

COMPOSITIONS AND METHODS FOR PRODUCING STEREOISOMERICALLY PURE STATINS AND SYNTHETIC INTERMEDIATES THEREFOR

1. TECHNICAL FIELD

[0001] The present disclosure relates to compositions and methods useful for the stereoselective reduction of hydroxy oxo esters, such as 5-hydroxy-3-oxo-hexanoate esters, to yield stereoisomerically pure corresponding *syn* dihydroxy esters. More specifically, the disclosure concerns non-naturally occurring engineered ketoreductase enzymes having improved properties as compared to the wild-type ketoreductases from which they were derived, polynucleotides encoding the engineered ketoreductase enzymes, host cells comprising such polynucleotides, methods of using the engineered ketoreductase enzymes to synthesize a variety of stereoisomerically pure compounds, and the stereoisomerically pure compounds synthesized therewith.

2. REFERENCE TO SEQUENCE LISTING, TABLE OR COMPUTER PROGRAM

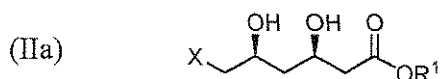
[0002] The Sequence Listing submitted concurrently herewith under 37 C.F.R. §§ 1.821(c) and 1.821(e) is herein incorporated by reference in its entirety.

3. BACKGROUND

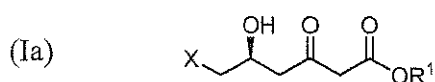
[0003] Stereoisomerically pure *syn* 3,5-dihydroxyhexanoate esters are key chiral intermediates for the synthesis of cholesterol lowering statins such as atorvastatin calcium (sold under the brand name LIPITOR® by Pfizer, Inc.), rosuvastatin calcium (sold under the brand name CRESTOR® by AstraZeneca, Ltd.), and pitavastatin (sold in Japan under the brand name Lipalo by Kowa Company Ltd. and Nissan Chemical Industries). While various methods for producing these chiral intermediates are known, including both chemical and enzymatic methods of reducing the corresponding 5-hydroxy-3-oxohexanoate ester, these methods suffer significant drawbacks, making them less than ideal for commercial scale synthesis. Given the importance of these key chiral intermediates in the synthesis of cholesterol lowering statins, compositions and methods useful for synthesizing these compounds in a cost effective and efficient manner would be highly desirable.

4. SUMMARY

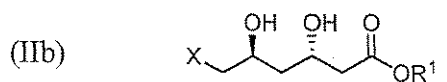
[0004] As mentioned above, stereoisomerically pure *syn* 3,5-dihydroxyhexanoate esters according to structural formula (IIa):



wherein X is selected from halo (*e.g.*, chloro and bromo), cyano and $-OR^6$, where R^6 is hydrogen or a protecting group, and R^1 is selected from (C2-C12) alkyl, (C6-C10) aryl and (C7-C12) arylalkyl, are key intermediates in the synthesis of cholesterol lowering statins, including but not limited to, atorvastatin; rosuvastatin, and pitavastatin. These key chiral intermediates are typically synthesized by reducing the corresponding enantiomerically pure 5-hydroxy-3-oxohexanoate ester according to structural formula (Ia):



under conditions in which the *syn* dihydroxy ester diastereomer of structural formula (IIa), *supra*, is obtained in diastereomeric excess over the corresponding *anti* dihydroxy ester diastereomer of structural formula (IIb):



[0005] Recently, certain ketoreductase enzymes have been identified that can be used to carry out this enantioselective reduction (see, *e.g.*, U.S. Patent No. 6,645,746 and WO 01/40450). The present inventors have discovered that ketoreductase enzymes capable of catalyzing the above-described enantioselective reduction can be engineered using laboratory evolution technologies, such as DNA shuffling, to yield non-naturally occurring engineered ketoreductases that have improved properties as compared to the naturally-occurring wild-type ketoreductase enzyme obtained from *Saccharomyces cerevisiae*. Further, the disclosure also provides isolated naturally-occurring ketoreductases that comprise any one of the sets of mutations disclosed herein for the engineered ketoreductases. Thus, such naturally-occurring ketoreductases that comprise such sets of mutations can be used in any one of the processes, kits, reaction mixtures, etc. disclosed herein.

[0006] The improved properties can be related to different aspects of the wild-type ketoreductase enzyme. For example, the improved properties can involve the stability of the enzyme under the conditions of the stereoselective reduction reaction, the enzymatic activity of the ketoreductase enzyme, and/or sensitivity to inhibition (*e.g.*, product inhibition).

[0007] Thus, in one aspect, there is provided a engineered ketoreductase enzyme derived from the wild type ketoreductase enzyme

of *Saccharomyces cerevisiae* capable of stereoselectively reducing the 3-oxo group of a 5-hydroxy-3-oxohexanoate to yield the corresponding *syn* 3,5-dihydroxyhexanoate ester, which enzyme has a specific activity that is at least about 1.5-300 times or more greater than the specific activity of the wild-type ketoreductase enzyme of SEQ ID NO:2 and comprises an amino acid sequence

that is: (a) at least 90% identical to SEQ ID NO:2, and (b) has one or more of the following characteristics:

X⁶ is a polar or acidic amino acid residue;

X²⁷ is an aliphatic or basic amino acid residue;

X³¹ is a hydroxyl containing or aliphatic amino acid residue;

X³⁶ is a small amino acid residue;

X⁴⁸ is a basic amino acid residue;

X⁶³ is an aromatic amino acid residue;

X⁶⁵ is a hydroxyl containing or small amino acid residue;

X⁸⁶ is an aliphatic or hydrophobic amino acid residue;

X¹²⁵ is an aliphatic or aromatic amino acid residue;

X¹⁵² is a basic amino acid residue;

X¹⁶⁰ is a hydroxyl containing or small amino acid residue;

X¹⁶⁵ is a polar or acidic amino acid residue;

X¹⁹⁴ is an aromatic amino acid or polar hydrophilic amino acid residue

X²¹⁴ is a polar hydrophilic amino acid residue;

X²¹⁸ is a hydroxyl containing amino acid residue,;

X²³⁴ is a polar hydrophilic amino acid residue;

X²⁴⁸ is an aliphatic amino acid residue;

X²⁵⁰ is a basic amino acid residue;

X²⁶³ is a acidic or polar amino acid residue;

X²⁹⁰ is an acidic amino acid residue;

X²⁹⁶ is an aliphatic amino acid residue

X²⁹⁷ is an aromatic amino acid residue;

X³⁰¹ is an aliphatic or hydroxyl containing or acidic or hydrophilic or basic amino acid

residue; and

X³⁰⁷ is an aromatic, a polar or a hydroxyl containing amino acid residue.

The present disclosure provides engineered (or isolated naturally-

occurring variant) ketoreductase enzymes having an improved property as compared to the naturally-occurring wild-type ketoreductase enzyme obtained from *Saccharomyces cerevisiae*. The engineered ketoreductases can possess a single improved property, or they can possess two or more improved properties, in any combination(s). In some embodiments, the engineered ketoreductases can comprise an amino acid sequence that is at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to the wild-type ketoreductase enzyme amino acid sequence, with the proviso that the engineered amino acid sequence comprises one or more mutations that are sufficient to provide an improved property.

[0008] In some embodiments, the engineered ketoreductase enzyme has increased enzymatic activity as compared to the wild-type ketoreductase enzyme. Improvements in enzymatic activity can be measured by comparing the specific activity of the engineered ketoreductase with that of the wild-type ketoreductase enzyme using standard enzyme assays. The amount of the improvement can range from 1.5 times the enzymatic activity of the corresponding wild-type ketoreductase enzyme, to as much as 2 times, 5 times, 10 times, 20 times, 25 times, 50 times, 75 times, 100 times, 150 times, 200 times, 250 times, 300 times, or more enzymatic activity. In specific embodiments, the engineered ketoreductase enzyme exhibits improved enzymatic activity in the range of 1.5 to 50 times, 1.5 to 100 times, 1.5 to 150 times, 1.5 to 200 times, 1.5 to 250 times, or 1.5 to 300 times greater than that of the wild-type ketoreductase enzyme. Improvements in enzyme activity also include increases in stereoselectivity or reduced product inhibition.

[0009] In some embodiments, the engineered ketoreductase enzyme exhibits improved thermal stability as compared to the wild-type ketoreductase enzyme. Improvements in thermal stability can be measured by comparing the degree of enzymatic activity retained by the engineered ketoreductase enzyme following a specified period of incubation at a specified temperature with that retained by the corresponding wild-type enzyme under similar conditions.

[0010] The engineered ketoreductase enzymes described herein can be obtained by mutagenizing the gene encoding naturally-occurring wild-type ketoreductase enzyme of *Saccharomyces* utilizing standard laboratory techniques, including the various mutagenesis and recombination techniques.

[0011] In some embodiments, the engineered ketoreductase enzymes described herein have a sequence that corresponds to the amino acid sequence of the wild-type ketoreductase from which they are derived and include one or more amino acid mutations that result in an improvement in the property of the enzyme. In some embodiments, the mutations are a selected combination of mutations that overall improve one or more properties of the enzyme. In some embodiments, such as where the improved property is from a single mutation or specific combination of mutations, the engineered ketoreductase may optionally include one or more conservative mutations at other residue positions within the polypeptide sequence.

[0012] In some embodiments, the ketoreductase enzyme comprises an amino acid sequence that corresponds to SEQ ID NO:2, or is at least about 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to SEQ ID NO:2, and wherein the amino acid sequence comprises at least one mutation over SEQ ID NO:2 at one of the following residue positions: 6, 27, 31, 36, 48, 63, 65, 86, 125, 152, 160, 165, 194, 214, 218, 234, 248, 250, 263, 290, 296, 297, 301, and 307. In one embodiment, the at least one mutation at one of the above positions must be a non-conservative mutation as compared to the wild-type SEQ ID NO:2 sequence.

[0013] In some embodiments, the ketoreductase enzyme comprises an amino acid sequence that corresponds to SEQ ID NO:2, or is at least about 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to SEQ ID NO:2, and wherein the amino acid sequence comprises an aromatic residue at position 63. In one embodiment, the aromatic residue is tryptophan.

[0014] In some embodiments, the ketoreductase enzyme has an amino acid sequence that is at least about 80, 85, 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identical to any one of the amino acid sequences listed in the Sequence Listing, with the proviso that the amino acid sequence is not identical to the wild-type sequence (SEQ ID NO:2). In some embodiments, the ketoreductase has an amino acid sequence that is identical to any one of the amino acid sequences listed in the Sequence Listing and includes one or more conservative mutations (including for example, 1, 2, 3, 1-5, 1-10-, 1-20, or more conservative mutations).

[0015] In some embodiments, the ketoreductase comprises an amino acid sequence that corresponds to SEQ ID NO:2, or is at least about 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identical to SEQ ID NO:2, and comprises one or more of the following characteristics:

X⁶ is a polar or acidic amino acid residue;
X²⁷ is an aliphatic or basic amino acid residue;
X³¹ is a hydroxyl containing or aliphatic amino acid residue;
X³⁶ is a small amino acid residue;
X⁴⁸ is a basic amino acid residue;
X⁶³ is a hydrophobic or aromatic amino acid;
X⁶⁵ is a hydroxyl containing or small amino acid residue;
X⁸⁶ is an aliphatic or hydrophobic amino acid residue;
X¹²⁵ is an aliphatic or aromatic amino acid residue;
X¹⁵² is a basic amino acid residue;
X¹⁶⁰ is a hydroxyl containing or small amino acid residue;
X¹⁶⁵ is a polar or acidic amino acid residue;
X¹⁹⁴ is an aromatic amino acid or polar hydrophilic amino acid residue
X²¹⁴ is a polar hydrophilic amino acid residue;
X²¹⁸ is a hydroxyl containing amino acid residue;;
X²³⁴ is a polar hydrophilic amino acid residue;
X²⁴⁸ is an aliphatic amino acid residue;
X²⁵⁰ is a basic amino acid residue;
X²⁶³ is a acidic or polar amino acid residue;
X²⁹⁰ is an acidic amino acid residue;
X²⁹⁶ is an aliphatic amino acid residue
X²⁹⁷ is an aromatic amino acid residue;
X³⁰¹ is an aliphatic or hydroxyl containing or acidic or hydrophilic or basic amino acid residue; and

X³⁰⁷ is an aromatic, a polar or a hydroxyl containing amino acid residue. In one embodiment, the ketoreductase comprises all of the above characteristics. In one embodiment, the ketoreductase comprises at least one characteristic such that at least one residue is mutated as compared to SEQ ID NO:2. In one embodiment, the ketoreductase comprises at least one characteristic such that at least one residue is non-conservatively mutated as compared to SEQ ID NO:2.

[0016] In some embodiments, the ketoreductase enzyme comprises an amino acid sequence that corresponds to SEQ ID NO:2, or is at least about 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identical to SEQ ID NO:2, and comprises one or more of the following characteristics:

X⁶ is a polar or acidic amino acid residue;
X²⁷ is an aliphatic or basic amino acid residue;
X³¹ is a hydroxyl containing or aliphatic amino acid residue;
X³⁶ is a small amino acid residue;
X⁴⁸ is a basic amino acid residue;
X⁶³ is an aromatic amino acid;
X⁶⁵ is a hydroxyl containing or small amino acid residue;
X⁸⁶ is an aliphatic or hydrophobic amino acid residue;
X¹²⁵ is an aliphatic or aromatic amino acid residue;
X¹⁵² is a basic amino acid residue;
X¹⁶⁰ is a hydroxyl containing or small amino acid residue;
X¹⁶⁵ is a polar or acidic amino acid residue;
X¹⁹⁴ is an aromatic amino acid or polar hydrophilic amino acid residue
X²¹⁴ is a polar hydrophilic amino acid residue;
X²¹⁸ is a hydroxyl containing amino acid residue;
X²³⁴ is a polar hydrophilic amino acid residue;
X²⁴⁸ is an aliphatic amino acid residue;
X²⁵⁰ is a basic amino acid residue;
X²⁶³ is a acidic or polar amino acid residue;
X²⁹⁰ is an acidic amino acid residue;
X²⁹⁶ is an aliphatic amino acid residue
X²⁹⁷ is an aromatic amino acid residue;
X³⁰¹ is an aliphatic or hydroxyl containing or acidic or hydrophilic or basic amino acid residue; and

X³⁰⁷ is an aromatic, a polar or a hydroxyl containing amino acid residue. In one embodiment, the ketoreductase comprises all of the above characteristics. In one embodiment, the ketoreductase comprises at least one characteristic such that at least one residue is mutated as compared to SEQ ID NO:2. In one embodiment, the ketoreductase

comprises at least one characteristic such that at least one residue is non-conservatively mutated as compared to SEQ ID NO:2.

[0017] In some embodiments, the ketoreductase comprises a ketoreductase having an improved activity as compared to a ketoreductase of SEQ ID NO:2, and that has an amino acid sequence that corresponds to the wild-type sequence ketoreductase of FIG. 3 (SEQ ID NO:2) and includes one or more mutations selected from: R27A, R27K, N31S, A36V, Y48H, I63W, R65G, R65S, L86I, F125L, K152R, A160T, Y194C, A218T, V248I, K250R, E290D, L296V, Y297W, Y297F, L301K, L301R, L301A, L301S, L301E, L301P, L301Q, L301V, L301T, L301Y, L301DY307H, Y307N, and Y307S. In some embodiments, such improved engineered ketoreductases comprise an amino acid sequence that is at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to SEQ ID NO:2, with the proviso that the amino acid sequence comprises at least one or more of the above listed mutations (in some embodiments, at least 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20 or more of the mutations).

[0018] In some embodiments, the engineered ketoreductase comprises a ketoreductase with an improved enzyme stability having an amino acid sequence that corresponds to the wild-type sequence of FIG. 3 (SEQ ID NO:2) and includes one or more mutations selected from: E44D, I46L, I55V, I56V, A60T, I63V, L76M,, G103S, L106I, D114G, L121I, Q144R, S148T, N158H, Q223H, I237G, I237N, I237R, S239T, and V253A.

[0019] In some embodiments, the engineered ketoreductase comprises a ketoreductase with a combination of improved enzyme activity and improved enzyme stability having a amino acid sequence that corresponds to the wild type sequence of FIG. 3 (SEQ ID NO:2) and that includes one or more mutations selected from: Q6E, N31P, A160S, Q165E, Q214H, Q214R, E234Q, and Q263E. In one embodiment, the ketoreductase comprises all of these mutations.

[0020] In some embodiments, the engineered ketoreductase comprises a ketoreductase with a combination of improved enzyme activity and/or improved enzyme stability having an amino acid sequence that corresponds to the wild type sequence of FIG. 3 (SEQ ID NO:2) and includes one or more mutations selected from: N40Y, V43L, K51E, I58V, E62Q, A73P, K79R, K152Q, K169E, F185I, Q189H, G192D, H200L, D201G, K215E, K215M, K216R, D221V, S233C, I237D, K250E, I265V, L287R, K304R, Q310R, K311E, V312S, and V312E.

[0021] Specific exemplary embodiments of such engineered ketoreductases include SEQ ID NOS: 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198, 200, 202, 204, 206, 208, 210, 212, 214, 216, 218, 220, 222, 224, 226, 228, 230, 232, 234, 236, 238, 240, 242, 244, 246, 248, 250, 252, 254, 256, 258, 260, 262, 266, 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 292, 294, 296, 298, 300, 302, 304, 306, 308, 310, 312, 314, 316, 318, 320, 322, 324, 326, 328, 330, 332, 334, 336, 338, 340, 342, 344, 346, 348, 350, 352, 354, 356, 358, 360, 362, 364, and 366.

[0022] In some embodiments, the engineered ketoreductase enzyme has an amino acid sequence that is at least about 80, 85, 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identical to an amino acid sequence listed in Table 1.

[0023] In some embodiments, the ketoreductase comprises an amino acid sequence that is at least about 95, 96, 97, 98, or 99% identical to SEQ ID NO:316 or 318. In one embodiment, the ketoreductase comprises the amino acid sequence of SEQ ID NO:316 or 318, but with one or more conservative mutations (including 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or more) at residues that have not been mutated as compared to SEQ ID NO:2.

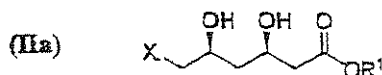
[0024] In another aspect, there is provided a polynucleotide comprising a sequence that encodes a ketoreductase enzyme as described herein. The present disclosure provides polynucleotides encoding the engineered ketoreductases described herein or polynucleotides that hybridize to such polynucleotides under highly stringent conditions. The polynucleotide can include promoters and other regulatory elements useful for expression of the encoded engineered ketoreductase, and can utilize codons optimized for specific desired expression systems.

[0025] In still another aspect, there is provided an expression system comprising the polynucleotide as described herein operably linked to a control sequence suitable for directing expression in a host cell. In yet another aspect, there is provided a host cell comprising the expression system as defined above. The present disclosure provides host cells comprising the polynucleotides and/or expression vectors described herein. The host cells may be *Saccharomyces cerevisiae*, which the engineered ketoreductase enzyme was derived from, or they may be a different organism. The host cells can be used for the expression and isolation of the engineered ketoreductase enzymes described herein, or, alternatively, they can be used in the various methods described further below.

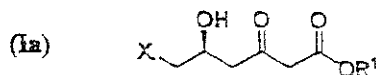
[0026] The ketoreductase enzymes can be used to reduce hydroxy oxo ester enantiomers of structural formula (Ia) to their corresponding *syn* dihydroxys in high yield and with a high degree of stereoselectivity.

[0027] In one embodiment, the ketoreductase enzymes are used in purified or isolated form. In another embodiment, extracts from cells expressing the enzymes are used.

[0028] Thus, in another aspect, there is provided a process for preparing a *syn* 3,5-dihydroxyhexanoate compound according to formula (IIa):



wherein X is selected from halo, cyano and $-OR^6$, where R^6 is hydrogen or a protecting group, and R^1 is selected from (C1-C12) alkyl, (C6-C10) aryl and (C7-C12) arylalkyl, comprising stereoselectively reducing an enantiomer of a 5-hydroxy-3-oxohexanoate compound according to structural formula (Ia):



wherein X and R^1 are as defined for structural formula (IIa);

using a ketoreductase as described herein under conditions suitable for reducing the 3-oxo group to a 3-hydroxy group.

In yet another aspect, there is provided a reaction mixture comprising a ketoreductase enzyme as described herein, a cofactor for said ketoreductase enzyme and a substrate according to structural formula (Ia):



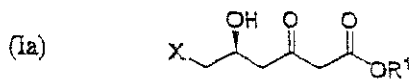
wherein X is selected from halo, cyano and $-OR^6$, where R^6 is hydrogen or a protecting group, and R^1 is selected from (C1-C12) alkyl, (C6-C10) aryl and (C7-C12) arylalkyl.

In still another aspect, there is provided a reaction mixture comprising a ketoreductase enzyme as described herein, a cofactor for said ketoreductase enzyme and a substrate according to structural formula (IIa):

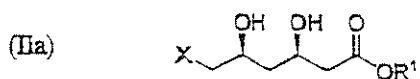


wherein X is selected from halo, cyano and $-OR^6$, where R^6 is hydrogen or a protecting group, and R^1 is selected from (C1-C12) alkyl, (C6-C10) aryl and (C7-C12) arylalkyl.

In still another aspect, there is provided in a method of synthesizing a statin compound that includes as one step the enantioselective reduction of a compound according to structural formula (Ia) to yield a compound according to structural formula (IIa), the improvement comprising carrying out the enantioselective reduction of compound (Ia) to compound (IIa) with a ketoreductase enzyme as described herein; wherein structural formula (Ia) is:

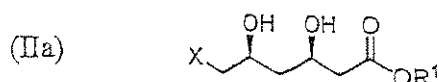


wherein X is selected from halo, cyano and $-OR^6$, where R^6 is hydrogen or a protecting group, and R^1 is selected from (C1-C12) alkyl, (C6-C10) aryl and (C7-C12) arylalkyl; and wherein structural formula (IIa) is:

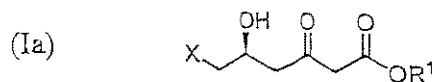


wherein X and R^1 are defined as for structural formula (Ia).

The present disclosure provides methods of producing a syn dihydroxy ester according to structural formula (IIa):



wherein X and R^1 are as previously defined. The methods generally comprise selectively reducing a hydroxy oxo ester enantiomer according to structural formula (Ia):



wherein X and R^1 are as defined for structural formula (IIa), using an engineered ketoreductase enzyme described herein. The method may be carried out using whole cells that express the engineered ketoreductase enzyme, such as the host cells described herein, extracts or lysates from such cells, or purified engineered ketoreductase enzymes.

[0029] As will be appreciated by skilled artisans, the reduction reaction illustrated above generally requires a cofactor, which is normally NADH or NADPH, and a system for regenerating the cofactor, for example glucose and glucose dehydrogenase. Since cells generally provide such cofactors and cofactor regeneration systems, in embodiments employing whole cells cell extracts or cell lysates, the addition of such cofactors and cofactor regeneration systems may be unnecessary. In embodiments employing purified engineered ketoreductase enzyme(s), such cofactors and optionally such cofactor regeneration systems will typically be added to the reaction medium along with the hydroxy oxo ester substrate and the ketoreductase enzyme(s). Like the engineered ketoreductase enzyme, any enzyme(s) comprising the cofactor regeneration system can be supplied to the reaction mixture in the form of extracts or lysates of such cells, or as purified enzyme(s). In embodiments employing cell extracts or cell lysates, the cells used to generate the extracts or lysates can be engineered to express the enzyme(s) comprising the cofactor regeneration systems alone, or

together with the engineered ketoreductase enzyme. In embodiments employing whole cells, the cells can be engineered to express the enzyme(s) comprising the cofactor regeneration systems and the engineered ketoreductase enzyme together.

[0030] Whether carrying out the method with whole cells, cell extracts or purified ketoreductase enzymes, a single ketoreductase enzyme may be used or, alternatively, mixtures of two or more ketoreductase enzymes may be used.

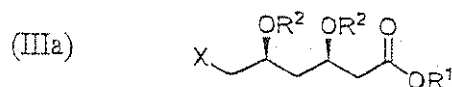
[0031] The ketoreductase enzymes described herein are highly specific for the enantiomer of structural formula (Ia) and catalyze the above-described reduction reaction in high yield and with a high degree of stereoselectivity. Depending upon the particular engineered ketoreductase enzyme used, yields in the range of about 80 to 99.9% with a diastereomeric excess ("d.e.") of $\geq 99.5\%$, can be readily achieved. For example, it has been discovered that engineered ketoreductase enzymes of the present disclosure can be used to stereoselectively reduce the 5-hydroxyoxo ester enantiomer of structural formula (Ia), *supra*, to the corresponding *syn* dihydroxy of structural formula (IIa) with yields in the range of 90 to 99.9% and with a degree of stereoselectivity of $\geq 99.7\%$.

[0032] In many embodiments, diastereoselectivities of $\geq 99.8\%$, 99.9%, 99.91%, 99.92%, 99.93%, 99.94%, 99.5%, 99.96%, 99.97%, 99.98% and even 99.99% d.e. can be achieved. Indeed, as will be discussed in more detail below in connection with FIGS. 6 and 7, a crude, unpurified reduction product obtained from a starting substrate that was $> 99\%$ pure in the enantiomer of structural formula (Ia) using the engineered ketoreductase enzyme of SEQ ID NO:316 was $>99.99\%$ pure in the *syn* diastereomer of structural formula (IIa).

[0033] Because the engineered ketoreductase enzymes described herein are so highly stereoselective, the resultant *syn* dihydroxy ester of structural formula (IIa) can be recovered in substantially stereochemically pure form without the need to chirally separate it from the corresponding *anti* or any other diastereomer. Indeed, owing to the high yield and high stereoselectivity of the reaction, if the hydroxy oxo ester substrate of structural formula (I) is substantially pure in the enantiomer of structural formula (Ia), the specific *syn* dihydroxy ester diastereomer of structural formula (IIa) can be recovered from the reaction medium as a substantially pure or pure diastereomer without purification.

[0034] The chiral dihydroxy ester of structural formula (IIa) can be used as a starting material to synthesize cholesterol-lowering statins, including but not limited to, atorvastatin,

rosuvastatin, and pitavastatin. A key step in many of these methods is protecting the hydroxyl groups of the *syn* dihydroxy ester of structural formula (IIa), yielding a protected *syn* dihydroxy ester according to structural formula (IIIa):



wherein X and R¹ are as previously defined for structural formula (IIa) and each R² is a protecting group or, alternatively, the two R² groups can be taken together to form a substituted or unsubstituted alkylene bridge. Hence, in an aspect, there is provided a process for the preparation of a protected *syn* 3,5-dihydroxy-3-oxohexanoate compound according to structural formula (IIIa):



wherein:

X is selected from halo, cyano and -OR⁶, where R⁶ is hydrogen or a protecting group;

R¹ is selected from (C1-C12) alkyl, (C6-C10) aryl and (C7-C12) arylalkyl; and

each R² is a protecting group, or, alternatively, the R² groups may be taken together to form an alkylene bridge of the formula -CR³R⁴-, or a boronate of -BR⁵- wherein R³ and R⁴ are each, independently of one another, selected from hydrogen, (C1-C12) alkyl, (C6-C10) aryl and (C7-C12) arylalkyl, or alternatively, R³ and R⁴ taken together form a (C4-C10) cycloalkyl or heterocycloalkyl, and R⁵ is selected from (C1-C12) alkyl, (C6-C10) aryl and (C7-C12) arylalkyl, comprising the steps of:

(i) stereoselectively reducing a 5-hydroxy-3-oxohexanoate enantiomer of structural formula

(Ia)

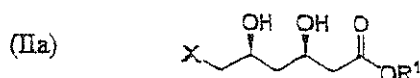
wherein structural formula (Ia) is:



wherein X is selected from halo, cyano and -OR⁶, where R⁶ is hydrogen or a protecting group, and R¹ is selected from (C1-C12) alkyl, (C6-C10) aryl and (C7-C12) arylalkyl;

using a ketoreductase enzyme as described herein under conditions suitable to reduce the 3-oxo group to a 3-hydroxy group to yield a first reaction product comprising a *syn* 3,5-dihydroxyhexanoate compound according to structural formula (IIa)

wherein structural formula (IIa) is:

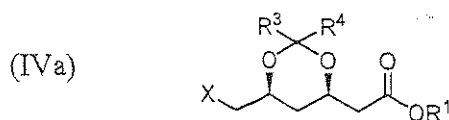


wherein X and R¹ are defined as for structural formula (Ia);

and

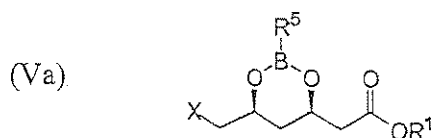
(ii) protecting the hydroxyl groups of the *syn* 3,5-dihydroxyhexanoate compound to yield a second reaction product comprising the protected *syn* 3,5-dihydroxy-3-oxohexanoate compound according to structural formula (IIIa).

In some embodiments, the protected *syn* dihydroxy ester is a compound according to structural formula (IVa):



wherein X and R¹ are as previously defined for structural formula (IIa) and R³ and R⁴ are each, independently of one another, selected from hydrogen, (C1-C12) alkyl, (C6-C10) aryl and (C7-C12) arylalkyl, or alternatively, R³ and R⁴ taken together form a (C4-C10) cycloalkyl or heterocycloalkyl. In a specific embodiment, R³ and R⁴ are each methyl.

[0035] In some embodiments, the protected *syn* dihydroxy ester is a compound according to structural formula (Va):

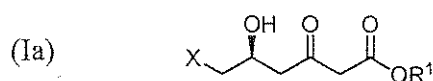


wherein X and R¹ are as previously defined for structural formula (IIa), and R⁵ is selected from (C1-C12) alkyl, (C6-C10) aryl and (C7-C12) arylalkyl. In some embodiments, R⁵ is phenyl.

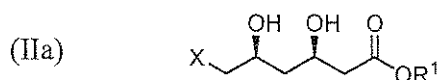
[0036] Owing to their stereoselectivity, the engineered ketoreductase enzymes described herein can be used to synthesize stereoisomerically pure preparations of protected *syn* dihydroxy esters according to structural formula (IIIa), (IVa) and (Va). The methods generally comprise enantioselectively reducing a hydroxyoxoester enantiomer according to

structural formula (Ia), *supra*, using an engineered ketoreductase enzyme as described herein to yield a first reaction product comprising a *syn* dihydroxy ester according to structural formula (IIa), *supra*, and protecting the hydroxyl groups of the *syn* dihydroxy ester to yield the protected *syn* dihydroxy ester of structural formula (IIIa). Owing to the high stereoselectivity of the engineered ketoreductase enzymes, the protected *syn* dihydroxy ester of structural formula (IIIa) can be recovered as a substantially stereochemically pure or pure diastereomer, *i.e.*, substantially free of the corresponding *anti* diastereomer and any other diastereomers, without chiral separation.

[0037] The *syn* dihydroxy esters and/or protected *syn* dihydroxy esters can be used as reactants in known methods to synthesize cholesterol lowering statins. Exemplary synthetic routes for preparing exemplary statins are illustrated in FIGS. 8, 9, and 10. Thus, in another aspect, the present disclosure provides methods of producing substantially stereoisomerically pure preparations of statins, such as, for example, atorvastatin, rosuvastatin, and pitavastatin. The methods generally comprises: (i) reducing a substantially enantiomerically pure hydroxy oxo ester enantiomer according to structural formula (Ia):



wherein R¹ and X are as previously defined, with an engineered ketoreductase enzyme described herein to yield a first reaction product comprising a substantially diastereomerically pure *syn* dihydroxy ester according to structural formula (IIa):



wherein X and R¹ are as defined for structural formula (Ia); and (ii) thereafter using the *syn* dihydroxy ester of structural formula (IIa) to synthesize a statin. Since the engineered ketoreductases described herein catalyze the reduction of step (i) with a high degree of enantioselectivity, the *syn* dihydroxy ester of structural formula (IIa) can be used to synthesize statins having a high degree of stereoisomeric purity using reactions carried out at nearly ambient temperature and without the need for chiral separations. Indeed, the high degree of stereoselectivity of the reduction reaction allows preparation of statins having a % d.e. that is within about 90 to 99.99 % of the %e.e. of the hydroxy oxo ester starting substrate, readily and economically in high yield.

5. BRIEF DESCRIPTION OF THE FIGURES

[0038] FIG.1 illustrates the role of ketoreductases and halohydrin dehalogenases in converting an alkyl 4-halo-3-oxobutyrate to various intermediates useful in the synthesis of statins.

[0039] FIG 2 illustrates various routes for synthesizing t-butyl (6R)-(2-cyanoethyl)-2,2 dimethyl-1,3-dioxane from a t-butyl-3,5-dihydroxy-6-haloheptanoate.

[0040] FIG. 3 provides the wild-type sequence of the ketoreductase encoded by the *Ydl124wp* gene (Genbank Acc. No.:NP_010159.1; GI:6320079) from *Saccharomyces cerevisiae* (SEQ ID NO:2).

[0041] FIG. 4 provides the amino acid sequence of the ketoreductase from *Saccharomyces cerevisiae* with the residues marked that can be modified to generate engineered polypeptides with improved ketoreductase properties.

[0042] FIG. 5 provides an illustration of plasmid pCK110900 in which cloned ketoreductase genes are operatively linked to the lac promoter under control of the lacI repressor for expressing engineered ketoreductase enzymes.

[0043] FIG. 6 shows LC/MS/MS chromatograms of t-butyl 6-cyano-(3R,5R)-dihydroxyhexanoate samples of Example 17 (a sample prepared by an embodiment of the methods described herein)(upper panel) and a sample prepared from commercial crystalline t-butyl (6R)-(2-cyanoethyl)-2,2 dimethyl-1,3-dioxane-(4R)-acetate (lower panel).

[0044] FIG. 7 shows GC/MS chromatograms of t-butyl (6R)-(2-cyanoethyl)-2,2 dimethyl-1,3 dioxane-(4R)-acetate samples of Example 23 (a sample prepared by the method of the invention) and a commercial crystalline sample.

[0045] FIG. 8 illustrates a synthetic scheme for rosuvastatin; R represents H or a suitable protecting group.

[0046] FIG. 9 illustrates a synthetic scheme for pitavastatin; R represents H or a suitable protecting group.

[0047] FIG. 10 illustrates a synthetic scheme for atorvastatin; R represents H or a suitable protecting group.

6. DETAILED DESCRIPTION

6.1 Definitions

[0048] As used herein, the following terms are intended to have the following meanings:

[0049] “Alkyl” by itself or as part of another substituent refers to a saturated or unsaturated branched, straight-chain or cyclic monovalent hydrocarbon radical having the stated number of carbon atoms (*i.e.*, C1-C6 means one to six carbon atoms) that is derived by the removal of one hydrogen atom from a single carbon atom of a parent alkane, alkene or alkyne. Typical alkyl groups include, but are not limited to, methyl; ethyls such as ethanyl, ethenyl, ethynyl; propyls such as propan-1-yl, propan-2-yl, cyclopropan-1-yl, prop-1-en-1-yl, prop-1-en-2-yl, prop-2-en-1-yl, cycloprop-1-en-1-yl; cycloprop-2-en-1-yl, prop-1-yn-1-yl, prop-2-yn-1-yl, *etc.*; butyls such as butan-1-yl, butan-2-yl, 2-methyl-propan-1-yl, 2-methyl-propan-2-yl, cyclobutan-1-yl, but-1-en-1-yl, but-1-en-2-yl, 2-methyl-prop-1-en-1-yl, but-2-en-1-yl, but-2-en-2-yl, buta-1,3-dien-1-yl, buta-1,3-dien-2-yl, cyclobut-1-en-1-yl, cyclobut-1-en-3-yl, cyclobuta-1,3-dien-1-yl, but-1-yn-1-yl, but-1-yn-3-yl, but-3-yn-1-yl, *etc.*; and the like. Where specific levels of saturation are intended, the nomenclature “alkanyl,” “alkenyl” and/or “alkynyl” is used, as defined below. “Lower alkyl” refers to an alkyl group containing from 1 to 6 carbon atoms.

[0050] “Alkanyl” by itself or as part of another substituent refers to a saturated branched, straight-chain or cyclic alkyl derived by the removal of one hydrogen atom from a single carbon atom of a parent alkane. Typical alkanyl groups include, but are not limited to, methanyl; ethanyl; propanyls such as propan-1-yl, propan-2-yl (isopropyl), cyclopropan-1-yl, *etc.*; butanyls such as butan-1-yl, butan-2-yl (*sec*-butyl), 2-methyl-propan-1-yl (isobutyl), 2-methyl-propan-2-yl (*t*-butyl), cyclobutan-1-yl, *etc.*; and the like.

[0051] “Alkenyl” by itself or as part of another substituent refers to an unsaturated branched, straight-chain or cyclic alkyl having at least one carbon-carbon double bond derived by the removal of one hydrogen atom from a single carbon atom of a parent alkene. The group may be in either the *cis* or *trans* conformation about the double bond(s). Typical alkenyl groups include, but are not limited to, ethenyl; propenyls such as prop-1-en-1-yl, prop-1-en-2-yl, prop-2-en-1-yl, prop-2-en-2-yl, cycloprop-1-en-1-yl; cycloprop-2-en-1-yl; butenyls such as but-1-en-1-yl, but-1-en-2-yl, 2-methyl-prop-1-en-1-yl, but-2-en-1-yl, but-2-en-2-yl, buta-1,3-dien-1-yl, buta-1,3-dien-2-yl, cyclobut-1-en-1-yl, cyclobut-1-en-3-yl, cyclobuta-1,3-dien-1-yl, *etc.*; and the like.

[0052] “Alkynyl” by itself or as part of another substituent refers to an unsaturated branched, straight-chain or cyclic alkyl having at least one carbon-carbon triple bond derived by the removal of one hydrogen atom from a single carbon atom of a parent alkyne. Typical alkynyl groups include, but are not limited to, ethynyl; propynyls such as prop-1-yn-1-yl, prop-2-yn-1-yl, *etc.*; butynyls such as but-1-yn-1-yl, but-1-yn-3-yl, but-3-yn-1-yl, *etc.*; and the like.

[0053] “Alkylidiyl” by itself or as part of another substituent refers to a saturated or unsaturated, branched, straight-chain or cyclic divalent hydrocarbon group having the stated number of carbon atoms (*i.e.*, C1-C6 means from one to six carbon atoms) derived by the removal of one hydrogen atom from each of two different carbon atoms of a parent alkane, alkene or alkyne, or by the removal of two hydrogen atoms from a single carbon atom of a parent alkane, alkene or alkyne. The two monovalent radical centers or each valency of the divalent radical center can form bonds with the same or different atoms. Typical alkylidiyl groups include, but are not limited to, methandiyl; ethylidiyls such as ethan-1,1-diyl, ethan-1,2-diyl, ethen-1,1-diyl, ethen-1,2-diyl; propylidiyls such as propan-1,1-diyl, propan-1,2-diyl, propan-2,2-diyl, propan-1,3-diyl, cyclopropan-1,1-diyl, cyclopropan-1,2-diyl, prop-1-en-1,1-diyl, prop-1-en-1,2-diyl, prop-2-en-1,2-diyl, prop-1-en-1,3-diyl, cycloprop-1-en-1,2-diyl, cycloprop-2-en-1,2-diyl, cycloprop-2-en-1,1-diyl, prop-1-yn-1,3-diyl, *etc.*; butylidiyls such as, butan-1,1-diyl, butan-1,2-diyl, butan-1,3-diyl, butan-1,4-diyl, butan-2,2-diyl, 2-methyl-propan-1,1-diyl, 2-methyl-propan-1,2-diyl, cyclobutan-1,1-diyl; cyclobutan-1,2-diyl, cyclobutan-1,3-diyl, but-1-en-1,1-diyl, but-1-en-1,2-diyl, but-1-en-1,3-diyl, but-1-en-1,4-diyl, 2-methyl-prop-1-en-1,1-diyl, 2-methanylidene-propan-1,1-diyl, buta-1,3-dien-1,1-diyl, buta-1,3-dien-1,2-diyl, buta-1,3-dien-1,3-diyl, buta-1,3-dien-1,4-diyl, cyclobut-1-en-1,2-diyl, cyclobut-1-en-1,3-diyl, cyclobut-2-en-1,2-diyl, cyclobuta-1,3-dien-1,2-diyl, cyclobuta-1,3-dien-1,3-diyl, but-1-yn-1,3-diyl, but-1-yn-1,4-diyl, buta-1,3-diyn-1,4-diyl, *etc.*; and the like. Where specific levels of saturation are intended, the nomenclature alkanyldiyl, alkenyldiyl and/or alkynyldiyl is used. Where it is specifically intended that the two valencies be on the same carbon atom, the nomenclature “alkylidene” is used. A “lower alkylidiyl” is an alkylidiyl group containing 1 to 6 carbon atoms. In some embodiments the alkylidiyl groups are saturated acyclic alkanyldiyl groups in which the radical centers are at

the terminal carbons, *e.g.*, methandiyl (methano); ethan-1,2-diyl (ethano); propan-1,3-diyl (propano); butan-1,4-diyl (butano); and the like (also referred to as alkylenes, defined *infra*).

[0054] “Alkylene” by itself or as part of another substituent refers to a straight-chain saturated or unsaturated alkylidiyl group having two terminal monovalent radical centers derived by the removal of one hydrogen atom from each of the two terminal carbon atoms of straight-chain parent alkane, alkene or alkyne. The locant of a double bond or triple bond, if present, in a particular alkylene is indicated in square brackets. Typical alkylene groups include, but are not limited to, methylene (methano); ethylenes such as ethano, etheno, ethyno; propylenes such as propano, prop[1]eno, propa[1,2]dieno, prop[1]yno, etc.; butylenes such as butano, but[1]eno, but[2]eno, buta[1,3]dieno, but[1]yno, but[2]yno, buta[1,3]diyno, etc.; and the like. Where specific levels of saturation are intended, the nomenclature alkano, alkeno and/or alkyno is used. In some embodiments, the alkylene group is (C1-C6) or (C1-C3) alkylene. In some embodiments, the alkylene group is a straight-chain saturated alkano group, *e.g.*, methano, ethano, propano, butano, and the like.

[0055] “Cycloalkyl” by itself or as part of another substituent refers to a cyclic version of an “alkyl” group. Typical cycloalkyl groups include, but are not limited to, cyclopropyl; cyclobutyls such as cyclobutanyl and cyclobutenyl; cyclopentyls such as cyclopentanyl and cyclopentenyl; cyclohexyls such as cyclohexanyl and cyclohexenyl; and the like.

[0056] “Parent Aromatic Ring System” refers to an unsaturated cyclic or polycyclic ring system having a conjugated π electron system. Specifically included within the definition of “parent aromatic ring system” are fused ring systems in which one or more of the rings are aromatic and one or more of the rings are saturated or unsaturated, such as, for example, fluorene, indane, indene, phenalene, tetrahydronaphthalene, etc. Typical parent aromatic ring systems include, but are not limited to, aceanthrylene, acenaphthylene, acephenanthrylene, anthracene, azulene, benzene, chrysene, coronene, fluoranthene, fluorene, hexacene, hexaphene, hexalene, indacene, *s*-indacene, indane, indene, naphthalene, octacene, octaphene, octalene, ovalene, penta-2,4-diene, pentacene, pentalene, pentaphene, perylene, phenalene, phenanthrene, picene, pleiadene, pyrene, pyranthrene, rubicene, tetrahydronaphthalene, triphenylene, trinaphthalene, and the like.

[0057] “Aryl” by itself or as part of another substituent refers to a monovalent aromatic hydrocarbon group having the stated number of carbon atoms (*i.e.*, C5-C15 means from 5 to

15 carbon atoms) derived by the removal of one hydrogen atom from a single carbon atom of a parent aromatic ring system. Typical aryl groups include, but are not limited to, groups derived from aceanthrylene, acenaphthylene, acephenanthrylene, anthracene, azulene, benzene, chrysene, coronene, fluoranthene, fluorene, hexacene, hexaphene, hexalene, *as*-indacene, *s*-indacene, indane, indene, naphthalene, octacene, octaphene, octalene, ovalene, penta-2,4-diene, pentacene, pentalene, pentaphene, perylene, phenalene, phenanthrene, picene, pleiadene, pyrene, pyranthrene, rubicene, triphenylene, trinaphthalene, and the like, as well as the various hydro isomers thereof. In some embodiments, the aryl group is (C6-C10). Specific examples are phenyl and naphthyl.

[0058] “Arylalkyl” by itself or as part of another substituent refers to an acyclic alkyl group in which one of the hydrogen atoms bonded to a carbon atom, typically a terminal or *sp*³ carbon atom, is replaced with an aryl group. Typical arylalkyl groups include, but are not limited to, benzyl, 2-phenylethan-1-yl, 2-phenylethen-1-yl, naphthylmethyl, 2-naphthylethan-1-yl, 2-naphthylethen-1-yl, naphthobenzyl, 2-naphthophenylethan-1-yl and the like. Where specifically saturated or unsaturated alkyl moieties are intended, the nomenclature arylalkanyl, arylalkenyl and/or arylalkynyl is used. In some embodiments, the arylalkyl group is (C7-C12) arylalkyl. In a specific embodiment the alkanyl, alkenyl or alkynyl moiety of the arylalkyl group is (C1-C2) and the aryl moiety is (C6-C10).

[0059] “Ketoreductase” and “KRED” are used interchangeably herein to refer to a polypeptide that is capable of enantioselectively reducing the 3-oxo group of a 5-hydroxy-3-oxohexanoate ester enantiomer to yield the corresponding *syn* 3,-5-dihydroxyhexanoate ester. The polypeptide typically utilizes the cofactor reduced nicotinamide adenine dinucleotide (NADH) or reduced nicotinamide adenine dinucleotide phosphate (NADPH) as the reducing agent. Ketoreductases as used herein include naturally occurring (wild type) ketoreductases as well as non-naturally occurring engineered polypeptides generated by human manipulation.

[0060] “Coding sequence” refers to that portion of a nucleic acid (*e.g.*, a gene) that encodes an amino acid sequence of a protein.

[0061] “Naturally-occurring” or “wild-type” refers to the form found in nature. For example, a naturally occurring or wild-type polypeptide or polynucleotide sequence is a sequence

present in an organism that can be isolated from a source in nature and which has not been intentionally modified by human manipulation.

[0062] “Recombinant” when used with reference to, *e.g.*, a cell, nucleic acid, or polypeptide, refers to a material, or a material corresponding to the natural or native form of the material, that has been modified in a manner that would not otherwise exist in nature, or is identical thereto but produced or derived from synthetic materials and/or by manipulation using recombinant techniques. Non-limiting examples include, among others, recombinant cells expressing genes that are not found within the native (non-recombinant) form of the cell or express native genes that are otherwise expressed at a different level.

[0063] “Percentage of sequence identity” and “percentage homology” are used interchangeably herein to refer to comparisons among polynucleotides and polypeptides, and are determined by comparing two optimally aligned sequences over a comparison window, wherein the portion of the polynucleotide or polypeptide sequence in the comparison window may comprise additions or deletions (*i.e.*, gaps) as compared to the reference sequence (which does not comprise additions or deletions) for optimal alignment of the two sequences. The percentage may be calculated by determining the number of positions at which the identical nucleic acid base or amino acid residue occurs in both sequences to yield the number of matched positions, dividing the number of matched positions by the total number of positions in the window of comparison and multiplying the result by 100 to yield the percentage of sequence identity. Alternatively, the percentage may be calculated by determining the number of positions at which either the identical nucleic acid base or amino acid residue occurs in both sequences or a nucleic acid base or amino acid residue is aligned with a gap to yield the number of matched positions, dividing the number of matched positions by the total number of positions in the window of comparison and multiplying the result by 100 to yield the percentage of sequence identity. Those of skill in the art appreciate that there are many established algorithms available to align two sequences. Optimal alignment of sequences for comparison can be conducted, *e.g.*, by the local homology algorithm of Smith and Waterman, 1981, *Adv. Appl. Math.* 2:482, by the homology alignment algorithm of Needleman and Wunsch, 1970, *J. Mol. Biol.* 48:443, by the search for similarity method of Pearson and Lipman, 1988, *Proc. Natl. Acad. Sci. USA* 85:2444, by computerized implementations of these algorithms (GAP, BESTFIT, FASTA, and TFASTA in the GCG Wisconsin Software Package), or by visual inspection (see generally, *Current Protocols in*

Molecular Biology, F. M. Ausubel et al., eds., Current Protocols, a joint venture between Greene Publishing Associates, Inc. and John Wiley & Sons, Inc., (1995 Supplement) (Ausubel)). Examples of algorithms that are suitable for determining percent sequence identity and sequence similarity are the BLAST and BLAST 2.0 algorithms, which are described in Altschul et al., 1990, *J. Mol. Biol.* 215: 403-410 and Altschul et al., 1977, *Nucleic Acids Res.* 3389-3402, respectively. Software for performing BLAST analyses is publicly available through the National Center for Biotechnology Information website. This algorithm involves first identifying high scoring sequence pairs (HSPs) by identifying short words of length W in the query sequence, which either match or satisfy some positive-valued threshold score T when aligned with a word of the same length in a database sequence. T is referred to as, the neighborhood word score threshold (Altschul et al, supra). These initial neighborhood word hits act as seeds for initiating searches to find longer HSPs containing them. The word hits are then extended in both directions along each sequence for as far as the cumulative alignment score can be increased. Cumulative scores are calculated using, for nucleotide sequences, the parameters M (reward score for a pair of matching residues; always >0) and N (penalty score for mismatching residues; always <0). For amino acid sequences, a scoring matrix is used to calculate the cumulative score. Extension of the word hits in each direction are halted when: the cumulative alignment score falls off by the quantity X from its maximum achieved value; the cumulative score goes to zero or below, due to the accumulation of one or more negative-scoring residue alignments; or the end of either sequence is reached. The BLAST algorithm parameters W, T, and X determine the sensitivity and speed of the alignment. The BLASTN program (for nucleotide sequences) uses as defaults a wordlength (W) of 11, an expectation (E) of 10, M=5, N=-4, and a comparison of both strands. For amino acid sequences, the BLASTP program uses as defaults a wordlength (W) of 3, an expectation (E) of 10, and the BLOSUM62 scoring matrix (see Henikoff and Henikoff, 1989, *Proc Natl Acad Sci USA* 89:10915). Exemplary determination of sequence alignment and % sequence identity can employ the BESTFIT or GAP programs in the GCG Wisconsin Software package (Accelrys, Madison WI), using default parameters provided.

[0064] "Reference sequence" refers to a defined sequence used as a basis for a sequence comparison. A reference sequence may be a subset of a larger sequence, for example, a segment of a full-length gene or polypeptide sequence. Generally, a reference sequence is at

least 20 nucleotide or amino acid residues in length, at least 25 residues in length, at least 50 residues in length, or the full length of the nucleic acid or polypeptide. Since two polynucleotides or polypeptides may each (1) comprise a sequence (*i.e.*, a portion of the complete sequence) that is similar between the two sequences, and (2) may further comprise a sequence that is divergent between the two sequences, sequence comparisons between two (or more) polynucleotides or polypeptide are typically performed by comparing sequences of the two polynucleotides over a “comparison window” to identify and compare local regions of sequence similarity.

[0065] “Comparison window” refers to a conceptual segment of at least about 20 contiguous nucleotide positions or amino acids residues wherein a sequence may be compared to a reference sequence of at least 20 contiguous nucleotides or amino acids and wherein the portion of the sequence in the comparison window may comprise additions or deletions (*i.e.*, gaps) of 20 percent or less as compared to the reference sequence (which does not comprise additions or deletions) for optimal alignment of the two sequences. The comparison window can be longer than 20 contiguous residues, and includes, optionally 30, 40, 50, 100, or longer windows.

[0066] “Substantial identity” refers to a polynucleotide or polypeptide sequence that has at least 80 percent sequence identity, at least 85 percent identity and 89 to 95 percent sequence identity, more usually at least 99 percent sequence identity as compared to a reference sequence over a comparison window of at least 20 residue positions, frequently over a window of at least 30-50 residues, wherein the percentage of sequence identity is calculated by comparing the reference sequence to a sequence that includes deletions or additions which total 20 percent or less of the reference sequence over the window of comparison. In specific embodiments applied to polypeptides, the term “substantial identity” means that two polypeptide sequences, when optimally aligned, such as by the programs GAP or BESTFIT using default gap weights, share at least 80 percent sequence identity, preferably at least 89 percent sequence identity, at least 95 percent sequence identity or more (*e.g.*, 99 percent sequence identity). Preferably, residue positions which are not identical differ by conservative amino acid substitutions.

[0067] “Stereoselectivity” refers to the preferential formation in a chemical or enzymatic reaction of one stereoisomer over another. Stereoselectivity can be partial, where the formation of one stereoisomer is favored over the other, or it may be complete where only

one stereoisomer is formed. When the stereoisomers are enantiomers, the stereoselectivity is referred to as enantioselectivity, the fraction (typically reported as a percentage) of one enantiomer in the sum of both. It is commonly reported in the art (typically as a percentage) as the enantiomeric excess calculated therefrom according to the formula $[\text{major enantiomer} - \text{minor enantiomer}] / [\text{major enantiomer} + \text{minor enantiomer}]$. Where the stereoisomers are diastereoisomers, the stereoselectivity is referred to as diastereoselectivity, the fraction (typically reported as a percentage) of one diastereomer in the sum with others. In the context of the present disclosure, diastereoselectivity refers to the fraction (typically reported as a percentage) of the hydroxy oxo ester of structural formula (Ia) that gets converted into the *syn* dihydroxy ester of structural formula IIa, as opposed to the anti dihydroxy ester of formula IIb. It may also be reported (typically as a percentage) as the diastereomeric excess calculated therefrom according to the formula $[\text{syn IIa} - \text{anti IIb}] / [\text{syn IIa} + \text{anti IIb}]$.

6.2 Ketoreductase Enzymes

[0068] The present disclosure provides engineered ketoreductase (“KRED”) enzymes that are capable of enantioselectively reducing the 3-oxo group of a 5-hydroxy-3-oxohexanoate ester enantiomer to produce the corresponding *syn* 3,5-dihydroxyhexanoate ester, and have at least one improved property when compared with the naturally-occurring, wild-type KRED enzyme obtained from *Saccharomyces cerevisiae*. As noted above, the stereoisomerically pure *syn* 3,5-dihydroxyhexanoate esters produced by the ketoreductase can serve as intermediates for the synthesis of several cholesterol lowering statins. Improvements in various enzyme properties can facilitate use of these engineered ketoreductases in large scale production of this intermediate compound. Any number of improvements in enzymatic properties would be useful for the described application, for example, enzymatic activity, thermal stability, and reduced co-factor requirement.

[0069] Ketoreductase enzymes having improved properties can be obtained by mutating the genetic material encoding the ketoreductase enzyme of *Saccharomyces cerevisiae* and identifying polynucleotides that express engineered enzymes with a desired property. These non-naturally occurring ketoreductases can be generated by various well-known techniques, such as *in vitro* mutagenesis or directed evolution. In some embodiments, directed evolution is an attractive method for generating engineered enzymes because of the relative ease of generating mutations throughout the whole of the gene coding for the polypeptide, as well as providing the ability to take previously mutated polynucleotides and subjecting them to

additional cycles of mutagenesis and/or recombination to obtain further improvements in a selected enzyme property. Subjecting the whole gene to mutagenesis can reduce the bias that may result from restricting the changes to a limited region of the gene. It can also enhance generation of enzymes affected in different enzyme properties since distantly spaced parts of the enzyme may play a role in various aspects of enzyme function. Mutagenesis and directed evolution techniques useful for the purposes herein are amply described in the literature:

Ling, et al., 1997, "Approaches to DNA mutagenesis: an overview," *Anal. Biochem.* 254(2):157-78; Dale et al., 1996, "Oligonucleotide-directed random mutagenesis using the phosphorothioate method," *Methods Mol. Biol.* 57:369-74; Smith, 1985, "In vitro mutagenesis," *Ann. Rev. Genet.* 19:423-462; Botstein et al., 1985, "Strategies and applications of in vitro mutagenesis," *Science* 229:1193-1201; Carter, 1986, "Site-directed mutagenesis," *Biochem. J.* 237:1-7; Kramer et al., 1984, "Point Mismatch Repair," *Cell*, 38:879-887; Wells et al., 1985, "Cassette mutagenesis: an efficient method for generation of multiple mutations at defined sites," *Gene* 34:315-323; Minshull et al., 1999, "Protein evolution by molecular breeding," *Curr Opin Chem Biol* 3:284-290; Christians et al., 1999, "Directed evolution of thymidine kinase for AZT phosphorylation using DNA family shuffling," *Nature Biotech* 17:259-264; Crameri et al., 1998, "DNA shuffling of a family of genes from diverse species accelerates directed evolution," *Nature* 391:288-291; Crameri et al., 1997, "Molecular evolution of an arsenate detoxification pathway by DNA shuffling," *Nature Biotech* 15:436-438; Zhang et al., 1997, "Directed evolution of an effective fructosidase from a galactosidase by DNA shuffling and screening," *Proc Natl Acad Sci USA* 94:4509-4509; Crameri et al., 1996, "Improved green fluorescent protein by molecular evolution using DNA shuffling," *Nature Biotech* 14:315-319; Stemmer, 1994, "Rapid evolution of a protein in vitro by DNA shuffling," *Nature* 370:389-391; Stemmer, 1994, "DNA shuffling by random fragmentation and reassembly: In vitro recombination for molecular evolution," *Proc Natl Acad Sci USA* 91:10747-10751; WO 95/22625; WO 97/0078; WO 97/35966; WO 98/27230; WO 00/42651; WO 01/75767 and U.S. Pat. 6,537,746. All publications are incorporated herein by reference.

[0070] The naturally occurring polynucleotide encoding the naturally occurring ketoreductase of *Saccharomyces cerevisiae* can be obtained from the isolated polynucleotide known to encode the ketoreductase activity (Genbank accession no. NP_010159 GI:6320079). Alternatively, a polynucleotide encoding the naturally occurring

ketoreductases can be synthesized by polynucleotide synthesis methodologies known in the art based on the reported polynucleotide sequence of the *Saccharomyces cerevisiae* ketoreductase-encoding gene. In various embodiments, as further described below, the naturally occurring polynucleotide encoding the ketoreductase can be codon optimized to the codons preferred by a specific host cell used for expression of the enzyme. See *e.g.*, Example 1.

[0071] The parent or reference polynucleotide encoding the naturally occurring or wild type ketoreductase is subjected to mutagenic processes, for example random mutagenesis and recombination, to introduce mutations into the polynucleotide. The mutated polynucleotide is expressed and translated, thereby generating engineered ketoreductase enzymes with modifications to the polypeptide. As used herein, “modifications” include amino acid substitutions, deletions, and insertions. Any one or a combination of modifications can be introduced into the naturally occurring enzymatically active polypeptide to generate engineered enzymes, which are then screened by various methods to identify polypeptides, and corresponding polynucleotides, having a desired improvement in a specific enzyme property. A polynucleotide encoding an engineered ketoreductase with an improved property can be subjected to additional rounds of mutagenesis treatments to generate polypeptides with further improvements in the desired enzyme property.

[0072] As used herein, a ketoreductase enzyme that has an “improved enzyme property” refers to a ketoreductase enzyme that exhibits an improvement in any enzyme property as compared to a reference ketoreductase enzyme. For the engineered ketoreductase enzymes described herein, the comparison is generally made to the wild-type *Saccharomyces cerevisiae* ketoreductase enzyme (SEQ ID NO:2), although in some embodiments, the reference ketoreductase can be another improved engineered ketoreductase. Enzyme properties for which improvement is desirable include, but are not limited to, enzymatic activity, thermal stability, pH activity profile, cofactor requirements, refractoriness to inhibitors (*e.g.*, product inhibition), stereospecificity, and stereoselectivity.

[0073] As used herein the context of engineered ketoreductase enzymes, “derived from” identifies the originating ketoreductase enzyme, and/or the gene encoding such ketoreductase enzyme, upon which the engineering was based. For example, the engineered ketoreductase enzyme of SEQ ID NO:80 was obtained by artificially evolving, over multiple generations the gene encoding the *Saccharomyces cerevisiae* ketoreductase enzyme of SEQ ID NO:2.

Thus, this engineered ketoreductase enzyme is “derived from” the wild-type ketoreductase of SEQ ID NO.: 2.

[0074] While not intending to be bound by any theory of operation, it is believed that the improvements in enzyme properties arise from introduction of modifications into a polypeptide chain that, in effect, perturb the structure-function of the enzyme and/or its interactions with another molecule (*e.g.*, substrate). Some regions of the polypeptide may be critical to enzyme activity, for example amino acids involved in catalysis and substrate binding domains, such that small perturbations to these regions may have significant effects on enzyme function. Some amino acid residues may be at important positions for maintaining the secondary or tertiary structure of the enzyme, and thus also produce noticeable changes in enzyme properties when modified. On the other hand, some regions of the polypeptide may have a global structural role or form part of the enzyme less involved in the critical aspects of enzyme function (*e.g.*, a peptide loop connecting alpha helices) and produce a measurable effect on enzyme function only when a large number of substitutions have accumulated in the region. Thus, in some embodiments, the number of modifications to the naturally occurring polypeptide that produces an improved ketoreductase property may comprise one or more amino acids, 2 or more amino acids, 5 or more amino acids, 10 or more amino acids, or 20 or more amino acids, up to 10% of the total number of amino acids, up to 20% of the total number of amino acids, or up to 30% of the total number of amino acids of the reference enzyme sequence.

[0075] Because of the nature of the technique, gene evolution approaches, such as DNA mutagenesis and recombination, biases the modification towards amino acid substitutions. Thus, in various embodiments, the improvements in enzyme properties can arise from substitutions at one amino acid residue, 2 or more amino acid residues, 5 or more amino acid residues, 10 or more amino acid residue, 15 or more amino acid residues, 20 or more amino acid residues, up to 10% of the total number of amino acids, up to 20% of the total number of amino acids, or up to 30% of the total number of amino acids making up the reference enzyme sequence.

[0076] As will be apparent to the skilled artisan, an analysis of amino acid substitutions for a large number of engineered ketoreductase with an improved enzyme property shows that the substitutions recur at certain amino acid residues in the ketoreductase polypeptide as well as a bias towards certain types of amino acids. This recurrence of substitutions at certain defined

positions within the polypeptide may reflect the effect of amino acid residue on that particular enzyme property and its retention by the continued imposition of selection for the particular improved enzyme property. The recurrence of substitutions as well as the bias of the types of substituted amino acids can be grouped to describe the types of substitutions allowable for generating the improved enzyme property. Typically, genetically encoded amino acids can be grouped into the following classes based on their side chain properties:

[0077] “Hydrophilic Amino Acid or Residue” refers to an amino acid or residue having a side chain exhibiting a hydrophobicity of less than zero according to the normalized consensus hydrophobicity scale of Eisenberg *et al.*, 1984, *J. Mol. Biol.* 179:125-142. Genetically encoded hydrophilic amino acids include L-Thr (T), L-Ser (S), L-His (H), L-Glu (E), L-Asn (N), L-Gln (Q), L-Asp (D), L-Lys (K) and L-Arg (R).

[0078] “Acidic Amino Acid or Residue” refers to a hydrophilic amino acid or residue having a side chain exhibiting a pK value of less than about 6 when the amino acid is included in a peptide or polypeptide. Acidic amino acids typically have negatively charged side chains at physiological pH due to loss of a hydrogen ion. Genetically encoded acidic amino acids include L-Glu (E) and L-Asp (D).

[0079] “Basic Amino Acid or Residue” refers to a hydrophilic amino acid or residue having a side chain exhibiting a pK value of greater than about 6 when the amino acid is included in a peptide or polypeptide. Basic amino acids typically have positively charged side chains at physiological pH due to association with hydronium ion. Genetically encoded basic amino acids include L-His (H), L-Arg (R) and L-Lys (K).

[0080] “Polar Amino Acid or Residue” refers to a hydrophilic amino acid or residue having a side chain that is uncharged at physiological pH, but which has at least one bond in which the pair of electrons shared in common by two atoms is held more closely by one of the atoms. Genetically encoded polar amino acids include L-Asn (N), L-Gln (Q), L-Ser (S) and L-Thr (T).

[0081] “Hydrophobic Amino Acid or Residue” refers to an amino acid or residue having a side chain exhibiting a hydrophobicity of greater than zero according to the normalized consensus hydrophobicity scale of Eisenberg *et al.*, 1984, *J. Mol. Biol.* 179:125-142. Genetically encoded hydrophobic amino acids include L-Pro (P), L-Ile (I), L-Phe (F), L-Val (V), L-Leu (L), L-Trp (W), L-Met (M), L-Ala (A) and L-Tyr (Y).

[0082] “Aromatic Amino Acid or Residue” refers to a hydrophilic or hydrophobic amino acid or residue having a side chain that includes at least one aromatic or heteroaromatic ring. Genetically encoded aromatic amino acids include L-Phe (F), L-Tyr (Y) and L-Trp (W). Although owing to the pKa of its heteroaromatic nitrogen atom L-His (H) is classified above as a basic residue, as its side chain includes a heteroaromatic ring, it may also be classified as an aromatic residue.

[0083] “Non-polar Amino Acid or Residue” refers to a hydrophobic amino acid or residue having a side chain that is uncharged at physiological pH and which has bonds in which the pair of electrons shared in common by two atoms is generally held equally by each of the two atoms (*i.e.*, the side chain is not polar). Genetically encoded non-polar amino acids include L-Leu (L), L-Val (V), L-Ile (I), L-Met (M) and L-Ala (A).

[0084] “Aliphatic Amino Acid or Residue” refers to a hydrophobic amino acid or residue having an aliphatic hydrocarbon side chain. Genetically encoded aliphatic amino acids include L-Ala (A), L-Val (V), L-Leu (L) and L-Ile (I).

[0085] The amino acid L-Cys (C) is unusual in that it can form disulfide bridges with other L-Cys (C) amino acids or other sulfanyl- or sulfhydryl-containing amino acids. The “cysteine-like residues” include cysteine and other amino acids that contain sulfhydryl moieties that are available for formation of disulfide bridges. The ability of L-Cys (C) (and other amino acids with -SH containing side chains) to exist in a peptide in either the reduced free -SH or oxidized disulfide-bridged form affects whether L-Cys (C) contributes net hydrophobic or hydrophilic character to a peptide. While L-Cys (C) exhibits a hydrophobicity of 0.29 according to the normalized consensus scale of Eisenberg (Eisenberg *et al.*, 1984, *supra*), it is to be understood that for purposes of the present disclosure L-Cys (C) is categorized as a polar hydrophilic amino acid, notwithstanding the general classifications defined above.

[0086] The amino acid Gly (G) is also unusual in that it bears no side chain on its α -carbon and, as a consequence, contributes only a peptide bond to a particular peptide sequence. Moreover, owing to the lack of a side chain, it is the only genetically-encoded amino acid having an achiral α -carbon. Although Gly (G) exhibits a hydrophobicity of 0.48 according to the normalized consensus scale of Eisenberg (Eisenberg *et al.*, 1984, *supra*), for purposes of the present invention, Gly is categorized as an aliphatic amino acid or residue.

[0087] “Small Amino Acid or Residue” refers to an amino acid or residue having a side chain that is composed of a total three or fewer carbon and/or heteroatoms (excluding the α -carbon and hydrogens). The small amino acids or residues may be further categorized as aliphatic, non-polar, polar or acidic small amino acids or residues, in accordance with the above definitions. Genetically-encoded small amino acids include Gly, L-Ala (A), L-Val (V), L-Cys (C), L-Asn (N), L-Ser (S), L-Thr (T) and L-Asp (D).

[0088] “Hydroxyl-containing Amino Acid or Residue” refers to an amino acid containing a hydroxyl (-OH) moiety. Genetically-encoded hydroxyl-containing amino acids include L-Ser (S) L-Thr (T) and L-Tyr (Y).

[0089] As will be appreciated by those of skill in the art, the above-defined categories are not mutually exclusive. Indeed, the delineated category of small amino acids includes amino acids from all of the other delineated categories except the aromatic category. Thus, amino acids having side chains exhibiting two or more physico-chemical properties can be included in multiple categories. As a specific example, amino acid side chains having heteroaromatic moieties that include ionizable heteroatoms, such as His, may exhibit both aromatic properties and basic properties, and can therefore be included in both the aromatic and basic categories. The appropriate classification of any amino acid or residue will be apparent to those of skill in the art, especially in light of the detailed disclosure provided herein.

[0090] In some embodiments, the substitution in the engineered ketoreductase may be a conservative substitution. The term “conservative amino acid substitutions” refer to the interchangeability of residues having similar side chains, and thus typically involves substitution of the amino acid in the polypeptide with amino acids within the same or similar defined class of amino acids. By way of example and not limitation, an amino acid with an aliphatic side chain may be substituted with another aliphatic amino acid, *e.g.*, alanine, valine, leucine, isoleucine, and methionine; an amino acid with hydroxyl side chain is substituted with another amino acid with a hydroxyl side chain, *e.g.*, serine and threonine; an amino acids having aromatic side chains is substituted with another amino acid having an aromatic side chain, *e.g.*, phenylalanine, tyrosine, tryptophan, and histidine; an amino acid with a basic side chain is substituted with another amino acid with a basis side chain, *e.g.*, lysine, arginine, and histidine; an amino acid with an acidic side chain is substituted with another amino acid with an acidic side chain, *e.g.*, aspartic acid or glutamic acid; and a

hydrophobic or hydrophilic amino acid is replaced with another hydrophobic or hydrophilic amino acid, respectively.

[0091] In some embodiments, the substitution in the engineered ketoreductase may be a conservative substitution. The term “conservative amino acid substitutions” refer to the interchangeability of residues having similar side chains, and thus typically involves substitution of the amino acid in the polypeptide with amino acids within the same or similar defined class of amino acids. By way of example and not limitation, an amino acid with an aliphatic side chain may be substituted with another aliphatic amino acid, *e.g.*, alanine, valine, leucine, isoleucine, and methionine; an amino acid with hydroxyl side chain is substituted with another amino acid with a hydroxyl side chain, *e.g.*, serine and threonine; an amino acids having aromatic side chains is substituted with another amino acid having an aromatic side chain, *e.g.*, phenylalanine, tyrosine, tryptophan, and histidine; an amino acid with a basic side chain is substituted with another amino acid with a basis side chain, *e.g.*, lysine, arginine, and histidine; an amino acid with an acidic side chain is substituted with another amino acid with an acidic side chain, *e.g.*, aspartic acid or glutamic acid; and a hydrophobic or hydrophilic amino acid is replaced with another hydrophobic or hydrophilic amino acid, respectively.

[0092] In various embodiments, the substitutions for generating an improved ketoreductase can comprise conservative substitutions, non-conservative substitutions, as well as combinations of conservative and non-conservative substitutions.

[0093] In some embodiments, the improved engineered ketoreductase enzymes comprise deletions of the naturally occurring ketoreductase polypeptides as well as deletions of other improved ketoreductase polypeptides. The term “deletion” refers to modification to the polypeptide by removal of one or more amino acids from the reference polypeptide. Deletions can comprise removal of 1 or more amino acids, 2 or more amino acids, 5 or more amino acids, 10 or more amino acids, 15 or more amino acids, or 20 or more amino acids, up to 10% of the total number of amino acids, or up to 20% of the total number of amino acids making up the reference enzyme while retaining enzymatic activity and/or retaining the improved properties of an engineered ketoreductase enzyme. Deletions can be directed to the internal portions and/or terminal portions of the polypeptide. In various embodiments, the deletion can comprise a continuous segment or can be discontinuous.

[0094] In other embodiments, the improved engineered ketoreductase enzymes comprise insertions of one or more amino acids to the naturally occurring ketoreductase polypeptide as well as insertions of one or more amino acids to other improved ketoreductase polypeptides. Insertions can be in the internal portions of the polypeptide, or to the carboxy or amino terminus. Insertions as used herein include fusion proteins as is known in the art. The insertion can be a contiguous segment of amino acids or separated by one or more of the amino acids in the naturally occurring polypeptide.

[0095] As described above the various modifications introduced into the naturally occurring polypeptide to generate an engineered ketoreductase enzyme can be targeted to a specific property of the enzyme. Thus, in some embodiments, the improved property of the engineered ketoreductase polypeptides is an increased enzymatic activity, typically represented by an increase in specific activity (*e.g.*, product produced/time/weight protein) as compared to the reference ketoreductase enzyme (*i.e.*, the naturally occurring ketoreductase). Exemplary methods to determine enzyme activity are provided in the Examples. Any property relating to enzyme activity may be affected, including the classical enzyme properties of K_m , V_{max} or k_{cat} , changes of which can lead to increased enzymatic activity. Improvements in enzyme activity can be from about 1.5 times the enzymatic activity of the corresponding wild-type ketoreductase enzyme, to as much as 2 times, 5 times, 10 times, 20 times, 25 times, 50 times, 75 times, 100 times, 150 times, 200 times, 250 times, 300 times, or more enzymatic activity than the naturally occurring ketoreductase of SEQ ID NO:2. In specific embodiments, the engineered ketoreductase enzyme exhibits improved enzymatic activity in the range of 1.5 to 50 times, 1.5 to 100 times, 1.5 to 150 times, 1.5 to 200 times, 1.5 to 250 times, or 1.5 to 300 times greater than that of the wild-type ketoreductase enzyme. It is understood by the skilled artisan that the activity of any enzyme is diffusion limited such that the catalytic turnover rate cannot exceed the diffusion rate of the substrate, including any required cofactors. The theoretical maximum of the diffusion limit, or k_{cat}/K_m , is generally about 10^8 to 10^9 ($M^{-1} s^{-1}$). Hence, any improvements in the enzyme activity of the ketoreductase will have an upper limit related to the diffusion rate of the substrates acted on by the ketoreductase enzyme. Ketoreductase activity can be measured by any one of standard assays used for measuring ketoreductase, such as a decrease in absorbance or fluorescence of NADPH due to its oxidation with the concomitant reduction of a ketone to the corresponding alcohol, or by product produced in a coupled assay. Comparisons of enzyme activities are

made using a defined preparation of enzyme and a defined assay under a set condition, as further described in detail herein. Generally, when lysates are compared, the numbers of cells and the amount of protein assayed are determined as well as use of identical expression systems and identical host cells to minimize variations in amount of enzyme produced by the host cells and present in the lysates.

[0096] In some embodiments, the engineered ketoreductase with improved enzyme activity comprise engineered polypeptides derived from *Saccharomyces cerevisiae* ketoreductase of SEQ ID NO:2. In some embodiments, the engineered ketoreductase comprises an amino acid sequence that is at least about 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identical to SEQ ID NO:2. Amino acid residues that can be modified to generate engineered polypeptides with improved enzyme activity are shown in FIG. 4 in which Xⁿ represents the modified amino acid residue. In some embodiments, one or more of the naturally occurring amino acid residue of

SEQ ID NO:2 can be substituted as follows :

- X⁶ is a polar or acidic amino acid residue;
- X²⁷ is an aliphatic or basic amino acid residue;
- X³¹ is a hydroxyl containing or aliphatic amino acid residue;
- X³⁶ is a small amino acid residue;
- X⁴⁸ is a basic amino acid residue;
- X⁶³ is a hydrophobic or aromatic amino acid;
- X⁶⁵ is a hydroxyl containing or small amino acid residue;
- X⁸⁶ is an aliphatic or hydrophobic amino acid residue;
- X¹²⁵ is an aliphatic or aromatic amino acid residue;
- X¹⁵² is a basic amino acid residue;
- X¹⁶⁰ is a hydroxyl containing or small amino acid residue;
- X¹⁶⁵ is a polar or acidic amino acid residue;
- X¹⁹⁴ is an aromatic amino acid or polar hydrophilic amino acid residue
- X²¹⁴ is a polar hydrophilic amino acid residue;
- X²¹⁸ is a hydroxyl containing amino acid residue,;
- X²³⁴ is a polar hydrophilic amino acid residue;
- X²⁴⁸ is an aliphatic amino acid residue;
- X²⁵⁰ is a basic amino acid residue;
- X²⁶³ is a acidic or polar amino acid residue;

X²⁹⁰ is an acidic amino acid residue;

X²⁹⁶ is an aliphatic amino acid residue

X²⁹⁷ is an aromatic amino acid residue;

X³⁰¹ is an aliphatic, hydroxyl containing, acidic, hydrophilic, or basic amino acid residue; and/or

X³⁰⁷ is an aromatic, a polar or a hydroxyl containing amino acid residue. In some embodiments, the ketoreductase has all of these residue characteristics.

[0097] In some embodiments, the ketoreductase has one or more of these residue characteristics. In some embodiments, at least one of these residue positions does not include a substitution that is a conservative mutation with respect to SEQ ID NO:2. In some embodiments, X⁶³ is an aromatic residue. In some embodiments, X⁶³ is tryptophan. In some embodiments, residues at other positions can be conservatively mutated with respect to SEQ ID NO:2.

[0098] In some embodiments, the amino acid residues of the ketoreductase of SEQ ID NO:2 can be substituted with one or more specific amino acids as follows:

X⁶ is E;

X²⁷ is A or K;

X³¹ is S or P;

X³⁶ is V;

X⁴⁸ is H;

X⁶³ is W;

X⁶⁵ is G or S;

X⁸⁶ is I;

X¹²⁵ is L;

X¹⁵² is R;

X¹⁶⁰ is T or S;

X¹⁶⁵ is E;

X¹⁹⁴ is C;

X²¹⁴ is R or H;

X²¹⁸ is T;

X²³⁴ is Q;

X²⁴⁸ is I;

X^{250} is R;
 X^{263} is E;
 X^{290} is V or D;
 X^{296} is I;
 X^{297} is F or W;
 X^{301} is R, K, A, V, S, T, Y, D, E, P, or Q; and/or
 X^{307} is H, N or S.

[0099] In some embodiments, the engineered ketoreductases with improved enzyme activity have substitutions in a subset of the amino acid residues indicated above. Thus, in some embodiments the amino acid substitutions can occur in one or more of the amino acid positions: X^{27} , X^{31} , X^{36} , X^{48} , X^{63} , X^{65} , X^{86} , X^{125} , X^{152} , X^{160} , X^{194} , X^{218} , X^{248} , X^{250} , X^{290} , X^{296} , X^{297} , X^{301} , and X^{307} , wherein the amino acid residues for substitution are selected as indicated above.

[0100] In some embodiments, the engineered ketoreductase comprises one or more mutations selected from: R27A, R27K, N31S, A36V, Y48H, I63W, R65G, R65S, L86I, F125L, K152R, A160T, Y194C, A218T, V248I, K250R, E290D, L296V, Y297W, Y297F, L301K, L301R, L301A, L301S, L301E, L301P, L301Q, L301V, L301T, L301Y, L301D, Y307H, Y307N, and Y307S.

[0101] It is also shown herein that the various amino acid residue positions whose substitutions result in a ketoreductase with improved properties are found to cluster in certain segments of the ketoreductase enzyme, which allows targeted modifications of the segments. Accordingly, in some embodiments, selected segments of the ketoreductase polypeptide may be subject to modification. For the reference sequence of SEQ ID NO:2, the segments affecting ketoreductase enzymatic activity include, among others, those represented by amino acid residues 27 to 36, 40 to 65, 103 to 125, 144 to 169, 233 to 265, and/or 287 to 312. One or more of the amino acid residues within each segment or combination of segments may be modified. In some embodiments, the corresponding amino acid sequences and positions for substitutions comprise:

X^{27} WYKX³¹EETDX³⁶

X^{40} SLX⁴³X⁴⁴QX⁴⁶VX⁴⁸ALX⁵¹LPGX⁵⁵X⁵⁶HX⁵⁸DX⁶⁰AX⁶²X⁶³YX⁶⁵

X^{103} LDX¹⁰⁶ALKK MGTX¹¹⁴YVDLYLX¹²¹HSPX¹²⁵

X¹⁴⁴LYKX¹⁴⁸GKAX¹⁵²NIGVSX¹⁵⁸F X¹⁶⁰VEDLX¹⁶⁵RILX¹⁶⁹

X²³³X²³⁴KYX²³⁷KX²³⁹EAQILRWX²⁴⁸TX²⁵⁰RGX²⁵³LPVTTSS KPX²⁶³RX²⁶⁵; and

X²⁹⁰HEPLRX²⁹⁶X²⁹⁷WNKX³⁰¹YGKYNX³⁰⁷AAX³¹⁰X³¹¹X³¹²

wherein Xⁿ indicates positions of the amino acid substitutions.

[0102] In some embodiments, the engineered ketoreductase enzyme with improved enzymatic activity has an amino acid sequence selected from the amino acid sequences recited in Table 1:

TABLE 1					
Nucleic Acid SEQ ID NO.	Protein SEQ ID NO.	Residue substitutions	Activity	temperature for stability test (°C)	Stability
15	16	L106I;	*	37	+
17	18	G112R; A160T;	*	37	+
19	20	E44D; Y307S;	*	37	+
21	22	I22M; S148T;	*	37	+
23	24	E290D;	*	37	+
25	26	R27A;	*	40	-
27	28	V253A; Y307N;	*	40	-
29	30	R27A; Y48H;	*	40	-
31	32	A60T;	*	40	+
33	34	D114G;	*	40	+
35	36	F185L;	*	40	-
37	38	N31S;	*	40	-
39	40	L296V;	*	40	-

TABLE 1

Nucleic Acid SEQ ID NO.	Protein SEQ ID NO.	Residue substitutions	Activity	temperature for stability test (°C)	Stability
41	42	E78K; A160T;	*	40	-
43	44	N40Y; S233C;	*	40	-
45	46	Q214H;	*	40	-
47	48	V248I;	*	40	-
49	50	E62Q; F185I;	*	40	-
51	52	A60T;	*	40	+
53	54	R27A; Y48H; A160T;	*	40	-
55	56	I22M; A101V; G112R; A160T; Y307S;	*	40	-
57	58	R27A; Y307S;	*	40	-
59	60	R27K; K51E; S148T; I237N;	*	40	+
61	62	A60T; D102G; I237N;	*	40	+
63	64	I237N;	*	40	+
65	66	R27A; Y48H; A160T;	*	40	-
67	68	A60T; I237N;	*	40	+
69	70	I22M; A60T; I237N;	*	40	+
71	72	R27A; A160T; K261R;	*	40	-
73	74	I22M; I237N; V253A;	*	40	+
75	76	I22M; E44D; I237N; E290Q;	*	40	+
77	78	A160T; E290D;	*	40	-
79	80	I22M; I237N; E290D;	*	40	+
81	82	G112R; A160T; Y307S;	*	40	-
83	84	I22M; T77A; G112R; A160T;	*	40	-

TABLE 1

Nucleic Acid SEQ ID NO.	Protein SEQ ID NO.	Residue substitutions	Activity	temperature for stability test (°C)	Stability
85	86	I22M; I237N;	*	40	+
87	88	N31S; I237N;	*	40	+
89	90	A60T; I237T;	*	40	+
91	92	A160T; Y307S;	*	40	-
93	94	K147R; A160T; I237N; Y307S;	*	40	+
95	96	R27K; A160T; I237N;	*	40	+
97	98	R27K; K79R; A160T;	*	40	-
99	100	R27A; G112R; A160T; I237N;	*	40	-
101	102	A60T; K195R; I237N;	*	40	+
103	104	A160T;	*	40	-
105	106	I63V; E78K; A160T; Q214R;	*	40	-
107	108	K51E; Y194C;	*	40	-
109	110	N31S; I237T;	*	40	-
111	112	R27K; A160T; Q214R; I237N;	**	40	+
113	114	R27K; A160T; S233G; I237N;	**	40	-
115	116	R27K; D114N; A160T; I237N; V248I;	**	40	-
117	118	R27K; A160T; I237N; V253A;	*	40	+
119	120	R27K; V43F; A160T; I237N;	**	40	-
121	122	R27K; A160T; V229I; I237N;	*	40	+
123	124	R27K; F125L; A160T; I237N;	**	40	-
125	126	R27K; L121I; A160T; I237N;	*	40	+
127	128	R27K; A160T; I237N; K261M;	**	40	-

TABLE 1

Nucleic Acid SEQ ID NO.	Protein SEQ ID NO.	Residue substitutions	Activity	temperature for stability test (°C)	Stability
129	130	A160S; I237R;	**	40	+
131	132	A160S; I237G;	**	40	+
133	134	A160S; I237Q;	**	40	+
135	136	R27K; L76M; A160T; I237N;	*	40	+
137	138	R27K; S148R; A160T; I237N;	**	40	-
139	140	R27K; A160T; I237N; S239T;	*	40	+
141	142	R27K; A160T; S222R; Q223H; I237N;	*	40	+
143	144	R27K; V47L; A160T; D221V; I237N;	*	40	+
145	146	R27K; A160T; I237N; L296Q;	**	40	-
147	148	R27K; A160S; Q214R; I237N;	**	43	+
149	150	R27K; Y48H; A160T; Q214R; I237N;	***	43	-
151	152	R27K; K51E; I63V; L121I; A160T; Q214R; I237G;	**	43	+
153	154	R27K; N31S; L121I; A160T; Q214R; K215M; I237N;	***	43	+
155	156	R27A; N31S; A160T; H200L; Q214R; K215E; I237N;	***	43	-
157	158	R27A; N31S; A160T; Q214R; I237N; V312E;	***	43	-
159	160	R27K; N31S; I58V; A160T; Q214R; I237N; I265V;	***	43	-
161	162	R27A; N31S; Y48H; A160T; Q214R; I237N;	***	43	-
163	164	R27K; A160T; G192D; Q214R;	***	43	-

TABLE 1

Nucleic Acid SEQ ID NO.	Protein SEQ ID NO.	Residue substitutions	Activity	temperature for stability test (°C)	Stability
		I237N; K250E;			
165	166	R27K; I63V; L121I; F125L; A160T; Q214R; I237N;	**	43	+
167	168	R27K; K152R; A160T; Q214R; I237N;	***	43	-
169	170	R27A; N31S; A160T; Q214R; I237N;	***	43	-
171	172	R27K; G103S; A160T; Q214R; I237N;	**	43	+
173	174	R27K; A60T; I84V; A160T; Q214R; I237N;	*	43	+
175	176	R27K; A160T; Q214R; I237R; Y307S;	***	43	-
177	178	R27A; N31S; F125L; A160T; K169R; Q214R; I237N;	***	43	-
179	180	R27K; Q144R; A160T; Q214R; I237N;	**	43	+
181	182	R27K; L121I; A160T; Q214R; I237D;	***	43	+
183	184	R27K; N31S; A160T; Q214R; I237N; Y307S;	***	43	-
185	186	R27K; L121I; A160T; Y194C; Q214R; I237N;	***	43	+
187	188	R27K; N31S; E78K; A160T; Q214R; T217A; S222G; I237N;	***	43	-
189	190	R27K; L121I; A160T; Q214R; I237G;	**	43	+
191	192	R27K; A160T; Q214R; Q223H; I237N;	**	43	+

TABLE 1

Nucleic Acid SEQ ID NO.	Protein SEQ ID NO.	Residue substitutions	Activity	temperature for stability test (°C)	Stability
193	194	R27K; E78K; A160T; Q214R; I237N; Y307S;	***	43	-
195	196	R27A; N31S; L121I; A160T; Q214R; I237N;	***	43	+
197	198	R27K; L121I; A160T; Y194C; Q214R; I237N;	***	43	+
199	200	R27K; N31S; L121I; A160T; Q214R; I237N;	***	43	+
201	202	R27K; N31S; A160T; Q214R; I237G;	***	43	-
203	204	I19T; R27K; N31S; A160T; Q214R; I237G;	***	43	-
205	206	R27K; I63V; A160T; Q214R; I237N;	**	43	+
207	208	R27K; N31S; K51E; A160T; Q214R; I237N; K304R;	***	43	-
209	210	R27K; N31S; L121I; A160T; Y194C; Q214R; I237R;	***	43	+
211	212	R27K; A160T; G192D; Q214R; I237N; Y307S;	***	43	-
213	214	R27A; N31S; A160T; Y194C; Q214R; I237R;	***	43	-
215	216	R27K; E78K; L121I; A160T; Q214R; K216R; I237G;	**	43	+
217	218	R27K; A160T; Q214R; I237G;	**	43	+
219	220	R27K; I56V; A160T; Q214R; I237N;	**	43	+
221	222	R27K; N31S; I63V; A160T; Q214R; I237N;	**	43	+

TABLE 1

Nucleic Acid SEQ ID NO.	Protein SEQ ID NO.	Residue substitutions	Activity	temperature for stability test (°C)	Stability
223	224	R27K; A160T; Q214R; I237N; K250R;	***	43	-
225	226	R27K; V130G; A160T; Q214R; I237N;	***	43	-
227	228	R27K; L121I; A160T; Q214R; I237N;	**	43	+
229	230	R27K; A160T; Q189H; Q214R; I237N; L287R;	**	43	+
231	232	R27K; A73P; A160T; D201G; Q214R; I237G;	***	43	-
233	234	R27K; A160T; Q214R; I237N; Y307H;	***	43	-
235	236	R27K; N31S; L121I; A160T; Y194C; Q214R; I237N;	***	43	+
237	238	R27K; N31S; L121I; A160S; Y194C; Q214R; I237N;	***	43	+
239	240	R27K; N31S; S148T; A160T; Q214R; I237N; Y307S;	***	43	-
241	242	R27K; L121I; A160S; Y194C; Q214R; I237N;	***	43	+
243	244	R27K; N31S; E78K; A160T; Q214R; I237G; Y307S;	***	43	-
245	246	R27K; N31S; L121I; S127T; A160T; Y194C; Q214R; I237N;	***	43	+
247	248	R27A; N31S; L121I; A160S; Y194C; Q214R; I237N;	****	43	+
249	250	R27K; N31S; L121I; S148T; A160T; Y194C; Q214R; I237N;	****	43	+
251	252	R27K; N31S; L121I; A160T; Y194C; Q214R; I237G;	****	43	+

TABLE 1

Nucleic Acid SEQ ID NO.	Protein SEQ ID NO.	Residue substitutions	Activity	temperature for stability test (°C)	Stability
253	254	R27K; N31S; L106I; L121I; A160S; Y194C; Q214R; I237N;	****	43	+
255	256	R27A; N31S; L121I; A160S; Q214R; I237N;	****	43	+
257	258	R27K; N31S; L121I; S148T; A160S; Y194C; Q214R; I237N;	****	43	+
259	260	R27A; N31S; F125L; A160T; Y194C; Q214R; I237N;	****	45	-
261	262	R27A; N31S; F125L; A160T; K169R; Q214R; I237N;	****	45	-
263	264	R27A; N31S; F125L; A160T; Q214R; I237R;	****	45	-
265	266	R27K; N31S; L121I; F125L; A160T; Y194C; Q214R; K215M; I237N;	****	45	+
267	268	R27A; N31S; S148T; A160T; K169R; Q214R; I237N;	****	45	-
269	270	I21T; R27A; N31S; L121I; F125L; A160T; Q214R; I237N;	****	45	-
271	272	R27A; N31S; F125L; A160T; Y194C; Q214R; I237R;	****	45	-
273	274	R27A; N31S; F125L; A160T; Q214R; I237N;	****	45	-
275	276	R27A; N31S; L121I; F125L; A160T; Y194C; Q214R; I237N;	****	45	-
277	278	R27A; N31P; L121I; F125L; A160T; Y194C; Q214R; I237N;	****	48	-
279	280	I19V; R27A; N31S; E44D; K72R; D105E; L121I; F125L; A160T; F185L; Y194C; Q214R; I237N;	****	48	-

TABLE 1

Nucleic Acid SEQ ID NO.	Protein SEQ ID NO.	Residue substitutions	Activity	temperature for stability test (°C)	Stability
		I243V; E290D;			
281	282	Q6E; R27A; N31S; S41T; L121I; F125L; A160T; Y194C; E199Q; Q214R; I237N; L271I;	****	48	+
283	284	Q6E; R27A; N31S; S41T; I46L; I55V; L121I; F125L; A160T; Y194C; E199Q; Q214R; I237N;	****	48	+
285	286	Q6E; R27A; N31S; S41T; I46L; F125L; Q144E; A160T; Y194C; E199Q; Q214R; I237N; S239T; L271I;	****	48	+
287	288	Q6E; R27A; N31S; I46L; L121I; F125L; A160T; Y194C; Q214R; I237N; S239T; I244L;	****	48	+
289	290	Q6E; R27A; N31S; L121I; F125L; A160T; Y194C; Q214R; I237N; S239T;	****	48	+
291	292	Q6E; R27A; N31S; S41T; L121I; F125L; A160T; Y194C; Q214R; I237N; L271I;	****	48	+
293	294	Q6E; R27A; N31S; L121I; F125L; A160T; Y194C; Q214R; E234Q; I237N; S239T;	****	48	+
295	296	Q6E; R27A; N31S; I58L; F125L; A160T; Y194C; E199Q; Q214R; I237N; I244L;	****	48	-
297	298	Q6E; R27A; N31S; I46L; L121I; F125L; A160T; Y194C; E199Q; Q214R; I237N; S239T; I244L;	****	48	+
299	300	Q6E; R27A; N31S; I58L; L86I; L121I; F125L; A160T; Y194C;	****	48	+

TABLE 1

Nucleic Acid SEQ ID NO.	Protein SEQ ID NO.	Residue substitutions	Activity	temperature for stability test (°C)	Stability
		Q214R; I237N; S239T; I244L;			
301	302	Q6E; R27A; N31S; I46L; L121I; F125L; A160T; Y194C; Q214R; I237N; S239T;	****	48	+
303	304	Q6E; R27A; N31S; L121I; F125L; A160T; Y194C; Q214R; I237N; L271I;	****	48	+
305	306	Q6E; R27A; N31S; I46L; I58L; L121I; F125L; Q144E; A160T; Y194C; Q214R; I237N; A309T;	****	48	-
307	308	Q6E; R27A; N31S; L121I; F125L; Q144E; A160T; Q165E; Y194C; E199Q; Q214R; I237N; S239T; I244L; Y305H;	****	48	-
309	310	Q6E; R27A; N31S; S41T; I46L; L121I; F125L; A160T; Y194C; Q214R; I237N;	****	48	+
311	312	Q6E; R27A; N31S; S41T; I46L; L121I; F125L; A160T; Y194C; Q214R; I237N;	****	48	+
313	314	Q6E; R27A; N31P; I46L; L86I; L121I; F125L; A160T; Y194C; Q214R; I237N; S239T;	****	50	+
315	316	R27A; N31P; I63W; L121I; F125L; A160T; Y194C; Q214R; I237N;	****	50	-
317	318	R27A; N31P; I63W; L121I; F125L; A160T; Y194C; Q214R; I237N;	****	50	-
319	320	R27A; N31P; L121I; F125L; A160T; Y194C; Q214R; I237N; Y297W;	****	50	-

TABLE 1

Nucleic Acid SEQ ID NO.	Protein SEQ ID NO.	Residue substitutions	Activity	temperature for stability test (°C)	Stability
321	322	R27A; N31P; L121I; F125L; A160T; Y194C; Q214R; I237N; L301R;	****	50	-
323	324	R27A; N31P; L121I; F125L; A160T; Y194C; Q214R; I237N; L301K;	****	50	-
325	326	R27A; N31P; I63W; L121I; F125L; A160T; Y194C; Q214R; I237N; Y297W;	****	50	-
327	328	R27A; N31P; I63W; L121I; F125L; A160T; Y194C; Q214R; I237N; Y297W; L301K;	****	50	-
329	330	Q6E; R27A; N31P; I46L; I63W; L86I; L121I; F125L; A160T; Y194C; Q214R; I237N; S239T;	****	50	+
331	332	R27A; N31P; I63W; L121I; F125L; A160T; Y194C; Q214R; I237N; Y297W; L301A;	****	ND	ND
333	334	R27A; N31P; I63W; L121I; F125L; A160T; Y194C; Q214R; I237N; Y297W; L301S;	****	ND	ND
335	336	R27A; N31P; I63W; L121I; F125L; A160T; Y194C; Q214R; I237N; Y297W; L301E;	****	ND	ND
337	338	R27A; N31P; I63W; L121I; F125L; A160T; Y194C; Q214R; I237N; Y297W; L301P;	****	ND	ND
339	340	R27A; N31P; I63W; L121I; F125L; A160T; Y194C; Q214R; I237N; Y297W; L301Q;	****	ND	ND
341	342	R27A; N31P; I63W; L121I; F125L; A160T; Y194C; Q214R; I237N; L301E;	****	50	-

TABLE 1

Nucleic Acid SEQ ID NO.	Protein SEQ ID NO.	Residue substitutions	Activity	temperature for stability test (°C)	Stability
343	344	R27A; N31P; S41G; I63W; L121I; F125L; A160T; Y194C; Q214R; I237N; L301A;	****	50	-
345	346	R27A; N31P; I63W; L121I; F125L; A160T; Y194C; Q214R; I237N; Y297F; L301E;	****	50	-
347	348	R27A; N31P; I63W; R65G; L121I; F125L; A160T; Y194C; Q214R; I237N; Y297W; L301Q;	****	50	-
349	350	R27A; N31P; I63W; R65S; L121I; F125L; A160T; Y194C; Q214R; I237N; Y297W; L301Q;	****	50	-
351	352	R27A; N31P; A36V; I63W; L121I; F125L; A160T; Y194C; Q214R; I237N; Y297W; L301Q;	****	50	-
353	354	R27A; N31P; I63W; L121I; F125L; A160T; Y194C; Q214R; I237N; Y297W; L301Q; Q310R; K311E; V312S; *313V;	****	50	-
355	356	R27A; N31P; I63W; L121I; F125L; A160T; Y194C; Q214R; A218T; I237N; Y297W; L301Q;	****	50	-
357	358	R27A; N31P; I63W; L121I; F125L; A160T; Y194C; Q214R; I237N; Y297W; L301Q; Q310P; K311E; V312S; *313V;	****	50	-
359	360	Q6E; R27A; N31P; I46L; I63W; L86I; L121I; F125L; A160T; Y194C; Q214R; I237N; S239T; L301E;	****	ND	ND
361	362	Q6E; R27A; N31P; I46L; L86I; L121I; F125L; A160T; Y194C; Q214R; I237N; S239T; Y297W;	****	ND	ND

TABLE 1					
Nucleic Acid SEQ ID NO.	Protein SEQ ID NO.	Residue substitutions	Activity	temperature for stability test (°C)	Stability
363	364	Q6E; R27A; N31P; I46L; I63W; L86I; L121I; F125L; A160T; Y194C; Q214R; I237N; S239T; Y297W;	****	ND	ND
365	366	Q6E; R27A; N31P; I46L; I63W; L86I; L121I; F125L; A160T; Y194C; Q214R; I237N; S239T; Y297W; L301Q;	****	ND	ND

- * = 150-500% enzymatic activity of SEQ ID NO: 2
 ** = 500-900% enzymatic activity of SEQ ID NO: 2
 *** = 900-1600% enzymatic activity of SEQ ID NO: 2
 **** = greater than 1600% enzymatic activity of SEQ ID NO: 2
 + = variant retains residual activity after heat treatment at indicated temperature for 16 hrs.
 ND = Not Determined

[0103] In other embodiments, the engineered ketoreductase comprises a ketoreductase with improved thermal stability as compared to the naturally occurring ketoreductase from which the engineered enzymes are derived. Thermally stable enzymes allow longer incubations with substrate, such as in conditions of high substrate concentrations used in large scale production, and also minimize the amount of enzyme needed. An enzyme that has “improved thermal stability” refers to an enzyme that displays increased resistance to inactivation when exposed to a set temperature or set of temperatures in defined assay conditions as compared to the resistance to inactivation of a reference enzyme.

[0104] A number of methods are available for measuring enzyme thermal stability. Enzymes may be treated for a defined time period at various temperatures under a standard set of assay conditions (*e.g.*, ionic strength, pH, protein concentration, etc.). Half-inactivation temperatures, *i.e.*, temperatures at which 50% inactivation occurs after heat treatment for the defined time are used to compare the thermal stabilities of the enzymes. Another method of determining thermal stability is to treat the enzyme at a set temperature and measure the amount of enzyme activity remaining. The amount of enzyme activity remaining is

compared to the activity remaining of the naturally occurring enzyme prepared under similar or identical conditions. Useful temperatures for analysis of thermal stability are temperature encompassing the reaction temperature for used for carrying out the reaction, for example as in large scale reactions, and/or temperatures at which the engineered enzymes have been selected for improved thermal stability. For example, the engineered enzymes can have improved thermal stability as compared to a reference enzyme (*e.g.*, a naturally occurring enzyme) at temperatures of about 30°C or above, about 35°C or above, 40°C or above, 45°C or above, 50°C or above, 55°C or above, to about 65°C. In some embodiments, the enzyme can have an improved thermal stability in which the engineered enzyme retains, as compared to a reference enzyme, about 10% or more activity, about 15% or more activity, about 20% or more activity, about 30% or more activity, about 50% or more activity, about 70% or more activity, about 90% or more activity. Under the conditions of treatment, the times at which enzyme activity shows enhanced thermal stability can include, about 5 hrs or more, about 6 hrs or more, about 12 hrs or more, about 18 hrs or more, about 24 hrs or more, about 36 hrs or more, about 48 hrs or more, about 72 hrs or more. Substrate may or may not be present during thermal treatment, although presence of substrate is known to stabilize enzyme structures in some instances.

[0105] In other embodiments, the thermal stability of an enzyme can be measured by determining protein folding stability, such as by detecting protein unfolding with calorimetry or circular dichroism. For example, to determine the thermal stability of the engineered and naturally occurring ketoreductase, changes in CD profile at various temperatures can be used. An Arrhenius plot of the unfolding rate constants of the enzymes is generated by use of temperature-jumps (*e.g.*, from a temperature where an enzyme is active to a temperature where the enzyme is inactive) and measuring changes in protein structure. The first-order rate constants, activation enthalpies, and activation free energies between the stable and transition state of the unfolding reaction at an inactivating temperature may be compared. Typically, the activation free energy increases with more thermally stable enzymes. Other methods for determining thermal stability will be apparent to the skilled artisan.

[0106] In some embodiments, the improved thermal stability is separable from other properties of the ketoreductase enzymes, while in other embodiments, the thermal stability is also observed with another improved property. In some embodiments, the ketoreductases comprise engineered ketoreductases with improved thermal stability is derived from the

Saccharomyces cerevisiae ketoreductase of SEQ ID NO:2. In some embodiments, the engineered ketoreductase with improved thermal stability retains about 20 % or more of enzyme activity following treatment at temperature ranging from 37 to 50°C for 16 hrs at pH 7.0. By comparison, the naturally occurring ketoreductase of SEQ ID NO:2 retains only 5-10% of its activity after incubation at 37°C for 16 hrs at pH 7.0 and retains essentially no activity when incubated at higher temperatures under the same conditions.

[0107] In some embodiments, the engineered ketoreductases with improved thermal stability comprises an amino acid sequence corresponding to SEQ ID NO:2 and includes one or more of the following substitutions:

- X⁶ is a polar or acidic amino acid residue;
- X³¹ is a hydroxyl containing or aliphatic amino acid residue;
- X⁴⁴ is an acidic amino acid residue;
- X⁴⁶ is an aliphatic amino acid residue
- X⁵⁵ is an aliphatic amino acid residue;
- X⁵⁶ is an aliphatic amino acid;
- X⁶⁰ is an hydroxyl containing or small amino acid;
- X⁶³ is a hydrophobic or aromatic amino acid;
- X⁷⁶ is a amino acid residue M;
- X¹⁰³ is a hydroxyl containing amino acid residue;
- X¹⁰⁶ is an aliphatic amino acid residue;
- X¹¹⁴ is a small amino acid residue;
- X¹²¹ is a hydrophobic or aliphatic amino acid residue;
- X¹⁴⁴ is a hydrophilic or basic amino acid residue
- X¹⁴⁸ is a hydroxyl containing amino acid residue
- X¹⁵⁸ is an aromatic amino acid residue
- X¹⁶⁰ is a hydroxyl containing or small amino acid residue;
- X¹⁶⁵ is a polar or acidic amino acid residue;
- X¹⁶⁹ is a aliphatic or basic amino acid residue;
- X¹⁸⁵ is an aromatic or aliphatic amino acid residue;
- X¹⁹⁴ is an aromatic amino acid or polar hydrophilic amino acid residue
- X¹⁹⁹ is a polar amino acid residue;
- X²¹⁴ is an aromatic or basic amino acid residue;

X²²³ is an aromatic amino acid residue;
X²³⁴ is a polar hydrophilic amino acid residue;
X²³⁷ is a hydrophilic or small amino acid residue;
X²³⁹ is a hydroxyl containing amino acid residue;
X²⁵³ is an aliphatic amino acid residue; and/or
X²⁶³ is a acidic or polar amino acid residue.

[0108] In some embodiments, X⁶³ is an aromatic residue. In some embodiments, X⁶³ is tryptophan. In some embodiments, the ketoreductase comprises one or more conservative mutations at other positions than those listed above.

[0109] In some embodiments, the engineered ketoreductases with improved thermal stability comprises an amino acid sequence corresponding to SEQ ID NO:2 and includes one or more of the following substitutions:

X⁶ is E;
X³¹ is P;
X⁴⁴ is D;
X⁴⁶ is L;
X⁵⁵ is V;
X⁵⁶ is V;
X⁶⁰ is T;
X⁶³ is V;
X⁷⁶ is M;
X¹⁰³ is S;
X¹⁰⁶ is I;
X¹¹⁴ is G;
X¹²¹ is I or M;
X¹⁴⁴ is R;
X¹⁴⁸ is T;
X¹⁵⁸ is H;
X¹⁶⁰ is S;
X¹⁶⁵ is E;
X²¹⁴ is R or H;
X²²³ is H, R or G;

X²³⁴ is Q;
X²³⁷ is N, G, R or Q,;
X²³⁹ is T; and/or
X²⁵³ is A.

[0110] In some embodiments, the engineered ketoreductase with improved thermal stability have substitutions in a subset of the amino acid residues indicated above. Thus, in some embodiments the amino acid substitutions can occur at one or more of the amino acid positions X⁴⁴, X⁴⁶, X⁵⁵, X⁵⁶, X⁶⁰, X⁶³, X⁷⁶, X¹⁰³, X¹⁰⁶, X¹¹⁴, X¹²¹, X¹⁴⁴, X¹⁴⁸, X¹⁵⁸, X²²³, X²³⁷, X²³⁹, and X²⁵³, wherein the amino acid residues for substitution are selected as indicated above.

[0111] In some embodiments, the engineered ketoreductase with improved thermal stability comprises one or more of the following substitutions as compared to SEQ ID NO:2: E44D, I46L, I55V, I56V, A60T, I63V, L76M,, G103S, L106I, D114G, L121I, Q144R, S148T, N158H, Q223H, I237G, I237N, I237R, S239T, and V253A.

[0112] As observed for the engineered ketoreductases with improved enzymatic activity, various amino acid residue positions whose substitutions result in an engineered ketoreductase with improved thermal stability are also found to cluster in certain segments of the ketoreductase of SEQ ID NO:2, which allows targeted modifications. Substitutions resulting in improved thermal stability overlap with those that occur in engineered enzymes with improved enzymatic activity, although some do not. Accordingly, in some embodiments, selected segments of the ketoreductase polypeptide may be subject to modification to generate engineered ketoreductases with improved thermal stability. For the reference sequence of SEQ ID NO:2, the segments affecting ketoreductase enzymatic activity include, among others, those represented by amino acid residues 27 to 36, 40 to 65, 103 to 125, 144 to 169, 233 to 265, and 287 to 312. In some embodiments, the segments affecting ketoreductase enzymatic activity include, among others, those represented by amino acid residues 27-32, 60-65, 90-93, 120-125, 157-159, 208-211, and 293-306. One or more of the amino acid residues in each segment or combination of segments may be modified.

[0113] In some embodiments, the corresponding amino acid sequences and positions for substitutions comprise:

$X^{27}WYKX^{31}EETDX^{36}$
 $X^{40}SLX^{43}X^{44}QX^{46}VX^{48}ALX^{51}LPGX^{55}X^{56}HX^{58}DX^{60}AX^{62}X^{63}YX^{65}$
 $X^{103}LDX^{106}ALKKMGTX^{114}YVDLYLX^{121}HSPX^{125}$
 $X^{144}LYKX^{148}GKAX^{152}NIGVSX^{158}FX^{160}VEDLX^{165}RILX^{169}$
 $X^{233}X^{234}KYX^{237}KX^{239}EAQILRWX^{248}TX^{250}RGX^{253}LPVTTSSKPX^{263}RX^{265}$; and
 $X^{290}HEPLRX^{296}X^{297}WNKX^{301}YGKYNX^{307}AAX^{310}X^{311}X^{312}$

wherein X^n indicates positions of the amino acid substitutions. Both conservative and non-conservative substitutions can be made in the segments as indicated.

[0114] In some embodiments, the improved property can be a combination of properties, such as improved enzymatic activity and improved thermal stability. In some embodiments, the engineered ketoreductase comprises a ketoreductase with a combination of improved enzyme activity and improved enzyme stability having a amino acid sequence that corresponds to the wild type sequence of the ketoreductase of SEQ ID NO:2 and includes one or more mutations selected from: Q6E, N31P, A160S, Q165E, Q214H, Q214R, E234Q, Q263E.

[0115] In some embodiments, the engineered ketoreductase comprises a ketoreductase with a combination of improved enzyme activity and/or stability having an amino acid sequence that corresponds to the wild type sequence of the ketoreductase SEQ ID NO:2 and includes one or more mutations selected from: N40Y, V43L, K51E, I58V, E62Q, A73P, K79R, K152Q, K169E, F185I, Q189H, G192D, H200L, D201G, K215E, K215M, K216R, D221V, S233C, I237D, K250E, I265V, L287R, K304R, Q310R, K311E, V312S, V312E.

[0116] It is to be understood that the engineered ketoreductases are not limited to those identified directly by mutagenesis or other gene evolution techniques, but also include variants or analogs of the improved engineered ketoreductase polypeptides. The term “variant” or “analog” as used herein refers to polypeptides which are comprised of a segment having ketoreductase activity, with or without retention of the improved property, and has substantial identity to a portion of the engineered ketoreductase. In some embodiments, analog polypeptides comprise a conservative amino acid substitution, or addition or deletion of one or more amino acid residues with respect to the engineered sequence. Analogs typically are at least an enzymatically active fragment and typically as long as the full-length naturally-occurring reference polypeptide of SEQ ID NO:2 (*e.g.*, 312 amino acid residues).

[0117] In some embodiments, the variant or analog of the engineered ketoreductase polypeptides can comprise an enzymatically active ketoreductase polypeptide that has about 70% or more amino acid identity, about 80% or more amino acid identity, about 90% or more amino acid identity, about 95% or more amino acid identity, about 97% or more amino acid identity, about 98% or more amino acid identity, or about 99% or more amino acid identity to a reference engineered ketoreductase or an enzymatically active fragment of an engineered ketoreductase.

[0118] In some embodiments, the reference engineered ketoreductase is selected from the amino acid sequences recited in Table 1. An exemplary reference sequence of an improved ketoreductase is SEQ ID NO:314. In some embodiments, the variant or analog of the engineered ketoreductase polypeptides can comprise an enzymatically active ketoreductase polypeptide that has about 95.5% or more amino acid identity, about 97% or more amino acid identity, about 98% or more amino acid identity, or about 99% or more amino acid identity to SEQ ID NO:314, or an enzymatically active fragment of SEQ ID NO:314.

[0119] Another exemplary reference sequence of an improved ketoreductase is SEQ ID NO:316. In some embodiments, the variant or analog of the engineered ketoreductase polypeptides can comprise an enzymatically active ketoreductase polypeptide that has about 95.5% or more amino acid identity, about 97% or more amino acid identity, about 98% or more amino acid identity, or about 99% or more amino acid identity to SEQ ID NO:316 or an enzymatically active fragment of SEQ ID NO:316.

[0120] Another exemplary reference sequence of an improved ketoreductase is SEQ ID NO:318. In some embodiments, the variant or analog of the engineered ketoreductase polypeptides can comprise an enzymatically active ketoreductase polypeptide that has about 95.5% or more amino acid identity, about 97% or more amino acid identity, about 98% or more amino acid identity, or about 99% or more amino acid identity to SEQ ID NO:318 or an enzymatically active fragment of SEQ ID NO:318.

[0121] Another exemplary reference sequence of an improved ketoreductase is SEQ ID NO:376. In some embodiments, the variant or analog of the engineered ketoreductase polypeptides can comprise an enzymatically active ketoreductase polypeptide that has about 95.5% or more amino acid identity, about 97% or more amino acid identity, about 98% or

more amino acid identity, or about 99% or more amino acid identity to SEQ ID NO:376 or an enzymatically active fragment of SEQ ID NO:376.

[0122] In some embodiments, segments of the improved ketoreductase polypeptides can be deleted to generate polypeptide fragments. The term “fragment” as used herein refers to a polypeptide that has an amino-terminal and/or carboxy-terminal deletion, but where the remaining amino acid sequence is identical to the corresponding positions in the sequence. Fragments can be at least 14 amino acids long, at least 20 amino acids long, at least 50 amino acids long or longer, and up to 70%, 80%, 90%, 95%, 98%, and 99% of the full-length naturally-occurring ketoreductase polypeptide of SEQ ID NO:2.

[0123] The improved ketoreductase enzymes may be present within a cell, present in the cellular medium, or prepared in various forms, such as lysates or isolated preparations. As such, in some embodiments, the improved ketoreductase enzyme can be an isolated polypeptide. The term “isolated polypeptide” refers to a polypeptide which is substantially separated from other contaminants that naturally accompany it, *e.g.*, protein, lipids, and polynucleotides. The term embraces polypeptides which have been removed or purified from their naturally-occurring environment or expression system (*e.g.*, host cell or *in vitro* synthesis).

[0124] In some embodiments, the isolated improved ketoreductases polypeptide is a substantially pure polypeptide composition. The term “substantially pure polypeptide” refers to a composition in which the polypeptide species is the predominant species present (*i.e.*, on a molar or weight basis it is more abundant than any other individual macromolecular species in the composition), and is generally a substantially purified composition when the object species comprises at least about 50 percent of the macromolecular species present by mole or % weight. Generally, a substantially pure ketoreductase composition will comprise about 60 % or more, about 70% or more, about 80% or more, about 90% or more, about 95% or more, and about 98% or more of all macromolecular species by mole or % weight present in the composition. In some embodiments, the object species is purified to essential homogeneity (*i.e.*, contaminant species cannot be detected in the composition by conventional detection methods) wherein the composition consists essentially of a single macromolecular species. Solvent species, small molecules (<500 Daltons), and elemental ion species are not considered macromolecular species.

6.3 Polynucleotides Encoding Engineered Ketoreductases

[0125] In another aspect, the present disclosure provides polynucleotides encoding the engineered ketoreductase enzymes. The polynucleotides may be operatively linked to one or more heterologous regulatory sequences that control gene expression to create a recombinant polynucleotide capable of expressing the polypeptide. Expression constructs containing a heterologous polynucleotide encoding the engineered ketoreductase can be introduced into appropriate host cells to express the corresponding ketoreductase polypeptide. The term "heterologous" polynucleotide refers to any polynucleotide that is introduced into a host cell by laboratory techniques, and includes polynucleotides that are removed from a host cell, subjected to laboratory manipulation, and then reintroduced into a host cell.

[0126] Because of the knowledge of the codons corresponding to the various amino acids, availability of a protein sequence provides a description of all the polynucleotides capable of encoding the subject. The degeneracy of the genetic code, where the same amino acids are encoded by alternative or synonymous codons allows an extremely large number of nucleic acids to be made, all of which encode the improved ketoreductase enzymes disclosed herein. Thus, having identified a particular amino acid sequence, those skilled in the art could make any number of different nucleic acids by simply modifying the sequence of one or more codons in a way which does not change the amino acid sequence of the protein. In this regard, the present disclosure specifically contemplates each and every possible variation of polynucleotides that could be made by selecting combinations based on the possible codon choices, and all such variations are to be considered specifically disclosed for any polypeptide disclosed herein, including the amino acid sequences presented in Table 1.

[0127] In some embodiments, the polynucleotides encoding the ketoreductases enzymes may be codon optimized for optimal production from the host organism selected for expression. The term "codon optimized" refers to changes in the codons of the polynucleotide encoding a protein to those preferentially used in a particular organism such that the encoded protein is efficiently expressed in the organism of interest. Although the genetic code is degenerate in that most amino acids are represented by several codons, called "synonyms" or "synonymous" codons, it is well known that codon usage by particular organisms is nonrandom and biased towards particular codon triplets. This codon usage bias may be higher in reference to a given gene, genes of common function or ancestral origin, highly expressed

proteins versus low copy number proteins, and the aggregate protein coding regions of an organism's genome.

[0128] The terms “preferred,” “optimal,” or “high codon usage bias” codons refers interchangeably to codons that are used at higher frequency in the protein coding regions than other codons that code for the same amino acid. The preferred codons may be determined in relation to codon usage in a single gene, a set of genes of common function or origin, highly expressed genes, the codon frequency in the aggregate protein coding regions of the whole organism, codon frequency in the aggregate protein coding regions of related organisms, or combinations thereof. Codons whose frequency increases with the level of gene expression are typically optimal codons for expression.

[0129] A variety of methods are known for determining the codon frequency (*e.g.*, codon usage, relative synonymous codon usage) and codon preference in specific organisms, including multivariate analysis, for example, using cluster analysis or correspondence analysis, and the effective number of codons used in a gene (see GCG CodonPreference, Genetics Computer Group Wisconsin Package; CodonW, John Peden, University of Nottingham; McInerney, J. O, 1998, *Bioinformatics* 14:372-73; Stenico et al., 1994, *Nucleic Acids Res.* 22:2437-46; Wright, F., 1990, *Gene* 87:23-29).

[0130] Codon usage tables are available for a growing list of organisms (see for example, Wada et al., 1992, *Nucleic Acids Res.* 20:2111-2118; Nakamura et al., 2000, *Nucl. Acids Res.* 28:292; Duret, et al., *supra*; Henaut and Danchin, “*Escherichia coli* and *Salmonella*,” 1996, Neidhardt, et al. Eds., ASM Press, Washington D.C., p. 2047-2066. The data source for obtaining codon usage may rely on any available nucleotide sequence capable of coding for a protein. These data sets include nucleic acid sequences actually known to encode expressed proteins (*e.g.*, complete protein coding sequences-CDS), expressed sequence tags (ESTS), or predicted coding regions of genomic sequences (see for example, Mount, D., *Bioinformatics: Sequence and Genome Analysis*, Chapter 8, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y., 2001; Uberbacher, E. C., 1996, *Methods Enzymol.* 266:259-281; Tiwari et al., 1997, *Comput. Appl. Biosci.* 13:263-270).

[0131] In various embodiments, the codons are preferably selected to fit the host cell in which the protein is being produced. For example, preferred codons used in bacteria are used to express the gene in bacteria; preferred codons used in yeast are used for expression in

yeast; and preferred codons used in mammals are used for expression in mammalian cells. By way of example, the polynucleotide of SEQ ID NO: 1 has been codon optimized for expression in *E. coli*, but otherwise encodes the naturally occurring ketoreductase of *Saccharomyces cerevisiae*.

[0132] In certain embodiments, all codons need not be replaced to optimize the codon usage of the ketoreductases since the natural sequence will comprise preferred codons and because use of preferred codons may not be required for all amino acid residues. Consequently, codon optimized polynucleotides encoding the ketoreductase enzymes may contain preferred codons at about 40%, 50%, 60%, 70%, 80%, or greater than 90% of codon positions of the full length coding region.

[0133] In the embodiments, the polynucleotides encoding the engineered ketoreductases are derived from *Saccharomyces cerevisiae ydl* gene. In some embodiments, the polynucleotides encoding the engineered ketoreductases are selected from SEQ ID NOS: 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197, 199, 201, 203, 205, 207, 209, 211, 213, 215, 217, 219, 221, 223, 225, 227, 229, 231, 233, 235, 237, 239, 241, 243, 245, 247, 249, 251, 253, 255, 257, 259, 261, 263, 265, 267, 269, 271, 273, 275, 277, 279, 281, 283, 285, 287, 289, 291, 293, 295, 297, 299, 301, 303, 305, 307, 309, 311, 313, 315, 317, 319, 321, 323, 325, 327, 329, 331, 333, 335, 337, 339, 341, 343, 345, 347, 349, 351, 353, 355, 357, 359, 361, 363, and 365.

[0134] These polynucleotides encode the corresponding polypeptides represented by the amino acid sequences listed in Table 1, which were derived by subjecting the *E. coli* codon optimized *Saccharomyces ydl* gene to directed gene evolution techniques described herein.

[0135] In other embodiments, the polynucleotides comprise polynucleotides that have about 80% or more sequence identity, about 85% or more sequence identity, about 90% or more sequence identity, about 95% or more sequence identity, about 98% or more sequence identity, or 99% or more sequence identity at the nucleotide level to a reference polynucleotide encoding an engineered ketoreductase with improved enzymatic properties or a fragment of an engineered ketoreductase with improved properties. In some embodiments,

the reference polynucleotide is selected from polynucleotide sequences represented by SED ID NOS: 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197, 199, 201, 203, 205, 207, 209, 211, 213, 215, 217, 219, 221, 223, 225, 227, 229, 231, 233, 235, 237, 239, 241, 243, 245, 247, 249, 251, 253, 255, 257, 259, 261, 263, 265, 267, 269, 271, 273, 275, 277, 279, 281, 283, 285, 287, 289, 291, 293, 295, 297, 299, 301, 303, 305, 307, 309, 311, 313, 315, 317, 319, 321, 323, 325, 327, 329, 331, 333, 335, 337, 339, 341, 343, 345, 347, 349, 351, 353, 355, 357, 359, 361, 363, and 365.

[0136] In some embodiments, the polynucleotide encodes an enzymatically active ketoreductase and hybridizes under defined conditions, such as moderately stringent or highly stringent conditions, to the complement of a sequence encoding an engineered ketoreductase enzyme of the present disclosure. The phrase “stringent hybridization” is used herein to refer to conditions under which nucleic acid hybrids are stable. As known to those of skill in the art, the stability of hybrids is reflected in the melting temperature (T_m) of the hybrids. In general, the stability of a hybrid is a function of ion strength, temperature, G/C content, and the presence of chaotropic agents. The T_m values for polynucleotides can be calculated using known methods for predicting melting temperatures (see, e.g., Baldino et al., *Methods Enzymology* 168:761-777; Bolton et al., 1962, *Proc. Natl. Acad. Sci. USA* 48:1390; Bresslauer et al., 1986, *Proc. Natl. Acad. Sci USA* 83:8893-8897; Freier et al., 1986, *Proc. Natl. Acad. Sci USA* 83:9373-9377; Kierzek et al., *Biochemistry* 25:7840-7846; Rychlik et al., 1990, *Nucleic Acids Res* 18:6409-6412 (erratum, 1991, *Nucleic Acids Res* 19:698); Sambrook et al., *supra*); Suggs et al., 1981, In *Developmental Biology Using Purified Genes* (Brown et al., eds.), pp. 683-693, Academic Press; and Wetmur, 1991, *Crit Rev Biochem Mol Biol* 26:227-259. All publications incorporate herein by reference).

[0137] Generally, hybridization reactions are performed under conditions of lower stringency, followed by washes of varying but higher stringency. Typically, reference to “hybridization stringency” relates to such washing conditions. The term “moderately stringent hybridization” refers to conditions that permit target-DNA to bind a complementary nucleic acid that has about 60% identity, preferably about 75% identity, about 85% identity to

the target DNA; with greater than about 90% identity to target-polynucleotide. Exemplary moderately stringent conditions are conditions equivalent to hybridization in 50% formamide, 5× Denhart's solution, 5×SSPE, 0.2% SDS at 42°C., followed by washing in 0.2×SSPE, 0.2% SDS, at 42°C.

[0138] The term “high stringency hybridization” refers generally to conditions that are about 10°C or less from the thermal melting temperature T_m as determined under the solution condition for a defined polynucleotide sequence. In some embodiments, a high stringency condition refers to conditions that permit hybridization of only those nucleic acid sequences that form stable hybrids in 0.018M NaCl at 65°C. (*i.e.*, if a hybrid is not stable in 0.018M NaCl at 65°C, it will not be stable under high stringency conditions, as contemplated herein). High stringency conditions can be provided, for example, by hybridization in conditions equivalent to 50% formamide, 5× Denhart's solution, 5×SSPE, 0.2% SDS at 42°C, followed by washing in 0.1×SSPE, and 0.1% SDS at 65°C. Other high stringency hybridization conditions, as well as moderately stringent conditions, are described in the references cited above.

[0139] An isolated polynucleotide encoding an improved ketoreductase polypeptide may be manipulated in a variety of ways to provide for expression of the polypeptide. Manipulation of the isolated polynucleotide prior to its insertion into a vector may be desirable or necessary depending on the expression vector. The techniques for modifying polynucleotides and nucleic acid sequences utilizing recombinant DNA methods are well known in the art. Guidance is provided in Sambrook et al., 2001, *Molecular Cloning: A Laboratory Manual*, 3rd Ed., Cold Spring Harbor Laboratory Press; and *Current Protocols in Molecular Biology*, Ausubel, F. ed., Greene Pub. Associates, 1998, updates to 2006.

[0140] The term “control sequence” is defined herein to include all components, which are necessary or advantageous for the expression of a polypeptide of the present disclosure. Each control sequence may be native or foreign to the nucleic acid sequence encoding the polypeptide. Such control sequences include, but are not limited to, a leader, polyadenylation sequence, propeptide sequence, promoter, signal peptide sequence, and transcription terminator. At a minimum, the control sequences include a promoter, and transcriptional and translational stop signals. The control sequences may be provided with linkers for the purpose of introducing specific restriction sites facilitating ligation of the control sequences with the coding region of the nucleic acid sequence encoding a polypeptide.

[0141] The term "operably linked" is defined herein as a configuration in which a control sequence is appropriately placed at a position relative to the coding sequence of the DNA sequence such that the control sequence directs the expression of a polynucleotide and/or polypeptide.

[0142] The control sequence may be an appropriate promoter sequence. The "promoter sequence" is a nucleic acid sequence that is recognized by a host cell for expression of the coding region. The promoter sequence contains transcriptional control sequences, which mediate the expression of the polypeptide. The promoter may be any nucleic acid sequence which shows transcriptional activity in the host cell of choice including mutant, truncated, and hybrid promoters, and may be obtained from genes encoding extracellular or intracellular polypeptides either homologous or heterologous to the host cell.

[0143] For bacterial host cells, suitable promoters for directing transcription of the nucleic acid constructs of the present disclosure, include the promoters obtained from the *E. coli* lac operon, *Streptomyces coelicolor* agarase gene (dagA), *Bacillus subtilis* levansucrase gene (sacB), *Bacillus licheniformis* alpha-amylase gene (amyL), *Bacillus stearothermophilus* maltogenic amylase gene (amyM), *Bacillus amyloliquefaciens* alpha-amylase gene (amyQ), *Bacillus licheniformis* penicillinase gene (penP), *Bacillus subtilis* xylA and xylB genes, and prokaryotic beta-lactamase gene (Villa-Kamaroff et al., 1978, *Proc. Natl Acad. Sci. USA* 75: 3727-3731), as well as the *tac* promoter (DeBoer et al., 1983, *Proc. Natl Acad. Sci. USA* 80: 21-25). Further promoters are described in "Useful proteins from recombinant bacteria" in *Scientific American*, 1980, 242:74-94; and in Sambrook et al., *supra*.

[0144] For filamentous fungal host cells, suitable promoters for directing the transcription of the nucleic acid constructs of the present disclosure include promoters obtained from the genes for *Aspergillus oryzae* TKA amylase, *Rhizomucor miehei* aspartic proteinase, *Aspergillus niger* neutral alpha-amylase, *Aspergillus niger* acid stable alpha-amylase, *Aspergillus niger* or *Aspergillus awamori* glucoamylase (glaA), *Rhizomucor miehei* lipase, *Aspergillus oryzae* alkaline protease, *Aspergillus oryzae* triose phosphate isomerase, *Aspergillus nidulans* acetamidase, and *Fusarium oxysporum* trypsin-like protease (WO 96/00787), as well as the NA2-tpi promoter (a hybrid of the promoters from the genes for *Aspergillus niger* neutral alpha-amylase and *Aspergillus oryzae* triose phosphate isomerase), and mutant, truncated, and hybrid promoters thereof.

[0145] In a yeast host, useful promoters can be from the genes for *Saccharomyces cerevisiae* enolase (ENO-1), *Saccharomyces cerevisiae* galactokinase (GAL1), *Saccharomyces cerevisiae* alcohol dehydrogenase/glyceraldehyde-3-phosphate dehydrogenase (ADH2/GAP), and *Saccharomyces cerevisiae* 3-phosphoglycerate kinase. Other useful promoters for yeast host cells are described by Romanos et al., 1992, *Yeast* 8:423-488.

[0146] The control sequence may also be a suitable transcription terminator sequence, a sequence recognized by a host cell to terminate transcription. The terminator sequence is operably linked to the 3' terminus of the nucleic acid sequence encoding the polypeptide. Any terminator which is functional in the host cell of choice may be used in the present invention.

[0147] For example, exemplary transcription terminators for filamentous fungal host cells can be obtained from the genes for *Aspergillus oryzae* TAKA amylase, *Aspergillus niger* glucoamylase, *Aspergillus nidulans* anthranilate synthase, *Aspergillus niger* alpha-glucosidase, and *Fusarium oxysporum* trypsin-like protease.

[0148] Exemplary terminators for yeast host cells can be obtained from the genes for *Saccharomyces cerevisiae* enolase, *Saccharomyces cerevisiae* cytochrome C (CYC1), and *Saccharomyces cerevisiae* glyceraldehyde-3-phosphate dehydrogenase. Other useful terminators for yeast host cells are described by Romanos et al., 1992, *supra*.

[0149] The control sequence may also be a suitable leader sequence, a nontranslated region of an mRNA that is important for translation by the host cell. The leader sequence is operably linked to the 5' terminus of the nucleic acid sequence encoding the polypeptide. Any leader sequence that is functional in the host cell of choice may be used. Exemplary leaders for filamentous fungal host cells are obtained from the genes for *Aspergillus oryzae* TAKA amylase and *Aspergillus nidulans* triose phosphate isomerase. Suitable leaders for yeast host cells are obtained from the genes for *Saccharomyces cerevisiae* enolase (ENO-1), *Saccharomyces cerevisiae* 3-phosphoglycerate kinase, *Saccharomyces cerevisiae* alpha-factor, and *Saccharomyces cerevisiae* alcohol dehydrogenase/glyceraldehyde-3-phosphate dehydrogenase (ADH2/GAP).

[0150] The control sequence may also be a polyadenylation sequence, a sequence operably linked to the 3' terminus of the nucleic acid sequence and which, when transcribed, is recognized by the host cell as a signal to add polyadenosine residues to transcribed mRNA. Any polyadenylation sequence which is functional in the host cell of choice may be used in

the present invention. Exemplary polyadenylation sequences for filamentous fungal host cells can be from the genes for *Aspergillus oryzae* TAKA amylase, *Aspergillus niger* glucoamylase, *Aspergillus nidulans* anthranilate synthase, *Fusarium oxysporum* trypsin-like protease, and *Aspergillus niger* alpha-glucosidase. Useful polyadenylation sequences for yeast host cells are described by Guo and Sherman, 1995, *Mol Cell Bio* 15:5983-5990.

[0151] The control sequence may also be a signal peptide coding region that codes for an amino acid sequence linked to the amino terminus of a polypeptide and directs the encoded polypeptide into the cell's secretory pathway. The 5' end of the coding sequence of the nucleic acid sequence may inherently contain a signal peptide coding region naturally linked in translation reading frame with the segment of the coding region that encodes the secreted polypeptide. Alternatively, the 5' end of the coding sequence may contain a signal peptide coding region that is foreign to the coding sequence. The foreign signal peptide coding region may be required where the coding sequence does not naturally contain a signal peptide coding region.

[0152] Alternatively, the foreign signal peptide coding region may simply replace the natural signal peptide coding region in order to enhance secretion of the polypeptide. However, any signal peptide coding region which directs the expressed polypeptide into the secretory pathway of a host cell of choice may be used in the present invention.

[0153] Effective signal peptide coding regions for bacterial host cells are the signal peptide coding regions obtained from the genes for *Bacillus* NCIB 11837 maltogenic amylase, *Bacillus stearothermophilus* alpha-amylase, *Bacillus licheniformis* subtilisin, *Bacillus licheniformis* beta-lactamase, *Bacillus stearothermophilus* neutral proteases (nprT, nprS, nprM), and *Bacillus subtilis* prsA. Further signal peptides are described by Simonen and Palva, 1993, *Microbiol Rev* 57: 109-137.

[0154] Effective signal peptide coding regions for filamentous fungal host cells can be the signal peptide coding regions obtained from the genes for *Aspergillus oryzae* TAKA amylase, *Aspergillus niger* neutral amylase, *Aspergillus niger* glucoamylase, *Rhizomucor miehei* aspartic proteinase, *Humicola insolens* cellulase, and *Humicola lanuginosa* lipase.

[0155] Useful signal peptides for yeast host cells can be from the genes for *Saccharomyces cerevisiae* alpha-factor and *Saccharomyces cerevisiae* invertase. Other useful signal peptide coding regions are described by Romanos et al., 1992, *supra*.

[0156] The control sequence may also be a propeptide coding region that codes for an amino acid sequence positioned at the amino terminus of a polypeptide. The resultant polypeptide is known as a proenzyme or propolypeptide (or a zymogen in some cases). A propolypeptide is generally inactive and can be converted to a mature active polypeptide by catalytic or autocatalytic cleavage of the propeptide from the propolypeptide. The propeptide coding region may be obtained from the genes for *Bacillus subtilis* alkaline protease (aprE), *Bacillus subtilis* neutral protease (nprT), *Saccharomyces cerevisiae* alpha-factor, *Rhizomucor miehei* aspartic proteinase, and *Myceliophthora thermophila* lactase (WO 95/33836).

[0157] Where both signal peptide and propeptide regions are present at the amino terminus of a polypeptide, the propeptide region is positioned next to the amino terminus of a polypeptide and the signal peptide region is positioned next to the amino terminus of the propeptide region.

[0158] It may also be desirable to add regulatory sequences, which allow the regulation of the expression of the polypeptide relative to the growth of the host cell. Examples of regulatory systems are those which cause the expression of the gene to be turned on or off in response to a chemical or physical stimulus, including the presence of a regulatory compound. In prokaryotic host cells, suitable regulatory sequences include the lac, tac, and trp operator systems. In yeast host cells, suitable regulatory systems include, as examples, the ADH2 system or GAL1 system. In filamentous fungi, suitable regulatory sequences include the TAKA alpha-amylase promoter, *Aspergillus niger* glucoamylase promoter, and *Aspergillus oryzae* glucoamylase promoter.

[0159] Other examples of regulatory sequences are those which allow for gene amplification. In eukaryotic systems, these include the dihydrofolate reductase gene, which is amplified in the presence of methotrexate, and the metallothionein genes, which are amplified with heavy metals. In these cases, the nucleic acid sequence encoding the KRED polypeptide of the present invention would be operably linked with the regulatory sequence.

[0160] Thus, in another aspect, the present disclosure is also directed to a recombinant expression vector comprising a polynucleotide encoding an improved ketoreductase polypeptide or a variant thereof, and one or more expression regulating regions such as a promoter and a terminator, a replication origin, etc., depending on the type of hosts into which they are to be introduced. The various nucleic acid and control sequences described

above may be joined together to produce a recombinant expression vector which may include one or more convenient restriction sites to allow for insertion or substitution of the nucleic acid sequence encoding the polypeptide at such sites. Alternatively, the nucleic acid sequence of the present disclosure may be expressed by inserting the nucleic acid sequence or a nucleic acid construct comprising the sequence into an appropriate vector for expression. In creating the expression vector, the coding sequence is located in the vector so that the coding sequence is operably linked with the appropriate control sequences for expression.

[0161] The recombinant expression vector may be any vector (*e.g.*, a plasmid or virus), which can be conveniently subjected to recombinant DNA procedures and can bring about the expression of the polynucleotide sequence. The choice of the vector will typically depend on the compatibility of the vector with the host cell into which the vector is to be introduced. The vectors may be linear or closed circular plasmids.

[0162] The expression vector may be an autonomously replicating vector, *i.e.*, a vector that exists as an extrachromosomal entity, the replication of which is independent of chromosomal replication, *e.g.*, a plasmid, an extrachromosomal element, a minichromosome, or an artificial chromosome. The vector may contain any means for assuring self-replication. Alternatively, the vector may be one which, when introduced into the host cell, is integrated into the genome and replicated together with the chromosome(s) into which it has been integrated. Furthermore, a single vector or plasmid or two or more vectors or plasmids which together contain the total DNA to be introduced into the genome of the host cell, or a transposon may be used.

[0163] The expression vector of the present invention preferably contains one or more selectable markers, which permit easy selection of transformed cells. A selectable marker is a gene the product of which provides for biocide or viral resistance, resistance to heavy metals, prototrophy to auxotrophs, and the like. Examples of bacterial selectable markers are the *dal* genes from *Bacillus subtilis* or *Bacillus licheniformis*, or markers, which confer antibiotic resistance such as ampicillin, kanamycin, chloramphenicol (Example 1) or tetracycline resistance. Suitable markers for yeast host cells are ADE2, HIS3, LEU2, LYS2, MET3, TRP1, and URA3.

[0164] Selectable markers for use in a filamentous fungal host cell include, but are not limited to, *amdS* (acetamidase), *argB* (ornithine carbamoyltransferase), *bar* (phosphinothricin

acetyltransferase), hph (hygromycin phosphotransferase), niaD (nitrate reductase), pyrG (orotidine-5'-phosphate decarboxylase), sC (sulfate adenylyltransferase), and trpC (anthranilate synthase), as well as equivalents thereof. Embodiments for use in an *Aspergillus* cell include the amdS and pyrG genes of *Aspergillus nidulans* or *Aspergillus oryzae* and the bar gene of *Streptomyces hygroscopicus*.

[0165] The expression vectors of the present invention preferably contain an element(s) that permits integration of the vector into the host cell's genome or autonomous replication of the vector in the cell independent of the genome. For integration into the host cell genome, the vector may rely on the nucleic acid sequence encoding the polypeptide or any other element of the vector for integration of the vector into the genome by homologous or nonhomologous recombination.

[0166] Alternatively, the expression vector may contain additional nucleic acid sequences for directing integration by homologous recombination into the genome of the host cell. The additional nucleic acid sequences enable the vector to be integrated into the host cell genome at a precise location(s) in the chromosome(s). To increase the likelihood of integration at a precise location, the integrational elements should preferably contain a sufficient number of nucleic acids, such as 100 to 10,000 base pairs, preferably 400 to 10,000 base pairs, and most preferably 800 to 10,000 base pairs, which are highly homologous with the corresponding target sequence to enhance the probability of homologous recombination. The integrational elements may be any sequence that is homologous with the target sequence in the genome of the host cell. Furthermore, the integrational elements may be non-encoding or encoding nucleic acid sequences. On the other hand, the vector may be integrated into the genome of the host cell by non-homologous recombination.

[0167] For autonomous replication, the vector may further comprise an origin of replication enabling the vector to replicate autonomously in the host cell in question. Examples of bacterial origins of replication are P15A ori (as shown in the plasmid of FIG. 5) or the origins of replication of plasmids pBR322, pUC19, pACYC177 (which plasmid has the P15A ori), or pACYC184 permitting replication in *E. coli*, and pUB110, pE194, pTA1060, or pAM β 1 permitting replication in *Bacillus*. Examples of origins of replication for use in a yeast host cell are the 2 micron origin of replication, ARS1, ARS4, the combination of ARS1 and CEN3, and the combination of ARS4 and CEN6. The origin of replication may be one

having a mutation which makes it's functioning temperature-sensitive in the host cell (see, *e.g.*, Ehrlich, 1978, *Proc Natl Acad Sci. USA* 75:1433).

[0168] More than one copy of a nucleic acid sequence of the present invention may be inserted into the host cell to increase production of the gene product. An increase in the copy number of the nucleic acid sequence can be obtained by integrating at least one additional copy of the sequence into the host cell genome or by including an amplifiable selectable marker gene with the nucleic acid sequence where cells containing amplified copies of the selectable marker gene, and thereby additional copies of the nucleic acid sequence, can be selected for by cultivating the cells in the presence of the appropriate selectable agent.

[0169] Many of the expression vectors for use in the present invention are commercially available. Suitable commercial expression vectors include p3xFLAGTMTM expression vectors from Sigma-Aldrich Chemicals, St. Louis MO., which includes a CMV promoter and hGH polyadenylation site for expression in mammalian host cells and a pBR322 origin of replication and ampicillin resistance markers for amplification in *E. coli*. Other suitable expression vectors are pBluescriptII SK(-) and pBK-CMV, which are commercially available from Stratagene, LaJolla CA, and plasmids which are derived from pBR322 (Gibco BRL), pUC (Gibco BRL), pREP4, pCEP4 (Invitrogen) or pPoly (Lathe et al., 1987, *Gene* 57:193-201).

6.4 Host Cells for Expression of Ketoreductase Polypeptides

[0170] In another aspect, the present disclosure provides a host cell comprising a polynucleotide encoding an improved ketoreductase polypeptide of the present disclosure, the polynucleotide being operatively linked to one or more control sequences for expression of the ketoreductase enzyme in the host cell. Host cells for use in expressing the KRED polypeptides encoded by the expression vectors of the present invention are well known in the art and include but are not limited to, bacterial cells, such as *E. coli*, *Streptomyces* and *Salmonella typhimurium* cells; fungal cells, such as yeast cells (*e.g.*, *Saccharomyces cerevisiae* or *Pichia pastoris* (ATCC Accession No. 201178)); insect cells such as *Drosophila* S2 and *Spodoptera Sf9* cells; animal cells such as CHO, COS, BHK, 293, and Bowes melanoma cells; and plant cells. Appropriate culture mediums and growth conditions for the above-described host cells are well known in the art.

[0171] Polynucleotides for expression of the ketoreductase may be introduced into cells by various methods known in the art. Techniques include among others, electroporation, biolistic particle bombardment, liposome mediated transfection, calcium chloride transfection, and protoplast fusion. Various methods for introducing polynucleotides into cells will be apparent to the skilled artisan.

[0172] An exemplary host cell is *Escherichia coli* W3110 as described in Example 1. The expression vector was created by operatively linking a polynucleotide encoding an improved ketoreductase into the plasmid pCK110900 operatively linked to the *lac* promoter under control of the *lacI* repressor. The expression vector also contained the P15a origin of replication and the chloramphenicol resistance gene. Cells containing the subject polynucleotide in *Escherichia coli* W3110 were isolated by subjecting the cells to chloramphenicol selection.

6.5 Methods of Generating Engineered Ketoreductase Polypeptides.

[0173] To make the improved KRED polynucleotides and polypeptides of the present disclosure, the naturally-occurring ketoreductase enzyme that catalyzes the reduction reaction is obtained from *Saccharomyces cerevisiae*. In some embodiments, the parent polynucleotide sequence is codon optimized to enhance expression of the ketoreductase in a specified host cell. As an illustration, the parental polynucleotide sequence encoding the wild-type KRED polypeptide (*ydI*) of *Saccharomyces cerevisiae* was constructed from oligonucleotides composed of 42 nucleotides based upon the known polypeptide sequence of *Saccharomyces cerevisiae* KRED sequence (*ydI*) available in Genbank database (NP_010159; GI:6320079). The parental polynucleotide sequence, designated as SEQ ID NO: 1, was codon optimized for expression in *E. coli* and the codon-optimized polynucleotide cloned into the *SfiI* cloning sites of the expression vector, pCK110900 (depicted in FIG. 5), placing the expression of the ketoreductase gene under the control of the *lac* promoter and *lacI* repressor gene. The expression vector also contained the P15A origin of replication and the chloramphenicol resistance gene. Clones expressing the active ketoreductase in *E. coli* W3110 were identified and the genes sequenced to confirm their identity. The sequence designated *ydIC* (SEQ ID NO: 1) was the parent sequence utilized as the starting point for all experiments and library construction of engineered ketoreductases evolved from the *S. cerevisiae* ketoreductase.

[0174] The engineered ketoreductases can be obtained by subjecting the polynucleotide encoding the naturally occurring ketoreductase to mutagenesis and/or directed evolution methods. An exemplary directed evolution technique is mutagenesis and/or DNA shuffling as described in Stemmer, 1994, *Proc Natl Acad Sci USA* 91:10747-10751; WO 95/22625; WO 97/0078; WO 97/35966; WO 98/27230; WO 00/42651; WO 01/75767 and U.S. Pat. 6,537,746. Other directed evolution procedures that can be used include, among others, staggered extension process (StEP), in vitro recombination (Zhao et al., 1998, *Nat. Biotechnol.* 16:258–261), mutagenic PCR (Caldwell et al., 1994, *PCR Methods Appl.* 3:S136-S140), and cassette mutagenesis (Black et al., 1996, *Proc Natl Acad Sci USA* 93:3525-3529).

[0175] The clones obtained following mutagenesis treatment are screened for engineered ketoreductases having a desired improved enzyme property. Measuring enzyme activity from the expression libraries can be performed using the standard biochemistry technique of monitoring the rate of decrease (via a decrease in absorbance or fluorescence) of NADH or NADPH concentration, as it is converted into NAD^+ or NADP^+ . In this reaction, the NADH or NADPH is consumed (oxidized) by the ketoreductase as the ketoreductase reduces a ketone substrate to the corresponding hydroxyl group. The rate of decrease of NADH or NADPH concentration, as measured by the decrease in absorbance or fluorescence, per unit time indicates the relative (enzymatic) activity of the KRED polypeptide in a fixed amount of the lysate (or a lyophilized powder made therefrom). Example 11 discloses an exemplary biochemical assay for ketoreductase activity. Where the improved enzyme property desired is thermal stability, enzyme activity may be measured after subjecting the enzyme preparations to a defined temperature and measuring the amount of enzyme activity remaining after heat treatments, such as in Example 12. Clones containing a polynucleotide encoding a ketoreductase are then isolated, sequenced to identify the nucleotide sequence changes (if any), and used to express the enzyme in a host cell.

[0176] Where the sequence of the engineered polypeptide is known, the polynucleotides encoding the enzyme can be prepared by standard solid-phase methods, according to known synthetic methods. In some embodiments, fragments of up to about 100 bases can be individually synthesized, then joined (e.g., by enzymatic or chemical ligation methods, or polymerase mediated methods) to form any desired continuous sequence. For example, polynucleotides and oligonucleotides of the invention can be prepared by chemical synthesis using, e.g., the classical phosphoramidite method described by Beaucage et al., 1981, *Tet Lett*

22:1859-69, or the method described by Matthes et al., 1984, *EMBO J.* 3:801-05, *e.g.*, as it is typically practiced in automated synthetic methods. According to the phosphoramidite method, oligonucleotides are synthesized, *e.g.*, in an automatic DNA synthesizer, purified, annealed, ligated and cloned in appropriate vectors. In addition, essentially any nucleic acid can be obtained from any of a variety of commercial sources, such as The Midland Certified Reagent Company, Midland, TX, The Great American Gene Company, Ramona, CA, ExpressGen Inc. Chicago, IL, Operon Technologies Inc., Alameda, CA, and many others.

[0177] Engineered ketoreductase enzymes expressed in a host cell can be recovered from the cells and or the culture medium using any one or more of the well known techniques for protein purification, including, among others, lysozyme treatment, sonication, filtration, salting-out, ultra-centrifugation, and chromatography. Suitable solutions for lysing and the high efficiency extraction of proteins from bacteria, such as *E. coli*, are commercially available under the trade name CelLytic BTM from Sigma-Aldrich of St. Louis MO.

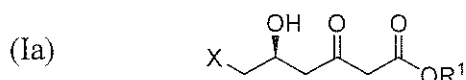
[0178] Chromatographic techniques for isolation of the ketoreductase polypeptide include, among others, reverse phase chromatography high performance liquid chromatography, ion exchange chromatography, gel electrophoresis, and affinity chromatography. Conditions for purifying a particular enzyme will depend, in part, on factors such as net charge, hydrophobicity, hydrophilicity, molecular weight, molecular shape, etc., and will be apparent to those having skill in the art.

[0179] In some embodiments, affinity techniques may be used to isolate the improved ketoreductase enzymes. For affinity chromatography purification, any antibody which specifically binds the ketoreductase polypeptide may be used. For the production of antibodies, various host animals, including but not limited to rabbits, mice, rats, etc., may be immunized by injection with a compound. The compound may be attached to a suitable carrier, such as BSA, by means of a side chain functional group or linkers attached to a side chain functional group. Various adjuvants may be used to increase the immunological response, depending on the host species, including but not limited to Freund's (complete and incomplete), mineral gels such as aluminum hydroxide, surface active substances such as lysolecithin, pluronic polyols, polyanions, peptides, oil emulsions, keyhole limpet hemocyanin, dinitrophenol, and potentially useful human adjuvants such as BCG (bacilli Calmette Guerin) and *Corynebacterium parvum*.

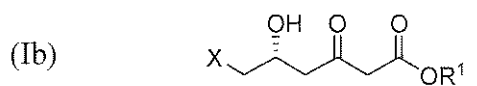
[0180] An exemplary process for recovering the KRED polypeptides from cell lysate for applications in a chemical process is disclosed in Example 2.

11.4 Methods of Using the Engineered Ketoreductase Enzymes and Compounds Prepared Therewith

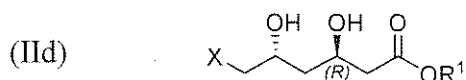
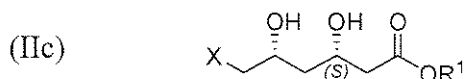
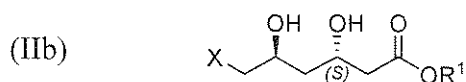
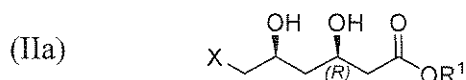
[0181] The engineered ketoreductase enzymes described herein catalyze the reduction of 5-hydroxy-3-oxohexanoate enantiomers according to structural formula (Ia):



wherein X and R¹ are as previously defined, to yield the corresponding *syn* 3,5-dihydroxyhexanoate ester compound. As will be recognized by skilled artisans, the carbon at the 5-position of the compound of structural formula (I) is chiral. As a consequence, the compound can exist in two different enantiomeric forms: the enantiomer of structural formula (Ia) above and the enantiomer of structural formula (Ib):



[0182] Skilled artisans will also recognize that when the oxo group at the 3-position is reduced to a hydroxy group, the carbon atom of the 3-position in the resultant 3,5-dihydroxy ester is also chiral. Thus, each of the enantiomers of structural formulae (Ia) and (Ib) can yield two different reduction products: a *syn* diastereomer and *anti* diastereomer. The *syn* and *anti* diastereomers produced by reduction of enantiomer (Ia) are illustrated below as compounds (IIa) and (IIb), respectively, and those produced by reduction of enantiomer (Ib) are illustrated as compounds (IIc) and (IId), respectively:



[0183] The absolute configurations about the 3-carbon are illustrated in the above structural diagrams. The *R*- or *S*- designations for the absolute configurations about the 5-carbon will depend upon the identity of the X. When X is cyano, the 5-carbon is designated *R*- in structures (Ia), (IIa) and (IIb) and designated *S*- in structures (Ib), (IIc) and (IIId). When X is halo or hydroxy, the 5-carbon is designated *S*- in structures (Ia), (IIa) and (IIb) and designated *R*- in structures (Ib), (IIc) and (IIId). This is due to the conventions for designating *R* or *S*, which reverse between X = cyano and X = halo or hydroxyl.

[0184] In some embodiments, the substrate (Ia) is of high enantiopurity, substantially free of (Ib).

[0185] In some embodiments, the reduction reaction is also highly diastereoselective, producing the *syn* diastereomer of structural formula (IIa) in $\geq 99.95\%$ diastereomeric purity, *i.e.* $\leq 0.05\%$ of the *anti* diastereomer of structural formula (IIb) (*i.e.*, $\geq 99.9\%$ diastereomeric excess). Many embodiments of the engineered ketoreductases described herein exhibit even higher stereoselectivities. For example, in reactions of *t*-butyl 6-cyano-(5*R*)-hydroxy-3-oxohexanoate (structural formula (Ia), X=CN, R¹=*t*-butyl) carried out with the engineered ketoreductases referenced in Table 2, diastereoselectivities for 6-cyano-(3*R*,5*R*)-dihydroxyhexanoate (structural formula (IIa), X=CN, R¹=*t*-butyl) of $\geq 99.99\%$ have been observed. Thus, diastereoselective reductions ranging from $\geq 99.9\%$, $\geq 99.91\%$, $\geq 99.92\%$, $\geq 99.93\%$, $\geq 99.94\%$, $\geq 99.95\%$, $\geq 99.96\%$, $\geq 99.97\%$, $\geq 99.98\%$ and even $\geq 99.99\%$ diastereoselectivity can be readily achieved with the engineered ketoreductase enzymes described herein.

[0186] The high degree of diastereoselectivity observed in reduction reactions catalyzed by the engineered ketoreductases described herein enables the ability to produce preparations of the *syn* 3,5-dihydroxyhexanoate ester of structural formula (IIa) that are substantially diastereomerically pure, *i.e.*, that are substantially free of all other diastereomers, without having to perform chiral isolation or separation steps. Because the reaction can be performed in high yield, utilizing highly enantiopure 5-hydroxy-3-oxohexanoate ester (Ia) starting materials, the present disclosure enables the preparation of *syn* 3,5-dihydroxyhexanoate esters of structural formula (IIa) that are substantially diastereomerically pure with minimal or no purification. In contrast to the present disclosure, prior reduction methods (*e.g.*, U.S. Patent 6,596,879) produced 3-4% (IIb) (X=CN, R¹=*t*-butyl), which is an oil, and which was then reacted to form ((*t*-butyl 6-cyanomethyl-2,2-dimethyl-1,3-dioxane-4-acetate) (X=CN, R¹=*t*-

butyl, R³,R⁴= methyl), a crystalline compound. In the prior known methods, the purity was improved by crystallization to lower the (IIb) content, which resulted in yield losses of (IIa).

[0187] The high degree of diastereomeric purity of the reduction products obtained with the engineered ketoreductase enzymes described herein is illustrated in FIG. 6, which compares the LC/MS/MS chromatogram of *tert*-butyl 6-cyanoethyl-(3R,5R)-dihydroxyhexanoate (structural formula (IIa), X=CN, R¹=*t*-butyl) prepared from commercially available crystalline *t*-butyl (6R)-cyanomethyl-2,2-dimethyl-1,3-dioxane-(4R)-acetate (structural formula (IVa), X=CN, R¹=*t*-butyl, R³,R⁴= methyl) (Aldrich, St. Louis, MO) with that of crude *tert*-butyl 6-cyano-(3R,5R)-dihydroxyhexanoate oil prepared from *t*-butyl 6-cyano-(5R)-hydroxy-3-oxohexanoate (structural formula (Ia), X=CN, R¹=*t*-butyl) using an engineered ketoreductase enzyme of the present disclosure. As illustrated in FIG. 6, compared to a *tert*-butyl (6R)-cyanoethyl-3,5-dihydroxyhexanoate sample prepared from commercially available crystalline *t*-butyl (6R)-cyanomethyl-2,2-dimethyl-1,3-dioxane-(4R)-acetate containing less than about 0.1% of the undesired (3S,5R) diastereomer (IIb), the crude *tert*-butyl 6-cyano-(3R,5R)-dihydroxyhexanoate oil prepared using the engineered ketoreductase of the disclosure contains no more than possibly 0.005% of the undesired (3S,5R) diastereomer.

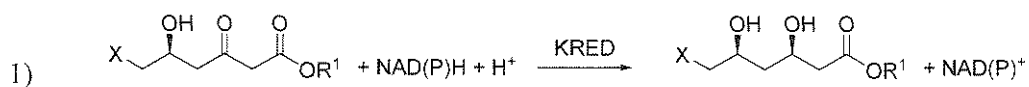
[0188] Similarly striking differences in diastereomeric purity are observed for *t*-butyl (6R)-cyanomethyl-2,2-dimethyl-1,3-dioxane-(4R)-acetate (see Example 23 and FIG. 7). GC/MS chromatograms comparing the stereoisomeric purity of the commercially available crystalline TBIN ((4R, *cis*)-1,1-dimethyl-6-cyanomethyl-2,2-dimethyl-1,3-dioxane-4-acetate)) and crude, extracted, but never crystallized TBIN prepared from crude C7 diol prepared using an engineered ketoreductase enzyme of the present invention are illustrated in FIG. 7. Likewise, the diastereomeric purity of atorvastatin produced from C7 diol prepared using the methods of the present disclosure are greater than what is currently present in commercial preparations (*e.g.*, 0.03% atorvastatin diastereomer present in a Lipitor® pill).

[0189] As used herein, a compound is “enriched” in a particular stereoisomer when that stereoisomer is present in excess over any other stereoisomer present in the compound. A compound that is enriched in a particular stereoisomer will typically comprise at least about 60%, 70%, 80%, 90%, or even more, of the specified stereoisomer. The amount of enrichment of a particular stereoisomer can be confirmed using conventional analytical methods routinely used by those of skill in the art, as will be discussed in more detail, below.

[0190] In some embodiments, the amount of undesired stereoisomers may be less than 10%, for example, less than 9%, less than 8%, less than 7%, less than 6%, less than 5%, less than 4%, less than 3%, less than 2%, less than 1% or even less than 0.9%, 0.8%, 0.7%, 0.6%, 0.5%, 0.4%, 0.2%, or 0.1%. Stereoisomerically enriched compounds that contain at least about 99.5% or more of the desired stereoisomer are referred to herein as “substantially pure” stereoisomers. In some embodiments, compounds that are substantially pure in a specified stereoisomer contain greater than 99.6%, 99.7%, 99.8%, 99.9%, 99.91%, 99.92%, 99.93%, 99.94%, 99.95%, 99.96%, 99.97%, 99.98% or even 99.99% of the particular stereoisomer. Stereoisomerically enriched compounds that contain $\geq 99.99\%$ of the desired stereoisomer are referred to herein as “pure” stereoisomers.

[0191] The stereoisomeric purity of any chiral compound described herein can be determined or confirmed using conventional analytical methods known in the art. Highly sensitive LC/MS and GC/MS methods and for assessing diastereoisomeric purity of the synthetic intermediates described herein are provided in Examples 5-7. A method for determining diastereomeric purity of atorvastatin is given in Ertürk et al., 2003, *J Pharm Biomed Anal.* 33(5):1017-23.

[0192] As is known by those of skill in the art, ketoreductase-catalyzed reduction reactions typically require a cofactor. Reduction reactions catalyzed by the engineered ketoreductase enzymes described herein also typically require a cofactor, although many embodiments of the engineered ketoreductases require far less cofactor than reactions catalyzed with wild-type ketoreductase enzymes. As used herein, the term “cofactor” refers to a non-protein compound that operates in combination with a ketoreductase enzyme. Cofactors suitable for use with the engineered ketoreductase enzymes described herein include, but are not limited to, NADP^+ (nicotinamide adenine dinucleotide phosphate), NADPH (the reduced form of NADP^+), NAD^+ (nicotinamide adenine dinucleotide) and NADH (the reduced form of NAD^+). Equation (1), below, illustrates an embodiment of a ketoreductase (“KRED”)-catalyzed reduction reaction utilizing NADH or NADPH as a cofactor, which are represented as alternatives by the designation NAD(P)H :



[0193] As illustrated, the reduced form of the cofactor is added to the reaction mixture. The reduced NAD(P)H form can be optionally regenerated from the oxidized NAD(P)⁺ form using a cofactor regeneration system.

[0194] The term “cofactor regeneration system” refers to a set of reactants that participate in a reaction that reduces the oxidized form of the cofactor (*e.g.*, NADP⁺ to NADPH).

Cofactors oxidized by the ketoreductase-catalyzed reduction of the 5-hydroxy-3-oxo-hexanoate ester are regenerated in reduced form by the cofactor regeneration system.

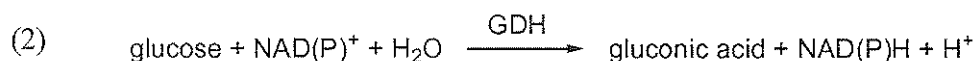
Cofactor regeneration systems comprise a stoichiometric reductant that is a source of reducing hydrogen equivalents and is capable of reducing the oxidized form of the cofactor.

The cofactor regeneration system may further comprise a catalyst, for example an enzyme catalyst, that catalyzes the reduction of the oxidized form of the cofactor by the reductant.

Cofactor regeneration systems to regenerate NADH or NADPH from NAD⁺ or NADP⁺, respectively, are known in the art and may be used in the methods described herein.

[0195] Suitable exemplary cofactor regeneration systems that may be employed include, but are not limited to, glucose and glucose dehydrogenase, formate and formate dehydrogenase, glucose-6-phosphate and glucose-6-phosphate dehydrogenase, a secondary (*e.g.*, isopropanol) alcohol and secondary alcohol dehydrogenase, phosphite and phosphite dehydrogenase, molecular hydrogen and hydrogenase, and the like. These systems may be used in combination with either NADP⁺/NADPH or NAD⁺/NADH as the cofactor. Electrochemical regeneration using hydrogenase may also be used as a cofactor regeneration system. *See, e.g.*, U.S. Pat. Nos. 5,538,867 and 6,495,023, both of which are incorporated herein by reference. Chemical cofactor regeneration systems comprising a metal catalyst and a reducing agent (for example, molecular hydrogen or formate) are also suitable. *See, e.g.*, PCT publication WO 2000/053731, which is incorporated herein by reference.

[0196] The terms “glucose dehydrogenase” and “GDH” are used interchangeably herein to refer to an NAD⁺ or NADP⁺-dependent enzyme that catalyzes the conversion of D-glucose and NAD⁺ or NADP⁺ to gluconic acid and NADH or NADPH, respectively. Equation (2), below, describes the glucose dehydrogenase-catalyzed reduction of NAD⁺ or NADP⁺ by glucose.



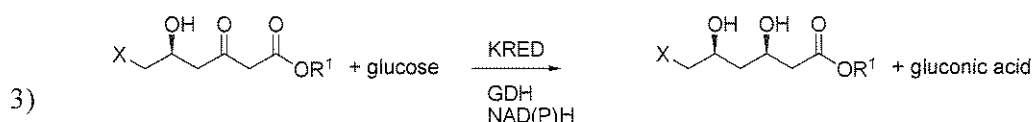
[0197] Glucose dehydrogenases that are suitable for use in the practice of the methods described herein include both naturally occurring glucose dehydrogenases, as well as non-naturally occurring glucose dehydrogenases. Naturally occurring glucose dehydrogenase encoding genes have been reported in the literature. For example, the *Bacillus subtilis* 61297 GDH gene was expressed in *E. coli* and was reported to exhibit the same physicochemical properties as the enzyme produced in its native host (Vasanthan et al., 1983, *Proc. Natl. Acad. Sci. USA* 80:785). The gene sequence of the *B. subtilis* GDH gene, which corresponds to Genbank Acc. No. M12276, was reported by Lampel et al., 1986, *J. Bacteriol.* 166:238-243, and in corrected form by Yamane et al., 1996, *Microbiology* 142:3047-3056 as Genbank Acc. No. D50453. Naturally occurring GDH genes also include those that encode the GDH from *B. cereus* ATCC 14579 (*Nature*, 2003, 423:87-91; Genbank Acc. No. AE017013) and *B. megaterium* (*Eur. J. Biochem.*, 1988, 174:485-490, Genbank Acc. No. X12370; *J. Ferment. Bioeng.*, 1990, 70:363-369, Genbank Acc. No. GI216270). Glucose dehydrogenases from *Bacillus sp.* are provided in PCT publication WO 2005/018579 as SEQ ID NOS: 10 and 12 (encoded by polynucleotide sequences corresponding to SEQ ID NOS: 9 and 11, respectively, of the PCT publication), the disclosure of which is incorporated herein by reference.

[0198] Non-naturally occurring glucose dehydrogenases may be generated using known methods, such as, for example, mutagenesis, directed evolution, and the like. GDH enzymes having suitable activity, whether naturally occurring or non-naturally occurring, may be readily identified using the assay described in Example 4 of PCT publication WO 2005/018579, the disclosure of which is incorporated herein by reference. Exemplary non-naturally occurring glucose dehydrogenases are provided in PCT publication WO 2005/018579 as SEQ ID NOS: 62, 64, 66, 68, 122, 124, and 126. The polynucleotide sequences that encode them are provided in PCT publication WO 2005/018579 as SEQ ID NOS: 61, 63, 65, 67, 121, 123, and 125, respectively. All of these sequences are incorporated herein by reference. Additional non-naturally occurring glucose dehydrogenases that are suitable for use in the ketoreductase-catalyzed reduction reactions disclosed herein are provided in U.S. application publication Nos. 2005/0095619 and 2005/0153417, the disclosures of which are incorporated herein by reference.

[0199] Glucose dehydrogenases employed in the ketoreductase-catalyzed reduction reactions described herein may exhibit an activity of at least about 10 $\mu\text{mol}/\text{min}/\text{mg}$ and sometimes at

least about 10^2 $\mu\text{mol}/\text{min}/\text{mg}$ or about 10^3 $\mu\text{mol}/\text{min}/\text{mg}$, up to about 10^4 $\mu\text{mol}/\text{min}/\text{mg}$ or higher in the assay described in Example 4 of PCT publication WO 2005/018579.

[0200] When glucose and glucose dehydrogenase are employed as the cofactor regeneration system, as the 5-hydroxy-3-oxohexanoate ester substrate is reduced by the engineered ketoreductase and NADH or NADPH, the resulting NAD^+ or NADP^+ is reduced by the coupled oxidation of glucose to gluconic acid by the glucose dehydrogenase. The net reaction is described by equation (3), which is the summation of equations (1) and (2):



[0201] The ketoreductase-catalyzed reduction reactions described herein are generally carried out in a solvent. Suitable solvents include water, organic solvents (*e.g.*, ethyl acetate, butyl acetate, 1-octanol, heptane, octane, methyl t-butyl ether (MTBE), toluene, and the like), ionic liquids (*e.g.*, 1-ethyl 4-methylimidazolium tetrafluoroborate, 1-butyl-3-methylimidazolium tetrafluoroborate, 1-butyl-3-methylimidazolium hexafluorophosphate, and the like). In some embodiments, aqueous solvents, including water and aqueous co-solvent systems, are used.

[0202] Exemplary aqueous co-solvent systems have water and one or more organic solvent. In general, an organic solvent component of an aqueous co-solvent system is selected such that it does not completely inactivate the ketoreductase enzyme. Appropriate co-solvent systems can be readily identified by measuring the enzymatic activity of the specified engineered ketoreductase enzyme with the 5-hydroxy-3-oxohexanoate ester of interest in the candidate solvent system, utilizing an enzyme activity assay, such as those described in the Examples.

[0203] The organic solvent component of an aqueous co-solvent system may be miscible with the aqueous component, providing a single liquid phase, or may be partly miscible or immiscible with the aqueous component, providing two liquid phases. Generally, when an aqueous co-solvent system is employed, it is selected to be biphasic, with water dispersed in an organic solvent, or vice-versa. Generally, when an aqueous co-solvent system is utilized, it is desirable to select an organic solvent that can be readily separated from the aqueous phase. In general, the ratio of water to organic solvent in the co-solvent system is typically in

the range of from about 90:10 to about 10:90 (v/v) organic solvent to water, and between 80:20 and 20:80 (v/v) organic solvent to water. The co-solvent system may be pre-formed prior to addition to the reaction mixture, or it may be formed *in situ* in the reaction vessel.

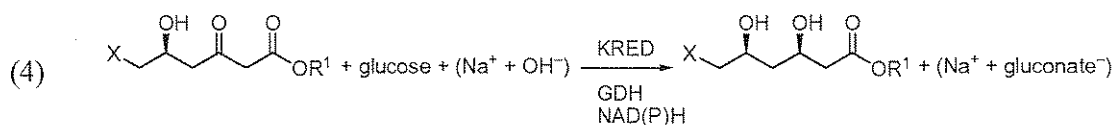
[0204] The aqueous solvent (water or aqueous co-solvent system) may be pH-buffered or unbuffered. The reduction of the 5-hydroxy-3-oxohexanoate ester to the corresponding 3,5-dihydroxyhexanoate ester can be carried out at a pH of about 5 or above. Generally, the reduction is carried out at a pH of about 10 or below, usually in the range of from about 5 to about 10. In some embodiments, the reduction is carried out at a pH of about 9 or below, usually in the range of from about 5 to about 9. In some embodiments, the reduction is carried out at a pH of about 8 or below, often in the range of from about 5 to about 8, and usually in the range of from about 6 to about 8. The reduction may also be carried out at a pH of about 7.8 or below, or 7.5 or below. Alternatively, the reduction may be carried out at a neutral pH, *i.e.*, about 7.

[0205] During the course of the reduction reactions, the pH of the reaction mixture may change. The pH of the reaction mixture may be maintained at a desired pH or within a desired pH range by the addition of an acid or a base during the course of the reaction. Alternatively, the pH may be controlled by using an aqueous solvent that comprises a buffer. Suitable buffers to maintain desired pH ranges are known in the art and include, for example, phosphate buffer, triethanolamine buffer, and the like. Combinations of buffering and acid or base addition may also be used.

[0206] When the glucose/glucose dehydrogenase cofactor regeneration system is employed, the co-production of gluconic acid ($pK_a=3.6$), as represented in equation (3) causes the pH of the reaction mixture to drop if the resulting aqueous gluconic acid is not otherwise neutralized. The pH of the reaction mixture may be maintained at the desired level by standard buffering techniques, wherein the buffer neutralizes the gluconic acid up to the buffering capacity provided, or by the addition of a base concurrent with the course of the conversion. Combinations of buffering and base addition may also be used. Suitable buffers to maintain desired pH ranges are described above. Suitable bases for neutralization of gluconic acid are organic bases, for example amines, alkoxides and the like, and inorganic bases, for example, hydroxide salts (*e.g.*, NaOH), carbonate salts (*e.g.*, K_2CO_3), bicarbonate salts (*e.g.*, $NaHCO_3$), basic phosphate salts (*e.g.*, K_2HPO_4 , Na_3PO_4), and the like. The addition of a base concurrent with the course of the conversion may be done manually while

monitoring the reaction mixture pH or, more conveniently, by using an automatic titrator as a pH stat. A combination of partial buffering capacity and base addition can also be used for process control.

[0207] In such reduction reactions when the pH is maintained by buffering or by addition of a base over the course of the conversion, an aqueous gluconate salt rather than aqueous gluconic acid is the product of the overall process. For example, equation (4) represents the overall process when aqueous sodium hydroxide ($\text{Na}^+ + \text{OH}^-$) is added over the course of the reaction to maintain an initial pH below about 5 or above.



[0208] When base addition is employed to neutralize the gluconic acid released during the ketoreductase-catalyzed reduction reaction, the progress of the conversion may be monitored by the amount of base added to maintain the pH. Typically, bases added to unbuffered or partially buffered reaction mixtures over the course of the reduction are added in aqueous solutions.

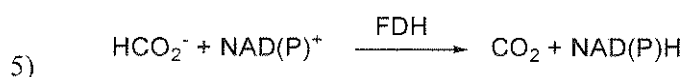
[0209] In some embodiments, when the process is carried out using whole cells of the host organism, the whole cell may natively provide the cofactor. Alternatively or in combination, the cell may natively or recombinantly provide the glucose dehydrogenase.

[0210] The terms “formate dehydrogenase” and “FDH” are used interchangeably herein to refer to an NAD^+ or NADP^+ -dependent enzyme that catalyzes the conversion of formate and NAD^+ or NADP^+ to carbon dioxide and NADH or NADPH, respectively. Formate dehydrogenases that are suitable for use as cofactor regenerating systems in the ketoreductase-catalyzed reduction reactions described herein include both naturally occurring formate dehydrogenases, as well as non-naturally occurring formate dehydrogenases. Formate dehydrogenases include those corresponding to SEQ ID NOS: 70 (*Pseudomonas* sp.) and 72 (*Candida boidinii*) of PCT publication WO 2005/018579, which are encoded by polynucleotide sequences corresponding to SEQ ID NOS: 69 and 71, respectively, of PCT publication 2005/018579, the disclosures of which are incorporated herein by reference. Formate dehydrogenases employed in the methods described herein, whether naturally

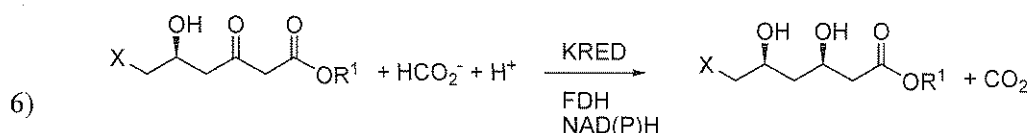
occurring or non-naturally occurring, may exhibit an activity of at least about 1 $\mu\text{mol}/\text{min}/\text{mg}$, sometimes at least about 10 $\mu\text{mol}/\text{min}/\text{mg}$, or at least about 10^2 $\mu\text{mol}/\text{min}/\text{mg}$, up to about 10^3 $\mu\text{mol}/\text{min}/\text{mg}$ or higher, and can be readily screened for activity in the assay described in Example 4 of PCT publication WO 2005/018579.

[0211] As used herein, the term “formate” refers to formate anion (HCO_2^-), formic acid (HCO_2H), and mixtures thereof. Formate may be provided in the form of a salt, typically an alkali or ammonium salt (for example, HCO_2Na , KHCO_2NH_4 , and the like), in the form of formic acid, typically aqueous formic acid, or mixtures thereof. Formic acid is a moderate acid. In aqueous solutions within several pH units of its pK_a ($\text{pK}_a=3.7$ in water) formate is present as both HCO_2^- and HCO_2H in equilibrium concentrations. At pH values above about pH 4, formate is predominantly present as HCO_2^- . When formate is provided as formic acid, the reaction mixture is typically buffered or made less acidic by adding a base to provide the desired pH, typically of about pH 5 or above. Suitable bases for neutralization of formic acid include, but are not limited to, organic bases, for example amines, alkoxides and the like, and inorganic bases, for example, hydroxide salts (*e.g.*, NaOH), carbonate salts (*e.g.*, K_2CO_3), bicarbonate salts (*e.g.*, NaHCO_3), basic phosphate salts (*e.g.*, K_2HPO_4 , Na_3PO_4), and the like.

[0212] For pH values above about pH 5, at which formate is predominantly present as HCO_2^- , equation (5), below, describes the formate dehydrogenase-catalyzed reduction of NAD^+ or NADP^+ by formate.

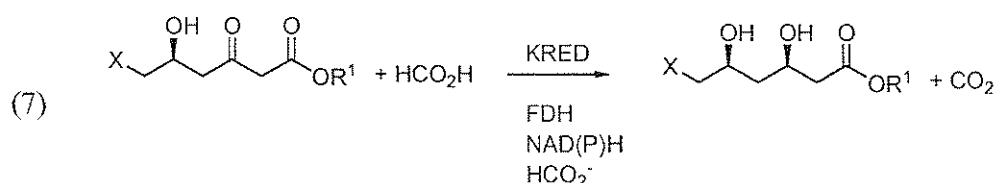


[0213] When formate and formate dehydrogenase are employed as the cofactor regeneration system, the 5-hydroxy-3-oxohexanoate ester is reduced by the ketoreductase and NADH or NADPH , the resulting NAD^+ or NADP^+ is reduced by the coupled oxidation of formate to carbon dioxide by the formate dehydrogenase. An embodiment of the net reaction is described by equation (6), which is the summation of equations (1) and (5):



[0214] Equation (6) shows that when the formate/formate dehydrogenase cofactor regeneration system is employed for the reduction of 5-hydroxy-3-oxohexanoate ester in

aqueous solution at a pH above about pH 5, protons in solution are consumed and the reaction causes the pH of the reaction mixture to rise if it is not otherwise buffered or re-acidified. The pH of the reaction mixture may be maintained at the desired level by standard buffering techniques, wherein the buffer releases protons up to the buffering capacity provided, or by the addition of an acid concurrent with the course of the conversion. Suitable acids to add during the course of the reaction to maintain the pH include organic acids, for example carboxylic acids, sulfonic acids, phosphonic acids, and the like, mineral acids, for example hydrohalic acids (such as hydrochloric acid), sulfuric acid, phosphoric acid, and the like, acidic salts, for example dihydrogenphosphate salts (*e.g.*, KH_2PO_4), bisulfate salts (*e.g.*, NaHSO_4) and the like. Some embodiments utilize formic acid, whereby both the formate concentration and the pH of the solution are maintained. For example, equation (7) represents the overall process when formic acid (HCO_2H) is added over the course of the reaction to maintain an initial pH above about pH 5. While the formate is present predominantly as HCO_2^- in the reaction mixture, the HCO_2^- concentration is maintained while the conversion in net consumes the added formic acid.



[0215] When acid addition is employed to maintain the pH during a reduction reaction using the formate/formate dehydrogenase cofactor regeneration system, the progress of the conversion may be monitored by the amount of acid added to maintain the pH. Typically, acids added to unbuffered or partially buffered reaction mixtures over the course of conversion are added in aqueous solutions.

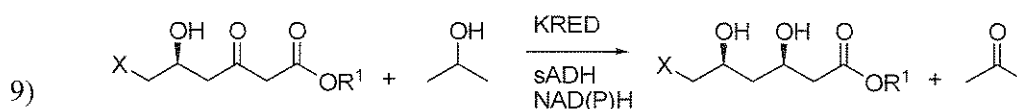
[0216] The terms “secondary alcohol dehydrogenase” and “sADH” are used interchangeably herein to refer to an NAD^+ or NADP^+ -dependent enzyme that catalyzes the conversion of a secondary alcohol and NAD^+ or NADP^+ to a ketone and NADH or NADPH , respectively. Equation (8), below, describes the reduction of NAD^+ or NADP^+ by a secondary alcohol, illustrated by isopropanol.



[0217] Secondary alcohol dehydrogenases that are suitable for use as cofactor regenerating systems in the ketoreductase-catalyzed reduction reactions described herein include both naturally occurring secondary alcohol dehydrogenases, as well as non-naturally occurring secondary alcohol dehydrogenases. Naturally occurring secondary alcohol dehydrogenases include known alcohol dehydrogenases from, *Thermoanaerobium brockii*, *Rhodococcus erythropolis*, *Lactobacillus kefir*, and *Lactobacillus brevis*, and non-naturally occurring secondary alcohol dehydrogenases include engineered alcohol dehydrogenases derived therefrom. Secondary alcohol dehydrogenases employed in the methods described herein, whether naturally occurring or non-naturally occurring, may exhibit an activity of at least about 1 $\mu\text{mol}/\text{min}/\text{mg}$, sometimes at least about 10 $\mu\text{mol}/\text{min}/\text{mg}$, or at least about 10^2 $\mu\text{mol}/\text{min}/\text{mg}$, up to about 10^3 $\mu\text{mol}/\text{min}/\text{mg}$ or higher.

[0218] Suitable secondary alcohols include lower secondary alkanols and aryl-alkyl carbinols. Examples of lower secondary alcohols include isopropanol, 2-butanol, 3-methyl-2-butanol, 2-pentanol, 3-pentanol, 3,3-dimethyl-2-butanol, and the like. In one embodiment the secondary alcohol is isopropanol. Suitable aryl-alkyl carbinols include unsubstituted and substituted 1-arylethanol.

[0219] When a secondary alcohol and secondary alcohol dehydrogenase are employed as the cofactor regeneration system, as the 5-hydroxy-3-oxohexanoate ester substrate is reduced by the engineered ketoreductase and NADH or NADPH, the resulting NAD^+ or NADP^+ is reduced by the coupled oxidation of the secondary alcohol to the ketone by the secondary alcohol dehydrogenase. The net reaction is described by equation (9), illustrated with isopropanol, which is the summation of equations (1) and (8):



[0220] It will be appreciated by the skilled artisan this reaction of a ketone and alcohol to the corresponding alcohol and ketone, respectively, is reversible, and will reach an equilibrium. The inventors found that the forward reaction is thermodynamically favored, and that only a modest excess of isopropanol is required to obtain high conversion of the 3-oxohexanoate ester to the desired 3,5-dihydroxyhexanoate ester at the equilibrium. Typically, the molar ratio of the secondary alcohol to the 3-oxohexanoate ester provided to the reaction is in the range of 1 to 20. In some embodiments this molar ratio is 1 to 10, 1 to 5, or 1 to 2.

[0221] Some engineered ketoreductases also have activity to dehydrogenate a secondary alcohol reductant. In some embodiments using secondary alcohol as reductant, the engineered ketoreductase and the secondary alcohol dehydrogenase are the same enzyme.

[0222] In carrying out embodiments of the ketoreductase-catalyzed reduction reactions described herein employing a cofactor regeneration system, either the oxidized or reduced form of the cofactor may be provided initially. As described above, the cofactor regeneration system converts oxidized cofactor to its reduced form, which is then utilized in the reduction of the ketoreductase substrate (*i.e.*, 5-hydroxy-3-oxohexanoate ester) to the corresponding 3,5-dihydroxyhexanoate ester.

[0223] In some embodiments, cofactor regeneration systems are not used. For reduction reactions carried out without the use of a cofactor regenerating systems, the cofactor is added to the reaction mixture in reduced form.

[0224] In carrying out the enantioselective reduction reactions described herein, the engineered ketoreductase enzyme, and any enzymes comprising the optional cofactor regeneration system, may be added to the reaction mixture in the form of the purified enzymes, whole cells transformed with gene(s) encoding the enzymes, and/or cell extracts and/or lysates of such cells. The gene(s) encoding the engineered ketoreductase enzyme and the optional cofactor regeneration enzymes can be transformed into host cells separately or together into the same host cell. For example, in some embodiments one set of host cells can be transformed with gene(s) encoding the engineered ketoreductase enzyme and another set can be transformed with gene(s) encoding the cofactor regeneration enzymes. Both sets of transformed cells can be utilized together in the reaction mixture in the form of whole cells, or in the form of lysates or extracts derived therefrom. In other embodiments, a host cell can be transformed with gene(s) encoding both the engineered ketoreductase enzyme and the cofactor regeneration enzymes.

[0225] Whole cells transformed with gene(s) encoding the engineered ketoreductase enzyme and/or the optional cofactor regeneration enzymes, or cell extracts and/or lysates thereof, may be employed in a variety of different forms, including solid (*e.g.*, lyophilized, spray-dried, and the like) or semisolid (*e.g.*, a crude paste).

[0226] The cell extracts or cell lysates may be partially purified by precipitation (ammonium sulfate, polyethyleneimine, heat treatment or the like, followed by a desalting procedure prior

to lyophilization (*e.g.*, ultrafiltration, dialysis, and the like). Any of the cell preparations may be stabilized by crosslinking using known crosslinking agents, such as, for example, glutaraldehyde or immobilization to a solid phase (*e.g.*, Eupergit C, and the like).

[0227] The solid reactants (*e.g.*, enzyme, salts, etc.) may be provided to the reaction in a variety of different forms, including powder (*e.g.*, lyophilized, spray dried, and the like), solution, emulsion, suspension, and the like. The reactants can be readily lyophilized or spray dried using methods and equipment that are known to those having ordinary skill in the art. For example, the protein solution can be frozen at -80°C in small aliquots, then added to a prechilled lyophilization chamber, followed by the application of a vacuum. After the removal of water from the samples, the temperature is typically raised to 4°C for two hours before release of the vacuum and retrieval of the lyophilized samples.

[0228] The quantities of reactants used in the reduction reaction will generally vary depending on the quantities of 3,5-dihydroxyhexanoate ester desired, and concomitantly the amount of ketoreductase substrate employed. The following guidelines can be used to determine the amounts of ketoreductase, cofactor, and optional cofactor regeneration system to use. Generally, 5-hydroxy-3-oxo-hexanoate ester substrates are employed at a concentration of about 20 to 300 grams/liter using from about 50 mg to about 5 g of ketoreductase and about 10 mg to about 150 mg of cofactor. Those having ordinary skill in the art will readily understand how to vary these quantities to tailor them to the desired level of productivity and scale of production. Appropriate quantities of optional cofactor regeneration system may be readily determined by routine experimentation based on the amount of cofactor and/or ketoreductase utilized. In general, the reductant (*e.g.*, glucose, formate, isopropanol) is utilized at levels above the equimolar level of ketoreductase substrate to achieve essentially complete or near complete conversion of the ketoreductase substrate.

[0229] The order of addition of reactants is not critical. The reactants may be added together at the same time to a solvent (*e.g.*, monophasic solvent, biphasic aqueous co-solvent system, and the like), or alternatively, some of the reactants may be added separately, and some together at different time points. For example, the cofactor regeneration system, cofactor, ketoreductase, and ketoreductase substrate may be added first to the solvent.

[0230] For improved mixing efficiency when an aqueous co-solvent system is used, the cofactor regeneration system, ketoreductase, and cofactor may be added and mixed into the aqueous phase first. The organic phase may then be added and mixed in, followed by addition of the ketoreductase substrate. Alternatively, the ketoreductase substrate may be premixed in the organic phase, prior to addition to the aqueous phase

[0231] Suitable conditions for carrying out the ketoreductase-catalyzed reduction reactions described herein include a wide variety of conditions which can be readily optimized by routine experimentation that includes, but is not limited to, contacting the engineered ketoreductase enzyme and substrate at an experimental pH and temperature and detecting product, for example, using the methods described in the Examples provided herein.

[0232] The ketoreductase catalyzed reduction is typically carried out at a temperature in the range of from about 15°C to about 75°C. For some embodiments, the reaction is carried out at a temperature in the range of from about 20°C to about 55°C. In still other embodiments, it is carried out at a temperature in the range of from about 20°C to about 45°C. The reaction may also be carried out under ambient conditions.

[0233] The reduction reaction is generally allowed to proceed until essentially complete, or near complete, reduction of substrate is obtained. Reduction of substrate to product can be monitored using known methods by detecting substrate and/or product. Suitable methods include gas chromatography, HPLC, and the like. Conversion yields of the 3,5-dihydroxyhexanoate ester reduction product generated in the reaction mixture are generally greater than about 50%, may also be greater than about 60%, may also be greater than about 70%, may also be greater than about 80%, may also be greater than 90%, and are often greater than about 97%.

[0234] The 3,5-dihydroxyhexanoate reduction product can be recovered from the reaction mixture and optionally further purified using methods that are known to those of skill in the art. Suitable methods are described in U.S. Patents 6,001,615, 6,472,544, 6,596,879, and 6,645,746, the disclosures of which are incorporated herein by reference. Additional suitable methods are provided in the Examples below.

[0235] As previously discussed, the ketoreductase-catalyzed reduction of the 5-hydroxy-3-oxohexanoate ester enantiomer (Ia) generates a new stereogenic carbon at the 3-position of the 3,5-dihydroxyhexanoate ester product. As also previously discussed, in reactions carried

out with the engineered ketoreductase enzymes described herein, the reduction product is generated with a high degree of *syn*- stereoselectivity at the 3-position: Thus, the 3,5-dihydroxyhexanoate esters generated using the engineered ketoreductase enzymes described herein are chiral and non-racemic. As mentioned above, the ketoreductase reactions described herein typically generate chiral *syn* 3,5-dihydroxyhexanoate esters according to structural formula (IIa) having a diastereomeric purity of at least about 99.5%, usually at least about 99.9%, and typically at least about 99.95%. The Examples illustrate embodiments providing *tert*-butyl 6-cyano-(3*R*,5*R*)-dihydroxyhexanoate ester with a diastereomeric purity of $\geq 99.993\%$.

[0236] Certain of the substrates described herein have been found to be particularly useful in the synthesis of clinically important cholesterol-lowering statin drugs. Such compounds include those in which R^1 is a lower alkyl, in some embodiments, *tert*-butyl; X is selected from chloro, cyano and hydroxyl and OR^2 , is as defined herein. Thus, some embodiments of the compounds according to structural formulae (Ia), (IIa), (IIIa), (IVa) and (Va) described herein include those compounds in which R^1 is a lower alkyl or *tert*-butyl and/or X is selected from chloro, cyano and hydroxy.

[0237] In embodiments of the compounds according to structural formulae (Ia), (IIa), (IIIa), (IVa) and (Va) in which X is $-OR^6$, where R^6 is a protecting group, the group can be virtually any protecting group known to be useful for protecting hydroxyl groups during organic syntheses. The identity of the specific protecting group will depend upon the various synthetic reaction conditions, and can be readily selected for specific situation by those of skill in the art. Suitable exemplary protecting groups are described in Greene & Wuts, "Protective Groups in Organic Synthesis," 3rd Ed., 1999, John Wiley & Sons, NY (see, for example, pp.17-200). In some embodiments, the protecting group is selected from ether protection groups (*e.g.*, benzyl, *t*-butyl, tetrahydropyranyl, methoxyethoxymethyl, methoxymethyl, etc.), silyl ether protection groups (*e.g.*, trimethylsilyl, triethylsilyl, *t*-butyldimethylsilyl, triphenylsilyl, etc.), ester protection groups (*e.g.*, benzoate, alkylate, haloalkylate, etc.), carbonate protecting groups (*e.g.*, alkyl methyl, methoxymethyl, alkyl 2,2,2,-trichloroethyl, allyl alkyl carbonate, alkyl benzyl, etc.), and sulfonate protecting groups (*e.g.*, allylsulfonate, methanesulfonate, benzylsulfonate, tosylate, etc.).

[0238] The 5-hydroxy-3-oxohexanoate ester enantiomers of structural formulae (Ia) can be prepared using standard methods that are well-known in the art. Suitable exemplary methods

are described in U.S. Patent No. 6,399,339 (for specific examples in which X = Cl and R¹ = *tert*-butyl, see Example 1); U.S. Patent No. 5,155,251 and the various references cited therein (X = CN, R¹ = *tert*-butyl), Japanese Patent Publication No. 1723728 (X = Cl, R¹ = *tert*-butyl) and PCT publication WO 2005/018579 (X = Cl or CN, R¹ = *tert*-butyl), the disclosures of which are incorporated herein by reference. FIG. 1 provides a diagram illustrating exemplary methods for synthesizing the substrates in both enantiomerically pure form and as racemic mixtures (International Publication Nos. WO 2003/070733 and WO 2004/113314).

[0239] The *syn* 3,5-dihydroxyhexanoate esters produced by the engineered ketoreductase-catalyzed reduction reactions described herein can be used as starting materials to synthesize clinically important cholesterol-lowering statin drugs, such as atorvastatin, rosuvastatin, and pitavastatin. A key intermediate in the synthesis of these statins is the protected *syn* 3,5-dihydroxyhexanoate ester of structural formula (IIIa) or (IVa), *supra*. Methods for synthesizing such protected esters are well known. In embodiments in which the R² substituents in the compounds of structural formula (IIIa) represent unbridged protecting groups, the protecting groups can be selected from those described above. Compounds including these protecting groups can be synthesized as described, for example, in Greene & Wuts, "Protective Groups in Organic Synthesis," 3rd Ed., 1999, John Wiley & Sons, NY (see, for example, pp. 17-200). The actual methods used will depend upon the identity of the protecting group(s).

[0240] Embodiments in which the R² groups are taken together to form an optionally substituted alkylene bridge can be synthesized from the *syn* 3,5-dihydroxyhexanoate esters using the methods described in U.S. Patent No. 5,097,045 (X=cyano), U.S. Patent No. 6,472,544 (X=halo or OH) and U.S. Patent No. 6,344,569 (X=halo or CN), the disclosures of which are incorporated herein by reference. Compounds including these protecting groups can be synthesized as described, for example, in Greene & Wuts, "Protective Groups in Organic Synthesis," 3rd Ed., 1999, John Wiley & Sons, NY (see, for example, pp. 201-245).

[0241] As a specific example, compounds according to structural formula (IVa) in which X is cyano can be prepared by treating the corresponding (3R,5R)-6-cyano-3,5-dihydroxyhexanoate ester with an acetal forming reagent as described in U.S. Patent No. 6,344,569, at Col. 7, line 30 through Col. 8, line 40, the disclosure of which is incorporated herein by reference.

[0242] As another specific example, compounds according to structural formula (IVa) in which X is halo can be prepared by treating the corresponding (3R,5S)-6-halo-3,5-dihydroxyhexanoate ester with an acetal forming reagent as described in U.S. Patent No. 6,344,569 at Col. 9, line 21 through Col. 10, line 34, the disclosure of which is incorporated herein by reference.

[0243] As yet another specific example, compounds according to structural formula (IVa) in which X is cyano can be prepared by treating the chloro analog (prepared as described above), with a cyanating reagent as described in U.S. Patent No. 6,344,569 at Col. 11, line 17 through Col. 12, line 5, the disclosure of which is incorporated herein by reference.

[0244] In some embodiments, the R² groups of the protected *syn* 3,5-dihydroxyhexanoate taken together can form a cyclic boronate protecting group of -BR⁵-, wherein the R⁵ is selected from (C1-C12) alkyl, (C6-C10) aryl and (C7-C12) arylalkyl. In a specific embodiment, R⁵ is phenyl. Compounds with cyclic boronate based protecting groups can be synthesized as described, for example, in Greene & Wuts, "Protective Groups in Organic Synthesis," 3rd Ed., 1999, John Wiley & Sons, NY (see, for example, pp. 243-245). An exemplary phenyl boronate protected *syn* 3,5-dihydroxyhexanoate ester is described in U.S. Patent No. 6,867,306, incorporated herein by reference.

[0245] Exemplary embodiments of these and other reactions are illustrated in FIG. 2. Specific methods of synthesizing tert-butyl (4R,6R)-6-cyanomethyl-2,2-dimethyl-1,3-dioxane-4-acetate from tert-butyl (3R,5R)-6-cyano-3,5-dihydroxyhexanoate and tert-butyl (4R,6S)-6-chloromethyl-2,2-dimethyl-1,3-dioxane-4-acetate from tert-butyl (3R,5S)-6-chloro-3,5-dihydroxyhexanoate are described in Example 2 and 3, respectively, of U.S. Patent No. 6,344,569, the disclosure of which is incorporated herein by reference. A specific method for synthesizing tert-butyl (4R,6R)-6-cyanomethyl-2,2-dimethyl-1,3-dioxane-4-acetate from tert-butyl (4R,6S)-6-chloromethyl-2,2-dimethyl-1,3-dioxane-4-acetate is described in Example 3 of U.S. Patent No., 6,344,569, the disclosure of which is incorporated herein by reference.

[0246] The protected and unprotected *syn* dihydroxy esters of structural formulas (IIa), (IIIa), (IVa), and (Va) can be used to synthesize cholesterol lowering statins, as well as other useful compounds including a 1,3- *syn* dihydroxy moiety, using methods that are well-known in the art. For example, methods of synthesizing atorvastatin using tert-butyl (3R,5R)-6-cyano-3,5-

dihydroxyhexanoate are described in U.S. Patent No. 6,596,879 (see especially Example 2 at Col. 14, line 22-58), and U.S. Patent No. 5,097,045, the disclosures of which is incorporated herein by reference.

[0247] Methods of synthesizing rosuvastatin using tert-butyl (3R,5S)-6-chloro-3,5-dihydroxyhexanoate are described in U.S. Patent No. 5,278,313 and U.S. Patent No. 6,472,544, respectively, the disclosures of which are incorporated herein by reference. Methods of synthesizing rosuvastatin using tert-butyl (3R,5S,6)-trihydroxyhexanoate are described in PCT application no. WO 01/85975, the disclosure of which is incorporated herein by reference. Synthesis of other statins using the compounds produced by the methods herein will be apparent to the skilled artisan.

7. EXAMPLES

[0248] Various features and embodiments of the disclosure are illustrated in the following representative examples, which are intended to be illustrative, and not limiting.

[0249] In the following description, wherever glucose dehydrogenase (GDH) is used, it is GDH-CDX901, obtainable from Julich Chiral Solutions, Jülich, Germany.

7.1 Example 1: Wild-type Ketoreductase Gene Acquisition and Construction of Expression Vectors.

[0250] The *Ydl124wp* gene (Genbank Acc. No.:NP_010159.1; GI:6320079) encoding a *Saccharomyces cerevisiae* ketoreductase was codon optimized (SEQ ID NO:1) for expression in *E. coli* based on the amino acid sequence (SEQ ID NO:2) of the ketoreductase ("YDL") encoded by the *Ydl124wp* gene. The gene was synthesized using oligonucleotides composed of 42 nucleotides and cloned into expression vector pCK110900 (depicted in FIG. 5) under the control of a *lac* promoter. The expression vector also contained the P15a origin of replication and the chloramphenicol resistance gene. Resulting plasmids were transformed into *E. coli* W3110 using standard methods. Several clones were selected for sequencing the putative KRED-encoding gene. Genes having the desired designed sequence were identified and used as the starting material for the development of genes encoding engineered ketoreductases.

[0251] This Example illustrates the acquisition of a recombinant polynucleotide encoding the wild-type ketoreductase YDL from which genes encoding engineered ketoreductases can be derived, and expression vectors and host cells suitable for such engineering.

[0252] Polynucleotides encoding engineered ketoreductases of the present disclosure were likewise cloned into vector pCK110900 for expression in *E. coli* W3110.

7.2 Example 2 Production of Ketoreductase Powders; Shake Flask Procedure.

[0253] A single microbial colony of *E. coli* containing a plasmid with the ketoreductase gene of interest was inoculated into 50 ml Luria Bertani broth containing 30 µg/ml chloramphenicol and 1% glucose. Cells were grown overnight (at least 16 hrs) in an incubator at 30°C with shaking at 250 rpm. The culture was diluted into 250 ml Terrific Broth (12 g/L bacto-tryptone, 24g/L yeast extract, 4 ml/L glycerol, 65mM potassium phosphate, pH 7.0, 1mM MgSO₄, 30 µg/ml chloramphenicol) in 1 liter flask) to an optical density at 600 nm (OD₆₀₀) of 0.2 and allowed to grow at 30°C. Expression of the ketoreductase gene was induced with 1mM IPTG when the OD₆₀₀ of the culture is 0.6 to 0.8 and incubated overnight (at least 16 hrs). Cells were harvested by centrifugation (5000rpm, 15 min, 4°C) and the supernatant discarded. The cell pellet was resuspended with an equal volume of cold (4°C) 100mM triethanolamine (chloride) buffer, pH 7.0, and harvested by centrifugation as above. The washed cells were resuspended in two volumes of the cold triethanolamine (chloride) buffer and passed through a French Press twice at 12000psi while maintained at 4°C. Cell debris was removed by centrifugation (9000 rpm, 45 min., 4°C). The clear lysate supernatant was collected and stored at -20°C. Lyophilization of frozen, clear lysate provided a dry powder of crude ketoreductase enzyme.

[0254] This Example illustrates the production of ketoreductases powders suitable for use to test enzyme properties.

7.3 Example 3: Preparation of t-butyl 6-cyano-(5*R*)-hydroxy-3-oxohexanoate.

[0255] To an 1 L 3-neck flask with an addition funnel and a PTFE-coated magnetic stirring bar, under a nitrogen atmosphere and immersed in a -20 °C dry ice/acetone bath, was added 120 mL anhydrous tetrahydrofuran and 75 mL (540 mmol) diisopropylamine. The solution was stirred and cooled to -20°C, and 200 mL (500 mmol) 2.5 M n-butyllithium in hexane was added dropwise over 45 minutes, giving a pale yellow solution. After an additional 30 minutes, 70 mL (520 mmol) t-butyl acetate was added dropwise with stirring over 25 minutes, turning the solution cloudy. After an additional 1 hour maintained at -20°C, a solution of 22.0 g ethyl 4-cyano-(3*R*)-hydroxybutyrate (>99.9% e.e., 140 mmol) in 30 mL anhydrous tetrahydrofuran was added dropwise with stirring over 35 minutes, giving a pale

yellow solution. The solution was maintained at -20°C for an additional 1 hour, then transferred via cannula over 30 minutes subsurface into a stirred biphasic mixture of 350 mL 1 M citric acid and 250 mL toluene immersed in an ice bath ($\sim 5^{\circ}\text{C}$). During this quench, the temperature of the mixture was maintained between $5-10^{\circ}\text{C}$. Upon completion, the phases separated, giving a pale yellow organic phase above and an orange aqueous phase, pH ~ 6 , below. The aqueous phase was separated and extracted with 250 mL toluene. The combined organic phases were washed with 100 mL 1 N HCl followed by 3 x 100 mL of distilled water. The final water wash gave pH ~ 5 . The solvent was removed from the organic phase by rotary evaporation at 60°C under vacuum to give 31.7 g of a yellow oil.

[0256] ^1H -NMR of the oil showed the presence of t-butyl 6-cyano-(5R)-hydroxy-3-oxohexanoate, t-butyl 3-oxobutyrate, and t-butyl 4-cyano-(3R)-hydroxybutyrate in 1.00:0.27:0.14 mole ratio, corresponding to 77 weight % t-butyl 6-cyano-(5R)-hydroxy-3-oxohexanoate if no other components are present. The actual weight % was likely slightly lower, but was not more accurately measured. 77 weight % of 31.7 g oil corresponds to a 77% mole yield on ethyl 4-cyano-(3R)-hydroxybutyrate (theoretical yield = 31.8 g).

[0257] This and similarly prepared crude t-butyl 6-cyano-(5R)-hydroxy-3-oxohexanoate, typically having purity ranging from 60 to 75 weight %, the balance being t-butyl 3-oxobutyrate and t-butyl 4-cyano-(3R)-hydroxybutyrate, were used in the following Examples, except when the purified substrate is specified. The specified amounts of t-butyl 6-cyano-(5R)-hydroxy-3-oxohexanoate used in the Examples refer to the amount of the crude preparation, uncorrected for its actual composition.

7.4 Example 4: LC/MS/MS Assay for Substrate Specificity and Conversion.

[0258] An LC/MS/MS method was developed to analyze the conversion of t-butyl 6-cyano-(5R)-hydroxy-3-oxohexanoate to t-butyl 6-cyano-(3R,5R)-dihydroxyhexanoate and the possible conversion of t-butyl 3-oxobutyrate in the crude substrate (Example 4) to t-butyl 3-hydroxybutyrate:

Instrument: Agilent 1100 with Waters Micromass Quattro Premier LC/MS/MS

Column: Agilent SB C18 (50mm x 4.6 mm, $5\mu\text{m}$)

Mobile phase: 50% aqueous 0.25 vol% acetic acid, 50% acetonitrile

Flow rate: 1.0 mL/min.

Backpressure: 60 bar

Temperature: ambient room temperature

Injection: 5 μ L, $\sim$ 0.1 mg/ml in methanol or other water miscible solvent.

Retention times:	t-butyl 6-cyano-(3R,5R)-dihydroxyhexanoate	1.0 min.
	t-butyl 6-cyano-(5R)-hydroxy-3-oxohexanoate	1.3 min.
	t-butyl 3-hydroxybutyrate	1.5 min.
	t-butyl 3-oxobutyrate	2.1 min.

Ionization/Detection: APCI+ using the transitions $MH^+ > MH-56$ (loss of t-butene)

[0259] The response ratio for t-butyl 6-cyano-(3R,5R)-dihydroxyhexanoate to t-butyl 6-cyano-(5R)-hydroxy-3-oxohexanoate substrate was typically 0.84 at 0.1 mg/ml. The MS/MS transitions for t-butyl 3-oxobutyrate and t-butyl 3-hydroxybutyrate were not optimized.

7.5 Example 5 Diastereomeric Analysis of t-butyl-6-cyano-3,(5R)-dihydroxyhexanoate by LC/MS/MS.

[0260] An LC/MS/MS method was developed to separate and analyze the (3R,5R) and (3S,5R) diastereomers of t-butyl 6-cyano-3,(5R)-dihydroxyhexanoate. The LC conditions provided baseline resolution of the diastereomers. The response was linear from 0.0001 to 1.0 mg/ml with a detection limit under 0.0001 mg/ml.

Instrument: Agilent 1100 with Waters Micromass Quattro Premier LC/MS/MS

Column: Agilent SB C8 (50mm x 4.6 mm, 5 μ m)

Mobile phase: Isocratic 65% of 0.25% aq acetic acid, 35% acetonitrile

Flow rate: 1.0 mL/min.

Temperature: ambient room temperature

Retention times: (3S,5R) 12.77 min: (3R, 5R) 13.67 min.

Ionization/Detection: APCI+ using the transitions $MH^+ > MH-56$ (loss of t-butene)

7.6 Example 6: Diastereomeric Analysis of t-butyl (6R)-cyanomethyl-2,2-dimethyl-1,3-dioxane-4-acetate by Gas Chromatography.

[0261] A GC/MS method was developed to separate and analyze the (4R,6R) and (4S,6R) diastereomers of t-butyl (6R)-cyanomethyl-2,2-dimethyl-1,3-dioxane-4-acetate:

Column: HP5MS (0.25mm i.d., 25 μ m df, 30m)

Carrier gas: Helium, 9.44 psi, 0.7mL/minute.

Oven: 60°C for 1min, then 15 °C/min to 280°C, then hold at 280°C for 2 min.

Retention Times: (4S,6R) 11.44 min.; (4R, 6R) 11.55 min.

Detection: total ion count

7.7 Example 7: Diastereomeric Analysis of t-butyl-6-cyano-3,(5R)-dihydroxyhexanoate via derivatization to t-butyl (6R)-cyanomethyl-2,2-dimethyl-1,3-dioxane-4-acetate.

[0262] To a 30 mg sample comprising t-butyl 6-cyano-3,(5R)-dihydroxyhexanoate was added 1 mL of ethyl acetate, 200 μ L of 2,2-dimethoxypropane, and 20 μ L of methanesulfonic acid. The mixture was stirred for 20 minutes at room temperature. After addition of 200 μ L of saturated aqueous sodium bicarbonate, a sample of the top ethyl acetate layer was analyzed by the method of Example 6.

[0263] Each of the (3R,5R) and (3S,5R) diastereomers of t-butyl-6-cyano-3,(5R)-dihydroxyhexanoate are quantitatively derivatized under these conditions. Accordingly the 3,(5R) diastereomeric composition of the t-butyl-6-cyano-3,(5R)-dihydroxyhexanoate corresponds to the analyzed 4,(6R) diastereomeric composition of the (6R)-cyanomethyl-2,2-dimethyl-1,3-dioxane-4-acetate derivative.

7.8 Example 8: Evaluation of Wild-Type Ketoreductase YDL for Activity to Reduce t-butyl 6-cyano-(5R)-hydroxy-3-oxohexanoate.

[0264] To a reaction mixture of 950 μ L 100mM triethanolamine (chloride) buffer, pH 7.0, 200 μ L isopropanol, 9 mg t-butyl 6-cyano-(5R)-hydroxy-3-oxohexanoate and 8 mg NAD(P)H was added 15 mg ketoreductase powder comprising ketoreductase YDL. The reaction mixture was stirred at room temperature for 24 hours, then extracted with 1 mL ethyl acetate. After centrifugation, the organic phase was separated and the solvent was removed by rotary evaporation to leave a nonvolatile oil. The nonvolatile oil was analyzed by the method of Example 4 for the conversion of the t-butyl 6-cyano-(5R)-hydroxy-3-oxohexanoate and, if present, the diastereomeric composition of the product, t-butyl 6-cyano-(3,5R)-dihydroxyhexanoate by the method of Example 7. The analyses showed 85% conversion of the t-butyl 6-cyano-(5R)-hydroxy-3-oxohexanoate to produce t-butyl 6-cyano-(3R,5R)-dihydroxyhexanoate having >99% d.e.

[0265] The Example illustrates the identification of wild-type ketoreductase YDL as a candidate for engineering to improve properties for the reduction of a 3-oxo group of an enantiomer of a 5-hydroxy-3-oxohexanoate ester to yield the corresponding *syn* 3,5-dihydroxyhexanoate ester.

7.9 Example 9: Evaluation of Wild-Type Ketoreductase YDL for Activity to Reduce t-butyl 6-cyano-(5R)-hydroxy-3-oxohexanoate using Glucose and Glucose Dehydrogenase for Cofactor Regeneration.

[0266] To a reaction mixture of 1 mL 100mM triethanolamine (chloride) buffer, pH 7.0, 100 μ L butyl acetate, 20mg t-butyl 6-cyano-(5R)-hydroxy-3-oxohexanoate, 1mg NAD(P)⁺, and 35 mg glucose, was added 3 mg of glucose dehydrogenase powder and 20mg ketoreductase powder comprising ketoreductase YDL. The reaction mixture was stirred at room temperature for 22 hours, then extracted with 1 mL ethyl acetate. After centrifugation, the organic phase was separated and the solvent was removed by rotary evaporation to leave a nonvolatile oil. The nonvolatile oil was analyzed by the method of Example 4 for the conversion of the t-butyl 6-cyano-(5R)-hydroxy-3-oxohexanoate and, if present, the diastereomeric composition of the product, t-butyl 6-cyano-(3,5R)-dihydroxyhexanoate by the method of Example 5. The analyses showed 92.6% conversion of the t-butyl 6-cyano-(5R)-hydroxy-3-oxohexanoate to produce t-butyl 6-cyano-(3R,5R)-dihydroxyhexanoate having >99.9% d.e.

[0267] The Example illustrates the evaluation of wild-type ketoreductase YDL for activity and diastereoselectivity when used in combination with a cofactor regeneration system (glucose and glucose dehydrogenase).

7.10 Example 10: Evaluation of Substrate and Cofactor Specificities of Wild-Type Ketoreductase YDL in the Reaction to Reduce crude t-butyl 6-cyano-(5R)-hydroxy-3-oxohexanoate.

[0268] The specificity of wild-type ketoreductase YDL powder for the reductions of t-butyl-(R)-5-hydroxy-3-oxohexanoate and of t-butyl 3-oxobutyrate by NADH and NADPH was evaluated by measuring the increase in NAD(P) absorbance at 340 nm in reaction mixtures comprising 3 mg/mL purified t-butyl-(R)-5-hydroxy-3-oxohexanoate or ~13 mM t-butyl 3-oxobutyrate and 0.2-0.3 mM NADH or NADPH in the total volume of 1mL 100 mM triethanolamine (chloride) buffer, pH 7.2.

[0269] Ketoreductase YDL powder was active for the reduction of t-butyl-(R)-5-hydroxy-3-oxohexanoate by NADPH but not by NADH. Ketoreductase YDL powder showed only very

low activity for the reduction of t-butyl 3-oxobutyrate by NADPH, relative to that on t-butyl-(*R*)-5-hydroxy-3-oxohexanoate.

7.11 Example 11: High Throughput Assay for Ketoreductase Activity on t-butyl 6-cyano-(5*R*)-hydroxy-3-oxohexanoate.

[0270] **A. High Throughput NAD(P)H Fluorescence Assay:** Library colonies were picked using a Q-bot® robotic colony picker (Genetix USA, Inc., Beaverton, OR) into 96-well shallow well microtiter plates containing 180 μ L Luria Bertani broth (LB), 1% glucose and 30 μ g/mL chloramphenicol (CAM). Cells were grown overnight at 30°C with shaking at 250 rpm. 13 μ L of this culture was then transferred into 96-deep well plates containing 400 μ L Terrific broth (TB) and 30 μ g/mL CAM. After incubation of deep-well plates at 30°C with shaking at 250 rpm for 2.5 to 3 hours (OD_{600} 0.6-0.8), recombinant gene expression by the cell cultures was induced by isopropyl thiogalactoside (IPTG) to a final concentration of 1 mM. The plates were then incubated at 30°C with shaking at 250 rpm for overnight.

[0271] Cells were pelleted via centrifugation, resuspended in 300 to 400 μ L lysis buffer and lysed by shaking at room temperature for at least 2 hours. The lysis buffer contained 100 mM triethanolamine (chloride) buffer, pH 7.0-7.2, 1 mg/mL lysozyme and 500 μ g/mL polymixin B sulfate.

[0272] Ketoreductase activity was measured by transferring measured quantities of the lysis mixtures into the wells of microtiter plates containing an assay mixture of 100 mM triethanolamine (chloride) buffer, pH 7-7.2, 0.2-0.3 mM NAD(P)H, 2 to 3 mg/mL t-butyl 6-cyano-(5*R*)-hydroxy-3-oxohexanoate, 0 to 2 mg/ml t-butyl 6-cyano-(3*R*,5*R*)-dihydroxyhexanoate, 0 to 600 mM glucose and 0 to 600 mM sodium gluconate. The reactions were monitored by measuring the decrease of fluorescent emission of NAD(P)H at 440nm as a function of time. The results were plotted as relative fluorescent units (RFU) of NAD(P)H verses time and the slope of the plot (RFU/min) was used to determine the rate of reaction.

[0273] **B. Medium Throughput LC/MS/MS Assay for Substrate Specificity and Conversion:** To determine the extent to which the NAD(P)H consumption measured in the fluorescence assay was due to conversion of the t-butyl 6-cyano-(5*R*)-hydroxy-3-oxohexanoate substrate to t-butyl 6-cyano-(3*R*,5*R*)-dihydroxyhexanoate product or to reduction of t-butyl 3-oxobutyrate in the crude substrate to t-butyl 3-hydroxybutyrate, the reaction mixtures showing NAD(P)H consumption activity of interest were consolidated into fewer

96-well microtiter plates and extracted with ethyl acetate. The separated ethyl acetate extracts were diluted with acetonitrile/water (1/1) and analyzed by the LC/MS/MS method of Example 4.

7.12 Example 12: High Throughput Screen for More Stable Engineered Ketoreductases.

[0274] Lysis mixtures comprising engineered ketoreductases prepared and identified as in Example 11A were incubated for at least 16 hrs at a temperature in the range of 37 °C to 50 °C. The ketoreductase activity remaining in the lysis mixtures after the incubation was then measured at ambient temperature by the procedure of Example 4. The ratio of the ketoreductase activity remaining after the incubation to the activity of the corresponding uninoculated lysis mixture, 0 to 1, was used as a measure of the stability of the engineered ketoreductase in the lysis mixture.

7.13 Example 13: Improved Activity of Engineered Ketoreductases Derived from Wild-type YDL for the Reduction of t-butyl 6-cyano-(5R)-hydroxy-3-oxohexanoate to t-butyl 6-cyano-(3R,5R)-dihydroxyhexanoate.

[0275] To a 25 mL three-neck vessel equipped with a PTFE-coated magnetic stirring bar and a pH electrode connected to an automatic titrator for pH-controlled addition of base on-demand via a feeding tube into the vessel, was charged 19 mL 100 mM triethanolamine (chloride) buffer, pH 7, 3.0 g glucose, ketoreductase powder comprising the ketoreductase specified by SEQ ID NOS. in Table 2 in the amount specified in Table 2, 13 mg glucose dehydrogenase powder, 1.0 mg NaNADP, and lastly 3 g t-butyl 6-cyano-(5R)-hydroxy-3-oxohexanoate. The reaction mixture was stirred at 22°C. The automatic titrator maintained the pH at 7 by the addition of 4N NaOH, which was continuously recorded. Reaction progress was monitored by the rate and cumulative addition of the base and periodic sampling of the reaction mixture for extraction and analysis by the method of Example 4. After the reaction time specified in Table 2, the reaction mixture was extracted twice with 10 mL ethyl acetate twice. The combined organic extract was filtered through a short pad of diatomaceous earth and the solvent was removed by rotary evaporation under vacuum. Diastereomeric analysis of the residual oil by the method of Example 5 showed the product t-butyl 6-cyano-(3R,5R)-dihydroxyhexanoate from each such reaction reported Table 2 to have >99.99% diastereopurity. (No other diastereomers were detectable.)

[0276] Table 2 gives the SEQ ID NOS. corresponding to the ketoreductase powder, the number of amino acid mutations from the wild-type ketoreductase YDL, the amount of ketoreductase powder used, the reaction time, and the conversion of t-butyl 6-cyano-(5R)-hydroxy-3-oxohexanoate to t-butyl 6-cyano-(3R,5R)-dihydroxyhexanoate reached in that reaction time.

[0277] This Example illustrates, by comparisons of ketoreductase amounts, reaction times, and conversions in Table 2, engineered ketoreductases derived from the wild-type ketoreductase YDL providing improved activity compared to ketoreductase YDL.

Table 2: Activities of engineered ketoreductases derived from YDL.				
ketoreductase SEQ ID NO.	mutations from YDL	ketoreductase amount (mg)	reaction time (h)	conversion (%)
2 (YDL)	0	120	67	87
70	3	120	67	99.6
112	4	60	24	94
178	7	30	24	95
276	8	30	23	96
278	8	30	22	99.0
318	9	30	5	99.7

7.14 Example 14: Improved Stability of Engineered Ketoreductases Derived from Wild-type YDL for the Reduction of t-butyl 6-cyano-(5R)-hydroxy-3-oxohexanoate to t-butyl 6-cyano-(3R,5R)-dihydroxyhexanoate.

[0278] To a 25 mL three-neck vessel equipped with a PTFE-coated magnetic stirring bar and a pH electrode connected to an automatic titrator for pH-controlled addition of base on-demand via a feeding tube into the vessel, was charged 20 mL 100 mM triethanolamine (chloride) buffer, pH 7, 0.5 g glucose, the amount of ketoreductase powder specified in Table 3, 8 mg glucose dehydrogenase, 2.0 mg NaNADP, and lastly 0.3 g t-butyl 6-cyano-(5R)-hydroxy-3-oxohexanoate. The reaction mixture was stirred at the temperature specified in Table 3. The automatic titrator maintained the pH at 7 by the addition of 4N NaOH, which was continuously recorded. Reaction progress was monitored by the rate and cumulative addition of the base and periodic sampling of the reaction mixture for extraction and analysis by the method of Example 4. After 22 hours, the reaction mixture was extracted twice with

10 mL ethyl acetate twice. The combined organic extract was filtered through a short pad of diatomaceous earth and the solvent was removed by rotary evaporation under vacuum.

Analysis of the residual oil by the method of Example 5 showed the product t-butyl 6-cyano-(3R,5R)-dihydroxyhexanoate from each such reaction reported Table 3 having >99.99% diastereopurity. (No other diastereomers was detectable.)

[0279] Table 3 gives the SEQ ID NOS. corresponding to the ketoreductase powder, the number of amino acid mutations from the wild-type ketoreductase YDL, the amount of ketoreductase powder used, the temperature of the reaction, and the conversion of t-butyl 6-cyano-(5R)-hydroxy-3-oxohexanoate to t-butyl 6-cyano-(3R,5R)-dihydroxyhexanoate reached at the specified cumulative reaction time.

Table 3: Activities of YDL and engineered ketoreductases derived from YDL.						
ketoreductase SEQ ID NO.	mutations from YDL	ketoreductase amount (mg)	temperature (°C)	conversion (%)		
				at 3 hours	at 17 hours	at 22 hours
2(YDL)	0	30	22	29	50	75
2(YDL)	0	30	30	25	25	25
154	7	30	30	43	78	78
312	11	30	30	40	90	>99
316	9	10	30	33	92	96

[0280] This Example illustrates, by comparisons of the ketoreductase amounts, reaction times, and conversions in Table 3 engineered ketoreductases derived from the wild-type ketoreductase YDL providing improved stability compared to YDL. While in the reaction at 22 °C, YDL retained activity and the reaction reached 75% conversion in 22 hours, in the reaction at 30 °C, YDL lost all activity within 3 hours reaching only 25% conversion. The engineered ketoreductase having the amino acid sequence SEQ ID NO. 156 is partially improved in stability; it retained beyond 3 hours at 30 °C, but lost all activity within 17 hours, having reached 78% conversion. The engineered ketoreductase having the amino acid sequence SEQ ID NO. 312 retained activity beyond 17 hours at 30°C and reached essentially complete conversion within 22 hours.

- 7.15 Example 15: Improved Activity and Diastereoselectivity of Engineered Ketoreductases Derived from Wild-type YDL for the Reduction of t-butyl 6-chloro-(5S)-hydroxy-3-oxohexanoate to t-butyl 6-chloro-(3R,5S)-dihydroxyhexanoate.

[0281] To a 50 mL three-neck vessel equipped with a PTFE-coated magnetic stirring bar and a pH electrode connected to an automatic titrator for pH-controlled addition of base on-demand via a feeding tube into the vessel, was charged 21 mL 100 mM triethanolamine (chloride) buffer, pH 7, 0.5 g glucose, 2 mL of the same buffer containing 10 mg of ketoreductase powder comprising the ketoreductase specified by SEQ ID NO. in Table 4, 10 mg glucose dehydrogenase powder, 2.0 mg NAD or NaNADP, and lastly 0.3 g t-butyl 6-chloro-(5S)-hydroxy-3-oxohexanoate. The reaction mixture was stirred at 22°C. The automatic titrator maintained the pH at 6.9 by the addition of 4N NaOH, which was continuously recorded. Reaction progress was monitored by the rate and cumulative addition of the base and periodic sampling of the reaction mixture for extraction and analysis by the method of Example 4. After the reaction time specified in Table 4, the reaction mixture was extracted twice with 10 mL ethyl acetate twice. The combined organic extract was filtered through diatomaceous earth and the solvent was removed by rotary evaporation under vacuum to give 0.2 g residual oil.

[0282] Diastereopurity of the t-butyl 6-chloro-(3R,5S)-dihydroxyhexanoate product in the residual oil was determined by the method of Example 7. The (3R,5S)-diol is a *syn* diastereomer. (The convention for labeling the 5-position R or S is reversed between 6-cyanomethyl and 6-chloromethyl.)

[0283] Table 4 gives the SEQ ID NOS. corresponding to the ketoreductase powder, the number of amino acid mutations from the wild-type ketoreductase YDL, the amount of ketoreductase powder used, the cofactor used, the reaction time, the conversion of t-butyl 6-chloro-(5S)-hydroxy-3-oxohexanoate, and the diastereopurity of the t-butyl 6-chloro-(3R,5S)-dihydroxyhexanoate product.

[0284] This Example illustrates an engineered ketoreductases derived from the wild-type ketoreductase YDL providing improved activity and improved diastereoselectivity compared to ketoreductase YDL and the use of such engineered ketoreductases for the preparation of t-butyl 6-chloro-(3R,5S)-dihydroxyhexanoate.

Table 4: Activities and stereoselectivities of YDL and engineered keto-reductases derived from YDL to produce t-butyl 6-chloro-(3R,5S)-dihydroxyhexanoate.					
cofactor	ketoreductase SEQ ID NO.	mutations from YDL	reaction time (h)	conversion (%)	d.e.(%) (3R,5S)
NADP	2(YDL)	0	20	37	97.3
	326	10	4	99.8	99.2
	328	11	4	99.6	99.4
NAD	2(YDL)	0	20	28	98.9
	326	10	5	99.5	99.8
	328	11	20	98.5	99.6

7.16 Example 16: Reduction of t-butyl 6-cyano-(5R)-hydroxy-3-oxohexanoate t-butyl 6-cyano-(3R,5R)-dihydroxyhexanoate by an Engineered Ketoreductase using Isopropanol and a Secondary Alcohol Dehydrogenase for Cofactor Regeneration.

[0285] To a reaction mixture of 2 mL 100mM triethanolamine (chloride) buffer, pH 7.2, containing 2 mM MgSO₄, 360 mg t-butyl 6-cyano-(5R)-hydroxy-3-oxohexanoate, and 200 µL isopropanol, were added 30 mg ketoreductase powder comprising the engineered ketoreductase having the amino acid sequence of SEQ ID NO. 330, secondary alcohol dehydrogenase powder comprising an engineered secondary alcohol dehydrogenase derived from ADH-LK and having activity to oxidize isopropanol to acetone, and 5 mg NaNADP. The reaction mixture was stirred at room temperature for 1 hour, then extracted with 1 mL ethyl acetate. After centrifugation, the organic phase was separated and the solvent was removed by rotary evaporation to leave a nonvolatile oil. The nonvolatile oil was analyzed by the methods of Examples 4 and 7. The t-butyl 6-cyano-(5R)-hydroxy-3-oxohexanoate was 100% converted to t-butyl 6-cyano-(3R,5R)-dihydroxyhexanoate with >99.9% d.e. (=>99.95% diastereoselectivity).

[0286] This Example illustrates the reduction of the 3-oxo group of an enantiomer of a 5-hydroxy-3-oxohexanoate ester to yield the corresponding *syn* 3,5-dihydroxyhexanoate ester using an engineered ketoreductase in combination with a cofactor regeneration system comprising a secondary alcohol (isopropanol) and a secondary alcohol dehydrogenase.

7.17 Example 17: Preparation of t-butyl 6-cyano-(3R,5R)-dihydroxyhexanoate (a compound of structural formula IIa).

[0287] To a 100 mL three-neck flask equipped with a PTFE-coated magnetic stirring bar and a pH electrode connected to an automatic titrator for pH-controlled addition of base on-

demand via a feeding tube into the flask, was charged 19 mL 100 mM triethanolamine (chloride) buffer, pH 7, 8.68 g glucose, 100 mg ketoreductase powder comprising the engineered ketoreductase having the amino acid sequence SEQ ID NO. 316, 40 mg glucose dehydrogenase powder, 6 mg NaNADP, and lastly 12 g t-butyl 6-cyano-(5R)-hydroxy-3-oxohexanoate. The reaction mixture was stirred at 22°C. The automatic titrator maintained the pH at 6.9 by the addition of 4N NaOH, which was continuously recorded. After 22 hours, 8.9 ml 4 N NaOH had been consumed, and an extract of a sample analyzed by the method of Example 4 showed >99% conversion. The reaction mixture was filtered through diatomaceous earth and 20 mL ethyl acetate was added through the diatomaceous earth. The aqueous phase was separated and extracted with 20 mL ethyl acetate. The solvent was removed from the combined organic extracts by rotary evaporation under vacuum to obtain 9.80 g crude t-butyl 6-cyano-(3R,5R)-dihydroxyhexanoate as an oil.

[0288] This Example illustrates the preparation and recovery of a *syn* 3,5-dihydroxyhexanoate ester using an engineered ketoreductase by the method of the invention.

7.18 Example 18: Preparation of t-butyl (6R)-cyanomethyl-2,2-dimethyl-1,3-dioxane-(4R)-acetate (a compound of structural formula IVa).

[0289] To the 9.80 g crude t-butyl 6-cyano-(3R,5R)-dihydroxyhexanoate obtained in Example 17 was added 26 mL 2,2-dimethoxypropane and 260 μ L methanesulfonic acid. The mixture was stirred at for 2 hours at 22°C. After addition of 25 mL 5% (half saturated) aqueous sodium bicarbonate, the pH of the aqueous phase was 7.5. The mixture was extracted with 52 mL heptane, and the separated organic phase was extracted with 25 mL 5% aqueous sodium bicarbonate. The solvents were removed from the organic phase by rotary evaporation under vacuum. The residue was taken up in 70 mL heptane with mild heating (~45°C), cooled and maintained at room temperature for 30 minutes, then cooled maintained at 0°C to complete the crystallization. Filtration and drying yielded at 8.1 g t-butyl (6R)-cyanomethyl-2,2-dimethyl-1,3-dioxane-(4R)-acetate as a slightly yellow solid. Analysis by the method of Example 6 showed 97.8 area % purity and no detectable (4S,6R) diastereomer.

[0290] This Example illustrates the preparation and recovery of a protected *syn* dihydroxy hexanoate ester from a *syn* 3,5-dihydroxyhexanoate ester prepared by the method of the invention.

7.19 Example 19: Preparation of t-butyl 6-cyano-(3R,5R)-dihydroxyhexanoate.

[0291] To a jacketed 3 L three-neck flask equipped with a PTFE-coated magnetic stirring bar, an addition funnel, and a pH electrode connected to an automatic titrator for pH-controlled addition of base on-demand via a feeding tube into the flask, was charged 6.36 g triethanolamine and 427 mL water. The pH of the solution was adjusted to 6.9 by addition of 3.85 g concentrated hydrochloric acid. 195 g D-glucose, 0.90 g glucose dehydrogenase powder, 2.25 g ketoreductase powder comprising the engineered ketoreductase having the amino acid sequence SEQ ID NO. 316, and 0.135 g NaNADP were added. With stirring at 22 °C and the automatic titrator prepared to provide 4N NaOH on demand, 270 g t-butyl 6-cyano-(5R)-hydroxy-3-oxohexanoate was added from the addition funnel. The automatic titrator maintained the pH at 6.9 by the addition of 4N NaOH, which was continuously recorded. After 22 hours, 196.7 mL 4 N NaOH had been consumed, and an extract of a sample analyzed by the method of Example 4 showed >99% conversion. 450 mL ethyl acetate was added and the mixture was filtered through diatomaceous earth. The aqueous phase was separated and extracted with 450 mL ethyl acetate. The solvent was removed from the combined organic extracts by rotary evaporation under vacuum to obtain 232 g crude t-butyl 6-cyano-(3R,5R)-dihydroxyhexanoate as an oil.

[0292] This Example illustrates a larger scale preparation and recovery of a *syn* 3,5-dihydroxyhexanoate ester using an engineered ketoreductase by the method of the invention.

7.20 Example 20: Reduction of t-butyl 6-cyano-(5S)-hydroxy-3-oxohexanoate.

[0293] The S-enantiomer of t-butyl 6-cyano-5-hydroxy-3-oxohexanoate was prepared from ethyl 4-cyano-(3S)-hydroxybutyrate (98% e.e.) following a procedure analogous to the preparation of the R-enantiomer from ethyl 4-cyano-(3S)-hydroxybutyrate described in Example 3.

[0294] To a 25 mL three-neck vessel equipped with a PTFE-coated magnetic stirring bar and a pH electrode connected to an automatic titrator for pH-controlled addition of base on-demand via a feeding tube into the vessel, was charged 20 mL 100 mM triethanolamine (chloride) buffer, pH 7, 1.80 g glucose, 9 mg glucose dehydrogenase powder, 30 mg

ketoreductase powder comprising the engineered ketoreductase having the amino acid sequence SEQ ID NO. 316, 2.5 mg NaNADP, and lastly 3 g t-butyl 6-cyano-(5S)-hydroxy-3-oxohexanoate. The reaction mixture was stirred at 22°C. The automatic titrator maintained the pH at 7 by the addition of 4N NaOH, which was continuously recorded. Reaction progress was monitored by the rate and cumulative addition of the base and periodic sampling of the reaction mixture for extraction and analysis by the method of Example 4. After 38 hours, the conversion was 47%. The reaction was extracted with twice with 10 mL ethyl acetate. The combined organic extract was filtered through diatomaceous earth and the solvent was removed by rotary evaporation under vacuum to leave an oil.

[0295] Crude t-butyl 6-cyanomethyl-2,2 dimethyl-1,3-dioxane-4-acetate was obtained from the oil (Example 7) and analyzed by the method of Example 6, showing 95.3% d.e. (4R,6S) diastereomer, corresponding to the ((3R,5S) diastereomer of the diol product of the reduction reaction. (Note: The (4R,6S) diastereomer has the same retention time as its (4S,6R) enantiomer, and the (4S,6S) diastereomer has the same retention time as its (4R,6R) enantiomer.)

[0296] When the engineered ketoreductase of this example is used to reduce the R-enantiomer of t-butyl 6-cyano-5-hydroxy-3-oxohexanoate, it provides the *syn* (3R,5R) diol in essentially perfect diastereoselectivity (see Examples 13, 14, and FIG. 6 and FIG. 7) This example illustrates that it is also 3R-selective when used to reduce the 5S-enantiomer of t-butyl 6-cyano-5-hydroxy-3-oxohexanoate.

7.21 Example 21: Reduction of a 97% 5R, 3% 5S mixture of enantiomers of t-butyl 6-cyano-5-hydroxy-3-oxohexanoate (94% e.e.).

[0297] The procedure was identical to the preceding Example with the exception that 2.91g t-butyl 6-cyano-(5R)-hydroxy-3-oxohexanoate and 0.09g t-butyl 6-cyano-(5S)-hydroxy-3-oxohexanoate were added to the reaction. The reaction reached 97% conversion in 20 hours, after which point the product oil was recovered as in the preceding example.

[0298] Crude t-butyl (4,6)-6-cyanomethyl-2,2 dimethyl-1,3-dioxane-4-acetate was obtained from the oil (Example 7) and analyzed by GC/MS by the method of Example 6, showing a mixture of 99.73% (4R, 6R) diastereomer, corresponding to the *syn*-(3R,5R) diastereomer of

of the diol (*i.e.*, 99.46% d.e.).

[0299] In combination with the preceding Example, this Example illustrates an engineered ketoreductase having stereospecificity for reduction of the R-enantiomer of t-butyl 6-cyano-5-hydroxy-3-oxohexanoate over the S-enantiomer. The stereopurity at the 5-position of the (3R,5)-diol (and the 6-position of the (4R,6)-dioxane derived therefrom) is substantially upgraded compared to that of the 5-hydroxy-3-oxohexanoate substrate, 99.46% d.e. vs. 94% e.e.. The engineered ketoreductase reacted less than one tenth of the 3% S-substrate added to the reaction, while reacting essentially all of the 97% R-substrate. Thus, engineered ketoreductases of the present disclosure can provide a higher degree of stereopurity in the *syn*-3,5-dihydroxyhexanoate product when the 5-hydroxy-3-oxohexanoate substrate is of lower stereopurity. Further, when the 5-hydroxy-3-oxohexanoate substrate is prepared from a 3-hydroxybutyrate ester, as exemplified in Example 3, a higher degree of stereopurity in the *syn*-3,5-dihydroxyhexanoate product can be obtained, in net, from 3-hydroxybutyrate ester of lower stereopurity.

7.22 Example 22: Diastereopurity of t-butyl 6-cyano-(3R,5R)-dihydroxyhexanoate prepared by the method of the invention.

[0300] Crude t-butyl 6-cyano-(3R,5R)-dihydroxyhexanoate was prepared as an oil by the method of Example 17. A sample of the oil was dissolved at 1.0 mg/mL in 9 % acetonitrile in water and analyzed by the LC/MS/MS method of Example 5. The chromatogram is shown, blown up in scale in FIG. 6, upper panel. No diastereomer of t-butyl 6-cyano-(3R,5R)-dihydroxyhexanoate was detected above 0.005%.

[0301] For comparison, a solution of t-butyl 6-cyano-(3R,5R)-dihydroxyhexanoate was prepared from crystalline t-butyl (6R)-(2-cyanoethyl)-2,2-dimethyl-1,3-dioxane-(4R)-acetate obtained from a commercial source (Aldrich Cat# 53,901-5), containing 0.1% of the (4S,6R) diastereomer (analyzed by the method of Example 6; see Example 23). 250 mg of the commercial t-butyl (6R)-(2-cyanoethyl)-2,2-dimethyl-1,3-dioxane-(4R)-acetate was suspended in 2 mL 1:1 methanol:water containing 200 μ L 1N HCl. The mixture was stirred for 16 hours at room temperature. 500 μ L saturated aqueous sodium bicarbonate and 5 mL of ethyl acetate were added. The organic phase was separated and solvents were removed by rotary evaporation under vacuum to yield 187 mg t-butyl 6-cyano-(3R,5R)-dihydroxyhexanoate as a slightly yellow oil.

[0302] A sample of this oil was dissolved at 1.0 mg/mL in 9 % acetonitrile in water and also analyzed by the LC/MS/MS method of Example 5. The chromatogram is shown, blown up in scale, in FIG. 6, lower panel. The chromatogram shows the peak for the 0.1% (3S,5R) diastereomer of t-butyl 6-cyano-3,5-dihydroxyhexanoate resulting from the 0.1% of the (4S,6R) diastereomer in the commercial t-butyl (6R)-(2-cyanoethyl)-2,2-dimethyl-1,3-dioxane-(4R)-acetate.

[0303] This example, by comparison of the upper and lower chromatograms in FIG. 6, illustrates the process of the invention providing a substantially diastereomerically pure *syn* 3,5-dihydroxyhexanoate compound.

7.23 Example 23: Diastereopurity of uncrystallized t-butyl (6R)-(2-cyanoethyl)-2,2-dimethyl-1,3-dioxane-(4R)-acetate prepared by the method of the invention.

[0304] Crude t-butyl 6-cyano-(5R)-hydroxy-3-oxohexanoate prepared from ethyl 4-cyano-(3R)-hydroxybutyrate of >99.9% e.e. in Example 3 was converted to t-butyl (6R)-(2-cyanoethyl)-2,2-dimethyl-1,3-dioxane-(4R)-acetate, which was analyzed for diastereopurity by GC/MS prior to crystallization.

[0305] To a 100 mL three-neck flask equipped with a PTFE-coated magnetic stirring bar and a pH electrode connected to an automatic titrator for pH-controlled addition of base on-demand via a feeding tube into the flask, was charged 18 mL 100 mM triethanolamine (chloride) buffer, pH 7.0, 12 g crude t-butyl 6-cyano-(5R)-hydroxy-3-oxohexanoate, and 7.99 g glucose. The pH of the solution was readjusted to 7.0 with 0.26 mL 4N NaOH. 1 mL of the same buffer containing 200 mg ketoreductase powder comprising the engineered ketoreductase having the amino acid sequence SEQ ID NO. 316, 15 mg glucose dehydrogenase powder, and 5 mg NaNADP was added and the reaction mixture was stirred at 22°C. The automatic titrator maintained the pH at 6.9 by the addition of 4N NaOH, which was continuously recorded. An additional 15 mg glucose dehydrogenase powder and 1 g glucose were added after 4.6 hours and an additional 15 mg glucose dehydrogenase powder and 1.5 mg NaNADP were added after 7 hours. After a total of 12 hours 9.04 ml 4 N NaOH had been consumed, and an extract of a sample analyzed by the method of Example 4 showed 99.3% conversion. 2.5 g diatomaceous earth was added to the reaction mixture, which was then extracted three times with 50 mL ethyl acetate. The solvent was removed from the

combined organic extracts by rotary evaporation under vacuum to obtain 10.40 g crude t-butyl 6-cyano-(3R,5R)-dihydroxyhexanoate as an oil.

[0306] To the crude t-butyl 6-cyano-(3R,5R)-dihydroxyhexanoate was added 22 mL 2,2-dimethoxypropane and 100 μ L methanesulfonic acid. The mixture was stirred at for 2 hours at room temperature. After addition of 5 mL saturated aqueous sodium bicarbonate, the pH of the aqueous phase was 8.0. The mixture was extracted with 60 mL hexane, and the solvent was removed from the extract by rotary evaporation under vacuum to leave a golden oil comprising t-butyl (6R)-(2-cyanoethyl)-2,2-dimethyl-1,3-dioxane-(4R)-acetate.

[0307] A sample of the oil was dissolved in ethyl acetate to 5 mg/mL, which was analyzed by the following GC/MS method:

[0308] Column: HP5MS (0.25mm i.d., 25 μ m df, 30m)

Carrier gas: Helium, 9.44 psi, 0.7mL/minute.

Oven: 50°C for 1 min, then 30 °C/min to 220 °C, then hold at 220 °C for 3 min.

Retention Times: (4S,6R) 7.9 min.; (4R, 6R) 8.0 min.

Detection: single ion monitoring, m/z 198.

[0309] The GC/MS analysis showed the t-butyl (6R)-(2-cyanoethyl)-2,2-dimethyl-1,3-dioxane-(4R)-acetate oil to be substantially diastereomerically pure. For comparison a sample of commercially obtained (Aldrich, catalog no. 53,901-5), crystalline t-butyl (6R)-(2-cyanoethyl)-2,2-dimethyl-1,3-dioxane-(4R)-acetate was dissolved in ethyl acetate to 5 mg/mL, and likewise analyzed, showing 0.10% of the (4S,6R) diastereomer. FIG. 7 shows the overlapped GC/MS chromatograms of the oil and the crystalline t-butyl (6R)-(2-cyanoethyl)-2,2-dimethyl-1,3-dioxane-(4R)-acetate.

[0310] The oil was then dissolved in 17 mL hexane and 50°C, and the solution was cooled to 0°C for crystallization. Filtration and drying in air yielded 8.1 g crystalline t-butyl (6R)-(2-cyanoethyl)-2,2-dimethyl-1,3-dioxane-(4R)-acetate of 98.7 area % chemical purity.

[0311] This example illustrates the process of the invention providing a substantially diastereomerically pure protected *syn* 3,5-dihydroxyhexanoate compound without any diastereomeric purification, for example, by crystallization.

7.24 Example 24: Preparation of t-butyl (6R)-(2-aminoethyl)-2,2-dimethyl-1,3-dioxane-(4R)-acetate (Formula V).

[0312] t-butyl (6R)-(2-cyanoethyl)-2,2-dimethyl-1,3-dioxane-(4R)-acetate, such as prepared in Examples 18 and 23, is converted to the title compound using the methodology disclosed in U.S. Pat. No. 5,003,080 at column 49, lines 16-43, which is incorporated herein by reference. In particular, a solution of t-butyl (6R)-(2-cyanoethyl)-2,2-dimethyl-1,3-dioxane-(4R)-acetate, 5.63 g (0.048 mol), in 100 mL of methanol saturated with gaseous ammonia is treated with 0.5 g of Raney nickel #30 and hydrogen gas in a shaker at 50 psi and 40°C. After 16 hours, thin layer chromatography indicates that no starting nitrile present. The suspension is cooled, filtered through a filter aid, and concentrated to an oil. This crude oil is purified by flash chromatography on silica gel with 30:20:1 (ethyl acetate:methanol:ammonium hydroxide) as eluent to give 4.93 g of the titled compound: t-butyl (6R)-(2-aminoethyl)-2,2-dimethyl-1,3-dioxane-(4R)-acetate of Formula V (98.2 area %), as a clear oil with acceptable IR, NMR, C-NMR and MS spectra.

7.25 Example 25: Preparation of t-butyl (6R)-[2[2-(fluorophenyl)-5-(1-methylethyl)-3-phenyl-4-[(phenylamino)carbonyl]-1H-pyrrol-1-yl]ethyl]-2,2-dimethyl-1,3-dioxane-(4R)-acetate (Formula VI).

[0313] t-butyl (6R)-(2-aminoethyl)-2,2-dimethyl-1,3-dioxane-(4R)-acetate, such as prepared in Example 24, is converted to the title compound using the methodology disclosed in U.S. Pat. No. 5,003,080 at column 49, lines 43-60, which is incorporated herein by reference. In particular, a solution of t-butyl (6R)-(2-aminoethyl)-2,2-dimethyl-1,3-dioxane-(4R)-acetate (formula IV), 1.36 g (4.97 mol), and ($\pm$)-4-fluoro- α -[2-methyl-1-oxopropyl]- γ -oxo-N, β -diphenylbenzenebutaneamide (formula V), which is a mixture of [R-(R',R')], [R-(R',S')], [S-(R',R')] and [S-R',S')] isomers, 1.60 g (3.83 mol), in 50 mL of heptane:toluene (9:1) is heated at reflux for 24 hours. The solution is cooled slightly and 15 mL of 2-propanol added. The mixture is allowed to cool to 25°C. and filtered to give 1.86 g of the titled compound: t-butyl (6R)-[2[2-(fluorophenyl)-5-(1-methylethyl)-3-phenyl-4-[(phenylamino)carbonyl]-1H-pyrrol-1-yl]ethyl]-2,2-dimethyl-1,3-dioxane-(4R)-acetate of formula VI, as a yellow solid with acceptable NMR spectra.

- 7.26 Example 26: Preparation of (2R-trans)-5-(4-fluorophenyl)-2-(1-methylethyl)-N,4-diphenyl-1-[2-(tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl)ethyl]-1H-pyrrole-3-carboxamide (a.k.a. atorvastatin lactone) (Formula VII).

[0314] t-butyl (6R)-[2[2-(fluorophenyl)-5-(-(1-methylethyl)-3-phenyl-4-[(phenylamino)carbonyl]-1H-pyrrol-1-yl)ethyl]-2,2-dimethyl-1,3-dioxane-(4R)-acetate, such as prepared in Example 25, is converted to the title compound using the methodology disclosed in U.S. Pat. No. 5,003,080 at col. 50, lines 4-30, which is incorporated herein by reference. In particular, 4.37 g (6.68 mol) of t-butyl (6R)-[2[2-(fluorophenyl)-5-(-(1-methylethyl)-3-phenyl-4-[(phenylamino)carbonyl]-1H-pyrrol-1-yl)ethyl]-2,2-dimethyl-1,3-dioxane-(4R)-acetate is dissolved in 200 mL of tetrahydrofuran and 15 mL of 10% hydrochloric acid solution is added, and the solution is stirred for 15 hours. To this solution is added sodium hydroxide (3.6 g) and the mixture is stirred for 30 hours. The reaction is stopped by adding 150 mL of water, 90 mL of hexane, and separating the layers. The aqueous layer is acidified with dilute hydrochloric acid solution, stirred for three hours and extracted with 150 mL of ethyl acetate. A drop of concentrated hydrochloric acid is added to the ethyl acetate solution and the solution is allowed to stand 18 hours. The solution is concentrated *in vacuo* and the concentrate is redissolved in 50 mL of ethyl acetate and treated with one drop of concentrated hydrochloric acid. The solution is stirred two hours, concentrated *in vacuo*, and dissolved in 3.0 mL of toluene. The titled compound, (2R-trans)-5-(4-fluorophenyl)-2-(1-methyl-ethyl)-N,4-diphenyl-1-[2-(tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl)ethyl]-1H-pyrrole-3-carboxamide (3.01 g) of Formula VII, which is also known as atorvastatin lactone, is isolated in two crops.

- 7.27 Example 27: Preparation of [R-(R*,R*)]-2-(4-fluorophenyl)- β - δ -dihydroxy-5-(1-methylethyl)-3-phenyl-4-[(phenylamino)carbonyl]-1H-pyrrole-1-heptanoic acid, calcium salt (2:1) of Formula VIII.

[0315] (2R-trans)-5-(4-fluorophenyl)-2-(1-methylethyl)-N,4-diphenyl-1-[2-(tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl)ethyl]-1H-pyrrole-3-carboxamide, such as prepared in Example 26, is converted to the title compound of Formula VIII using the methodology disclosed in Examples 1A or 1B of U.S. Pat. 5,969,156, entitled "Crystalline [R-(R*,R*)]-2-(4-fluorophenyl)- β , δ -dihydroxy-5-(1-methylethyl)-3-phenyl-4-[(phenylamino)carbonyl]-1H-pyrrole-1-heptanoic acid hemi calcium salt (atorvastatin)," which issued on 10/19/99 and which examples are incorporated herein by reference. The title compound is well known

under the generic name atorvastatin, hemi calcium salt and the brand name LIPITOR®.

Preparation of the calcium salt from the lactone of Example 26 is disclosed in Example 10 of U.S. Pat. 5,273,995, which is incorporated herein by reference.

i. Sodium Salt

[0316] In particular, dissolve one mole of the lactone (540.6 g) from Example 26 in 5 L of methanol. After dissolution, add 1 L of H₂O. While stirring, add 0.98 equivalents NaOH and follow the reaction by HPLC until 2% or less lactone and methyl ester of the diol acid remains. An excess of NaOH is not used because Ca(OH)₂ can form upon the addition of CaCl₂ in a subsequent step. Upon hydrolysis of the lactone, [R-(R*,R*)]-2-(4-fluorophenyl)-β-δ-dihydroxy-5-(1-methylethyl)-3-phenyl-4-[(phenylamino)carbonyl]-1H-pyrrole-1-heptanoic acid, sodium salt (atorvastatin, sodium salt) is formed.

ii. Calcium Salt

[0317] Upon completion of hydrolysis, add 10 L H₂O, then wash at least two times with a 1:1 mixture of EtOAc/hexane. Each wash should contain 10 L each of EtOAc/hexane. If sodium salt is pure, add 15 L of methanol. If it is impure and/or contains color, add 100 g of G-60 charcoal, stir for two hours, filter over supercel and then wash with 15 L MeOH. Perform an analysis on the reaction mixture by HPLC to determine the exact amount of the sodium salt of atorvastatin that is in the aqueous methanol solution.

[0318] Dissolve 1 equivalent or slight excess of CaCl₂·2H₂O (73.5 g) in 20 L H₂O. Heat both the CaCl₂ solution and the aqueous methanol solution to 60°C. Add the CaCl₂ solution slowly, with high agitation to the 60°C aqueous methanol solution of atorvastatin, sodium salt. After complete addition, cool the mixture slowly to 15°C and filter the precipitating calcium salt of formula VIII. Wash the filter cake with 5 L H₂O. Dry at 50°C in a vacuum oven.

The calcium salt from the dried filter cake can be recrystallized by dissolving in 4 L of EtOAc (50° C), filtering over Supercel®, washing the filtrate with 1 L EtOAc (50° C), then adding 3 L of a nonpolar solvent such as hexane to the 50°C EtOAc solution. The resulting crystals of formula VIII are then dried by air or with heating.

11.5 Example 28: Production of Ketoreductases; Fermentation Procedure.

[0319] In an aerated agitated 15L fermenter, 6.0L of growth medium containing 0.88 g/L ammonium sulfate, 0.98 g/L of sodium citrate; 12.5 g/L of dipotassium hydrogen phosphate

trihydrate, 6.25g/L of potassium dihydrogen phosphate, 6.2 g/L of Tastone-154 yeast extract, 0.083 g/L ferric ammonium citrate, and 8.3 ml/L of a trace element solution containing 2 g/L of calcium chloride dihydrate, 2.2 g/L of zinc sulfate septahydrate, 0.5 g/L manganese sulfate monohydrate, 1 g/L cuprous sulfate heptahydrate, 0.1 g/L ammonium molybdate tetrahydrate and 0.02 g/L sodium tetraborate decahydrate was brought to a temperature of 30. The fermenter was inoculated with a late exponential culture of *E. coli* W3110, containing a plasmid with the ketoreductase gene of interest, grown in a shake flask as described in Example 3 to a starting OD₆₀₀ of 0.5 to 2.0. The fermenter was agitated at 500-1500 rpm and air was supplied to the fermentation vessel at 1.0-15.0 L/min to maintain a dissolved oxygen level of 30% saturation or greater. The pH of the culture was controlled at 7.0 by addition of 20% v/v ammonium hydroxide. Growth of the culture was maintained by the addition of a feed solution containing 500g/L cerelose, 12 g/L ammonium chloride and 10.4 g/L magnesium sulfate heptahydrate. After the culture reached an OD₆₀₀ of 50, the expression of ketoreductase was induced by the addition of isopropyl-b-D-thiogalactoside (IPTG) to a final concentration of 1mM. The culture was grown for another 14 hours. The culture was then chilled to 4°C and maintained at 4°C until harvested. Cells were harvested by centrifugation at 5000G for 40 minutes in a Sorval RC12BP centrifuge at 4°C. Harvested cells were used directly in the following downstream recovery process or were stored at 4°C until such use.

[0320] The cell pellet was resuspended in 2 volumes of 100 mM triethanolamine (chloride) buffer, pH 6.8, at 4 °C to each volume of wet cell paste. The intracellular ketoreductase was released from the cells by passing the suspension through a homogenizer fitted with a two-stage homogenizing valve assembly using a pressure of 12000 psig. The cell homogenate was cooled to 4°C immediately after disruption. A solution of 10% w/v polyethyleneimine, pH 7.2, was added to the lysate to a final concentration of 0.5% w/v and stirred for 30 minutes. The resulting suspension was clarified by centrifugation at 5000G in a standard laboratory centrifuge for 30 minutes. The clear supernatant was decanted and concentrated ten fold using a cellulose ultrafiltration membrane with a molecular weight cut off of 30Kd. The final concentrate was dispensed into shallow containers, frozen at -20°C and lyophilized to powder. The ketoreductase powder was stored at -80°C.

[0321] This Example illustrates the production of ketoreductase powders by a practical scaleable procedure.

[0322] All publications, patents, patent applications and other documents cited in this application are hereby incorporated by reference in their entireties for all purposes to the same extent as if each individual publication, patent, patent application or other document were individually indicated to be incorporated by reference for all purposes.

[0323] While various specific embodiments have been illustrated and described, it will be appreciated that various changes can be made without departing from the spirit and scope of the invention(s).

WHAT IS CLAIMED IS:

1. A engineered ketoreductase enzyme derived from the wild-type ketoreductase enzyme of *Saccharomyces cerevisiae* capable of stereoselectively reducing the 3-oxo group of a 5-hydroxy-3-oxohexanoate to yield the corresponding *syn* 3,5-dihydroxyhexanoate ester, which enzyme has a specific activity that is at least about 1.5-300 times or more greater than the specific activity of the wild-type ketoreductase enzyme of SEQ ID NO:2 and comprises an amino acid sequence that is : (a) at least 90% identical to SEQ ID NO:2, and (b) has one or more of the following characteristics:

- X⁶ is a polar or acidic amino acid residue;
- X²⁷ is an aliphatic or basic amino acid residue;
- X³¹ is a hydroxyl containing or aliphatic amino acid residue;
- X³⁶ is a small amino acid residue;
- X⁴⁸ is a basic amino acid residue;
- X⁶³ is an aromatic amino acid residue;
- X⁶⁵ is a hydroxyl containing or small amino acid residue;
- X⁸⁶ is an aliphatic or hydrophobic amino acid residue;
- X¹²⁵ is an aliphatic or aromatic amino acid residue;
- X¹⁵² is a basic amino acid residue;

X^{160} is a hydroxyl containing or small amino acid residue;
 X^{165} is a polar or acidic amino acid residue;
 X^{194} is an aromatic amino acid or polar hydrophilic amino acid residue
 X^{214} is a polar hydrophilic amino acid residue;
 X^{218} is a hydroxyl containing amino acid residue;
 X^{234} is a polar hydrophilic amino acid residue;
 X^{248} is an aliphatic amino acid residue;
 X^{250} is a basic amino acid residue;
 X^{263} is a acidic or polar amino acid residue;
 X^{290} is an acidic amino acid residue;
 X^{296} is an aliphatic amino acid residue
 X^{297} is an aromatic amino acid residue;
 X^{301} is an aliphatic or hydroxyl containing or acidic or hydrophilic or basic amino acid residue; and
 X^{307} is an aromatic, a polar or a hydroxyl containing amino acid residue.

2. The engineered ketoreductase enzyme of claim 1 which includes one or more mutations selected from:

X^6 is E;
 X^{27} is A or K;
 X^{31} is S or P;
 X^{36} is V;
 X^{48} is H;
 X^{63} is W;
 X^{65} is G or S;
 X^{86} is I;
 X^{125} is L;
 X^{152} is R;

X^{160} is T or S;
 X^{165} is E;
 X^{194} is C;
 X^{214} is R or H;
 X^{218} is T;
 X^{234} is Q;
 X^{248} is I;
 X^{250} is R;
 X^{263} is E;
 X^{290} is V;
 X^{296} is I;
 X^{297} is F or W;
 X^{301} is R, K, A, V, S, T, Y, D, E, P, or Q; and
 X^{307} is H, N or S.

3. The engineered ketoreductase enzyme of claim 1 which includes one or more mutations selected from:

X^6 is E;
 X^{31} is P;
 X^{44} is D;
 X^{46} is L;
 X^{55} is V;
 X^{56} is V;
 X^{60} is T;
 X^{63} is V;
 X^{76} is M;
 X^{103} is S;
 X^{106} is I;
 X^{114} is G;
 X^{121} is I or M;

X¹⁴⁴ is R;
X¹⁴⁸ is T;
X¹⁵⁸ is H;
X¹⁶⁰ is S;
X¹⁶⁵ is E;
X²¹⁴ is R or H;
X²²³ is R or G;
X²³⁴ is Q;
X²³⁷ is N, G or Q,;
X²³⁹ is T;
X²⁵³ is A; and
X²⁶³ is E.

4. The engineered ketoreductase enzyme of claim 3 which includes one or more mutations selected from:

X⁴⁴ is D;
X⁴⁶ is L;
X⁵⁵ is V;
X⁵⁶ is V;
X⁶⁰ is T;
X⁶³ is V;
X⁷⁶ is M;
X¹⁰³ is S;
X¹⁰⁶ is I;
X¹¹⁴ is G;
X¹²¹ is I or M;
X¹⁴⁴ is R;
X¹⁴⁸ is T;
X¹⁵⁸ is H;
X²²³ is R or G;

X²³⁴ is Q;

X²³⁷ is N, G, R or Q;

X²³⁹ is T; and

X²⁵³ is A.

5. The engineered ketoreductase enzyme of **claim 1** in which the amino acid sequence corresponds to SEQ ID NO:2 and includes one or more of mutations selected from: R27A, R27K, N31S, A36V, Y48H, I63W, R65G, R65S, L86I, F125L, K152R, A160T, Y194C, A218T, V248I, K250R, E290D, L296V, Y297W, Y297F, L301K, L301R, L301A, L301S, L301E, L301P, L301Q, L301V, L301T, L301Y, L301D, Y307H, Y307N, and Y307S.

6. The engineered ketoreductase enzyme of **claim 1** in which the amino acid sequence corresponds to SEQ ID NO:2 and includes one or more mutations selected from: Q6E, N31P, A160S, Q165E, Q214H, Q214R, E234Q, and Q263E.

7. The engineered ketoreductase enzyme of **claim 1** in which the amino acid sequence corresponds to SEQ ID NO:2 and includes one or more mutations selected from: N40Y, V43L, K51E, I58V, B62Q, A73P, K79R, K152Q, K169E, F185I, Q189H, G192D, H200L, D201G, K215E, K215M, K216R, D221V, S233C, I237D, K250E, I265V, L287R, K304R, Q310R, K311E, V312S, and V312E.

8. The engineered ketoreductase enzyme of **claim 1** in which the amino acid sequence corresponds to SEQ ID NO:2 and includes mutations Q6E; R27A; N31P; I46L; L86I; L121I; F125L; A160T; Y194C; Q214R; I237N; and S239T.

9. The engineered ketoreductase enzyme of **claim 1** in which the amino acid sequence corresponds to SEQ ID NO:2 and includes mutations R27A; N31P; I63W; L121I; F125L; A160T; Y194C; Q214R; and I237N.

10. The engineered ketoreductase enzyme of **claim 1** in which the amino acid sequence is selected from the group consisting of SEQ ID NOS: 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198, 200, 202, 204, 206, 208, 210, 212, 214, 216, 218, 220, 222, 224, 226, 228, 230, 232, 234, 236, 238, 240, 242, 244, 246, 248, 250, 252, 254, 256, 258, 260, 262, 266, 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 292, 294, 296, 298, 300, 302, 304, 306, 308, 310, 312, 314, 316, 318, 320, 322, 324, 326, 328, 330, 332, 334, 336, 338, 340, 342, 344, 346, 348, 350, 352, 354, 356, 358, 360, 362, 364, and 366.

11. The engineered ketoreductase enzyme of **claim 1** in which the amino acid sequence is selected from the group consisting of SEQ ID NOS: 314, 316, and 318.

12. A polynucleotide comprising a sequence that encodes a ketoreductase enzyme according to any one of claims 1 to 11.

13. The polynucleotide of claim 12 which is selected from the group consisting of SEQ ID NOS: 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197, 199, 201, 203, 205, 207, 209, 211, 213, 215, 217, 219, 221, 223, 225, 227, 229, 231, 233, 235, 237, 239, 241, 243, 245, 247, 249, 251, 253, 255, 257, 259, 261, 263, 265, 267, 269, 271, 273, 275, 277, 279, 281, 283, 285, 287, 289, 291, 293, 295, 297, 299, 301, 303, 305, 307, 309, 311, 313, 315, 317, 319, 321, 323, 325, 327, 329, 331, 333, 335, 337, 339, 341, 343, 345, 347, 349, 351, 353, 355, 357, 359, 361, 363, and 365.

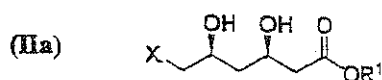
14. An expression system comprising the polynucleotide of claim 12 or 13 operably linked to a control sequence suitable for directing expression in a host cell.

15. A host cell comprising the expression system of claim 14.

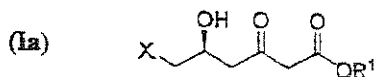
16. The host cell of claim 15 which is *E. coli*.

17. The host cell of claim 16 in which the codons comprising the expression vector have been optimized for expression in said host cell.

18. A process for preparing a syn 3,5-dihydroxyhexanoate compound according to formula (IIa):



wherein X is selected from halo, cyano and $-OR^6$, where R^6 is hydrogen or a protecting group, and R^1 is selected from (C1-C12) alkyl, (C6-C10) aryl and (C7-C12) arylalkyl, comprising stereoselectively reducing an enantiomer of a 5-hydroxy-3-oxohexanoate compound according to structural formula (Ia):



wherein X and R^1 are as defined for structural formula (IIa);

using a ketoreductase according to any one of claims 1 to 5 under conditions suitable for reducing the 3-oxo group to a 3-hydroxy group.

19. The process of claim 18 which further comprises recovering the 3,5-dihydroxyhexanoate compound according to structural formula (IIa) from the reaction mixture.

20. The process of claim 18 in which the 5-hydroxy-3-oxohexanoate compound is substantially pure in the enantiomer of structural formula (Ia).

21. The process of claim 18 which is carried out with whole cells that express the ketoreductase enzyme, or an extract or lysate of such cells.

22. The process of claim 18 in which the ketoreductase is isolated and/or purified and the enantioselective reduction reaction is carried out in the presence of a cofactor for the ketoreductase and optionally a regeneration system for the cofactor.

23. The process of claim 18 which is carried out at a temperature in the range of about 15°C to about 75°C.

24. The process of claim 18 which is carried out at a pH in the range of about pH 5 to pH 8.

25. The process of claim 18 in which the weight ratio of the 5-hydroxy-3-oxohexanoate compound of structural formula (Ia) to the ketoreductase enzyme is in the range of about 10:1 to 200:1.

26. The process of claim 18 in which X is selected from chloro, cyano and hydroxyl, and in which R¹ is a lower alkanyl or *t*-butyl.

27. The process of claim 18 which is carried out in the presence of a cofactor and optionally a cofactor regeneration system.

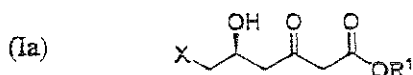
28. The process of claim 27 in which the cofactor is NADH and/or NADPH, and in which the weight ratio of the cofactor to the ketoreductase enzyme is in the range of about 10:1 to 100:1.

29. The process of claim 27 in which the cofactor regenerating system comprises glucose dehydrogenase and glucose; formate dehydrogenase and formate; or isopropanol and a secondary alcohol dehydrogenase.

30. The process of claim 29 wherein the secondary alcohol dehydrogenase is the ketoreductase.

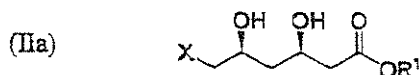
31. The process of claim 18 in which the preparation of 3,5-dihydroxyhexanoate compound is a substantially pure in the *syn* diastereomer.

32. A reaction mixture comprising a ketoreductase enzyme according to any one of claims 1 to 11, a cofactor for said ketoreductase enzyme and a substrate according to structural formula (Ia):



wherein X is selected from halo, cyano and $-OR^6$, where R^6 is hydrogen or a protecting group, and R^1 is selected from (C1-C12) alkyl, (C6-C10) aryl and (C7-C12) arylalkyl.

33. A reaction mixture comprising a ketoreductase enzyme according to any one of claims 1 to 11, a cofactor for said ketoreductase enzyme and a substrate according to structural formula (IIa):



wherein X is selected from halo, cyano and $-OR^6$, where R^6 is hydrogen or a protecting group, and R^1 is selected from (C1-C12) alkyl, (C6-C10) aryl and (C7-C12) arylalkyl.

34. The mixture of claim 32 or 33 in which the weight ratio of the 5-hydroxy-3-oxohexanoate compound of structural formula (Ia) or (IIa) to the ketoreductase enzyme is in the range of about 10:1 to 200:1.

35. The mixture of claim 32 or 33 in which X is selected from chloro, cyano and hydroxyl, and in which R^1 is a lower alkanyl or *t*-butyl.

36. The mixture of claim 32 or 33 in which the cofactor is NADH and/or NADPH, and in which the weight ratio of the cofactor to the ketoreductase enzyme is in the range of about 10:1 to 100:1.

37. The mixture of claim 32 or 33 further comprising a cofactor regeneration system.

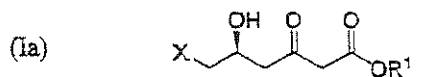
38. The mixture of claim 37 in which the cofactor regenerating system comprises glucose dehydrogenase and glucose; formate dehydrogenase and formate; or isopropanol and a secondary alcohol dehydrogenase.

39. The mixture of claim 38 wherein the secondary alcohol dehydrogenase is the ketoreductase.

40. In a method of synthesizing a statin compound that includes as one step the enantioselective reduction of a compound according to structural formula (Ia) to yield a compound

according to structural formula (IIa), the improvement comprising carrying out the enantioselective reduction of compound (Ia) to compound (IIa) with a ketoreductase enzyme according to any one of claims 1 to 11;

wherein structural formula (Ia) is:



wherein X is selected from halo, cyano and $-OR^6$, where R^6 is hydrogen or a protecting group, and R^1 is selected from (C1-C12) alkyl, (C6-C10) aryl and (C7-C12) arylalkyl; and

wherein structural formula (IIa) is:



wherein X and R^1 are defined as for structural formula (Ia).

41. The method of claim 40 in which the statin is selected from atorvastatin, rosuvastatin, and pitavastatin.

42. A process for the preparation of a protected syn 3,5-dihydroxy-3-oxohexanoate compound according to structural formula (IIIa):



wherein:

X is selected from halo, cyano and $-OR^6$, where R^6 is hydrogen or a protecting group;

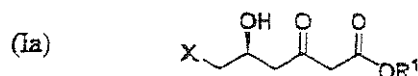
R^1 is selected from (C1-C12) alkyl, (C6-C10) aryl and (C7-C12) arylalkyl; and

each R^2 is a protecting group, or, alternatively, the R^2 groups may be taken together to form an alkylene bridge of the formula $-CR^3R^4-$, or a boronate of $-BR^5-$ wherein R^3 and R^4 are each, independently of one another, selected from hydrogen, (C1-C12) alkyl, (C6-C10) aryl and (C7-C12) arylalkyl, or alternatively, R^3 and R^4 taken together form a (C4-C10) cycloalkyl or heterocycloalkyl, and R^5 is selected from (C1-C12) alkyl, (C6-C10) aryl and (C7-C12) arylalkyl, comprising the steps of:

(i) stereoselectively reducing a 5-hydroxy-3-oxohexanoate enantiomer of structural formula

(Ia)

wherein structural formula (Ia) is:



wherein X is selected from halo, cyano and $-OR^6$, where R^6 is hydrogen or a protecting group, and R^1 is selected from (C1-C12) alkyl, (C6-C10) aryl and (C7-C12) arylalkyl;

using a ketoreductase enzyme according to any one of claims 1 to 11 under conditions suitable to reduce the 3-oxo group to a 3-hydroxy group to yield a first reaction product comprising a *syn* 3,5-dihydroxyhexanoate compound according to structural formula (IIa)

wherein structural formula (IIa) is:



wherein X and R^1 are defined as for structural formula (Ia);

and

(ii) protecting the hydroxyl groups of the *syn* 3,5-dihydroxyhexanoate compound to yield a second reaction product comprising the protected *syn* 3,5-dihydroxy-3-oxohexanoate compound according to structural formula (IIIa).

43. The process of claim 42 in which R^3 and R^4 are each methyl.
44. The process of claim 42 in which X is selected from chloro, cyano and hydroxyl.
45. The process of claim 42 in which R^1 is a lower alkyanyl.

SEQUENCE LISTING

<110> Giver, Lorraine Joan
 Newman, Lisa Marie
 Mundorff, Emily
 Huisman, Gjalte W.
 Jenne, Stephane J.
 Zhu, Jun
 Behrouzian, Behnaz
 Grate, John H.
 Lalonde, James

<120> Compositions and Methods for Producing Stereoisomerically Pure Statins and Synthetic Intermediates Therefor

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ggtttcttcc agagtcttta tgaggcatcg gttacgggtac cttattgggg cgctcgtaat 900
gaactgatcg aattgatcga tctggcgcat gctgggtattt tcgacattgc cgttgagacc 960
ttctctttgg ataatgggtc agaggcctat cgtcgcctgg ctgcgggcac actgtcaggc 1020
cgtgcggtag tcgtcccgga cctgtaatga 1050

```

<210> 6

<211> 349

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 6

```

Met Lys Ala Ile Gln Tyr Thr Arg Ile Gly Ala Glu Pro Glu Leu Thr
1           5           10           15
Glu Ile Pro Lys Pro Glu Pro Gly Pro Gly Glu Val Leu Leu Glu Val
          20           25           30
Thr Ala Ala Gly Val Cys His Ser Asp Asp Phe Ile Met Ser Leu Pro
          35           40           45
Glu Glu Gln Tyr Thr Tyr Gly Leu Pro Leu Thr Leu Gly His Glu Gly
          50           55           60
Ala Gly Lys Val Ala Ala Val Gly Glu Gly Val Glu Gly Leu Asp Ile
65           70           75           80
Gly Thr Asn Val Val Val Tyr Gly Pro Trp Gly Cys Gly Asn Cys Trp
          85           90           95
His Cys Ser Gln Gly Leu Glu Asn Tyr Cys Ser Arg Ala Gln Glu Leu
          100          105          110
Gly Ile Asn Pro Pro Gly Leu Gly Ala Pro Gly Ala Leu Ala Glu Phe
          115          120          125
Met Ile Val Asp Ser Pro Arg His Leu Val Pro Ile Gly Asp Leu Asp
          130          135          140
Pro Val Lys Thr Val Pro Leu Thr Asp Ala Gly Leu Thr Pro Tyr His
145          150          155          160
Ala Ile Lys Arg Ser Leu Pro Lys Leu Arg Gly Gly Ser Tyr Ala Val
          165          170          175
Val Ile Gly Thr Gly Gly Leu Gly His Val Ala Ile Gln Leu Leu Arg
          180          185          190
His Leu Ser Ala Ala Thr Val Ile Ala Leu Asp Val Ser Ala Asp Lys
          195          200          205
Leu Glu Leu Ala Thr Lys Val Gly Ala His Glu Val Val Leu Ser Asp
          210          215          220
Lys Asp Ala Ala Glu Asn Val Arg Lys Ile Thr Gly Ser Gln Gly Ala
225          230          235          240
Ala Leu Val Leu Asp Phe Val Gly Tyr Gln Pro Thr Ile Asp Thr Ala
          245          250          255
Met Ala Val Ala Gly Val Gly Ser Asp Val Thr Ile Val Gly Ile Gly
          260          265          270

```

Asp	Gly	Gln	Ala	His	Ala	Lys	Val	Gly	Phe	Phe	Gln	Ser	Pro	Tyr	Glu
	275						280				285				
Ala	Ser	Val	Thr	Val	Pro	Tyr	Trp	Gly	Ala	Arg	Asn	Glu	Leu	Ile	Glu
	290					295					300				
Leu	Ile	Asp	Leu	Ala	His	Ala	Gly	Ile	Phe	Asp	Ile	Ala	Val	Glu	Thr
305					310					315				320	
Phe	Ser	Leu	Asp	Asn	Gly	Ala	Glu	Ala	Tyr	Arg	Arg	Leu	Ala	Ala	Gly
			325						330					335	
Thr	Leu	Ser	Gly	Arg	Ala	Val	Val	Val	Pro	Gly	Leu				
			340					345							

<210> 7
 <211> 1050
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 7

atgaccacgg	aaaaaacggt	agtgttcgtg	tcaggcgoga	ccggttttat	tgctctgcac	60
gtggtagatg	acctgctgaa	aactggttac	aaagtaattg	gttccgggtcg	ttctcaggaa	120
aaaaatgacg	gtttgctgaa	gaagttcaag	tccaaccoga	atctgagcat	ggaaattgtg	180
gaagatattg	cggcaccaaa	cgccttcgat	aaagtattcc	agaaacatgg	taaagaaatt	240
aaagtgggcc	tgcatatcgc	gtccccgggc	catttcaaca	ctaccgattt	cgaaaaagac	300
ttactgatcc	cggcggtaaa	cggtaacaaa	tctattttgg	aagcaattaa	gaactatgcc	360
gcagacaccg	tggaaaaagt	ggttattact	tcactctgtg	ccgcgttggc	ctctccgggt	420
gatatgaaag	ataccagctt	cgtgggttaac	gaagaatcct	ggaataaaga	cacctgggaa	480
tcgtgtcagg	cgaatgctgt	gtccgcttat	tgccggttcta	aaaaattcgc	agagaaaacg	540
gcgtgggact	tcttggaaga	aaaccagagc	agcattaaat	ttactctgtc	cacgattaac	600
ccaggcttcg	tttttggtcc	gcagctgttc	gccgactcct	tgcgcaatgg	tattaactct	660
agcagtgcga	ttattgcaaa	cctgggtgtc	tataaattag	gggataactt	ctacaattat	720
agcggcccg	ttatcgacgt	ccgtgacgtt	tccaaagctc	atctgctggc	atttgagaaa	780
cctgaatgcg	ccggtcagcg	cctgtttctg	tgcgaggata	tggtctgttc	ccaggaagcc	840
ctggacattc	tgaacgaaga	atttccacag	ctgaagggca	agatcgcaac	gggccaacct	900
ggcagcggct	cgaccttcct	gactaaaaat	tggtgcaaat	gcgacaatcg	taaaactaaa	960
aacttgctgg	gcttccagtt	caacaaattc	cgcgactgca	ttgtcgatac	tgcgccocag	1020
ttgctggaag	tgcaaagcaa	aagctaatga				1050

<210> 8
 <211> 349
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 8

Met	Thr	Thr	Glu	Lys	Thr	Val	Val	Phe	Val	Ser	Gly	Ala	Thr	Gly	Phe
1				5				10					15		
Ile	Ala	Leu	His	Val	Val	Asp	Asp	Leu	Leu	Lys	Thr	Gly	Tyr	Lys	Val
			20					25					30		
Ile	Gly	Ser	Gly	Arg	Ser	Gln	Glu	Lys	Asn	Asp	Gly	Leu	Leu	Lys	Lys
		35					40					45			
Phe	Lys	Ser	Asn	Pro	Asn	Leu	Ser	Met	Glu	Ile	Val	Glu	Asp	Ile	Ala
	50					55					60				
Ala	Pro	Asn	Ala	Phe	Asp	Lys	Val	Phe	Gln	Lys	His	Gly	Lys	Glu	Ile
65					70				75					80	
Lys	Val	Val	Leu	His	Ile	Ala	Ser	Pro	Val	His	Phe	Asn	Thr	Thr	Asp

<210> 10
 <211> 313
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 10

```

Met Pro Ala Thr Leu Lys Asn Ser Ser Ala Thr Leu Lys Leu Asn Thr
1          5          10          15
Gly Ala Ser Ile Pro Val Leu Gly Phe Gly Thr Trp Arg Ser Val Asp
20          25          30
Asn Asn Gly Tyr His Ser Val Ile Ala Ala Leu Lys Ala Gly Tyr Arg
35          40          45
His Ile Asp Ala Ala Ala Ile Tyr Leu Asn Glu Glu Glu Val Gly Arg
50          55          60
Ala Ile Lys Asp Ser Gly Val Pro Arg Glu Glu Ile Phe Ile Thr Thr
65          70          75          80
Lys Leu Trp Gly Thr Glu Gln Arg Asp Pro Glu Ala Ala Leu Asn Lys
85          90          95
Ser Leu Lys Arg Leu Gly Leu Asp Tyr Val Asp Leu Tyr Leu Met His
100         105         110
Trp Pro Val Pro Leu Lys Thr Asp Arg Val Thr Asp Gly Asn Val Leu
115         120         125
Cys Ile Pro Thr Leu Glu Asp Gly Thr Val Asp Ile Asp Thr Lys Glu
130         135         140
Trp Asn Phe Ile Lys Thr Trp Glu Leu Met Gln Glu Leu Pro Lys Thr
145         150         155         160
Gly Lys Thr Lys Ala Val Gly Val Ser Asn Phe Ser Ile Asn Asn Ile
165         170         175
Lys Glu Leu Leu Glu Ser Pro Asn Asn Lys Val Val Pro Ala Thr Asn
180         185         190
Gln Ile Glu Ile His Pro Leu Leu Pro Gln Asp Glu Leu Ile Ala Phe
195         200         205
Cys Lys Glu Lys Gly Ile Val Val Glu Ala Tyr Ser Pro Phe Gly Ser
210         215         220
Ala Asn Ala Pro Leu Leu Lys Glu Gln Ala Ile Ile Asp Met Ala Lys
225         230         235         240
Lys His Gly Val Glu Pro Ala Gln Leu Ile Ile Ser Trp Ser Ile Gln
245         250         255
Arg Gly Tyr Val Val Leu Ala Lys Ser Val Asn Pro Glu Arg Ile Val
260         265         270
Ser Asn Phe Lys Ile Phe Thr Leu Pro Glu Asp Asp Phe Lys Thr Ile
275         280         285
Ser Asn Leu Ser Lys Val His Gly Thr Lys Arg Val Val Asp Met Lys
290         295         300
Trp Gly Ser Phe Pro Ile Phe Gln
305         310

```

<210> 11
 <211> 1032
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 11

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atgtctgtgt tctgtgtcagg cgcgaatggt tttattgctc agcacatcgt agatctgctg 60
ctgaaagaag attacaaagt aattggttcc gcacgttctc aggaaaaagc tgaaaatttg 120
accgaagcct tcggttaacaa cccgaaattt agcatggaag tgggtgctga tattagcaaa 180
ctggatgcct tcgatcatgt attccagaaa catggttaaag atattaaaaat cgtcctgcat 240
accgcgtccc cgttttgttt cgatattacc gattccgaac gtgacttact gatccccggc 300
gtaaacggtg tcaaaggtat tttgcacagt attaagaaat atgccgcaga cagcgtggaa 360
cgcgtggttc tgacttcac ttaacgcgcg gtatttgata tggcgaagga aaacgataag 420
agcctgacct tcaacgaaga atcctggaat ccggcgacct ggaatcgtg tcagagtgat 480
ccggtgaacg cttattgcgg ttctaaaaaa ttccgagaga aagcagcgtg ggaattcttg 540
gaagaaaacc gtgatagcgt gaaatttgag ctgacagcgg tcaaccaggt ttacgttttt 600
ggtccgcaga tgttcgataa agatgttaaa aaacacttga acaccagctg cgaactgggt 660
aactctctga tgcattctgag ccctgaagat aaaattccgg aactgttttg cgtttacatc 720
gacgtccgtg acgttgcgaa agctcatctg gttgcatttc agaaacgtga aacaatcgg 780
cagcgcctga tctgttcgga ggcacgtttc acgatgcagg acgttctgga cattctgaac 840
gaagactttc cagtactgaa gggcaatata ccggtcggca agcctggcag cggcgccacc 900
cataatactc tgggcgccac cctggacaat aaaaaaagca aaaaattgct gggcttcaaa 960
ttccgtaata tgaaagagac tattgacgat actgcgtccc agatcctgaa attogaaggt 1020
cgcatttaat ga 1032

```

<210> 12

<211> 343

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 12

```

Met Ser Val Phe Val Ser Gly Ala Asn Gly Phe Ile Ala Gln His Ile
1          5          10          15
Val Asp Leu Leu Leu Lys Glu Asp Tyr Lys Val Ile Gly Ser Ala Arg
          20          25          30
Ser Gln Glu Lys Ala Glu Asn Leu Thr Glu Ala Phe Gly Asn Asn Pro
          35          40          45
Lys Phe Ser Met Glu Val Val Pro Asp Ile Ser Lys Leu Asp Ala Phe
          50          55          60
Asp His Val Phe Gln Lys His Gly Lys Asp Ile Lys Ile Val Leu His
65          70          75          80
Thr Ala Ser Pro Phe Cys Phe Asp Ile Thr Asp Ser Glu Arg Asp Leu
          85          90          95
Leu Ile Pro Ala Val Asn Gly Val Lys Gly Ile Leu His Ser Ile Lys
          100          105          110
Lys Tyr Ala Ala Asp Ser Val Glu Arg Val Val Leu Thr Ser Ser Tyr
          115          120          125
Ala Ala Val Phe Asp Met Ala Lys Glu Asn Asp Lys Ser Leu Thr Phe
          130          135          140
Asn Glu Glu Ser Trp Asn Pro Ala Thr Trp Glu Ser Cys Gln Ser Asp
145          150          155          160
Pro Val Asn Ala Tyr Cys Gly Ser Lys Lys Phe Ala Glu Lys Ala Ala
          165          170          175
Trp Glu Phe Leu Glu Glu Asn Arg Asp Ser Val Lys Phe Glu Leu Thr
          180          185          190
Ala Val Asn Pro Val Tyr Val Phe Gly Pro Gln Met Phe Asp Lys Asp
          195          200          205
Val Lys Lys His Leu Asn Thr Ser Cys Glu Leu Val Asn Ser Leu Met
210          215          220
His Leu Ser Pro Glu Asp Lys Ile Pro Glu Leu Phe Gly Gly Tyr Ile
225          230          235          240
Asp Val Arg Asp Val Ala Lys Ala His Leu Val Ala Phe Gln Lys Arg
          245          250          255

```

Glu	Thr	Ile	Gly	Gln	Arg	Leu	Ile	Val	Ser	Glu	Ala	Arg	Phe	Thr	Met
		260						265					270		
Gln	Asp	Val	Leu	Asp	Ile	Leu	Asn	Glu	Asp	Phe	Pro	Val	Leu	Lys	Gly
	275						280					285			
Asn	Ile	Pro	Val	Gly	Lys	Pro	Gly	Ser	Gly	Ala	Thr	His	Asn	Thr	Leu
	290					295					300				
Gly	Ala	Thr	Leu	Asp	Asn	Lys	Lys	Ser	Lys	Lys	Leu	Leu	Gly	Phe	Lys
305				310					315					320	
Phe	Arg	Asn	Leu	Lys	Glu	Thr	Ile	Asp	Asp	Thr	Ala	Ser	Gln	Ile	Leu
			325					330						335	
Lys	Phe	Glu	Gly	Arg	Ile										
		340													

<210> 13
 <211> 759
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 13
 atgaccgatc gtctgaaggg caaagtagcc atcgtaaccg gcgggactct gggatatcgg 60
 ttggcaatcg ccgataaatt tgtagaggag ggtgcgaaag tagttattac tggtcgtcac 120
 gcggatgtag gtgaaaaggc cgccaaatca atcggcggca ctgatgttat tcgctttgtc 180
 cagcacgatg catccgatga agcaggctgg acgaaactgt tcgacaaccac cgaggaggca 240
 ttgggcccggt ttacgaccgt cgtgaacaat gcagggattg cagtttccaa aagcgttgaa 300
 gacactacca cggaggaatg gcgtaaactg ctgtccgtta atctggatgg tgttttttcc 360
 ggcaccpgtc tgggcattca gcgcatgaaa aataaaggct tgggcgctag catcatcaat 420
 atgagcagta ttgaggggtt cgtaggcgat ccgacgctgg gggcatacaa cgcttccaag 480
 ggggcggtac gtatcatgtc gaaaagcgca gcgctggatt gcgcaactgaa ggactacgat 540
 gtgcgtgtca acacagtaca tccgggctat atcaagaccc cgctgggtcga tgatctggaa 600
 ggtgctgagg aaatgatgtc acagcgtacg aaaaccoccta tgggcacat tggcgaaccg 660
 aatgacatcg catggatctg tgtgtacctg gcatctgacg aatcgaaatt tgcgacgggt 720
 gcagaatttg tggtcgacgg cgggtatacc gcacagtga 759

<210> 14
 <211> 252
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 14
 Met Thr Asp Arg Leu Lys Gly Lys Val Ala Ile Val Thr Gly Gly Thr
 1 5 10 15
 Leu Gly Ile Gly Leu Ala Ile Ala Asp Lys Phe Val Glu Glu Gly Ala
 20 25 30
 Lys Val Val Ile Thr Gly Arg His Ala Asp Val Gly Glu Lys Ala Ala
 35 40 45
 Lys Ser Ile Gly Gly Thr Asp Val Ile Arg Phe Val Gln His Asp Ala
 50 55 60
 Ser Asp Glu Ala Gly Trp Thr Lys Leu Phe Asp Thr Thr Glu Glu Ala
 65 70 75 80
 Phe Gly Pro Val Thr Thr Val Val Asn Asn Ala Gly Ile Ala Val Ser
 85 90 95
 Lys Ser Val Glu Asp Thr Thr Thr Glu Trp Arg Lys Leu Leu Ser
 100 105 110

Val	Asn	Leu	Asp	Gly	Val	Phe	Phe	Gly	Thr	Arg	Leu	Gly	Ile	Gln	Arg
	115						120					125			
Met	Lys	Asn	Lys	Gly	Leu	Gly	Ala	Ser	Ile	Ile	Asn	Met	Ser	Ser	Ile
	130					135					140				
Glu	Gly	Phe	Val	Gly	Asp	Pro	Thr	Leu	Gly	Ala	Tyr	Asn	Ala	Ser	Lys
145					150					155					160
Gly	Ala	Val	Arg	Ile	Met	Ser	Lys	Ser	Ala	Ala	Leu	Asp	Cys	Ala	Leu
				165					170					175	
Lys	Asp	Tyr	Asp	Val	Arg	Val	Asn	Thr	Val	His	Pro	Gly	Tyr	Ile	Lys
			180					185					190		
Thr	Pro	Leu	Val	Asp	Asp	Leu	Glu	Gly	Ala	Glu	Glu	Met	Met	Ser	Gln
		195					200					205			
Arg	Thr	Lys	Thr	Pro	Met	Gly	His	Ile	Gly	Glu	Pro	Asn	Asp	Ile	Ala
	210					215					220				
Trp	Ile	Cys	Val	Tyr	Leu	Ala	Ser	Asp	Glu	Ser	Lys	Phe	Ala	Thr	Gly
225					230					235					240
Ala	Glu	Phe	Val	Val	Asp	Gly	Gly	Tyr	Thr	Ala	Gln				
				245					250						

<210> 15
 <211> 942
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 15
 atgtcttttt accaacagtt tttcacgctg aacaacggca ataaaatccc ggcgattggc 60
 atcatcggca ctggtacacg ttggtataaa aatgaagaaa ctgacgcgac cttctccaat 120
 agtctggttg aacaaatcgt gtacgcgttg aaactgccgg ggattatcca catcgacgcc 180
 gcggagattt atcgcaccta cccggaagtg ggtaaagcac tgtccctgac cgaaaagcct 240
 cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactccoct 300
 gcggacggtc tggatatagc attgaagaaa atgggtacag attatgttga tttatatctg 360
 ttacattccc cgtttgtttc gaaggaagtg aatggcttaa gcttagaaga ggcttggaaa 420
 gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggttc caatttcgca 480
 gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
 gagttctctc cgttcctgca aaaccaaaaca ccaggcattt ataaattctg tcaggagcac 600
 gatatccttg tggaagcata ttctccgctg ggcccgtgac agaagaaaac cgcgcaggat 660
 gacagccaac cattttttga gtacgtcaaa gaattgagcg aaaaatacat caaatccgag 720
 gccagatca tcttgccgtg ggtcactaaa cgcggtgtgc tgccagttac cacctcttca 780
 aagcctcagc gcatttagca tgctcagaac ctgttttctt togacctgac agcgggaagag 840
 gttgataaaa tcacggagct gggtctggaa catgaaccgc tgcgcctgta ctggaataaa 900
 ttgtatggca aatataacta cgcgcgccag aaagtgtaat ga 942

<210> 16
 <211> 313
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 16
 Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
 1 5 10 15
 Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Arg Trp Tyr Lys Asn Glu
 20 25 30
 Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr

35	40	45
Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Ile Tyr		
50	55	60
Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro		
65	70	75
Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met		80
85	90	95
Ser Asp Ser Pro Ala Asp Gly Leu Asp Ile Ala Leu Lys Lys Met Gly		
100	105	110
Thr Asp Tyr Val Asp Leu Tyr Leu Leu His Ser Pro Phe Val Ser Lys		
115	120	125
Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln		
130	135	140
Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Ala		
145	150	155
Val Glu Asp Leu Gln Arg Ile Leu Lys Val Ala Glu Val Lys Pro Gln		160
165	170	175
Val Asn Gln Ile Glu Phe Ser Pro Phe Leu Gln Asn Gln Thr Pro Gly		
180	185	190
Ile Tyr Lys Phe Cys Gln Glu His Asp Ile Leu Val Glu Ala Tyr Ser		
195	200	205
Pro Leu Gly Pro Leu Gln Lys Lys Thr Ala Gln Asp Asp Ser Gln Pro		
210	215	220
Phe Phe Glu Tyr Val Lys Glu Leu Ser Glu Lys Tyr Ile Lys Ser Glu		
225	230	235
Ala Gln Ile Ile Leu Arg Trp Val Thr Lys Arg Gly Val Leu Pro Val		240
245	250	255
Thr Thr Ser Ser Lys Pro Gln Arg Ile Ser Asp Ala Gln Asn Leu Phe		
260	265	270
Ser Phe Asp Leu Thr Ala Glu Glu Val Asp Lys Ile Thr Glu Leu Gly		
275	280	285
Leu Glu His Glu Pro Leu Arg Leu Tyr Trp Asn Lys Leu Tyr Gly Lys		
290	295	300
Tyr Asn Tyr Ala Ala Gln Lys Val		
305	310	

<210> 17

<211> 942

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 17

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atgtcttttc accaacagtt tttcacgctg aacaacggca ataaaatccc ggcgattgcc 60
atcatcggca ctggtacacg ttggtataaa aatgaagaaa ctgacgcgac cttctccaat 120
agtctggttg aacaaatcgt gtatgcgttg aaactgcggg ggattatcca catcgacgcc 180
goggagattt atcgcaccta ccggaagtg ggtaaagcac tgtccctgac cgaaaagcct 240
cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactcccct 300
gcggacggtc tggatttagc attgaagaaa atgcgtacag attatgttga tttatatctg 360
ttacattccc cgtttgtttc gaaggaagtg aatggcttaa gcttagaaga ggcttggaaa 420
gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggttc caatttcaca 480
gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
gagttctctc cgttcctgca aaaccaaaaca ccaggcattt ataaattctg tcaggagcac 600
gatatcctgg tggaagcata ttctccgctg ggcccgtgca agaagaaaac cgcgcaggat 660
gacagtcaac cattttttga gtacgtcaaa gaattgagcg aaaaatacat caaatccgag 720
gcccagatca tcttgcgctg ggtcactaaa cgcggtgtgc tgccagttac caoctottca 780
aagcctcagc gcattagcga tgctcagaac ctgttttccct tcgacctgac agcgggaagag 840
gttgataaaa tcacggagct gggtctggaa catgaaccgc tgcgcctgta ctggaataaa 900

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ttgtatggca aatataacta cgccgcccag aaagtgtaat ga

942

<210> 18

<211> 313

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 18

Met	Ser	Phe	His	Gln	Gln	Phe	Phe	Thr	Leu	Asn	Asn	Gly	Asn	Lys	Ile		
1				5					10					15			
Pro	Ala	Ile	Ala	Ile	Ile	Gly	Thr	Gly	Thr	Arg	Trp	Tyr	Lys	Asn	Glu		
			20					25					30				
Glu	Thr	Asp	Ala	Thr	Phe	Ser	Asn	Ser	Leu	Val	Glu	Gln	Ile	Val	Tyr		
		35					40					45					
Ala	Leu	Lys	Leu	Pro	Gly	Ile	Ile	His	Ile	Asp	Ala	Ala	Glu	Ile	Tyr		
	50					55				60							
Arg	Thr	Tyr	Pro	Glu	Val	Gly	Lys	Ala	Leu	Ser	Leu	Thr	Glu	Lys	Pro		
65					70					75					80		
Arg	Asn	Ala	Ile	Phe	Leu	Thr	Asp	Lys	Tyr	Ser	Pro	Gln	Ile	Lys	Met		
				85					90					95			
Ser	Asp	Ser	Pro	Ala	Asp	Gly	Leu	Asp	Leu	Ala	Leu	Lys	Lys	Met	Arg		
			100					105					110				
Thr	Asp	Tyr	Val	Asp	Leu	Tyr	Leu	Leu	His	Ser	Pro	Phe	Val	Ser	Lys		
		115					120						125				
Glu	Val	Asn	Gly	Leu	Ser	Leu	Glu	Glu	Ala	Trp	Lys	Asp	Met	Glu	Gln		
	130					135					140						
Leu	Tyr	Lys	Ser	Gly	Lys	Ala	Lys	Asn	Ile	Gly	Val	Ser	Asn	Phe	Thr		
145					150					155					160		
Val	Glu	Asp	Leu	Gln	Arg	Ile	Leu	Lys	Val	Ala	Glu	Val	Lys	Pro	Gln		
				165					170					175			
Val	Asn	Gln	Ile	Glu	Phe	Ser	Pro	Phe	Leu	Gln	Asn	Gln	Thr	Pro	Gly		
			180					185					190				
Ile	Tyr	Lys	Phe	Cys	Gln	Glu	His	Asp	Ile	Leu	Val	Glu	Ala	Tyr	Ser		
	195						200					205					
Pro	Leu	Gly	Pro	Leu	Gln	Lys	Lys	Thr	Ala	Gln	Asp	Asp	Ser	Gln	Pro		
	210					215					220						
Phe	Phe	Glu	Tyr	Val	Lys	Glu	Leu	Ser	Glu	Lys	Tyr	Ile	Lys	Ser	Glu		
225					230					235					240		
Ala	Gln	Ile	Ile	Leu	Arg	Trp	Val	Thr	Lys	Arg	Gly	Val	Leu	Pro	Val		
				245					250					255			
Thr	Thr	Ser	Ser	Lys	Pro	Gln	Arg	Ile	Ser	Asp	Ala	Gln	Asn	Leu	Phe		
			260					265					270				
Ser	Phe	Asp	Leu	Thr	Ala	Glu	Glu	Val	Asp	Lys	Ile	Thr	Glu	Leu	Gly		
		275					280					285					
Leu	Glu	His	Glu	Pro	Leu	Arg	Leu	Tyr	Trp	Asn	Lys	Leu	Tyr	Gly	Lys		
	290					295					300						
Tyr	Asn	Tyr	Ala	Ala	Gln	Lys	Val										
305					310												

<210> 19

<211> 942

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 19

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atgtcttttc atcaacagtt tttcacgctg aataacggca ataaaatccc ggcgattgcc 60
atcatcggca ctggtacacg ttggtataaa aatgaagaaa ctgacgcgac cttctccaat 120
agtctgggtg atcaaatcgt gtatgcgttg aaactgccgg ggattatcca catcgacgcc 180
gcggagattt atcgcaccta cccggaagtg ggtaaagcac tgtccctgac cgaaaagcct 240
cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactcccct 300
gcggacggtc tggatttagc attgaagaaa atgggtaccg attatgttga tttatatctg 360
ttacattccc cgtttgtttc gaaggaagtg aatggcttaa gcttagaaga ggcttggaag 420
gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggttc caatttcgca 480
gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
gagttctctc cgttcctgca aaaccaaaca ccaggcattt ataaattctg tcaggagcac 600
gatatcctgg tgggaagcata ttctccgctg ggcccgtgac agaagaaaac cgcgcaggat 660
gacagccaac cattttttga gtacgtcaaa gaattgagcg aaaaatacat caaatccgag 720
gcccagatca tctctgcgtg ggtcactaaa cgcgggtgtg tgccagttac cacctcttca 780
aagcctcagc gcattagcga tgctcagaac ctgttttctt tcgacctgac agcgggaagag 840
gttgataaaa tcacggagct gggctctggaa catgaaccgc tgcgcctgta ctggaataaa 900
ttgtatggca aatataactc cgccgccagc aaagtgtaat ga 942
```

<210> 20

<211> 313

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 20

```
Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
1          5          10          15
Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Arg Trp Tyr Lys Asn Glu
          20          25          30
Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Asp Gln Ile Val Tyr
          35          40          45
Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Ile Tyr
          50          55          60
Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
65          70          75          80
Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
          85          90          95
Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
          100         105         110
Thr Asp Tyr Val Asp Leu Tyr Leu Leu His Ser Pro Phe Val Ser Lys
          115         120         125
Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
          130         135         140
Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Ala
145         150         155         160
Val Glu Asp Leu Gln Arg Ile Leu Lys Val Ala Glu Val Lys Pro Gln
          165         170         175
Val Asn Gln Ile Glu Phe Ser Pro Phe Leu Gln Asn Gln Thr Pro Gly
          180         185         190
Ile Tyr Lys Phe Cys Gln Glu His Asp Ile Leu Val Glu Ala Tyr Ser
          195         200         205
Pro Leu Gly Pro Leu Gln Lys Lys Thr Ala Gln Asp Asp Ser Gln Pro
          210         215         220
Phe Phe Glu Tyr Val Lys Glu Leu Ser Glu Lys Tyr Ile Lys Ser Glu
225         230         235         240
Ala Gln Ile Ile Leu Arg Trp Val Thr Lys Arg Gly Val Leu Pro Val
          245         250         255
```

Thr	Thr	Ser	Ser	Lys	Pro	Gln	Arg	Ile	Ser	Asp	Ala	Gln	Asn	Leu	Phe
			260					265					270		
Ser	Phe	Asp	Leu	Thr	Ala	Glu	Glu	Val	Asp	Lys	Ile	Thr	Glu	Leu	Gly
		275					280					285			
Leu	Glu	His	Glu	Pro	Leu	Arg	Leu	Tyr	Trp	Asn	Lys	Leu	Tyr	Gly	Lys
	290					295					300				
Tyr	Asn	Ser	Ala	Ala	Gln	Lys	Val								
305					310										

<210> 21
 <211> 942
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 21
 atgtcttttc accaacagtt tttcacgctg aacaacggca ataaaatccc ggcgattgcc 60
 atcatgggca ctggtacacg ttggtataaa aatgaagaaa ctgaocgcgac cttctccaat 120
 agtctggttg agcaaatcgt gtatgcgttg aaactgccgg ggattatcca catogacgcc 180
 gcggagattt atcgcaccta cccggaagtg ggtaaagcac tgtccctgac cgaaaagcct 240
 cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactcccct 300
 gcggacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
 ttacattccc cgtttgtttc gaaggaagtg aatggcttaa gcttagaaga ggcttggaaa 420
 gatattggagc agttatatataa aactggtaaa gctaaaaaca tcgggggttc caatttcgca 480
 gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
 gagttctctc cgttcctgca aaaccaaaca ccaggcattt ataaattctg tcaggagcac 600
 gatatacttg tggaagcata ttctccgtg ggcccgctgc agaagaaaac cgcgcaggat 660
 gacagccaac cattttttga gtacgtcaaa gaattgagcg aaaaatacat caaatccgag 720
 gccagatca tcctgcgctg ggtcactaaa cgcgggtgtg tgccagttac cacctottca 780
 aagcctcagc gcattagcga tgctcagaac ctgttttctc tcgacctgac agcgggaagag 840
 gttgataaaa tcacggagct gggtctggaa catgaaccgc tgcgcctgta ctggaataaa 900
 ttgtatggca aatataacta cgccgccag aaagtgtaat ga 942

<210> 22
 <211> 313
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 22
 Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
 1 5 10 15
 Pro Ala Ile Ala Ile Met Gly Thr Gly Thr Arg Trp Tyr Lys Asn Glu
 20 25 30
 Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
 35 40 45
 Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Ile Tyr
 50 55 60
 Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
 65 70 75 80
 Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
 85 90 95
 Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
 100 105 110
 Thr Asp Tyr Val Asp Leu Tyr Leu Leu His Ser Pro Phe Val Ser Lys

	115		120		125										
Glu	Val	Asn	Gly	Leu	Ser	Leu	Glu	Glu	Ala	Trp	Lys	Asp	Met	Glu	Gln
	130		135		140										
Leu	Tyr	Lys	Thr	Gly	Lys	Ala	Lys	Asn	Ile	Gly	Val	Ser	Asn	Phe	Ala
145				150					155						160
Val	Glu	Asp	Leu	Gln	Arg	Ile	Leu	Lys	Val	Ala	Glu	Val	Lys	Pro	Gln
			165						170					175	
Val	Asn	Gln	Ile	Glu	Phe	Ser	Pro	Phe	Leu	Gln	Asn	Gln	Thr	Pro	Gly
	180							185					190		
Ile	Tyr	Lys	Phe	Cys	Gln	Glu	His	Asp	Ile	Leu	Val	Glu	Ala	Tyr	Ser
	195						200					205			
Pro	Leu	Gly	Pro	Leu	Gln	Lys	Lys	Thr	Ala	Gln	Asp	Asp	Ser	Gln	Pro
	210					215					220				
Phe	Phe	Glu	Tyr	Val	Lys	Glu	Leu	Ser	Glu	Lys	Tyr	Ile	Lys	Ser	Glu
225				230					235						240
Ala	Gln	Ile	Ile	Leu	Arg	Trp	Val	Thr	Lys	Arg	Gly	Val	Leu	Pro	Val
			245					250					255		
Thr	Thr	Ser	Ser	Lys	Pro	Gln	Arg	Ile	Ser	Asp	Ala	Gln	Asn	Leu	Phe
	260						265					270			
Ser	Phe	Asp	Leu	Thr	Ala	Glu	Glu	Val	Asp	Lys	Ile	Thr	Glu	Leu	Gly
	275						280					285			
Leu	Glu	His	Glu	Pro	Leu	Arg	Leu	Tyr	Trp	Asn	Lys	Leu	Tyr	Gly	Lys
	290				295					300					
Tyr	Asn	Tyr	Ala	Ala	Gln	Lys	Val								
305				310											

<210> 23
 <211> 939
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 23
 atgtcttttc accaacagtt ttccacgctg aacaacggca ataaaatccc ggcgattgcc 60
 atcatcgga ctggtacacg ttggtataaa aatgaagaaa ctgaogogac cttotccaat 120
 agtctggttg aacaaatogt gtatgcgttg aaactgccgg ggattatoca catcgacgoc 180
 gcggagattt atcgcaccta cccggaagtg ggtaaagcac tgtccctgac cgaaaagcct 240
 cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactccctt 300
 gcggacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
 ttacattccc cgtttgttcc gaaggaagtg aatggcttaa gcttagaaga ggcttggaaa 420
 gatattggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggttc caatttcgca 480
 gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aaactcaggt caaccagatt 540
 gagttctctc cgttcctgca aaaccaaaca ccaggcattt ataaattctg tcaggagcac 600
 gatattcttg tggaagcata ttctccgctg ggcccgtgac agaagaaaac cgcgcaggat 660
 gacagccaac ctttttttga gtacgtcaaa gaattgagcg aaaaatacat caaatccgag 720
 gccagatca tcttgcgctg ggtaactaaa cgcgggtgtg tgccagttac cacctcttca 780
 aagcctcagc gcattagcga tgctcagaac ctgttttctt tcgacctgac agcgggaagag 840
 gttgataaaa tcacggagct gggtctggat catgaaccgc tgogcctgta ctggaataaa 900
 ttgtatggca aatataacta cgccgccag aaagtgtaa 939

<210> 24
 <211> 312
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 24

```
Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
1          5          10          15
Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Arg Trp Tyr Lys Asn Glu
20          25          30
Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
35          40          45
Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Ile Tyr
50          55          60
Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
65          70          75          80
Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
85          90          95
Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
100         105         110
Thr Asp Tyr Val Asp Leu Tyr Leu Leu His Ser Pro Phe Val Ser Lys
115         120         125
Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
130         135         140
Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Ala
145         150         155         160
Val Glu Asp Leu Gln Arg Ile Leu Lys Val Ala Glu Val Lys Pro Gln
165         170         175
Val Asn Gln Ile Glu Phe Ser Pro Phe Leu Gln Asn Gln Thr Pro Gly
180         185         190
Ile Tyr Lys Phe Cys Gln Glu His Asp Ile Leu Val Glu Ala Tyr Ser
195         200         205
Pro Leu Gly Pro Leu Gln Lys Lys Thr Ala Gln Asp Asp Ser Gln Pro
210         215         220
Phe Phe Glu Tyr Val Lys Glu Leu Ser Glu Lys Tyr Ile Lys Ser Glu
225         230         235         240
Ala Gln Ile Ile Leu Arg Trp Val Thr Lys Arg Gly Val Leu Pro Val
245         250         255
Thr Thr Ser Ser Lys Pro Gln Arg Ile Ser Asp Ala Gln Asn Leu Phe
260         265         270
Ser Phe Asp Leu Thr Ala Glu Glu Val Asp Lys Ile Thr Glu Leu Gly
275         280         285
Leu Asp His Glu Pro Leu Arg Leu Tyr Trp Asn Lys Leu Tyr Gly Lys
290         295         300
Tyr Asn Tyr Ala Ala Gln Lys Val
305          310
```

<210> 25

<211> 942

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 25

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atgtcttttt accaacagtt tttaacgctg aacaacggca ataaaatccc ggcgattgcc 60
atcatcggca ctggtacagc ttggtataaa aatgaagaaa ctgacgcgac cttctccaat 120
agtctggttg aacaaatcgt gtatgcgttg aaactgccgg ggattatoca catcgacgco 180
gcggagattt atcgcaocta cccggaagtg ggtaaagcac tgccoctgac ogaaaagcct 240
cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactcccct 300
gcggacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatotg 360
ttacattccc cgtttgtttc gaaggaagtg aatggcttaa gcttagaaga ggcttgga 420
gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggttc caatttcgca 480
```

```

gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
gagttctctc cgttcctgca aaaccaaaca ccaggcattt ataaattctg tcaggagcac 600
gatatcctgg tggaagcata ttctccgctg ggcccgtgac agaagaaaac cgcgcaggat 660
gacagccaac cattttttga gtacgtcaaa gaattgagcg aaaaatacat caaatccgag 720
gcccagatca tcttgcgctg ggctactaaa cgcggtgtgc tgccagttac cacctcttca 780
aagcctcagc gcattagcga tgctcagaac ctgttttctt tcgacctgac agcggaagag 840
gttgataaaa tcacggagct gggctctggaa catgaaccgc tgcgcctgta ctggaataaa 900
ttgtatggca aatataacta cgccgcccag aaagtgtaat ga 942

```

<210> 26

<211> 313

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 26

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Met Ser Phe His Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
1      5      10      15
Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Ala Trp Tyr Lys Asn Glu
20     25     30
Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
35     40     45
Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Ile Tyr
50     55     60
Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
65     70     75     80
Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
85     90     95
Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
100    105    110
Thr Asp Tyr Val Asp Leu Tyr Leu Leu His Ser Pro Phe Val Ser Lys
115    120    125
Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
130    135    140
Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Ala
145    150    155    160
Val Glu Asp Leu Gln Arg Ile Leu Lys Val Ala Glu Val Lys Pro Gln
165    170    175
Val Asn Gln Ile Glu Phe Ser Pro Phe Leu Gln Asn Gln Thr Pro Gly
180    185    190
Ile Tyr Lys Phe Cys Gln Glu His Asp Ile Leu Val Glu Ala Tyr Ser
195    200    205
Pro Leu Gly Pro Leu Gln Lys Lys Thr Ala Gln Asp Asp Ser Gln Pro
210    215    220
Phe Phe Glu Tyr Val Lys Glu Leu Ser Glu Lys Tyr Ile Lys Ser Glu
225    230    235    240
Ala Gln Ile Ile Leu Arg Trp Val Thr Lys Arg Gly Val Leu Pro Val
245    250    255
Thr Thr Ser Ser Lys Pro Gln Arg Ile Ser Asp Ala Gln Asn Leu Phe
260    265    270
Ser Phe Asp Leu Thr Ala Glu Glu Val Asp Lys Ile Thr Glu Leu Gly
275    280    285
Leu Glu His Glu Pro Leu Arg Leu Tyr Trp Asn Lys Leu Tyr Gly Lys
290    295    300
Tyr Asn Tyr Ala Ala Gln Lys Val
305    310

```


<210> 27
 <211> 942
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 27
 atgtcttttc accaacagtt ttccacgctg aacaacggca ataaaatccc ggcgattgcc 60
 atcatcggca ctggtacacg ttggtataaa aatgaagaaa ctgacgcgac cttotccaat 120
 agtctggttg agcaaatcgt gtatgcgttg aaactgccgg ggattatcca catcgacgcc 180
 gcggagatct atcgcaccta cccggaagtg ggtaaagcac tgccctgac cgaaaagcct 240
 cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactccct 300
 gcggacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
 ttacattccc cgtttgtttc gaaggaagtg aatggcttaa gcttagaaga ggcttggaaa 420
 gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggtttc caatttcgca 480
 gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
 gagttctctc cgttcctgca aaaccaaaca ccaggcattt ataaattctg tcaggagcac 600
 gatatcctgg tgggaagcata ttctccgctg ggcccgctgc agaagaaaac cgcgcaggat 660
 gacagccaac cattttttga gtacgtcaaa gaattgagcg aaaaatacat caaatccgag 720
 gccagatca tctcgcgctg ggctactaaa cgcggtgccc tgccagttac cacctcttca 780
 aagcctcagc gcattagcga tgctcagaac ctgttttccct tcgacctgac agcgggaagag 840
 gttgataaaa tcacggagct gggctctggaa catgaaccgc tcgcctgta ctggaataaa 900
 ttgtatggca aatataacaa cgccgccag aaagtgtaat ga 942

<210> 28
 <211> 313
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 28
 Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
 1 5 10 15
 Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Arg Trp Tyr Lys Asn Glu
 20 25 30
 Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
 35 40 45
 Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Ile Tyr
 50 55 60
 Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
 65 70 75 80
 Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
 85 90 95
 Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
 100 105 110
 Thr Asp Tyr Val Asp Leu Tyr Leu Leu His Ser Pro Phe Val Ser Lys
 115 120 125
 Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
 130 135 140
 Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Ala
 145 150 155 160
 Val Glu Asp Leu Gln Arg Ile Leu Lys Val Ala Glu Val Lys Pro Gln
 165 170 175
 Val Asn Gln Ile Glu Phe Ser Pro Phe Leu Gln Asn Gln Thr Pro Gly
 180 185 190
 Ile Tyr Lys Phe Cys Gln Glu His Asp Ile Leu Val Glu Ala Tyr Ser

195	200	205
Pro Leu Gly Pro Leu Gln Lys Lys Thr Ala Gln Asp Asp Ser Gln Pro		
210	215	220
Phe Phe Glu Tyr Val Lys Glu Leu Ser Glu Lys Tyr Ile Lys Ser Glu		
225	230	235
Ala Gln Ile Ile Leu Arg Trp Val Thr Lys Arg Gly Ala Leu Pro Val		
245	250	255
Thr Thr Ser Ser Lys Pro Gln Arg Ile Ser Asp Ala Gln Asn Leu Phe		
260	265	270
Ser Phe Asp Leu Thr Ala Glu Glu Val Asp Lys Ile Thr Glu Leu Gly		
275	280	285
Leu Glu His Glu Pro Leu Arg Leu Tyr Trp Asn Lys Leu Tyr Gly Lys		
290	295	300
Tyr Asn Asn Ala Ala Gln Lys Val		
305	310	

<210> 29
 <211> 942
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 29
 atgtctttt accaacagtt ttccacgctg aacaacggca ataaaatccc ggcgattgcc 60
 atcatcgga ctggtacagc ttggtacaaa aatgaagaaa ctgacgcgac cttctccaat 120
 agtctggttg aacaaatcgt gcatgcgttg aaactgcggg ggattatcca catcgacgcc 180
 gcggagattt atcgcaccta cccggaagtg ggtaaagcac tgtccctgac cgaaaagcct 240
 cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactcccct 300
 gcggacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
 ttacattccc cgtttgtttc gaaggaagtg aatggcttaa gcttagaaga ggcttgga 420
 gatattggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggtttc caatttcgca 480
 gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
 gagttctctc cgttcctgca aaaccaaaca ccaggcattt ataaattctg tcaggagcac 600
 gatattcctg tggaagcata ttctccgctg ggcccgtgca agaagaaaac cgcgcaggat 660
 gacagccaac cattttttga gtaagtcaaa gaattgagcg aaaaatacat caaatccgag 720
 gccagatca tcctgcgctg ggtcactaaa cgcgggtgtgc tgccagttac cacctcttca 780
 aagcctcagc gcattagcga tgctcagaac ctgttttctc tcgacctgac agcgggaagag 840
 gttgataaaa tcacggagct gggtctggaa catgaaccgc tgcgcctgta ctggaataaa 900
 ttgtatggca aatataacta cgcgcgccag aaagtgtaat ga 942

<210> 30
 <211> 313
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 30
 Met Ser Phe His Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
 1 5 10 15
 Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Ala Trp Tyr Lys Asn Glu
 20 25 30
 Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val His
 35 40 45
 Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Ile Tyr
 50 55 60

Arg	Thr	Tyr	Pro	Glu	Val	Gly	Lys	Ala	Leu	Ser	Leu	Thr	Glu	Lys	Pro
65					70					75					80
Arg	Asn	Ala	Ile	Phe	Leu	Thr	Asp	Lys	Tyr	Ser	Pro	Gln	Ile	Lys	Met
			85						90					95	
Ser	Asp	Ser	Pro	Ala	Asp	Gly	Leu	Asp	Leu	Ala	Leu	Lys	Lys	Met	Gly
			100					105					110		
Thr	Asp	Tyr	Val	Asp	Leu	Tyr	Leu	Leu	His	Ser	Pro	Phe	Val	Ser	Lys
		115					120					125			
Glu	Val	Asn	Gly	Leu	Ser	Leu	Glu	Glu	Ala	Trp	Lys	Asp	Met	Glu	Gln
	130					135					140				
Leu	Tyr	Lys	Ser	Gly	Lys	Ala	Lys	Asn	Ile	Gly	Val	Ser	Asn	Phe	Ala
145					150					155					160
Val	Glu	Asp	Leu	Gln	Arg	Ile	Leu	Lys	Val	Ala	Glu	Val	Lys	Pro	Gln
				165				170						175	
Val	Asn	Gln	Ile	Glu	Phe	Ser	Pro	Phe	Leu	Gln	Asn	Gln	Thr	Pro	Gly
			180					185					190		
Ile	Tyr	Lys	Phe	Cys	Gln	Glu	His	Asp	Ile	Leu	Val	Glu	Ala	Tyr	Ser
		195					200					205			
Pro	Leu	Gly	Pro	Leu	Gln	Lys	Lys	Thr	Ala	Gln	Asp	Asp	Ser	Gln	Pro
	210					215					220				
Phe	Phe	Glu	Tyr	Val	Lys	Glu	Leu	Ser	Glu	Lys	Tyr	Ile	Lys	Ser	Glu
225					230					235					240
Ala	Gln	Ile	Ile	Leu	Arg	Trp	Val	Thr	Lys	Arg	Gly	Val	Leu	Pro	Val
				245					250					255	
Thr	Thr	Ser	Ser	Lys	Pro	Gln	Arg	Ile	Ser	Asp	Ala	Gln	Asn	Leu	Phe
			260					265					270		
Ser	Phe	Asp	Leu	Thr	Ala	Glu	Glu	Val	Asp	Lys	Ile	Thr	Glu	Leu	Gly
		275					280					285			
Leu	Glu	His	Glu	Pro	Leu	Arg	Leu	Tyr	Trp	Asn	Lys	Leu	Tyr	Gly	Lys
	290					295					300				
Tyr	Asn	Tyr	Ala	Ala	Gln	Lys	Val								
305					310										

<210> 31

<211> 936

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 31

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atgtcttttt accaacagtt tttcacgctg aacaacggca ataaaatccc ggcgattgcc 60
atcatcgcca ctggtacacg ttggtataaa aatgaagaaa ctgacgogac cttctccaat 120
agtctggttg aacaaatcgt gtatgcgttg aaactgcogg ggattatcca catcgacacc 180
gcggagattt atcgcaccta cccggaagtg ggtaaagcac tgccctgac cgaaaagcct 240
cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactccct 300
gcggacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
ttacattccc cgtttgtttc gaaggaagtg aatggcttaa gcttagaaga ggcttgga 420
gatatggagc agttatacaa aagtggtaaa gctaaaaaca toggggtttc caatttcgca 480
gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
gagttctctc cgttcctgca aaaccaaaaca ccaggcattt ataaattctg tcaggagcac 600
gatatccttg tggaagcata ttctccgctg ggcccgtgc agaagaaaac cgcgcaggat 660
gacagccaac cattttttga gtaagtcaaa gaattgagcg aaaaatacat caaatccgag 720
gcccgatca tcttgcgctg ggtcactaaa cgcggtgtgc tgccagttac cacctottca 780
aagcctcagc gcattagcga tgctcagaac ctgttttctc tgacctgac agcggaagag 840
gttgataaaa tcacggagct gggtctggaa catgaaccgc tgcgcctgta ctggaataaa 900
ttgtatggca aatataacta cgccgccagc aaagtg 936

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<210> 32
 <211> 312
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 32
 Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
 1 5 10 15
 Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Arg Trp Tyr Lys Asn Glu
 20 25 30
 Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
 35 40 45
 Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Thr Ala Glu Ile Tyr
 50 55 60
 Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
 65 70 75 80
 Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
 85 90 95
 Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
 100 105 110
 Thr Asp Tyr Val Asp Leu Tyr Leu Leu His Ser Pro Phe Val Ser Lys
 115 120 125
 Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
 130 135 140
 Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Ala
 145 150 155 160
 Val Glu Asp Leu Gln Arg Ile Leu Lys Val Ala Glu Val Lys Pro Gln
 165 170 175
 Val Asn Gln Ile Glu Phe Ser Pro Phe Leu Gln Asn Gln Thr Pro Gly
 180 185 190
 Ile Tyr Lys Phe Cys Gln Glu His Asp Ile Leu Val Glu Ala Tyr Ser
 195 200 205
 Pro Leu Gly Pro Leu Gln Lys Lys Thr Ala Gln Asp Asp Ser Gln Pro
 210 215 220
 Phe Phe Glu Tyr Val Lys Glu Leu Ser Glu Lys Tyr Ile Lys Ser Glu
 225 230 235 240
 Ala Gln Ile Ile Leu Arg Trp Val Thr Lys Arg Gly Val Leu Pro Val
 245 250 255
 Thr Thr Ser Ser Lys Pro Gln Arg Ile Ser Asp Ala Gln Asn Leu Phe
 260 265 270
 Ser Phe Asp Leu Thr Ala Glu Glu Val Asp Lys Ile Thr Glu Leu Gly
 275 280 285
 Leu Glu His Glu Pro Leu Arg Leu Tyr Trp Asn Lys Leu Tyr Gly Lys
 290 295 300
 Tyr Asn Tyr Ala Ala Gln Lys Val
 305 310

<210> 33
 <211> 936
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 33
 atgtcttttc accaacagtt ttacacgctg aacaacggca ataaaatccc ggcgattgcc 60

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agtctggttg aacaaatcgt gtatgcgttg aaactgccgg ggattatcca catcgacgcc 180
gcggagattt atcgcaccta cccggaagtg ggtaaagcac tgtccctgac cgaaaagcct 240
cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactccctt 300
gcggacggtc tggatttagc attgaagaaa atgggtacag gttatgttga tttatatctg 360
ttacattccc cgtttgtttc gaaggaagtg aatggcttaa gcttagaaga ggcttggaaa 420
gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggttc caatttcgca 480
gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
gagttctctc cgttcctgca aaaccaaaca ccaggcattt ataaattctg tcaggagcac 600
gatatcctgg tggaagcata ttctccgctg ggcccgcctg agaagaaaac cgcgaggat 660
gacagccaac ctttttttga gtacgtcaaa gaattgagcg aaaaatacat caaatccgag 720
gccagatca tctcgcgctg ggtcactaaa cgcggtgtgc tgccagttac cacctcttca 780
aagcctcagc gcattagoga tgctcagaac ctgttttctt tcgacctgac agcgggaagag 840
gttgataaaa tcacggagct gggctctggaa catgaaccgc tgcgcctgta ctggaataaa 900
ttgtatggca aatataacta cgccgccag aaagtg 936

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<210> 34

<211> 312

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 34

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Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
1          5          10          15
Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Arg Trp Tyr Lys Asn Glu
          20          25          30
Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
          35          40          45
Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Ile Tyr
          50          55          60
Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
65          70          75          80
Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
          85          90          95
Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
          100          105          110
Thr Gly Tyr Val Asp Leu Tyr Leu Leu His Ser Pro Phe Val Ser Lys
          115          120          125
Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
          130          135          140
Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Ala
145          150          155          160
Val Glu Asp Leu Gln Arg Ile Leu Lys Val Ala Glu Val Lys Pro Gln
          165          170          175
Val Asn Gln Ile Glu Phe Ser Pro Phe Leu Gln Asn Gln Thr Pro Gly
          180          185          190
Ile Tyr Lys Phe Cys Gln Glu His Asp Ile Leu Val Glu Ala Tyr Ser
          195          200          205
Pro Leu Gly Pro Leu Gln Lys Lys Thr Ala Gln Asp Asp Ser Gln Pro
          210          215          220
Phe Phe Glu Tyr Val Lys Glu Leu Ser Glu Lys Tyr Ile Lys Ser Glu
225          230          235          240
Ala Gln Ile Ile Leu Arg Trp Val Thr Lys Arg Gly Val Leu Pro Val
          245          250          255
Thr Thr Ser Ser Lys Pro Gln Arg Ile Ser Asp Ala Gln Asn Leu Phe
          260          265          270
Ser Phe Asp Leu Thr Ala Glu Glu Val Asp Lys Ile Thr Glu Leu Gly

```

	275		280		285										
Leu	Glu	His	Glu	Pro	Leu	Arg	Leu	Tyr	Trp	Asn	Lys	Leu	Tyr	Gly	Lys
	290				295						300				
Tyr	Asn	Tyr	Ala	Ala	Gln	Lys	Val								
305					310										

<210> 35
 <211> 936
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 35
 atgtcttttc accaacagtt ttccacgctg aacaacggca ataaaatccc ggcgattgcc 60
 atcatcgaggc ctggtacacg ttggtataaa aatgaagaaa ctgacgcgac ctctctccaat 120
 agtctggttg aacaaatcgt gtatgcgttg aaactgcggg ggattatcca catcgacgcc 180
 gcgagagatt atcgaccta cccggaagtg ggtaaagcac tgccctgac cgaaaagcct 240
 cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactccctt 300
 gcgagcggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
 ttacattccc cgtttgtttc gaaggaagtg aatggcttaa gcttagaaga ggcttggaaa 420
 gatattggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggttc caatttcgca 480
 gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaagt caaccagatt 540
 gagttctctc cgctcctgca aaaccaaaca ccaggtattt ataaattctg tcaggagcac 600
 gatatcctgg tggaaagcata ttctccgctg ggcccgctgc agaagaaaac ogcgcaggat 660
 gacagccaac ctttttttga gtacgtcaaa gaattgagcg aaaaatacat caaatccgag 720
 gccagatca tcttgogctg ggtcactaaa cggcgtgtgc tgccagttac caactcttca 780
 aagcctcagc gcattagcga tgctcagaac ctgttttctt tcgacctgac agcgggaagag 840
 gttgataaaa tcacggagct gggctctggaa catgaaccgc tgcgcctgta ctggaataaa 900
 ttgtatggca aatataacta cgccgccagc aaagtg 936

<210> 36
 <211> 312
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 36
 Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
 1 5 10 15
 Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Arg Trp Tyr Lys Asn Glu
 20 25 30
 Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
 35 40 45
 Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Ile Tyr
 50 55 60
 Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
 65 70 75 80
 Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
 85 90 95
 Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
 100 105 110
 Thr Asp Tyr Val Asp Leu Tyr Leu Leu His Ser Pro Phe Val Ser Lys
 115 120 125
 Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
 130 135 140

Leu	Tyr	Lys	Ser	Gly	Lys	Ala	Lys	Asn	Ile	Gly	Val	Ser	Asn	Phe	Ala
145					150					155					160
Val	Glu	Asp	Leu	Gln	Arg	Ile	Leu	Lys	Val	Ala	Glu	Val	Lys	Pro	Gln
				165					170						175
Val	Asn	Gln	Ile	Glu	Phe	Ser	Pro	Leu	Leu	Gln	Asn	Gln	Thr	Pro	Gly
			180					185					190		
Ile	Tyr	Lys	Phe	Cys	Gln	Glu	His	Asp	Ile	Leu	Val	Glu	Ala	Tyr	Ser
	195						200					205			
Pro	Leu	Gly	Pro	Leu	Gln	Lys	Lys	Thr	Ala	Gln	Asp	Asp	Ser	Gln	Pro
	210					215					220				
Phe	Phe	Glu	Tyr	Val	Lys	Glu	Leu	Ser	Glu	Lys	Tyr	Ile	Lys	Ser	Glu
225					230					235					240
Ala	Gln	Ile	Ile	Leu	Arg	Trp	Val	Thr	Lys	Arg	Gly	Val	Leu	Pro	Val
				245					250					255	
Thr	Thr	Ser	Ser	Lys	Pro	Gln	Arg	Ile	Ser	Asp	Ala	Gln	Asn	Leu	Phe
			260					265					270		
Ser	Phe	Asp	Leu	Thr	Ala	Glu	Glu	Val	Asp	Lys	Ile	Thr	Glu	Leu	Gly
		275					280					285			
Leu	Glu	His	Glu	Pro	Leu	Arg	Leu	Tyr	Trp	Asn	Lys	Leu	Tyr	Gly	Lys
	290					295					300				
Tyr	Asn	Tyr	Ala	Ala	Gln	Lys	Val								
305					310										

<210> 37

<211> 936

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 37

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atcatcggca ctggtacacg ttggtataaa agtgaagaaa ctgacgogac cttctccaat 120
agtctggttg aacaaatcgt gtatgcgttg aaactgccgg ggattatoca catogaagcc 180
gcgagagatt atcgcaccta cccggaagtg ggtaaagcac tgtccctgac cgaaaagcct 240
cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactcccct 300
gcggacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
ttacattccc cgtttgtttc gaaggaagtg aatggcttaa gcttagaaga ggcttgaaa 420
gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcggggtttc caatttcgca 480
gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
gagttctctc cgttcctgca aaaccaaaca ccaggcattt ataaattctg tcaggagcac 600
gatattcttg tggaagcata ttctccgctg ggcccgcctg agaagaaaac cgogcaggat 660
gacagccaac cattttttga gtacgtcaaa gaattgagcg aaaaatacat caaatcogag 720
gccagatca tcctgcgctg ggtcactaaa cgcggtgtgc tgccagttac cacctcttca 780
aagcctcagc gcattagcga tgctcagaac ctgttttctt tcgaactgac agcgggaagag 840
gttgataaaa tcacggagct gggctctggaa catgaaccgc tcgcgctgta ctggaataaa 900
ttgtatggca aatataacta cgccgccagc aaagtg 936

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<210> 38

<211> 312

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 38

Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile

1				5					10					15					
Pro	Ala	Ile	Ala	Ile	Ile	Gly	Thr	Gly	Thr	Arg	Trp	Tyr	Lys	Ser	Glu				
			20					25					30						
Glu	Thr	Asp	Ala	Thr	Phe	Ser	Asn	Ser	Leu	Val	Glu	Gln	Ile	Val	Tyr				
		35					40					45							
Ala	Leu	Lys	Leu	Pro	Gly	Ile	Ile	His	Ile	Asp	Ala	Ala	Glu	Ile	Tyr				
	50					55				60									
Arg	Thr	Tyr	Pro	Glu	Val	Gly	Lys	Ala	Leu	Ser	Leu	Thr	Glu	Lys	Pro				
65					70				75						80				
Arg	Asn	Ala	Ile	Phe	Leu	Thr	Asp	Lys	Tyr	Ser	Pro	Gln	Ile	Lys	Met				
				85				90						95					
Ser	Asp	Ser	Pro	Ala	Asp	Gly	Leu	Asp	Leu	Ala	Leu	Lys	Lys	Met	Gly				
			100					105					110						
Thr	Asp	Tyr	Val	Asp	Leu	Tyr	Leu	Leu	His	Ser	Pro	Phe	Val	Ser	Lys				
		115					120					125							
Glu	Val	Asn	Gly	Leu	Ser	Leu	Glu	Glu	Ala	Trp	Lys	Asp	Met	Glu	Gln				
	130					135					140								
Leu	Tyr	Lys	Ser	Gly	Lys	Ala	Lys	Asn	Ile	Gly	Val	Ser	Asn	Phe	Ala				
145					150				155						160				
Val	Glu	Asp	Leu	Gln	Arg	Ile	Leu	Lys	Val	Ala	Glu	Val	Lys	Pro	Gln				
			165					170						175					
Val	Asn	Gln	Ile	Glu	Phe	Ser	Pro	Phe	Leu	Gln	Asn	Gln	Thr	Pro	Gly				
		180						185					190						
Ile	Tyr	Lys	Phe	Cys	Gln	Glu	His	Asp	Ile	Leu	Val	Glu	Ala	Tyr	Ser				
	195						200					205							
Pro	Leu	Gly	Pro	Leu	Gln	Lys	Lys	Thr	Ala	Gln	Asp	Asp	Ser	Gln	Pro				
	210					215					220								
Phe	Phe	Glu	Tyr	Val	Lys	Glu	Leu	Ser	Glu	Lys	Tyr	Ile	Lys	Ser	Glu				
225					230					235					240				
Ala	Gln	Ile	Ile	Leu	Arg	Trp	Val	Thr	Lys	Arg	Gly	Val	Leu	Pro	Val				
			245					250						255					
Thr	Thr	Ser	Ser	Lys	Pro	Gln	Arg	Ile	Ser	Asp	Ala	Gln	Asn	Leu	Phe				
		260						265					270						
Ser	Phe	Asp	Leu	Thr	Ala	Glu	Glu	Val	Asp	Lys	Ile	Thr	Glu	Leu	Gly				
		275					280					285							
Leu	Glu	His	Glu	Pro	Leu	Arg	Leu	Tyr	Trp	Asn	Lys	Leu	Tyr	Gly	Lys				
	290					295					300								
Tyr	Asn	Tyr	Ala	Ala	Gln	Lys	Val												
305					310														

<210> 39

<211> 936

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 39

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atcatcggca ctggtacacg ttggtataaa aatgaagaaa ctgacgcgac cttctocaat 120
agtctggttg aacaaatcgt gtatgcgttg aaactgcogg ggattatoca catcgacgcc 180
gcgagatatt atcgcaccta ccggaagtg ggtaaagcac tgtcooctgac cgaaaagcct 240
cgtaacgcga tttttctgac ggataaatat tctcgcgaga ttaaaatgag tgactoccoct 300
gcggacggto tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
ttacattccc cgtttgtttc gaaggaagtg aatggcttaa gcttagaaga ggcttggaag 420
gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggtttc caatttcgca 480
gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
gagttctctc cgttcctgca aaaccaaaca ccaggcattt ataaattctg tcaggagcac 600
gatatcctgg tggaagcata ttctcogctg ggcccgctgc agaagaaaac cgcgcaggat 660

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gacagccaac cattttttga gtacgtcaaa gaattgagcg aaaaatacat caaatccgag 720
goccagatca tcctgcgctg ggtcactaaa cgcggtgtgc tgccagttac cacctcttca 780
aagcctcagc gcattagcga tgctcagaac ctgttttccct tcgacctgac agcggaagag 840
gttgataaaa tcacggagct gggctctggag catgaaccgc tgcgcgtgta ctggaataaa 900
ttgtatggca aatataacta cgccgcccag aaagtg 936

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<210> 40
 <211> 312
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 40

Met	Ser	Phe	His	Gln	Gln	Phe	Phe	Thr	Leu	Asn	Asn	Gly	Asn	Lys	Ile
1				5					10					15	
Pro	Ala	Ile	Ala	Ile	Ile	Gly	Thr	Gly	Thr	Arg	Trp	Tyr	Lys	Asn	Glu
			20					25					30		
Glu	Thr	Asp	Ala	Thr	Phe	Ser	Asn	Ser	Leu	Val	Glu	Gln	Ile	Val	Tyr
		35					40					45			
Ala	Leu	Lys	Leu	Pro	Gly	Ile	Ile	His	Ile	Asp	Ala	Ala	Glu	Ile	Tyr
	50					55				60					
Arg	Thr	Tyr	Pro	Glu	Val	Gly	Lys	Ala	Leu	Ser	Leu	Thr	Glu	Lys	Pro
65					70					75				80	
Arg	Asn	Ala	Ile	Phe	Leu	Thr	Asp	Lys	Tyr	Ser	Pro	Gln	Ile	Lys	Met
				85					90					95	
Ser	Asp	Ser	Pro	Ala	Asp	Gly	Leu	Asp	Leu	Ala	Leu	Lys	Lys	Met	Gly
			100					105					110		
Thr	Asp	Tyr	Val	Asp	Leu	Tyr	Leu	Leu	His	Ser	Pro	Phe	Val	Ser	Lys
		115					120					125			
Glu	Val	Asn	Gly	Leu	Ser	Leu	Glu	Glu	Ala	Trp	Lys	Asp	Met	Glu	Gln
	130					135					140				
Leu	Tyr	Lys	Ser	Gly	Lys	Ala	Lys	Asn	Ile	Gly	Val	Ser	Asn	Phe	Ala
145					150				155					160	
Val	Glu	Asp	Leu	Gln	Arg	Ile	Leu	Lys	Val	Ala	Glu	Val	Lys	Pro	Gln
				165					170					175	
Val	Asn	Gln	Ile	Glu	Phe	Ser	Pro	Phe	Leu	Gln	Asn	Gln	Thr	Pro	Gly
		180						185					190		
Ile	Tyr	Lys	Phe	Cys	Gln	Glu	His	Asp	Ile	Leu	Val	Glu	Ala	Tyr	Ser
	195						200					205			
Pro	Leu	Gly	Pro	Leu	Gln	Lys	Lys	Thr	Ala	Gln	Asp	Asp	Ser	Gln	Pro
	210					215					220				
Phe	Phe	Glu	Tyr	Val	Lys	Glu	Leu	Ser	Glu	Lys	Tyr	Ile	Lys	Ser	Glu
225					230					235				240	
Ala	Gln	Ile	Ile	Leu	Arg	Trp	Val	Thr	Lys	Arg	Gly	Val	Leu	Pro	Val
				245					250					255	
Thr	Thr	Ser	Ser	Lys	Pro	Gln	Arg	Ile	Ser	Asp	Ala	Gln	Asn	Leu	Phe
			260					265					270		
Ser	Phe	Asp	Leu	Thr	Ala	Glu	Glu	Val	Asp	Lys	Ile	Thr	Glu	Leu	Gly
		275					280					285			
Leu	Glu	His	Glu	Pro	Leu	Arg	Val	Tyr	Trp	Asn	Lys	Leu	Tyr	Gly	Lys
	290					295					300				
Tyr	Asn	Tyr	Ala	Ala	Gln	Lys	Val								
305					310										

<210> 41
 <211> 936
 <212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 41

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atcatcggca ctggtacacg ttggtataaa aatgaagaaa ctgacgcgac cttctccaat 120
agtctgggtg aacaaatcgt gtatgcgttg aaactgccgg ggattatcca catcgacgcc 180
gcggagattt atcgcaccta cccggaagtg ggtaaagcac tgtccctgac caaaaagcct 240
cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactcccct 300
gcggacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
ttacattccc cgtttgtttc gaaggaagtg aatggcttaa gcttagaaga ggcttggaag 420
gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggttc caatttcaca 480
gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
gagttctctc cgttcctgca aaaccaaaca ccaggcattt ataaattctg tcaggagcac 600
gatatcctgg tgggaagcata ttctccgctg ggcccgtctc agaagaaaac cgcgcaggat 660
gacagccaac cattttttga gtacgtcaaa gaattgagcg aaaaatacat caaatccgag 720
gcccgatca tcctgcgctg ggctactaaa cgcggtgtgc tgccagttac cacctcttca 780
aagcctcagc gcattagcga tgctcagaac ctgttttcct tcgacctgac agcgggaagag 840
gttgataaaa tcacggagct gggtctggaa catgaaccgc tcgcgttgta ctggaataaa 900
ttgtatggca aatataacta cgccgccag aaagtg 936
```

<210> 42

<211> 312

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 42

```
Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
1          5          10          15
Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Arg Trp Tyr Lys Asn Glu
20          25          30
Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
35          40          45
Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Ile Tyr
50          55          60
Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Lys Lys Pro
65          70          75          80
Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
85          90          95
Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
100          105          110
Thr Asp Tyr Val Asp Leu Tyr Leu Leu His Ser Pro Phe Val Ser Lys
115          120          125
Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
130          135          140
Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Thr
145          150          155          160
Val Glu Asp Leu Gln Arg Ile Leu Lys Val Ala Glu Val Lys Pro Gln
165          170          175
Val Asn Gln Ile Glu Phe Ser Pro Phe Leu Gln Asn Gln Thr Pro Gly
180          185          190
Ile Tyr Lys Phe Cys Gln Glu His Asp Ile Leu Val Glu Ala Tyr Ser
195          200          205
Pro Leu Gly Pro Leu Gln Lys Lys Thr Ala Gln Asp Asp Ser Gln Pro
210          215          220
```

Phe	Phe	Glu	Tyr	Val	Lys	Glu	Leu	Ser	Glu	Lys	Tyr	Ile	Lys	Ser	Glu
225					230					235					240
Ala	Gln	Ile	Ile	Leu	Arg	Trp	Val	Thr	Lys	Arg	Gly	Val	Leu	Pro	Val
				245					250					255	
Thr	Thr	Ser	Ser	Lys	Pro	Gln	Arg	Ile	Ser	Asp	Ala	Gln	Asn	Leu	Phe
			260					265					270		
Ser	Phe	Asp	Leu	Thr	Ala	Glu	Glu	Val	Asp	Lys	Ile	Thr	Glu	Leu	Gly
		275					280					285			
Leu	Glu	His	Glu	Pro	Leu	Arg	Leu	Tyr	Trp	Asn	Lys	Leu	Tyr	Gly	Lys
	290					295					300				
Tyr	Asn	Tyr	Ala	Ala	Gln	Lys	Val								
305					310										

<210> 43

<211> 942

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 43

```

atgtcttttc accaacagtt tttcacgctg aacaacggca ataaaatccc ggcgattgcc 60
atcatcggca ctggtacacg ttggtataaa aatgaagaaa ctgacgcgac cttctcctat 120
agtctggttg aacaaatcgt gtatgcgttg aaactgccgg ggattatcca catcgacgcc 180
gcgagagattt atcgcaccta cccggaagtg ggtaaagcac tgtccctgac cgaaaagcct 240
cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactcccct 300
gcggacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
ttacattccc cgtttgtttc gaaggaagtg aatggcttaa gcttagaaga ggcttggaag 420
gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggtttc caatttcgca 480
gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
gagttctctc cgttctctga aaaccaaaca ccaggcattt ataaattctg tcaggagcac 600
gatatcctgg tggaagcata ctctccgctg ggcccgtctc agaagaaaac cgcgcaggat 660
gacagccaac cattttttga gtacgtcaaa gaattgtgcg aaaaatacat caaatccgag 720
gcccagatca tcctgcgctg ggtaactaaa cgcggtgtgc tgccagttac cacctcttca 780
aagcctcagc gcattagcga tgctcagaac ctgttttctc tcgacctgac agcgggaagag 840
gttgataaaa tcacggagct gggtctggaa catgaaccgc tcgcgctgta ctggaataaa 900
ttgtatggca aatataacta cgccgccagc aaagtgtaat ga 942

```

<210> 44

<211> 313

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 44

Met	Ser	Phe	His	Gln	Gln	Phe	Phe	Thr	Leu	Asn	Asn	Gly	Asn	Lys	Ile
1				5					10					15	
Pro	Ala	Ile	Ala	Ile	Ile	Gly	Thr	Gly	Thr	Arg	Trp	Tyr	Lys	Asn	Glu
			20					25					30		
Glu	Thr	Asp	Ala	Thr	Phe	Ser	Tyr	Ser	Leu	Val	Glu	Gln	Ile	Val	Tyr
		35					40					45			
Ala	Leu	Lys	Leu	Pro	Gly	Ile	Ile	His	Ile	Asp	Ala	Ala	Glu	Ile	Tyr
	50					55				60					
Arg	Thr	Tyr	Pro	Glu	Val	Gly	Lys	Ala	Leu	Ser	Leu	Thr	Glu	Lys	Pro
65				70					75					80	
Arg	Asn	Ala	Ile	Phe	Leu	Thr	Asp	Lys	Tyr	Ser	Pro	Gln	Ile	Lys	Met

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 46

```
Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
1          5          10          15
Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Arg Trp Tyr Lys Asn Glu
          20          25          30
Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
          35          40          45
Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Ile Tyr
          50          55          60
Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
65          70          75          80
Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
          85          90          95
Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
          100          105          110
Thr Asp Tyr Val Asp Leu Tyr Leu Leu His Ser Pro Phe Val Ser Lys
          115          120          125
Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
          130          135          140
Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Ala
145          150          155          160
Val Glu Asp Leu Gln Arg Ile Leu Lys Val Ala Glu Val Lys Pro Gln
          165          170          175
Val Asn Gln Ile Glu Phe Ser Pro Phe Leu Gln Asn Gln Thr Pro Gly
          180          185          190
Ile Tyr Lys Phe Cys Gln Glu His Asp Ile Leu Val Glu Ala Tyr Ser
          195          200          205
Pro Leu Gly Pro Leu His Lys Lys Thr Ala Gln Asp Asp Ser Gln Pro
          210          215          220
Phe Phe Glu Tyr Val Lys Glu Leu Ser Glu Lys Tyr Ile Lys Ser Glu
225          230          235          240
Ala Gln Ile Ile Leu Arg Trp Val Thr Lys Arg Gly Val Leu Pro Val
          245          250          255
Thr Thr Ser Ser Lys Pro Gln Arg Ile Ser Asp Ala Gln Asn Leu Phe
          260          265          270
Ser Phe Asp Leu Thr Ala Glu Glu Val Asp Lys Ile Thr Glu Leu Gly
          275          280          285
Leu Glu His Glu Pro Leu Arg Leu Tyr Trp Asn Lys Leu Tyr Gly Lys
          290          295          300
Tyr Asn Tyr Ala Ala Gln Lys Val
305          310
```

<210> 47

<211> 942

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 47

```
atgtcttttt accaacagtt tttcacgctg aacaacggca ataaaatccc ggcgattgcc 60
atcatcggca ctggtacacg ttggtataaa aatgaagaaa ctgaacgac cttotocaat 120
agtctggttg aacaaatcgt gtatgogttg aaactgcogg ggattatoca catogacgcc 180
gcggagattt atcgcaccta ccggaagtg ggtaaagcac tgtccctgac cgaaaagcct 240
```

```

cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactcccct 300
gcggacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
ttacattccc cgtttgtttc gaaggaagtg aatggcttaa gcttagaaga ggcttgaaa 420
gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggttc caatttcgca 480
gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
gagttctctc cgttcctgca aaaccaaaca ccaggcattt ataaattctg tcaggagcac 600
gatatcctgg tggaagcata ttctccgctg ggcccgctgc agaagaaaac cgcgcaggat 660
gacagccaac cattttttga gtacgtcaaa gaattgagcg aaaaatacat caaatccgag 720
gcccgatca tcctgcgctg gatcactaaa cgcggtgtgc tgccagttac cacctcttca 780
aagcctcagc gcattagcga tgctcagaac ctgttttcct tcgacctgac agcgggaagag 840
gttgataaaa tcacggagct gggctctgaa catgaaccgc tcgcctgtga ctggaataaa 900
ttgtatggca aatataacta cgcgcgccag aaagtgtaat ga 942

```

<210> 48

<211> 313

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 48

```

Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
1          5          10          15
Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Arg Trp Tyr Lys Asn Glu
20        25        30
Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
35        40        45
Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Ile Tyr
50        55        60
Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
65        70        75        80
Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
85        90        95
Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
100       105       110
Thr Asp Tyr Val Asp Leu Tyr Leu Leu His Ser Pro Phe Val Ser Lys
115       120       125
Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
130       135       140
Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Ala
145       150       155       160
Val Glu Asp Leu Gln Arg Ile Leu Lys Val Ala Glu Val Lys Pro Gln
165       170       175
Val Asn Gln Ile Glu Phe Ser Pro Phe Leu Gln Asn Gln Thr Pro Gly
180       185       190
Ile Tyr Lys Phe Cys Gln Glu His Asp Ile Leu Val Glu Ala Tyr Ser
195       200       205
Pro Leu Gly Pro Leu Gln Lys Lys Thr Ala Gln Asp Asp Ser Gln Pro
210       215       220
Phe Phe Glu Tyr Val Lys Glu Leu Ser Glu Lys Tyr Ile Lys Ser Glu
225       230       235       240
Ala Gln Ile Ile Leu Arg Trp Ile Thr Lys Arg Gly Val Leu Pro Val
245       250       255
Thr Thr Ser Ser Lys Pro Gln Arg Ile Ser Asp Ala Gln Asn Leu Phe
260       265       270
Ser Phe Asp Leu Thr Ala Glu Glu Val Asp Lys Ile Thr Glu Leu Gly
275       280       285
Leu Glu His Glu Pro Leu Arg Leu Tyr Trp Asn Lys Leu Tyr Gly Lys
290       295       300

```

Tyr Asn Tyr Ala Ala Gln Lys Val
305 310

<210> 49

<211> 942

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 49

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atgtcttttc accaacagtt tttcacgctg aacaacggca ataaaatccc ggcgattgcc 60
atcatcggca ctggtacacg ttggtataaa aatgaagaaa ctgacgcgac cttctccaat 120
agtctggttg aacaaatcgt gtatgcgttg aaactgccgg ggattatcca catcgacgcc 180
gcgcagattt atcgcaccta cccggaagtg ggtaaagcac tgtccctgac cgaaaagcct 240
cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactcccct 300
gcggacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
ttacattccc cgtttgtttc gaaggaagtg aatggcttaa gcttagaaga ggcttggaaa 420
gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggttc caatttcgca 480
gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
gagttctctc cgatcctgca aaaccaaact ccaggcattt ataaattctg tcaggagcac 600
gatatcctgg tggaagcata ttctccgctg ggcccgtgac agaagaaaac cgcgaggat 660
gacagccaac cattttttga gtacgtcaaa gaattgagcg aaaaatacat caaatccgag 720
gccagatca tcttgcgctg ggtcactaaa cgcggtgtgc tgccagttac cactcttca 780
aagcctcagc gcattagcga tgctcagaac ctgttttcct tcgacctgac agcggaagag 840
gttgataaaa tcacggagct gggtctggaa catgaaccgc tgcgcctgta ctggaataaa 900
ttgtatggca aatataacta cgccgccag aaagtgtaat ga 942
```

<210> 50

<211> 313

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 50

```
Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
1 5 10 15
Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Arg Trp Tyr Lys Asn Glu
20 25 30
Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
35 40 45
Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Gln Ile Tyr
50 55 60
Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
65 70 75 80
Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
85 90 95
Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
100 105 110
Thr Asp Tyr Val Asp Leu Tyr Leu Leu His Ser Pro Phe Val Ser Lys
115 120 125
Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
130 135 140
Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Ala
145 150 155 160
Val Glu Asp Leu Gln Arg Ile Leu Lys Val Ala Glu Val Lys Pro Gln
```

				165						170					175				
Val	Asn	Gln	Ile	Glu	Phe	Ser	Pro	Ile	Leu	Gln	Asn	Gln	Thr	Pro	Gly				
			180						185					190					
Ile	Tyr	Lys	Phe	Cys	Gln	Glu	His	Asp	Ile	Leu	Val	Glu	Ala	Tyr	Ser				
		195					200					205							
Pro	Leu	Gly	Pro	Leu	Gln	Lys	Lys	Thr	Ala	Gln	Asp	Asp	Ser	Gln	Pro				
	210					215					220								
Phe	Phe	Glu	Tyr	Val	Lys	Glu	Leu	Ser	Glu	Lys	Tyr	Ile	Lys	Ser	Glu				
225					230					235					240				
Ala	Gln	Ile	Ile	Leu	Arg	Trp	Val	Thr	Lys	Arg	Gly	Val	Leu	Pro	Val				
			245						250				255						
Thr	Thr	Ser	Ser	Lys	Pro	Gln	Arg	Ile	Ser	Asp	Ala	Gln	Asn	Leu	Phe				
		260						265					270						
Ser	Phe	Asp	Leu	Thr	Ala	Glu	Glu	Val	Asp	Lys	Ile	Thr	Glu	Leu	Gly				
		275					280					285							
Leu	Glu	His	Glu	Pro	Leu	Arg	Leu	Tyr	Trp	Asn	Lys	Leu	Tyr	Gly	Lys				
	290					295					300								
Tyr	Asn	Tyr	Ala	Ala	Gln	Lys	Val												
305					310														

<210> 51
 <211> 942
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 51
 atgtcttttt accaacagtt tttcacgctg aacaacggca ataaaatccc ggcgattgcc 60
 atcatoggca ctggtacacg ttggtataaa aatgaagaaa ctgacgogac ettctccaat 120
 agtctggttg aacaaatcgt gtatgcgttg aaactgccgg ggattatcca catcgacacc 180
 gcggagattt atcgcaacta cccggaagtg ggtaaagcac tgtccctgac cgaaaagcct 240
 cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactccpct 300
 gcggacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
 ttacattccc cgtttgtttc gaaggaagtg aatggcttaa gottagaaga ggcttggaaa 420
 gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggttc caatttcgca 480
 gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
 gagttctctc cattcctgca aaaccaaaaca ccaggcattt ataaattctg tcaggagcac 600
 gatatccttg tggaagcata ttctccgctg ggcccgtgac agaagaaaac cgcgaggat 660
 gacagccaac cattttttga gtacgtcaaa gaattgagcg aaaaatacat caaatccgag 720
 gccagatca tcttgccgtg ggtcactaaa cgcggtgtgc tgccagttac cacctcttca 780
 aagcctcagc gcattagcga tgctcagaac ctgttttctc tcgaacctgac agcgggaagag 840
 gttgataaaa tcacggagct gggtctggaa catgaaccgc tgccctgta ctggaataaa 900
 ttgtatggca aatataacta cgccgccag aaagtgtaat ga 942

<210> 52
 <211> 313
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 52
 Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
 1 5 10 15
 Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Arg Trp Tyr Lys Asn Glu
 20 25 30

Glu	Thr	Asp	Ala	Thr	Phe	Ser	Asn	Ser	Leu	Val	Glu	Gln	Ile	Val	Tyr
		35					40					45			
Ala	Leu	Lys	Leu	Pro	Gly	Ile	Ile	His	Ile	Asp	Thr	Ala	Glu	Ile	Tyr
		50				55					60				
Arg	Thr	Tyr	Pro	Glu	Val	Gly	Lys	Ala	Leu	Ser	Leu	Thr	Glu	Lys	Pro
65					70					75					80
Arg	Asn	Ala	Ile	Phe	Leu	Thr	Asp	Lys	Tyr	Ser	Pro	Gln	Ile	Lys	Met
				85					90					95	
Ser	Asp	Ser	Pro	Ala	Asp	Gly	Leu	Asp	Leu	Ala	Leu	Lys	Lys	Met	Gly
			100					105					110		
Thr	Asp	Tyr	Val	Asp	Leu	Tyr	Leu	Leu	His	Ser	Pro	Phe	Val	Ser	Lys
		115					120					125			
Glu	Val	Asn	Gly	Leu	Ser	Leu	Glu	Glu	Ala	Trp	Lys	Asp	Met	Glu	Gln
		130				135					140				
Leu	Tyr	Lys	Ser	Gly	Lys	Ala	Lys	Asn	Ile	Gly	Val	Ser	Asn	Phe	Ala
145					150					155					160
Val	Glu	Asp	Leu	Gln	Arg	Ile	Leu	Lys	Val	Ala	Glu	Val	Lys	Pro	Gln
				165					170					175	
Val	Asn	Gln	Ile	Glu	Phe	Ser	Pro	Phe	Leu	Gln	Asn	Gln	Thr	Pro	Gly
			180					185					190		
Ile	Tyr	Lys	Phe	Cys	Gln	Glu	His	Asp	Ile	Leu	Val	Glu	Ala	Tyr	Ser
		195					200					205			
Pro	Leu	Gly	Pro	Leu	Gln	Lys	Lys	Thr	Ala	Gln	Asp	Asp	Ser	Gln	Pro
		210				215					220				
Phe	Phe	Glu	Tyr	Val	Lys	Glu	Leu	Ser	Glu	Lys	Tyr	Ile	Lys	Ser	Glu
225					230					235					240
Ala	Gln	Ile	Ile	Leu	Arg	Trp	Val	Thr	Lys	Arg	Gly	Val	Leu	Pro	Val
				245					250					255	
Thr	Thr	Ser	Ser	Lys	Pro	Gln	Arg	Ile	Ser	Asp	Ala	Gln	Asn	Leu	Phe
			260					265					270		
Ser	Phe	Asp	Leu	Thr	Ala	Glu	Glu	Val	Asp	Lys	Ile	Thr	Glu	Leu	Gly
		275					280					285			
Leu	Glu	His	Glu	Pro	Leu	Arg	Leu	Tyr	Trp	Asn	Lys	Leu	Tyr	Gly	Lys
		290				295					300				
Tyr	Asn	Tyr	Ala	Ala	Gln	Lys	Val								
305					310										

<210> 53

<211> 942

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 53

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atgtctttttt accaacagtt ttctacgctg aacaacggca ataaaatccc ggcgattgcc 60
atcatcggca ctggtacagc ttggtacaaa aatgaagaaa ctgacgcgac cttctccaat 120
agtctggttg aacaaatcgt gcatgcgttg aaactgccgg ggattatcca catcgacgcc 180
gcggagattt atcgcaccta cccggaagtg ggtaaagcac tgtccctgac cgaaaagcct 240
cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactccoct 300
gcggacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
ttacattccc cgtttgtttc gaaggaagtg aatggcttaa gcttagaaga ggottggaaa 420
gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggttt caatttcaca 480
gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
gagttctctc cgttcctgca aaaccaaaca ccaggcattt ataaattctg ccaggagcac 600
gatatccttg tggaagcata ttctccgctg ggcccgtgac agaagaaaac cgcgaggat 660
gacagtcaac cattttttga gtacgtcaaa gaattgagcg aaaaatacat caaatccgag 720
gcccgatca tcttgccgtg ggtcactaaa cgcggtgtgc tgccagttac cacctcttca 780
aagcctcagc gcattagcga tgctcagaac ctgttttctt tcgacctgac agcgggaagag 840

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gttgataaaa tcacggagct gggctctggaa catgaaccgc tgcgcctgta ctggaataaa 900
 ttgtatggca aatataacta cgccgccag aaagtgtaat ga 942

<210> 54
 <211> 313
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 54
 Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
 1 5 10 15
 Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Ala Trp Tyr Lys Asn Glu
 20 25 30
 Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val His
 35 40 45
 Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Ile Tyr
 50 55 60
 Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
 65 70 75 80
 Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
 85 90 95
 Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
 100 105 110
 Thr Asp Tyr Val Asp Leu Tyr Leu Leu His Ser Pro Phe Val Ser Lys
 115 120 125
 Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
 130 135 140
 Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Thr
 145 150 155 160
 Val Glu Asp Leu Gln Arg Ile Leu Lys Val Ala Glu Val Lys Pro Gln
 165 170 175
 Val Asn Gln Ile Glu Phe Ser Pro Phe Leu Gln Asn Gln Thr Pro Gly
 180 185 190
 Ile Tyr Lys Phe Cys Gln Glu His Asp Ile Leu Val Glu Ala Tyr Ser
 195 200 205
 Pro Leu Gly Pro Leu Gln Lys Lys Thr Ala Gln Asp Asp Ser Gln Pro
 210 215 220
 Phe Phe Glu Tyr Val Lys Glu Leu Ser Glu Lys Tyr Ile Lys Ser Glu
 225 230 235 240
 Ala Gln Ile Ile Leu Arg Trp Val Thr Lys Arg Gly Val Leu Pro Val
 245 250 255
 Thr Thr Ser Ser Lys Pro Gln Arg Ile Ser Asp Ala Gln Asn Leu Phe
 260 265 270
 Ser Phe Asp Leu Thr Ala Glu Glu Val Asp Lys Ile Thr Glu Leu Gly
 275 280 285
 Leu Glu His Glu Pro Leu Arg Leu Tyr Trp Asn Lys Leu Tyr Gly Lys
 290 295 300
 Tyr Asn Tyr Ala Ala Gln Lys Val
 305 310

<210> 55
 <211> 942
 <212> DNA
 <213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 55

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atgtcttttc accaacagtt ttccacgctg aacaacggca ataaaatccc ggcgattgcc 60
atcatgggca ctggtacacg ttggtataaa aatgaagaaa ctgacgcgac cttctccaat 120
agcctggttg aacaaatcgt gtatgcgttg aaactgccgg ggattatcca catogaagcc 180
gcggagattt atcgcaccta cccggaagtg ggtaaagcac tgtccctgac cgaaaagcct 240
cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgaactccct 300
gtggacggtc tggatttagc attgaagaaa atgcgtacag attatgttga tttatatctg 360
ttacattccc cgtttgtttc gaaggaagtg aatggcttaa gcttagaaga ggcttggaag 420
gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggttc caatttcaca 480
gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
gagttctctc cgttcctgca aaaccaaaca ccaggcattt ataaattctg tcaggagcac 600
gatatcctgg tggaaagcata ttctccgctg ggcccgtctc agaagaaaac cgcgcaggat 660
gacagtcaac ctttttttga gtacgtcaaa gaattgagcg aaaaatacat caaatccgag 720
gccagatca tcttgccgtg ggtcactaaa cgcggtgtgc tgccagttac cacctcttca 780
aagcctcagc gcattagcga tgcacagaac ctgttttctt tcgaactgac agcggaagag 840
gttgataaaa tcacggagct gggctctggaa catgaaccgc tcgcgctgta ctggaataaa 900
ttgtatggca aatataactc cgccgccagc aaagtgtaat ga 942
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<210> 56

<211> 313

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 56

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Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
1          5          10          15
Pro Ala Ile Ala Ile Met Gly Thr Gly Thr Arg Trp Tyr Lys Asn Glu
20          25          30
Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
35          40          45
Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Ile Tyr
50          55          60
Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
65          70          75          80
Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
85          90          95
Ser Asp Ser Pro Val Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Arg
100          105          110
Thr Asp Tyr Val Asp Leu Tyr Leu Leu His Ser Pro Phe Val Ser Lys
115          120          125
Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
130          135          140
Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Thr
145          150          155          160
Val Glu Asp Leu Gln Arg Ile Leu Lys Val Ala Glu Val Lys Pro Gln
165          170          175
Val Asn Gln Ile Glu Phe Ser Pro Phe Leu Gln Asn Gln Thr Pro Gly
180          185          190
Ile Tyr Lys Phe Cys Gln Glu His Asp Ile Leu Val Glu Ala Tyr Ser
195          200          205
Pro Leu Gly Pro Leu Gln Lys Lys Thr Ala Gln Asp Asp Ser Gln Pro
210          215          220
Phe Phe Glu Tyr Val Lys Glu Leu Ser Glu Lys Tyr Ile Lys Ser Glu
225          230          235          240
Ala Gln Ile Ile Leu Arg Trp Val Thr Lys Arg Gly Val Leu Pro Val
```

				245					250					255			
Thr	Thr	Ser	Ser	Lys	Pro	Gln	Arg	Ile	Ser	Asp	Ala	Gln	Asn	Leu	Phe		
			260					265					270				
Ser	Phe	Asp	Leu	Thr	Ala	Glu	Glu	Val	Asp	Lys	Ile	Thr	Glu	Leu	Gly		
		275					280					285					
Leu	Glu	His	Glu	Pro	Leu	Arg	Leu	Tyr	Trp	Asn	Lys	Leu	Tyr	Gly	Lys		
	290					295					300						
Tyr	Asn	Ser	Ala	Ala	Gln	Lys	Val										
305					310												

<210> 57
 <211> 942
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 57
 atgtcttttc atcaacagtt cttcacgctg aataacggca ataaaatccc ggcgattgcc 60
 atcatcggca ctggtacagc ttggtataaa aatgaagaaa ctgacgcgac cttctccaat 120
 agtctggttg aacaaatcgt gtatgcgttg aaactgccgg ggattatcca catcgacgcc 180
 gcggagattt atcgcaccta cccggaagtg ggtaaagcac tgtccctgac cgaaaagcct 240
 cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactcccct 300
 gcggacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
 ttacattccc cgtttgtttc gaaggaagtg aatggcttaa gottagaaga ggcttggaaa 420
 gatattggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggttc caatttogca 480
 gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
 gagttctctc cgttcctgca aaaccaaaca ccaggcattt ataaattctg tcaggagcac 600
 gatatacttg tggaagcata ttctccgctg ggcccgctgc agaagaaaac cgcgcaggat 660
 gacagccaac cattttttga gtacgtcaaa gaattgagcg aaaaatacat caaatccgag 720
 gccagatca tcttgccgtg ggtcactaaa cgcgggtgtg tgccagttac cacctottca 780
 aagcctcagc gcattagcga tgctcagaac ctgttttctc tcgacctgac agcgggaagag 840
 gttgataaaa tcacggagct gggctctggaa catgaaccgc tgcgcctgta ctggaataaa 900
 ttgtatggca aatataactc cgcgcgccag aaagtgtaat ga 942

<210> 58
 <211> 313
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 58
 Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
 1 5 10 15
 Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Ala Trp Tyr Lys Asn Glu
 20 25 30
 Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
 35 40 45
 Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Ile Tyr
 50 55 60
 Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
 65 70 75 80
 Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
 85 90 95
 Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
 100 105 110

Thr	Asp	Tyr	Val	Asp	Leu	Tyr	Leu	Leu	His	Ser	Pro	Phe	Val	Ser	Lys
	115						120					125			
Glu	Val	Asn	Gly	Leu	Ser	Leu	Glu	Glu	Ala	Trp	Lys	Asp	Met	Glu	Gln
	130						135				140				
Leu	Tyr	Lys	Ser	Gly	Lys	Ala	Lys	Asn	Ile	Gly	Val	Ser	Asn	Phe	Ala
	145				150				155					160	
Val	Glu	Asp	Leu	Gln	Arg	Ile	Leu	Lys	Val	Ala	Glu	Val	Lys	Pro	Gln
			165				170							175	
Val	Asn	Gln	Ile	Glu	Phe	Ser	Pro	Phe	Leu	Gln	Asn	Gln	Thr	Pro	Gly
		180					185						190		
Ile	Tyr	Lys	Phe	Cys	Gln	Glu	His	Asp	Ile	Leu	Val	Glu	Ala	Tyr	Ser
	195						200					205			
Pro	Leu	Gly	Pro	Leu	Gln	Lys	Lys	Thr	Ala	Gln	Asp	Asp	Ser	Gln	Pro
	210					215					220				
Phe	Phe	Glu	Tyr	Val	Lys	Glu	Leu	Ser	Glu	Lys	Tyr	Ile	Lys	Ser	Glu
	225				230				235					240	
Ala	Gln	Ile	Ile	Leu	Arg	Trp	Val	Thr	Lys	Arg	Gly	Val	Leu	Pro	Val
			245					250						255	
Thr	Thr	Ser	Ser	Lys	Pro	Gln	Arg	Ile	Ser	Asp	Ala	Gln	Asn	Leu	Phe
		260					265						270		
Ser	Phe	Asp	Leu	Thr	Ala	Glu	Glu	Val	Asp	Lys	Ile	Thr	Glu	Leu	Gly
	275					280						285			
Leu	Glu	His	Glu	Pro	Leu	Arg	Leu	Tyr	Trp	Asn	Lys	Leu	Tyr	Gly	Lys
	290					295					300				
Tyr	Asn	Ser	Ala	Ala	Gln	Lys	Val								
305					310										

<210> 59
 <211> 942
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 59
 atgtcttttc accaacagtt ttccacgctg aacaacggca ataaaatccc ggcgattgcc 60
 atcatcggca ctggtacaaa atggtataaa aatgaagaaa ctgacgogac cttctccaat 120
 agtctggttg aacaaatcgt gtatgcgttg gaactgcogg ggattatcca catcgacgcc 180
 gcggagattt atgcaccta cccggaagtg ggtaaagcac tgccctgac cgaaaagcct 240
 cgtaacgoga tttttctgac ggataaatat ttccgcaga ttaaaatgag tgactccct 300
 gcggacggtc tggatttagc attgaagaaa atgggtacag attatgttg tttatatotg 360
 ttacattccc cgtttgtttc gaaggaagtg aatggcttaa gcttagaaga ggcttggaaa 420
 gatatggagc agttatataa aactggtaaa gctaaaaaca tcggggtttc caatttgcga 480
 gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
 gagttctctc cgttcctgca aaaccaaaca ccaggcattt ataaattctg tcaggagcac 600
 gatatcctgg tggaagcata ttctccgctg ggcccgctgc agaagaaaac cgcgcaggat 660
 gacagccaac ctttttttga gtacgtcaaa gaattgagcg aaaaatacaa caaatccgag 720
 gccagatca tcctgcgctg ggctactaaa cgcggtgtgc tgccagttac cacctottca 780
 aagcctcagc gcattagcga tgctcagaac ctgttttctt tcgacctgac agcggaagag 840
 gttgataaaa tcacggagct ggtctggaa catgaaccgc tcgcctgta ctggaataaa 900
 ttgtatggca aatataacta cgccgccag aaagtgtaat ga 942

<210> 60
 <211> 313
 <212> PRT
 <213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 60

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Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
1      5      10      15
Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Lys Trp Tyr Lys Asn Glu
20     25     30
Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
35     40     45
Ala Leu Glu Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Ile Tyr
50     55     60
Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
65     70     75     80
Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
85     90     95
Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
100    105    110
Thr Asp Tyr Val Asp Leu Tyr Leu Leu His Ser Pro Phe Val Ser Lys
115    120    125
Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
130    135    140
Leu Tyr Lys Thr Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Ala
145    150    155    160
Val Glu Asp Leu Gln Arg Ile Leu Lys Val Ala Glu Val Lys Pro Gln
165    170    175
Val Asn Gln Ile Glu Phe Ser Pro Phe Leu Gln Asn Gln Thr Pro Gly
180    185    190
Ile Tyr Lys Phe Cys Gln Glu His Asp Ile Leu Val Glu Ala Tyr Ser
195    200    205
Pro Leu Gly Pro Leu Gln Lys Lys Thr Ala Gln Asp Asp Ser Gln Pro
210    215    220
Phe Phe Glu Tyr Val Lys Glu Leu Ser Glu Lys Tyr Asn Lys Ser Glu
225    230    235    240
Ala Gln Ile Ile Leu Arg Trp Val Thr Lys Arg Gly Val Leu Pro Val
245    250    255
Thr Thr Ser Ser Lys Pro Gln Arg Ile Ser Asp Ala Gln Asn Leu Phe
260    265    270
Ser Phe Asp Leu Thr Ala Glu Glu Val Asp Lys Ile Thr Glu Leu Gly
275    280    285
Leu Glu His Glu Pro Leu Arg Leu Tyr Trp Asn Lys Leu Tyr Gly Lys
290    295    300
Tyr Asn Tyr Ala Ala Gln Lys Val
305    310
```

<210> 61

<211> 942

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 61

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atgtcttttc accaacagtt ttccacgctg aacaacggca ataaaatccc ggogattgcc 60
atcatcgga ctggtacacg ttggtataaa aatgaagaaa ctgacgcgac ctctccaat 120
agtctggttg aacaaatcgt gtatgcgttg aaactgccgg ggattatcca catgcacacc 180
gcggagattt atcgcaccta cccggaagtg ggtaaagcac tgcacctgac cgaaaagcct 240
cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactccoct 300
gcgggcggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
ttacattccc cgtttgttgc gaaggaagtg aatggcttaa gcttagaaga ggcttgga 420
```

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gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggtttc caatttcgca 480
gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
gagtttctctc cgttccctgca aaaccaaaca ccaggcattt ataaattctg tcaggagcac 600
gatatcctgg tggaagcata ttctccgctg ggcccgtgc agaagaaaac cgcgcaggat 660
gacagccaac cattttttga gtacgtcaaa gaattgagcg aaaaatacaa caaatccgag 720
gcccagatca tcttgcgctg ggtcactaaa cgcgggtgtg tgccagttac cacctcttca 780
aagcctcagc gcattagcga tgctcagaac ctgttctcct tcgacctgac agcggaagag 840
gttgataaaa tcacggagct ggggtctggaa catgaaccgc tgcgcctgta ctggaataaa 900
ttgtatggca aatataacta cgccgcccag aaagtgtaat ga 942

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<210> 62

<211> 313

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 62

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Met Ser Phe His Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
1      5      10      15
Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Arg Trp Tyr Lys Asn Glu
20     25     30
Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
35     40     45
Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Thr Ala Glu Ile Tyr
50     55     60
Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
65     70     75     80
Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
85     90     95
Ser Asp Ser Pro Ala Gly Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
100    105    110
Thr Asp Tyr Val Asp Leu Tyr Leu Leu His Ser Pro Phe Val Ser Lys
115    120    125
Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
130    135    140
Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Ala
145    150    155    160
Val Glu Asp Leu Gln Arg Ile Leu Lys Val Ala Glu Val Lys Pro Gln
165    170    175
Val Asn Gln Ile Glu Phe Ser Pro Phe Leu Gln Asn Gln Thr Pro Gly
180    185    190
Ile Tyr Lys Phe Cys Gln Glu His Asp Ile Leu Val Glu Ala Tyr Ser
195    200    205
Pro Leu Gly Pro Leu Gln Lys Lys Thr Ala Gln Asp Asp Ser Gln Pro
210    215    220
Phe Phe Glu Tyr Val Lys Glu Leu Ser Glu Lys Tyr Asn Lys Ser Glu
225    230    235    240
Ala Gln Ile Ile Leu Arg Trp Val Thr Lys Arg Gly Val Leu Pro Val
245    250    255
Thr Thr Ser Ser Lys Pro Gln Arg Ile Ser Asp Ala Gln Asn Leu Phe
260    265    270
Ser Phe Asp Leu Thr Ala Glu Glu Val Asp Lys Ile Thr Glu Leu Gly
275    280    285
Leu Glu His Glu Pro Leu Arg Leu Tyr Trp Asn Lys Leu Tyr Gly Lys
290    295    300
Tyr Asn Tyr Ala Ala Gln Lys Val
305    310

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<210> 63
<211> 942
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 63
atgtcttttc accaacagtt ttccacgctg aacaacggca ataaaatccc ggcgattgcc 60
atcatcggca ctggtacacg ttggtataaa aatgaagaaa ctgacgcgac cttctccaat 120
agtctggttg aacaaatcgt gtatgcgttg aaactgcggg ggattatoca catogaagcc 180
gcggagattt atcgcaccta cccggaagtg ggtaaagcac tgtccctgac cgaaaagcct 240
cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactcccct 300
gcggacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
ttacattccc cgtttgtttc gaaggaagtg aatggcttaa gcttagaaga ggcttggaaa 420
gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggttc caatttcgca 480
gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatc 540
gagttctctc cgttctctgca aaaccaaaca ccaggcattt ataaattctg tcaggagcac 600
gatatcctgg tggaagcata ttctccgctg ggcccgcgtc agaagaaaac cgcgcaggat 660
gacagccaac cattttttga gtacgtcaaa gaattgagcg aaaaatacaa caaatccgag 720
gccagatca tcctgcgctg ggctactaaa cgcggtgtgc tgccagttac cacctcttca 780
aagcctcagc gcattagcga tgctcagaac ctgttttctt tcgacctgac agcgggaagag 840
gttgataaaa tcacggagct gggctctggaa catgaaccgc tcgcgctgta ctggaataaa 900
ttgtatggca aatataacta cgccgccag aaagtgtaat ga 942

<210> 64
<211> 313
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 64
Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
1 5 10 15
Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Arg Trp Tyr Lys Asn Glu
20 25 30
Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
35 40 45
Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Ile Tyr
50 55 60
Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
65 70 75 80
Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
85 90 95
Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
100 105 110
Thr Asp Tyr Val Asp Leu Tyr Leu Leu His Ser Pro Phe Val Ser Lys
115 120 125
Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
130 135 140
Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Ala
145 150 155 160
Val Glu Asp Leu Gln Arg Ile Leu Lys Val Ala Glu Val Lys Pro Gln
165 170 175
Val Asn Gln Ile Glu Phe Ser Pro Phe Leu Gln Asn Gln Thr Pro Gly
180 185 190

50	Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro	55		60
65	Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met	70		75
		85		90
	Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly	100		105
	Thr Asp Tyr Val Asp Leu Tyr Leu Leu His Ser Pro Phe Val Ser Lys	115		120
	Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln	130		135
	Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Thr	145		150
	Val Glu Asp Leu Gln Arg Ile Leu Lys Val Ala Glu Val Lys Pro Gln	165		170
	Val Asn Gln Ile Glu Phe Ser Pro Phe Leu Gln Asn Gln Thr Pro Gly	180		185
	Ile Tyr Lys Phe Cys Gln Glu His Asp Ile Leu Val Glu Ala Tyr Ser	195		200
	Pro Leu Gly Pro Leu Gln Lys Lys Thr Ala Gln Asp Asp Ser Gln Pro	210		215
	Phe Phe Glu Tyr Val Lys Glu Leu Ser Glu Lys Tyr Ile Lys Ser Glu	225		230
	Ala Gln Ile Ile Leu Arg Trp Val Thr Lys Arg Gly Val Leu Pro Val	245		250
	Thr Thr Ser Ser Lys Pro Gln Arg Ile Ser Asp Ala Gln Asn Leu Phe	260		265
	Ser Phe Asp Leu Thr Ala Glu Glu Val Asp Lys Ile Thr Glu Leu Gly	275		280
	Leu Glu His Glu Pro Leu Arg Leu Tyr Trp Asn Lys Leu Tyr Gly Lys	290		295
	Tyr Asn Tyr Ala Ala Gln Lys Val	305		310

<210> 67
 <211> 942
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 67
 atgtcttttc accaacagtt ttccacgctg aacaacggca ataaaatccc ggcgattgcc 60
 atcatcggca ctggtacacg ttggtataaa aatgaagaaa ctgacgcgac cttctccaat 120
 agtctggttg agcaaatcgt gtatgcgttg aaactaccgg ggattatcca catcgacacc 180
 gcggagattt atcgcaccta cccggaagtg ggtaaagcac tgtccctgac cgaagagcct 240
 cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactccccct 300
 gcggacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
 ttacattccc cgtttggttc gaaggaagtg aatggcttaa gcttagaaga ggcttggaag 420
 gatattggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggtttc caattttcgca 480
 gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatc 540
 gagttctctc cgttcctgca aaaccaaaaca ccaggcattt ataaattctg tcaggagcac 600
 gatatcctgg tggaagcata ttctccgctg ggcccgctgc agaagaaaac cgcgcaggat 660
 gacagccaac cattttttga gtacgtcaaa gaattgagcg aaaaatacaa caaatccgag 720
 gccagatca tcctgcgctg ggtaactaaa cgcggtgtgc tgccagttac cacctcttca 780
 aagcctcagc gcattagcga tgctcagaac ctgttttctc tcgacctgac agcgggaagag 840
 gttgataaaa tcacggagct gggtctggaa catgaaccgc tgcgcctgta ctggaataaa 900
 ttgtatggca aatataacta cgccgccag aaagtgtaat ga 942

<210> 68
 <211> 313
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 68
 Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
 1 5 10 15
 Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Arg Trp Tyr Lys Asn Glu
 20 25 30
 Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
 35 40 45
 Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Thr Ala Glu Ile Tyr
 50 55 60
 Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
 65 70 75 80
 Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
 85 90 95
 Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
 100 105 110
 Thr Asp Tyr Val Asp Leu Tyr Leu Leu His Ser Pro Phe Val Ser Lys
 115 120 125
 Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
 130 135 140
 Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Ala
 145 150 155 160
 Val Glu Asp Leu Gln Arg Ile Leu Lys Val Ala Glu Val Lys Pro Gln
 165 170 175
 Val Asn Gln Ile Glu Phe Ser Pro Phe Leu Gln Asn Gln Thr Pro Gly
 180 185 190
 Ile Tyr Lys Phe Cys Gln Glu His Asp Ile Leu Val Glu Ala Tyr Ser
 195 200 205
 Pro Leu Gly Pro Leu Gln Lys Lys Thr Ala Gln Asp Asp Ser Gln Pro
 210 215 220
 Phe Phe Glu Tyr Val Lys Glu Leu Ser Glu Lys Tyr Asn Lys Ser Glu
 225 230 235 240
 Ala Gln Ile Ile Leu Arg Trp Val Thr Lys Arg Gly Val Leu Pro Val
 245 250 255
 Thr Thr Ser Ser Lys Pro Gln Arg Ile Ser Asp Ala Gln Asn Leu Phe
 260 265 270
 Ser Phe Asp Leu Thr Ala Glu Glu Val Asp Lys Ile Thr Glu Leu Gly
 275 280 285
 Leu Glu His Glu Pro Leu Arg Leu Tyr Trp Asn Lys Leu Tyr Gly Lys
 290 295 300
 Tyr Asn Tyr Ala Ala Gln Lys Val
 305 310

<210> 69
 <211> 942
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 69

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atgtcttttc accaacagtt ttccacgctg aacaacggca ataaaaatccc ggcgattgcc 60
atcatgggca ctggtacacg ttggtataaa aatgaagaaa ctgacgcgac cttctccaat 120
agtctggttg agcaaatcgt gtatgcgttg aaactgccgg ggattatcca catcgacacc 180
gcgagagatt atcgcaccta cccggaagtg ggtaaagcac tgtccctgac cgaaaagcct 240
cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactccctt 300
gcgacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
ttacattccc cgtttgtttc gaaggaagtg aacggcttaa gcttagaaga ggcttggaaa 420
gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggttc caatttcgca 480
gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
gagttctctc cgttcctgca aaaccaaaca ccaggcattt ataaattctg tcaggagcac 600
gatatcctgg tgggaagcata ttctccgctg ggcccgtgc agaagaaaac cgcgcaggat 660
gacagccaac cattttttga gtacgtcaaa gaattgagcg aaaaatacaa caaatccgag 720
gccagatca tcttgcgctg ggtcactaaa cgcggtgtgc tgccagttac cacctcttca 780
aagcctcagc gcattagcga tgctcagaac ctgttttctt tcgacctgac agcgggaagag 840
gttgataaaa tcacggagct gggctctggaa catgaaccgc tcgcctgta ctggaataaa 900
ttgtacggca aatataacta cgccgccag aaagtgtaat ga 942

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<210> 70

<211> 313

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 70

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Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
1          5          10          15
Pro Ala Ile Ala Ile Met Gly Thr Gly Thr Arg Trp Tyr Lys Asn Glu
          20          25          30
Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
          35          40          45
Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Thr Ala Glu Ile Tyr
          50          55          60
Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
65          70          75          80
Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
          85          90          95
Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
          100          105          110
Thr Asp Tyr Val Asp Leu Tyr Leu Leu His Ser Pro Phe Val Ser Lys
          115          120          125
Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
          130          135          140
Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Ala
145          150          155          160
Val Glu Asp Leu Gln Arg Ile Leu Lys Val Ala Glu Val Lys Pro Gln
          165          170          175
Val Asn Gln Ile Glu Phe Ser Pro Phe Leu Gln Asn Gln Thr Pro Gly
          180          185          190
Ile Tyr Lys Phe Cys Gln Glu His Asp Ile Leu Val Glu Ala Tyr Ser
          195          200          205
Pro Leu Gly Pro Leu Gln Lys Lys Thr Ala Gln Asp Asp Ser Gln Pro
          210          215          220
Phe Phe Glu Tyr Val Lys Glu Leu Ser Glu Lys Tyr Asn Lys Ser Glu
225          230          235          240
Ala Gln Ile Ile Leu Arg Trp Val Thr Lys Arg Gly Val Leu Pro Val
          245          250          255
Thr Thr Ser Ser Lys Pro Gln Arg Ile Ser Asp Ala Gln Asn Leu Phe
          260          265          270

```

Ser Phe Asp Leu Thr Ala Glu Glu Val Asp Lys Ile Thr Glu Leu Gly
 275 280 285
 Leu Glu His Glu Pro Leu Arg Leu Tyr Trp Asn Lys Leu Tyr Gly Lys
 290 295 300
 Tyr Asn Tyr Ala Ala Gln Lys Val
 305 310

<210> 71
 <211> 942
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 71
 atgtcttttc accaacagtt ttccacgctg aacaacggca ataaaatccc ggcgattgco 60
 atcatcggca ctggtacagc ttggtataaa aatgaagaaa ctgacgcgac cttctccaat 120
 agtctgggtg aacaaatcgt gtatgcgttg aaactgccgg ggattatcca catcgacgcc 180
 gcggagattt atcgcaccta cccggaagtg ggtaaagcac tgtccctgac cgaaaagcct 240
 cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgaotccoct 300
 gcggacggto tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
 ttacattccc cgtttgtttc gaaggaagtg aatggcttaa gcttagaaga ggcttgga 420
 gatattggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggttc caatttcaca 480
 gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
 gagttctctc cgttcctgca aaaccaaaca ccaggcattt ataaattctg tcaggagcac 600
 gatattcctgg tggaaagcata ttctccgctg ggcccgtgc agaagaaaac cgcacaggat 660
 gacagtcaac cattttttga gtacgtcaaa gaattgagcg aaaaatacat caaatccgag 720
 gccagatca tccctgcgctg ggctactaaa cgcgggtgtg tgcagttac cacctcttca 780
 aggccccagc gcattagcga tgctcagaac ctgttttctc tcgacctgac agcggaagag 840
 gttgataaaa tcacggagct gggctctggaa catgaaccgc tggcctgta ctggaataaa 900
 ttgtatggca aatataacta cgcgcgccag aaagtgtaat ga 942

<210> 72
 <211> 313
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 72
 Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
 1 5 10 15
 Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Ala Trp Tyr Lys Asn Glu
 20 25 30
 Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
 35 40 45
 Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Ile Tyr
 50 55 60
 Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
 65 70 75 80
 Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
 85 90 95
 Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
 100 105 110
 Thr Asp Tyr Val Asp Leu Tyr Leu Leu His Ser Pro Phe Val Ser Lys
 115 120 125
 Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln

130		135		140
Leu Tyr Lys Ser Gly	Lys Ala Lys Asn Ile Gly	Val Ser Asn Phe Thr		
145	150	155		160
Val Glu Asp Leu Gln Arg	Ile Leu Lys Val Ala Glu Val Lys Pro Gln			
	165	170		175
Val Asn Gln Ile Glu Phe Ser Pro Phe Leu Gln Asn Gln Thr Pro Gly				
	180	185		190
Ile Tyr Lys Phe Cys Gln Glu His Asp Ile Leu Val Glu Ala Tyr Ser				
	195	200		205
Pro Leu Gly Pro Leu Gln Lys Lys Thr Ala Gln Asp Asp Ser Gln Pro				
	210	215		220
Phe Phe Glu Tyr Val Lys Glu Leu Ser Glu Lys Tyr Ile Lys Ser Glu				
225	230	235		240
Ala Gln Ile Ile Leu Arg Trp Val Thr Lys Arg Gly Val Leu Pro Val				
	245	250		255
Thr Thr Ser Ser Arg Pro Gln Arg Ile Ser Asp Ala Gln Asn Leu Phe				
	260	265		270
Ser Phe Asp Leu Thr Ala Glu Glu Val Asp Lys Ile Thr Glu Leu Gly				
	275	280		285
Leu Glu His Glu Pro Leu Arg Leu Tyr Trp Asn Lys Leu Tyr Gly Lys				
	290	295		300
Tyr Asn Tyr Ala Ala Gln Lys Val				
305	310			

<210> 73
 <211> 942
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 73
 atgtcttttt accaacagtt tttcacgctg aacaacggca ataaaatccc ggogattgcc 60
 atcatgggca ctggtacacg ttggtataaa aatgaagaaa ctgacgcgac cttctccaat 120
 agtctggttg aacaaatcgt gtatgcgttg aaactgccgg ggattatcca catcgacgcc 180
 gcggagattt atcgcaccta cccggaagtg ggtaaagcac tgccctgac cgaaaagcct 240
 cgtaacgcga tttttctgac ggataaatat totccgcaga ttaaaatgag tgactccct 300
 gcggacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
 ttacattccc cgtttgtttc gaaggaagtg aatggcttaa gcttagaaga ggcttgga 420
 gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggttc caatttcgca 480
 gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
 gagttctctc cgttcctgca aaaccaaaca ccaggcattt ataaattctg tcaggagcac 600
 gatatccttg tggaagcata ttctccgctg ggcccgtgc agaagaaaac cgcgcaggat 660
 gacagccaac ctttttttga gtacgtcaaa gaattgagcg aaaaatacaa caaatccgag 720
 gccagatca tcctgcgctg ggtcactaaa cgcggtgcgc tgccagttac cacctcttca 780
 aagcctcagc gcattagcga tgctcagaac ctgttttctc tcgacctgac agcggaagag 840
 gttgataaaa tcacggagct gggctctggaa catgaaccgc tcgcctgtga ctggaataaa 900
 ttgtatggca aatataacta cgccgccag aaagtgtaat ga 942

<210> 74
 <211> 313
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 74

Met	Ser	Phe	His	Gln	Gln	Phe	Phe	Thr	Leu	Asn	Asn	Gly	Asn	Lys	Ile
1			5						10					15	
Pro	Ala	Ile	Ala	Ile	Met	Gly	Thr	Gly	Thr	Arg	Trp	Tyr	Lys	Asn	Glu
			20					25					30		
Glu	Thr	Asp	Ala	Thr	Phe	Ser	Asn	Ser	Leu	Val	Glu	Gln	Ile	Val	Tyr
		35					40					45			
Ala	Leu	Lys	Leu	Pro	Gly	Ile	Ile	His	Ile	Asp	Ala	Ala	Glu	Ile	Tyr
	50					55					60				
Arg	Thr	Tyr	Pro	Glu	Val	Gly	Lys	Ala	Leu	Ser	Leu	Thr	Glu	Lys	Pro
65					70					75					80
Arg	Asn	Ala	Ile	Phe	Leu	Thr	Asp	Lys	Tyr	Ser	Pro	Gln	Ile	Lys	Met
				85					90					95	
Ser	Asp	Ser	Pro	Ala	Asp	Gly	Leu	Asp	Leu	Ala	Leu	Lys	Lys	Met	Gly
			100					105					110		
Thr	Asp	Tyr	Val	Asp	Leu	Tyr	Leu	Leu	His	Ser	Pro	Phe	Val	Ser	Lys
	115						120					125			
Glu	Val	Asn	Gly	Leu	Ser	Leu	Glu	Glu	Ala	Trp	Lys	Asp	Met	Glu	Gln
	130					135					140				
Leu	Tyr	Lys	Ser	Gly	Lys	Ala	Lys	Asn	Ile	Gly	Val	Ser	Asn	Phe	Ala
145					150					155					160
Val	Glu	Asp	Leu	Gln	Arg	Ile	Leu	Lys	Val	Ala	Glu	Val	Lys	Pro	Gln
				165					170					175	
Val	Asn	Gln	Ile	Glu	Phe	Ser	Pro	Phe	Leu	Gln	Asn	Gln	Thr	Pro	Gly
	180							185					190		
Ile	Tyr	Lys	Phe	Cys	Gln	Glu	His	Asp	Ile	Leu	Val	Glu	Ala	Tyr	Ser
	195						200					205			
Pro	Leu	Gly	Pro	Leu	Gln	Lys	Lys	Thr	Ala	Gln	Asp	Asp	Ser	Gln	Pro
	210					215					220				
Phe	Phe	Glu	Tyr	Val	Lys	Glu	Leu	Ser	Glu	Lys	Tyr	Asn	Lys	Ser	Glu
225					230					235					240
Ala	Gln	Ile	Ile	Leu	Arg	Trp	Val	Thr	Lys	Arg	Gly	Ala	Leu	Pro	Val
				245					250					255	
Thr	Thr	Ser	Ser	Lys	Pro	Gln	Arg	Ile	Ser	Asp	Ala	Gln	Asn	Leu	Phe
			260					265					270		
Ser	Phe	Asp	Leu	Thr	Ala	Glu	Glu	Val	Asp	Lys	Ile	Thr	Glu	Leu	Gly
	275						280					285			
Leu	Glu	His	Glu	Pro	Leu	Arg	Leu	Tyr	Trp	Asn	Lys	Leu	Tyr	Gly	Lys
	290					295					300				
Tyr	Asn	Tyr	Ala	Ala	Gln	Lys	Val								
305					310										

<210> 75

<211> 942

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 75

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atgtcttttc accaacagtt tttcacgctg aacaacggca ataaaatccc ggcgattgcc 60
atcatgggca ctggtacacg ttggtataaa aatgaagaaa ctgacgogac cttctccaat 120
agtctggttg atcaaatcgt gtatgcgttg aaactgccgg ggattatcca catogaogcc 180
gcggagattt atcgcaccta cccggaagtg ggtaaagcac tgccoctgac cgaagaagcct 240
cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactccoct 300
gcggacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
ttacattccc cgtttgtttc gaaggaagtg aatggottaa gottagaaga ggcttggaag 420
gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggttc caatttcgca 480
gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatc 540
gagttctctc cgttctctgca aaaccaaaaca ccaggcattt ataaattctg tcaggagcac 600

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gatatcctgg tggaagcata ttctccgctg ggcccgcgtgc agaagaaaac cgcgcaggat 660
gacagccaac cattttttga gtacgtcaaa gaattgagcg aaaaatacaa caaatccgag 720
gccagatca tcctgcgctg ggctactaaa cgcggtgtgc tgccagttac cacctcttca 780
aagcctcagc gcattagcga tgctcagaac ctgttttctc tcgacctgac agcgggaagag 840
gttgataaaa tcacggagct gggctctgcaa catgaaccgc tgcgcctgta ctggaataaa 900
ttgtatggca aatataacta cgccgcccag aaagtgtaat ga 942

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<210> 76

<211> 313

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 76

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Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
1          5          10          15
Pro Ala Ile Ala Ile Met Gly Thr Gly Thr Arg Trp Tyr Lys Asn Glu
          20          25          30
Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Asp Gln Ile Val Tyr
          35          40          45
Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Ile Tyr
          50          55          60
Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
65          70          75          80
Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
          85          90          95
Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
          100          105          110
Thr Asp Tyr Val Asp Leu Tyr Leu Leu His Ser Pro Phe Val Ser Lys
          115          120          125
Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
          130          135          140
Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Ala
145          150          155          160
Val Glu Asp Leu Gln Arg Ile Leu Lys Val Ala Glu Val Lys Pro Gln
          165          170          175
Val Asn Gln Ile Glu Phe Ser Pro Phe Leu Gln Asn Gln Thr Pro Gly
          180          185          190
Ile Tyr Lys Phe Cys Gln Glu His Asp Ile Leu Val Glu Ala Tyr Ser
          195          200          205
Pro Leu Gly Pro Leu Gln Lys Lys Thr Ala Gln Asp Asp Ser Gln Pro
210          215          220
Phe Phe Glu Tyr Val Lys Glu Leu Ser Glu Lys Tyr Asn Lys Ser Glu
225          230          235          240
Ala Gln Ile Ile Leu Arg Trp Val Thr Lys Arg Gly Val Leu Pro Val
          245          250          255
Thr Thr Ser Ser Lys Pro Gln Arg Ile Ser Asp Ala Gln Asn Leu Phe
          260          265          270
Ser Phe Asp Leu Thr Ala Glu Glu Val Asp Lys Ile Thr Glu Leu Gly
          275          280          285
Leu Gln His Glu Pro Leu Arg Leu Tyr Trp Asn Lys Leu Tyr Gly Lys
          290          295          300
Tyr Asn Tyr Ala Ala Gln Lys Val
305          310

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<210> 77

<211> 942

<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 77
atgtcttttc accaacagtt tttcacgctg aacaacggca ataaaatccc ggcgattgcc 60
atcatcggca ctggtacacg ttggtataaa aatgaagaaa ctgacgcgac cttctccaat 120
agtctggttg aacaaatcgt gtatgcgttg aaactgccgg ggattatcca catcgacgcc 180
gcggagattt atcgaccta cccggaagtg ggtaaagcac tgcacctgac cgaaaagcct 240
cgtaacgca tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactccct 300
gcggacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
ttacattccc cgtttgtttc gaaggaagtg aatggcttaa gottagaaga ggcttggaaa 420
gatatggagc agttatacaa aagtggtaaa gotaaaaaca tcggggtttc caatttcaca 480
gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
gagttctctc cgttctctgca aaaccaaaca ccaggcattt ataaattctg tcaggagcac 600
gatatcctgg tgggaagcata ttctccgctg ggcccgtgca agaagaaaac cgcgcaggat 660
gacagtcaac ctttttttga gtacgtcaaa gaattgagcg aaaaatacat caaatccgag 720
gccagatca tcttgcgctg ggtcactaaa cgcgggtgtgc tgccagttac cacctottca 780
aagcctcagc gcattagcga tgcacagaac ctgttttctc tcgacctgac agcgggaagag 840
gttgataaaa tcacggagct gggctctggat catgaaccgc tgcgcctgta ctggaataaa 900
ttgtatggca aatataacta cgcgcgccag aaagtgtaat ga 942

<210> 78
<211> 313
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 78
Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
1 5 10 15
Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Arg Trp Tyr Lys Asn Glu
20 25 30
Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
35 40 45
Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Ile Tyr
50 55 60
Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
65 70 75 80
Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
85 90 95
Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
100 105 110
Thr Asp Tyr Val Asp Leu Tyr Leu Leu His Ser Pro Phe Val Ser Lys
115 120 125
Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
130 135 140
Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Thr
145 150 155 160
Val Glu Asp Leu Gln Arg Ile Leu Lys Val Ala Glu Val Lys Pro Gln
165 170 175
Val Asn Gln Ile Glu Phe Ser Pro Phe Leu Gln Asn Gln Thr Pro Gly
180 185 190
Ile Tyr Lys Phe Cys Gln Glu His Asp Ile Leu Val Glu Ala Tyr Ser
195 200 205
Pro Leu Gly Pro Leu Gln Lys Lys Thr Ala Gln Asp Asp Ser Gln Pro

210		215		220
Phe Phe Glu Tyr Val	Lys Glu Leu Ser Glu	Lys Tyr Ile Lys Ser Glu		
225	230	235		240
Ala Gln Ile Ile Leu	Arg Trp Val Thr	Lys Arg Gly Val Leu	Pro Val	
	245	250		255
Thr Thr Ser Ser Lys	Pro Gln Arg Ile	Ser Asp Ala Gln	Asn Leu Phe	
	260	265		270
Ser Phe Asp Leu Thr	Ala Glu Glu Val	Asp Lys Ile Thr	Glu Leu Gly	
	275	280		285
Leu Asp His Glu Pro	Leu Arg Leu Tyr	Trp Asn Lys	Leu Tyr Gly Lys	
	290	295		300
Tyr Asn Tyr Ala Ala	Gln Lys Val			
305	310			

<210> 79
 <211> 942
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 79
 atgtcttttt accaacagtt tttcacgctg aacaacggca ataaaatccc ggcgattgcc 60
 atcatgggca ctggtacacg ttggtataaa aatgaagaaa ctgacgogac cttctccaat 120
 agtctggttg aacaaatcgt gtatgcgttg aaactgccgg ggattatoca catcgacgcc 180
 gcgagagatt atcgcaccta cccggaagtg ggtaaagcac tgccctgac cgaaaagcct 240
 cgtaacgcga tttttctgac ggataaatat tctcgcaga ttaaaatgag tgactccct 300
 gcggacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
 ttacattccc cgtttgtttc gaaggaagtg aatggcttaa gcttagaaga ggcttggaaa 420
 gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggttt caatttgcga 480
 gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
 gagttctctc cgttcctgca aaaccaaaca ccaggcattt ataaattctg tcaggagcac 600
 gatatccttg tggaaagcata ttctcgcgtg ggcccgtgca agaagaaaac cgcgcaggat 660
 gacagccaac ctttttttga gtacgtcaaa gaattgagcg aaaaatacaa caaatcogag 720
 gccagatca tcttgcgctg ggtaactaaa cggggtgtgc tgccagttac caoctottca 780
 aagcctcagc gcattagcga tgctcagaac ctgttttctt tcgacctgac agcggaagag 840
 gttgataaaa tcacggagct gggctctggat catgaacggc tgcgcctgta ctggaataaa 900
 ttgtatggca aatataacta cgcgcgccag aaagtgtaat ga 942

<210> 80
 <211> 313
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 80
 Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
 1 5 10 15
 Pro Ala Ile Ala Ile Met Gly Thr Gly Thr Arg Trp Tyr Lys Asn Glu
 20 25 30
 Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
 35 40 45
 Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Ile Tyr
 50 55 60
 Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
 65 70 75 80

Arg	Asn	Ala	Ile	Phe	Leu	Thr	Asp	Lys	Tyr	Ser	Pro	Gln	Ile	Lys	Met	
			85						90					95		
Ser	Asp	Ser	Pro	Ala	Asp	Gly	Leu	Asp	Leu	Ala	Leu	Lys	Lys	Met	Gly	
			100					105					110			
Thr	Asp	Tyr	Val	Asp	Leu	Tyr	Leu	Leu	His	Ser	Pro	Phe	Val	Ser	Lys	
		115					120					125				
Glu	Val	Asn	Gly	Leu	Ser	Leu	Glu	Glu	Ala	Trp	Lys	Asp	Met	Glu	Gln	
	130					135					140					
Leu	Tyr	Lys	Ser	Gly	Lys	Ala	Lys	Asn	Ile	Gly	Val	Ser	Asn	Phe	Ala	
145					150					155					160	
Val	Glu	Asp	Leu	Gln	Arg	Ile	Leu	Lys	Val	Ala	Glu	Val	Lys	Pro	Gln	
			165						170					175		
Val	Asn	Gln	Ile	Glu	Phe	Ser	Pro	Phe	Leu	Gln	Asn	Gln	Thr	Pro	Gly	
			180					185					190			
Ile	Tyr	Lys	Phe	Cys	Gln	Glu	His	Asp	Ile	Leu	Val	Glu	Ala	Tyr	Ser	
	195						200					205				
Pro	Leu	Gly	Pro	Leu	Gln	Lys	Lys	Thr	Ala	Gln	Asp	Asp	Ser	Gln	Pro	
	210					215					220					
Phe	Phe	Glu	Tyr	Val	Lys	Glu	Leu	Ser	Glu	Lys	Tyr	Asn	Lys	Ser	Glu	
225					230					235					240	
Ala	Gln	Ile	Ile	Leu	Arg	Trp	Val	Thr	Lys	Arg	Gly	Val	Leu	Pro	Val	
			245						250					255		
Thr	Thr	Ser	Ser	Lys	Pro	Gln	Arg	Ile	Ser	Asp	Ala	Gln	Asn	Leu	Phe	
		260					265						270			
Ser	Phe	Asp	Leu	Thr	Ala	Glu	Glu	Val	Asp	Lys	Ile	Thr	Glu	Leu	Gly	
	275						280					285				
Leu	Asp	His	Glu	Pro	Leu	Arg	Leu	Tyr	Trp	Asn	Lys	Leu	Tyr	Gly	Lys	
	290					295					300					
Tyr	Asn	Tyr	Ala	Ala	Gln	Lys	Val									
305					310											

<210> 81
 <211> 942
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 81
 atgtcttttt accaacagtt tttaoagctg aacaaogggca ataaaatccc ggcgattgcc 60
 atcatcggca ctggtacaag ttggtataaa aatgaagaaa ctgacgogac cttctccaat 120
 agtctggttg aacaaatcgt gtatgcgttg aaactgccgg ggattatcca catcgacgcc 180
 gcggagattt atcgcaccta cccggaagtg ggtaaagcac tgcccttgac cgaaaagcct 240
 cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactccoct 300
 gcggacggtc tggatttagc attgaagaaa atgcgtacag attatgttga tttatatctg 360
 ttacattccc cgtttgtttc gaaggaagtg aatggcttaa gcttagaaga ggcttggaaa 420
 gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggttc caatttcaca 480
 gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
 gagttctctc cgttcctgca aaaccaaaca ccaggcattt ataaattctg tcaggagcac 600
 gatatcctgg tggaaagcata ttctcogctg ggcccgtgc agaagaaaac cgcgcaggat 660
 gacagccaac cattttttga gtacgtcaaa gaattgagcg aaaaatacat caaatccgag 720
 gccagatca tcttgccgtg ggtcactaaa cgcgggtgtg tgccagttac cacctcttca 780
 aagcctcagc gcattagcga tgctcagaac ctgttttctc tcgacctgac agcgggaagag 840
 gttgataaaa tcacggagct gggctctggaa catgaaccgc tcgcgcctgta ctggaataaa 900
 ttgtatggca aatataactc cgcgcgccag aaagtgtaat ga 942

<210> 82
 <211> 313

<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 82
Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
1 5 10 15
Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Arg Trp Tyr Lys Asn Glu
20 25 30
Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
35 40 45
Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Ile Tyr
50 55 60
Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
65 70 75 80
Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
85 90 95
Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Arg
100 105 110
Thr Asp Tyr Val Asp Leu Tyr Leu Leu His Ser Pro Phe Val Ser Lys
115 120 125
Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
130 135 140
Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Thr
145 150 155 160
Val Glu Asp Leu Gln Arg Ile Leu Lys Val Ala Glu Val Lys Pro Gln
165 170 175
Val Asn Gln Ile Glu Phe Ser Pro Phe Leu Gln Asn Gln Thr Pro Gly
180 185 190
Ile Tyr Lys Phe Cys Gln Glu His Asp Ile Leu Val Glu Ala Tyr Ser
195 200 205
Pro Leu Gly Pro Leu Gln Lys Lys Thr Ala Gln Asp Asp Ser Gln Pro
210 215 220
Phe Phe Glu Tyr Val Lys Glu Leu Ser Glu Lys Tyr Ile Lys Ser Glu
225 230 235 240
Ala Gln Ile Ile Leu Arg Trp Val Thr Lys Arg Gly Val Leu Pro Val
245 250 255
Thr Thr Ser Ser Lys Pro Gln Arg Ile Ser Asp Ala Gln Asn Leu Phe
260 265 270
Ser Phe Asp Leu Thr Ala Glu Glu Val Asp Lys Ile Thr Glu Leu Gly
275 280 285
Leu Glu His Glu Pro Leu Arg Leu Tyr Trp Asn Lys Leu Tyr Gly Lys
290 295 300
Tyr Asn Ser Ala Ala Gln Lys Val
305 310

<210> 83
<211> 942
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 83
atgtctttttc accaacagtt ttccacgctg aacaacggca ataaaatccc ggcgattgcc 60
atcatgggca ctggtacacg ttggtataaa aatgaagaaa ctgacgcgac cttctccaat 120
agtctggttg agcaaatcgt gtatgcgttg aaactgcggg ggattatcca catcgacgcc 180

```

gcgagatatt atcgcaccta cccggaagtg ggtaaagcac tgtccctggc cgaaaagcct 240
cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactcccct 300
gcgagcggtc tggatttagc attgaagaaa atgcgtacag attatgttga tttatatctg 360
ttacattccc cgtttgtttc gaaggaagtg aatggcttaa gcttagaaga ggcttggaaa 420
gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggtttc caatttcaca 480
gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
gagttctctc cgttcctgca aaaccaaaca ccaggcattt ataaattctg tcaggagcac 600
gatatcctgg tggaagcata ttctccgctg ggcccgcctgc agaagaaaac cgcgcaggat 660
gacagtcaac cattttttga gtacgtcaaa gaattgagcg aaaaatacat caaatccgag 720
gccagatca tctgcgctg ggtcactaaa cgcgggtgtgc tgccagttac cacctcttca 780
aagcctcagc gcattagcga tgctcagaac ctgttttctc tcgacctgac agcgggaagag 840
gttgataaaa tcacggagct gggtctggaa catgaaccgc tcgcctgta ctggaataaa 900
ttgtatggca aatataacta cgcgcccgag aaagtgtaat ga 942

```

<210> 84

<211> 313

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 84

```

Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
1      5      10      15
Pro Ala Ile Ala Ile Met Gly Thr Gly Thr Arg Trp Tyr Lys Asn Glu
20     25     30
Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
35     40     45
Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Ile Tyr
50     55     60
Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Ala Glu Lys Pro
65     70     75     80
Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
85     90     95
Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Arg
100    105    110
Thr Asp Tyr Val Asp Leu Tyr Leu Leu His Ser Pro Phe Val Ser Lys
115    120    125
Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
130    135    140
Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Thr
145    150    155    160
Val Glu Asp Leu Gln Arg Ile Leu Lys Val Ala Glu Val Lys Pro Gln
165    170    175
Val Asn Gln Ile Glu Phe Ser Pro Phe Leu Gln Asn Gln Thr Pro Gly
180    185    190
Ile Tyr Lys Phe Cys Gln Glu His Asp Ile Leu Val Glu Ala Tyr Ser
195    200    205
Pro Leu Gly Pro Leu Gln Lys Lys Thr Ala Gln Asp Asp Ser Gln Pro
210    215    220
Phe Phe Glu Tyr Val Lys Glu Leu Ser Glu Lys Tyr Ile Lys Ser Glu
225    230    235    240
Ala Gln Ile Ile Leu Arg Trp Val Thr Lys Arg Gly Val Leu Pro Val
245    250    255
Thr Thr Ser Ser Lys Pro Gln Arg Ile Ser Asp Ala Gln Asn Leu Phe
260    265    270
Ser Phe Asp Leu Thr Ala Glu Glu Val Asp Lys Ile Thr Glu Leu Gly
275    280    285
Leu Glu His Glu Pro Leu Arg Leu Tyr Trp Asn Lys Leu Tyr Gly Lys

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290
Tyr Asn Tyr Ala Ala Gln Lys Val
305 310

300

<210> 85
<211> 942
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 85
atgtcttttt accaacagtt tttcacgctg aacaacggca ataaaatccc ggcgattgcc 60
atcatgggca ctggtacacg ttggtataaa aatgaagaaa ctgacgcgac cttctccaat 120
agtctggttg agcaaatcgt gtatgcgttg aaactgcggg ggattatcca catcgacgcc 180
gcgagagatt atcgcaccta cccggaagtg ggtaaagcac tgccctgac cgaaaagcct 240
cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaagatgag tgactccct 300
gcgacgggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
ttacattccc cgtttgtttc gaaggaagtg aatggcctaa gcttagaaga ggcttggaaa 420
gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggttc caatttcgca 480
gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
gagttctctc cgttcctgca aaaccaaaca ccaggcattt ataaattctg tcaggagcac 600
gatatcctgg tgggaagcgt tttctcgctg ggcccgtgc agaagaaaac cgcgaggat 660
gacagccaac ctttttttga gtacgtcaaa gaattgagcg aaaaatacaa caaatccgag 720
gccagatca tcctgcgctg ggctactaaa cgoggtgtgc tgccagttac cacctcttca 780
aagcctcagc gcattagcga tgctcagaac ctgttttctc tcgacctgac agcggaagag 840
gttgataaaa tcacggagct gggctctggaa catgaaccgc tcgcctgta ctggaataaa 900
ttgtatggca aatataacta cgccgccag aaagtgtaat ga 942

<210> 86
<211> 313
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 86
Met Ser Phe His Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
1 5 10 15
Pro Ala Ile Ala Ile Met Gly Thr Gly Thr Arg Trp Tyr Lys Asn Glu
20 25 30
Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
35 40 45
Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Ile Tyr
50 55 60
Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
65 70 75 80
Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
85 90 95
Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
100 105 110
Thr Asp Tyr Val Asp Leu Tyr Leu Leu His Ser Pro Phe Val Ser Lys
115 120 125
Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
130 135 140
Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Ala
145 150 155 160

Val	Glu	Asp	Leu	Gln	Arg	Ile	Leu	Lys	Val	Ala	Glu	Val	Lys	Pro	Gln
				165					170					175	
Val	Asn	Gln	Ile	Glu	Phe	Ser	Pro	Phe	Leu	Gln	Asn	Gln	Thr	Pro	Gly
			180					185					190		
Ile	Tyr	Lys	Phe	Cys	Gln	Glu	His	Asp	Ile	Leu	Val	Glu	Ala	Tyr	Ser
		195					200					205			
Pro	Leu	Gly	Pro	Leu	Gln	Lys	Lys	Thr	Ala	Gln	Asp	Asp	Ser	Gln	Pro
	210					215					220				
Phe	Phe	Glu	Tyr	Val	Lys	Glu	Leu	Ser	Glu	Lys	Tyr	Asn	Lys	Ser	Glu
225					230					235					240
Ala	Gln	Ile	Ile	Leu	Arg	Trp	Val	Thr	Lys	Arg	Gly	Val	Leu	Pro	Val
				245					250					255	
Thr	Thr	Ser	Ser	Lys	Pro	Gln	Arg	Ile	Ser	Asp	Ala	Gln	Asn	Leu	Phe
			260					265					270		
Ser	Phe	Asp	Leu	Thr	Ala	Glu	Glu	Val	Asp	Lys	Ile	Thr	Glu	Leu	Gly
		275					280					285			
Leu	Glu	His	Glu	Pro	Leu	Arg	Leu	Tyr	Trp	Asn	Lys	Leu	Tyr	Gly	Lys
	290					295					300				
Tyr	Asn	Tyr	Ala	Ala	Gln	Lys	Val								
305					310										

<210> 87
 <211> 942
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 87
 atgtctttttt accaacagtt tttcacgctg aacaacggca ataaaatccc ggcgattgcc 60
 atcatcggca ctggtacacg ttggtataaa agtgaagaaa ctgacgcgac cttctccaat 120
 agtctggttg aacaaatcgt gtatgcgttg aaactgcgag ggattatcca catcgacgac 180
 gcggagattt atcgaccta cccggaagtg ggtaaagcac tgccctgac cgaaaagcct 240
 cgtaacgcga tttttctgac ggataaatat tctcgcaga ttaaaatgag tgactccctt 300
 gcggacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
 ttacattccc cgtttgtttc gaaggaagtg aatggcttaa gcttagaaga ggcttggaag 420
 gatattggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggttt caatttcgca 480
 gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aaactcaggt caaccagatc 540
 gagttctctc cgttcctgca aaaccaaaca ccaggcattt ataaattctg tcaggagcac 600
 gatatcctgg tggaaagcata ttctccgctg ggcccgcgtc agaagaaaac cgcgcaggat 660
 gacagccaac cattttttga gtacgtcaaa gaattgagcg aaaaatacaa caaatccgag 720
 gccagatca tcttgcgctg ggtcactaaa cgcgggtgtc tgccagttac cacctcttca 780
 aagcctcagc gcattagcga tgcacagAAC ctgttttctc tcgacctgac agcggaagag 840
 gttgataaaa tcacggagct gggctctggaa catgaaccgc tcgcctctga ctggaataaa 900
 ttgtatggca aatataacta cgcgcgccag aaagtgtaat ga 942

<210> 88
 <211> 313
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 88
 Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
 1 5 10 15
 Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Arg Trp Tyr Lys Ser Glu


```

aagcctcagc gcattagcga tgctcagaac ctgttttctt tcgacctgac agcgggaagag 840
gttgataaaa tcacggagct gggctctggaa catgaaccgc tgcgcctgta ctggaataaa 900
ttgtatggca aatataacta cgccgcccag aaagtgtaat ga 942

```

```

<210> 90
<211> 313
<212> PRT
<213> Artificial Sequence

```

```

<220>
<223> Synthetic Construct

```

```

<400> 90
Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
1      5      10      15
Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Arg Trp Tyr Lys Asn Glu
20      25      30
Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
35      40      45
Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Thr Ala Glu Ile Tyr
50      55      60
Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
65      70      75      80
Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
85      90      95
Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
100     105     110
Thr Asp Tyr Val Asp Leu Tyr Leu Leu His Ser Pro Phe Val Ser Lys
115     120     125
Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
130     135     140
Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Ala
145     150     155     160
Val Glu Asp Leu Gln Arg Ile Leu Lys Val Ala Glu Val Lys Pro Gln
165     170     175
Val Asn Gln Ile Glu Phe Ser Pro Phe Leu Gln Asn Gln Thr Pro Gly
180     185     190
Ile Tyr Lys Phe Cys Gln Glu His Asp Ile Leu Val Glu Ala Tyr Ser
195     200     205
Pro Leu Gly Pro Leu Gln Lys Lys Thr Ala Gln Asp Asp Ser Gln Pro
210     215     220
Phe Phe Glu Tyr Val Lys Glu Leu Ser Glu Lys Tyr Thr Lys Ser Glu
225     230     235     240
Ala Gln Ile Ile Leu Arg Trp Val Thr Lys Arg Gly Val Leu Pro Val
245     250     255
Thr Thr Ser Ser Lys Pro Gln Arg Ile Ser Asp Ala Gln Asn Leu Phe
260     265     270
Ser Phe Asp Leu Thr Ala Glu Glu Val Asp Lys Ile Thr Glu Leu Gly
275     280     285
Leu Glu His Glu Pro Leu Arg Leu Tyr Trp Asn Lys Leu Tyr Gly Lys
290     295     300
Tyr Asn Tyr Ala Ala Gln Lys Val
305     310

```

```

<210> 91
<211> 942
<212> DNA
<213> Artificial Sequence

```

<220>

<223> Synthetic Construct

<400> 91

```
atgtcttttc accaacagtt ttccacgctg aacaacggca ataaaatccc ggcgattgcc 60
atcatcgcca ctggtacacg ttggtataaa aatgaagaaa ctgacggac cttctccaat 120
agtctggttg aacaaatcgt gtatgcgttg aaactgccgg ggattatcca catcgacgcc 180
gcggagattt atcgacaccta cccggaagtg ggtaaagcac tgtccctgac cgaaaagcct 240
cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactccoct 300
gcggaaggctc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
ttacattccc cgtttgtttc gaaggaagtg aatggcttaa gcttagaaga ggcttggaag 420
gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggttc caatttcaca 480
gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
gagttctctc cgttcctgca aaaccaaaca ccaggcattt ataaattctg tcaggagcac 600
gatatcctgg tgggaagcata ttctccgctg ggcccgtgc agaagaaaac cgcgcaggat 660
gacagtcaac cattttttga gtacgtcaaa gaattgagcg aaaaatacat caaatccgag 720
gcccagatca tctctgcctg ggtcactaaa cgcggtgtgc tgccagttac cacctcttca 780
aagccccagc gcattagcga tgctcagaac ctgttttctc tcgacctgac agcgggaagag 840
gttgataaaa tcacggagct gggctctgga catgaaccgc tgcgcctgta ctggaataaa 900
ttgtatggca aatataactc cgccgccagc aaagtgtgat ga 942
```

<210> 92

<211> 313

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 92

```
Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
1          5          10          15
Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Arg Trp Tyr Lys Asn Glu
20          25          30
Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
35          40          45
Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Ile Tyr
50          55          60
Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
65          70          75          80
Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
85          90          95
Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
100         105         110
Thr Asp Tyr Val Asp Leu Tyr Leu Leu His Ser Pro Phe Val Ser Lys
115         120         125
Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
130         135         140
Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Thr
145         150         155         160
Val Glu Asp Leu Gln Arg Ile Leu Lys Val Ala Glu Val Lys Pro Gln
165         170         175
Val Asn Gln Ile Glu Phe Ser Pro Phe Leu Gln Asn Gln Thr Pro Gly
180         185         190
Ile Tyr Lys Phe Cys Gln Glu His Asp Ile Leu Val Glu Ala Tyr Ser
195         200         205
Pro Leu Gly Pro Leu Gln Lys Lys Thr Ala Gln Asp Asp Ser Gln Pro
210         215         220
Phe Phe Glu Tyr Val Lys Glu Leu Ser Glu Lys Tyr Ile Lys Ser Glu
225         230         235         240
```

Ala	Gln	Ile	Ile	Leu	Arg	Trp	Val	Thr	Lys	Arg	Gly	Val	Leu	Pro	Val
				245					250					255	
Thr	Thr	Ser	Ser	Lys	Pro	Gln	Arg	Ile	Ser	Asp	Ala	Gln	Asn	Leu	Phe
				260				265					270		
Ser	Phe	Asp	Leu	Thr	Ala	Glu	Glu	Val	Asp	Lys	Ile	Thr	Glu	Leu	Gly
		275				280						285			
Leu	Glu	His	Glu	Pro	Leu	Arg	Leu	Tyr	Trp	Asn	Lys	Leu	Tyr	Gly	Lys
	290					295					300				
Tyr	Asn	Ser	Ala	Ala	Gln	Lys	Val								
305					310										

<210> 93

<211> 942

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 93

atgtcttttc	accaacagtt	tttcacgctg	aacaacggca	ataaaatccc	ggcgattgcc	60
atcatcggca	ctggtacacg	ttggtataaa	aatgaagaaa	ctgacgcgac	cttctccaat	120
agtctggttg	aacaaatcgt	gtatgcgttg	aaactgccgg	ggattatcca	catcgacgcc	180
gcggagattt	atcgcaccta	cccgagggtg	ggtaaagcac	tgtccctgac	cgaaaagcct	240
cgtaacgcga	tttttctgac	ggataaatat	tctccgcaga	ttaaaatgag	tgactccoct	300
gcggacggtc	tggatttagc	attgaagaaa	atgggtacag	attatgttga	tttatactcg	360
ttacattccc	cgtttgtttc	gaaggaagtg	aatggcttaa	gcttagaaga	ggcttggaaa	420
gatatggagc	agttatacag	aagtggtaaa	gctaaaaaca	tcgggggtttc	caatttcaca	480
gtggaagacc	tgcaacgtat	cctgaaagtc	gctgaagtta	agcctcaggt	caaccagatt	540
gagttctctc	cgttctctgca	aaaccaaaaca	ccaggcattt	ataaattctg	tcaggagcac	600
gatatcctgg	tggaagcata	ttctccgctg	ggcccgtctc	agaagaaaac	cgcgaggat	660
gacagccaac	cattttttga	gtacgtcaaa	gaattgagcg	aaaaatacaa	caaattccgag	720
gccagatca	tcttgccgtg	ggctactaaa	cgcggtgtgc	tgccagttac	cacctcttca	780
aagcctcagc	gcattagcga	tgctcagaac	ctgttttctt	tcgacctgac	agcgggaagag	840
gttgataaaa	tcacggagct	gggtctggaa	catgagcgcg	tgcgccctgta	ctggaataaa	900
ttgtatggca	aataataactc	cgccgcccag	aaagtgtaat	ga		942

<210> 94

<211> 313

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 94

Met	Ser	Phe	His	Gln	Gln	Phe	Phe	Thr	Leu	Asn	Asn	Gly	Asn	Lys	Ile
1			5						10					15	
Pro	Ala	Ile	Ala	Ile	Ile	Gly	Thr	Gly	Thr	Arg	Trp	Tyr	Lys	Asn	Glu
			20					25					30		
Glu	Thr	Asp	Ala	Thr	Phe	Ser	Asn	Ser	Leu	Val	Glu	Gln	Ile	Val	Tyr
		35				40					45				
Ala	Leu	Lys	Leu	Pro	Gly	Ile	Ile	His	Ile	Asp	Ala	Ala	Glu	Ile	Tyr
	50				55				60						
Arg	Thr	Tyr	Pro	Glu	Val	Gly	Lys	Ala	Leu	Ser	Leu	Thr	Glu	Lys	Pro
65			70					75					80		
Arg	Asn	Ala	Ile	Phe	Leu	Thr	Asp	Lys	Tyr	Ser	Pro	Gln	Ile	Lys	Met
		85				90							95		
Ser	Asp	Ser	Pro	Ala	Asp	Gly	Leu	Asp	Leu	Ala	Leu	Lys	Lys	Met	Gly

			100					105					110				
Thr	Asp	Tyr	Val	Asp	Leu	Tyr	Leu	Leu	His	Ser	Pro	Phe	Val	Ser	Lys		
		115						120					125				
Glu	Val	Asn	Gly	Leu	Ser	Leu	Glu	Glu	Ala	Trp	Lys	Asp	Met	Glu	Gln		
		130						135				140					
Leu	Tyr	Arg	Ser	Gly	Lys	Ala	Lys	Asn	Ile	Gly	Val	Ser	Asn	Phe	Thr		
145					150					155					160		
Val	Glu	Asp	Leu	Gln	Arg	Ile	Leu	Lys	Val	Ala	Glu	Val	Lys	Pro	Gln		
				165					170					175			
Val	Asn	Gln	Ile	Glu	Phe	Ser	Pro	Phe	Leu	Gln	Asn	Gln	Thr	Pro	Gly		
			180						185				190				
Ile	Tyr	Lys	Phe	Cys	Gln	Glu	His	Asp	Ile	Leu	Val	Glu	Ala	Tyr	Ser		
		195						200					205				
Pro	Leu	Gly	Pro	Leu	Gln	Lys	Lys	Thr	Ala	Gln	Asp	Asp	Ser	Gln	Pro		
		210				215					220						
Phe	Phe	Glu	Tyr	Val	Lys	Glu	Leu	Ser	Glu	Lys	Tyr	Asn	Lys	Ser	Glu		
225					230					235					240		
Ala	Gln	Ile	Ile	Leu	Arg	Trp	Val	Thr	Lys	Arg	Gly	Val	Leu	Pro	Val		
				245					250					255			
Thr	Thr	Ser	Ser	Lys	Pro	Gln	Arg	Ile	Ser	Asp	Ala	Gln	Asn	Leu	Phe		
			260						265				270				
Ser	Phe	Asp	Leu	Thr	Ala	Glu	Glu	Val	Asp	Lys	Ile	Thr	Glu	Leu	Gly		
		275					280						285				
Leu	Glu	His	Glu	Pro	Leu	Arg	Leu	Tyr	Trp	Asn	Lys	Leu	Tyr	Gly	Lys		
		290				295					300						
Tyr	Asn	Ser	Ala	Ala	Gln	Lys	Val										
305					310												

<210> 95
 <211> 942
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 95
 atgtcttttc accaacagtt tttcacgctg aacaacggca ataaaatccc ggcgattgcc 60
 atcatcggca ctggtacaaa atggtataaa aatgaagaaa ctgacgcgac cttctccaat 120
 agtctggttg aacaaatcgt gtatgcgttg aaactgccgg ggattatcca catcgacgcc 180
 gcgagagatt atcgaccta ccgggaagtg ggtaaacgac tgtccctgac cgaaaagcct 240
 cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactccoot 300
 gcggacggtc tggatttagc attgaagaaa atgggtacag attatggtga tttatatctg 360
 ttacattccc cgtttgtttc gaaggaagtg aatggcttaa gcttagaaga ggottggaaa 420
 gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggttt caatttcaca 480
 gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
 gagttctctc cgttcctgca aaaccaaaca ccaggcattt ataaattctg tcaggagcac 600
 gatatcctgg tggaagcata ttctccgctg ggcccgtgac agaagaaaac cgcgcaggat 660
 gacagccaac ctttttttga gtacgtcaaa gaattgagcg aaaaatacaa caaatccgag 720
 gccagatca tcctgcgctg ggtcactaaa cgcggtgtgc tgccagttac cactcttca 780
 aagcctcagc gcattagcga tgctcagaac ctgttttctc tcgacctgac agcgggaagag 840
 gttgataaaa tcacggagct gggtctggaa catgaaccgc tgcgcctgta ctggaataaa 900
 ttgtatggca aatataacta cgccgccag aaagtgtaat ga 942

<210> 96
 <211> 313
 <212> PRT
 <213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 96

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Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
1      5      10      15
Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Lys Trp Tyr Lys Asn Glu
      20      25      30
Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
      35      40      45
Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Ile Tyr
      50      55      60
Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
65      70      75      80
Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
      85      90      95
Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
      100     105     110
Thr Asp Tyr Val Asp Leu Tyr Leu Leu His Ser Pro Phe Val Ser Lys
      115     120     125
Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
      130     135     140
Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Thr
145     150     155     160
Val Glu Asp Leu Gln Arg Ile Leu Lys Val Ala Glu Val Lys Pro Gln
      165     170     175
Val Asn Gln Ile Glu Phe Ser Pro Phe Leu Gln Asn Gln Thr Pro Gly
      180     185     190
Ile Tyr Lys Phe Cys Gln Glu His Asp Ile Leu Val Glu Ala Tyr Ser
      195     200     205
Pro Leu Gly Pro Leu Gln Lys Lys Thr Ala Gln Asp Asp Ser Gln Pro
      210     215     220
Phe Phe Glu Tyr Val Lys Glu Leu Ser Glu Lys Tyr Asn Lys Ser Glu
225     230     235     240
Ala Gln Ile Ile Leu Arg Trp Val Thr Lys Arg Gly Val Leu Pro Val
      245     250     255
Thr Thr Ser Ser Lys Pro Gln Arg Ile Ser Asp Ala Gln Asn Leu Phe
      260     265     270
Ser Phe Asp Leu Thr Ala Glu Glu Val Asp Lys Ile Thr Glu Leu Gly
      275     280     285
Leu Glu His Glu Pro Leu Arg Leu Tyr Trp Asn Lys Leu Tyr Gly Lys
      290     295     300
Tyr Asn Tyr Ala Ala Gln Lys Val
305      310
```

<210> 97

<211> 942

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 97

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atgtctttttc accaacagtt tttaacgctg aacaacggca ataaaatccc ggcgattgcc 60
atcatcggca ctggtacaaa atggtataaa aatgaagaaa ctgacgcgac cttctccaat 120
agtctggttg aacaaatcgt gtatgcgttg aaactgcogg ggattatcca catcgacgcc 180
gcggagattt atcgcaccta cccggaagtg ggtaaagcac tgtccctgac cgaaaggcct 240
cggaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactccctt 300
gcggacggtc tggatttagc attgaagaaa atgggtaccg attatgttga tttatatctg 360
```

```

ttacattccc cgtttgtttc gaaggaagtg aatggcttaa gcttagaaga ggcttgga 420
gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggtttc caatttcaca 480
gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
gagttctctc cgttctctga aaaccaaaca ccaggcattt ataaattctg tcaggagcac 600
gatatcctgg tggaagcata ttctccgctg ggcccgtctg agaagaaaac cgcgcaggat 660
gacagtcaac ctttttttga gtacgtcaaa gaattgagcg aaaaatacat caaatccgag 720
gccagatca tcttgcgctg ggctactaaa cgcgggtgtg tgccagttac cacctcttca 780
aagcctcagc gcattagcga tgctcagaac ctgttttctt tcgacctgac agcgggaagag 840
gttgataaaa tcacggagct gggctctgaa catgaaccgc tcgcctgtga ctggaataaa 900
ttgtatggca aatataacta cgccgccag aaagtgtaat ga 942

```

<210> 98

<211> 313

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 98

```

Met Ser Phe His Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
1      5      10      15
Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Lys Trp Tyr Lys Asn Glu
20     25     30
Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
35     40     45
Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Ile Tyr
50     55     60
Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Arg Pro
65     70     75     80
Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
85     90     95
Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
100    105    110
Thr Asp Tyr Val Asp Leu Tyr Leu Leu His Ser Pro Phe Val Ser Lys
115    120    125
Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
130    135    140
Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Thr
145    150    155    160
Val Glu Asp Leu Gln Arg Ile Leu Lys Val Ala Glu Val Lys Pro Gln
165    170    175
Val Asn Gln Ile Glu Phe Ser Pro Phe Leu Gln Asn Gln Thr Pro Gly
180    185    190
Ile Tyr Lys Phe Cys Gln Glu His Asp Ile Leu Val Glu Ala Tyr Ser
195    200    205
Pro Leu Gly Pro Leu Gln Lys Lys Thr Ala Gln Asp Asp Ser Gln Pro
210    215    220
Phe Phe Glu Tyr Val Lys Glu Leu Ser Glu Lys Tyr Ile Lys Ser Glu
225    230    235    240
Ala Gln Ile Ile Leu Arg Trp Val Thr Lys Arg Gly Val Leu Pro Val
245    250    255
Thr Thr Ser Ser Lys Pro Gln Arg Ile Ser Asp Ala Gln Asn Leu Phe
260    265    270
Ser Phe Asp Leu Thr Ala Glu Glu Val Asp Lys Ile Thr Glu Leu Gly
275    280    285
Leu Glu His Glu Pro Leu Arg Leu Tyr Trp Asn Lys Leu Tyr Gly Lys
290    295    300
Tyr Asn Tyr Ala Ala Gln Lys Val
305    310

```

<210> 99
 <211> 942
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 99
 atgtcttttc accaacagtt tttcacgctg aacaacggca ataaaatccc ggcgattgcc 60
 atcatcggca ctggtacagc ttggtacaaa aatgaagaaa ctgacgcgac cttctccaat 120
 agtctggttg agcaaatcgt gtatgcgttg aaactgocgg ggattatcca catcgacgcc 180
 gcggagattt atcgcaccta cccggaagtg ggtaaagcac tgtccctgac cgaaaagcct 240
 cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactcccct 300
 gcggacggtc tggatttagc attgaagaaa atgcgtacag attatggtga tttatatctg 360
 ttacattccc cgtttgtttc gaaggaagtg aatggcttaa gcttagaaga ggottggaaa 420
 gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggtttc caatttcaca 480
 gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
 gagttctctc cgttcctgca aaaccaaaaca ccaggcattt ataaattctg tcaggagcac 600
 gatatcctgg tggaaagcata ttctccgctg ggcccgctgc agaagaaaac cgcgcaggat 660
 gacagccaac cattttttga gtacgtcaaa gaattgagcg aaaaatacaa caaatccgag 720
 gccagatca tcttgcgctg ggtcactaaa cgcgggtgtg tgccagttac cacctcttca 780
 aagcctcagc gcattagcga tgctcagaac ctgttttctc tcgacctgac agcgggaagag 840
 gttgataaaa tcacggagct gggctctggaa catgaaccgc tgcgcctgta ctggaataaa 900
 ttgtatggca aatataacta cgccgccag aaagtgtaat ga 942

<210> 100
 <211> 313
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 100
 Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
 1 5 10 15
 Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Ala Trp Tyr Lys Asn Glu
 20 25 30
 Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
 35 40 45
 Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Ile Tyr
 50 55 60
 Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
 65 70 75 80
 Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
 85 90 95
 Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Arg
 100 105 110
 Thr Asp Tyr Val Asp Leu Tyr Leu Leu His Ser Pro Phe Val Ser Lys
 115 120 125
 Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
 130 135 140
 Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Thr
 145 150 155 160
 Val Glu Asp Leu Gln Arg Ile Leu Lys Val Ala Glu Val Lys Pro Gln
 165 170 175
 Val Asn Gln Ile Glu Phe Ser Pro Phe Leu Gln Asn Gln Thr Pro Gly

Ala	Leu	Lys	Leu	Pro	Gly	Ile	Ile	His	Ile	Asp	Thr	Ala	Glu	Ile	Tyr
50						55					60				
Arg	Thr	Tyr	Pro	Glu	Val	Gly	Lys	Ala	Leu	Ser	Leu	Thr	Glu	Lys	Pro
65					70					75					80
Arg	Asn	Ala	Ile	Phe	Leu	Thr	Asp	Lys	Tyr	Ser	Pro	Gln	Ile	Lys	Met
				85					90					95	
Ser	Asp	Ser	Pro	Ala	Asp	Gly	Leu	Asp	Leu	Ala	Leu	Lys	Lys	Met	Gly
			100					105					110		
Thr	Asp	Tyr	Val	Asp	Leu	Tyr	Leu	Leu	His	Ser	Pro	Phe	Val	Ser	Lys
		115					120					125			
Glu	Val	Asn	Gly	Leu	Ser	Leu	Glu	Glu	Ala	Trp	Lys	Asp	Met	Glu	Gln
	130					135					140				
Leu	Tyr	Lys	Ser	Gly	Lys	Ala	Lys	Asn	Ile	Gly	Val	Ser	Asn	Phe	Ala
145					150					155					160
Val	Glu	Asp	Leu	Gln	Arg	Ile	Leu	Lys	Val	Ala	Glu	Val	Lys	Pro	Gln
				165					170					175	
Val	Asn	Gln	Ile	Glu	Phe	Ser	Pro	Phe	Leu	Gln	Asn	Gln	Thr	Pro	Gly
			180					185					190		
Ile	Tyr	Arg	Phe	Cys	Gln	Glu	His	Asp	Ile	Leu	Val	Glu	Ala	Tyr	Ser
	195						200					205			
Pro	Leu	Gly	Pro	Leu	Gln	Lys	Lys	Thr	Ala	Gln	Asp	Asp	Ser	Gln	Pro
	210					215					220				
Phe	Phe	Glu	Tyr	Val	Lys	Glu	Leu	Ser	Glu	Lys	Tyr	Asn	Lys	Ser	Glu
225					230					235					240
Ala	Gln	Ile	Ile	Leu	Arg	Trp	Val	Thr	Lys	Arg	Gly	Val	Leu	Pro	Val
				245					250					255	
Thr	Thr	Ser	Ser	Lys	Pro	Gln	Arg	Ile	Ser	Asp	Ala	Gln	Asn	Leu	Phe
			260					265					270		
Ser	Phe	Asp	Leu	Thr	Ala	Glu	Glu	Val	Asp	Lys	Ile	Thr	Glu	Leu	Gly
		275					280					285			
Leu	Glu	His	Glu	Pro	Leu	Arg	Leu	Tyr	Trp	Asn	Lys	Leu	Tyr	Gly	Lys
	290					295					300				
Tyr	Asn	Tyr	Ala	Ala	Gln	Lys	Val								
305					310										

<210> 103

<211> 942

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 103

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atgtcttttc accaacagtt tttaacgctg aacaacggca ataaaatccc ggcgattgcc 60
atcatcggca ctggtacacg ttggtataaa aatgaagaaa ctgacgcgac cttctccaat 120
agtctggttg aacaaatcgt gtagcgcttg aaactgccgg ggattatcca catcgacgcc 180
gcggagattt atcgcaccta cccggaagtg ggtaaagcac tgtccctgac cgaaaagcct 240
cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactccoct 300
gcggacggtc tggatttagc actgaagaaa atgggtacag attatgttga tttatatctg 360
ttacattccc cgtttggttc gaaggaagtg aatggcttaa gcttagaaga ggcttggaag 420
gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggttc caatttcaca 480
gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacotcaggt caaccagatt 540
gagttctctc cgttcctgca aaaccaaaaca ccaggcattt ataaattctg tcaggagcac 600
gatatccttg tggaagcata ttctccgctg ggcccgtgac agaagaaaac cgcgcaggat 660
gacagccaac cattttttga gtacgtcaaa gaattgagcg aaaaatacat caaatccgag 720
gccagatca tcttgcgctg ggtcactaaa cgcgggtgtg tgccagttac cactcttca 780
aagcctcagc gcattagcga tgctcagaac ctgttttctc tcgacctgac agcgggaagag 840
gttgataaaa tcacggagct gggctctggaa catgaacgcg tgcgcctgta ctggaataaa 900
ttgtatggca aatataacta cgccgccag aaagtgtaat ga 942

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<210> 104
 <211> 313
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 104
 Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
 1 5 10 15
 Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Arg Trp Tyr Lys Asn Glu
 20 25 30
 Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
 35 40 45
 Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Ile Tyr
 50 55 60
 Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
 65 70 75 80
 Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
 85 90 95
 Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
 100 105 110
 Thr Asp Tyr Val Asp Leu Tyr Leu Leu His Ser Pro Phe Val Ser Lys
 115 120 125
 Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
 130 135 140
 Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Thr
 145 150 155 160
 Val Glu Asp Leu Gln Arg Ile Leu Lys Val Ala Glu Val Lys Pro Gln
 165 170 175
 Val Asn Gln Ile Glu Phe Ser Pro Phe Leu Gln Asn Gln Thr Pro Gly
 180 185 190
 Ile Tyr Lys Phe Cys Gln Glu His Asp Ile Leu Val Glu Ala Tyr Ser
 195 200 205
 Pro Leu Gly Pro Leu Gln Lys Lys Thr Ala Gln Asp Asp Ser Gln Pro
 210 215 220
 Phe Phe Glu Tyr Val Lys Glu Leu Ser Glu Lys Tyr Ile Lys Ser Glu
 225 230 235 240
 Ala Gln Ile Ile Leu Arg Trp Val Thr Lys Arg Gly Val Leu Pro Val
 245 250 255
 Thr Thr Ser Ser Lys Pro Gln Arg Ile Ser Asp Ala Gln Asn Leu Phe
 260 265 270
 Ser Phe Asp Leu Thr Ala Glu Glu Val Asp Lys Ile Thr Glu Leu Gly
 275 280 285
 Leu Glu His Glu Pro Leu Arg Leu Tyr Trp Asn Lys Leu Tyr Gly Lys
 290 295 300
 Tyr Asn Tyr Ala Ala Gln Lys Val
 305 310

<210> 105
 <211> 942
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 105

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atgtcttttc accaacagtt tttcacgctg aacaacggca ataaaatccc ggcgattgcc 60
atcatcggca ctggtacacg ttggtataaa aatgaagaaa ctgacgcgac cttctccaat 120
agtcctggtg aacaaatcgt gtatgcgttg aaactgccgg ggattatcca catcgacgcc 180
gcgagaggtt atcgcaccta cccggaagtg ggtaaagcac tgtccctgac caaaaagcct 240
cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactcccct 300
gcgacaggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
ttacattccc cgtttgtttc gaaggaagtg aatggcttaa gcttagaaga ggcttggaag 420
gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggttc caatttcaca 480
gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
gagttctctc cgttcctgca aaaccaaaca ccaggcattt ataaattctg tcaggagcac 600
gatatcctgg tgggaagcata ttctccgttg ggcccgtgac ggaagaaaac cgcgaggat 660
gacagccaac cattttttga gtacgtcaaa gaattgagcg aaaaatacat caaatccgag 720
gcccagatca tctcgcgctg ggctactaaa cgcggtgtgc tgccagttac cacctcttca 780
aagcctcagc gcattagcga tgctcagaac ctgttttctt tcgacctgac agcggaagag 840
gttgataaaa tcacggagct gggctctggaa catgaaccgc tgcgcttgta ctggaataaa 900
ttgtatggca aatataacta cgccgccag aaagtgtaat ga 942
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<210> 106

<211> 313

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 106

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Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
1          5          10          15
Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Arg Trp Tyr Lys Asn Glu
20        25        30
Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
35        40        45
Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Val Tyr
50        55        60
Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Lys Lys Pro
65        70        75        80
Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
85        90        95
Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
100       105       110
Thr Asp Tyr Val Asp Leu Tyr Leu Leu His Ser Pro Phe Val Ser Lys
115       120       125
Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
130       135       140
Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Thr
145       150       155       160
Val Glu Asp Leu Gln Arg Ile Leu Lys Val Ala Glu Val Lys Pro Gln
165       170       175
Val Asn Gln Ile Glu Phe Ser Pro Phe Leu Gln Asn Gln Thr Pro Gly
180       185       190
Ile Tyr Lys Phe Cys Gln Glu His Asp Ile Leu Val Glu Ala Tyr Ser
195       200       205
Pro Leu Gly Pro Leu Arg Lys Lys Thr Ala Gln Asp Asp Ser Gln Pro
210       215       220
Phe Phe Glu Tyr Val Lys Glu Leu Ser Glu Lys Tyr Ile Lys Ser Glu
225       230       235       240
Ala Gln Ile Ile Leu Arg Trp Val Thr Lys Arg Gly Val Leu Pro Val
245       250       255
Thr Thr Ser Ser Lys Pro Gln Arg Ile Ser Asp Ala Gln Asn Leu Phe
```


Glu	Val	Asn	Gly	Leu	Ser	Leu	Glu	Glu	Ala	Trp	Lys	Asp	Met	Glu	Gln
130						135					140				
Leu	Tyr	Lys	Ser	Gly	Lys	Ala	Lys	Asn	Ile	Gly	Val	Ser	Asn	Phe	Ala
145					150					155					160
Val	Glu	Asp	Leu	Gln	Arg	Ile	Leu	Lys	Val	Ala	Glu	Val	Lys	Pro	Gln
			165						170					175	
Val	Asn	Gln	Ile	Glu	Phe	Ser	Pro	Phe	Leu	Gln	Asn	Gln	Thr	Pro	Gly
		180						185					190		
Ile	Cys	Lys	Phe	Cys	Gln	Glu	His	Asp	Ile	Leu	Val	Glu	Ala	Tyr	Ser
	195						200					205			
Pro	Leu	Gly	Pro	Leu	Gln	Lys	Lys	Thr	Ala	Gln	Asp	Asp	Ser	Gln	Pro
	210					215					220				
Phe	Phe	Glu	Tyr	Val	Lys	Glu	Leu	Ser	Glu	Lys	Tyr	Ile	Lys	Ser	Glu
225					230					235					240
Ala	Gln	Ile	Ile	Leu	Arg	Trp	Val	Thr	Lys	Arg	Gly	Val	Leu	Pro	Val
			245						250					255	
Thr	Thr	Ser	Ser	Lys	Pro	Gln	Arg	Ile	Ser	Asp	Ala	Gln	Asn	Leu	Phe
		260						265					270		
Ser	Phe	Asp	Leu	Thr	Ala	Glu	Glu	Val	Asp	Lys	Ile	Thr	Glu	Leu	Gly
	275						280					285			
Leu	Glu	His	Glu	Pro	Leu	Arg	Leu	Tyr	Trp	Asn	Lys	Leu	Tyr	Gly	Lys
	290					295					300				
Tyr	Asn	Tyr	Ala	Ala	Gln	Lys	Val								
305					310										

<210> 109
 <211> 942
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 109
 atgtcttttc accaacagtt ttccacgctg aacaacggca ataaaatccc ggcgattgcc 60
 atcatcggca ctggtacacg ttggtataaa agtgaagaaa ctgacgcgac cttctccaat 120
 agtctggttg aacaaatcgt gtatgcgttg aaactgccgg ggattatcca catcgacgcc 180
 gcggagattt atcgcaccta cccggaagtg ggtaaagcac tgtccctgac cgaaaagcct 240
 cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactcccct 300
 gcggacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
 ttacattccc cgtttgtttc gaaggaagtg aatggcttaa gcttagaaga ggcttggaaa 420
 gatattggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggttc caatttcgca 480
 gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
 gagttctctc cgttcctgca aaaccaaaca ccaggcattt ataaattctg tcaggagcac 600
 gatatcctgg tgggaagcata ttctccgctg ggcccgtgca agaagaaaac cgcgcaggat 660
 gacagccaac cattttttga gtacgtcaaa gaattgagcg aaaaatacac caaatccgag 720
 gccagatca tcctgcgctg ggtcactaaa cgcgggtgtg tgccagttac cacctcttca 780
 aagcctcagc gcattagcga tgctcagaac ctgttttctt tcgacctgac agcgggaagag 840
 gttgataaaa tcacggagct gggtctggaa catgaaccgc tcgcctgtga ctggaataaa 900
 ttgtatggca aatataacta cgccgccag aaagtgtaat ga 942

<210> 110
 <211> 313
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 110

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Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
1      5      10      15
Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Arg Trp Tyr Lys Ser Glu
20      25      30
Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
35      40      45
Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Ile Tyr
50      55      60
Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
65      70      75      80
Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
85      90      95
Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
100     105     110
Thr Asp Tyr Val Asp Leu Tyr Leu Leu His Ser Pro Phe Val Ser Lys
115     120     125
Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
130     135     140
Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Ala
145     150     155     160
Val Glu Asp Leu Gln Arg Ile Leu Lys Val Ala Glu Val Lys Pro Gln
165     170     175
Val Asn Gln Ile Glu Phe Ser Pro Phe Leu Gln Asn Gln Thr Pro Gly
180     185     190
Ile Tyr Lys Phe Cys Gln Glu His Asp Ile Leu Val Glu Ala Tyr Ser
195     200     205
Pro Leu Gly Pro Leu Gln Lys Lys Thr Ala Gln Asp Asp Ser Gln Pro
210     215     220
Phe Phe Glu Tyr Val Lys Glu Leu Ser Glu Lys Tyr Thr Lys Ser Glu
225     230     235     240
Ala Gln Ile Ile Leu Arg Trp Val Thr Lys Arg Gly Val Leu Pro Val
245     250     255
Thr Thr Ser Ser Lys Pro Gln Arg Ile Ser Asp Ala Gln Asn Leu Phe
260     265     270
Ser Phe Asp Leu Thr Ala Glu Glu Val Asp Lys Ile Thr Glu Leu Gly
275     280     285
Leu Glu His Glu Pro Leu Arg Leu Tyr Trp Asn Lys Leu Tyr Gly Lys
290     295     300
Tyr Asn Tyr Ala Ala Gln Lys Val
305      310
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<210> 111

<211> 942

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 111

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atgtctttttc accaacagtt tttcacgctg aacaacggca ataaaatccc ggcgattgcc 60
atcatcgcca ctggtacaaa atggtataaa aatgaagaaa ctgacgcgac cttctccaat 120
agtctggttg aacaaatcgt gtatgcgttg aaactgccgg ggattatcca catcgacgcc 180
gcggagattt atcgcaccta ccggaagtg ggtaaagcac tgccoctgac cgaaaagcct 240
cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactcccct 300
gcggacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
ttacattccc cgtttgtttc gaaggaagtg aatggcttaa gcttagaaga ggcttggaaa 420
gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggttc caatttcaca 480
gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
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gagttctctc cgttcctgca aaaccaaaca ccaggcattt ataaattctg tcaggagcac 600
gatatcctgg tggaagcata ttctcogctg ggcccgtgc ggaagaaaac cgcgcaggat 660
gacagccaac ctttttttga gtacgtcaaa gaattgagcg aaaaatacaa caaatccogag 720
gcccgatca tcctgcgctg ggtcactaaa cgcgggtgtg tgccagttac cacctcttca 780
aagcctcagc gcattagcga tgctcagaac ctgttttcct tcgacctgac agcggaagag 840
gttgataaaa tcacggagct gggctctggaa catgaaccgc tcgcctgtga ctggaataaa 900
ttgtatggca aatataacta cgccgccag aaagtgtaat ga 942

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<210> 112

<211> 313

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 112

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Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
1          5          10          15
Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Lys Trp Tyr Lys Asn Glu
20          25          30
Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
35          40          45
Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Ile Tyr
50          55          60
Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
65          70          75          80
Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
85          90          95
Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
100         105         110
Thr Asp Tyr Val Asp Leu Tyr Leu Leu His Ser Pro Phe Val Ser Lys
115         120         125
Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
130         135         140
Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Thr
145         150         155         160
Val Glu Asp Leu Gln Arg Ile Leu Lys Val Ala Glu Val Lys Pro Gln
165         170         175
Val Asn Gln Ile Glu Phe Ser Pro Phe Leu Gln Asn Gln Thr Pro Gly
180         185         190
Ile Tyr Lys Phe Cys Gln Glu His Asp Ile Leu Val Glu Ala Tyr Ser
195         200         205
Pro Leu Gly Pro Leu Arg Lys Lys Thr Ala Gln Asp Asp Ser Gln Pro
210         215         220
Phe Phe Glu Tyr Val Lys Glu Leu Ser Glu Lys Tyr Asn Lys Ser Glu
225         230         235         240
Ala Gln Ile Ile Leu Arg Trp Val Thr Lys Arg Gly Val Leu Pro Val
245         250         255
Thr Thr Ser Ser Lys Pro Gln Arg Ile Ser Asp Ala Gln Asn Leu Phe
260         265         270
Ser Phe Asp Leu Thr Ala Glu Glu Val Asp Lys Ile Thr Glu Leu Gly
275         280         285
Leu Glu His Glu Pro Leu Arg Leu Tyr Trp Asn Lys Leu Tyr Gly Lys
290         295         300
Tyr Asn Tyr Ala Ala Gln Lys Val
305          310

```

<210> 113

<211> 942
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 113
atgtcttttc accaacagtt tttcacgctg aacaacggca ataaaatccc ggcgattgcc 60
atcatcggca ctggtacaaa atggtataaa aatgaagaaa ctgacgcgac cttctccaat 120
agtctgggtg aacaaatcgt gtatgcgttg aaactgcggg ggattatcca catcgacgcc 180
gcggagattt atcgcaccta cccggaagtg ggtaaagcac tgtccctgac cgaaaagcct 240
cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactccctt 300
gcggacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
ttacattccc cgtttgtttc gaaggaagtg aatggcttaa gcttagaaga ggcttggaaa 420
gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggttc caatttcaca 480
gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
gagttctctc cgttcctgca aaaccaaaaca ccaggcattt ataaattctg tcaggagcac 600
gatatcctgg tgggaagcata ttctccgctg ggcccgtgc agaagaaaac cgcgcaggat 660
gacagccaac cattttttga gtacgtcaaa gaattgggcg aaaaatacaa caaatccgag 720
gcccgatca tcctgcgctg ggtaactaaa cgcgggtgtg tgccagttac cacctcttca 780
aagcctcagc gcattagcga tgctcagaac ctgttttctt tcgacctgac agcgggaagag 840
gttgataaaa tcacggagct ggggtctggaa catgaaccgc tcgcctgtga ctggaataaa 900
ttgtatggca aatataacta cgccgccag aaagtgtaat ga 942

<210> 114
<211> 313
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 114
Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
1 5 10 15
Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Lys Trp Tyr Lys Asn Glu
20 25 30
Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
35 40 45
Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Ile Tyr
50 55 60
Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
65 70 75 80
Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
85 90 95
Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
100 105 110
Thr Asp Tyr Val Asp Leu Tyr Leu Leu His Ser Pro Phe Val Ser Lys
115 120 125
Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
130 135 140
Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Thr
145 150 155 160
Val Glu Asp Leu Gln Arg Ile Leu Lys Val Ala Glu Val Lys Pro Gln
165 170 175
Val Asn Gln Ile Glu Phe Ser Pro Phe Leu Gln Asn Gln Thr Pro Gly
180 185 190
Ile Tyr Lys Phe Cys Gln Glu His Asp Ile Leu Val Glu Ala Tyr Ser
195 200 205

Pro	Leu	Gly	Pro	Leu	Gln	Lys	Lys	Thr	Ala	Gln	Asp	Asp	Ser	Gln	Pro
210						215					220				
Phe	Phe	Glu	Tyr	Val	Lys	Glu	Leu	Gly	Glu	Lys	Tyr	Asn	Lys	Ser	Glu
225					230					235					240
Ala	Gln	Ile	Ile	Leu	Arg	Trp	Val	Thr	Lys	Arg	Gly	Val	Leu	Pro	Val
				245					250					255	
Thr	Thr	Ser	Ser	Lys	Pro	Gln	Arg	Ile	Ser	Asp	Ala	Gln	Asn	Leu	Phe
			260					265					270		
Ser	Phe	Asp	Leu	Thr	Ala	Glu	Glu	Val	Asp	Lys	Ile	Thr	Glu	Leu	Gly
		275					280					285			
Leu	Glu	His	Glu	Pro	Leu	Arg	Leu	Tyr	Trp	Asn	Lys	Leu	Tyr	Gly	Lys
	290					295					300				
Tyr	Asn	Tyr	Ala	Ala	Gln	Lys	Val								
305					310										

<210> 115
 <211> 942
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 115
 atgtcttttc accaacagtt tttcacgctg aacaacggca ataaaatccc ggcgattgcc 60
 atcatcggca ctggtacaaa atggtataaa aatgaagaaa ctgatgcgac cttctocaat 120
 agtctggttg aacaaatcgt gtatgcgttg aaactgccgg ggattatcca catcgacgcc 180
 gcggagattt atcgcaccta cccggaagtg ggtaaagcac tgtccctgac cgaaaagcct 240
 cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactcccct 300
 gcggacggtc tggatttagc attgaagaaa atgggtacaa attatgttga tttatatctg 360
 ttacattccc cgtttgtttc gaaggaagtg aatggcttaa gcttagaaga ggcttggaag 420
 gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggttc caatttcaca 480
 gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
 gagttctctc cgttcctgca aaaccaaaaca ccaggcattt ataaattctg tcaggagcac 600
 gatatcctgg tggaagcata ttctccgctg ggcccgtgc agaagaaaac cgcgcaggat 660
 gacagccaac cattttttga gtacgtcaaa gaattgagcg aaaaatacaa caaatccgag 720
 gccagatca tctcgcgctg gatcactaaa cgcgggtgtg tgccagttac cacctcttca 780
 aagcctcagc gcattagcga tgctcagaac ctgttttctc tcgacctgac agcggaagag 840
 gttgataaaa tcacggagct gggtctggaa catgaaccgc tgcgcctgta ctggaataaa 900
 ttgtatggca aatataacta cgccgccag aaagtgtaat ga 942

<210> 116
 <211> 313
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 116
 Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
 1 5 10 15
 Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Lys Trp Tyr Lys Asn Glu
 20 25 30
 Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
 35 40 45
 Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Ile Tyr
 50 55 60
 Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro

65		70		75		80									
Arg	Asn	Ala	Ile	Phe	Leu	Thr	Asp	Lys	Tyr	Ser	Pro	Gln	Ile	Lys	Met
		85						90						95	
Ser	Asp	Ser	Pro	Ala	Asp	Gly	Leu	Asp	Leu	Ala	Leu	Lys	Lys	Met	Gly
		100						105					110		
Thr	Asn	Tyr	Val	Asp	Leu	Tyr	Leu	Leu	His	Ser	Pro	Phe	Val	Ser	Lys
		115					120					125			
Glu	Val	Asn	Gly	Leu	Ser	Leu	Glu	Glu	Ala	Trp	Lys	Asp	Met	Glu	Gln
		130				135					140				
Leu	Tyr	Lys	Ser	Gly	Lys	Ala	Lys	Asn	Ile	Gly	Val	Ser	Asn	Phe	Thr
145					150					155					160
Val	Glu	Asp	Leu	Gln	Arg	Ile	Leu	Lys	Val	Ala	Glu	Val	Lys	Pro	Gln
				165					170					175	
Val	Asn	Gln	Ile	Glu	Phe	Ser	Pro	Phe	Leu	Gln	Asn	Gln	Thr	Pro	Gly
		180						185					190		
Ile	Tyr	Lys	Phe	Cys	Gln	Glu	His	Asp	Ile	Leu	Val	Glu	Ala	Tyr	Ser
		195					200					205			
Pro	Leu	Gly	Pro	Leu	Gln	Lys	Lys	Thr	Ala	Gln	Asp	Asp	Ser	Gln	Pro
		210				215					220				
Phe	Phe	Glu	Tyr	Val	Lys	Glu	Leu	Ser	Glu	Lys	Tyr	Asn	Lys	Ser	Glu
225					230					235					240
Ala	Gln	Ile	Ile	Leu	Arg	Trp	Ile	Thr	Lys	Arg	Gly	Val	Leu	Pro	Val
				245					250					255	
Thr	Thr	Ser	Ser	Lys	Pro	Gln	Arg	Ile	Ser	Asp	Ala	Gln	Asn	Leu	Phe
			260					265					270		
Ser	Phe	Asp	Leu	Thr	Ala	Glu	Glu	Val	Asp	Lys	Ile	Thr	Glu	Leu	Gly
		275					280					285			
Leu	Glu	His	Glu	Pro	Leu	Arg	Leu	Tyr	Trp	Asn	Lys	Leu	Tyr	Gly	Lys
		290				295					300				
Tyr	Asn	Tyr	Ala	Ala	Gln	Lys	Val								
305					310										

<210> 117

<211> 942

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 117

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atgtcttttc accaacagtt tttcacgctg aacaacggca ataaaatccc ggogattgcc 60
atcatcggca ctggtacaaa atggtataaa aatgaagaaa ctgacgogac cttctocaat 120
agtctggttg aacaaatcgt gtatgcgttg aaactgccgg ggattatoca catcgacgcc 180
gcgagattt atcgcaccta ccggaagtg ggtaaagcac tgtccctgac cgaaaagcct 240
cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactccct 300
gcgacggctc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
ttacattccc cgtttgtttc gaaggaagtg aatggcttaa gcttagaaga ggcttgga 420
gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcggggtttc caatttcaca 480
gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
gagttctctc cgttcctgca aaaccaaaca ccaggcattt ataaattctg tcaggagcac 600
gatatcctgg tggaagctta ttctccgctg ggcccgtgc agaagaaaac cgcgcaggat 660
gacagccaac cattttttga gtacgtcaaa gaattgagcg aaaaatacaa caaatccgag 720
gccagatca tcctgcgctg ggtaactaaa cgcggtgcgc tgccagttac cacctcttca 780
aagcctcagc gcattagcga tgctcagaac ctgttttctc tcgacctgac agcggaagag 840
gttgataaaa tcacggagct gggtctggaa catgaacgc tcgcctgta ctggaataaa 900
ttgtatggca aatataacta cgccgccag aaagtgtaat ga 942

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<210> 118

<211> 313
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 118
 Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
 1 5 10 15
 Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Lys Trp Tyr Lys Asn Glu
 20 25 30
 Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
 35 40 45
 Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Ile Tyr
 50 55 60
 Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
 65 70 75 80
 Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
 85 90 95
 Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
 100 105 110
 Thr Asp Tyr Val Asp Leu Tyr Leu Leu His Ser Pro Phe Val Ser Lys
 115 120 125
 Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
 130 135 140
 Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Thr
 145 150 155 160
 Val Glu Asp Leu Gln Arg Ile Leu Lys Val Ala Glu Val Lys Pro Gln
 165 170 175
 Val Asn Gln Ile Glu Phe Ser Pro Phe Leu Gln Asn Gln Thr Pro Gly
 180 185 190
 Ile Tyr Lys Phe Cys Gln Glu His Asp Ile Leu Val Glu Ala Tyr Ser
 195 200 205
 Pro Leu Gly Pro Leu Gln Lys Lys Thr Ala Gln Asp Asp Ser Gln Pro
 210 215 220
 Phe Phe Glu Tyr Val Lys Glu Leu Ser Glu Lys Tyr Asn Lys Ser Glu
 225 230 235 240
 Ala Gln Ile Ile Leu Arg Trp Val Thr Lys Arg Gly Ala Leu Pro Val
 245 250 255
 Thr Thr Ser Ser Lys Pro Gln Arg Ile Ser Asp Ala Gln Asn Leu Phe
 260 265 270
 Ser Phe Asp Leu Thr Ala Glu Glu Val Asp Lys Ile Thr Glu Leu Gly
 275 280 285
 Leu Glu His Glu Pro Leu Arg Leu Tyr Trp Asn Lys Leu Tyr Gly Lys
 290 295 300
 Tyr Asn Tyr Ala Ala Gln Lys Val
 305 310

<210> 119
 <211> 942
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 119
 atgtcttttc accaacagtt tttcacgctg aacaacggca ataaaaatccc ggcgattgcc 60
 atcatcggca ctggtacaaa atggtataaa aatgaagaaa ctgacgogac cttctccaat 120

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agtctgtttg aacaaatcgt gtatgcgttg aaactgccgg ggattatcca catcgacgoc 180
gcgagagatt atcgcaccta cccggaagtg ggtaaagcac tgtccctgac cgaaaagcct 240
cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactcccoct 300
gcgagacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
ttacattccc cgtttgttgc gaaggaagtg aatggcttaa gcttagaaga ggcttggaaa 420
gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggttgc caatttcaca 480
gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
gagttctctc cgttcctgca aaaccaaaca ccaggcattt ataaattctg tcaggagcac 600
gataccttgg tggaagcata ttctccgctg ggcccgtgc agaagaaaac cgcgcaggat 660
gacagccaac cattttttga gtacgtcaaa gaattgagcg aaaaatacaa caaatccgag 720
gcccagatca tcctgcgctg ggtcactaaa cgcggtgtgc tgccagttac cacctottca 780
aagcctcagc gcattagcga tgctcagaac ctgttttctc tcgacctgac agcgggaagag 840
gttgataaaa tcacggagct gggctctggaa catgaaccgc tgcgcctgta ctggaataaa 900
ttgtatggca aatataacta cgccgccag aaagtgtaat ga 942

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<210> 120

<211> 313

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 120

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Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
1          5          10          15
Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Lys Trp Tyr Lys Asn Glu
20        25        30
Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Phe Glu Gln Ile Val Tyr
35        40        45
Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Ile Tyr
50        55        60
Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
65        70        75        80
Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
85        90        95
Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
100       105       110
Thr Asp Tyr Val Asp Leu Tyr Leu Leu His Ser Pro Phe Val Ser Lys
115       120       125
Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
130       135       140
Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Thr
145       150       155       160
Val Glu Asp Leu Gln Arg Ile Leu Lys Val Ala Glu Val Lys Pro Gln
165       170       175
Val Asn Gln Ile Glu Phe Ser Pro Phe Leu Gln Asn Gln Thr Pro Gly
180       185       190
Ile Tyr Lys Phe Cys Gln Glu His Asp Ile Leu Val Glu Ala Tyr Ser
195       200       205
Pro Leu Gly Pro Leu Gln Lys Lys Thr Ala Gln Asp Asp Ser Gln Pro
210       215       220
Phe Phe Glu Tyr Val Lys Glu Leu Ser Glu Lys Tyr Asn Lys Ser Glu
225       230       235       240
Ala Gln Ile Ile Leu Arg Trp Val Thr Lys Arg Gly Val Leu Pro Val
245       250       255
Thr Thr Ser Ser Lys Pro Gln Arg Ile Ser Asp Ala Gln Asn Leu Phe
260       265       270
Ser Phe Asp Leu Thr Ala Glu Glu Val Asp Lys Ile Thr Glu Leu Gly
275       280       285

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Leu Glu His Glu Pro Leu Arg Leu Tyr Trp Asn Lys Leu Tyr Gly Lys
 290 295 300
 Tyr Asn Tyr Ala Ala Gln Lys Val
 305 310

<210> 121
 <211> 942
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 121
 atgtcttttc accaacagtt tttcacgctg aacaacggca ataaaatccc ggogattgcc 60
 atcatcgga ctggtacaaa atggtataaa aatgaagaaa ctgacgcgac cttctccaat 120
 agtctgggtg aacaaatcgt gtatgcgttg aaactgccgg ggattatcca catcgacgcc 180
 gcggagattt atcgcaccta cccggaagtg ggtaaagcac tgtccctgac cgaagagcct 240
 cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactccctt 300
 gcggacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
 ttacattccc cgtttgtttc gaaggaagtg aatgggttaa gottagaaga ggcttggaaa 420
 gatattggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggtttc caatttcaca 480
 gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
 gatttctctc cgttcctgca aaaccaaaca ccaggcattt ataaattctg tcaggagcac 600
 gatattcctg tggaagcata ttctccgctg ggcccgctgc agaagaaaac cgcgcaggat 660
 gacagccaac cattttttga gtacatcaaa gaattgagcg aaaaatacaa caaatccgag 720
 gccagatca tctcgcgctg ggctactaaa cgcggtgtgc tgccagttac caoctcttca 780
 aagcctcagc gcattagcga tgctcagaac ctgttttctc tcgacctgac agcgggaagag 840
 gttgataaaa tcacggagct gggtctggaa catgaacogo tgcgcctgta ctggaataaa 900
 ttgtatggca aatataacta cgcgcgccag aaagtgtaat ga 942

<210> 122
 <211> 313
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 122
 Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
 1 5 10 15
 Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Lys Trp Tyr Lys Asn Glu
 20 25 30
 Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
 35 40 45
 Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Ile Tyr
 50 55 60
 Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
 65 70 75 80
 Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
 85 90 95
 Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
 100 105 110
 Thr Asp Tyr Val Asp Leu Tyr Leu Leu His Ser Pro Phe Val Ser Lys
 115 120 125
 Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
 130 135 140
 Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Thr

145		150		155		160									
Val	Glu	Asp	Leu	Gln	Arg	Ile	Leu	Lys	Val	Ala	Glu	Val	Lys	Pro	Gln
		165		170		175									
Val	Asn	Gln	Ile	Glu	Phe	Ser	Pro	Phe	Leu	Gln	Asn	Gln	Thr	Pro	Gly
		180		185		190									
Ile	Tyr	Lys	Phe	Cys	Gln	Glu	His	Asp	Ile	Leu	Val	Glu	Ala	Tyr	Ser
	195				200						205				
Pro	Leu	Gly	Pro	Leu	Gln	Lys	Lys	Thr	Ala	Gln	Asp	Asp	Ser	Gln	Pro
	210				215						220				
Phe	Phe	Glu	Tyr	Ile	Lys	Glu	Leu	Ser	Glu	Lys	Tyr	Asn	Lys	Ser	Glu
225				230					235						240
Ala	Gln	Ile	Ile	Leu	Arg	Trp	Val	Thr	Lys	Arg	Gly	Val	Leu	Pro	Val
		245						250						255	
Thr	Thr	Ser	Ser	Lys	Pro	Gln	Arg	Ile	Ser	Asp	Ala	Gln	Asn	Leu	Phe
		260						265					270		
Ser	Phe	Asp	Leu	Thr	Ala	Glu	Glu	Val	Asp	Lys	Ile	Thr	Glu	Leu	Gly
	275					280					285				
Leu	Glu	His	Glu	Pro	Leu	Arg	Leu	Tyr	Trp	Asn	Lys	Leu	Tyr	Gly	Lys
	290				295					300					
Tyr	Asn	Tyr	Ala	Ala	Gln	Lys	Val								
305				310											

<210> 123
 <211> 942
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 123
 atgtcttttt accaacagtt tttcacgctg aacaacggca ataaaatccc ggcgattgcc 60
 atcatcgga ctggtacaaa atggtataaa aatgaagaaa ctgaacgcac cttctccaat 120
 agtctggttg aacaaatcgt gtatgcgttg aaactgcgg ggattatcca catogaagcc 180
 gcggagattt atcgaccta cccggaagtg ggtaaagcac tgtccctgac cgaagagcct 240
 cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactccccc 300
 gcggacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatcta 360
 ttacattccc cgcttggttc gaaggaagtg aatgggttaa gcttagaaga ggcttgga 420
 gatattggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggttc caatttcaca 480
 gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
 gaggttcttc cgttcctgca aaaccaaaca ccaggcattt ataaattctg ccaggagcac 600
 gatattcctg tggaagcata ttctccgctg ggcccgtgac agaagaaaac cgcgcaggat 660
 gacagccaac cattttttga gtacgtcaaa gaattgagcg aaaaatacaa caaatccag 720
 gccagatca tctgcgctg ggtcactaaa cgcggtgtgc tgccagttac cactottca 780
 aagcctcagc gcattagcga tgctcagaac ctgttttctc tcgatctgac agcgggaag 840
 gttgataaaa tcacggagct gggctctgga catgaacgc tgccgctgta ctggaataaa 900
 ttgtatggca aatataacta cgcgcgccag aaagtgtaat ga 942

<210> 124
 <211> 313
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 124
 Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
 1 5 10 15

<400>	125							
atgtcttttc	accaacagtt	tttcacgctg	aacaacggca	ataaaatccc	ggcgattgcc	60		
atcatcggca	ctggtaaaaa	atgggtataaa	aatgaagaaa	ctgacgcgac	cttctccaat	120		
agtctggttg	aacaaatcgt	gtatgcgttg	aaactgccgg	ggattatcca	catcgacgcc	180		
gcggagattt	atcgcaccta	cccggaagtg	ggtaaagcac	tgtccctgac	cgagaagcct	240		
cgtaacgcga	tttttctgac	ggataaatat	tctccgcaga	ttaaaatgag	tgactccctt	300		
gcggacggtc	tggatttagc	attgaagaaa	atgggtacag	attatgttga	tttatatctg	360		
atacattccc	cgtttgtttc	gaaggaagtg	aatggcttaa	gcttagaaga	ggcttggaag	420		
gatatggagc	agttatacaa	aagtggtaaa	gctaaaaaca	tcgggggttc	caatttcaca	480		
gtggaagacc	tgcaacgtat	cctgaaagtc	gctgaagtta	aacctcaggt	caaccagatt	540		
gagttctctc	cgttcctgca	aaaccaaaaca	ccaggcattt	ataaattctg	tcaggagcac	600		
gatatcctgg	tggaagcata	ttctccgctg	ggcccgctgc	agaagaaaac	cgcgagggat	660		
gacaqccaac	catttttttga	gtacgtcaaa	gaattgagcg	aaaaatacaa	caaattccgag	720		

<220>

<223> Synthetic Construct

<400> 127

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atgtcttttc accaacagtt tttcacgctg aacaacggca ataaaatccc ggcgattgcc 60
atcatcggca ctggtacaaa atggtataaa aatgaagaaa ctgacgcgac cttctccaat 120
agtctggttg aacaaatcgt gtatgcgttg aaactgccgg ggattatcca catcgacgcc 180
gcggagattt atcgcaccta cccggaagtg ggtaaagcac tgtccctgac cgaaaagcct 240
cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactccoct 300
gcggacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
ttacattccc cgtttgtttc gaaggaagtg aatggcttaa gcttagaaga ggcttgga 420
gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggttc caatttcaca 480
gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
gagttctctc cgttcctgca aaaccaaaca ccaggcattt ataaattctg tcaggagcac 600
gatatcctgg tggaaagcata ttctccactg ggcccgtctc agaagaaaac cgcgcaggat 660
gacagccaac cattttttga gtacgtcaaa gaattgagcg aaaaatacaa caaatccgag 720
gccagatca tcttgcgctg ggtcactaaa cgcggtgtgc tgccagttac cacctcttca 780
atgcctcagc gcattagcga tgctcagaac ctgttttctt tcgacctgac agcgggaagag 840
gttgataaaa tcacggagct gggctctggaa catgaaccgc tgcgcctgta ctggaataaa 900
ttgtatggca aatataacta cgccgccagc aaagtgtaat ga 942
```

<210> 128

<211> 313

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 128

```
Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
1          5          10          15
Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Lys Trp Tyr Lys Asn Glu
20          25          30
Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
35          40          45
Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Ile Tyr
50          55          60
Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
65          70          75          80
Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
85          90          95
Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
100         105         110
Thr Asp Tyr Val Asp Leu Tyr Leu Leu His Ser Pro Phe Val Ser Lys
115         120         125
Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
130         135         140
Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Thr
145         150         155         160
Val Glu Asp Leu Gln Arg Ile Leu Lys Val Ala Glu Val Lys Pro Gln
165         170         175
Val Asn Gln Ile Glu Phe Ser Pro Phe Leu Gln Asn Gln Thr Pro Gly
180         185         190
Ile Tyr Lys Phe Cys Gln Glu His Asp Ile Leu Val Glu Ala Tyr Ser
195         200         205
Pro Leu Gly Pro Leu Gln Lys Lys Thr Ala Gln Asp Asp Ser Gln Pro
210         215         220
Phe Phe Glu Tyr Val Lys Glu Leu Ser Glu Lys Tyr Asn Lys Ser Glu
```

225		230		235		240									
Ala	Gln	Ile	Ile	Leu	Arg	Trp	Val	Thr	Lys	Arg	Gly	Val	Leu	Pro	Val
		245		250		255									
Thr	Thr	Ser	Ser	Met	Pro	Gln	Arg	Ile	Ser	Asp	Ala	Gln	Asn	Leu	Phe
		260		265		270									
Ser	Phe	Asp	Leu	Thr	Ala	Glu	Glu	Val	Asp	Lys	Ile	Thr	Glu	Leu	Gly
		275		280		285									
Leu	Glu	His	Glu	Pro	Leu	Arg	Leu	Tyr	Trp	Asn	Lys	Leu	Tyr	Gly	Lys
	290			295		300									
Tyr	Asn	Tyr	Ala	Ala	Gln	Lys	Val								
305				310											

<210> 129
 <211> 942
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 129
 atgtcttttc accaacagtt tttcacgctg aacaacggca ataaaatccc ggcgattgcc 60
 atcatcggca ctggtacacg ttggtataaa aatgaagaaa ctgacgcgac cttctocaat 120
 agtctggttg aacaaatcgt gtatgcgttg aaactgccgg ggattatcca catogacgcc 180
 gcggagattt atcgcaccta ccggaagtg ggtaaagcac tgtccctgac cgaaaagcct 240
 cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactcccct 300
 gcggacggtc tggatttagc attgaagaaa atgggtacag attatggtga tttatatctg 360
 ttacattccc cgtttgtttc gaaggaagtg aatggcttaa gcttagaaga ggcttggaag 420
 gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggtttc caatttctcg 480
 gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
 gagttctctc cgttcctgca aaaccaaaca ccaggcattt ataaattctg tcaggagcac 600
 gatatcctgg tggaaagcata ttctccgctg ggcccgtgac agaagaaaac cgcgcaggat 660
 gacagccaac cattttttga gtacgtcaaa gaattgagcg aaaaataccg gaaatccgag 720
 gccagatca tcctgcgctg ggtcactaaa cgcggtgtgc tgccagttac cacctcttca 780
 aagcctcagc gcattagoga tgcacagaac ctgttttctc tcgacctgac agcgggaagag 840
 gttgataaaa tcacggagct gggtctggaa catgaaccgc tcgcgctgta ctggaataaa 900
 ttgtatggca aatataacta cgcgcgccag aaagtgtaat ga 942

<210> 130
 <211> 313
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 130
 Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
 1 5 10 15
 Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Arg Trp Tyr Lys Asn Glu
 20 25 30
 Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
 35 40 45
 Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Ile Tyr
 50 55 60
 Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
 65 70 75 80
 Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
 85 90 95

Ser	Asp	Ser	Pro	Ala	Asp	Gly	Leu	Asp	Leu	Ala	Leu	Lys	Lys	Met	Gly
			100					105					110		
Thr	Asp	Tyr	Val	Asp	Leu	Tyr	Leu	Leu	His	Ser	Pro	Phe	Val	Ser	Lys
		115					120					125			
Glu	Val	Asn	Gly	Leu	Ser	Leu	Glu	Glu	Ala	Trp	Lys	Asp	Met	Glu	Gln
		130				135					140				
Leu	Tyr	Lys	Ser	Gly	Lys	Ala	Lys	Asn	Ile	Gly	Val	Ser	Asn	Phe	Ser
145					150					155					160
Val	Glu	Asp	Leu	Gln	Arg	Ile	Leu	Lys	Val	Ala	Glu	Val	Lys	Pro	Gln
				165					170					175	
Val	Asn	Gln	Ile	Glu	Phe	Ser	Pro	Phe	Leu	Gln	Asn	Gln	Thr	Pro	Gly
			180					185					190		
Ile	Tyr	Lys	Phe	Cys	Gln	Glu	His	Asp	Ile	Leu	Val	Glu	Ala	Tyr	Ser
		195					200					205			
Pro	Leu	Gly	Pro	Leu	Gln	Lys	Lys	Thr	Ala	Gln	Asp	Asp	Ser	Gln	Pro
		210				215					220				
Phe	Phe	Glu	Tyr	Val	Lys	Glu	Leu	Ser	Glu	Lys	Tyr	Arg	Lys	Ser	Glu
225					230					235					240
Ala	Gln	Ile	Ile	Leu	Arg	Trp	Val	Thr	Lys	Arg	Gly	Val	Leu	Pro	Val
				245					250					255	
Thr	Thr	Ser	Ser	Lys	Pro	Gln	Arg	Ile	Ser	Asp	Ala	Gln	Asn	Leu	Phe
			260					265					270		
Ser	Phe	Asp	Leu	Thr	Ala	Glu	Glu	Val	Asp	Lys	Ile	Thr	Glu	Leu	Gly
		275					280					285			
Leu	Glu	His	Glu	Pro	Leu	Arg	Leu	Tyr	Trp	Asn	Lys	Leu	Tyr	Gly	Lys
		290				295					300				
Tyr	Asn	Tyr	Ala	Ala	Gln	Lys	Val								
305					310										

<210> 131
 <211> 942
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 131
 atgtcttttc accaacagtt tttcacgctg aacaacggca ataaaatccc ggcgattgcc 60
 atcatcggga ctggtacacg ttggtataaa aatgaagaaa ctgacgcgac ottctccaat 120
 agtctggttg aacaaatcgt gtatgcgttg aaactgccgg ggattatoca catcgacgcc 180
 gcggagattt atcgcaccta cccggaagtg ggtaaagcac tgtccctgac cgaaaagcct 240
 cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactcccct 300
 gcggacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
 ttacattccc cgtttgtttc gaaggaagtg aatggcttaa gcttagaaga ggcttgga 420
 gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggttc caatttctcc 480
 gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
 gagttctctc cgttcctgca aaaccaaaca ccaggcattt ataaattctg tcaggagcac 600
 gatatcctgg tggaagcata ttctccgctg ggcccgtgac agaagaaaac cgcgcaggat 660
 gacagccaac cattttttga gtacgtcaaa gaattgagcg aaaaatacgg caaatccgag 720
 gccagatca tcctgcgctg ggtcactaaa cgcggtgtgc tgccagttac cacctcttca 780
 aagcctcagc gcattagcga tgctcagaac ctgttttctc tcgacctgac agcgggaagag 840
 gttgataaaa tcacggagct gggtctggaa catgaaccgc tgcgcctgta ctggaataaa 900
 ttgtatggca aatataacta cgccgccagc aaagtgtaat ga 942

<210> 132
 <211> 313
 <212> PRT
 <213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 132

```
Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
1      5      10      15
Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Arg Trp Tyr Lys Asn Glu
      20      25      30
Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
      35      40      45
Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Ile Tyr
      50      55      60
Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
65      70      75      80
Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
      85      90      95
Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
      100      105      110
Thr Asp Tyr Val Asp Leu Tyr Leu Leu His Ser Pro Phe Val Ser Lys
      115      120      125
Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
130      135      140
Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Ser
145      150      155      160
Val Glu Asp Leu Gln Arg Ile Leu Lys Val Ala Glu Val Lys Pro Gln
      165      170      175
Val Asn Gln Ile Glu Phe Ser Pro Phe Leu Gln Asn Gln Thr Pro Gly
      180      185      190
Ile Tyr Lys Phe Cys Gln Glu His Asp Ile Leu Val Glu Ala Tyr Ser
195      200      205
Pro Leu Gly Pro Leu Gln Lys Lys Thr Ala Gln Asp Asp Ser Gln Pro
210      215      220
Phe Phe Glu Tyr Val Lys Glu Leu Ser Glu Lys Tyr Gly Lys Ser Glu
225      230      235      240
Ala Gln Ile Ile Leu Arg Trp Val Thr Lys Arg Gly Val Leu Pro Val
      245      250      255
Thr Thr Ser Ser Lys Pro Gln Arg Ile Ser Asp Ala Gln Asn Leu Phe
260      265      270
Ser Phe Asp Leu Thr Ala Glu Glu Val Asp Lys Ile Thr Glu Leu Gly
275      280      285
Leu Glu His Glu Pro Leu Arg Leu Tyr Trp Asn Lys Leu Tyr Gly Lys
290      295      300
Tyr Asn Tyr Ala Ala Gln Lys Val
305      310
```

<210> 133

<211> 942

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 133

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atgtcttttc accaacagtt ttccacgctg aacaacggca ataaaatccc ggcgattgcc 60
atcatcggca ctggtacacg ttggtataaa aatgaagaaa ctgacgcgac cttctccaat 120
agtctggttg aacaaatcgt gtatgcgttg aaactgocgg ggattatcca catcgacgcc 180
gcggagattt atcgcaccta cccggaagtg ggtaaagcac tgtccctgac cgaaaagcct 240
cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactccoct 300
```

```

gcggacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
ttacattccc cgtttgtttc gaaggaagtg aatggcttaa gcttagaaga ggcttggaaa 420
gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggttc caatttcagc 480
gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
gagttctctc cgttcctgca aaaccaaaaca ccaggcattt ataaattctg tcaggagcac 600
gatatcctgg tggaagcata ttctccgctg ggcccgcctgc agaagaaaac cgcgcaggat 660
gacagccaac cattttttga gtacgtcaaa gaattgagcg aaaaatacca aaaatccgag 720
gccagatca tcctgcgctg ggtcactaaa cgcggtgtgc tgccagttac cacctcttca 780
aagcctcagc gcattagcga tgctcagaac ctgttttctt togacctgac agcggaagag 840
gttgataaaa tcacggagct gggtctggaa catgaaccgc tgcgcctgta ctggaataaa 900
ttgtatggca aatataacta cgcgcgccag aaagtgtaat ga 942

```

<210> 134

<211> 313

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 134

```

Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
1          5          10          15
Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Arg Trp Tyr Lys Asn Glu
          20          25          30
Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
          35          40          45
Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Ile Tyr
          50          55          60
Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
65          70          75          80
Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
          85          90          95
Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
          100          105          110
Thr Asp Tyr Val Asp Leu Tyr Leu Leu His Ser Pro Phe Val Ser Lys
          115          120          125
Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
          130          135          140
Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Ser
145          150          155          160
Val Glu Asp Leu Gln Arg Ile Leu Lys Val Ala Glu Val Lys Pro Gln
          165          170          175
Val Asn Gln Ile Glu Phe Ser Pro Phe Leu Gln Asn Gln Thr Pro Gly
          180          185          190
Ile Tyr Lys Phe Cys Gln Glu His Asp Ile Leu Val Glu Ala Tyr Ser
          195          200          205
Pro Leu Gly Pro Leu Gln Lys Lys Thr Ala Gln Asp Asp Ser Gln Pro
          210          215          220
Phe Phe Glu Tyr Val Lys Glu Leu Ser Glu Lys Tyr Gln Lys Ser Glu
225          230          235          240
Ala Gln Ile Ile Leu Arg Trp Val Thr Lys Arg Gly Val Leu Pro Val
          245          250          255
Thr Thr Ser Ser Lys Pro Gln Arg Ile Ser Asp Ala Gln Asn Leu Phe
          260          265          270
Ser Phe Asp Leu Thr Ala Glu Glu Val Asp Lys Ile Thr Glu Leu Gly
          275          280          285
Leu Glu His Glu Pro Leu Arg Leu Tyr Trp Asn Lys Leu Tyr Gly Lys
290          295          300
Tyr Asn Tyr Ala Ala Gln Lys Val

```

<210> 135
 <211> 942
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 135
 atgtcttttc accaacagtt tttcacgctg aacaacggca ataaaatccc ggcgattgcc 60
 atcatcggca ctggtacaaa atggtataaa aatgaagaaa ctgacgcgac cttctccaat 120
 agtctggttg aacaaatcgt gtatgcgttg aaactgccgg ggattatcca catcgacgcc 180
 gcggagattt atcgcaccta cccggaagtg ggtaaagcac tgtocatgac cgaaaagcct 240
 cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactcccct 300
 gcggacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
 ttacattccc cgtttgtttc gaaggaagtg aatggcttaa gottagaaga ggcttgga 420
 gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggtttc caatttcaca 480
 gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
 gagttctctc cgttcctgca aaaccaaaaca ccaggcattt ataaattctg tcaggagcac 600
 gatatcctgg tggaagcata ttctccgctg ggcccgtgac agaagaaaac cgcgcaggat 660
 gacagccaac cattttttga gtacgtcaaa gaattgagcg aaaaatacaa caaatccgag 720
 gccagatca tctgcgctg ggtcactaaa cgcggtgtgc tgccagttac cacctcttca 780
 aagcctcagc gcattagcga tgctcagaac ctgttttctt tcgacctgac agcgggaagag 840
 gttgataaaa tcacggagct gggtctggaa catgaaccgc tcgcctgta ctggaataaa 900
 ttgtatggca aatataacta cgccgccag aaagtgtaat ga 942

<210> 136
 <211> 313
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 136
 Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
 1 5 10 15
 Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Lys Trp Tyr Lys Asn Glu
 20 25 30
 Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
 35 40 45
 Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Ile Tyr
 50 55 60
 Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Met Thr Glu Lys Pro
 65 70 75 80
 Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
 85 90 95
 Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
 100 105 110
 Thr Asp Tyr Val Asp Leu Tyr Leu Leu His Ser Pro Phe Val Ser Lys
 115 120 125
 Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
 130 135 140
 Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Thr
 145 150 155 160
 Val Glu Asp Leu Gln Arg Ile Leu Lys Val Ala Glu Val Lys Pro Gln
 165 170 175

Val	Asn	Gln	Ile	Glu	Phe	Ser	Pro	Phe	Leu	Gln	Asn	Gln	Thr	Pro	Gly
			180					185					190		
Ile	Tyr	Lys	Phe	Cys	Gln	Glu	His	Asp	Ile	Leu	Val	Glu	Ala	Tyr	Ser
		195					200					205			
Pro	Leu	Gly	Pro	Leu	Gln	Lys	Lys	Thr	Ala	Gln	Asp	Asp	Ser	Gln	Pro
	210					215					220				
Phe	Phe	Glu	Tyr	Val	Lys	Glu	Leu	Ser	Glu	Lys	Tyr	Asn	Lys	Ser	Glu
225					230					235					240
Ala	Gln	Ile	Ile	Leu	Arg	Trp	Val	Thr	Lys	Arg	Gly	Val	Leu	Pro	Val
			245						250					255	
Thr	Thr	Ser	Ser	Lys	Pro	Gln	Arg	Ile	Ser	Asp	Ala	Gln	Asn	Leu	Phe
			260					265					270		
Ser	Phe	Asp	Leu	Thr	Ala	Glu	Glu	Val	Asp	Lys	Ile	Thr	Glu	Leu	Gly
		275					280					285			
Leu	Glu	His	Glu	Pro	Leu	Arg	Leu	Tyr	Trp	Asn	Lys	Leu	Tyr	Gly	Lys
	290					295					300				
Tyr	Asn	Tyr	Ala	Ala	Gln	Lys	Val								
305					310										

<210> 137
 <211> 942
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 137
 atgtcttttt accaacagtt tttcacgctg aacaacggca ataaaatccc ggogattgcc 60
 atcatcggca ctggtacaaa atggtataaa aatgaagaaa ctgaacgcgac cttctccaat 120
 agtctggttg aacaaatcgt gtatgcgttg aaactgccgg ggattatcca catcgaagcc 180
 gcggagatat atcgcaccta cccggaagtg ggtaaagcac tgtccctgac cgaaaagcct 240
 cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactccoct 300
 gcggacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
 ttacattccc cgtttgtttc gaaggaagtg aatggcttaa gcttagaaga ggcttggaag 420
 gatattggagc agttatacaa acgtggtaaa gctaaaaaca tcgggggttt caatttcaca 480
 gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
 gagttctctc cgttcctgca aaaccaaaaca ccaggcattt ataaattctg tcaggagcac 600
 gatattcctg tggaagcata ttctccgctg ggcccgtgac agaagaaaac cggcaggat 660
 gacagccaac cattttttga gtacgtcaaa gaattgagcg aaaaatacaa caaatccgag 720
 gccagatca tcttgccgtg ggtcactaaa cgcggtgtgc tgccagttac cacctcttca 780
 aagcctcagc gcattagcga tgctcagaac ctgttttctt togaactgac agcgggaagag 840
 gttgataaaa tcacggagct gggtctggaa catgaaccgc tgcgcctgta ctggaataaa 900
 ttgtatggca aatataacta cgcgcgccag aaagtgtaat ga 942

<210> 138
 <211> 313
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 138
 Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
 1 5 10 15
 Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Lys Trp Tyr Lys Asn Glu
 20 25 30
 Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr

35	40	45
Ala Leu Lys Leu Pro Gly Ile	Ile His Ile Asp	Ala Ala Glu Ile Tyr
50	55	60
Arg Thr Tyr Pro Glu Val Gly	Lys Ala Leu Ser	Leu Thr Glu Lys Pro
65	70	75
Arg Asn Ala Ile Phe Leu Thr	Asp Lys Tyr Ser	Pro Gln Ile Lys Met
85	90	95
Ser Asp Ser Pro Ala Asp Gly	Leu Asp Leu Ala	Leu Lys Lys Met Gly
100	105	110
Thr Asp Tyr Val Asp Leu Tyr	Leu Leu His Ser	Pro Phe Val Ser Lys
115	120	125
Glu Val Asn Gly Leu Ser Leu	Glu Glu Ala Trp	Lys Asp Met Glu Gln
130	135	140
Leu Tyr Lys Arg Gly Lys Ala	Lys Asn Ile Gly	Val Ser Asn Phe Thr
145	150	155
Val Glu Asp Leu Gln Arg Ile	Leu Lys Val Ala	Glu Val Lys Pro Gln
165	170	175
Val Asn Gln Ile Glu Phe Ser	Pro Phe Leu Gln	Asn Gln Thr Pro Gly
180	185	190
Ile Tyr Lys Phe Cys Gln Glu	His Asp Ile Leu	Val Glu Ala Tyr Ser
195	200	205
Pro Leu Gly Pro Leu Gln Lys	Lys Thr Ala Gln	Asp Asp Ser Gln Pro
210	215	220
Phe Phe Glu Tyr Val Lys Glu	Leu Ser Glu Lys	Tyr Asn Lys Ser Glu
225	230	235
Ala Gln Ile Ile Leu Arg Trp	Val Thr Lys Arg	Gly Val Leu Pro Val
245	250	255
Thr Thr Ser Ser Lys Pro Gln	Arg Ile Ser Asp	Ala Gln Asn Leu Phe
260	265	270
Ser Phe Asp Leu Thr Ala Glu	Glu Val Asp Lys	Ile Thr Glu Leu Gly
275	280	285
Leu Glu His Glu Pro Leu Arg	Leu Tyr Trp Asn	Lys Leu Tyr Gly Lys
290	295	300
Tyr Asn Tyr Ala Ala Gln Lys	Val	
305	310	

<210> 139
 <211> 942
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 139
 atgtcttttt accaacagtt ttctacgctg aacaacggca ataaaatccc ggcgattgcc 60
 atcatcggca ctggtacaaa atggtataaa aatgaagaaa ctgaacgcgac cttctccaat 120
 agtctggttg aacaaatcgt gtatgcgttg aaactgccgg ggattatcca catcgacgcc 180
 gcggagattt atcgcaccta cccggaagtg ggtaaagcac tgtccctgac cgaaaagcct 240
 cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactccoct 300
 gcggacgggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
 ttacattccc cgtttgtttc gaaggaagtg aatggcttaa gcttagaaga ggcttgga 420
 gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggtttc caatttcaca 480
 gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
 gagttctctc cgttcctgca aaaccaaaca ccaggcattt ataaattctg tcaggagcac 600
 gatatccttg tggaagcata ttctcogctg ggcccgtgc agaagaaaac cgcgaggat 660
 gacagccaac cattttttga gtacgtcaaa gaattgagcg aaaaatacaa caaacccgag 720
 gccagatca tcttgcgctg ggtcactaaa cgcggtgtgc tgccagttac cacctcttca 780
 aagcctcagc gcattagcga tgctcagaac ctgttttctc tcgacctgac agcgggaagag 840
 gttgataaaa tcacggagct gggctctggaa catgaaccgc tcgcctgta ctggaataaa 900

ttgtatggca aatataacta cgccgccag aaagtgtaat ga

942

<210> 140

<211> 313

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 140

Met	Ser	Phe	His	Gln	Gln	Phe	Phe	Thr	Leu	Asn	Asn	Gly	Asn	Lys	Ile	
1				5					10					15		
Pro	Ala	Ile	Ala	Ile	Ile	Gly	Thr	Gly	Thr	Lys	Trp	Tyr	Lys	Asn	Glu	
			20					25					30			
Glu	Thr	Asp	Ala	Thr	Phe	Ser	Asn	Ser	Leu	Val	Glu	Gln	Ile	Val	Tyr	
		35					40					45				
Ala	Leu	Lys	Leu	Pro	Gly	Ile	Ile	His	Ile	Asp	Ala	Ala	Glu	Ile	Tyr	
	50					55				60						
Arg	Thr	Tyr	Pro	Glu	Val	Gly	Lys	Ala	Leu	Ser	Leu	Thr	Glu	Lys	Pro	
65				70						75					80	
Arg	Asn	Ala	Ile	Phe	Leu	Thr	Asp	Lys	Tyr	Ser	Pro	Gln	Ile	Lys	Met	
				85					90					95		
Ser	Asp	Ser	Pro	Ala	Asp	Gly	Leu	Asp	Leu	Ala	Leu	Lys	Lys	Met	Gly	
			100					105					110			
Thr	Asp	Tyr	Val	Asp	Leu	Tyr	Leu	Leu	His	Ser	Pro	Phe	Val	Ser	Lys	
	115						120					125				
Glu	Val	Asn	Gly	Leu	Ser	Leu	Glu	Glu	Ala	Trp	Lys	Asp	Met	Glu	Gln	
	130					135					140					
Leu	Tyr	Lys	Ser	Gly	Lys	Ala	Lys	Asn	Ile	Gly	Val	Ser	Asn	Phe	Thr	
145				150					155						160	
Val	Glu	Asp	Leu	Gln	Arg	Ile	Leu	Lys	Val	Ala	Glu	Val	Lys	Pro	Gln	
				165				170						175		
Val	Asn	Gln	Ile	Glu	Phe	Ser	Pro	Phe	Leu	Gln	Asn	Gln	Thr	Pro	Gly	
			180					185					190			
Ile	Tyr	Lys	Phe	Cys	Gln	Glu	His	Asp	Ile	Leu	Val	Glu	Ala	Tyr	Ser	
	195						200					205				
Pro	Leu	Gly	Pro	Leu	Gln	Lys	Lys	Thr	Ala	Gln	Asp	Asp	Ser	Gln	Pro	
	210					215					220					
Phe	Phe	Glu	Tyr	Val	Lys	Glu	Leu	Ser	Glu	Lys	Tyr	Asn	Lys	Thr	Glu	
225					230					235					240	
Ala	Gln	Ile	Ile	Leu	Arg	Trp	Val	Thr	Lys	Arg	Gly	Val	Leu	Pro	Val	
				245					250					255		
Thr	Thr	Ser	Ser	Lys	Pro	Gln	Arg	Ile	Ser	Asp	Ala	Gln	Asn	Leu	Phe	
			260				265						270			
Ser	Phe	Asp	Leu	Thr	Ala	Glu	Glu	Val	Asp	Lys	Ile	Thr	Glu	Leu	Gly	
		275					280					285				
Leu	Glu	His	Glu	Pro	Leu	Arg	Leu	Tyr	Trp	Asn	Lys	Leu	Tyr	Gly	Lys	
	290					295					300					
Tyr	Asn	Tyr	Ala	Ala	Gln	Lys	Val									
305					310											

<210> 141

<211> 942

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 141

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atgtcttttc accaacagtt tttcacgctg aacaacggca ataaaatccc ggcgattgcc 60
atcatcggca ctggtacaaa atggtataaa aatgaagaaa ctgaacgcac cttctccaat 120
agtctggttg aacaaatcgt gtatgcgttg aaactgccgg ggattatcca catcgacgcc 180
gcgagagattt atcgcaccta cccggaagtg ggtaaagcac tgccctgac cgaaaagcct 240
cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactcccct 300
gcgatggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
ttacattccc cgtttgttc gaaggaagtg aatggcttaa gcttagaaga ggcttggaaa 420
gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcggggtttc caatttcaca 480
gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
gagttctctc cgttcctgca aaaccaaaca ccaggcattt ataaattctg tcaggagcac 600
gatatcctgg tggaaagcata ttctcogctg ggcccgtgc agaagaaaac cgcgcaggat 660
gacagacacc cattttttga gtacgtcaaa gaattgagcg aaaaatacaa caaatccgag 720
gccagatca tctgcgctg ggtcactaaa cgcggtgtgc tgccagttac cacctcttca 780
aagcctcagc gcattagcga tgctcagaac ctgttttctc tcgacctgac agcgggaagag 840
gttgataaaa tcacggagct gggctcggaa catgaaccgc tcgcctgta ctggaataaa 900
ttgtatggca aatataacta cgccgccag aaagtgtaat ga 942
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<210> 142

<211> 313

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 142

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Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
1          5          10          15
Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Lys Trp Tyr Lys Asn Glu
          20          25          30
Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
          35          40          45
Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Ile Tyr
          50          55          60
Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
65          70          75          80
Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
          85          90          95
Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
          100          105          110
Thr Asp Tyr Val Asp Leu Tyr Leu Leu His Ser Pro Phe Val Ser Lys
          115          120          125
Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
          130          135          140
Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Thr
145          150          155          160
Val Glu Asp Leu Gln Arg Ile Leu Lys Val Ala Glu Val Lys Pro Gln
          165          170          175
Val Asn Gln Ile Glu Phe Ser Pro Phe Leu Gln Asn Gln Thr Pro Gly
          180          185          190
Ile Tyr Lys Phe Cys Gln Glu His Asp Ile Leu Val Glu Ala Tyr Ser
          195          200          205
Pro Leu Gly Pro Leu Gln Lys Lys Thr Ala Gln Asp Asp Arg His Pro
210          215          220
Phe Phe Glu Tyr Val Lys Glu Leu Ser Glu Lys Tyr Asn Lys Ser Glu
225          230          235          240
Ala Gln Ile Ile Leu Arg Trp Val Thr Lys Arg Gly Val Leu Pro Val
          245          250          255
```

Thr	Thr	Ser	Ser	Lys	Pro	Gln	Arg	Ile	Ser	Asp	Ala	Gln	Asn	Leu	Phe
			260					265					270		
Ser	Phe	Asp	Leu	Thr	Ala	Glu	Glu	Val	Asp	Lys	Ile	Thr	Glu	Leu	Gly
		275					280					285			
Leu	Glu	His	Glu	Pro	Leu	Arg	Leu	Tyr	Trp	Asn	Lys	Leu	Tyr	Gly	Lys
	290					295					300				
Tyr	Asn	Tyr	Ala	Ala	Gln	Lys	Val								
305					310										

<210> 143
 <211> 942
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 143
 atgtcttttc accaacagtt tttcacgctg aacaacggca ataaaatccc ggcgattgcc 60
 atcatcggca ctggtacaaa atggtataaa aatgaagaaa ctgaacgogac cttctccaac 120
 agtctggttg aacaaatctt gtatgcgttg aaactgccgg ggattatcca catcgacgcc 180
 gcggagattt atcgcaccta cccggaagtg ggtaaagcac tgtccctgac cgaaaagcct 240
 cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactccct 300
 gcggacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
 ttacattccc cgtttgtttc gaaggaagtg aatggcttaa gcttagaaga ggcttggaaa 420
 gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggttc caatttcaca 480
 gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
 gagttctctc cgttcctgca aaaccaaaca ccaggcattt ataaattctg tcaggagcac 600
 gatatcctgg tgggaagcata ttctccgctg ggcccgtgac agaagaaaac cgcgcaggat 660
 gtcagccaac cattttttga gtacgtcaaa gaattgagcg aaaaatacaa caaatccgag 720
 gccagatca tcttgcgctg ggtcactaaa cgcgggtgtg tgccagttac cacctottca 780
 aagcctcagc gcattagcga tgctcagaac ctgttttctc tcgacctgac agcggaagag 840
 gttgataaaa tcacggagct gggctctggaa catgaaccgc tgcgcctgta ctggaataaa 900
 ttgtatggca aatataacta cgccgccag aaagtgtaat ga 942

<210> 144
 <211> 313
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 144
 Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
 1 5 10 15
 Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Lys Trp Tyr Lys Asn Glu
 20 25 30
 Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Leu Tyr
 35 40 45
 Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Ile Tyr
 50 55 60
 Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
 65 70 75 80
 Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
 85 90 95
 Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
 100 105 110
 Thr Asp Tyr Val Asp Leu Tyr Leu Leu His Ser Pro Phe Val Ser Lys

	115		120		125										
Glu	Val	Asn	Gly	Leu	Ser	Leu	Glu	Glu	Ala	Trp	Lys	Asp	Met	Glu	Gln
	130					135					140				
Leu	Tyr	Lys	Ser	Gly	Lys	Ala	Lys	Asn	Ile	Gly	Val	Ser	Asn	Phe	Thr
145					150					155					160
Val	Glu	Asp	Leu	Gln	Arg	Ile	Leu	Lys	Val	Ala	Glu	Val	Lys	Pro	Gln
			165						170					175	
Val	Asn	Gln	Ile	Glu	Phe	Ser	Pro	Phe	Leu	Gln	Asn	Gln	Thr	Pro	Gly
	180							185					190		
Ile	Tyr	Lys	Phe	Cys	Gln	Glu	His	Asp	Ile	Leu	Val	Glu	Ala	Tyr	Ser
	195						200				205				
Pro	Leu	Gly	Pro	Leu	Gln	Lys	Lys	Thr	Ala	Gln	Asp	Val	Ser	Gln	Pro
	210					215				220					
Phe	Phe	Glu	Tyr	Val	Lys	Glu	Leu	Ser	Glu	Lys	Tyr	Asn	Lys	Ser	Glu
225					230					235					240
Ala	Gln	Ile	Ile	Leu	Arg	Trp	Val	Thr	Lys	Arg	Gly	Val	Leu	Pro	Val
			245					250						255	
Thr	Thr	Ser	Ser	Lys	Pro	Gln	Arg	Ile	Ser	Asp	Ala	Gln	Asn	Leu	Phe
		260					265					270			
Ser	Phe	Asp	Leu	Thr	Ala	Glu	Glu	Val	Asp	Lys	Ile	Thr	Glu	Leu	Gly
	275					280					285				
Leu	Glu	His	Glu	Pro	Leu	Arg	Leu	Tyr	Trp	Asn	Lys	Leu	Tyr	Gly	Lys
	290					295				300					
Tyr	Asn	Tyr	Ala	Ala	Gln	Lys	Val								
305					310										

<210> 145
 <211> 942
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 145
 atgtcttttt accaacagtt tttcacgctg aacaaaggca ataaaatccc ggcgattgcc 60
 atcatcggca ctggtacaaa atggtataaa aatgaagaaa ctgacgcgac cttctccaat 120
 agtctggttg aacaaatcgt gtatgcgttg aaactgcggg ggattatcca catcgacgcc 180
 gcggagattt atcgcaocta ccgggaagtg ggtaaagcac tgccoctgac cgaaaagcct 240
 cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactcccct 300
 gcggacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
 ttacattccc cgtttgtttc gaaggaagtg aatggcttaa gcttagaaga ggcttggaaa 420
 gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggttc caatttcaca 480
 gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
 gagttctctc cgttcctgca aaaccaaaca ccaggcattt ataaattctg tcaggagcac 600
 gatatccttg tggaagcata ttctccgctg ggcccgctgc agaagaaaac cgcgcaggat 660
 gacagccaac ctttttttga gtacgtcaaa gaattgagcg aaaaatacaa caaatccgag 720
 gccagatca tcttgogctg ggtaactaaa cgcggtgtgc tgccagttac cacctottca 780
 aagcctcagc gcattagcga tgctcagaac ctgttttctt tcgacctgac agcgggaagag 840
 gttgataaaa tcacggagct gggctctggaa catgaaccgc tcgcgcagta ctggaataaa 900
 ttgtatggca aatataacta cgccgccagc aaagtgtaat ga 942

<210> 146
 <211> 313
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 146

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Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
1          5          10          15
Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Lys Trp Tyr Lys Asn Glu
20          25          30
Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
35          40          45
Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Ile Tyr
50          55          60
Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
65          70          75          80
Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
85          90          95
Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
100         105         110
Thr Asp Tyr Val Asp Leu Tyr Leu Leu His Ser Pro Phe Val Ser Lys
115         120         125
Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
130         135         140
Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Thr
145         150         155         160
Val Glu Asp Leu Gln Arg Ile Leu Lys Val Ala Glu Val Lys Pro Gln
165         170         175
Val Asn Gln Ile Glu Phe Ser Pro Phe Leu Gln Asn Gln Thr Pro Gly
180         185         190
Ile Tyr Lys Phe Cys Gln Glu His Asp Ile Leu Val Glu Ala Tyr Ser
195         200         205
Pro Leu Gly Pro Leu Gln Lys Lys Thr Ala Gln Asp Asp Ser Gln Pro
210         215         220
Phe Phe Glu Tyr Val Lys Glu Leu Ser Glu Lys Tyr Asn Lys Ser Glu
225         230         235         240
Ala Gln Ile Ile Leu Arg Trp Val Thr Lys Arg Gly Val Leu Pro Val
245         250         255
Thr Thr Ser Ser Lys Pro Gln Arg Ile Ser Asp Ala Gln Asn Leu Phe
260         265         270
Ser Phe Asp Leu Thr Ala Glu Glu Val Asp Lys Ile Thr Glu Leu Gly
275         280         285
Leu Glu His Glu Pro Leu Arg Gln Tyr Trp Asn Lys Leu Tyr Gly Lys
290         295         300
Tyr Asn Tyr Ala Ala Gln Lys Val
305          310
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<210> 147

<211> 942

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 147

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atgtcttttc accaacagtt ttccacgctg aacaacggca ataaaatccc ggcgattgcc 60
atcatcggca ctggtacaaa atggtataaa aatgaagaaa ctgacgogac otttccaat 120
agtctggttg aacaaatcgt gtatgcgttg aaactgcggg ggattatcca catcgacgcc 180
gcggagattt atcgaccta cccggaagtg ggtaaagcac tgccctgac cgaagacct 240
cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactcccct 300
gcggacggtc tggatttagc attgaagaaa atgggtacag attatgttg tttatatctg 360
ttacattccc cgtttgtttc gaaggaagtg aatggcttaa gcttagaaga ggcttgaaa 420
gatattggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggttc caatttctcc 480
```

```

gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aaccccaggt caaccagatt 540
gagttctctc cgttcctgca aaaccaaaca ccaggcattt ataaattctg tcaggagcac 600
gatatcctgg tggaagcata ttctccgctg ggcccgtgct ggaagaaaac cgcgcaggat 660
gacagccaac cattttttga gtacgtcaaa gaattgagcg aaaaatacaa caaatccgag 720
gcccagatca tcctgcgctg ggctactaaa cgcggtgtgc tgccagttac cacctcttca 780
aagcctcagc gcattagcga tgctcagaac ctgttttctt tcgacctgac agcgggaagag 840
gttgataaaa tcacggagct gggctctggaa catgaaccgc tcgcgctgta ctggaataaa 900
ttgtatggca aatataacta cgccgccag aaagtgtaat ga 942

```

<210> 148

<211> 313

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 148

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Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
1          5          10          15
Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Lys Trp Tyr Lys Asn Glu
20          25          30
Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
35          40          45
Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Ile Tyr
50          55          60
Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
65          70          75          80
Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
85          90          95
Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
100         105         110
Thr Asp Tyr Val Asp Leu Tyr Leu Leu His Ser Pro Phe Val Ser Lys
115         120         125
Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
130         135         140
Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Ser
145         150         155         160
Val Glu Asp Leu Gln Arg Ile Leu Lys Val Ala Glu Val Lys Pro Gln
165         170         175
Val Asn Gln Ile Glu Phe Ser Pro Phe Leu Gln Asn Gln Thr Pro Gly
180         185         190
Ile Tyr Lys Phe Cys Gln Glu His Asp Ile Leu Val Glu Ala Tyr Ser
195         200         205
Pro Leu Gly Pro Leu Arg Lys Lys Thr Ala Gln Asp Asp Ser Gln Pro
210         215         220
Phe Phe Glu Tyr Val Lys Glu Leu Ser Glu Lys Tyr Asn Lys Ser Glu
225         230         235         240
Ala Gln Ile Ile Leu Arg Trp Val Thr Lys Arg Gly Val Leu Pro Val
245         250         255
Thr Thr Ser Ser Lys Pro Gln Arg Ile Ser Asp Ala Gln Asn Leu Phe
260         265         270
Ser Phe Asp Leu Thr Ala Glu Glu Val Asp Lys Ile Thr Glu Leu Gly
275         280         285
Leu Glu His Glu Pro Leu Arg Leu Tyr Trp Asn Lys Leu Tyr Gly Lys
290         295         300
Tyr Asn Tyr Ala Ala Gln Lys Val
305         310

```

<210> 149
<211> 942
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 149
atgtcttttc accaacagtt tttcacgctg aacaacggca ataaaatccc ggcgattgcc 60
atcatcggca ctggtacaaa atggtataaa aatgaagaaa ctgacgcgac cttctccaat 120
agtctggttg agcaaatcgt gcatgcgttg aaactgccgg ggattatcca catcgacgcc 180
gcgagagattt atcgcaccta cccggaagtg ggtaaagcac tgtccctgac cgaaaagcct 240
cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactcccct 300
gcgacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
ttacattccc cgtttggttc gaaggaagtg aatggcttaa gcttagaaga ggcttggaag 420
gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggttc caatttcaca 480
gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
gagttctctc cgttcctgca aaaccaaaca ccaggcattt ataaattctg tcaggagcac 600
gatatcctgg tggaagcata ttctccgctg ggcccgtctg ggaagaaaac cgcgcaggat 660
gacagccaac cattttttga gtacgtcaaa gaattgagcg aaaaatacaa caaatccgag 720
gccagatca tctcgcgctg ggctactaaa cgcggtgtgc tgccagttac cacctcttca 780
aagcctcagc gcattagcga tgctcagaac ctgttttctt tcgacctgac agcgggaagag 840
gttgataaaa tcacggagct gggctctggaa catgaaccgc tcgcctgtga ctggaataaa 900
ttgtatggca aatataacta cgccgccag aaagtgtaat ga 942

<210> 150
<211> 313
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 150
Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
1 5 10 15
Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Lys Trp Tyr Lys Asn Glu
20 25 30
Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val His
35 40 45
Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Ile Tyr
50 55 60
Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
65 70 75 80
Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
85 90 95
Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
100 105 110
Thr Asp Tyr Val Asp Leu Tyr Leu Leu His Ser Pro Phe Val Ser Lys
115 120 125
Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
130 135 140
Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Thr
145 150 155 160
Val Glu Asp Leu Gln Arg Ile Leu Lys Val Ala Glu Val Lys Pro Gln
165 170 175
Val Asn Gln Ile Glu Phe Ser Pro Phe Leu Gln Asn Gln Thr Pro Gly
180 185 190
Ile Tyr Lys Phe Cys Gln Glu His Asp Ile Leu Val Glu Ala Tyr Ser

195	200	205
Pro Leu Gly Pro Leu Arg Lys Lys Thr Ala Gln Asp Asp Ser Gln Pro		
210	215	220
Phe Phe Glu Tyr Val Lys Glu Leu Ser Glu Lys Tyr Asn Lys Ser Glu		
225	230	235
Ala Gln Ile Ile Leu Arg Trp Val Thr Lys Arg Gly Val Leu Pro Val		
245	250	255
Thr Thr Ser Ser Lys Pro Gln Arg Ile Ser Asp Ala Gln Asn Leu Phe		
260	265	270
Ser Phe Asp Leu Thr Ala Glu Glu Val Asp Lys Ile Thr Glu Leu Gly		
275	280	285
Leu Glu His Glu Pro Leu Arg Leu Tyr Trp Asn Lys Leu Tyr Gly Lys		
290	295	300
Tyr Asn Tyr Ala Ala Gln Lys Val		
305	310	

<210> 151
 <211> 942
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 151
 atgtcttttc accaacagtt tttcacgctg aacaacggca ataaaatccc ggcgattgcc 60
 atcatcggca ctggtacaaa atggtataaa aatgaagaaa ctgacgcgac cttctccaat 120
 agtctggttg aacaaatcgt gtacgcgttg gagctgccgg gaattatoca catcgaogcc 180
 gcggaggttt atcgcaccta cccggaagtg ggtaaagcac tgtccctgac cgaaaagcct 240
 cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactcccct 300
 gcggacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
 attcattccc cgtttgtttc gaaggaagtg aatggcttaa gcttagaaga ggcttgga 420
 gatattggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggtttc caatttcaca 480
 gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
 gagttctctc cgttcctgca aaaccaaaaca ccaggcattt ataaattctg tcaggagcac 600
 gatatcctgg tgggaagcata ttctccgctg ggcccgtgc ggaagaaaac cgcgcaggat 660
 gacagccaac cattttttga gtacgtcaaa gaattgagcg aaaaatacgg caaatccgag 720
 gccagatca tcctgcgctg ggtaactaaa cgcggtgtgc tgccagttac cacctcttca 780
 aagcctcagc gcattagcga tgctcagaac ctgttttctc tcgacctgac agcggaagag 840
 gttgataaaa tcacggagct gggtctggaa catgaaccgc tgcgcctgta ctggaataaa 900
 ttgtatggca aatataacta cgccgccag aaagtgtaat ga 942

<210> 152
 <211> 313
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 152
 Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
 1 5 10 15
 Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Lys Trp Tyr Lys Asn Glu
 20 25 30
 Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
 35 40 45
 Ala Leu Glu Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Val Tyr
 50 55 60

Arg	Thr	Tyr	Pro	Glu	Val	Gly	Lys	Ala	Leu	Ser	Leu	Thr	Glu	Lys	Pro
65					70					75					80
Arg	Asn	Ala	Ile	Phe	Leu	Thr	Asp	Lys	Tyr	Ser	Pro	Gln	Ile	Lys	Met
				85					90					95	
Ser	Asp	Ser	Pro	Ala	Asp	Gly	Leu	Asp	Leu	Ala	Leu	Lys	Lys	Met	Gly
			100					105					110		
Thr	Asp	Tyr	Val	Asp	Leu	Tyr	Leu	Ile	His	Ser	Pro	Phe	Val	Ser	Lys
		115					120					125			
Glu	Val	Asn	Gly	Leu	Ser	Leu	Glu	Glu	Ala	Trp	Lys	Asp	Met	Glu	Gln
	130					135					140				
Leu	Tyr	Lys	Ser	Gly	Lys	Ala	Lys	Asn	Ile	Gly	Val	Ser	Asn	Phe	Thr
145					150					155					160
Val	Glu	Asp	Leu	Gln	Arg	Ile	Leu	Lys	Val	Ala	Glu	Val	Lys	Pro	Gln
				165					170					175	
Val	Asn	Gln	Ile	Glu	Phe	Ser	Pro	Phe	Leu	Gln	Asn	Gln	Thr	Pro	Gly
			180					185					190		
Ile	Tyr	Lys	Phe	Cys	Gln	Glu	His	Asp	Ile	Leu	Val	Glu	Ala	Tyr	Ser
		195					200					205			
Pro	Leu	Gly	Pro	Leu	Arg	Lys	Lys	Thr	Ala	Gln	Asp	Asp	Ser	Gln	Pro
	210					215					220				
Phe	Phe	Glu	Tyr	Val	Lys	Glu	Leu	Ser	Glu	Lys	Tyr	Gly	Lys	Ser	Glu
225					230					235					240
Ala	Gln	Ile	Ile	Leu	Arg	Trp	Val	Thr	Lys	Arg	Gly	Val	Leu	Pro	Val
				245					250					255	
Thr	Thr	Ser	Ser	Lys	Pro	Gln	Arg	Ile	Ser	Asp	Ala	Gln	Asn	Leu	Phe
			260					265					270		
Ser	Phe	Asp	Leu	Thr	Ala	Glu	Glu	Val	Asp	Lys	Ile	Thr	Glu	Leu	Gly
		275					280					285			
Leu	Glu	His	Glu	Pro	Leu	Arg	Leu	Tyr	Trp	Asn	Lys	Leu	Tyr	Gly	Lys
	290					295					300				
Tyr	Asn	Tyr	Ala	Ala	Gln	Lys	Val								
305					310										

<210> 153

<211> 942

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 153

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atgtcttttc accaacagtt ttccacgctg aacaacggca ataaaatccc ggcgattgcc 60
atcatcggca ctggtacaaa gtggtataaa agtgaagaaa ctgacgcgac cttctccaat 120
agtctggttg aacaaatcgt gtatgcgttg aaactgcggg ggattatcca catcgacgcc 180
gcggagattt atcgcaccta cccggaagtg ggtaaagcac tgtccctgac cgaaaagcct 240
cgtaacgcga tttttctgac ggataaatat tctcgcgaga ttaaaatgag tgactccoct 300
gcggacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
attcattccc cgtttgtttc gaaggaagtg aatggcttaa gcttagaaga ggcttgga 420
gatattggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggttc caatttcaca 480
gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
gagttctctc cgttcctgca aaaccaaacg ccaggcattt ataaattctg tcaggagcac 600
gatatcctgg tggaagcata ctctccgctg ggcccgtgac ggatgaaaac cgcgcaggat 660
gacagccaac cattttttga gtacgtcaaa gagttgagcg aaaaatacaa caaatccgag 720
gcccagatca tcctgcgctg ggtcactaaa cgcgggtgtg tgccagttac cacctcttca 780
aagcctcagc gcattagcga tgctcagaac ctgttttctc tcgacctgac agcgggaagag 840
gttgataaaa tcacggagct gggtctggaa catgaaccgc tgcgcctgta ctggaataaa 900
ttgtatggca aatataacta cgcgcgccag aaagtgtaat ga 942

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<210> 154
 <211> 313
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 154
 Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
 1 5 10 15
 Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Lys Trp Tyr Lys Ser Glu
 20 25 30
 Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
 35 40 45
 Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Ile Tyr
 50 55 60
 Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
 65 70 75 80
 Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
 85 90 95
 Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
 100 105 110
 Thr Asp Tyr Val Asp Leu Tyr Leu Ile His Ser Pro Phe Val Ser Lys
 115 120 125
 Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
 130 135 140
 Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Thr
 145 150 155 160
 Val Glu Asp Leu Gln Arg Ile Leu Lys Val Ala Glu Val Lys Pro Gln
 165 170 175
 Val Asn Gln Ile Glu Phe Ser Pro Phe Leu Gln Asn Gln Thr Pro Gly
 180 185 190
 Ile Tyr Lys Phe Cys Gln Glu His Asp Ile Leu Val Glu Ala Tyr Ser
 195 200 205
 Pro Leu Gly Pro Leu Arg Met Lys Thr Ala Gln Asp Asp Ser Gln Pro
 210 215 220
 Phe Phe Glu Tyr Val Lys Glu Leu Ser Glu Lys Tyr Asn Lys Ser Glu
 225 230 235 240
 Ala Gln Ile Ile Leu Arg Trp Val Thr Lys Arg Gly Val Leu Pro Val
 245 250 255
 Thr Thr Ser Ser Lys Pro Gln Arg Ile Ser Asp Ala Gln Asn Leu Phe
 260 265 270
 Ser Phe Asp Leu Thr Ala Glu Glu Val Asp Lys Ile Thr Glu Leu Gly
 275 280 285
 Leu Glu His Glu Pro Leu Arg Leu Tyr Trp Asn Lys Leu Tyr Gly Lys
 290 295 300
 Tyr Asn Tyr Ala Ala Gln Lys Val
 305 310

<210> 155
 <211> 942
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 155
 atgtcttttc accaacagtt ttacacgctg aacaacggca ataaaatccc ggcgattgcc 60

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atcatcgga ctggtacagc ctggtataaa agtgaagaaa ctgacgcgac cttctccaat 120
agtctggttg aacaaatcgt gtatgcgttg aaactgcogg ggattatcca catcgacgcc 180
gcggagattt atcgcaccta cccggaagtg ggtaaagcac tgtccctgac cgaaaagcct 240
cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactccccct 300
gcggacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
ttacattccc cgtttggttc gaaggaagtg aatggcttaa gottagaaga ggcttggaag 420
gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggttc caatttcaca 480
gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
gagttctctc cgttcctgca aaaccaaaca ccaggcattt ataaattctg tcaggagctc 600
gatatecttg tggaagcata ttctccgtg ggcgcgctgc gggagaaaac cgcgcaggat 660
gacagccaac ctttttttga gtacgtcaaa gaattgagcg aaaaatacaa caaatccgag 720
gcccagatca tctcgcgctg ggtcactaaa cgcggtgtgc tgccagttac caoctttca 780
aagcctcagc gcattagcga tgctcagaac ctgttttctc tcgacctgac agcgggaagag 840
gttgataaaa tcacggagct gggctcggaa catgaaccgc tgcgcctgta ctggaataaa 900
ttgtatggca aatataacta cgccgccag aaagtgtaat ga 942

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<210> 156

<211> 313

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 156

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Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
1          5          10          15
Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Ala Trp Tyr Lys Ser Glu
20         25         30
Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
35         40         45
Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Ile Tyr
50         55         60
Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
65         70         75         80
Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
85         90         95
Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
100        105        110
Thr Asp Tyr Val Asp Leu Tyr Leu Leu His Ser Pro Phe Val Ser Lys
115        120        125
Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
130        135        140
Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Thr
145        150        155        160
Val Glu Asp Leu Gln Arg Ile Leu Lys Val Ala Glu Val Lys Pro Gln
165        170        175
Val Asn Gln Ile Glu Phe Ser Pro Phe Leu Gln Asn Gln Thr Pro Gly
180        185        190
Ile Tyr Lys Phe Cys Gln Glu Leu Asp Ile Leu Val Glu Ala Tyr Ser
195        200        205
Pro Leu Gly Pro Leu Arg Glu Lys Thr Ala Gln Asp Asp Ser Gln Pro
210        215        220
Phe Phe Glu Tyr Val Lys Glu Leu Ser Glu Lys Tyr Asn Lys Ser Glu
225        230        235        240
Ala Gln Ile Ile Leu Arg Trp Val Thr Lys Arg Gly Val Leu Pro Val
245        250        255
Thr Thr Ser Ser Lys Pro Gln Arg Ile Ser Asp Ala Gln Asn Leu Phe
260        265        270
Ser Phe Asp Leu Thr Ala Glu Glu Val Asp Lys Ile Thr Glu Leu Gly

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	275		280		285
Leu	Glu His Glu Pro Leu Arg Leu Tyr Trp Asn Lys	Leu Tyr Gly Lys			
	290		295		300
Tyr Asn Tyr Ala Ala Gln Lys Val					
305		310			

<210> 157
 <211> 942
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 157
 atgtcttttc accaacagtt ttccacgctg aacaacggca ataaaatccc ggcgattgcc 60
 atcatcggca ctggtacagc ctggtataaa agtgaagaaa ctgacgcgac cttctccaat 120
 agtctggttg aacaaatcgt gtatgcgttg aaactgcggg ggattatcca catcgacgcc 180
 gcggagattt atcgcaccta cccggaagtg ggtaaagcac tgtccctgac cgaaaagcct 240
 cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactccoct 300
 gcggacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
 ttacattccc cgtttggttc gaaggaagtg aatggcttaa gcttagaaga ggcttgga 420
 gatattggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggttc caatttcaca 480
 gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
 gagttctctc cgttcctgca aaaccaaaca ccaggcattt ataaattctg tcaggagcac 600
 gatattcctg tggaagcata ttctccgtg ggcgcgctgc ggaagaaaac cgcgcaggat 660
 gacagccaac cattttttga gtacgtcaaa gaattgagcg aaaaatacaa caaatccgag 720
 gccagatca tcttgcgctg ggtcactaaa cgcggtgtgc tgccagttac cacctcttca 780
 aagcctcagc gcattagcga tgcacagaac ctgttttctc tcgacctgac agcgggaagag 840
 gttgataaaa tcacggagct gggtctggaa catgaacgcg tcgcgctgta ctggaataaa 900
 ttgtatggca aatataacta cgccgccag aaagaataat ga 942

<210> 158
 <211> 313
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 158
 Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
 1 5 10 15
 Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Ala Trp Tyr Lys Ser Glu
 20 25 30
 Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
 35 40 45
 Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Ile Tyr
 50 55 60
 Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
 65 70 75 80
 Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
 85 90 95
 Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
 100 105 110
 Thr Asp Tyr Val Asp Leu Tyr Leu Leu His Ser Pro Phe Val Ser Lys
 115 120 125
 Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
 130 135 140

Leu	Tyr	Lys	Ser	Gly	Lys	Ala	Lys	Asn	Ile	Gly	Val	Ser	Asn	Phe	Thr
145					150					155					160
Val	Glu	Asp	Leu	Gln	Arg	Ile	Leu	Lys	Val	Ala	Glu	Val	Lys	Pro	Gln
			165						170					175	
Val	Asn	Gln	Ile	Glu	Phe	Ser	Pro	Phe	Leu	Gln	Asn	Gln	Thr	Pro	Gly
			180					185					190		
Ile	Tyr	Lys	Phe	Cys	Gln	Glu	His	Asp	Ile	Leu	Val	Glu	Ala	Tyr	Ser
	195						200					205			
Pro	Leu	Gly	Pro	Leu	Arg	Lys	Lys	Thr	Ala	Gln	Asp	Asp	Ser	Gln	Pro
	210					215					220				
Phe	Phe	Glu	Tyr	Val	Lys	Glu	Leu	Ser	Glu	Lys	Tyr	Asn	Lys	Ser	Glu
225					230					235					240
Ala	Gln	Ile	Ile	Leu	Arg	Trp	Val	Thr	Lys	Arg	Gly	Val	Leu	Pro	Val
				245					250					255	
Thr	Thr	Ser	Ser	Lys	Pro	Gln	Arg	Ile	Ser	Asp	Ala	Gln	Asn	Leu	Phe
			260				265						270		
Ser	Phe	Asp	Leu	Thr	Ala	Glu	Glu	Val	Asp	Lys	Ile	Thr	Glu	Leu	Gly
		275					280					285			
Leu	Glu	His	Glu	Pro	Leu	Arg	Leu	Tyr	Trp	Asn	Lys	Leu	Tyr	Gly	Lys
	290					295					300				
Tyr	Asn	Tyr	Ala	Ala	Gln	Lys	Glu								
305					310										

<210> 159

<211> 942

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 159

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atgtcttttc accaacagtt ttccacgctg aacaacggca ataaaatccc ggcgattgcc 60
atcatcggca ctggtacaaa atggtataaa agtgaagaaa ctgacgogac cttctccaat 120
agtctggttg agcaaatcgt gtatgcgttg aaactgocgg ggattatoca cgtcgacgcc 180
gcggagattt atcgcaccta cccggaagtg ggtaaagcac tgtccctgac cgaagagcct 240
cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactccoct 300
gcggacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
ttacattccc cgtttgtttc gaaggaagtg aatggcttaa gcttagaaga ggcttggaag 420
gatattggagc agttatacaa aagtggtaaa gctaaaaaca tcggggtttc caatttcaca 480
gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
gagttctctc cgttcctgca aaaccaaaca ccaggcattt ataaattctg tcaggagcac 600
gatatcctgg tggaagcata ttctccgctg ggcccgctgc ggaagaaaac cgcgcaggat 660
gacagccaac cattttttga gtacgtcaaa gaattgagcg aaaaatacaa caaatccgag 720
gcccagatca tcctgcgctg ggtaactaaa cgcgggtgtg tgccagttac caactottca 780
aagcctcagc gcgttagcga tgctcagaac ctgttttctt tcgacctgac agcgggaagag 840
gttgataaaa tcacggagct gggtctggaa catgaaccgc tgcgcctgta ctggaataaa 900
ttgtatggca aatataacta cgccgccagc aaagtgtaat ga 942

```

<210> 160

<211> 313

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 160

Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile

1				5					10					15					
Pro	Ala	Ile	Ala	Ile	Ile	Gly	Thr	Gly	Thr	Lys	Trp	Tyr	Lys	Ser	Glu				
			20					25					30						
Glu	Thr	Asp	Ala	Thr	Phe	Ser	Asn	Ser	Leu	Val	Glu	Gln	Ile	Val	Tyr				
		35					40					45							
Ala	Leu	Lys	Leu	Pro	Gly	Ile	Ile	His	Val	Asp	Ala	Ala	Glu	Ile	Tyr				
	50				55					60									
Arg	Thr	Tyr	Pro	Glu	Val	Gly	Lys	Ala	Leu	Ser	Leu	Thr	Glu	Lys	Pro				
65				70					75					80					
Arg	Asn	Ala	Ile	Phe	Leu	Thr	Asp	Lys	Tyr	Ser	Pro	Gln	Ile	Lys	Met				
			85					90					95						
Ser	Asp	Ser	Pro	Ala	Asp	Gly	Leu	Asp	Leu	Ala	Leu	Lys	Lys	Met	Gly				
			100					105					110						
Thr	Asp	Tyr	Val	Asp	Leu	Tyr	Leu	Leu	His	Ser	Pro	Phe	Val	Ser	Lys				
	115						120					125							
Glu	Val	Asn	Gly	Leu	Ser	Leu	Glu	Glu	Ala	Trp	Lys	Asp	Met	Glu	Gln				
	130					135					140								
Leu	Tyr	Lys	Ser	Gly	Lys	Ala	Lys	Asn	Ile	Gly	Val	Ser	Asn	Phe	Thr				
145				150				155						160					
Val	Glu	Asp	Leu	Gln	Arg	Ile	Leu	Lys	Val	Ala	Glu	Val	Lys	Pro	Gln				
			165					170					175						
Val	Asn	Gln	Ile	Glu	Phe	Ser	Pro	Phe	Leu	Gln	Asn	Gln	Thr	Pro	Gly				
	180							185					190						
Ile	Tyr	Lys	Phe	Cys	Gln	Glu	His	Asp	Ile	Leu	Val	Glu	Ala	Tyr	Ser				
	195						200					205							
Pro	Leu	Gly	Pro	Leu	Arg	Lys	Lys	Thr	Ala	Gln	Asp	Asp	Ser	Gln	Pro				
	210					215					220								
Phe	Phe	Glu	Tyr	Val	Lys	Glu	Leu	Ser	Glu	Lys	Tyr	Asn	Lys	Ser	Glu				
225				230					235					240					
Ala	Gln	Ile	Ile	Leu	Arg	Trp	Val	Thr	Lys	Arg	Gly	Val	Leu	Pro	Val				
			245					250					255						
Thr	Thr	Ser	Ser	Lys	Pro	Gln	Arg	Val	Ser	Asp	Ala	Gln	Asn	Leu	Phe				
			260					265					270						
Ser	Phe	Asp	Leu	Thr	Ala	Glu	Glu	Val	Asp	Lys	Ile	Thr	Glu	Leu	Gly				
	275						280					285							
Leu	Glu	His	Glu	Pro	Leu	Arg	Leu	Tyr	Trp	Asn	Lys	Leu	Tyr	Gly	Lys				
	290					295					300								
Tyr	Asn	Tyr	Ala	Ala	Gln	Lys	Val												
305					310														

<210> 161

<211> 942

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 161

```

atgtcttttc accaacagtt tttcacgctg aacaacggca ataaaatccc ggcgattgcc 60
atcatcggca ctggtacagc ctggtataaa agtgaagaaa ctgacgogac cttctccaat 120
agtctggttg aacaaatcgt gcatgcgttg aaactgccgg ggattatoca catcgacgcc 180
gcggagattt atcgcaccta cccggaagtg ggtaaagcac tgtccctgac cgaaaagcct 240
cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactcccct 300
gcggacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
ttacattccc cgtttgtttc gaaggaagtg aatggcttaa gcttagaaga ggcttgga 420
gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcggggtttc caatttcaca 480
gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
gagttctctc cgttcctgca aaaccaaaca ccaggcattt ataaattctg tcaggagcac 600
gatatcctgg tggaagcata ttctccgctg ggcccgctgc ggaagaaaac cgcgcaggat 660

```


<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 163

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atgtcttttc accaacagtt tttcacgctg aacaacggca ataaaatccc ggcgattgcc 60
atcatcggca ctggtacaaa atggtataaa aatgaagaaa ctgacgcgac cttctccaat 120
agtctgggtg aacaaatcgt gtatgcgttg aaactgccgg ggattatcca catcgacgcc 180
gcggagattt atcgcaccta cccggaagtg ggtaaagcac tgtccctgac cgaaaagcct 240
cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgaotcccct 300
gcggacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
ttacattccc cgtttgtttc gaaggaagtg aatggcttaa gcttagaaga ggcttggaag 420
gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggttc caatttcaca 480
gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
gagttctctc cgttcctgca aaaccaaaca ccagacattt ataaattctg tcaggagcac 600
gatatcctgg tggaagcata ttctccgctg ggcccgcctg ggaagaaaac cgcgcaggat 660
gacagccaac ctttttttga gtacgtcaaa gaattgagcg aaaaatacaa caaatccgag 720
gcccagatca tcctgcgctg ggtcactgaa cgcggtgtgc tgccagttac cacctcttca 780
aagcctcagc gcattagcga tgctcagaac ctgttttctt tcgacctgac agcgggaagag 840
gttgataaaa tcacggagct gggctctggaa catgaaccgc tcgcgctgta ctggaataaa 900
ttgtatggca aatataacta cgccgccag aaagtgtaat ga 942
```

<210> 164

<211> 313

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 164

```
Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
1          5          10          15
Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Lys Trp Tyr Lys Asn Glu
20          25          30
Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
35          40          45
Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Ile Tyr
50          55          60
Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
65          70          75          80
Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
85          90          95
Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
100         105         110
Thr Asp Tyr Val Asp Leu Tyr Leu Leu His Ser Pro Phe Val Ser Lys
115         120         125
Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
130         135         140
Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Thr
145         150         155         160
Val Glu Asp Leu Gln Arg Ile Leu Lys Val Ala Glu Val Lys Pro Gln
165         170         175
Val Asn Gln Ile Glu Phe Ser Pro Phe Leu Gln Asn Gln Thr Pro Asp
180         185         190
Ile Tyr Lys Phe Cys Gln Glu His Asp Ile Leu Val Glu Ala Tyr Ser
195         200         205
Pro Leu Gly Pro Leu Arg Lys Lys Thr Ala Gln Asp Asp Ser Gln Pro
210         215         220
```


Phe	Phe	Glu	Tyr	Val	Lys	Glu	Leu	Ser	Glu	Lys	Tyr	Asn	Lys	Ser	Glu
225					230					235					240
Ala	Gln	Ile	Ile	Leu	Arg	Trp	Val	Thr	Glu	Arg	Gly	Val	Leu	Pro	Val
				245						250					255
Thr	Thr	Ser	Ser	Lys	Pro	Gln	Arg	Ile	Ser	Asp	Ala	Gln	Asn	Leu	Phe
				260						265					270
Ser	Phe	Asp	Leu	Thr	Ala	Glu	Glu	Val	Asp	Lys	Ile	Thr	Glu	Leu	Gly
		275					280						285		
Leu	Glu	His	Glu	Pro	Leu	Arg	Leu	Tyr	Trp	Asn	Lys	Leu	Tyr	Gly	Lys
	290					295					300				
Tyr	Asn	Tyr	Ala	Ala	Gln	Lys	Val								
305					310										

<210> 165
 <211> 942
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 165

atgtcttttc	accaacagtt	tttcacgctg	aacaacggca	ataaaatccc	ggcgattgcc	60
atcatcggca	ctggtacaaa	atggtataaa	aatgaagaaa	ctgacgcgac	cttctccaat	120
agtctggttg	aacaaatcgt	gtatgcgttg	aaactgccgg	ggattatcca	catcgacgcc	180
gcggagggtt	atcgcaccta	cccggaagtg	ggtaaagcac	tgtccctgac	cgaaaagcct	240
cgtaacgcga	ttttctgac	ggataaatat	tctccgcaga	ttaaaatgag	tgactcccct	300
gcggacggtc	tggatttagc	attgaagaaa	atgggtacag	attatgttga	tttatatctg	360
attcattccc	cgcttgtttc	gaaggaagtg	aatggcttaa	gcttagaaga	ggcttgga	420
gatatggagc	agttatacaa	aagtggtaaa	gctaaaaaca	tcgggggttc	caatttcaca	480
gtggaagacc	tgcaacgtat	cctgaaagtc	gctgaagtta	aacctcaggt	caaccagatt	540
gagttctctc	cgttcctgca	aaaccaaaca	ccaggcattt	ataaattctg	tcaggagcac	600
gatatcctgg	tggaagcata	ttctccgctg	ggcccgtctg	ggaagaaaac	cgcgaggat	660
gacagccaac	cattttttga	gtacgtcaaa	gaattgagcg	aaaaatacaa	caaatccgag	720
gcccagatca	tcctgcgctg	ggtcactaaa	cgcggtgtgc	tgccagttac	cacctcttca	780
aagcctcagc	gcattagcga	tgctcagaac	ctgttttctt	tcgacctgac	agcggaagag	840
gttgataaaa	tcacggagct	gggtctggaa	catgaaccgc	tgcgctgtga	ctggaataaa	900
ttgtatggca	aatataacta	cgccgcccag	aaagtgtaat	ga		942

<210> 166
 <211> 313
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 166

Met	Ser	Phe	His	Gln	Gln	Phe	Phe	Thr	Leu	Asn	Asn	Gly	Asn	Lys	Ile
1			5						10					15	
Pro	Ala	Ile	Ala	Ile	Ile	Gly	Thr	Gly	Thr	Lys	Trp	Tyr	Lys	Asn	Glu
			20						25					30	
Glu	Thr	Asp	Ala	Thr	Phe	Ser	Asn	Ser	Leu	Val	Glu	Gln	Ile	Val	Tyr
		35					40					45			
Ala	Leu	Lys	Leu	Pro	Gly	Ile	Ile	His	Ile	Asp	Ala	Ala	Glu	Val	Tyr
	50					55				60					
Arg	Thr	Tyr	Pro	Glu	Val	Gly	Lys	Ala	Leu	Ser	Leu	Thr	Glu	Lys	Pro
65				70					75					80	
Arg	Asn	Ala	Ile	Phe	Leu	Thr	Asp	Lys	Tyr	Ser	Pro	Gln	Ile	Lys	Met

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 168

```
Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
1      5      10      15
Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Lys Trp Tyr Lys Asn Glu
20     25     30
Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
35     40     45
Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Ile Tyr
50     55     60
Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
65     70     75     80
Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
85     90     95
Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
100    105    110
Thr Asp Tyr Val Asp Leu Tyr Leu Leu His Ser Pro Phe Val Ser Lys
115    120    125
Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
130    135    140
Leu Tyr Lys Ser Gly Lys Ala Arg Asn Ile Gly Val Ser Asn Phe Thr
145    150    155    160
Val Glu Asp Leu Gln Arg Ile Leu Lys Val Ala Glu Val Lys Pro Gln
165    170    175
Val Asn Gln Ile Glu Phe Ser Pro Phe Leu Gln Asn Gln Thr Pro Gly
180    185    190
Ile Tyr Lys Phe Cys Gln Glu His Asp Ile Leu Val Glu Ala Tyr Ser
195    200    205
Pro Leu Gly Pro Leu Arg Lys Lys Thr Ala Gln Asp Asp Ser Gln Pro
210    215    220
Phe Phe Glu Tyr Val Lys Glu Leu Ser Glu Lys Tyr Asn Lys Ser Glu
225    230    235    240
Ala Gln Ile Ile Leu Arg Trp Val Thr Lys Arg Gly Val Leu Pro Val
245    250    255
Thr Thr Ser Ser Lys Pro Gln Arg Ile Ser Asp Ala Gln Asn Leu Phe
260    265    270
Ser Phe Asp Leu Thr Ala Glu Glu Val Asp Lys Ile Thr Glu Leu Gly
275    280    285
Leu Glu His Glu Pro Leu Arg Leu Tyr Trp Asn Lys Leu Tyr Gly Lys
290    295    300
Tyr Asn Tyr Ala Ala Gln Lys Val
305    310
```

<210> 169

<211> 942

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 169

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atgtctttt accaacagtt tttcacgctg aacaacggca ataaaatccc ggcgattgcc 60
atcatcggca ctggtacagc ctggtataaa agtgaagaaa ctgacgcgac cttctccaat 120
agtctggttg aacaaatcgt gtatgcgttg aaactgccgg ggattatcca catcgacgcc 180
gcggagattt atcgcaccta cccggaagtg ggtaaagcac tgtccctgac cgaaaagcct 240
```

```

cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactcccct 300
gcgagacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
ttacattccc cgtttgtttc gaaggaagtg aatggcttaa gcttagaaga ggcttgga 420
gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggtttc caatttcaca 480
gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
gagttctctc cgttcctgca aaaccaaaca ccaggcattt ataaattctg tcaggagcac 600
gatatcctgg tggaagcata ttctccgctg ggcccgcctgc ggaagaaaac cgcgcaggat 660
gacagccaac cattttttga gtacgtcaaa gaattgagcg aaaaatacaa caaatccgag 720
goccagatca tctcgcgctg ggtcactaaa cgcggtgtgc tgccagttac cacctcttca 780
aagcctcagc gcattagcga tgctcagaac ctgttttctc tcgacctgac agcgggaagag 840
gttgataaaa tcacggagct gggctcggaa catgaaccgc tgcgcctgta ctggaataaa 900
ttgtatggca aatataacta cgcgcgccag aaagtgtaat ga 942

```

<210> 170

<211> 313

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 170

```

Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
1          5          10          15
Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Ala Trp Tyr Lys Ser Glu
20        25        30
Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
35        40        45
Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Ile Tyr
50        55        60
Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
65        70        75        80
Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
85        90        95
Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
100       105       110
Thr Asp Tyr Val Asp Leu Tyr Leu Leu His Ser Pro Phe Val Ser Lys
115       120       125
Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
130       135       140
Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Thr
145       150       155       160
Val Glu Asp Leu Gln Arg Ile Leu Lys Val Ala Glu Val Lys Pro Gln
165       170       175
Val Asn Gln Ile Glu Phe Ser Pro Phe Leu Gln Asn Gln Thr Pro Gly
180       185       190
Ile Tyr Lys Phe Cys Gln Glu His Asp Ile Leu Val Glu Ala Tyr Ser
195       200       205
Pro Leu Gly Pro Leu Arg Lys Lys Thr Ala Gln Asp Asp Ser Gln Pro
210       215       220
Phe Phe Glu Tyr Val Lys Glu Leu Ser Glu Lys Tyr Asn Lys Ser Glu
225       230       235       240
Ala Gln Ile Ile Leu Arg Trp Val Thr Lys Arg Gly Val Leu Pro Val
245       250       255
Thr Thr Ser Ser Lys Pro Gln Arg Ile Ser Asp Ala Gln Asn Leu Phe
260       265       270
Ser Phe Asp Leu Thr Ala Glu Glu Val Asp Lys Ile Thr Glu Leu Gly
275       280       285
Leu Glu His Glu Pro Leu Arg Leu Tyr Trp Asn Lys Leu Tyr Gly Lys
290       295       300

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Tyr Asn Tyr Ala Ala Gln Lys Val
305 310

<210> 171
<211> 942
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 171
atgtcttttt accaacagtt tttcacgctg aacaacggca ataaaatccc ggcgattgcc 60
atcatcgcca ctggtacaaa atggtataaa aatgaagaaa ctgacgcgac cttctccaat 120
agtctggttg aacaaatcgt gtatgcgttg aaactgccgg ggattatcca catcgacgcc 180
gcggagattt atcgcaccta cccggaagtg ggtaaagcac tgtccctgac cgaaaagcct 240
cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactccoct 300
gcggacagtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
ttacattccc cgtttgtttc gaaggaagtg aatggcttaa gcttagaaga ggcttggaaa 420
gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggtttc caatttcaca 480
gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
gagttctctc cgttcctgca aaaccaaaca ccaggcattt ataaattctg tcaggagcac 600
gatatcctgg tggaagcata ttctccgctg ggcccgcctgc ggaagaaaac cgcgcaggat 660
gacagccaac cattttttga gtacgtcaaa gaattgagcg aaaaatacaa caaatccgag 720
gcccagatca tcctgcgctg ggtcactaaa cgcggtgtgc tgctgtttac cacctcttca 780
aagcctcagc gcattagcga tgctcagaac ctgttttctt tcgacctgac agcgggaagag 840
gttgataaaa tcacggagct gggctctggaa catgaaccgc tcgcctgtga ctggaataaa 900
ttgtatggca aatataacta cgcgcgccag aaagtgtaat ga 942

<210> 172
<211> 313
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 172
Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
1 5 10 15
Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Lys Trp Tyr Lys Asn Glu
20 25 30
Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
35 40 45
Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Ile Tyr
50 55 60
Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
65 70 75 80
Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
85 90 95
Ser Asp Ser Pro Ala Asp Ser Leu Asp Leu Ala Leu Lys Lys Met Gly
100 105 110
Thr Asp Tyr Val Asp Leu Tyr Leu Leu His Ser Pro Phe Val Ser Lys
115 120 125
Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
130 135 140
Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Thr
145 150 155 160
Val Glu Asp Leu Gln Arg Ile Leu Lys Val Ala Glu Val Lys Pro Gln

Glu	Thr	Asp	Ala	Thr	Phe	Ser	Asn	Ser	Leu	Val	Glu	Gln	Ile	Val	Tyr
	35						40					45			
Ala	Leu	Lys	Leu	Pro	Gly	Ile	Ile	His	Ile	Asp	Thr	Ala	Glu	Ile	Tyr
	50					55					60				
Arg	Thr	Tyr	Pro	Glu	Val	Gly	Lys	Ala	Leu	Ser	Leu	Thr	Glu	Lys	Pro
	65				70					75					80
Arg	Asn	Ala	Val	Phe	Leu	Thr	Asp	Lys	Tyr	Ser	Pro	Gln	Ile	Lys	Met
			85						90					95	
Ser	Asp	Ser	Pro	Ala	Asp	Gly	Leu	Asp	Leu	Ala	Leu	Lys	Lys	Met	Gly
			100					105					110		
Thr	Asp	Tyr	Val	Asp	Leu	Tyr	Leu	Leu	His	Ser	Pro	Phe	Val	Ser	Lys
		115					120					125			
Glu	Val	Asn	Gly	Leu	Ser	Leu	Glu	Glu	Ala	Trp	Lys	Asp	Met	Glu	Gln
	130					135					140				
Leu	Tyr	Lys	Ser	Gly	Lys	Ala	Lys	Asn	Ile	Gly	Val	Ser	Asn	Phe	Thr
	145				150					155					160
Val	Glu	Asp	Leu	Gln	Arg	Ile	Leu	Lys	Val	Ala	Glu	Val	Lys	Pro	Gln
				165				170						175	
Val	Asn	Gln	Ile	Glu	Phe	Ser	Pro	Phe	Leu	Gln	Asn	Gln	Thr	Pro	Gly
			180					185					190		
Ile	Tyr	Lys	Phe	Cys	Gln	Glu	His	Asp	Ile	Leu	Val	Glu	Ala	Tyr	Ser
	195						200					205			
Pro	Leu	Gly	Pro	Leu	Arg	Lys	Lys	Thr	Ala	Gln	Asp	Asp	Ser	Gln	Pro
	210					215					220				
Phe	Phe	Glu	Tyr	Val	Lys	Glu	Leu	Ser	Glu	Lys	Tyr	Asn	Lys	Ser	Glu
	225				230					235					240
Ala	Gln	Ile	Ile	Leu	Arg	Trp	Val	Thr	Lys	Arg	Gly	Val	Leu	Pro	Val
				245					250					255	
Thr	Thr	Ser	Ser	Lys	Pro	Gln	Arg	Ile	Ser	Asp	Ala	Gln	Asn	Leu	Phe
			260					265					270		
Ser	Phe	Asp	Leu	Thr	Ala	Glu	Glu	Val	Asp	Lys	Ile	Thr	Glu	Leu	Gly
		275					280					285			
Leu	Glu	His	Glu	Pro	Leu	Arg	Leu	Tyr	Trp	Asn	Lys	Leu	Tyr	Gly	Lys
	290					295					300				
Tyr	Asn	Tyr	Ala	Ala	Gln	Lys	Val								
305					310										

<210> 175

<211> 942

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 175

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atgtcttttc accaacagtt tttcacgctg aacaacggca ataaaatccc ggcgattgcc 60
atcatcggca ctggtacaaa atggtataaa aatgaagaaa ctgacgcgac cttctccaat 120
agtctggttg aacaaatcgt gtatgcgttg aaactgccgg ggattatcca catcgacgcc 180
gcggagattt atcgcaccta cccggaagtg ggtaaagcac tgtccctgac cgaaaagcct 240
cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactccoct 300
gcggacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
ttacattccc cgtttgtttc gaaggaagtg aatggcttaa gcttagaaga ggcttggaag 420
gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggttc caatttcaca 480
gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
gagttctctc cgttcctgca aaaccaaaac ccaggcattt ataaattctg tcaggagcac 600
gatatcctgg tggaagcata ttctccgctg ggcccgtgct ggaagaaaac cgcgcaggat 660
gacagccaac cattttttga gtacgtcaaa gaattgagcg aaaaataccg caaatccgag 720
gccagatca tcttgcgctg ggtcactaaa cgcgggtgtg tgccagttac cacctcttca 780
aagcctcagc gcattagcga tgctcagaac ctgttttctc tcgacctgac agcgggaagag 840

```

gttgataaaa tcacggagct gggctctggaa catgaaccgc tgcgcctgta ctggaataaa 900
 ttgtatggca aatataactc tgccgcccag aaagtgtaat ga 942

<210> 176
 <211> 313
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 176
 Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
 1 5 10 15
 Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Lys Trp Tyr Lys Asn Glu
 20 25 30
 Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
 35 40 45
 Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Ile Tyr
 50 55 60
 Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
 65 70 75 80
 Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
 85 90 95
 Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
 100 105 110
 Thr Asp Tyr Val Asp Leu Tyr Leu Leu His Ser Pro Phe Val Ser Lys
 115 120 125
 Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
 130 135 140
 Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Thr
 145 150 155 160
 Val Glu Asp Leu Gln Arg Ile Leu Lys Val Ala Glu Val Lys Pro Gln
 165 170 175
 Val Asn Gln Ile Glu Phe Ser Pro Phe Leu Gln Asn Gln Thr Pro Gly
 180 185 190
 Ile Tyr Lys Phe Cys Gln Glu His Asp Ile Leu Val Glu Ala Tyr Ser
 195 200 205
 Pro Leu Gly Pro Leu Arg Lys Lys Thr Ala Gln Asp Asp Ser Gln Pro
 210 215 220
 Phe Phe Glu Tyr Val Lys Glu Leu Ser Glu Lys Tyr Arg Lys Ser Glu
 225 230 235 240
 Ala Gln Ile Ile Leu Arg Trp Val Thr Lys Arg Gly Val Leu Pro Val
 245 250 255
 Thr Thr Ser Ser Lys Pro Gln Arg Ile Ser Asp Ala Gln Asn Leu Phe
 260 265 270
 Ser Phe Asp Leu Thr Ala Glu Glu Val Asp Lys Ile Thr Glu Leu Gly
 275 280 285
 Leu Glu His Glu Pro Leu Arg Leu Tyr Trp Asn Lys Leu Tyr Gly Lys
 290 295 300
 Tyr Asn Ser Ala Ala Gln Lys Val
 305 310

<210> 177
 <211> 942
 <212> DNA
 <213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 177

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atgtcttttc accaacagtt ttccacgctg aacaacggca ataaaatccc ggcgattgcc 60
atcatcggca ctggtacagc ctggtataaa agtgaagaaa ctgacgcgac cttctccaat 120
agtctggttg aacaaatcgt gtatgcgttg aaactgccgg ggattatcca catcgacgcc 180
gcggagattt atcgcaccta cccggaagtg ggtaaagcac tgtccctgac cgaaaagcct 240
cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactcccct 300
gcggacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
ttacattccc cgcttgtttc gaaggaagtg aatggcttaa gcttagaaga ggcttggaag 420
gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggttc caatttcaca 480
gtggaagacc tgcaacgtat cctgagagtc gctgaagtta aacctcaggt caaccagatt 540
gagttctctc cgttcctgca aaaccaaaca ccaggcattt ataaattctg tcaggagcac 600
gatatcctgg tggaaagcata ttctccgctg ggcccgtctg ggaagaaaac cgcgcaggat 660
gacagccaac cattttttga gtacgtcaaa gaattgagcg aaaaatacaa caaatccgag 720
gccagatca tctgcgctg ggctactaaa cgcggtgtgc tgccagttac cacctcttca 780
aagcctcagc gcattagcga tgctcagaac ctgttttcct tcgacctgac agcgggaagag 840
gttgataaaa tcacggagct gggtctggaa catgaaccgc tcgcctgta ctggaataaa 900
ttgtatggca aatataacta cgccgccag aaagtgtaat ga 942
```

<210> 178

<211> 313

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 178

```
Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
1          5          10          15
Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Ala Trp Tyr Lys Ser Glu
20          25          30
Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
35          40          45
Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Ile Tyr
50          55          60
Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
65          70          75          80
Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
85          90          95
Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
100          105          110
Thr Asp Tyr Val Asp Leu Tyr Leu Leu His Ser Pro Leu Val Ser Lys
115          120          125
Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
130          135          140
Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Thr
145          150          155          160
Val Glu Asp Leu Gln Arg Ile Leu Arg Val Ala Glu Val Lys Pro Gln
165          170          175
Val Asn Gln Ile Glu Phe Ser Pro Phe Leu Gln Asn Gln Thr Pro Gly
180          185          190
Ile Tyr Lys Phe Cys Gln Glu His Asp Ile Leu Val Glu Ala Tyr Ser
195          200          205
Pro Leu Gly Pro Leu Arg Lys Lys Thr Ala Gln Asp Asp Ser Gln Pro
210          215          220
Phe Phe Glu Tyr Val Lys Glu Leu Ser Glu Lys Tyr Asn Lys Ser Glu
225          230          235          240
Ala Gln Ile Ile Leu Arg Trp Val Thr Lys Arg Gly Val Leu Pro Val
```

				245					250					255					
Thr	Thr	Ser	Ser	Lys	Pro	Gln	Arg	Ile	Ser	Asp	Ala	Gln	Asn	Leu	Phe				
			260					265					270						
Ser	Phe	Asp	Leu	Thr	Ala	Glu	Glu	Val	Asp	Lys	Ile	Thr	Glu	Leu	Gly				
		275					280					285							
Leu	Glu	His	Glu	Pro	Leu	Arg	Leu	Tyr	Trp	Asn	Lys	Leu	Tyr	Gly	Lys				
	290					295					300								
Tyr	Asn	Tyr	Ala	Ala	Gln	Lys	Val												
305					310														

<210> 179

<211> 942

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 179

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atgtcttttc accaacagtt tttcacgctg aacaacggca ataaaatccc ggcgattgcc 60
atcatcgcca ctggtacaaa atggtataaa aatgaagaaa ctgacgcgac cttctccaat 120
agtctggttg aacaaatcgt gtatgcgttg aaactgccgg ggattatcca catogaagcc 180
gcggagattt atcgcaccta cccggaagtg ggtaaagcac tgccctgac cgaaaagcct 240
cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactccoct 300
gcggacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
ttacattccc cgtttgtttc gaaggaagtg aatggcttaa gcttagaaga ggcttggaag 420
gatatggagc gggtatacaa aagtggtaaa gctaaaaaca tcggggtttc caatttcaca 480
gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
gagttctctc cgttcctgca aaaccaaaca ccaggcattt ataaattctg tcaggagcac 600
gatatcctgg tggaagcata ttctccgctg ggcccgtctg ggaagaaaac cgcgcaggat 660
gacagccaac cattttttga gtacgtcaaa gaattgagcg aaaaatacaa caaatccogag 720
gccagatca tcttgccgtg ggtcactaaa cgcggtgtgc tgccagttac cacctottca 780
aagcctcagc gcattagcga tgcacagaac ctgttttctt tcgacctgac agcgggaagag 840
gttgataaaa tcaoggagct gggtctggaa catgaaccgc tcgcctgtga ctggaataaa 900
ttgtatggca aatataacta cgccgccagc aaagtgtaat ga 942

```

<210> 180

<211> 313

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 180

Met	Ser	Phe	His	Gln	Gln	Phe	Phe	Thr	Leu	Asn	Asn	Gly	Asn	Lys	Ile				
1			5					10					15						
Pro	Ala	Ile	Ala	Ile	Ile	Gly	Thr	Gly	Thr	Lys	Trp	Tyr	Lys	Asn	Glu				
		20					25					30							
Glu	Thr	Asp	Ala	Thr	Phe	Ser	Asn	Ser	Leu	Val	Glu	Gln	Ile	Val	Tyr				
	35					40					45								
Ala	Leu	Lys	Leu	Pro	Gly	Ile	Ile	His	Ile	Asp	Ala	Ala	Glu	Ile	Tyr				
	50				55					60									
Arg	Thr	Tyr	Pro	Glu	Val	Gly	Lys	Ala	Leu	Ser	Leu	Thr	Glu	Lys	Pro				
65			70						75					80					
Arg	Asn	Ala	Ile	Phe	Leu	Thr	Asp	Lys	Tyr	Ser	Pro	Gln	Ile	Lys	Met				
		85				90							95						
Ser	Asp	Ser	Pro	Ala	Asp	Gly	Leu	Asp	Leu	Ala	Leu	Lys	Lys	Met	Gly				
		100				105						110							

Thr	Asp	Tyr	Val	Asp	Leu	Tyr	Leu	Leu	His	Ser	Pro	Phe	Val	Ser	Lys
	115						120					125			
Glu	Val	Asn	Gly	Leu	Ser	Leu	Glu	Glu	Ala	Trp	Lys	Asp	Met	Glu	Arg
	130					135					140				
Leu	Tyr	Lys	Ser	Gly	Lys	Ala	Lys	Asn	Ile	Gly	Val	Ser	Asn	Phe	Thr
145					150					155					160
Val	Glu	Asp	Leu	Gln	Arg	Ile	Leu	Lys	Val	Ala	Glu	Val	Lys	Pro	Gln
			165						170					175	
Val	Asn	Gln	Ile	Glu	Phe	Ser	Pro	Phe	Leu	Gln	Asn	Gln	Thr	Pro	Gly
			180					185						190	
Ile	Tyr	Lys	Phe	Cys	Gln	Glu	His	Asp	Ile	Leu	Val	Glu	Ala	Tyr	Ser
		195						200					205		
Pro	Leu	Gly	Pro	Leu	Arg	Lys	Lys	Thr	Ala	Gln	Asp	Asp	Ser	Gln	Pro
	210					215					220				
Phe	Phe	Glu	Tyr	Val	Lys	Glu	Leu	Ser	Glu	Lys	Tyr	Asn	Lys	Ser	Glu
225					230					235					240
Ala	Gln	Ile	Ile	Leu	Arg	Trp	Val	Thr	Lys	Arg	Gly	Val	Leu	Pro	Val
				245					250					255	
Thr	Thr	Ser	Ser	Lys	Pro	Gln	Arg	Ile	Ser	Asp	Ala	Gln	Asn	Leu	Phe
			260					265						270	
Ser	Phe	Asp	Leu	Thr	Ala	Glu	Glu	Val	Asp	Lys	Ile	Thr	Glu	Leu	Gly
		275					280						285		
Leu	Glu	His	Glu	Pro	Leu	Arg	Leu	Tyr	Trp	Asn	Lys	Leu	Tyr	Gly	Lys
	290					295					300				
Tyr	Asn	Tyr	Ala	Ala	Gln	Lys	Val								
305					310										

<210> 181
 <211> 942
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 181
 atgtcttttc accaacagtt ttccacgctg aacaacggca ataaaatccc ggcgattgcc 60
 atcatcggca ctggtacaaa atggtataaa aatgaagaaa ctgacgcgac cttctccaat 120
 agtctggttg aacaaatcgt gtatgcgttg aaactgccgg ggattatcca catcgacgcc 180
 gcggagattt atcgcaccta cccggaagtg ggtaaagcac tgtccctgac cgaaaagcct 240
 cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactccoct 300
 gcggacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
 attcattccc cgtttgtttc gaaggaagtg aatggcttaa gcttagaaga ggcttgga 420
 gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggttt caatttcaca 480
 gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
 gagttctctc cgttcctgca aaaccaaaca ccaggcattt ataaattctg tcaggagcac 600
 gatatccttg tggaagcata ttctccgctg ggcccgctgc ggaagaaaac cgcgcaggat 660
 gacagccaac ctttttttga gtacgtcaaa gaattgagcg aaaaatacga caaatccgag 720
 gccagatca tcttgccgtg ggtcactaaa cgcgggtgtg tgccagttac cacctcttca 780
 aagcctcagc gcattagcga tgctcagaac ctgttttctc tcgacctgac agcgggaagag 840
 gttgataaaa tcacggagct gggtctggaa catgaaccgc tgcgcctgta ctggaataaa 900
 ttgtatggca aatataacta cgccgccag aaagtgtaat ga 942

<210> 182
 <211> 313
 <212> PRT
 <213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 182

```
Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
1      5      10      15
Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Lys Trp Tyr Lys Asn Glu
20     25     30
Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
35     40     45
Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Ile Tyr
50     55     60
Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
65     70     75     80
Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
85     90     95
Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
100    105    110
Thr Asp Tyr Val Asp Leu Tyr Leu Ile His Ser Pro Phe Val Ser Lys
115    120    125
Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
130    135    140
Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Thr
145    150    155    160
Val Glu Asp Leu Gln Arg Ile Leu Lys Val Ala Glu Val Lys Pro Gln
165    170    175
Val Asn Gln Ile Glu Phe Ser Pro Phe Leu Gln Asn Gln Thr Pro Gly
180    185    190
Ile Tyr Lys Phe Cys Gln Glu His Asp Ile Leu Val Glu Ala Tyr Ser
195    200    205
Pro Leu Gly Pro Leu Arg Lys Lys Thr Ala Gln Asp Asp Ser Gln Pro
210    215    220
Phe Phe Glu Tyr Val Lys Glu Leu Ser Glu Lys Tyr Asp Lys Ser Glu
225    230    235    240
Ala Gln Ile Ile Leu Arg Trp Val Thr Lys Arg Gly Val Leu Pro Val
245    250    255
Thr Thr Ser Ser Lys Pro Gln Arg Ile Ser Asp Ala Gln Asn Leu Phe
260    265    270
Ser Phe Asp Leu Thr Ala Glu Glu Val Asp Lys Ile Thr Glu Leu Gly
275    280    285
Leu Glu His Glu Pro Leu Arg Leu Tyr Trp Asn Lys Leu Tyr Gly Lys
290    295    300
Tyr Asn Tyr Ala Ala Gln Lys Val
305    310
```

<210> 183

<211> 942

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 183

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atgtcttttc accaacagtt ttccacgctg aacaacggca ataaaaatccc ggcgattgcc 60
atcatcggca ctggtacaaa atggtataaa agtgaagaaa ctgacgcgac cttctccaat 120
agtctggttg aacaaatcgt gtatgcgttg aaactgccgg ggattatcca cattgacgcc 180
gcggagattt atcgcaccta cccggaagtg ggtaaggcac tgtccctgac cgaaaagcct 240
cgtaacgcga tttttctgac ggataaatat tccccgcaga ttaaaatgag tgactccoct 300
gcggacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
ttacattccc cgtttgtttc gaaggaagtg aatggcttaa gcttagaaga ggcttgga 420
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gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggtttc caatttcaca 480
gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
gagttctctc cgttcctgca aaaccaaaca ccaggcattt ataaattctg tcaggagcac 600
gatatcctgg tggaagcata ttctccgctg ggcccgcctgc ggaagaaaaac cgcgcaggat 660
gacagccaac cattttttga gtacgtcaaa gaattgagcg aaaaatacaa caaatccgag 720
gcccagatca tcttgcgctg ggtcactaaa cgcggtgtgc tgccagttac cacctcttca 780
aagcctcagc gcattagcga tgctcagaac ctgttttcct tcgacctgac agcgggaagag 840
gttgataaaa tcacggagct gggctctggaa catgaaccgc tcgcgctgta ctggaataaa 900
ttgtatggca aatataactc tgccgcccag aaagtgtaat ga 942

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<210> 184

<211> 313

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 184

```

Met Ser Phe His Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
1      5      10      15
Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Lys Trp Tyr Lys Ser Glu
20     25     30
Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
35     40     45
Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Ile Tyr
50     55     60
Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
65     70     75     80
Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
85     90     95
Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
100    105    110
Thr Asp Tyr Val Asp Leu Tyr Leu Leu His Ser Pro Phe Val Ser Lys
115    120    125
Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
130    135    140
Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Thr
145    150    155    160
Val Glu Asp Leu Gln Arg Ile Leu Lys Val Ala Glu Val Lys Pro Gln
165    170    175
Val Asn Gln Ile Glu Phe Ser Pro Phe Leu Gln Asn Gln Thr Pro Gly
180    185    190
Ile Tyr Lys Phe Cys Gln Glu His Asp Ile Leu Val Glu Ala Tyr Ser
195    200    205
Pro Leu Gly Pro Leu Arg Lys Lys Thr Ala Gln Asp Asp Ser Gln Pro
210    215    220
Phe Phe Glu Tyr Val Lys Glu Leu Ser Glu Lys Tyr Asn Lys Ser Glu
225    230    235    240
Ala Gln Ile Ile Leu Arg Trp Val Thr Lys Arg Gly Val Leu Pro Val
245    250    255
Thr Thr Ser Ser Lys Pro Gln Arg Ile Ser Asp Ala Gln Asn Leu Phe
260    265    270
Ser Phe Asp Leu Thr Ala Glu Glu Val Asp Lys Ile Thr Glu Leu Gly
275    280    285
Leu Glu His Glu Pro Leu Arg Leu Tyr Trp Asn Lys Leu Tyr Gly Lys
290    295    300
Tyr Asn Ser Ala Ala Gln Lys Val
305    310

```

<210> 185
<211> 942
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 185
atgtcttttc accaacagtt tttcacgctg aacaacggca ataaaatccc ggcgattgcc 60
atcatcggca ctggtacaaa atggtataaa aatgaagaaa ctgacgcgac cttctccaat 120
agtctggttg aacaaatcgt gtatgcgttg aaactgcggg ggattatcca catcgacgcc 180
gcggagattt atcgcaccta cccggaagtg ggtaaagcac tgtccctgac cgaaaagcct 240
cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactcccct 300
gcggacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
attcattccc cgtttgtttc gaaggaagtg aatggcttaa gcttagaaga ggcttggaaa 420
gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggttc caatttcaca 480
gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
gagttctctc cgttcctgca aaaccaaaca ccaggcattt gcaaattctg tcaggagcac 600
gatatccttg tggaagcata ttctccgctg ggcccgtctg ggaagaaaac cgcgcaggat 660
gacagccaac cattttttga gtacgtcaaa gaattgagcg aaaaatacaa caaatccgag 720
gccagatca tcttgcgctg ggtcactaaa cgcggtgtgc tgccagttac cacctcttca 780
aagcctcagc gcattagcga tgctcagaac ctgttttcct tcgacctgac agcgggaagag 840
gttgataaaa tcacggagct gggctctggaa catgaaccgc tcgcctgta ctggaataaa 900
ttgtatggca aatataacta cgcgcccag aaagtgtaat ga 942

<210> 186
<211> 313
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 186
Met Ser Phe His Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
1 5 10 15
Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Lys Trp Tyr Lys Asn Glu
20 25 30
Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
35 40 45
Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Ile Tyr
50 55 60
Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
65 70 75 80
Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
85 90 95
Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
100 105 110
Thr Asp Tyr Val Asp Leu Tyr Leu Ile His Ser Pro Phe Val Ser Lys
115 120 125
Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
130 135 140
Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Thr
145 150 155 160
Val Glu Asp Leu Gln Arg Ile Leu Lys Val Ala Glu Val Lys Pro Gln
165 170 175
Val Asn Gln Ile Glu Phe Ser Pro Phe Leu Gln Asn Gln Thr Pro Gly
180 185 190

Ile	Cys	Lys	Phe	Cys	Gln	Glu	His	Asp	Ile	Leu	Val	Glu	Ala	Tyr	Ser		
	195					200					205						
Pro	Leu	Gly	Pro	Leu	Arg	Lys	Lys	Thr	Ala	Gln	Asp	Asp	Ser	Gln	Pro		
	210					215					220						
Phe	Phe	Glu	Tyr	Val	Lys	Glu	Leu	Ser	Glu	Lys	Tyr	Asn	Lys	Ser	Glu		
225					230					235					240		
Ala	Gln	Ile	Ile	Leu	Arg	Trp	Val	Thr	Lys	Arg	Gly	Val	Leu	Pro	Val		
				245					250					255			
Thr	Thr	Ser	Ser	Lys	Pro	Gln	Arg	Ile	Ser	Asp	Ala	Gln	Asn	Leu	Phe		
			260					265					270				
Ser	Phe	Asp	Leu	Thr	Ala	Glu	Glu	Val	Asp	Lys	Ile	Thr	Glu	Leu	Gly		
		275					280					285					
Leu	Glu	His	Glu	Pro	Leu	Arg	Leu	Tyr	Trp	Asn	Lys	Leu	Tyr	Gly	Lys		
	290					295					300						
Tyr	Asn	Tyr	Ala	Ala	Gln	Lys	Val										
305					310												

<210> 187

<211> 942

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 187

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atcatcgcca ctggtacaaa atggtataaa agtgaagaaa ctgacgcgac cttctccaat 120
agtctggttg aacaaatcgt gtatgcgttg aaactgccgg ggattatcca catcgacgcc 180
gcggagattt atcgcaccta cccggaagtg ggtaaagcac tgtccctgac caaaaagcct 240
cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactccoct 300
gcggacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
ttacattccc cgtttgtttc gaaggaagtg aatggcttaa gcttagaaga ggcttgga 420
gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcggggtttc caatttcaca 480
gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
gagttctctc cgttcctgca aaaccaaaca ccaggcattt ataaattctg tcaggagcac 600
gatatcctgg tggaagcata ttctccgctg ggcccgtg gcgaagaaagc cgcgcaggat 660
gacggccaac cattttttga gtacgtcaaa gaattgagcg aaaaatacaa caaatccgag 720
gccagatca tcttgcgctg ggtcactaaa cgcggtgtgc tgccagttac cacctottca 780
aagcctcagc gcattagcga tgctcagaac ctgttttctc tcgacctgac agcgggaagag 840
gttgataaaa tcacggagct gggtctggaa catgaaccgc tcgcctgta ctggaataaa 900
ttgtatggca aatataacta cgcgcgccag aaagtgtaat ga 942

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<210> 188

<211> 313

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 188

Met	Ser	Phe	His	Gln	Phe	Phe	Thr	Leu	Asn	Asn	Gly	Asn	Lys	Ile			
1			5				10					15					
Pro	Ala	Ile	Ala	Ile	Ile	Gly	Thr	Gly	Thr	Lys	Trp	Tyr	Lys	Ser	Glu		
		20					25					30					
Glu	Thr	Asp	Ala	Thr	Phe	Ser	Asn	Ser	Leu	Val	Glu	Gln	Ile	Val	Tyr		
		35				40					45						
Ala	Leu	Lys	Leu	Pro	Gly	Ile	Ile	His	Ile	Asp	Ala	Ala	Glu	Ile	Tyr		

50	55	60
Arg Thr Tyr Pro Glu Val	Gly Lys Ala Leu Ser	Leu Thr Lys Lys Pro
65	70	75
Arg Asn Ala Ile Phe Leu Thr	Asp Lys Tyr Ser	Pro Gln Ile Lys Met
85	90	95
Ser Asp Ser Pro Ala Asp	Gly Leu Asp Leu Ala	Leu Lys Lys Met Gly
100	105	110
Thr Asp Tyr Val Asp Leu Tyr	Leu Leu His Ser	Pro Phe Val Ser Lys
115	120	125
Glu Val Asn Gly Leu Ser	Leu Glu Glu Ala Trp	Lys Asp Met Glu Gln
130	135	140
Leu Tyr Lys Ser Gly Lys	Ala Lys Asn Ile Gly	Val Ser Asn Phe Thr
145	150	155
Val Glu Asp Leu Gln Arg	Ile Leu Lys Val Ala	Glu Val Lys Pro Gln
165	170	175
Val Asn Gln Ile Glu Phe	Ser Pro Phe Leu Gln	Asn Gln Thr Pro Gly
180	185	190
Ile Tyr Lys Phe Cys Gln	Glu His Asp Ile Leu	Val Glu Ala Tyr Ser
195	200	205
Pro Leu Gly Pro Leu Arg	Lys Lys Ala Ala Gln	Asp Asp Gly Gln Pro
210	215	220
Phe Phe Glu Tyr Val Lys	Glu Leu Ser Glu Lys	Tyr Asn Lys Ser Glu
225	230	235
Ala Gln Ile Ile Leu Arg	Trp Val Thr Lys Arg	Gly Val Leu Pro Val
245	250	255
Thr Thr Ser Ser Lys Pro	Gln Arg Ile Ser Asp	Ala Gln Asn Leu Phe
260	265	270
Ser Phe Asp Leu Thr Ala	Glu Glu Val Asp Lys	Ile Thr Glu Leu Gly
275	280	285
Leu Glu His Glu Pro Leu	Arg Leu Tyr Trp Asn	Lys Leu Tyr Gly Lys
290	295	300
Tyr Asn Tyr Ala Ala Gln	Lys Val	
305	310	

<210> 189
 <211> 942
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 189
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 atcatcggca ctggtacaaa gtggtataaa aatgaagaaa ctgacgcgac cttctccaat 120
 agtctggttg aacaaatcgt gtatgcgttg aaactgccgg ggattatcca catcgacgcc 180
 gcggagattt atcgcaccta cccggaagtg ggtaaagcac tgtccctgac cgaaaagcct 240
 cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactccct 300
 gcggacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
 attcattccc cgtttgtttc gaaggaagtg aatggcttaa gcttagaaga ggcttgga 420
 gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggtttc caatttcaca 480
 gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
 gagttctctc cgttcctgca aaaccaaaaca ccaggcattt ataaattctg tcaggagcac 600
 gatatccttg tggaagcata ttctccgctg ggcccgtgc ggaagaaaac cgcgcaggat 660
 gacagccaac cattttttga gtacgtcaaa gaattgagcg aaaaatacgg caaatccgag 720
 gccagatca tcttgccgtg ggtcactaaa cgcgggtgtg tgccagttac cacctcttca 780
 aagcctcagc gcattagcga tgctcagaac ctgttttctc tcgacctgac agcgggaagag 840
 gttgataaaa tcacggagct gggtctggaa catgaaccgc tcgcctgta ctggaataaa 900
 ttgtatggca aatataacta cgccgccag aaagtgtaat ga 942

<210> 190
 <211> 313
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 190
 Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
 1 5 10 15
 Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Lys Trp Tyr Lys Asn Glu
 20 25 30
 Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
 35 40 45
 Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Ile Tyr
 50 55 60
 Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
 65 70 75 80
 Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
 85 90 95
 Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
 100 105 110
 Thr Asp Tyr Val Asp Leu Tyr Leu Ile His Ser Pro Phe Val Ser Lys
 115 120 125
 Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
 130 135 140
 Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Thr
 145 150 155 160
 Val Glu Asp Leu Gln Arg Ile Leu Lys Val Ala Glu Val Lys Pro Gln
 165 170 175
 Val Asn Gln Ile Glu Phe Ser Pro Phe Leu Gln Asn Gln Thr Pro Gly
 180 185 190
 Ile Tyr Lys Phe Cys Gln Glu His Asp Ile Leu Val Glu Ala Tyr Ser
 195 200 205
 Pro Leu Gly Pro Leu Arg Lys Lys Thr Ala Gln Asp Asp Ser Gln Pro
 210 215 220
 Phe Phe Glu Tyr Val Lys Glu Leu Ser Glu Lys Tyr Gly Lys Ser Glu
 225 230 235 240
 Ala Gln Ile Ile Leu Arg Trp Val Thr Lys Arg Gly Val Leu Pro Val
 245 250 255
 Thr Thr Ser Ser Lys Pro Gln Arg Ile Ser Asp Ala Gln Asn Leu Phe
 260 265 270
 Ser Phe Asp Leu Thr Ala Glu Glu Val Asp Lys Ile Thr Glu Leu Gly
 275 280 285
 Leu Glu His Glu Pro Leu Arg Leu Tyr Trp Asn Lys Leu Tyr Gly Lys
 290 295 300
 Tyr Asn Tyr Ala Ala Gln Lys Val
 305 310

<210> 191
 <211> 942
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 191

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atgtcttttt accaacagtt tttcacgctg aacaacggca ataaaatccc ggcgattgcc 60
atcatcggca ctggtacaaa atggtataaa aatgaagaaa ctgacgcgac cttctccaat 120
agtctggttg aacaaatcgt gtatgcgttg aaactgccgg ggattatcca catcgacgcc 180
gcgagagattt atcgcaccta cccggaagtg ggtaaagcac tgccctgac cgaaaagcct 240
cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactcccct 300
gcgacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
ttacattccc cgtttgtttc gaaggaagtg aatggcttaa gcttagaaga ggcttggaaa 420
gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggttc caatttcaca 480
gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
gagttctctc cgttcctgca aaaccaaaca ccaggcattt ataaattctg tcaggagcac 600
gatatcctgg tggaaagcata ttctccgctg ggcccgtgc ggaagaaaac cgcgcaggat 660
gacagccatc cattttttga gtacgtcaaa gaattgagcg aaaaatacaa caaatccgag 720
gcccagatca tctgcgctg ggctactaaa cgcggtgtgc tgccagttac cacctcttca 780
aagcctcagc gcattagcga tgctcagaac ctgttttctc tcgacctgac agcgggaagag 840
gttgataaaa tcacggagct gggctctggaa catgaaccgc tgcgcctgta ctggaataaa 900
ttgatatggca aatataacta cgccgccag aaagtgtaat ga 942

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<210> 192

<211> 313

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 192

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Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
1          5          10          15
Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Lys Trp Tyr Lys Asn Glu
          20          25          30
Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
          35          40          45
Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Ile Tyr
          50          55          60
Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
65          70          75          80
Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
          85          90          95
Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
          100          105          110
Thr Asp Tyr Val Asp Leu Tyr Leu Leu His Ser Pro Phe Val Ser Lys
          115          120          125
Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
          130          135          140
Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Thr
145          150          155          160
Val Glu Asp Leu Gln Arg Ile Leu Lys Val Ala Glu Val Lys Pro Gln
          165          170          175
Val Asn Gln Ile Glu Phe Ser Pro Phe Leu Gln Asn Gln Thr Pro Gly
          180          185          190
Ile Tyr Lys Phe Cys Gln Glu His Asp Ile Leu Val Glu Ala Tyr Ser
          195          200          205
Pro Leu Gly Pro Leu Arg Lys Lys Thr Ala Gln Asp Asp Ser His Pro
210          215          220
Phe Phe Glu Tyr Val Lys Glu Leu Ser Glu Lys Tyr Asn Lys Ser Glu
225          230          235          240
Ala Gln Ile Ile Leu Arg Trp Val Thr Lys Arg Gly Val Leu Pro Val
          245          250          255
Thr Thr Ser Ser Lys Pro Gln Arg Ile Ser Asp Ala Gln Asn Leu Phe
260          265          270

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Ser	Phe	Asp	Leu	Thr	Ala	Glu	Glu	Val	Asp	Lys	Ile	Thr	Glu	Leu	Gly
		275					280					285			
Leu	Glu	His	Glu	Pro	Leu	Arg	Leu	Tyr	Trp	Asn	Lys	Leu	Tyr	Gly	Lys
		290				295					300				
Tyr	Asn	Tyr	Ala	Ala	Gln	Lys	Val								
305					310										

<210> 193
 <211> 942
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 193
 atgtcttttc accaacagtt tttcacgctg aacaacggca ataaaatccc ggcgattgcc 60
 atcatcggca ctggtacaaa atggtataaa aatgaagaaa ctgacgcgac cttctccaat 120
 agtctggttg aacaaatcgt gtatgcgttg aaactgccgg ggattatcca catogaagcc 180
 ggcgagattt atcgcaccta ccggaagtg ggtaaagcac tgtccctgac caaaaagcct 240
 cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactccctt 300
 gcggacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
 ttacattccc cgtttgtttc gaaggaagtg aatggcttaa gcttagaaga ggcttggaaa 420
 gatattgagc agttatacaa aagtggtaaa gctaaaaaca tcgggggttc caatttcaca 480
 gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
 gagttctctc cgttcctgca aaaccaaaca ccaggcattt ataaattctg tcaggagcac 600
 gatatcctgg tgggaagcata ttctccgctg ggcccgtgc ggaagaaaac cgcgcaggat 660
 gacagccaac ctttttttga gtacgtcaaa gaattgagcg aaaaatacaa caaatccgag 720
 gccagatca tctcgcgctg ggtcactaaa cgcggtgtgc tgccagttac cacctcttca 780
 aagcctcagc gcattagcga tgctcagaac ctgttttctt tcgacctgac agcgggaagag 840
 gttgataaaa tcacggagct gggctctggaa catgaaccgc tgcgcctgta ctggaataaa 900
 ttatatggca aatataactc tgccgcccg aaagtgtaat ga 942

<210> 194
 <211> 313
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 194
 Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
 1 5 10 15
 Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Lys Trp Tyr Lys Asn Glu
 20 25 30
 Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
 35 40 45
 Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Ile Tyr
 50 55 60
 Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Lys Lys Pro
 65 70 75 80
 Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
 85 90 95
 Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
 100 105 110
 Thr Asp Tyr Val Asp Leu Tyr Leu Leu His Ser Pro Phe Val Ser Lys
 115 120 125
 Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln

130		135		140
Leu Tyr Lys Ser Gly	Lys Ala Lys Asn Ile Gly	Val Ser Asn Phe Thr		
145	150	155	160	
Val Glu Asp Leu Gln Arg	Ile Leu Lys Val Ala Glu	Val Lys Pro Gln		
	165	170	175	
Val Asn Gln Ile Glu Phe	Ser Pro Phe Leu Gln	Asn Gln Thr Pro Gly		
	180	185	190	
Ile Tyr Lys Phe Cys Gln	Glu His Asp Ile Leu	Val Glu Ala Tyr Ser		
	195	200	205	
Pro Leu Gly Pro Leu Arg	Lys Lys Thr Ala Gln	Asp Asp Ser Gln Pro		
	210	215	220	
Phe Phe Glu Tyr Val Lys	Glu Leu Ser Glu Lys	Tyr Asn Lys Ser Glu		
225	230	235	240	
Ala Gln Ile Ile Leu Arg	Trp Val Thr Lys Arg	Gly Val Leu Pro Val		
	245	250	255	
Thr Thr Ser Ser Lys Pro	Gln Arg Ile Ser Asp	Ala Gln Asn Leu Phe		
	260	265	270	
Ser Phe Asp Leu Thr Ala	Glu Glu Val Asp Lys	Ile Thr Glu Leu Gly		
	275	280	285	
Leu Glu His Glu Pro Leu	Arg Leu Tyr Trp Asn	Lys Leu Tyr Gly Lys		
	290	295	300	
Tyr Asn Ser Ala Ala Gln	Lys Val			
305	310			

<210> 195
 <211> 942
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 195
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 atcatcgcca ctggtacagc ctggtataaa agtgaagaaa ctgacgcgac cttctccaat 120
 agtctggttg aacaaatcgt gtatgcgttg aaactgccgg ggattatcca catcgacgcc 180
 gcggagattt atcgcaccta cccggaagtg ggtaaagcac tgtccctgac cgaaaagcct 240
 cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactccct 300
 gcggacggtc tggatttagc attgaagaaa atgggtacag attatggtga tttatatctg 360
 attcattccc cgtttgtttc gaaggaagtg aatggcttaa gcttagaaga ggcttggaaa 420
 gatattgagc agttatacaa aagtggtaaa gctaaaaaca tcgggggttc caatttcaca 480
 gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
 gagttctctc cgttctctgca aaaccaaaca ccaggcattt ataaattctg tcaggagcac 600
 gatattcttg tggaaagcata ttctccgctg ggcccgctgc ggaagaaaac cgcgcaggat 660
 gacagccaac ctttttttga gtacgtcaaa gaattgagcg aaaaatacaa caaatccgag 720
 gccagatca tcttgcgctg ggtcactaaa cgcgggtgtg tgccagttac cacctcttca 780
 aagcctcagc gcattagcga tgctcagaac ctgttttcc tgcacctgac agcgggaagag 840
 gttgataaaa tcacggagct ggtctggaa catgaaccgc tgcgcctgta ctggaataaa 900
 ttgtatggca aatataacta cgccgccag aaagtgtaat ga 942

<210> 196
 <211> 313
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 196

Met	Ser	Phe	His	Gln	Gln	Phe	Phe	Thr	Leu	Asn	Asn	Gly	Asn	Lys	Ile
1			5						10					15	
Pro	Ala	Ile	Ala	Ile	Ile	Gly	Thr	Gly	Thr	Ala	Trp	Tyr	Lys	Ser	Glu
		20						25					30		
Glu	Thr	Asp	Ala	Thr	Phe	Ser	Asn	Ser	Leu	Val	Glu	Gln	Ile	Val	Tyr
		35					40					45			
Ala	Leu	Lys	Leu	Pro	Gly	Ile	Ile	His	Ile	Asp	Ala	Ala	Glu	Ile	Tyr
	50					55					60				
Arg	Thr	Tyr	Pro	Glu	Val	Gly	Lys	Ala	Leu	Ser	Leu	Thr	Glu	Lys	Pro
65				70						75					80
Arg	Asn	Ala	Ile	Phe	Leu	Thr	Asp	Lys	Tyr	Ser	Pro	Gln	Ile	Lys	Met
			85						90					95	
Ser	Asp	Ser	Pro	Ala	Asp	Gly	Leu	Asp	Leu	Ala	Leu	Lys	Lys	Met	Gly
			100					105					110		
Thr	Asp	Tyr	Val	Asp	Leu	Tyr	Leu	Ile	His	Ser	Pro	Phe	Val	Ser	Lys
		115					120					125			
Glu	Val	Asn	Gly	Leu	Ser	Leu	Glu	Glu	Ala	Trp	Lys	Asp	Met	Glu	Gln
	130					135					140				
Leu	Tyr	Lys	Ser	Gly	Lys	Ala	Lys	Asn	Ile	Gly	Val	Ser	Asn	Phe	Thr
145				150					155						160
Val	Glu	Asp	Leu	Gln	Arg	Ile	Leu	Lys	Val	Ala	Glu	Val	Lys	Pro	Gln
			165					170						175	
Val	Asn	Gln	Ile	Glu	Phe	Ser	Pro	Phe	Leu	Gln	Asn	Gln	Thr	Pro	Gly
		180						185					190		
Ile	Tyr	Lys	Phe	Cys	Gln	Glu	His	Asp	Ile	Leu	Val	Glu	Ala	Tyr	Ser
	195						200					205			
Pro	Leu	Gly	Pro	Leu	Arg	Lys	Lys	Thr	Ala	Gln	Asp	Asp	Ser	Gln	Pro
	210					215					220				
Phe	Phe	Glu	Tyr	Val	Lys	Glu	Leu	Ser	Glu	Lys	Tyr	Asn	Lys	Ser	Glu
225				230						235					240
Ala	Gln	Ile	Ile	Leu	Arg	Trp	Val	Thr	Lys	Arg	Gly	Val	Leu	Pro	Val
			245						250					255	
Thr	Thr	Ser	Ser	Lys	Pro	Gln	Arg	Ile	Ser	Asp	Ala	Gln	Asn	Leu	Phe
		260						265					270		
Ser	Phe	Asp	Leu	Thr	Ala	Glu	Glu	Val	Asp	Lys	Ile	Thr	Glu	Leu	Gly
		275					280					285			
Leu	Glu	His	Glu	Pro	Leu	Arg	Leu	Tyr	Trp	Asn	Lys	Leu	Tyr	Gly	Lys
	290					295					300				
Tyr	Asn	Tyr	Ala	Ala	Gln	Lys	Val								
305					310										

<210> 197

<211> 942

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 197

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agtctggttg aacaaatcgt gtatgcgttg aaactgccgg ggattatcca catcgacgcc 180
gcggagattt atcgcaacct cccggaagtg ggtaaagcac tgtccctgac cgaaaagcct 240
cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactcccct 300
gcggacggtc tggatttggc attgaagaaa atgggtacag attatgttga tttatatctg 360
attcattccc cgtttgtttc gaaggaagtg aatggcctaa gcttagaaga ggcttggaaa 420
gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggttc caatttcaca 480
gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
gagttctctc cgttcctgca aaaccaaaca ccaggcattt gcaaattctg tcaggagcac 600

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gatatcctgg tggaagcata ttctccgctg ggcccgcgtgc ggaagaaaac cgcgcaggat 660
gacagccaac cattttttga gtacgtcaaa gaattgagcg aaaaatacaa caaatccgag 720
gccagatca tctgcgctg ggctactaaa cgcgggtgtgc tgccagttac cacctcttca 780
aagcctcagc gcattagcga tgctcagaac ctgttttctt tcgacctgac agcgggaagag 840
gttgataaaa tcacggagct gggctctggaa catgaaccgc tcgcgcctgta ctggaataaa 900
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<210> 198

<211> 313

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 198

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Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
1          5          10          15
Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Lys Trp Tyr Lys Asn Glu
20          25          30
Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
35          40          45
Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Ile Tyr
50          55          60
Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
65          70          75          80
Arg Asp Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
85          90          95
Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
100         105         110
Thr Asp Tyr Val Asp Leu Tyr Leu Ile His Ser Pro Phe Val Ser Lys
115         120         125
Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
130         135         140
Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Thr
145         150         155         160
Val Glu Asp Leu Gln Arg Ile Leu Lys Val Ala Glu Val Lys Pro Gln
165         170         175
Val Asn Gln Ile Glu Phe Ser Pro Phe Leu Gln Asn Gln Thr Pro Gly
180         185         190
Ile Cys Lys Phe Cys Gln Glu His Asp Ile Leu Val Glu Ala Tyr Ser
195         200         205
Pro Leu Gly Pro Leu Arg Lys Lys Thr Ala Gln Asp Asp Ser Gln Pro
210         215         220
Phe Phe Glu Tyr Val Lys Glu Leu Ser Glu Lys Tyr Asn Lys Ser Glu
225         230         235         240
Ala Gln Ile Ile Leu Arg Trp Val Thr Lys Arg Gly Val Leu Pro Val
245         250         255
Thr Thr Ser Ser Lys Pro Gln Arg Ile Ser Asp Ala Gln Asn Leu Phe
260         265         270
Ser Phe Asp Leu Thr Ala Glu Glu Val Asp Lys Ile Thr Glu Leu Gly
275         280         285
Leu Glu His Glu Pro Leu Arg Leu Tyr Trp Asn Lys Leu Tyr Gly Lys
290         295         300
Tyr Asn Tyr Ala Ala Gln Lys Val
305         310

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<210> 199

<211> 942

<212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 199
 atgtcttttc accaacagtt tttcacgctg aacaacggca ataaaatccc ggcgattgcc 60
 atcatcggca ctggtacaaa gtggtataaa agtgaagaaa ctgacgcgac cttctccaat 120
 agtctgggtg aacaaatcgt gtatgcgttg aaactgccgg ggattatcca catcgaagcc 180
 gcggagattt atcgcaccta cccggaagtg ggtaaagcac tgccctgac cgaaaagcct 240
 cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactcccct 300
 gcggacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
 attcattccc cgtttgtttc gaaggaagtg aatggcttaa gcttagaaga ggcttgga 420
 gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggttc caatttcaca 480
 gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
 gagttctctc cgttcctgca aaaccaaaca ccaggcattt ataaattctg tcaggagcac 600
 gatatcctgg tggaagcata ttctccgctg ggcccgtg gcgagaaaac cgcgcaggat 660
 gacagccaac cattttttga gtacgtcaaa gaattgagcg aaaaatacaa caaatccgag 720
 gccagatca tcctgcgctg ggtcactaaa cgcggtgtgc tgccagttac cacctcttca 780
 aagcctcagc gcattagcga tgctcagaac ctgttttctc tcgacctgac agcgggaagag 840
 gttgataaaa tcacggagct gggtctggaa catgaaccgc tcgcgctgta ctggaataaa 900
 ttgtatggca aatataacta cgccgccag aaagtgtaat ga 942

<210> 200
 <211> 313
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 200
 Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
 1 5 10 15
 Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Lys Trp Tyr Lys Ser Glu
 20 25 30
 Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
 35 40 45
 Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Ile Tyr
 50 55 60
 Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
 65 70 75 80
 Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
 85 90 95
 Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
 100 105 110
 Thr Asp Tyr Val Asp Leu Tyr Leu Ile His Ser Pro Phe Val Ser Lys
 115 120 125
 Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
 130 135 140
 Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Thr
 145 150 155 160
 Val Glu Asp Leu Gln Arg Ile Leu Lys Val Ala Glu Val Lys Pro Gln
 165 170 175
 Val Asn Gln Ile Glu Phe Ser Pro Phe Leu Gln Asn Gln Thr Pro Gly
 180 185 190
 Ile Tyr Lys Phe Cys Gln Glu His Asp Ile Leu Val Glu Ala Tyr Ser
 195 200 205
 Pro Leu Gly Pro Leu Arg Lys Lys Thr Ala Gln Asp Asp Ser Gln Pro

210		215		220
Phe Phe Glu Tyr Val Lys Glu Leu Ser Glu Lys Tyr Asn Lys Ser Glu				
225		230		235
Ala Gln Ile Ile Leu Arg Trp Val Thr Lys Arg Gly Val Leu Pro Val				240
	245		250	255
Thr Thr Ser Ser Lys Pro Gln Arg Ile Ser Asp Ala Gln Asn Leu Phe				
	260		265	270
Ser Phe Asp Leu Thr Ala Glu Glu Val Asp Lys Ile Thr Glu Leu Gly				
	275		280	285
Leu Glu His Glu Pro Leu Arg Leu Tyr Trp Asn Lys Leu Tyr Gly Lys				
	290		295	300
Tyr Asn Tyr Ala Ala Gln Lys Val				
305		310		

<210> 201
 <211> 942
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 201
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 attatcggca ctggtacaaa gtggtataaaa agtgaagaaa ctgacgogac cttctccaat 120
 agtctgggtg aacaaatcgt gtatgctgtg aaactgcggg ggattatcca catcgacgcc 180
 gcggagattt atcgcaccta cccggaagtg ggtaaagcac tgtccctgac cgaaaagcct 240
 cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactcccct 300
 gcggacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
 ttacattccc cgtttgtttc gaaggaagtg aatggcttaa gcttagaaga ggcttgga 420
 gatattggagc agttatacaa aagtggtaaa gctaaaaaca tgggggtttc caatttcaca 480
 gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
 gagttctctc cgttcctgca aaaccaaaca ccaggcattt ataaattctg tcaggagcac 600
 gatatcctgg tggaaagcata ttctccgctg ggcccgotgc ggaagaaaac cgcgcaggat 660
 gacagccaac cattttttga gtacgtcaaa gaattgagcg aaaaatacgg caaatccgag 720
 gccagatca tccctgcctg ggtaactaaa cgcgggtgtg tgcagttac cacctcttca 780
 aagcctcagc gcattagcga tgctcagaac ctgttttctt tcgacctgac agcggaagag 840
 gttgataaaa tcacggagct gggctctggaa catgaaccgc tgcgcctgta ctggaataaa 900
 ttgtatggca aatataacta cgccgccag aaagtgtaat ga 942

<210> 202
 <211> 313
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 202
 Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
 1 5 10 15
 Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Lys Trp Tyr Lys Ser Glu
 20 25 30
 Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
 35 40 45
 Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Ile Tyr
 50 55 60
 Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
 65 70 75 80

Arg	Asn	Ala	Ile	Phe	Leu	Thr	Asp	Lys	Tyr	Ser	Pro	Gln	Ile	Lys	Met	
			85						90					95		
Ser	Asp	Ser	Pro	Ala	Asp	Gly	Leu	Asp	Leu	Ala	Leu	Lys	Lys	Met	Gly	
			100					105					110			
Thr	Asp	Tyr	Val	Asp	Leu	Tyr	Leu	Leu	His	Ser	Pro	Phe	Val	Ser	Lys	
		115					120					125				
Glu	Val	Asn	Gly	Leu	Ser	Leu	Glu	Glu	Ala	Trp	Lys	Asp	Met	Glu	Gln	
	130					135					140					
Leu	Tyr	Lys	Ser	Gly	Lys	Ala	Lys	Asn	Ile	Gly	Val	Ser	Asn	Phe	Thr	
145					150					155					160	
Val	Glu	Asp	Leu	Gln	Arg	Ile	Leu	Lys	Val	Ala	Glu	Val	Lys	Pro	Gln	
				165					170					175		
Val	Asn	Gln	Ile	Glu	Phe	Ser	Pro	Phe	Leu	Gln	Asn	Gln	Thr	Pro	Gly	
			180					185					190			
Ile	Tyr	Lys	Phe	Cys	Gln	Glu	His	Asp	Ile	Leu	Val	Glu	Ala	Tyr	Ser	
		195					200					205				
Pro	Leu	Gly	Pro	Leu	Arg	Lys	Lys	Thr	Ala	Gln	Asp	Asp	Ser	Gln	Pro	
	210					215					220					
Phe	Phe	Glu	Tyr	Val	Lys	Glu	Leu	Ser	Glu	Lys	Tyr	Gly	Lys	Ser	Glu	
225					230					235					240	
Ala	Gln	Ile	Ile	Leu	Arg	Trp	Val	Thr	Lys	Arg	Gly	Val	Leu	Pro	Val	
				245					250					255		
Thr	Thr	Ser	Ser	Lys	Pro	Gln	Arg	Ile	Ser	Asp	Ala	Gln	Asn	Leu	Phe	
			260					265					270			
Ser	Phe	Asp	Leu	Thr	Ala	Glu	Glu	Val	Asp	Lys	Ile	Thr	Glu	Leu	Gly	
		275					280					285				
Leu	Glu	His	Glu	Pro	Leu	Arg	Leu	Tyr	Trp	Asn	Lys	Leu	Tyr	Gly	Lys	
	290					295					300					
Tyr	Asn	Tyr	Ala	Ala	Gln	Lys	Val									
305					310											

<210> 203

<211> 942

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 203

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atgtcttttc accaacagtt tttcacgctg aacaacggca ataaaatccc ggogactgcc 60
attatcggca ctggtacaaa gtggtataaa agtgaagaaa ctgacgcgac cttctccaat 120
agtctggttg aacaaatcgt gtacgcgttg aaactgccgg ggattatoca catogaogcc 180
gcggagattt atcgcaccta cccggaagtg ggtaaagcac tgtocotgac cgaaaagcct 240
cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactccct 300
gcggacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
ttacattccc cgtttgtttc gaaggaagtg aatggcttaa gcttagaaga ggcttggaaa 420
gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggttc caatttcaca 480
gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
gagttctctc cgttcctgca aaaccaaaca ccaggcattt ataaattctg tcaggagcac 600
gatatcctgg tggaagcata ttctccgctg ggcccgtgc ggaagaaaac cgcgcaggat 660
gacagccaac ctttttttga gtacgtcaaa gaattgagcg aaaaatacgg caaatccgag 720
gcccagatca tcctgcgctg ggtaactaaa cgcggtgtgc tgccagttac cacctcttca 780
aagcctcagc gcattagcga tgctcagaac ctgttttctt tcgacctgac agcggaagag 840
gttgataaaa tcacggagct ggggtctgaa catgaaccgc tgcgcctgta ctggaataaa 900
ttgtatggca aatataacta cgcgcgccag aaagtgtaat ga 942

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<210> 204

<211> 313

<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 204
Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
1 5 10 15
Pro Ala Thr Ala Ile Ile Gly Thr Gly Thr Lys Trp Tyr Lys Ser Glu
20 25 30
Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
35 40 45
Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Ile Tyr
50 55 60
Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
65 70 75 80
Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
85 90 95
Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
100 105 110
Thr Asp Tyr Val Asp Leu Tyr Leu Leu His Ser Pro Phe Val Ser Lys
115 120 125
Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
130 135 140
Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Thr
145 150 155 160
Val Glu Asp Leu Gln Arg Ile Leu Lys Val Ala Glu Val Lys Pro Gln
165 170 175
Val Asn Gln Ile Glu Phe Ser Pro Phe Leu Gln Asn Gln Thr Pro Gly
180 185 190
Ile Tyr Lys Phe Cys Gln Glu His Asp Ile Leu Val Glu Ala Tyr Ser
195 200 205
Pro Leu Gly Pro Leu Arg Lys Lys Thr Ala Gln Asp Asp Ser Gln Pro
210 215 220
Phe Phe Glu Tyr Val Lys Glu Leu Ser Glu Lys Tyr Gly Lys Ser Glu
225 230 235 240
Ala Gln Ile Ile Leu Arg Trp Val Thr Lys Arg Gly Val Leu Pro Val
245 250 255
Thr Thr Ser Ser Lys Pro Gln Arg Ile Ser Asp Ala Gln Asn Leu Phe
260 265 270
Ser Phe Asp Leu Thr Ala Glu Glu Val Asp Lys Ile Thr Glu Leu Gly
275 280 285
Leu Glu His Glu Pro Leu Arg Leu Tyr Trp Asn Lys Leu Tyr Gly Lys
290 295 300
Tyr Asn Tyr Ala Ala Gln Lys Val
305 310

<210> 205
<211> 942
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 205
atgtcttttc accaacagtt tttcacgctg aacaacggca ataaaatccc ggogattgcc 60
atcatcggca ctggtacaaa atggtataaa aatgaagaaa ctgacgcgac cttctccaat 120
agtctggttg aacaaatcgt gtatgcgttg aaactgcggg ggattatoca catcgacgcc 180

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gcgagggttt atcgcaccta cccggaagtg ggtaaagcac tgtccctgac cgaaaagcct 240
cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactcccct 300
gcggaacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
ttacattccc cgtttgtttc gaaggaagtg aatggcttaa gcttagaaga ggcttgaaa 420
gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggttc caatttcaca 480
gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
gagttctctc cgttcctgca aaaccaaaca ccaggcattt ataaattctg tcaggagcac 600
gatatcctgg tggaagcata ttctccgctg ggcccgtgc ggaagaaaac cgcgcaggat 660
gacagccaac cattttttga gtacgtcaaa gaattgagcg aaaaatacaa caaatccgag 720
gcccagatca tctgcgctg ggtcactaaa cgcggtgtgc tgccagttac cacctcttca 780
aagcctcagc gcattagcga tgctcagaac ctgttttcct tcgacctgac agcggaagag 840
gttgataaaa tcacggagct gggctcggaa catgaaccgc tgcgcctgta ctggaataaa 900
ttgtatggca aatataacta cgccgccag aaagtgtaat ga 942

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<210> 206

<211> 313

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 206

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Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
1                               5                               10                               15
Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Lys Trp Tyr Lys Asn Glu
20                               25                               30
Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
35                               40                               45
Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Val Tyr
50                               55                               60
Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
65                               70                               75                               80
Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
85                               90                               95
Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
100                              105                              110
Thr Asp Tyr Val Asp Leu Tyr Leu Leu His Ser Pro Phe Val Ser Lys
115                              120                              125
Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
130                              135                              140
Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Thr
145                              150                              155                              160
Val Glu Asp Leu Gln Arg Ile Leu Lys Val Ala Glu Val Lys Pro Gln
165                              170                              175
Val Asn Gln Ile Glu Phe Ser Pro Phe Leu Gln Asn Gln Thr Pro Gly
180                              185                              190
Ile Tyr Lys Phe Cys Gln Glu His Asp Ile Leu Val Glu Ala Tyr Ser
195                              200                              205
Pro Leu Gly Pro Leu Arg Lys Lys Thr Ala Gln Asp Asp Ser Gln Pro
210                              215                              220
Phe Phe Glu Tyr Val Lys Glu Leu Ser Glu Lys Tyr Asn Lys Ser Glu
225                              230                              235                              240
Ala Gln Ile Ile Leu Arg Trp Val Thr Lys Arg Gly Val Leu Pro Val
245                              250                              255
Thr Thr Ser Ser Lys Pro Gln Arg Ile Ser Asp Ala Gln Asn Leu Phe
260                              265                              270
Ser Phe Asp Leu Thr Ala Glu Glu Val Asp Lys Ile Thr Glu Leu Gly
275                              280                              285
Leu Glu His Glu Pro Leu Arg Leu Tyr Trp Asn Lys Leu Tyr Gly Lys

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290
Tyr Asn Tyr Ala Ala Gln Lys Val
305 310

300

<210> 207
<211> 942
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 207
atgtcttttc accaacagtt tttcacgctg aacaacggca ataaaatccc ggcgattgcc 60
atcatcggca ctggtacaaa gtggtataaa agtgaagaaa ctgaacgcgac cttctccaat 120
agtctggttg aacaaatcgt gtatgcgttg gaactgccgg ggattatcca catcgacgcc 180
gcggagattt atcgcaccta cccggaagtg ggtaaagcac tgtccctgac cgaaaagcct 240
cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactcccct 300
gcggacggtc tggatttagc attgaagaaa atgggtacag attatggtga tttatatctg 360
ttacattccc cgtttggttc gaaggaagtg aatggcttaa gcttagaaga ggcttgga 420
gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggttc caatttcaca 480
gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
gagttctctc cgttcctgca aaaccaaaca ccaggcattt ataaattctg tcaggagcac 600
gatatcctgg tggaagcata ttctccgctg ggcccgtgc ggaagaaaac cgcgcaggat 660
gacagccaac cattttttga gtacgtcaaa gaattgagcg aaaaatacaa caaatccgag 720
gccagatca tctcgcgctg ggtcactaaa cgcggtgtgc tgccagttac cacctottca 780
aagcctcagc gcattagcga tgctcagaac ctgttttctc tcgacctgac agcgggaagag 840
gttgataaaa tcacggagct gggtctggaa catgaaccgc tgcgcctgta ctggaataaa 900
ttgtatggca gatataacta cgccgccag aaagtgtaat ga 942

<210> 208
<211> 313
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 208
Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
1 5 10 15
Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Lys Trp Tyr Lys Ser Glu
20 25 30
Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
35 40 45
Ala Leu Glu Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Ile Tyr
50 55 60
Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
65 70 75 80
Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
85 90 95
Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
100 105 110
Thr Asp Tyr Val Asp Leu Tyr Leu Leu His Ser Pro Phe Val Ser Lys
115 120 125
Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
130 135 140
Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Thr
145 150 155 160

Val	Glu	Asp	Leu	Gln	Arg	Ile	Leu	Lys	Val	Ala	Glu	Val	Lys	Pro	Gln
				165					170					175	
Val	Asn	Gln	Ile	Glu	Phe	Ser	Pro	Phe	Leu	Gln	Asn	Gln	Thr	Pro	Gly
			180					185					190		
Ile	Tyr	Lys	Phe	Cys	Gln	Glu	His	Asp	Ile	Leu	Val	Glu	Ala	Tyr	Ser
		195					200					205			
Pro	Leu	Gly	Pro	Leu	Arg	Lys	Lys	Thr	Ala	Gln	Asp	Asp	Ser	Gln	Pro
	210					215					220				
Phe	Phe	Glu	Tyr	Val	Lys	Glu	Leu	Ser	Glu	Lys	Tyr	Asn	Lys	Ser	Glu
225					230					235					240
Ala	Gln	Ile	Ile	Leu	Arg	Trp	Val	Thr	Lys	Arg	Gly	Val	Leu	Pro	Val
				245					250					255	
Thr	Thr	Ser	Ser	Lys	Pro	Gln	Arg	Ile	Ser	Asp	Ala	Gln	Asn	Leu	Phe
			260					265					270		
Ser	Phe	Asp	Leu	Thr	Ala	Glu	Glu	Val	Asp	Lys	Ile	Thr	Glu	Leu	Gly
		275					280					285			
Leu	Glu	His	Glu	Pro	Leu	Arg	Leu	Tyr	Trp	Asn	Lys	Leu	Tyr	Gly	Arg
	290					295					300				
Tyr	Asn	Tyr	Ala	Ala	Gln	Lys	Val								
305					310										

<210> 209
 <211> 942
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 209
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 atcatcggca ctggtacaaa atggtataaa agtgaagaaa ctgacgcgac cttctccaat 120
 agtctggttg aacaaatogt gtatgcgttg aaactgccgg ggattatcca catcgacgcc 180
 gcggagattt atcgcaccta cccggaagtg ggtaaagcac tgtccctgac cgaagagcct 240
 cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactccoct 300
 gcggacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
 attcattccc cgtttgtttc gaaggaagtg aatggcttaa gcttagaaga ggcttggaag 420
 gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggttc caatttcaca 480
 gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
 gagttctctc cgttcctgca aaaccaaaca ccaggcattt gcaaattctg tcaggagcac 600
 gatatcctgg tggaagcata ttctccgctg ggcccgcgtc ggaagaaaac cgcgcaggat 660
 gacagccaac cattttttga gtacgtcaaa gaattgagcg aaaaataccg caaatccgag 720
 gccagatca tccctgcgtg ggtcactaaa cgcggtgtgc tgccagttac cacctcttca 780
 aagcctcagc gcattagcga tgctcagaac ctgttttcct tcgacctgac agcggaagag 840
 gttgataaaa tcacggagct gggtctggaa catgaaccgc tgcgcctgta ctggaataaa 900
 ttgtatggca aatataacta cgccgccag aaagtgtaat ga 942

<210> 210
 <211> 313
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 210
 Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
 1 5 10 15
 Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Lys Trp Tyr Lys Ser Glu


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aagcctcagc gcattagcga tgctcagaac ctgttttcoct tcgacctgac agcgggaagag 840
gttgataaaa tcacggagct gggctctggaa catgaaccgc tgcgcctgta ctggaataaa 900
ttgtatggca aatataactc tgccgcccaa aaagtgtaat ga 942

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<210> 212
 <211> 313
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 212

Met	Ser	Phe	His	Gln	Gln	Phe	Phe	Thr	Leu	Asn	Asn	Gly	Asn	Lys	Ile
1			5						10				15		
Pro	Ala	Ile	Ala	Ile	Ile	Gly	Thr	Gly	Thr	Lys	Trp	Tyr	Lys	Asn	Glu
			20					25					30		
Glu	Thr	Asp	Ala	Thr	Phe	Ser	Asn	Ser	Leu	Val	Glu	Gln	Ile	Val	Tyr
		35					40				45				
Ala	Leu	Lys	Leu	Pro	Gly	Ile	Ile	His	Ile	Asp	Ala	Ala	Glu	Ile	Tyr
	50				55					60					
Arg	Thr	Tyr	Pro	Glu	Val	Gly	Lys	Ala	Leu	Ser	Leu	Thr	Glu	Lys	Pro
65				70					75					80	
Arg	Asn	Ala	Ile	Phe	Leu	Thr	Asp	Lys	Tyr	Ser	Pro	Gln	Ile	Lys	Met
			85					90					95		
Ser	Asp	Ser	Pro	Ala	Asp	Gly	Leu	Asp	Leu	Ala	Leu	Lys	Lys	Met	Gly
			100				105						110		
Thr	Asp	Tyr	Val	Asp	Leu	Tyr	Leu	Leu	His	Ser	Pro	Phe	Val	Ser	Lys
		115				120						125			
Glu	Val	Asn	Gly	Leu	Ser	Leu	Glu	Glu	Ala	Trp	Lys	Asp	Met	Glu	Gln
	130					135					140				
Leu	Tyr	Lys	Ser	Gly	Lys	Ala	Lys	Asn	Ile	Gly	Val	Ser	Asn	Phe	Thr
145				150					155					160	
Val	Glu	Asp	Leu	Gln	Arg	Ile	Leu	Lys	Val	Ala	Glu	Val	Lys	Pro	Gln
			165					170					175		
Val	Asn	Gln	Ile	Glu	Phe	Ser	Pro	Phe	Leu	Gln	Asn	Gln	Thr	Pro	Asp
		180					185						190		
Ile	Tyr	Lys	Phe	Cys	Gln	Glu	His	Asp	Ile	Leu	Val	Glu	Ala	Tyr	Ser
	195					200						205			
Pro	Leu	Gly	Pro	Leu	Arg	Lys	Lys	Thr	Ala	Gln	Asp	Asp	Ser	Gln	Pro
	210				215						220				
Phe	Phe	Glu	Tyr	Val	Lys	Glu	Leu	Ser	Glu	Lys	Tyr	Asn	Lys	Ser	Glu
225				230					235					240	
Ala	Gln	Ile	Ile	Leu	Arg	Trp	Val	Thr	Lys	Arg	Gly	Val	Leu	Pro	Val
			245					250					255		
Thr	Thr	Ser	Ser	Lys	Pro	Gln	Arg	Ile	Ser	Asp	Ala	Gln	Asn	Leu	Phe
		260					265						270		
Ser	Phe	Asp	Leu	Thr	Ala	Glu	Glu	Val	Asp	Lys	Ile	Thr	Glu	Leu	Gly
	275					280						285			
Leu	Glu	His	Glu	Pro	Leu	Arg	Leu	Tyr	Trp	Asn	Lys	Leu	Tyr	Gly	Lys
	290				295					300					
Tyr	Asn	Ser	Ala	Ala	Gln	Lys	Val								
305					310										

<210> 213
 <211> 942
 <212> DNA
 <213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 213
atgtcttttc accaacagtt tttcacgctg aacaacggca ataaaatccc ggcgattgcc 60
atcatcggca ctggtacagc ctggtataaa agtgaagaaa ctgacgcgac ctctctccaat 120
agtctgggtg aacaaatcgt gtatgcgttg aaactgccgg ggattatcca catcgacgcc 180
gcggagattt atcgcaccta cccggaagtg ggtaaagcac tgtccctgac cgaaaagcct 240
cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactccct 300
gcggacggtc tggatttagc attgaagaaa atgggtacag attatggtga tttatatctg 360
ttacattccc cgtttgtttc gaaggaagtg aatggcttaa gcttagaaga ggcttgga 420
gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggtttc caatttcaca 480
gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
gagttctctc cgttcctgca aaaccaaaca ccaggcattt gcaaattctg tcaggagcac 600
gatatcctgg tgggaagcata ttctccgctg ggcccgtctg ggaagaaaac cgcgcaggat 660
gacagccaac ctttttttga gtacgtcaaa gaattgagcg aaaaataccg caaatccgag 720
gccagatca tcctgcgctg ggtcactaaa cgcggtgtgc tgccagttac cacctcttca 780
aagcctcagc gcattagcga tgctcagaac ctgttttcct tcgacctgac agcgggaagag 840
gttgataaaa tcacggagct gggctcggaa catgaaccgc tgccgcctgta ctggaataaa 900
ttgtatggca aatataacta cgcgcgccag aaagtgtaat ga 942

<210> 214
<211> 313
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 214
Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
1 5 10 15
Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Ala Trp Tyr Lys Ser Glu
20 25 30
Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
35 40 45
Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Ile Tyr
50 55 60
Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
65 70 75 80
Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
85 90 95
Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
100 105 110
Thr Asp Tyr Val Asp Leu Tyr Leu Leu His Ser Pro Phe Val Ser Lys
115 120 125
Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
130 135 140
Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Thr
145 150 155 160
Val Glu Asp Leu Gln Arg Ile Leu Lys Val Ala Glu Val Lys Pro Gln
165 170 175
Val Asn Gln Ile Glu Phe Ser Pro Phe Leu Gln Asn Gln Thr Pro Gly
180 185 190
Ile Cys Lys Phe Cys Gln Glu His Asp Ile Leu Val Glu Ala Tyr Ser
195 200 205
Pro Leu Gly Pro Leu Arg Lys Lys Thr Ala Gln Asp Asp Ser Gln Pro
210 215 220
Phe Phe Glu Tyr Val Lys Glu Leu Ser Glu Lys Tyr Arg Lys Ser Glu
225 230 235 240

Ala	Gln	Ile	Ile	Leu	Arg	Trp	Val	Thr	Lys	Arg	Gly	Val	Leu	Pro	Val
				245					250					255	
Thr	Thr	Ser	Ser	Lys	Pro	Gln	Arg	Ile	Ser	Asp	Ala	Gln	Asn	Leu	Phe
			260					265					270		
Ser	Phe	Asp	Leu	Thr	Ala	Glu	Glu	Val	Asp	Lys	Ile	Thr	Glu	Leu	Gly
		275					280					285			
Leu	Glu	His	Glu	Pro	Leu	Arg	Leu	Tyr	Trp	Asn	Lys	Leu	Tyr	Gly	Lys
	290					295					300				
Tyr	Asn	Tyr	Ala	Ala	Gln	Lys	Val								
305					310										

<210> 215
 <211> 942
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 215
 atgtcttttc accaacagtt ttccacgctg aacaacggca ataaaatccc ggcgattgcc 60
 atcatcggca ctggtacaaa atggtataaa aatgaagaaa ctgacgcgac cttctccaat 120
 agtctggttg aacaaatcgt gtatgcgttg aaactgccgg ggattatcca catcgacgcc 180
 gcggagattt atcgcaccta cccggaagtg ggtaaagcac tgtccctgac caaaaagcct 240
 cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactcccct 300
 gcggacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
 attcattccc cgtttgtttc gaaggaagtg aatggcttaa gcttagaaga ggcttggaaa 420
 gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggtttc caatttcaca 480
 gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
 gagttctctc cgttcctgca aaaccaaaca ccaggcattt ataaattctg tcaggagcac 600
 gatatcctgg tggaagcata ttctccgctg ggcccgtctg ggaagagAAC cgcgcaggat 660
 gacagccaac cattctttga gtacgtcaaa gaattgagcg aaaaatacgg caaatccgag 720
 gccagatca tcctgcgctg ggtcactaaa cgcggtgtgc tgccagttac cacctcttca 780
 aagcctcagc gcattagoga tgctcagaac ctgttttctt togacctgac agcgggaagag 840
 gttgataaaa tcacggagct gggtctggaa catgaaccgc tgcgcctgta ctggaataaa 900
 ttgtatggca aatataacta cgccgccag aaagtgtaat ga 942

<210> 216
 <211> 313
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 216
 Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
 1 5 10 15
 Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Lys Trp Tyr Lys Asn Glu
 20 25 30
 Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
 35 40 45
 Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Ile Tyr
 50 55 60
 Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Lys Lys Pro
 65 70 75 80
 Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
 85 90 95
 Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly

			100					105					110				
Thr	Asp	Tyr	Val	Asp	Leu	Tyr	Leu	Ile	His	Ser	Pro	Phe	Val	Ser	Lys		
	115						120					125					
Glu	Val	Asn	Gly	Leu	Ser	Leu	Glu	Glu	Ala	Trp	Lys	Asp	Met	Glu	Gln		
	130					135					140						
Leu	Tyr	Lys	Ser	Gly	Lys	Ala	Lys	Asn	Ile	Gly	Val	Ser	Asn	Phe	Thr		
145					150					155					160		
Val	Glu	Asp	Leu	Gln	Arg	Ile	Leu	Lys	Val	Ala	Glu	Val	Lys	Pro	Gln		
			165					170					175				
Val	Asn	Gln	Ile	Glu	Phe	Ser	Pro	Phe	Leu	Gln	Asn	Gln	Thr	Pro	Gly		
	180							185					190				
Ile	Tyr	Lys	Phe	Cys	Gln	Glu	His	Asp	Ile	Leu	Val	Glu	Ala	Tyr	Ser		
	195						200					205					
Pro	Leu	Gly	Pro	Leu	Arg	Lys	Arg	Thr	Ala	Gln	Asp	Asp	Ser	Gln	Pro		
	210					215					220						
Phe	Phe	Glu	Tyr	Val	Lys	Glu	Leu	Ser	Glu	Lys	Tyr	Gly	Lys	Ser	Glu		
225					230					235					240		
Ala	Gln	Ile	Ile	Leu	Arg	Trp	Val	Thr	Lys	Arg	Gly	Val	Leu	Pro	Val		
			245					250					255				
Thr	Thr	Ser	Ser	Lys	Pro	Gln	Arg	Ile	Ser	Asp	Ala	Gln	Asn	Leu	Phe		
		260					265						270				
Ser	Phe	Asp	Leu	Thr	Ala	Glu	Glu	Val	Asp	Lys	Ile	Thr	Glu	Leu	Gly		
	275					280						285					
Leu	Glu	His	Glu	Pro	Leu	Arg	Leu	Tyr	Trp	Asn	Lys	Leu	Tyr	Gly	Lys		
	290					295				300							
Tyr	Asn	Tyr	Ala	Ala	Gln	Lys	Val										
305					310												

<210> 217
 <211> 942
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 217
 atgtcttttc accaacagtt tttcacgctg aacaacggca ataaaatccc ggcgattgcc 60
 atcatcggca ctggtacaaa atggtataaa aatgaagaaa ctgacgcgac cttctccaat 120
 agtctggttg aacaaatcgt gtatgcgttg aaactgcggg ggattatcca catcgacgcc 180
 gcggagattt atcgcaccta cccggaagtg ggtaaagcac tgcccctgac cgaaaagcct 240
 cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactccoct 300
 gcggacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
 ttacattccc cgtttgtttc gaaggaagtg aatggcttaa gottagaaga ggottggaaa 420
 gatattggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggttc caatttcaca 480
 gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
 gagttctctc cgttcctgca aaaccaaaca ccaggcattt ataaattctg tcaggagcac 600
 gatattcctg tggaagcata ctctccgctg ggcccgtgac ggaagaaaac cgcgcaggat 660
 gacagccaac ctttttttga gtacgtcaaa gaattgagcg aaaaatacgg caaatccgag 720
 gccagatca tcttcgcctg ggtcactaaa cgcgggtgtg tgccagttac cacctcttca 780
 aagcctcagc gcattagcga tgctcagaac ctgttttctc tcgaactgac agcgggaagag 840
 gttgataaaa tcacggagct ggggtctggaa catgaaccgc tgcgcctgta ctggaataaa 900
 ttgtatggca aatataacta cgccgcccag aaagtgtaat ga 942

<210> 218
 <211> 313
 <212> PRT
 <213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 218

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Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
1      5      10      15
Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Lys Trp Tyr Lys Asn Glu
      20      25      30
Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
      35      40      45
Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Ile Tyr
      50      55      60
Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
65      70      75      80
Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
      85      90      95
Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
      100     105     110
Thr Asp Tyr Val Asp Leu Tyr Leu Leu His Ser Pro Phe Val Ser Lys
      115     120     125
Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
      130     135     140
Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Thr
145     150     155     160
Val Glu Asp Leu Gln Arg Ile Leu Lys Val Ala Glu Val Lys Pro Gln
      165     170     175
Val Asn Gln Ile Glu Phe Ser Pro Phe Leu Gln Asn Gln Thr Pro Gly
      180     185     190
Ile Tyr Lys Phe Cys Gln Glu His Asp Ile Leu Val Glu Ala Tyr Ser
      195     200     205
Pro Leu Gly Pro Leu Arg Lys Lys Thr Ala Gln Asp Asp Ser Gln Pro
      210     215     220
Phe Phe Glu Tyr Val Lys Glu Leu Ser Glu Lys Tyr Gly Lys Ser Glu
225     230     235     240
Ala Gln Ile Ile Leu Arg Trp Val Thr Lys Arg Gly Val Leu Pro Val
      245     250     255
Thr Thr Ser Ser Lys Pro Gln Arg Ile Ser Asp Ala Gln Asn Leu Phe
      260     265     270
Ser Phe Asp Leu Thr Ala Glu Glu Val Asp Lys Ile Thr Glu Leu Gly
      275     280     285
Leu Glu His Glu Pro Leu Arg Leu Tyr Trp Asn Lys Leu Tyr Gly Lys
      290     295     300
Tyr Asn Tyr Ala Ala Gln Lys Val
305      310
```

<210> 219

<211> 942

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 219

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atgtcttttt accaacagtt tttaacgctg aacaacggca ataaaatccc ggcgattgcc 60
atcatcggca ctggtacaaa atggtataaa aatgaagaaa ctgacgcgac cttctccaat 120
agtctggttg aacaaatcgt gtatgcgttg aaactgccgg ggattgtcca catcgacgcc 180
gcggagattt atcgcaccta cccggaagtg ggtaaagcac tgtccctgac cgaaaagcct 240
cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactcccct 300
gcggacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
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<210> 221
 <211> 942
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 221
 atgtcttttt accaacagtt tttcacactg aacaacggca ataaaatccc ggcgattgcc 60
 atcatcggca ctggtacaaa atggtataaa agtgaagaaa ctgacgcgac cttctccaat 120
 agtctggttg aacaaatcgt gtatgcgttg aaactgccgg ggattatcca catcgacgcc 180
 gcggagggtt atcgcaccta cccggaagtg ggtaaagcac tgtccctgac cgaaaagcct 240
 cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactcccct 300
 gcggacgggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
 ttacattccc cgtttggttc gaaggaagtg aatggcttaa gcttagaaga ggcttggaaa 420
 gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggttc caatttcaca 480
 gtggaagacc tgcaacgtat cctgaaagtc gotgaagtta aacctcaggt caaccagatt 540
 gagttctctc cgttcctgca aaaccaaaaca ccaggcattt ataaattctg tcaggagcac 600
 gatatcctgg tgggaagcata ttctccgctg ggcccgcctgc ggaagaaaac cgcgcaggat 660
 gacagccaac cattttttga gtacgtcaaa gaattgagcg aaaaatacaa caaatccgag 720
 gcccgatca tctgcgctg ggtcactaaa cgcggtgtgc tgccagttac cacctcttca 780
 aagcctcagc gcattagcga tgctcagaac ctgttttctc tcgacctgac agcgggaagag 840
 gttgataaaa tcacggagct gggctctggaa catgaaccgc tcgcctgta ctggaataaa 900
 ttgtatggca aatataacta cgcgcgccag aaagtgtaat ga 942

<210> 222
 <211> 313
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 222
 Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
 1 5 10 15
 Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Lys Trp Tyr Lys Ser Glu
 20 25 30
 Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
 35 40 45
 Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Val Tyr
 50 55 60
 Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
 65 70 75 80
 Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
 85 90 95
 Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
 100 105 110
 Thr Asp Tyr Val Asp Leu Tyr Leu Leu His Ser Pro Phe Val Ser Lys
 115 120 125
 Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
 130 135 140
 Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Thr
 145 150 155 160
 Val Glu Asp Leu Gln Arg Ile Leu Lys Val Ala Glu Val Lys Pro Gln
 165 170 175
 Val Asn Gln Ile Glu Phe Ser Pro Phe Leu Gln Asn Gln Thr Pro Gly

Ala	Leu	Lys	Leu	Pro	Gly	Ile	Ile	His	Ile	Asp	Ala	Ala	Glu	Ile	Tyr
50						55					60				
Arg	Thr	Tyr	Pro	Glu	Val	Gly	Lys	Ala	Leu	Ser	Leu	Thr	Glu	Lys	Pro
65					70					75					80
Arg	Asn	Ala	Ile	Phe	Leu	Thr	Asp	Lys	Tyr	Ser	Pro	Gln	Ile	Lys	Met
			85						90					95	
Ser	Asp	Ser	Pro	Ala	Asp	Gly	Leu	Asp	Leu	Ala	Leu	Lys	Lys	Met	Gly
			100					105					110		
Thr	Asp	Tyr	Val	Asp	Leu	Tyr	Leu	Leu	His	Ser	Pro	Phe	Val	Ser	Lys
		115					120					125			
Glu	Val	Asn	Gly	Leu	Ser	Leu	Glu	Glu	Ala	Trp	Lys	Asp	Met	Glu	Gln
	130					135					140				
Leu	Tyr	Lys	Ser	Gly	Lys	Ala	Lys	Asn	Ile	Gly	Val	Ser	Asn	Phe	Thr
145					150					155					160
Val	Glu	Asp	Leu	Gln	Arg	Ile	Leu	Lys	Val	Ala	Glu	Val	Lys	Pro	Gln
				165					170					175	
Val	Asn	Gln	Ile	Glu	Phe	Ser	Pro	Phe	Leu	Gln	Asn	Gln	Thr	Pro	Gly
			180					185					190		
Ile	Tyr	Lys	Phe	Cys	Gln	Glu	His	Asp	Ile	Leu	Val	Glu	Ala	Tyr	Ser
	195						200					205			
Pro	Leu	Gly	Pro	Leu	Arg	Lys	Lys	Thr	Ala	Gln	Asp	Asp	Ser	Gln	Pro
	210					215					220				
Phe	Phe	Glu	Tyr	Val	Lys	Glu	Leu	Ser	Glu	Lys	Tyr	Asn	Lys	Ser	Glu
225					230					235					240
Ala	Gln	Ile	Ile	Leu	Arg	Trp	Val	Thr	Arg	Arg	Gly	Val	Leu	Pro	Val
				245					250					255	
Thr	Thr	Ser	Ser	Lys	Pro	Gln	Arg	Ile	Ser	Asp	Ala	Gln	Asn	Leu	Phe
			260					265					270		
Ser	Phe	Asp	Leu	Thr	Ala	Glu	Glu	Val	Asp	Lys	Ile	Thr	Glu	Leu	Gly
	275					280						285			
Leu	Glu	His	Glu	Pro	Leu	Arg	Leu	Tyr	Trp	Asn	Lys	Leu	Tyr	Gly	Lys
	290					295					300				
Tyr	Asn	Tyr	Ala	Ala	Gln	Lys	Val								
305					310										

<210> 225

<211> 942

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 225

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atgtcttttc accaacagtt tttcacgctg aacaacggca ataaaatccc ggcgattgcc 60
atcatcggca ctggtacaaa atggtataaa aatgaagaaa ctgacgcgac cttctccaat 120
agtctggttg aacaaatcgt gtatgcgttg aaactgccgg ggattatcca catcgacgcc 180
gcggagattt atcgcaccta cccggaagtg ggtaaagcac tgtccctgac cgaaaagcct 240
cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactccoct 300
gcggacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
ttacattccc cgtttgtttc gaaggaaggg aatggcttaa gcttagaaga ggcttggaaa 420
gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggtttc caatttcaca 480
gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
gagttctctc cgttcctgca aaaccaaaaca ccaggcattt ataaattctg tcaggagcac 600
gatatcctgg tggaagcata ttctccgctg ggcccgcctg ggaagaaaac cgcgcaggat 660
gacagccaac cattttttga gtacgtcaaa gaattgagcg aaaaatacaa caaatccgag 720
gccagatca tcttgcgctg ggtcactaaa cgcggtgtgc tgccagttac cacctcttca 780
aagcctcagc gcatttagcga tgctcagaac ctgttttccct tcgacctgac agcgggaagag 840
gttgataaaa tcacggagct gggtctggaa catgaaccgc tcgcgcctgta ctggaataaa 900
ttgtatggca aatataacta cgccgccag aaagtgtaat ga 942

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<210> 226
 <211> 313
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 226
 Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
 1 5 10 15
 Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Lys Trp Tyr Lys Asn Glu
 20 25 30
 Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
 35 40 45
 Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Ile Tyr
 50 55 60
 Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
 65 70 75 80
 Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
 85 90 95
 Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
 100 105 110
 Thr Asp Tyr Val Asp Leu Tyr Leu Leu His Ser Pro Phe Val Ser Lys
 115 120 125
 Glu Gly Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
 130 135 140
 Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Thr
 145 150 155 160
 Val Glu Asp Leu Gln Arg Ile Leu Lys Val Ala Glu Val Lys Pro Gln
 165 170 175
 Val Asn Gln Ile Glu Phe Ser Pro Phe Leu Gln Asn Gln Thr Pro Gly
 180 185 190
 Ile Tyr Lys Phe Cys Gln Glu His Asp Ile Leu Val Glu Ala Tyr Ser
 195 200 205
 Pro Leu Gly Pro Leu Arg Lys Lys Thr Ala Gln Asp Asp Ser Gln Pro
 210 215 220
 Phe Phe Glu Tyr Val Lys Glu Leu Ser Glu Lys Tyr Asn Lys Ser Glu
 225 230 235 240
 Ala Gln Ile Ile Leu Arg Trp Val Thr Lys Arg Gly Val Leu Pro Val
 245 250 255
 Thr Thr Ser Ser Lys Pro Gln Arg Ile Ser Asp Ala Gln Asn Leu Phe
 260 265 270
 Ser Phe Asp Leu Thr Ala Glu Glu Val Asp Lys Ile Thr Glu Leu Gly
 275 280 285
 Leu Glu His Glu Pro Leu Arg Leu Tyr Trp Asn Lys Leu Tyr Gly Lys
 290 295 300
 Tyr Asn Tyr Ala Ala Gln Lys Val
 305 310

<210> 227
 <211> 942
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 227

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atgtcttttc accaacagtt tttcacgctg aacaacggca ataaaatccc ggcgattgcc 60
atcatcggca ctggtacaaa atggtataaa aatgaagaaa ctgacgcgac cttctccaat 120
agtcctggttg aacaaatcgt gtatgcgttg aaactgccgg ggattatcca catcgacgcc 180
gcggagattt atcgcaccta cccggaagtg ggtaaagcac tgccctgac cgaaaagcct 240
cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactcccct 300
gcggacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
attcattccc cgtttgtttc gaaggaagtg aatggcttaa gcttagaaga ggcttgaaa 420
gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcggggtttc caatttcaca 480
gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
gagttctctc cgttcctgca aaaccaaaca ccaggcattt ataaattctg tcaggagcac 600
gatatcctgg tggaaagcata ttctccgctg ggcccgtgc ggaagaaaac cgcgcaggat 660
gacagccaac ctttttttga gtacgtcaaa gaattgagcg aaaaatacaa caaatccgag 720
gccagatca tcttgccgtg ggtcactaaa cgcggcgtgc tgccagttac cacctcttca 780
aagcctcagc gcattagcga tgctcagaac ctgttttctt tcgacctgac agcgggaagag 840
gttgataaaa tcacggagct gggctctggaa catgaaccgc tgcgcctgta ctggaataaa 900
ttgatggca aatataacta cgccgccag aaagtgtaat ga 942
```

<210> 228

<211> 313

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 228

```
Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
1          5          10          15
Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Lys Trp Tyr Lys Asn Glu
20          25          30
Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
35          40          45
Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Ile Tyr
50          55          60
Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
65          70          75          80
Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
85          90          95
Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
100          105          110
Thr Asp Tyr Val Asp Leu Tyr Leu Ile His Ser Pro Phe Val Ser Lys
115          120          125
Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
130          135          140
Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Thr
145          150          155          160
Val Glu Asp Leu Gln Arg Ile Leu Lys Val Ala Glu Val Lys Pro Gln
165          170          175
Val Asn Gln Ile Glu Phe Ser Pro Phe Leu Gln Asn Gln Thr Pro Gly
180          185          190
Ile Tyr Lys Phe Cys Gln Glu His Asp Ile Leu Val Glu Ala Tyr Ser
195          200          205
Pro Leu Gly Pro Leu Arg Lys Lys Thr Ala Gln Asp Asp Ser Gln Pro
210          215          220
Phe Phe Glu Tyr Val Lys Glu Leu Ser Glu Lys Tyr Asn Lys Ser Glu
225          230          235          240
Ala Gln Ile Ile Leu Arg Trp Val Thr Lys Arg Gly Val Leu Pro Val
245          250          255
Thr Thr Ser Ser Lys Pro Gln Arg Ile Ser Asp Ala Gln Asn Leu Phe
```


Glu	Val	Asn	Gly	Leu	Ser	Leu	Glu	Glu	Ala	Trp	Lys	Asp	Met	Glu	Gln
130						135					140				
Leu	Tyr	Lys	Ser	Gly	Lys	Ala	Lys	Asn	Ile	Gly	Val	Ser	Asn	Phe	Thr
145					150					155					160
Val	Glu	Asp	Leu	Gln	Arg	Ile	Leu	Lys	Val	Ala	Glu	Val	Lys	Pro	Gln
			165						170					175	
Val	Asn	Gln	Ile	Glu	Phe	Ser	Pro	Phe	Leu	Gln	Asn	His	Thr	Pro	Gly
			180					185					190		
Ile	Tyr	Lys	Phe	Cys	Gln	Glu	His	Asp	Ile	Leu	Val	Glu	Ala	Tyr	Ser
		195					200					205			
Pro	Leu	Gly	Pro	Leu	Arg	Lys	Lys	Thr	Ala	Gln	Asp	Asp	Ser	Gln	Pro
	210					215					220				
Phe	Phe	Glu	Tyr	Val	Lys	Glu	Leu	Ser	Glu	Lys	Tyr	Asn	Lys	Ser	Glu
225					230					235					240
Ala	Gln	Ile	Ile	Leu	Arg	Trp	Val	Thr	Lys	Arg	Gly	Val	Leu	Pro	Val
			245						250					255	
Thr	Thr	Ser	Ser	Lys	Pro	Gln	Arg	Ile	Ser	Asp	Ala	Gln	Asn	Leu	Phe
			260					265					270		
Ser	Phe	Asp	Leu	Thr	Ala	Glu	Glu	Val	Asp	Lys	Ile	Thr	Glu	Arg	Gly
		275					280					285			
Leu	Glu	His	Glu	Pro	Leu	Arg	Leu	Tyr	Trp	Asn	Lys	Leu	Tyr	Gly	Lys
	290					295					300				
Tyr	Asn	Tyr	Ala	Ala	Gln	Lys	Val								
305					310										

<210> 231
 <211> 942
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 231
 atgtcttttc accaacagtt ttccacgctg aacaacggca ataaaatccc ggcgattgcc 60
 atcatcggca ctggtacaaa atggtataaa aatgaagaaa ctgacgcgac cttctccaat 120
 agtctggttg aacaaatcgt gtatgcgttg aaactgcgag ggattatcca catogacgcc 180
 gcggagattt atgcaccta cccggaagtg ggtaaaccac tgtccctgac cgaaaagcct 240
 cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactcccct 300
 gcggacggtc tggatttagc attgaagaaa atgggtacag attatggtga tttatatctg 360
 ttacattccc cgtttgtttc gaaggaagtg aatggcttaa gcttagaaga ggcttgga 420
 gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggttc caatttcaca 480
 gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
 gagttctctc cgttcctgca aaaccaaaca ccaggcattt ataaattctg tcaggagcac 600
 ggtatcctgg tggaaagcata ttctccgctg ggcccgtgac ggaagaaaac cgcgcaggat 660
 gacagccaac ctttttttga gtacgtcaaa gaattgagcg aaaaatacgg caaatccgag 720
 gccagatca tcttgcgctg ggtcactaaa cgcggtgtgc tgccagttac cacctcttca 780
 aagcctcagc gcattagcga tgctcagaac ctgttttctc tcgacctgac agcgggaagag 840
 gttgataaaa tcacggagct gggctctggaa catgaaccgc tcgcgctgta ctggaataaa 900
 ttgtatggca aatataacta cgccgccag aaagtgtaat ga 942

<210> 232
 <211> 313
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 232

```
Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
1      5      10      15
Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Lys Trp Tyr Lys Asn Glu
      20      25      30
Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
      35      40      45
Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Ile Tyr
      50      55      60
Arg Thr Tyr Pro Glu Val Gly Lys Pro Leu Ser Leu Thr Glu Lys Pro
65      70      75      80
Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
      85      90      95
Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
      100     105     110
Thr Asp Tyr Val Asp Leu Tyr Leu Leu His Ser Pro Phe Val Ser Lys
      115     120     125
Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
      130     135     140
Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Thr
145     150     155     160
Val Glu Asp Leu Gln Arg Ile Leu Lys Val Ala Glu Val Lys Pro Gln
      165     170     175
Val Asn Gln Ile Glu Phe Ser Pro Phe Leu Gln Asn Gln Thr Pro Gly
      180     185     190
Ile Tyr Lys Phe Cys Gln Glu His Gly Ile Leu Val Glu Ala Tyr Ser
      195     200     205
Pro Leu Gly Pro Leu Arg Lys Lys Thr Ala Gln Asp Asp Ser Gln Pro
      210     215     220
Phe Phe Glu Tyr Val Lys Glu Leu Ser Glu Lys Tyr Gly Lys Ser Glu
225     230     235     240
Ala Gln Ile Ile Leu Arg Trp Val Thr Lys Arg Gly Val Leu Pro Val
      245     250     255
Thr Thr Ser Ser Lys Pro Gln Arg Ile Ser Asp Ala Gln Asn Leu Phe
      260     265     270
Ser Phe Asp Leu Thr Ala Glu Glu Val Asp Lys Ile Thr Glu Leu Gly
      275     280     285
Leu Glu His Glu Pro Leu Arg Leu Tyr Trp Asn Lys Leu Tyr Gly Lys
      290     295     300
Tyr Asn Tyr Ala Ala Gln Lys Val
305      310
```

<210> 233

<211> 942

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 233

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atgtcttttt accaacagtt tttcacgctg aacaacggca ataaaatccc ggcgattgcc 60
atcatcggca ctggtacaaa atggtataaa aatgaagaaa ctgacgcgac cttctccaat 120
agtctggttg aacaaatcgt gtatgcgttg aaactgcogg ggattatcca catogaogcc 180
gcgagagatt atcgcaccta cccggaagtg ggtaaagcac tgtccctgac cgaaaagcct 240
cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactccoct 300
gcggacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
ttacattccc cgtttgtttc gaaggaagtg aatggcttaa gcttagaaga ggcttggaaa 420
gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggttc caatttcaca 480
gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
```

```

gagttctctc cgttcctgca aaaccaaaca ccaggcattt ataaattctg tcaggagcac 600
gatatcctgg tggaagcata ttctccgctg ggcccgtgc ggaagaaaac cgcgcaggat 660
gacagccaac ctttttttga gtacgtcaaa gaattgagcg aaaaatacaa caaatccgag 720
gccagatca tcctgcgctg ggtcactaaa cgcggtgtgc tgccagttac cacctcttca 780
aagcctcagc gcattagcga tgctcagaac ctgttttcct tcgacctgac agcgggaagag 840
gttgataaaa tcacggagct gggctctggaa catgaaccgc tgcgcctgta ctggaataaa 900
ttgtatggca aatataacca cgccgccag aaagtgtaat ga 942

```

<210> 234

<211> 313

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 234

```

Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
1          5          10          15
Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Lys Trp Tyr Lys Asn Glu
20          25          30
Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
35          40          45
Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Ile Tyr
50          55          60
Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
65          70          75          80
Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
85          90          95
Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
100         105         110
Thr Asp Tyr Val Asp Leu Tyr Leu Leu His Ser Pro Phe Val Ser Lys
115         120         125
Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
130         135         140
Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Thr
145         150         155         160
Val Glu Asp Leu Gln Arg Ile Leu Lys Val Ala Glu Val Lys Pro Gln
165         170         175
Val Asn Gln Ile Glu Phe Ser Pro Phe Leu Gln Asn Gln Thr Pro Gly
180         185         190
Ile Tyr Lys Phe Cys Gln Glu His Asp Ile Leu Val Glu Ala Tyr Ser
195         200         205
Pro Leu Gly Pro Leu Arg Lys Lys Thr Ala Gln Asp Asp Ser Gln Pro
210         215         220
Phe Phe Glu Tyr Val Lys Glu Leu Ser Glu Lys Tyr Asn Lys Ser Glu
225         230         235         240
Ala Gln Ile Ile Leu Arg Trp Val Thr Lys Arg Gly Val Leu Pro Val
245         250         255
Thr Thr Ser Ser Lys Pro Gln Arg Ile Ser Asp Ala Gln Asn Leu Phe
260         265         270
Ser Phe Asp Leu Thr Ala Glu Glu Val Asp Lys Ile Thr Glu Leu Gly
275         280         285
Leu Glu His Glu Pro Leu Arg Leu Tyr Trp Asn Lys Leu Tyr Gly Lys
290         295         300
Tyr Asn His Ala Ala Gln Lys Val
305          310

```

<210> 235

<211> 942
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 235
atgtcttttc accaacagtt ttccacgctg aacaacggca ataaaatccc ggcgattgcc 60
atcatcggca ctggtacaaa atggtataaa agtgaagaaa ctgacgcgac cttctccaat 120
agtctggttg aacaaatcgt gtatgcgttg aaactgccgg ggattatcca catcgacgcc 180
gcggagattt atcgcaccta cccggaagtg ggtaaagcac tgccctgac cgaaaagcct 240
cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactcccct 300
gcggacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
attcattccc cgtttgttgc gaaggaagtg aatggcttaa gcttagaaga ggcttggaag 420
gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggttc caatttcaca 480
gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
gagttctctc cgttctctgca aaaccaaaaca ccaggcattt gcaaattctg tcaggagcac 600
gatatcctgg tgggaagcata ttctccgctg ggcccgcctgc ggaagaaaac cgcgcaggat 660
gacagccaac catttttttga gtacgtcaaa gaattgagcg aaaaatacaa caaatccgag 720
gccagatca tcttgccgtg ggtcactaaa cgcgggtgtgc tgccagttac cacctcttca 780
aagcctcagc gcattagcga tgctcagaac ctgttttctc tcgacctgac agcgggaagag 840
gttgataaaa tcacggagct gggtttgga catgaaccgc tcgcctgta ctggaataaa 900
ttgtatggca aatataacta cgccgccag aaagtgtaat ga 942

<210> 236
<211> 313
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 236
Met Ser Phe His Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
1 5 10 15
Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Lys Trp Tyr Lys Ser Glu
20 25 30
Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
35 40 45
Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Ile Tyr
50 55 60
Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
65 70 75 80
Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
85 90 95
Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
100 105 110
Thr Asp Tyr Val Asp Leu Tyr Leu Ile His Ser Pro Phe Val Ser Lys
115 120 125
Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
130 135 140
Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Thr
145 150 155 160
Val Glu Asp Leu Gln Arg Ile Leu Lys Val Ala Glu Val Lys Pro Gln
165 170 175
Val Asn Gln Ile Glu Phe Ser Pro Phe Leu Gln Asn Gln Thr Pro Gly
180 185 190
Ile Cys Lys Phe Cys Gln Glu His Asp Ile Leu Val Glu Ala Tyr Ser
195 200 205

Pro	Leu	Gly	Pro	Leu	Arg	Lys	Lys	Thr	Ala	Gln	Asp	Asp	Ser	Gln	Pro
210						215					220				
Phe	Phe	Glu	Tyr	Val	Lys	Glu	Leu	Ser	Glu	Lys	Tyr	Asn	Lys	Ser	Glu
225					230					235					240
Ala	Gln	Ile	Ile	Leu	Arg	Trp	Val	Thr	Lys	Arg	Gly	Val	Leu	Pro	Val
				245					250					255	
Thr	Thr	Ser	Ser	Lys	Pro	Gln	Arg	Ile	Ser	Asp	Ala	Gln	Asn	Leu	Phe
			260					265					270		
Ser	Phe	Asp	Leu	Thr	Ala	Glu	Glu	Val	Asp	Lys	Ile	Thr	Glu	Leu	Gly
		275					280					285			
Leu	Glu	His	Glu	Pro	Leu	Arg	Leu	Tyr	Trp	Asn	Lys	Leu	Tyr	Gly	Lys
	290					295					300				
Tyr	Asn	Tyr	Ala	Ala	Gln	Lys	Val								
305					310										

<210> 237
 <211> 942
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 237
 atgtcttttc accaacagtt ttccacgctg aacaacggca ataaaatccc ggcgattgcc 60
 atcatcgcca ctggtacaaa gtggtataaa agtgaagaaa ctgacggcag cttctccaat 120
 agtctggttg aacaaatcgt gtatgcgttg aaactgccgg ggattatcca catcgacgcc 180
 gcggagattt atcgcaccta cccggaagtg ggtaaagcac tgccctgac cgaaaagcct 240
 cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactcccct 300
 gcggacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
 attcattccc cgtttgtttc gaaggaagtg aatggcttaa gcttagaaga ggcttggaag 420
 gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcggggtttc caatttctcc 480
 gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
 gagttctctc cgttcctgca aaaccaaaca ccaggcattt gcaaattctg tcaggagcac 600
 gatatcctgg tggaagcata ttctccgctg ggcccgtg gcgaagaaac cgcgcaggat 660
 gacagccaac cattttttga gtacgtcaaa gaattgagcg aaaaatacaa caaatccgag 720
 gccagatca tcttgccgtg ggtaactaaa cgcgggtgtg tgccagttac cacctottca 780
 aagcctcagc gcattagcga tgcacagaac ctgttttctc tcgacctgac agcgggaagag 840
 gttgataaaa tcacggagct ggtcttgga catgaacgcg tcgcgctgta ctggaataaa 900
 ttgtatggca aatataacta cgcgcgccag aaagtgtaat ga 942

<210> 238
 <211> 313
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 238
 Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
 1 5 10 15
 Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Lys Trp Tyr Lys Ser Glu
 20 25 30
 Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
 35 40 45
 Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Ile Tyr
 50 55 60
 Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro

65					70					75				80
Arg	Asn	Ala	Ile	Phe	Leu	Thr	Asp	Lys	Tyr	Ser	Pro	Gln	Ile	Lys Met
				85					90					95
Ser	Asp	Ser	Pro	Ala	Asp	Gly	Leu	Asp	Leu	Ala	Leu	Lys	Lys	Met Gly
			100					105					110	
Thr	Asp	Tyr	Val	Asp	Leu	Tyr	Leu	Ile	His	Ser	Pro	Phe	Val	Ser Lys
		115					120					125		
Glu	Val	Asn	Gly	Leu	Ser	Leu	Glu	Glu	Ala	Trp	Lys	Asp	Met	Glu Gln
		130				135					140			
Leu	Tyr	Lys	Ser	Gly	Lys	Ala	Lys	Asn	Ile	Gly	Val	Ser	Asn	Phe Ser
145					150					155				160
Val	Glu	Asp	Leu	Gln	Arg	Ile	Leu	Lys	Val	Ala	Glu	Val	Lys	Pro Gln
				165					170					175
Val	Asn	Gln	Ile	Glu	Phe	Ser	Pro	Phe	Leu	Gln	Asn	Gln	Thr	Pro Gly
			180					185					190	
Ile	Cys	Lys	Phe	Cys	Gln	Glu	His	Asp	Ile	Leu	Val	Glu	Ala	Tyr Ser
		195					200					205		
Pro	Leu	Gly	Pro	Leu	Arg	Lys	Lys	Thr	Ala	Gln	Asp	Asp	Ser	Gln Pro
		210				215					220			
Phe	Phe	Glu	Tyr	Val	Lys	Glu	Leu	Ser	Glu	Lys	Tyr	Asn	Lys	Ser Glu
225					230					235				240
Ala	Gln	Ile	Ile	Leu	Arg	Trp	Val	Thr	Lys	Arg	Gly	Val	Leu	Pro Val
				245					250					255
Thr	Thr	Ser	Ser	Lys	Pro	Gln	Arg	Ile	Ser	Asp	Ala	Gln	Asn	Leu Phe
			260					265					270	
Ser	Phe	Asp	Leu	Thr	Ala	Glu	Glu	Val	Asp	Lys	Ile	Thr	Glu	Leu Gly
		275					280					285		
Leu	Glu	His	Glu	Pro	Leu	Arg	Leu	Tyr	Trp	Asn	Lys	Leu	Tyr	Gly Lys
		290				295					300			
Tyr	Asn	Tyr	Ala	Ala	Gln	Lys	Val							
305					310									

<210> 239

<211> 942

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 239

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atgtcttttc accaacagtt tttcacgctg aacaacggca ataaaatccc ggcgattgcc 60
atcatcggca ctggtacaaa gtggtataaa agtgaagaaa ctgacggcag cttctccaat 120
agtctggttg aacaaatcgt gtatgcgttg aagctgccgg ggattatcca catogacgcc 180
gcggagattt atcgcaccta cccggaagtg ggcaaagcac tgtccctgac cgaaaagcct 240
cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactcccct 300
gcggacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
ttacattccc cgtttgtttc gaaggaagtg aatggcttaa gcttagaaga ggcttggaaa 420
gatattggagc agttatacaa aaccggtaaa gctaaaaaca tcgggggttt caatttcaca 480
gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
gagttctctc cgttcctgca aaaccaaaca ccaggcattt ataaattctg tcaggagcac 600
gatatcctgg tggaagcata ttctccgctg ggcccgtgac ggaagaaaac cgcgcaggat 660
gacagccaac cattttttga gtacgtcaaa gaattgagcg aaaaatacaa caaatccgag 720
gcccgatca tcttgcgctg ggtcactaaa cgcggtgtgc tgccagttac cacctcttca 780
aagcctcagc gcattagcga tgctcagaac ctgttttctt tcgacctgac agcgggaagag 840
gttgataaaa tcacggagct gggtctggag catgaaccgc tgcgcctgta ctggaataaa 900
ttgtatggca aatataactc tgccgcccag aaagtgtaat ga 942

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<210> 240

<211> 313
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 240
 Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
 1 5 10 15
 Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Lys Trp Tyr Lys Ser Glu
 20 25 30
 Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
 35 40 45
 Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Ile Tyr
 50 55 60
 Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
 65 70 75 80
 Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
 85 90 95
 Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
 100 105 110
 Thr Asp Tyr Val Asp Leu Tyr Leu Leu His Ser Pro Phe Val Ser Lys
 115 120 125
 Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
 130 135 140
 Leu Tyr Lys Thr Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Thr
 145 150 155 160
 Val Glu Asp Leu Gln Arg Ile Leu Lys Val Ala Glu Val Lys Pro Gln
 165 170 175
 Val Asn Gln Ile Glu Phe Ser Pro Phe Leu Gln Asn Gln Thr Pro Gly
 180 185 190
 Ile Tyr Lys Phe Cys Gln Glu His Asp Ile Leu Val Glu Ala Tyr Ser
 195 200 205
 Pro Leu Gly Pro Leu Arg Lys Lys Thr Ala Gln Asp Asp Ser Gln Pro
 210 215 220
 Phe Phe Glu Tyr Val Lys Glu Leu Ser Glu Lys Tyr Asn Lys Ser Glu
 225 230 235 240
 Ala Gln Ile Ile Leu Arg Trp Val Thr Lys Arg Gly Val Leu Pro Val
 245 250 255
 Thr Thr Ser Ser Lys Pro Gln Arg Ile Ser Asp Ala Gln Asn Leu Phe
 260 265 270
 Ser Phe Asp Leu Thr Ala Glu Glu Val Asp Lys Ile Thr Glu Leu Gly
 275 280 285
 Leu Glu His Glu Pro Leu Arg Leu Tyr Trp Asn Lys Leu Tyr Gly Lys
 290 295 300
 Tyr Asn Ser Ala Ala Gln Lys Val
 305 310

<210> 241
 <211> 942
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 241
 atgtcttttc accaacagtt ttccacgctg aacaacggca ataaaatccc ggcgattgcc 60
 atcatcggca ctggtacaaa atggtataaa aatgaagaaa ctgacgcgac cttctccaat 120

```

agtctggttg aacaaatcgt gtatgcgttg aaactgccgg ggattatcca catcgacgoc 180
gcgagagatt atcgcaccta ccggaagtg ggtaaagcac tgtccctgac cgaaaagcct 240
cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactcccct 300
gcgagacggtc tggatttagc attgaagaaa atgggtacgg attatgttga tttatatctg 360
attcattccc cgtttgtttc gaaggaagtg aatggcttaa gcttagaaga ggcttggaag 420
gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggttc caatttctcc 480
gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
gagttctctc cgttcctgca aaaccaaaca ccaggcattt gcaaattctg tcaggagcac 600
gatatcctgg tggaaagcata ttctccgctg ggcccgtctg ggaagaaaac cgcgaggat 660
gacagccaac cattttttga gtacgtcaaa gaattgagcg aaaaatacaa caaatccgag 720
gcccagatca tcttgcgctg ggtcactaaa cgcggtgtgc tgccagttac cacctcttca 780
aagcctcagc gcattagcga tgcccagaac ctgttttctt tcgacctgac agcggaagag 840
gttgataaaa tcacggagct gggctctggaa catgaaccgc tgcgcctgta ctggaataaa 900
ttgtatggca aatataacta cgccgccag aaagtgtaat ga 942

```

<210> 242

<211> 313

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 242

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Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
1          5          10          15
Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Lys Trp Tyr Lys Asn Glu
20        25        30
Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
35        40        45
Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Ile Tyr
50        55        60
Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
65        70        75        80
Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
85        90        95
Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
100       105       110
Thr Asp Tyr Val Asp Leu Tyr Leu Ile His Ser Pro Phe Val Ser Lys
115       120       125
Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
130       135       140
Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Ser
145       150       155       160
Val Glu Asp Leu Gln Arg Ile Leu Lys Val Ala Glu Val Lys Pro Gln
165       170       175
Val Asn Gln Ile Glu Phe Ser Pro Phe Leu Gln Asn Gln Thr Pro Gly
180       185       190
Ile Cys Lys Phe Cys Gln Glu His Asp Ile Leu Val Glu Ala Tyr Ser
195       200       205
Pro Leu Gly Pro Leu Arg Lys Lys Thr Ala Gln Asp Asp Ser Gln Pro
210       215       220
Phe Phe Glu Tyr Val Lys Glu Leu Ser Glu Lys Tyr Asn Lys Ser Glu
225       230       235       240
Ala Gln Ile Ile Leu Arg Trp Val Thr Lys Arg Gly Val Leu Pro Val
245       250       255
Thr Thr Ser Ser Lys Pro Gln Arg Ile Ser Asp Ala Gln Asn Leu Phe
260       265       270
Ser Phe Asp Leu Thr Ala Glu Glu Val Asp Lys Ile Thr Glu Leu Gly
275       280       285

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Leu Glu His Glu Pro Leu Arg Leu Tyr Trp Asn Lys Leu Tyr Gly Lys
 290 295 300
 Tyr Asn Tyr Ala Ala Gln Lys Val
 305 310

<210> 243
 <211> 942
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 243
 atgtcttttc accaacagtt tttcacgctg aacaacggca ataaaatccc ggogattgcc 60
 atcatcggca ctggtacaaa gtggtataaa agtgaagaaa ctgacgcgac cttctccaat 120
 agtctggttg aacaaatcgt gtatgcgttg aaactgccgg ggattatcca catcgacggc 180
 gcggagattt atcgcaccta cccggaagtg ggtaaagcac tgtccctgac caaaaagcct 240
 cgtaacgoga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactccoct 300
 gcggacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
 ttacattccc cgtttgttgc gaaggaagtg aatggcttaa gcttagaaga ggcttggaaa 420
 gatattggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggttc caatttcaca 480
 gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
 gagttctctc cgttcctgca aaaccaaaca ccaggcattt ataaattctg tcaggagcac 600
 gatctcctgg tggaagcata ttctccgctg ggcccactgc ggaagaaaac cgcgcaggat 660
 gacagccaac cattttttga gtacgtcaaa gaattgagcg aaaaatacgg caaatccgag 720
 gccagatca tcttgcgctg ggctactaaa cgcggtgtgc tgccagttac cacctottca 780
 aagcctcagc gcattagcga tgctcagaac ctgttttctt tcgacctgac agcggaagag 840
 gttgataaaa tcacggagct gggctctggaa catgaaccgc tgcgcctgta ctggaataaa 900
 ttgtatggca aatataactc tgccgcccgag aaagtgtaat ga 942

<210> 244
 <211> 313
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 244
 Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
 1 5 10 15
 Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Lys Trp Tyr Lys Ser Glu
 20 25 30
 Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
 35 40 45
 Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Ile Tyr
 50 55 60
 Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Lys Lys Pro
 65 70 75 80
 Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
 85 90 95
 Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
 100 105 110
 Thr Asp Tyr Val Asp Leu Tyr Leu Leu His Ser Pro Phe Val Ser Lys
 115 120 125
 Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
 130 135 140
 Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Thr

145		150		155		160									
Val	Glu	Asp	Leu	Gln	Arg	Ile	Leu	Lys	Val	Ala	Glu	Val	Lys	Pro	Gln
		165		170		175									
Val	Asn	Gln	Ile	Glu	Phe	Ser	Pro	Phe	Leu	Gln	Asn	Gln	Thr	Pro	Gly
		180		185		190									
Ile	Tyr	Lys	Phe	Cys	Gln	Glu	His	Asp	Ile	Leu	Val	Glu	Ala	Tyr	Ser
		195		200		205									
Pro	Leu	Gly	Pro	Leu	Arg	Lys	Lys	Thr	Ala	Gln	Asp	Asp	Ser	Gln	Pro
		210		215		220									
Phe	Phe	Glu	Tyr	Val	Lys	Glu	Leu	Ser	Glu	Lys	Tyr	Gly	Lys	Ser	Glu
225				230		235									240
Ala	Gln	Ile	Ile	Leu	Arg	Trp	Val	Thr	Lys	Arg	Gly	Val	Leu	Pro	Val
		245		250		255									
Thr	Thr	Ser	Ser	Lys	Pro	Gln	Arg	Ile	Ser	Asp	Ala	Gln	Asn	Leu	Phe
		260		265		270									
Ser	Phe	Asp	Leu	Thr	Ala	Glu	Glu	Val	Asp	Lys	Ile	Thr	Glu	Leu	Gly
		275		280		285									
Leu	Glu	His	Glu	Pro	Leu	Arg	Leu	Tyr	Trp	Asn	Lys	Leu	Tyr	Gly	Lys
		290		295		300									
Tyr	Asn	Ser	Ala	Ala	Gln	Lys	Val								
305				310											

<210> 245
 <211> 942
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 245
 atgtcttttt accaacagtt tttcacgctg aacaacggca ataaaatccc ggcgattgcc 60
 atcatcgga ctggtacaaa gtggtataaa agtgaagaaa ctgacgcgac cttctccaat 120
 agtctggttg aacaaatcgt gtatgcgttg aaactgcgag ggattatcca catcgacgcc 180
 gcggagattt atcgcaccta cccggaagtg ggtaaagcac tgtccctgac cgaagaagcct 240
 cgtaacgcga tttttctgac ggataaatat tctcgcgaga ttaaaatgag tgactccccct 300
 gcggacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
 attcattccc cgtttggtac gaaggaagtg aatggcttaa gcttagaaga ggcttggaag 420
 gatattggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggttc caatttcaca 480
 gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
 gagttctctc cgttcctgca aaaccaaaca ccaggcattt gcaaattctg tcaggagcac 600
 gatatccttg tggaagcata ttctccgctg ggcccgcctg ggaagaaaac cgcgcaggat 660
 gacagccaac cattttttga gtacgtcaaa gaattgagcg aaaaatacaa caaatccgag 720
 gccagatca tctgcgctg ggtcactaaa cgcggtgtgc tgcagttac cactottca 780
 aagcctcagc gcattagcga tgctcagaac ctgttttctt tcgacctgac agcgggaagag 840
 gttgataaaa tcacggagct ggtcttgaa catgaaccgc tgcgcctgta ctggaataaa 900
 ttgtatggca aatataacta cgcgcgccag aaagtgtaat ga 942

<210> 246
 <211> 313
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 246
 Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
 1 5 10 15

Pro	Ala	Ile	Ala	Ile	Ile	Gly	Thr	Gly	Thr	Lys	Trp	Tyr	Lys	Ser	Glu
			20					25					30		
Glu	Thr	Asp	Ala	Thr	Phe	Ser	Asn	Ser	Leu	Val	Glu	Gln	Ile	Val	Tyr
		35					40					45			
Ala	Leu	Lys	Leu	Pro	Gly	Ile	Ile	His	Ile	Asp	Ala	Ala	Glu	Ile	Tyr
	50				55					60					
Arg	Thr	Tyr	Pro	Glu	Val	Gly	Lys	Ala	Leu	Ser	Leu	Thr	Glu	Lys	Pro
65					70				75						80
Arg	Asn	Ala	Ile	Phe	Leu	Thr	Asp	Lys	Tyr	Ser	Pro	Gln	Ile	Lys	Met
				85					90					95	
Ser	Asp	Ser	Pro	Ala	Asp	Gly	Leu	Asp	Leu	Ala	Leu	Lys	Lys	Met	Gly
			100					105					110		
Thr	Asp	Tyr	Val	Asp	Leu	Tyr	Leu	Ile	His	Ser	Pro	Phe	Val	Thr	Lys
		115					120					125			
Glu	Val	Asn	Gly	Leu	Ser	Leu	Glu	Glu	Ala	Trp	Lys	Asp	Met	Glu	Gln
	130					135					140				
Leu	Tyr	Lys	Ser	Gly	Lys	Ala	Lys	Asn	Ile	Gly	Val	Ser	Asn	Phe	Thr
145					150					155					160
Val	Glu	Asp	Leu	Gln	Arg	Ile	Leu	Lys	Val	Ala	Glu	Val	Lys	Pro	Gln
				165				170						175	
Val	Asn	Gln	Ile	Glu	Phe	Ser	Pro	Phe	Leu	Gln	Asn	Gln	Thr	Pro	Gly
			180					185					190		
Ile	Cys	Lys	Phe	Cys	Gln	Glu	His	Asp	Ile	Leu	Val	Glu	Ala	Tyr	Ser
	195						200					205			
Pro	Leu	Gly	Pro	Leu	Arg	Lys	Lys	Thr	Ala	Gln	Asp	Asp	Ser	Gln	Pro
	210					215					220				
Phe	Phe	Glu	Tyr	Val	Lys	Glu	Leu	Ser	Glu	Lys	Tyr	Asn	Lys	Ser	Glu
225					230					235					240
Ala	Gln	Ile	Ile	Leu	Arg	Trp	Val	Thr	Lys	Arg	Gly	Val	Leu	Pro	Val
				245					250					255	
Thr	Thr	Ser	Ser	Lys	Pro	Gln	Arg	Ile	Ser	Asp	Ala	Gln	Asn	Leu	Phe
			260					265					270		
Ser	Phe	Asp	Leu	Thr	Ala	Glu	Glu	Val	Asp	Lys	Ile	Thr	Glu	Leu	Gly
		275					280					285			
Leu	Glu	His	Glu	Pro	Leu	Arg	Leu	Tyr	Trp	Asn	Lys	Leu	Tyr	Gly	Lys
	290					295					300				
Tyr	Asn	Tyr	Ala	Ala	Gln	Lys	Val								
305					310										

<210> 247

<211> 942

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 247

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atgtcttttc accaacagtt tttcacgctg aacaacggca ataaaatccc ggcgattgcc 60
atcatcggca ctggtacagc ctggtataaa agtgaagaaa ctgacgcgac cttctccaat 120
agtctggttg aacaaatcgt gtatgcgttg aaactgccgg ggattatcca catcgacgcc 180
gcggagattt atcgcaccta ccoggaagtg ggtaaagcac tgtccctgac cgaaaagcct 240
cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactccoct 300
gcggacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
attcattccc cgtttgtttc gaaggaagtg aatggcttaa gcttagaaga ggcttgga 420
gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcggggtttc caatttctcc 480
gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
gagttctctc cgttcctgca aaaccaaaca ccaggcattt gcaaattctg tcaggagcac 600
gatatcctgg tggaagcata ttctccgctg ggcccgtgc ggaagaaaac cgcgcaggat 660
gacagccaac cattttttga gtacgtcaaa gaattgagcg aaaaatacaa caaatccgag 720

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gccagatca tctgcgctg ggtcactaaa cgcggtgtgc tgccagttac cacctcttca 780
aagcctcagc gcattagcga tgctcagaac ctgttttcct tcgacctgac agcggaagag 840
gttgataaaa tcacggagct gggctctggaa catgaaccgc tgcgcctgta ctggaataaa 900
ttgtatggca aatataacta cgccgccag aaagtgtaat ga 942

```

<210> 248
 <211> 313
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 248

Met	Ser	Phe	His	Gln	Gln	Phe	Phe	Thr	Leu	Asn	Asn	Gly	Asn	Lys	Ile	1	5	10	15
Pro	Ala	Ile	Ala	Ile	Ile	Gly	Thr	Gly	Thr	Ala	Trp	Tyr	Lys	Ser	Glu	20	25	30	
Glu	Thr	Asp	Ala	Thr	Phe	Ser	Asn	Ser	Leu	Val	Glu	Gln	Ile	Val	Tyr	35	40	45	
Ala	Leu	Lys	Leu	Pro	Gly	Ile	Ile	His	Ile	Asp	Ala	Ala	Glu	Ile	Tyr	50	55	60	
Arg	Thr	Tyr	Pro	Glu	Val	Gly	Lys	Ala	Leu	Ser	Leu	Thr	Glu	Lys	Pro	65	70	75	80
Arg	Asn	Ala	Ile	Phe	Leu	Thr	Asp	Lys	Tyr	Ser	Pro	Gln	Ile	Lys	Met	85	90	95	
Ser	Asp	Ser	Pro	Ala	Asp	Gly	Leu	Asp	Leu	Ala	Leu	Lys	Lys	Met	Gly	100	105	110	
Thr	Asp	Tyr	Val	Asp	Leu	Tyr	Leu	Ile	His	Ser	Pro	Phe	Val	Ser	Lys	115	120	125	
Glu	Val	Asn	Gly	Leu	Ser	Leu	Glu	Glu	Ala	Trp	Lys	Asp	Met	Glu	Gln	130	135	140	
Leu	Tyr	Lys	Ser	Gly	Lys	Ala	Lys	Asn	Ile	Gly	Val	Ser	Asn	Phe	Ser	145	150	155	160
Val	Glu	Asp	Leu	Gln	Arg	Ile	Leu	Lys	Val	Ala	Glu	Val	Lys	Pro	Gln	165	170	175	
Val	Asn	Gln	Ile	Glu	Phe	Ser	Pro	Phe	Leu	Gln	Asn	Gln	Thr	Pro	Gly	180	185	190	
Ile	Cys	Lys	Phe	Cys	Gln	Glu	His	Asp	Ile	Leu	Val	Glu	Ala	Tyr	Ser	195	200	205	
Pro	Leu	Gly	Pro	Leu	Arg	Lys	Lys	Thr	Ala	Gln	Asp	Asp	Ser	Gln	Pro	210	215	220	
Phe	Phe	Glu	Tyr	Val	Lys	Glu	Leu	Ser	Glu	Lys	Tyr	Asn	Lys	Ser	Glu	225	230	235	240
Ala	Gln	Ile	Ile	Leu	Arg	Trp	Val	Thr	Lys	Arg	Gly	Val	Leu	Pro	Val	245	250	255	
Thr	Thr	Ser	Ser	Lys	Pro	Gln	Arg	Ile	Ser	Asp	Ala	Gln	Asn	Leu	Phe	260	265	270	
Ser	Phe	Asp	Leu	Thr	Ala	Glu	Glu	Val	Asp	Lys	Ile	Thr	Glu	Leu	Gly	275	280	285	
Leu	Glu	His	Glu	Pro	Leu	Arg	Leu	Tyr	Trp	Asn	Lys	Leu	Tyr	Gly	Lys	290	295	300	
Tyr	Asn	Tyr	Ala	Ala	Gln	Lys	Val	305	310										

<210> 249
 <211> 942
 <212> DNA
 <213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 249

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atgtcttttc accaacagtt tttcacgctg aacaacggca ataaaatccc ggcgattgcc 60
atcatcggca ctggtacaaa gtggtataaa agtgaagaaa ctgacgcgac cttctccaat 120
agtctgggtg aacaaatcgt gtacgcgttg aagctgccgg ggattatcca catcgacgcc 180
gcggagattt atcgcaccta cccggaagtg ggtaaagcac tgtccctgac cgaaaagcct 240
cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactccoct 300
gcggacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
attcattccc cgtttgtttc gaaggaagtg aatggcttaa gottagaaga ggcttggaag 420
gatatggagc agttatacaa aaccggtaaa gctaaaaaca tcgggggtttc caatttcaca 480
gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
gagttctctc cgttcctgca aaaccaaaca ccaggcattt gcaaattctg tcaggagcac 600
gatatcctgg tgggaagcata ttctccgctg ggcccgctgc ggaagaaaac cgcgcaggat 660
gacagccaac ctttttttga gtacgtcaaa gaattgagcg aaaaatacaa caaatccgag 720
gcccgatca tcctgcgctg ggctactaaa cgcggtgtgc tgccagttac cacctottca 780
aagcctcagc gcattagcga tgctcagaac ctgttttctt tcgaacctgac agcgggaagag 840
gttgataaaa tcacggagct gggtctggaa catgaaccgc tgogcctgta ctggaataaa 900
ttgtatggca aatataacta cgcgcgccag aaagtgtaat ga 942
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<210> 250

<211> 313

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 250

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Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
1      5      10      15
Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Lys Trp Tyr Lys Ser Glu
20     25     30
Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
35     40     45
Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Ile Tyr
50     55     60
Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
65     70     75     80
Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
85     90     95
Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
100    105    110
Thr Asp Tyr Val Asp Leu Tyr Leu Ile His Ser Pro Phe Val Ser Lys
115    120    125
Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
130    135    140
Leu Tyr Lys Thr Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Thr
145    150    155    160
Val Glu Asp Leu Gln Arg Ile Leu Lys Val Ala Glu Val Lys Pro Gln
165    170    175
Val Asn Gln Ile Glu Phe Ser Pro Phe Leu Gln Asn Gln Thr Pro Gly
180    185    190
Ile Cys Lys Phe Cys Gln Glu His Asp Ile Leu Val Glu Ala Tyr Ser
195    200    205
Pro Leu Gly Pro Leu Arg Lys Lys Thr Ala Gln Asp Asp Ser Gln Pro
210    215    220
Phe Phe Glu Tyr Val Lys Glu Leu Ser Glu Lys Tyr Asn Lys Ser Glu
```

225		230		235		240									
Ala	Gln	Ile	Ile	Leu	Arg	Trp	Val	Thr	Lys	Arg	Gly	Val	Leu	Pro	Val
		245		250		255									
Thr	Thr	Ser	Ser	Lys	Pro	Gln	Arg	Ile	Ser	Asp	Ala	Gln	Asn	Leu	Phe
		260		265		270									
Ser	Phe	Asp	Leu	Thr	Ala	Glu	Glu	Val	Asp	Lys	Ile	Thr	Glu	Leu	Gly
		275		280		285									
Leu	Glu	His	Glu	Pro	Leu	Arg	Leu	Tyr	Trp	Asn	Lys	Leu	Tyr	Gly	Lys
		290		295		300									
Tyr	Asn	Tyr	Ala	Ala	Gln	Lys	Val								
305				310											

<210> 251
 <211> 942
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 251

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atgtcttttc accaacagtt ttccacgctg aacaacggca ataaaatccc ggcgattgcc 60
atcatcggca ctggtacaaa gtggtataaa agtgaagaaa ctgacgcgac cttctccaat 120
agtctggttg aacaaatcgt gtatgcgttg aaactgccgg ggattatcca catcgacgcc 180
gcggagattt atcgcaccta ccggaagtg ggcaaagcac tgccctgac cgaaaagcct 240
cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactccctc 300
gcggacggtc tggatttagc attgaagaaa atgggtacag attatggtga tttatatctg 360
attcattccc cgtttgtttc gaaggaagtg aatggcttaa gcttagaaga ggcttggaag 420
gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcggggtttc caatttcaca 480
gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
gagttctctc cgttcctgca aaaccaaaca ccaggcattt gcaaattctg tcaggagcac 600
gatatcctgg tggaagcata ttctccgctg ggcccgtgct ggaagaaaac cgcgcaggat 660
gacagccaac ctttttttga gtacgtcaaa gaattgagcg aaaaatacgg caaatccgag 720
gccagatca tcttgcgctg ggctactaaa cgcggtgtgc tgccagttac cactcttcca 780
aagcctcagc gcattagcga tgctcagaac ctgttttcc tgcacctgac agcgggaagag 840
gttgataaaa tcacggagct ggtctggaa catgaaccgc tgcgcctgta ctggaataaa 900
ttgtatggca aatataacta cgccgccagc aaagtataat ga 942

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<210> 252
 <211> 313
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 252

Met	Ser	Phe	His	Gln	Gln	Phe	Phe	Thr	Leu	Asn	Asn	Gly	Asn	Lys	Ile
1			5					10					15		
Pro	Ala	Ile	Ala	Ile	Ile	Gly	Thr	Gly	Thr	Lys	Trp	Tyr	Lys	Ser	Glu
			20					25					30		
Glu	Thr	Asp	Ala	Thr	Phe	Ser	Asn	Ser	Leu	Val	Glu	Gln	Ile	Val	Tyr
			35				40					45			
Ala	Leu	Lys	Leu	Pro	Gly	Ile	Ile	His	Ile	Asp	Ala	Ala	Glu	Ile	Tyr
			50			55				60					
Arg	Thr	Tyr	Pro	Glu	Val	Gly	Lys	Ala	Leu	Ser	Leu	Thr	Glu	Lys	Pro
65				70				75						80	
Arg	Asn	Ala	Ile	Phe	Leu	Thr	Asp	Lys	Tyr	Ser	Pro	Gln	Ile	Lys	Met
			85					90						95	

Ser	Asp	Ser	Pro	Ala	Asp	Gly	Leu	Asp	Leu	Ala	Leu	Lys	Lys	Met	Gly
			100					105					110		
Thr	Asp	Tyr	Val	Asp	Leu	Tyr	Leu	Ile	His	Ser	Pro	Phe	Val	Ser	Lys
		115					120					125			
Glu	Val	Asn	Gly	Leu	Ser	Leu	Glu	Glu	Ala	Trp	Lys	Asp	Met	Glu	Gln
	130					135					140				
Leu	Tyr	Lys	Ser	Gly	Lys	Ala	Lys	Asn	Ile	Gly	Val	Ser	Asn	Phe	Thr
145					150					155					160
Val	Glu	Asp	Leu	Gln	Arg	Ile	Leu	Lys	Val	Ala	Glu	Val	Lys	Pro	Gln
			165					170						175	
Val	Asn	Gln	Ile	Glu	Phe	Ser	Pro	Phe	Leu	Gln	Asn	Gln	Thr	Pro	Gly
			180					185					190		
Ile	Cys	Lys	Phe	Cys	Gln	Glu	His	Asp	Ile	Leu	Val	Glu	Ala	Tyr	Ser
		195					200					205			
Pro	Leu	Gly	Pro	Leu	Arg	Lys	Lys	Thr	Ala	Gln	Asp	Asp	Ser	Gln	Pro
	210					215					220				
Phe	Phe	Glu	Tyr	Val	Lys	Glu	Leu	Ser	Glu	Lys	Tyr	Gly	Lys	Ser	Glu
225					230					235					240
Ala	Gln	Ile	Ile	Leu	Arg	Trp	Val	Thr	Lys	Arg	Gly	Val	Leu	Pro	Val
			245					250						255	
Thr	Thr	Ser	Ser	Lys	Pro	Gln	Arg	Ile	Ser	Asp	Ala	Gln	Asn	Leu	Phe
		260						265					270		
Ser	Phe	Asp	Leu	Thr	Ala	Glu	Glu	Val	Asp	Lys	Ile	Thr	Glu	Leu	Gly
		275					280					285			
Leu	Glu	His	Glu	Pro	Leu	Arg	Leu	Tyr	Trp	Asn	Lys	Leu	Tyr	Gly	Lys
	290					295					300				
Tyr	Asn	Tyr	Ala	Ala	Gln	Lys	Val								
305					310										

<210> 253

<211> 942

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 253

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atgtcttttc accaacagtt tttcacgctg aacaacggca ataaaatccc ggcgattgcc 60
atcatcggca ctggtacaaa gtggtataaa agtgaagaaa ctgacgcgac cttctccaat 120
agtctggttg aacaaatcgt gtatgcgttg aaactgccgg ggattatcca catcgacgcc 180
gcggagattt atcgcaccta cccggaagtg ggtaaagcac tgtccctgac cgaaaagcct 240
cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactccoct 300
gcggacggtc tggatatagc attgaagaaa atgggtacag attatgttga tttatatctg 360
attcattccc cgtttgtttc gaaggaagtg aatggcttaa gcttagaaga ggcttggaag 420
gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcggggtttc caatttctcc 480
gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
gagttctctc cgttcctgca aaaccaaaca ccaggcattt gcaaattctg tcaggagcac 600
gatatcctgg tgaagcata ttctccgctg ggcccgtgac ggaagaaaac cgcgcaggat 660
gacagccaac cattttttga gtacgtcaaa gaattgagcg aaaaatacaa caaatccgag 720
gccagatca tctcgctgct ggtcactaaa cgcggtgtgc tgccagttac cactcttca 780
aagcctcagc gcattagcga tgctcagaac ctgttttctc tcgacctgac agcgggaagag 840
gttgataaaa tcacggagct ggtctgggaa catgaaccgc tgcgcctgta ctggaataaa 900
ttgtatggca aatataacta cgccgccagc aaagtgtaat ga 942

```

<210> 254

<211> 313

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 254

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Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
1      5      10      15
Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Lys Trp Tyr Lys Ser Glu
20     25     30
Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
35     40     45
Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Ile Tyr
50     55     60
Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
65     70     75     80
Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
85     90     95
Ser Asp Ser Pro Ala Asp Gly Leu Asp Ile Ala Leu Lys Lys Met Gly
100    105    110
Thr Asp Tyr Val Asp Leu Tyr Leu Ile His Ser Pro Phe Val Ser Lys
115    120    125
Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
130    135    140
Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Ser
145    150    155    160
Val Glu Asp Leu Gln Arg Ile Leu Lys Val Ala Glu Val Lys Pro Gln
165    170    175
Val Asn Gln Ile Glu Phe Ser Pro Phe Leu Gln Asn Gln Thr Pro Gly
180    185    190
Ile Cys Lys Phe Cys Gln Glu His Asp Ile Leu Val Glu Ala Tyr Ser
195    200    205
Pro Leu Gly Pro Leu Arg Lys Lys Thr Ala Gln Asp Asp Ser Gln Pro
210    215    220
Phe Phe Glu Tyr Val Lys Glu Leu Ser Glu Lys Tyr Asn Lys Ser Glu
225    230    235    240
Ala Gln Ile Ile Leu Arg Trp Val Thr Lys Arg Gly Val Leu Pro Val
245    250    255
Thr Thr Ser Ser Lys Pro Gln Arg Ile Ser Asp Ala Gln Asn Leu Phe
260    265    270
Ser Phe Asp Leu Thr Ala Glu Glu Val Asp Lys Ile Thr Glu Leu Gly
275    280    285
Leu Glu His Glu Pro Leu Arg Leu Tyr Trp Asn Lys Leu Tyr Gly Lys
290    295    300
Tyr Asn Tyr Ala Ala Gln Lys Val
305    310
```

<210> 255

<211> 942

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 255

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atgtctttt accaacagtt ttccacgctg aacaaaggca ataaaatccc ggcgattgcc 60
atcatcggca ctggtacagc ctggtataaa agtgaagaaa ctgacgcgac cttctccaat 120
agtctggttg aacaaatcgt gtacgcgttg aagctgcgag ggattatcca catcgacgcc 180
gcggagattt atcgcaccta cccggaagtg ggtaaagcac tgtccctgac cgaaaagcct 240
cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactccoct 300
```

```

gcggacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
attcattccc cgtttgtttc gaaggaagtg aatggcttaa gcttagaaga ggcttggaaa 420
gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggttc caatttctcc 480
gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
gagttctctc cgttcctgca aaaccaaaaca ccaggcattt ataaattctg tcaggagcac 600
gatatcctgg tggaagcata ttctccgctg ggcccgcctgc ggaagaaaac cgcgcaggat 660
gacagccaac cattttttga gtacgtcaaa gaattgagcg aaaaatacaa caaatccgag 720
gcccagatca tcctgcgctg ggtcactaaa cgcggtgtgc tgccagttac cacctcttca 780
aagcctcagc gcattagcga tgctcagaac ctgttttctt tcgacctgac agcggaagag 840
gttgataaaa tcacggagct gggctctggaa catgaaccgc tcgcctgtga ctggaataaa 900
ttgtatggca aatataacta cgccgccag aaagtgtaat ga 942

```

<210> 256

<211> 313

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 256

```

Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
1      5      10      15
Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Ala Trp Tyr Lys Ser Glu
      20      25      30
Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
      35      40      45
Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Ile Tyr
      50      55      60
Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
65      70      75      80
Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
      85      90      95
Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
      100     105     110
Thr Asp Tyr Val Asp Leu Tyr Leu Ile His Ser Pro Phe Val Ser Lys
      115     120     125
Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
      130     135     140
Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Ser
145     150     155     160
Val Glu Asp Leu Gln Arg Ile Leu Lys Val Ala Glu Val Lys Pro Gln
      165     170     175
Val Asn Gln Ile Glu Phe Ser Pro Phe Leu Gln Asn Gln Thr Pro Gly
      180     185     190
Ile Tyr Lys Phe Cys Gln Glu His Asp Ile Leu Val Glu Ala Tyr Ser
      195     200     205
Pro Leu Gly Pro Leu Arg Lys Lys Thr Ala Gln Asp Asp Ser Gln Pro
      210     215     220
Phe Phe Glu Tyr Val Lys Glu Leu Ser Glu Lys Tyr Asn Lys Ser Glu
225     230     235     240
Ala Gln Ile Ile Leu Arg Trp Val Thr Lys Arg Gly Val Leu Pro Val
      245     250     255
Thr Thr Ser Ser Lys Pro Gln Arg Ile Ser Asp Ala Gln Asn Leu Phe
      260     265     270
Ser Phe Asp Leu Thr Ala Glu Glu Val Asp Lys Ile Thr Glu Leu Gly
      275     280     285
Leu Glu His Glu Pro Leu Arg Leu Tyr Trp Asn Lys Leu Tyr Gly Lys
      290     295     300
Tyr Asn Tyr Ala Ala Gln Lys Val

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<210> 257
 <211> 942
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 257
 atgtcttttc accaacagtt tttcacgctg aacaacggca ataaaatccc ggcgattgcc 60
 atcatcggca ctggtacaaa gtggtataaa agtgaagaaa ctgacgcgac cttctccaat 120
 agtctggttg aacaaatcgt gtacgcgttg aagctgccgg ggattatcca catcgacgcc 180
 gcggagattt atcgcaccta cccggaagtg ggtaaagcac tgtccctgac cgaaaagcct 240
 cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactccctt 300
 gcggacggtc tggaatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
 attcattccc cgtttgtttc gaaggaagtg aatggcttaa gcttagaaga ggcttgga 420
 gatatggagc agttatacaa aaccggtaaa gctaaaaaca tcgggggttt caattttctc 480
 gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
 gagttctctc cgttcctgca aaaccaaaca ccaggcattt gcaaattctg tcaggagcac 600
 gatatcctgg tggaagcata ttctccgctg ggcccgtg gcgaagaaac cgcgcaggat 660
 gacagccaac cattttttga gtacgtcaaa gaattgagcg aaaaatacaa caaatccgag 720
 gccagatca tcttgcgctg ggtcactaaa cgcgggtgtg tgccagttac cacctcttca 780
 aagcctcagc gcattagcga tgctcagaac ctgttttctt tcgacctgac agcgggaagag 840
 gttgataaaa tcacggagct gggctctggaa catgaaccgc tcgcctgta ctggaataaa 900
 ttgtatggca aatataacta cgcgcgccag aaagtgtaat ga 942

<210> 258
 <211> 313
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 258
 Met Ser Phe His Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
 1 5 10 15
 Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Lys Trp Tyr Lys Ser Glu
 20 25 30
 Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
 35 40 45
 Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Ile Tyr
 50 55 60
 Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
 65 70 75 80
 Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
 85 90 95
 Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
 100 105 110
 Thr Asp Tyr Val Asp Leu Tyr Leu Ile His Ser Pro Phe Val Ser Lys
 115 120 125
 Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
 130 135 140
 Leu Tyr Lys Thr Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Ser
 145 150 155 160
 Val Glu Asp Leu Gln Arg Ile Leu Lys Val Ala Glu Val Lys Pro Gln
 165 170 175

Val	Asn	Gln	Ile	Glu	Phe	Ser	Pro	Phe	Leu	Gln	Asn	Gln	Thr	Pro	Gly
		180						185					190		
Ile	Cys	Lys	Phe	Cys	Gln	Glu	His	Asp	Ile	Leu	Val	Glu	Ala	Tyr	Ser
	195						200					205			
Pro	Leu	Gly	Pro	Leu	Arg	Lys	Lys	Thr	Ala	Gln	Asp	Asp	Ser	Gln	Pro
	210					215					220				
Phe	Phe	Glu	Tyr	Val	Lys	Glu	Leu	Ser	Glu	Lys	Tyr	Asn	Lys	Ser	Glu
225					230					235					240
Ala	Gln	Ile	Ile	Leu	Arg	Trp	Val	Thr	Lys	Arg	Gly	Val	Leu	Pro	Val
			245						250					255	
Thr	Thr	Ser	Ser	Lys	Pro	Gln	Arg	Ile	Ser	Asp	Ala	Gln	Asn	Leu	Phe
			260					265					270		
Ser	Phe	Asp	Leu	Thr	Ala	Glu	Glu	Val	Asp	Lys	Ile	Thr	Glu	Leu	Gly
		275					280					285			
Leu	Glu	His	Glu	Pro	Leu	Arg	Leu	Tyr	Trp	Asn	Lys	Leu	Tyr	Gly	Lys
	290					295					300				
Tyr	Asn	Tyr	Ala	Ala	Gln	Lys	Val								
305					310										

<210> 259

<211> 942

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 259

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atcatcggca ctggtacagc gtggtataaa agtgaagaaa ctgacgcgac cttctccaat 120
agtctggttg aacaaatcgt gtatgcgttg aaactgccgg ggattatcca catcgacgcc 180
gcgagatatt atcgcaccta cccggaagtg ggtaaagcac tgtccctgac cgaaaagcct 240
cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactcccct 300
gcggacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
ttacattccc cgttagtttc gaaggaagtg aatggcttaa gcttagaaga ggcttggaag 420
gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggttc caatttcaca 480
gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
gagttctctc cgttcctgca aaaccaaaca ccaggcattt gcaaattctg tcaggagcac 600
gatatcctgg tggaagcata ttctccgctg ggcccgtgct ggaagaaaac cgcgcaggat 660
gacagccaac cattttttga gtacgtcaaa gaattgagcg aaaaatacaa taaatccgag 720
gccagatca tcttgccgtg ggtcactaaa cgcgggtgtg tgccagttac cacctcttca 780
aagcctcagc gcattagcga tgctcagaac ctgttttccct tgacctgac agcgggaagag 840
gttgataaaa tcacggagct gggtctggaa catgaaccgc tcgcctgta ctggaataaa 900
ttgtatggca aatataacta cgccgccag aaagtgtaat ga 942

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<210> 260

<211> 313

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 260

Met	Ser	Phe	His	Gln	Gln	Phe	Phe	Thr	Leu	Asn	Asn	Gly	Asn	Lys	Ile
1			5						10					15	
Pro	Ala	Ile	Ala	Ile	Ile	Gly	Thr	Gly	Thr	Ala	Trp	Tyr	Lys	Ser	Glu
			20					25					30		
Glu	Thr	Asp	Ala	Thr	Phe	Ser	Asn	Ser	Leu	Val	Glu	Gln	Ile	Val	Tyr

35	40	45													
Ala	Leu	Lys	Leu	Pro	Gly	Ile	Ile	His	Ile	Asp	Ala	Ala	Glu	Ile	Tyr
50						55					60				
Arg	Thr	Tyr	Pro	Glu	Val	Gly	Lys	Ala	Leu	Ser	Leu	Thr	Glu	Lys	Pro
65					70					75					80
Arg	Asn	Ala	Ile	Phe	Leu	Thr	Asp	Lys	Tyr	Ser	Pro	Gln	Ile	Lys	Met
			85						90					95	
Ser	Asp	Ser	Pro	Ala	Asp	Gly	Leu	Asp	Leu	Ala	Leu	Lys	Lys	Met	Gly
			100					105					110		
Thr	Asp	Tyr	Val	Asp	Leu	Tyr	Leu	Leu	His	Ser	Pro	Leu	Val	Ser	Lys
		115					120					125			
Glu	Val	Asn	Gly	Leu	Ser	Leu	Glu	Glu	Ala	Trp	Lys	Asp	Met	Glu	Gln
	130					135					140				
Leu	Tyr	Lys	Ser	Gly	Lys	Ala	Lys	Asn	Ile	Gly	Val	Ser	Asn	Phe	Thr
145					150					155					160
Val	Glu	Asp	Leu	Gln	Arg	Ile	Leu	Lys	Val	Ala	Glu	Val	Lys	Pro	Gln
			165					170						175	
Val	Asn	Gln	Ile	Glu	Phe	Ser	Pro	Phe	Leu	Gln	Asn	Gln	Thr	Pro	Gly
		180						185					190		
Ile	Cys	Lys	Phe	Cys	Gln	Glu	His	Asp	Ile	Leu	Val	Glu	Ala	Tyr	Ser
	195						200					205			
Pro	Leu	Gly	Pro	Leu	Arg	Lys	Lys	Thr	Ala	Gln	Asp	Asp	Ser	Gln	Pro
	210					215					220				
Phe	Phe	Glu	Tyr	Val	Lys	Glu	Leu	Ser	Glu	Lys	Tyr	Asn	Lys	Ser	Glu
225				230					235						240
Ala	Gln	Ile	Ile	Leu	Arg	Trp	Val	Thr	Lys	Arg	Gly	Val	Leu	Pro	Val
			245					250						255	
Thr	Thr	Ser	Ser	Lys	Pro	Gln	Arg	Ile	Ser	Asp	Ala	Gln	Asn	Leu	Phe
		260					265						270		
Ser	Phe	Asp	Leu	Thr	Ala	Glu	Glu	Val	Asp	Lys	Ile	Thr	Glu	Leu	Gly
	275					280					285				
Leu	Glu	His	Glu	Pro	Leu	Arg	Leu	Tyr	Trp	Asn	Lys	Leu	Tyr	Gly	Lys
	290					295					300				
Tyr	Asn	Tyr	Ala	Ala	Gln	Lys	Val								
305					310										

<210> 261
 <211> 942
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 261
 atgtcttttc accaacagtt ttccacgctg aacaacggca ataaaatccc ggogattgcc 60
 atcatcgcca ctggtacagc gtggtataaa agtgaagaaa ctgacgogac cttctccaat 120
 agtctggttg aacaaatcgt gtatgcgttg aaactgccgg ggattatcca catcgacgcc 180
 gcggagattt atcgcaccta ccggaagtg ggtaaagcac tgtccctgac cgaaaagcct 240
 cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactccctc 300
 gcggacggtc tggatttagc attgaagaaa atgggtacag attatgttga ttatatctg 360
 ttacattccc cgttagtttc gaaggaagtg aatggcttaa gcttagaaga ggcttgga 420
 gatatggagc agttatacaa aagtggtaaa gctaaaaaca tgggggtttc caatttcaca 480
 gtggaagacc tgcaacgtat cctgcgtgct gctgaagtta aacctcaggt caaccagatt 540
 gagttctctc cgttcctgca aaaccaaaaca ccaggcattt acaaattctg tcaggagcac 600
 gatatcctgg tggaaagcata ttctccgctg ggcccgtgct ggaagaaaac cggcaggat 660
 gacagccaac ctttttttga gtacgtcaaa gaattgagcg aaaaatacaa taaatccgag 720
 gccagatca tcttgcgctg ggtcactaaa cgoggtgtgc tgccagttac cacctcttca 780
 aagcctcagc gcattagcga tgctcagaac ctgttttctc tcgacctgac agcgggaagag 840
 gttgataaaa tcacggagct gggtctggaa catgaaccgc tgcgcctgta ctggaataaa 900

ttgtatggca aatataacta cgccgccag aaagtgtaat ga

942

<210> 262

<211> 313

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 262

Met	Ser	Phe	His	Gln	Gln	Phe	Phe	Thr	Leu	Asn	Asn	Gly	Asn	Lys	Ile	
1				5					10					15		
Pro	Ala	Ile	Ala	Ile	Ile	Gly	Thr	Gly	Thr	Ala	Trp	Tyr	Lys	Ser	Glu	
			20					25					30			
Glu	Thr	Asp	Ala	Thr	Phe	Ser	Asn	Ser	Leu	Val	Glu	Gln	Ile	Val	Tyr	
		35					40					45				
Ala	Leu	Lys	Leu	Pro	Gly	Ile	Ile	His	Ile	Asp	Ala	Ala	Glu	Ile	Tyr	
	50					55				60						
Arg	Thr	Tyr	Pro	Glu	Val	Gly	Lys	Ala	Leu	Ser	Leu	Thr	Glu	Lys	Pro	
65					70					75					80	
Arg	Asn	Ala	Ile	Phe	Leu	Thr	Asp	Lys	Tyr	Ser	Pro	Gln	Ile	Lys	Met	
				85					90					95		
Ser	Asp	Ser	Pro	Ala	Asp	Gly	Leu	Asp	Leu	Ala	Leu	Lys	Lys	Met	Gly	
			100				105						110			
Thr	Asp	Tyr	Val	Asp	Leu	Tyr	Leu	Leu	His	Ser	Pro	Leu	Val	Ser	Lys	
		115					120					125				
Glu	Val	Asn	Gly	Leu	Ser	Leu	Glu	Glu	Ala	Trp	Lys	Asp	Met	Glu	Gln	
	130					135					140					
Leu	Tyr	Lys	Ser	Gly	Lys	Ala	Lys	Asn	Ile	Gly	Val	Ser	Asn	Phe	Thr	
145					150				155						160	
Val	Glu	Asp	Leu	Gln	Arg	Ile	Leu	Arg	Val	Ala	Glu	Val	Lys	Pro	Gln	
				165				170						175		
Val	Asn	Gln	Ile	Glu	Phe	Ser	Pro	Phe	Leu	Gln	Asn	Gln	Thr	Pro	Gly	
			180					185					190			
Ile	Tyr	Lys	Phe	Cys	Gln	Glu	His	Asp	Ile	Leu	Val	Glu	Ala	Tyr	Ser	
		195					200					205				
Pro	Leu	Gly	Pro	Leu	Arg	Lys	Lys	Thr	Ala	Gln	Asp	Asp	Ser	Gln	Pro	
	210					215					220					
Phe	Phe	Glu	Tyr	Val	Lys	Glu	Leu	Ser	Glu	Lys	Tyr	Asn	Lys	Ser	Glu	
225					230					235					240	
Ala	Gln	Ile	Ile	Leu	Arg	Trp	Val	Thr	Lys	Arg	Gly	Val	Leu	Pro	Val	
				245					250					255		
Thr	Thr	Ser	Ser	Lys	Pro	Gln	Arg	Ile	Ser	Asp	Ala	Gln	Asn	Leu	Phe	
			260					265					270			
Ser	Phe	Asp	Leu	Thr	Ala	Glu	Glu	Val	Asp	Lys	Ile	Thr	Glu	Leu	Gly	
		275					280					285				
Leu	Glu	His	Glu	Pro	Leu	Arg	Leu	Tyr	Trp	Asn	Lys	Leu	Tyr	Gly	Lys	
	290					295					300					
Tyr	Asn	Tyr	Ala	Ala	Gln	Lys	Val									
305					310											

<210> 263

<211> 942

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 263

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atgtcttttc accaacagtt ttccacgctg aacaacggca ataaaatccc ggcgattgcc 60
atcatcggca ctggtacagc gtggtataaa agtgaagaaa ctgacgcgcac cttctccaat 120
agtctggttg aacaaatcgt gtatgcgttg aaactgcgcg ggattatcca catcgacgcc 180
gcggagattt atcgcaccta cccggaagtg ggtaaagcac tgtccctgac cgaaaagcct 240
cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactccctt 300
gcggacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
ttacattccc cgttagtttc gaaggaagtg aatggcttaa gcttagaaga ggcttggaaa 420
gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggttc caatttcaca 480
gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
gagttctctc cgttcctgca aaaccaaaca ccaggcattt acaaattctg tcaggagcac 600
gatatcctgg tggaaagcata ttctccgctg ggcccgctgc ggaagaaaac cgcgcaggat 660
gacagccaac cattttttga gtacgtcaaa gaattgagcg aaaaataccg caaatccgag 720
gccagatca tcttgcgctg ggtcactaaa cgcggtgtgc tgccagttac cacctcttca 780
aagcctcagc gcattagcga tgctcagaac ctgttttctt tcgacctgac agcgggaagag 840
gttgataaaa tcacggagct gggctctggaa catgaaccgc tgcgcctgta ctggaataaa 900
ttgtatggca aatataacta cgccgccagc aaagtgtaat ga 942
```

<210> 264

<211> 313

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 264

```
Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
1          5          10          15
Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Ala Trp Tyr Lys Ser Glu
20          25          30
Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
35          40          45
Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Ile Tyr
50          55          60
Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
65          70          75          80
Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
85          90          95
Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
100         105         110
Thr Asp Tyr Val Asp Leu Tyr Leu Leu His Ser Pro Leu Val Ser Lys
115         120         125
Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
130         135         140
Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Thr
145         150         155         160
Val Glu Asp Leu Gln Arg Ile Leu Lys Val Ala Glu Val Lys Pro Gln
165         170         175         180
Val Asn Gln Ile Glu Phe Ser Pro Phe Leu Gln Asn Gln Thr Pro Gly
180         185         190
Ile Tyr Lys Phe Cys Gln Glu His Asp Ile Leu Val Glu Ala Tyr Ser
195         200         205
Pro Leu Gly Pro Leu Arg Lys Lys Thr Ala Gln Asp Asp Ser Gln Pro
210         215         220
Phe Phe Glu Tyr Val Lys Glu Leu Ser Glu Lys Tyr Arg Lys Ser Glu
225         230         235         240
Ala Gln Ile Ile Leu Arg Trp Val Thr Lys Arg Gly Val Leu Pro Val
245         250         255
```


Thr	Thr	Ser	Ser	Lys	Pro	Gln	Arg	Ile	Ser	Asp	Ala	Gln	Asn	Leu	Phe
			260					265					270		
Ser	Phe	Asp	Leu	Thr	Ala	Glu	Glu	Val	Asp	Lys	Ile	Thr	Glu	Leu	Gly
		275					280					285			
Leu	Glu	His	Glu	Pro	Leu	Arg	Leu	Tyr	Trp	Asn	Lys	Leu	Tyr	Gly	Lys
	290					295					300				
Tyr	Asn	Tyr	Ala	Ala	Gln	Lys	Val								
305					310										

<210> 265

<211> 942

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 265

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atgtcttttc accaacagtt tttcacgctg aacaacggca ataaaatccc ggogattgcc 60
atcatcggca ctggtacaaa atggtataaa agtgaagaaa ctgacgcgac cttctccaat 120
agtctggttg aacaaatcgt gtatgcgttg aaactgccgg ggattatcca catcgacgcc 180
gcggagattt atcgcaccta cccggaagtg ggtaaagcac tgtccctgac cgaaaagcct 240
cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactcccct 300
gcggacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
attcattccc cgttagtttc gaaggaagtg aatggcttaa gcttagaaga ggcttggaaa 420
gatattggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggttc caatttcaca 480
gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
gagttctctc cgttcctgca aaaccaaaca ccaggcattt gcaaattctg tcaggagcac 600
gatatactgg tggaagcata ttctccgctg ggcccgtg gcgatgaaaac cgcgcaggat 660
gacagccaac cattttttga gtacgtcaaa gaattgagcg aaaaatacaa taaatccgag 720
gccagatca tcttgcgctg ggtcactaaa cgcggtgtgc tgccagttac cacctottca 780
aagcctcagc gcattagcga tgctcagaac ctgttttctt tcgacctgac agcgggaagag 840
gttgataaaa tcacggagct gggctctggaa catgaaccgc tgcgcctgta ctggaataaa 900
ttgtatggca aatataacta cgccgccag aaagtgtaat ga 942

```

<210> 266

<211> 313

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 266

Met	Ser	Phe	His	Gln	Gln	Phe	Phe	Thr	Leu	Asn	Asn	Gly	Asn	Lys	Ile
1			5					10					15		
Pro	Ala	Ile	Ala	Ile	Ile	Gly	Thr	Gly	Thr	Lys	Trp	Tyr	Lys	Ser	Glu
			20					25					30		
Glu	Thr	Asp	Ala	Thr	Phe	Ser	Asn	Ser	Leu	Val	Glu	Gln	Ile	Val	Tyr
		35					40					45			
Ala	Leu	Lys	Leu	Pro	Gly	Ile	Ile	His	Ile	Asp	Ala	Ala	Glu	Ile	Tyr
	50					55					60				
Arg	Thr	Tyr	Pro	Glu	Val	Gly	Lys	Ala	Leu	Ser	Leu	Thr	Glu	Lys	Pro
65				70						75				80	
Arg	Asn	Ala	Ile	Phe	Leu	Thr	Asp	Lys	Tyr	Ser	Pro	Gln	Ile	Lys	Met
			85						90					95	
Ser	Asp	Ser	Pro	Ala	Asp	Gly	Leu	Asp	Leu	Ala	Leu	Lys	Lys	Met	Gly
			100					105					110		
Thr	Asp	Tyr	Val	Asp	Leu	Tyr	Leu	Ile	His	Ser	Pro	Leu	Val	Ser	Lys

	115		120		125										
Glu	Val	Asn	Gly	Leu	Ser	Leu	Glu	Glu	Ala	Trp	Lys	Asp	Met	Glu	Gln
	130					135					140				
Leu	Tyr	Lys	Ser	Gly	Lys	Ala	Lys	Asn	Ile	Gly	Val	Ser	Asn	Phe	Thr
145					150					155					160
Val	Glu	Asp	Leu	Gln	Arg	Ile	Leu	Lys	Val	Ala	Glu	Val	Lys	Pro	Gln
			165						170					175	
Val	Asn	Gln	Ile	Glu	Phe	Ser	Pro	Phe	Leu	Gln	Asn	Gln	Thr	Pro	Gly
		180						185					190		
Ile	Cys	Lys	Phe	Cys	Gln	Glu	His	Asp	Ile	Leu	Val	Glu	Ala	Tyr	Ser
	195						200				205				
Pro	Leu	Gly	Pro	Leu	Arg	Met	Lys	Thr	Ala	Gln	Asp	Asp	Ser	Gln	Pro
	210					215					220				
Phe	Phe	Glu	Tyr	Val	Lys	Glu	Leu	Ser	Glu	Lys	Tyr	Asn	Lys	Ser	Glu
225					230					235					240
Ala	Gln	Ile	Ile	Leu	Arg	Trp	Val	Thr	Lys	Arg	Gly	Val	Leu	Pro	Val
			245					250						255	
Thr	Thr	Ser	Ser	Lys	Pro	Gln	Arg	Ile	Ser	Asp	Ala	Gln	Asn	Leu	Phe
		260					265						270		
Ser	Phe	Asp	Leu	Thr	Ala	Glu	Glu	Val	Asp	Lys	Ile	Thr	Glu	Leu	Gly
	275					280					285				
Leu	Glu	His	Glu	Pro	Leu	Arg	Leu	Tyr	Trp	Asn	Lys	Leu	Tyr	Gly	Lys
	290					295				300					
Tyr	Asn	Tyr	Ala	Ala	Gln	Lys	Val								
305					310										

<210> 267
 <211> 942
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 267
 atgtcttttt accaacagtt ttccacgctg aacaaaggca ataaaatccc ggcgattgcc 60
 atcatcgcca ctggtacagc gtggtataaa agtgaagaaa ctgacgcgac cttctccaat 120
 agtctggttg aacaaatcgt gtatgcgttg aaactgccgg ggattatcca catcgacgcc 180
 gcggagattt atcgcaccta ccoggaagtg ggtaaagcac tgtccctgac cgaaaagcct 240
 cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactcccct 300
 gcggacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
 ttacattccc cgttcgttcc gaaggaagtg aatggcttaa gcttagaaga ggcttggaaa 420
 gatattggagc agttatacaa aaccggtaaa gctaaaaaca tcgggggttc caatttcaca 480
 gtggaagacc tgcaacgtat cctgcgtgct gctgaagtta aacctcaggt caaccagatt 540
 gagttctctc cgttcctgca aaaccaaaca ccaggcattt acaaattctg tcaggagcac 600
 gatatacttg tggaagcata ttctccgctg ggcccgcgtg ggaagaaaac cgcgcaggat 660
 gacagccaac ctttttttga gtacgtcaaa gaattgagcg aaaaatacaa taaatccgag 720
 gccagatca tctgcgctg ggtcactaaa cgcggtgtgc tgccagttac cactcttca 780
 aagcctcagc gcattagcga tgctcagaac ctgttttctt tcgacctgac agcggaagag 840
 gttgataaaa tcacggagct gggctctggaa catgaaccgc tgcgcctgta ctggaataaa 900
 ttgtatggca aatataacta cgccgccag aaagtgtaat ga 942

<210> 268
 <211> 313
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 268

```
Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
1      5      10      15
Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Ala Trp Tyr Lys Ser Glu
20      25      30
Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
35      40      45
Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Ile Tyr
50      55      60
Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
65      70      75      80
Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
85      90      95
Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
100     105     110
Thr Asp Tyr Val Asp Leu Tyr Leu Leu His Ser Pro Phe Val Ser Lys
115     120     125
Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
130     135     140
Leu Tyr Lys Thr Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Thr
145     150     155     160
Val Glu Asp Leu Gln Arg Ile Leu Arg Val Ala Glu Val Lys Pro Gln
165     170     175
Val Asn Gln Ile Glu Phe Ser Pro Phe Leu Gln Asn Gln Thr Pro Gly
180     185     190
Ile Tyr Lys Phe Cys Gln Glu His Asp Ile Leu Val Glu Ala Tyr Ser
195     200     205
Pro Leu Gly Pro Leu Arg Lys Lys Thr Ala Gln Asp Asp Ser Gln Pro
210     215     220
Phe Phe Glu Tyr Val Lys Glu Leu Ser Glu Lys Tyr Asn Lys Ser Glu
225     230     235     240
Ala Gln Ile Ile Leu Arg Trp Val Thr Lys Arg Gly Val Leu Pro Val
245     250     255
Thr Thr Ser Ser Lys Pro Gln Arg Ile Ser Asp Ala Gln Asn Leu Phe
260     265     270
Ser Phe Asp Leu Thr Ala Glu Glu Val Asp Lys Ile Thr Glu Leu Gly
275     280     285
Leu Glu His Glu Pro Leu Arg Leu Tyr Trp Asn Lys Leu Tyr Gly Lys
290     295     300
Tyr Asn Tyr Ala Ala Gln Lys Val
305      310
```

<210> 269

<211> 942

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 269

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atgtctttttc accaacagtt tttaacgctg aacaacggca ataaaatccc ggcgattgcc 60
accatcggca ctggtacagc gtggtataaa agtgaagaaa ctgacgcgac ctctccaat 120
agtctggttg aacaaatcgt gtatgcgttg aaactgccgg ggattatcca catcgacgcc 180
gcgagagatt atgcaccta cccggaagtg ggtaaagcac tgtccctgac cgaaaagcct 240
cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactcccct 300
gcggaaggctc tggatttagc attgaagaaa atgggtacag attatgttg tttatatctg 360
attcattccc cgtagtttc gaaggaagtg aatggcttaa gcttagaaga ggcttgga 420
gatattggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggttc caatttcaca 480
```

```

gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
gagttctctc cgttcctgca aaaccaaaca ccaggcattt acaaattctg tcaggagcac 600
gatatcctgg tggaagcata ttctccgctg ggcccgtgct ggaagaaaac cgcgccaggat 660
gacagccaac cattttttga gtacgtcaaa gaattgagcg aaaaatacaa taaatccgag 720
gcccagatca tcctgcgctg ggctactaaa cgcggtgtgc tgccagttac cacctcttca 780
aagcctcagc gcattagcga tgctcagaac ctgttttcct tcgacctgac agcgggaagag 840
gttgataaaa tcacggagct gggctctggaa catgaaccgc tgcgcctgta ctggaataaa 900
ttgtatggca aatataacta cgccgccag aaagtgtaat ga 942

```

<210> 270

<211> 313

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 270

```

Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
1          5          10          15
Pro Ala Ile Ala Thr Ile Gly Thr Gly Thr Ala Trp Tyr Lys Ser Glu
20          25          30
Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
35          40          45
Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Ile Tyr
50          55          60
Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
65          70          75          80
Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
85          90          95
Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
100         105         110
Thr Asp Tyr Val Asp Leu Tyr Leu Ile His Ser Pro Leu Val Ser Lys
115         120         125
Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
130         135         140
Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Thr
145         150         155         160
Val Glu Asp Leu Gln Arg Ile Leu Lys Val Ala Glu Val Lys Pro Gln
165         170         175
Val Asn Gln Ile Glu Phe Ser Pro Phe Leu Gln Asn Gln Thr Pro Gly
180         185         190
Ile Tyr Lys Phe Cys Gln Glu His Asp Ile Leu Val Glu Ala Tyr Ser
195         200         205
Pro Leu Gly Pro Leu Arg Lys Lys Thr Ala Gln Asp Asp Ser Gln Pro
210         215         220
Phe Phe Glu Tyr Val Lys Glu Leu Ser Glu Lys Tyr Asn Lys Ser Glu
225         230         235         240
Ala Gln Ile Ile Leu Arg Trp Val Thr Lys Arg Gly Val Leu Pro Val
245         250         255
Thr Thr Ser Ser Lys Pro Gln Arg Ile Ser Asp Ala Gln Asn Leu Phe
260         265         270
Ser Phe Asp Leu Thr Ala Glu Glu Val Asp Lys Ile Thr Glu Leu Gly
275         280         285
Leu Glu His Glu Pro Leu Arg Leu Tyr Trp Asn Lys Leu Tyr Gly Lys
290         295         300
Tyr Asn Tyr Ala Ala Gln Lys Val
305         310

```

<210> 271
<211> 942
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 271
atgtcttttc accaacagtt tttcacgctg aacaacggca ataaaatccc ggcgattgcc 60
atcatcggca ctggtacagc gtggtataaa agtgaagaaa ctgacgcgac cttctccaat 120
agtctggttg aacaaatcgt gtatgcgttg aaactgccgg ggattatcca catcgacgcc 180
gcgagatttt atcgcaccta cccggaagtg ggtaaagcac tgtccctgac cgaaaagcct 240
cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactcccct 300
gcgacaggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
ttacattccc cgttagtctt gaaggaagtg aatggcttaa gcttagaaga ggcttggaag 420
gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggttt caatttcaca 480
gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
gagttctctc cgttcctgca aaaccaaaaca ccaggcattt gcaaattctg tcaggagcac 600
gatatcctgg tgggaagcata ttctccgctg ggcccgtctg ggaagaaaac cgcgcaggat 660
gacagccaac cattttttga gtacgtcaaa gaattgagcg aaaaataccg caaatccgag 720
gccagatca tctcgcgctg ggtcactaaa cgcggtgtgc tgccagttac cacctcttca 780
aagcctcagc gcattagcga tgctcagaac ctgttttcct tcgacctgac agcggaagag 840
gttgataaaa tcacggagct gggctctggaa catgaaccgc tcgcctgta ctggaataaa 900
ttgtatggca aatataacta cgccgccag aaagtgtaat ga 942

<210> 272
<211> 313
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 272
Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
1 5 10 15
Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Ala Trp Tyr Lys Ser Glu
20 25 30
Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
35 40 45
Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Ile Tyr
50 55 60
Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
65 70 75 80
Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
85 90 95
Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
100 105 110
Thr Asp Tyr Val Asp Leu Tyr Leu Leu His Ser Pro Leu Val Ser Lys
115 120 125
Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
130 135 140
Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Thr
145 150 155 160
Val Glu Asp Leu Gln Arg Ile Leu Lys Val Ala Glu Val Lys Pro Gln
165 170 175
Val Asn Gln Ile Glu Phe Ser Pro Phe Leu Gln Asn Gln Thr Pro Gly
180 185 190
Ile Cys Lys Phe Cys Gln Glu His Asp Ile Leu Val Glu Ala Tyr Ser

Arg	Thr	Tyr	Pro	Glu	Val	Gly	Lys	Ala	Leu	Ser	Leu	Thr	Glu	Lys	Pro
65					70					75					80
Arg	Asn	Ala	Ile	Phe	Leu	Thr	Asp	Lys	Tyr	Ser	Pro	Gln	Ile	Lys	Met
			85					90						95	
Ser	Asp	Ser	Pro	Ala	Asp	Gly	Leu	Asp	Leu	Ala	Leu	Lys	Lys	Met	Gly
			100				105					110			
Thr	Asp	Tyr	Val	Asp	Leu	Tyr	Leu	Leu	His	Ser	Pro	Leu	Val	Ser	Lys
	115					120						125			
Glu	Val	Asn	Gly	Leu	Ser	Leu	Glu	Glu	Ala	Trp	Lys	Asp	Met	Glu	Gln
	130					135					140				
Leu	Tyr	Lys	Ser	Gly	Lys	Ala	Lys	Asn	Ile	Gly	Val	Ser	Asn	Phe	Thr
145					150				155						160
Val	Glu	Asp	Leu	Gln	Arg	Ile	Leu	Lys	Val	Ala	Glu	Val	Lys	Pro	Gln
			165				170							175	
Val	Asn	Gln	Ile	Glu	Phe	Ser	Pro	Phe	Leu	Gln	Asn	Gln	Thr	Pro	Gly
			180				185						190		
Ile	Tyr	Lys	Phe	Cys	Gln	Glu	His	Asp	Ile	Leu	Val	Glu	Ala	Tyr	Ser
	195					200						205			
Pro	Leu	Gly	Pro	Leu	Arg	Lys	Lys	Thr	Ala	Gln	Asp	Asp	Ser	Gln	Pro
	210					215					220				
Phe	Phe	Glu	Tyr	Val	Lys	Glu	Leu	Ser	Glu	Lys	Tyr	Asn	Lys	Ser	Glu
225					230				235						240
Ala	Gln	Ile	Ile	Leu	Arg	Trp	Val	Thr	Lys	Arg	Gly	Val	Leu	Pro	Val
			245				250							255	
Thr	Thr	Ser	Ser	Lys	Pro	Gln	Arg	Ile	Ser	Asp	Ala	Gln	Asn	Leu	Phe
			260				265						270		
Ser	Phe	Asp	Leu	Thr	Ala	Glu	Glu	Val	Asp	Lys	Ile	Thr	Glu	Leu	Gly
		275				280						285			
Leu	Glu	His	Glu	Pro	Leu	Arg	Leu	Tyr	Trp	Asn	Lys	Leu	Tyr	Gly	Lys
	290					295					300				
Tyr	Asn	Tyr	Ala	Ala	Gln	Lys	Val								
305					310										

<210> 275

<211> 942

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 275

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atgtcttttc accaacagtt ttccacgctg aacaacggca ataaaatccc ggcgattgcc 60
atcatcggca ctggtacagc gtggtataaa agtgaagaaa ctgacgogac cttctccaat 120
agtctggttg aacaaatcgt gtatgcgttg aaactgccgg ggattatoca catcgacgcc 180
gcggagattt atcgcaccta cccggaagtg ggtaaagcac tgtccctgac cgaaaagcct 240
cgtaacgcga tttttctgac ggataaatat totccgcaga ttaaaatgag tgactcccct 300
gcggacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
attcattccc cgttagtttc gaaggaagtg aatggcttaa gcttagaaga ggcttgga 420
gatattggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggttc caatttcaca 480
gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
gagttctctc cgttcctgca aaaccaaaca ccaggcattt gcaaattctg tcaggagcac 600
gatatcctgg tggaagcata ttctccgctg ggcccgtgc ggaagaaaac cgcgcaggat 660
gacagccaac cattttttga gtacgtcaaa gaattgagcg aaaaatacaa taaatccgag 720
gcccgatca tcctgcgctg ggtaactaaa cgcggtgtgc tgccagttac cacctcttca 780
aagcctcagc gcattagcga tgctcagaac ctgttttctc tcgacctgac agcggaagag 840
gttgataaaa tcacggagct ggtctcggaa catgaaccgc tcgcctgtga ctggaataaa 900
ttgtatggca aatataacta cgccgccag aaagtgtaat ga 942

```

<210> 276
 <211> 313
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 276
 Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
 1 5 10 15
 Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Ala Trp Tyr Lys Ser Glu
 20 25 30
 Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
 35 40 45
 Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Ile Tyr
 50 55 60
 Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
 65 70 75 80
 Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
 85 90 95
 Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
 100 105 110
 Thr Asp Tyr Val Asp Leu Tyr Leu Ile His Ser Pro Leu Val Ser Lys
 115 120 125
 Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
 130 135 140
 Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Thr
 145 150 155 160
 Val Glu Asp Leu Gln Arg Ile Leu Lys Val Ala Glu Val Lys Pro Gln
 165 170 175
 Val Asn Gln Ile Glu Phe Ser Pro Phe Leu Gln Asn Gln Thr Pro Gly
 180 185 190
 Ile Cys Lys Phe Cys Gln Glu His Asp Ile Leu Val Glu Ala Tyr Ser
 195 200 205
 Pro Leu Gly Pro Leu Arg Lys Lys Thr Ala Gln Asp Asp Ser Gln Pro
 210 215 220
 Phe Phe Glu Tyr Val Lys Glu Leu Ser Glu Lys Tyr Asn Lys Ser Glu
 225 230 235 240
 Ala Gln Ile Ile Leu Arg Trp Val Thr Lys Arg Gly Val Leu Pro Val
 245 250 255
 Thr Thr Ser Ser Lys Pro Gln Arg Ile Ser Asp Ala Gln Asn Leu Phe
 260 265 270
 Ser Phe Asp Leu Thr Ala Glu Glu Val Asp Lys Ile Thr Glu Leu Gly
 275 280 285
 Leu Glu His Glu Pro Leu Arg Leu Tyr Trp Asn Lys Leu Tyr Gly Lys
 290 295 300
 Tyr Asn Tyr Ala Ala Gln Lys Val
 305 310

<210> 277
 <211> 942
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 277
 atgtcttttc accaacagtt ttccacgctg aacaacggca ataaaatccc ggcgattgcc 60


```

atcatcggca ctggtacagc gtggtataaa cccgaagaaa ctgacgcgac cttctccaat 120
agtctggttg aacaaatcgt gtatgcgttg aaactgccgg ggattatcca catcgacgcc 180
gcggagattt atcgcaccta ccoggaagtg ggtaaagcac tgtccctgac cgaaaagcct 240
cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactcccct 300
gcggacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
attcattccc cgttagtttc gaaggaagtg aatggcttaa gcttagaaga ggcttggaaa 420
gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggttc caatttcaca 480
gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
gagttctctc cgttcctgca aaaccaaaca ccaggcattt gcaaattctg tcaggagcac 600
gatatcctgg tggaaacata ttctccgtg ggcccgtgc ggaagaaaac cgcgaggat 660
gacagccaac ctttttttga gtacgtcaaa gaattgagcg aaaaatacaa taaatccgag 720
gcccagatca tcttgcgctg ggctactaaa cgcggtgtgc tgccagttac cacctcttca 780
aagcctcagc gcattagcga tgctcagaac ctgttttctc tcgacctgac agcggaagag 840
gttgataaaa tcacggagct gggctcggaa catgaaccgc tcgcgctgta ctggaataaa 900
ttgtatggca aatataacta cgccgccag aaagtgtaat ga 942

```

<210> 278
 <211> 313
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 278

Met	Ser	Phe	His	Gln	Gln	Phe	Phe	Thr	Leu	Asn	Asn	Gly	Asn	Lys	Ile	1	5	10	15
Pro	Ala	Ile	Ala	Ile	Ile	Gly	Thr	Gly	Thr	Ala	Trp	Tyr	Lys	Pro	Glu	20	25	30	
Glu	Thr	Asp	Ala	Thr	Phe	Ser	Asn	Ser	Leu	Val	Glu	Gln	Ile	Val	Tyr	35	40	45	
Ala	Leu	Lys	Leu	Pro	Gly	Ile	Ile	His	Ile	Asp	Ala	Ala	Glu	Ile	Tyr	50	55	60	
Arg	Thr	Tyr	Pro	Glu	Val	Gly	Lys	Ala	Leu	Ser	Leu	Thr	Glu	Lys	Pro	65	70	75	80
Arg	Asn	Ala	Ile	Phe	Leu	Thr	Asp	Lys	Tyr	Ser	Pro	Gln	Ile	Lys	Met	85	90	95	
Ser	Asp	Ser	Pro	Ala	Asp	Gly	Leu	Asp	Leu	Ala	Leu	Lys	Lys	Met	Gly	100	105	110	
Thr	Asp	Tyr	Val	Asp	Leu	Tyr	Leu	Ile	His	Ser	Pro	Leu	Val	Ser	Lys	115	120	125	
Glu	Val	Asn	Gly	Leu	Ser	Leu	Glu	Glu	Ala	Trp	Lys	Asp	Met	Glu	Gln	130	135	140	
Leu	Tyr	Lys	Ser	Gly	Lys	Ala	Lys	Asn	Ile	Gly	Val	Ser	Asn	Phe	Thr	145	150	155	160
Val	Glu	Asp	Leu	Gln	Arg	Ile	Leu	Lys	Val	Ala	Glu	Val	Lys	Pro	Gln	165	170	175	
Val	Asn	Gln	Ile	Glu	Phe	Ser	Pro	Phe	Leu	Gln	Asn	Gln	Thr	Pro	Gly	180	185	190	
Ile	Cys	Lys	Phe	Cys	Gln	Glu	His	Asp	Ile	Leu	Val	Glu	Ala	Tyr	Ser	195	200	205	
Pro	Leu	Gly	Pro	Leu	Arg	Lys	Lys	Thr	Ala	Gln	Asp	Asp	Ser	Gln	Pro	210	215	220	
Phe	Phe	Glu	Tyr	Val	Lys	Glu	Leu	Ser	Glu	Lys	Tyr	Asn	Lys	Ser	Glu	225	230	235	240
Ala	Gln	Ile	Ile	Leu	Arg	Trp	Val	Thr	Lys	Arg	Gly	Val	Leu	Pro	Val	245	250	255	
Thr	Thr	Ser	Ser	Lys	Pro	Gln	Arg	Ile	Ser	Asp	Ala	Gln	Asn	Leu	Phe	260	265	270	
Ser	Phe	Asp	Leu	Thr	Ala	Glu	Glu	Val	Asp	Lys	Ile	Thr	Glu	Leu	Gly				

```

          275                               280                               285
Leu Glu His Glu Pro Leu Arg Leu Tyr Trp Asn Lys Leu Tyr Gly Lys
      290                               295                               300
Tyr Asn Tyr Ala Ala Gln Lys Val
    305                               310

```

Leu	Tyr	Lys	Ser	Gly	Lys	Ala	Lys	Asn	Ile	Gly	Val	Ser	Asn	Phe	Thr
145					150					155					160
Val	Glu	Asp	Leu	Gln	Arg	Ile	Leu	Lys	Val	Ala	Glu	Val	Lys	Pro	Gln
				165					170						175
Val	Asn	Gln	Ile	Glu	Phe	Ser	Pro	Leu	Leu	Gln	Asn	Gln	Thr	Pro	Gly
			180					185					190		
Ile	Cys	Lys	Phe	Cys	Gln	Glu	His	Asp	Ile	Leu	Val	Glu	Ala	Tyr	Ser
	195						200					205			
Pro	Leu	Gly	Pro	Leu	Arg	Lys	Lys	Thr	Ala	Gln	Asp	Asp	Ser	Gln	Pro
	210					215					220				
Phe	Phe	Glu	Tyr	Val	Lys	Glu	Leu	Ser	Glu	Lys	Tyr	Asn	Lys	Ser	Glu
225					230					235					240
Ala	Gln	Val	Ile	Leu	Arg	Trp	Val	Thr	Lys	Arg	Gly	Val	Leu	Pro	Val
				245					250						255
Thr	Thr	Ser	Ser	Lys	Pro	Gln	Arg	Ile	Ser	Asp	Ala	Gln	Asn	Leu	Phe
			260					265					270		
Ser	Phe	Asp	Leu	Thr	Ala	Glu	Glu	Val	Asp	Lys	Ile	Thr	Glu	Leu	Gly
		275					280					285			
Leu	Asp	His	Glu	Pro	Leu	Arg	Leu	Tyr	Trp	Asn	Lys	Leu	Tyr	Gly	Lys
	290					295					300				
Tyr	Asn	Tyr	Ala	Ala	Gln	Lys	Val								
305					310										

<210> 281

<211> 942

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 281

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atgtcttttc accaagaatt tttcacgctg aacaacggca ataaaatccc ggcgattgcc 60
atcatcggca ctggtacagc gtggtataaa agtgaagaaa ctgacgcgac cttctccaat 120
accctgggtg aacaaatcgt gtatgcgttg aaactgccgg ggattatcca catcgacgcc 180
gcggagatgt atcgcaccta cccggaagtg ggtaaagcac tgtccctgac cgaaaagcct 240
cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactccoct 300
gcggacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
attcattccc cgttagtttc gaaggaagtg aatggcttaa gottagaaga ggcttgga 420
gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggttc caatttcaca 480
gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
gagttctctc cgttcctgca aaaccaaaaca ccaggcattt gcaaattctg tcagcaaacac 600
gacatcctgg tggaagcata ttctccgctg ggcccgtgac ggaagaaaac cgcgcaggat 660
gacagccaac cattttttga gtacgtcaaa gaattgagcg aaaaatacaa taaatccgag 720
gcccagatca tctgcgctg ggtcactaaa cgcggtgtgc tgccagttac caoctottca 780
aagcctcagc gcattagcga tgctcagaac atcttttctc tcgacctgac agcgggaagag 840
gttgataaaa tcacggagct gggctctgaa catgaacgcg tcgcgctgta ctggaataaa 900
ttgtatggca aatataacta cgccgccag aaagtgtaat ga 942

```

<210> 282

<211> 313

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 282

Met Ser Phe His Gln Glu Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile

1		5		10		15	
Pro	Ala	Ile	Ala	Ile	Ile	Gly	Thr
		20		25		30	
Glu	Thr	Asp	Ala	Thr	Phe	Ser	Asn
		35		40		45	
Ala	Leu	Lys	Leu	Pro	Gly	Ile	His
	50			55		60	
Arg	Thr	Tyr	Pro	Glu	Val	Gly	Lys
65				70		75	
Arg	Asn	Ala	Ile	Phe	Leu	Thr	Asp
			85		90		95
Ser	Asp	Ser	Pro	Ala	Asp	Gly	Leu
		100		105		110	
Thr	Asp	Tyr	Val	Asp	Leu	Tyr	Leu
	115			120		125	
Glu	Val	Asn	Gly	Leu	Ser	Leu	Glu
	130			135		140	
Leu	Tyr	Lys	Ser	Gly	Lys	Ala	Lys
145				150		155	
Val	Glu	Asp	Leu	Gln	Arg	Ile	Leu
			165		170		175
Val	Asn	Gln	Ile	Glu	Phe	Ser	Pro
	180			185		190	
Ile	Cys	Lys	Phe	Cys	Gln	Gln	His
	195			200		205	
Pro	Leu	Gly	Pro	Leu	Arg	Lys	Lys
	210			215		220	
Phe	Phe	Glu	Tyr	Val	Lys	Glu	Leu
225				230		235	
Ala	Gln	Ile	Ile	Leu	Arg	Trp	Val
			245		250		255
Thr	Thr	Ser	Ser	Lys	Pro	Gln	Arg
		260		265		270	
Ser	Phe	Asp	Leu	Thr	Ala	Glu	Glu
	275			280		285	
Leu	Glu	His	Glu	Pro	Leu	Arg	Leu
	290			295		300	
Tyr	Asn	Tyr	Ala	Ala	Gln	Lys	Val
305				310			

<210> 283

<211> 942

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 283

```

atgtcttttc accaagaatt tttcacgctg aacaacggca ataaaatccc ggcgattgcc 60
atcatcggca ctggtacagc gtggtataaa agtgaagaaa ctgacgcgac cttctccaat 120
accctggttg aacaattagt gtatgcgttg aaactgccgg gggttatcca catcgacgcc 180
gcggagattt atcgcaccta cccggaagtg ggtaaagcac tgtccctgac cgaaaagcct 240
cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactcccct 300
gcggacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatotg 360
attcattccc cgttagtttc gaaggaagtg aatggottaa gcttagaaga ggcttggaaa 420
gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcggggtttc caatttcaca 480
gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
gagttctctc cgttcctgca aaaccaaaac ccaggcattt gcaaattctg tcagcaacac 600
gatatcctgg tggaagcata ttctccgctg ggcccgcctg ggaagaaaac cgcgcaggat 660

```


<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 285

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atgtcttttc accaagaatt tttcacgctg aacaacggca ataaaatccc ggcgattgcc 60
atcatcggca ctggtacagc gtggtataaa agtgaagaaa ctgacgcgac cttctocaat 120
acctgggttg aacaattagt gtatgcgttg aaactgccgg ggattatcca catogaagcc 180
gcggagattt atcgcaccta cccggaagtg ggtaaagcac tgtccctgac cgaaaagcct 240
cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactcccct 300
gcggacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
ctgcattccc cgttagtttc gaaggaagtg aatggcttaa gcttagaaga ggcttggaaa 420
gatatggagg agttatacaa aagtggtaaa gctaaaaaca tcgggggttc caatttcaca 480
gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
gagttctctc cgttcctgca aaaccaaaca ccaggcattt gcaaattctg tcagcaacac 600
gatatcctgg tggaaagcata ttctccgctg ggcccgtctc ggaagaaaac cgcgcaggat 660
gacagccaac cattttttga gtacgtcaaa gaattgagcg aaaaatacaa taaaaccogag 720
gcccgatca tcttgogctg ggtcactaaa cgcggtgtgc tgccagttac cacctcttca 780
aagcctcagc gcattagcga tgctcagaac atcttttcct tcgacctgac agcggaagag 840
gttgataaaa tcacggagct ggtctggaa catgaaccgc tcgcctgta ctggaataaa 900
ttgtatggca aatataacta cgcgcccgag aaagtgtaat ga 942
```

<210> 286

<211> 313

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 286

```
Met Ser Phe His Gln Glu Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
1          5          10          15
Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Ala Trp Tyr Lys Ser Glu
20          25          30
Glu Thr Asp Ala Thr Phe Ser Asn Thr Leu Val Glu Gln Leu Val Tyr
35          40          45
Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Ile Tyr
50          55          60
Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
65          70          75          80
Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
85          90          95
Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
100          105          110
Thr Asp Tyr Val Asp Leu Tyr Leu Leu His Ser Pro Leu Val Ser Lys
115          120          125
Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Glu
130          135          140
Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Thr
145          150          155          160
Val Glu Asp Leu Gln Arg Ile Leu Lys Val Ala Glu Val Lys Pro Gln
165          170          175
Val Asn Gln Ile Glu Phe Ser Pro Phe Leu Gln Asn Gln Thr Pro Gly
180          185          190
Ile Cys Lys Phe Cys Gln Gln His Asp Ile Leu Val Glu Ala Tyr Ser
195          200          205
Pro Leu Gly Pro Leu Arg Lys Lys Thr Ala Gln Asp Asp Ser Gln Pro
210          215          220
```

Phe	Phe	Glu	Tyr	Val	Lys	Glu	Leu	Ser	Glu	Lys	Tyr	Asn	Lys	Thr	Glu
225					230					235					240
Ala	Gln	Ile	Ile	Leu	Arg	Trp	Val	Thr	Lys	Arg	Gly	Val	Leu	Pro	Val
				245					250					255	
Thr	Thr	Ser	Ser	Lys	Pro	Gln	Arg	Ile	Ser	Asp	Ala	Gln	Asn	Ile	Phe
			260					265					270		
Ser	Phe	Asp	Leu	Thr	Ala	Glu	Glu	Val	Asp	Lys	Ile	Thr	Glu	Leu	Gly
		275					280						285		
Leu	Glu	His	Glu	Pro	Leu	Arg	Leu	Tyr	Trp	Asn	Lys	Leu	Tyr	Gly	Lys
	290					295					300				
Tyr	Asn	Tyr	Ala	Ala	Gln	Lys	Val								
305					310										

<210> 287
 <211> 942
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 287

atgtcttttc	accaagaatt	tttcacgctg	aacaacggca	ataaaatccc	ggcgattgcc	60
atcatcggca	ctggtacagc	gtggtataaa	agtgaagaaa	ctgacgcgac	cttctccaat	120
agtctggttg	aacaattagt	gtatgcgttg	aaactgccgg	ggattatcca	catcgacgcc	180
gcggagattt	atcgcaccta	cccggaagtg	ggtaaagcac	tgtocttgac	cgaaaagcct	240
cgtaacgcga	tttttctgac	ggataaatat	tctccgcaga	ttaaaatgag	tgactccctt	300
gcggacggtc	tggatttagc	attgaagaaa	atgggtacag	attatgttga	tttatatctg	360
attcattccc	cgtagttttc	gaaggaagtg	aatggcttaa	gcttagaaga	ggcttggaaa	420
gatatggagc	agttatacaa	aagtggtaaa	gctaaaaaca	tcggggtttc	caatttcaca	480
gtggaagacc	tgcaacgtat	cctgaaagtc	gctgaagtta	aacctcaggt	caaccagatt	540
gagttctctc	cgttcctgca	aaaccaaaca	ccaggcattt	gcaaattctg	tcaggagcac	600
gatatcctgg	tggaagcata	ttctccgctg	ggcccgtctc	ggaagaaaac	cgcgcaggat	660
gacagccaac	cattttttga	gtacgtcaaa	gaattgagcg	aaaaatacaa	taaaaccgag	720
gccagatct	tactgcgctg	ggctactaaa	cgcggtgtgc	tgccagttac	cacctcttca	780
aagcctcagc	gcattagcga	tgctcagaac	ctgttttcct	tgcacctgac	agcgggaagag	840
gttgataaaa	tcacggagct	gggtctggaa	catgaaccgc	tgcgcctgta	ctggaataaa	900
ttgtatggca	aataataacta	cgccgcccag	aaagtgtaat	ga		942

<210> 288
 <211> 313
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 288

Met	Ser	Phe	His	Gln	Glu	Phe	Phe	Thr	Leu	Asn	Asn	Gly	Asn	Lys	Ile
1			5						10				15		
Pro	Ala	Ile	Ala	Ile	Ile	Gly	Thr	Gly	Thr	Ala	Trp	Tyr	Lys	Ser	Glu
			20					25					30		
Glu	Thr	Asp	Ala	Thr	Phe	Ser	Asn	Ser	Leu	Val	Glu	Gln	Leu	Val	Tyr
		35					40					45			
Ala	Leu	Lys	Leu	Pro	Gly	Ile	Ile	His	Ile	Asp	Ala	Ala	Glu	Ile	Tyr
	50					55				60					
Arg	Thr	Tyr	Pro	Glu	Val	Gly	Lys	Ala	Leu	Ser	Leu	Thr	Glu	Lys	Pro
65				70					75					80	
Arg	Asn	Ala	Ile	Phe	Leu	Thr	Asp	Lys	Tyr	Ser	Pro	Gln	Ile	Lys	Met

```
<210> 290
<211> 313
<212> PRT
```


<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 290

```
Met Ser Phe His Gln Glu Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
1          5          10          15
Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Ala Trp Tyr Lys Ser Glu
          20          25          30
Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
          35          40          45
Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Ile Tyr
          50          55          60
Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
65          70          75          80
Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
          85          90          95
Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
          100         105         110
Thr Asp Tyr Val Asp Leu Tyr Leu Ile His Ser Pro Leu Val Ser Lys
          115         120         125
Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
          130         135         140
Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Thr
145         150         155         160
Val Glu Asp Leu Gln Arg Ile Leu Lys Val Ala Glu Val Lys Pro Gln
          165         170         175
Val Asn Gln Ile Glu Phe Ser Pro Phe Leu Gln Asn Gln Thr Pro Gly
          180         185         190
Ile Cys Lys Phe Cys Gln Glu His Asp Ile Leu Val Glu Ala Tyr Ser
          195         200         205
Pro Leu Gly Pro Leu Arg Lys Lys Thr Ala Gln Asp Asp Ser Gln Pro
          210         215         220
Phe Phe Glu Tyr Val Lys Glu Leu Ser Glu Lys Tyr Asn Lys Thr Glu
225         230         235         240
Ala Gln Ile Ile Leu Arg Trp Val Thr Lys Arg Gly Val Leu Pro Val
          245         250         255
Thr Thr Ser Ser Lys Pro Gln Arg Ile Ser Asp Ala Gln Asn Leu Phe
          260         265         270
Ser Phe Asp Leu Thr Ala Glu Glu Val Asp Lys Ile Thr Glu Leu Gly
          275         280         285
Leu Glu His Glu Pro Leu Arg Leu Tyr Trp Asn Lys Leu Tyr Gly Lys
          290         295         300
Tyr Asn Tyr Ala Ala Gln Lys Val
305          310
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<210> 291

<211> 942

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 291

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atgtcttttt accaagaatt tttaacgctg aacaacggca ataaaaatccc ggcgattgcc 60
atcatcggca ctggtacagc gtggtataaa agtgaagaaa ctgacgcgac cttctccaat 120
accctggttg aacaaatcgt gtatgcgttg aaactgcggg ggattatcca catcgacgcc 180
gcggagattt atcgcaccta ccggaagtg ggtaaagcac tgtccctgac cgaaaagcct 240
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cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactcccct 300
gcggacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
attcattccc cgttagtttc gaaggaagtg aatggcttaa gcttagaaga ggcttgga 420
gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggttc caatttcaca 480
gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
gagttctctc cgttcctgca aaaccaaaaca ccaggcattt gcaaattctg tcaggagcac 600
gatatcctgg tggaagcata ttctccgctg ggcccgtg gcgaagaaaac cgcgcaggat 660
gacagccaac catTTTTTga gtacgtcaaa gaattgagcg aaaaatacaa taaatccgag 720
gccagatca tcctgcgctg ggtcactaaa cgcggtgtgc tgccagttac cacctcttca 780
aagcctcagc gcattagcga tgctcagaac atcttttctc tcgacctgac agcggaagag 840
gttgataaaa tcacggagct gggctctggaa catgaaccgc tgcgcctgta ctggaataaa 900
ttgtatggca aatataacta cgccgccag aaagtgtaat ga 942

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<210> 292

<211> 313

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 292

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Met Ser Phe His Gln Glu Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
1          5          10          15
Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Ala Trp Tyr Lys Ser Glu
          20          25          30
Glu Thr Asp Ala Thr Phe Ser Asn Thr Leu Val Glu Gln Ile Val Tyr
          35          40          45
Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Ile Tyr
          50          55          60
Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
65          70          75          80
Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
          85          90          95
Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
          100          105          110
Thr Asp Tyr Val Asp Leu Tyr Leu Ile His Ser Pro Leu Val Ser Lys
          115          120          125
Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
          130          135          140
Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Thr
145          150          155          160
Val Glu Asp Leu Gln Arg Ile Leu Lys Val Ala Glu Val Lys Pro Gln
          165          170          175
Val Asn Gln Ile Glu Phe Ser Pro Phe Leu Gln Asn Gln Thr Pro Gly
          180          185          190
Ile Cys Lys Phe Cys Gln Glu His Asp Ile Leu Val Glu Ala Tyr Ser
          195          200          205
Pro Leu Gly Pro Leu Arg Lys Lys Thr Ala Gln Asp Asp Ser Gln Pro
          210          215          220
Phe Phe Glu Tyr Val Lys Glu Leu Ser Glu Lys Tyr Asn Lys Ser Glu
225          230          235          240
Ala Gln Ile Ile Leu Arg Trp Val Thr Lys Arg Gly Val Leu Pro Val
          245          250          255
Thr Thr Ser Ser Lys Pro Gln Arg Ile Ser Asp Ala Gln Asn Ile Phe
          260          265          270
Ser Phe Asp Leu Thr Ala Glu Glu Val Asp Lys Ile Thr Glu Leu Gly
          275          280          285
Leu Glu His Glu Pro Leu Arg Leu Tyr Trp Asn Lys Leu Tyr Gly Lys
          290          295          300

```

Tyr Asn Tyr Ala Ala Gln Lys Val
305 310

<210> 293
<211> 942
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 293
atgtcttttt accaagaatt ttctacgctg aacaacggca ataaaatccc ggcgattgcc 60
atcatcggca ctggtacagc gtggtataaa agtgaagaaa ctgacgcgac cttctccaat 120
agtctggttg aacaaatcgt gtatgcgttg aaactgccgg ggattatcca catcgacgcc 180
gcggagattt atcgcaccta cccggaagtg ggtaaagcac tgtccctgac cgaaaagcct 240
cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactcccct 300
gcggacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
attcattccc cgttagtctt gaaggaagtg aatggcttaa gcttagaaga ggcttggaaa 420
gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggttt caatttcaca 480
gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
gagttctctc cgttcctgca aaaccaaaca ccaggcattt gcaaattctg tcaggagcac 600
gatatcctgg tggaagcata ttctccgctg ggcccgtctg ggaagaaaac cgcgcaggat 660
gacagccaac cattttttga gtacgtcaaa gaattgagcc agaaatacaa taaaaccgag 720
gccagatca tctgcgctg ggtcactaaa cgcggtgtgc tgccagttac cacctcttca 780
aaacctcagc gcattagcga tgctcagaac ctgttttctt tcgacctgac agcgggaagag 840
gttgataaaa tcacggagct gggctctggaa catgaacgc tcgcctgta ctggaataaa 900
ttgtatggca aatataacta cgcgcgcag aaagtgtaat ga 942

<210> 294
<211> 313
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 294
Met Ser Phe His Gln Glu Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
1 5 10 15
Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Ala Trp Tyr Lys Ser Glu
20 25 30
Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
35 40 45
Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Ile Tyr
50 55 60
Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
65 70 75 80
Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
85 90 95
Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
100 105 110
Thr Asp Tyr Val Asp Leu Tyr Leu Ile His Ser Pro Leu Val Ser Lys
115 120 125
Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
130 135 140
Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Thr
145 150 155 160
Val Glu Asp Leu Gln Arg Ile Leu Lys Val Ala Glu Val Lys Pro Gln

				165					170					175			
Val	Asn	Gln	Ile	Glu	Phe	Ser	Pro	Phe	Leu	Gln	Asn	Gln	Thr	Pro	Gly		
			180					185					190				
Ile	Cys	Lys	Phe	Cys	Gln	Glu	His	Asp	Ile	Leu	Val	Glu	Ala	Tyr	Ser		
		195					200					205					
Pro	Leu	Gly	Pro	Leu	Arg	Lys	Lys	Thr	Ala	Gln	Asp	Asp	Ser	Gln	Pro		
	210					215					220						
Phe	Phe	Glu	Tyr	Val	Lys	Glu	Leu	Ser	Gln	Lys	Tyr	Asn	Lys	Thr	Glu		
225					230					235					240		
Ala	Gln	Ile	Ile	Leu	Arg	Trp	Val	Thr	Lys	Arg	Gly	Val	Leu	Pro	Val		
			245					250					255				
Thr	Thr	Ser	Ser	Lys	Pro	Gln	Arg	Ile	Ser	Asp	Ala	Gln	Asn	Leu	Phe		
			260					265					270				
Ser	Phe	Asp	Leu	Thr	Ala	Glu	Glu	Val	Asp	Lys	Ile	Thr	Glu	Leu	Gly		
		275					280					285					
Leu	Glu	His	Glu	Pro	Leu	Arg	Leu	Tyr	Trp	Asn	Lys	Leu	Tyr	Gly	Lys		
	290					295					300						
Tyr	Asn	Tyr	Ala	Ala	Gln	Lys	Val										
305					310												

<210> 295
 <211> 942
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 295
 atgtcttttt accaagaatt tttcacgctg aacaacggca ataaaatccc ggcgattgcc 60
 atcatcgga ctggtacagc gtggtataaa agtgaagaaa ctgacgcgac cttctccaat 120
 agtctggttg aacaaatcgt gtatgcgttg aaactgccgg ggattatcca cctggaagcc 180
 gcggagattt atcgcaccta cccggaagtg ggtaaagcac tgtccctgac cgaaaagcct 240
 cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactcccct 300
 gcggacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
 ctgcattccc cgttagtttc gaaggaagtg aatggcttaa gcttagaaga ggcttggaaa 420
 gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggttc caatttcaca 480
 gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
 gagttctctc cgttcctgca aaaccaaaaca ccaggcattt gcaaattctg tcagcaaacac 600
 gatatacttg tggaagcata ttctccgctg ggcccgtgct ggaagaaaac cgcgaggat 660
 gacagccaac ctttttttga gtacgtcaaa gaattgagcg aaaaatacaa taaatccgag 720
 gccagatct tactgcgctg ggtcactaaa cgcggtgtgc tgccagttac cacctcttca 780
 aagcctcagc gcattagcga tgctcagaac ctgttttctc tcgacctgac agcgggaagag 840
 gttgataaaa tcacggagct gggtctggaa catgaaccgc tcgcctgta ctggaataaa 900
 ttgtatggca aatataacta cgccgccag aaagtgtaat ga 942

<210> 296
 <211> 313
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 296
 Met Ser Phe His Gln Glu Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
 1 5 10 15
 Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Ala Trp Tyr Lys Ser Glu
 20 25 30

Glu	Thr	Asp	Ala	Thr	Phe	Ser	Asn	Ser	Leu	Val	Glu	Gln	Ile	Val	Tyr
	35						40					45			
Ala	Leu	Lys	Leu	Pro	Gly	Ile	Ile	His	Leu	Asp	Ala	Ala	Glu	Ile	Tyr
	50					55					60				
Arg	Thr	Tyr	Pro	Glu	Val	Gly	Lys	Ala	Leu	Ser	Leu	Thr	Glu	Lys	Pro
	65				70					75					80
Arg	Asn	Ala	Ile	Phe	Leu	Thr	Asp	Lys	Tyr	Ser	Pro	Gln	Ile	Lys	Met
			85						90					95	
Ser	Asp	Ser	Pro	Ala	Asp	Gly	Leu	Asp	Leu	Ala	Leu	Lys	Lys	Met	Gly
			100					105					110		
Thr	Asp	Tyr	Val	Asp	Leu	Tyr	Leu	Leu	His	Ser	Pro	Leu	Val	Ser	Lys
	115						120					125			
Glu	Val	Asn	Gly	Leu	Ser	Leu	Glu	Glu	Ala	Trp	Lys	Asp	Met	Glu	Gln
	130					135					140				
Leu	Tyr	Lys	Ser	Gly	Lys	Ala	Lys	Asn	Ile	Gly	Val	Ser	Asn	Phe	Thr
	145				150					155					160
Val	Glu	Asp	Leu	Gln	Arg	Ile	Leu	Lys	Val	Ala	Glu	Val	Lys	Pro	Gln
			165					170						175	
Val	Asn	Gln	Ile	Glu	Phe	Ser	Pro	Phe	Leu	Gln	Asn	Gln	Thr	Pro	Gly
	180							185					190		
Ile	Cys	Lys	Phe	Cys	Gln	Gln	His	Asp	Ile	Leu	Val	Glu	Ala	Tyr	Ser
	195						200					205			
Pro	Leu	Gly	Pro	Leu	Arg	Lys	Lys	Thr	Ala	Gln	Asp	Asp	Ser	Gln	Pro
	210					215					220				
Phe	Phe	Glu	Tyr	Val	Lys	Glu	Leu	Ser	Glu	Lys	Tyr	Asn	Lys	Ser	Glu
	225				230					235					240
Ala	Gln	Ile	Leu	Leu	Arg	Trp	Val	Thr	Lys	Arg	Gly	Val	Leu	Pro	Val
			245						250					255	
Thr	Thr	Ser	Ser	Lys	Pro	Gln	Arg	Ile	Ser	Asp	Ala	Gln	Asn	Leu	Phe
			260					265					270		
Ser	Phe	Asp	Leu	Thr	Ala	Glu	Glu	Val	Asp	Lys	Ile	Thr	Glu	Leu	Gly
	275						280					285			
Leu	Glu	His	Glu	Pro	Leu	Arg	Leu	Tyr	Trp	Asn	Lys	Leu	Tyr	Gly	Lys
	290					295					300				
Tyr	Asn	Tyr	Ala	Ala	Gln	Lys	Val								
	305					310									

<210> 297

<211> 942

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 297

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atgtcttttc accaagaatt ttccacgctg aacaacggca ataaaatccc ggcgattgcc 60
atcatcggca ctggtacagc gtggtataaa agtgaagaaa ctgacgcgac cttctccaat 120
agtctggttg aacaattagt gtatgcgttg aaactgccgg ggattatcca catcgacgcc 180
gcggagattt atcgcaccta cccggaagtg ggtaaagcac tgccctgac cgaaaagcct 240
cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactccctc 300
gcggacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
attcattccc cgtagtttgc gaaggaagtg aatggcttaa gottagaaga ggcttggaag 420
gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggttc caatttcaca 480
gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
gagttctctc cgttcctgca aaaccaaaca ccaggcattt gcaaattctg tcagcaaacac 600
gatatcctgg tggaagcata ttctccgctg ggcccgtgct ggaagaaaac cgcgcaggat 660
gacagccaac cattttttga gtacgtcaaa gaattgagcg aaaaatacaa taaaaccgag 720
gccagatct tactgcgctg ggtcactaaa cgcggtgtgc tgccagttac cacctottca 780
aagcctcagc gcattagcga tgctcagaac ctgttttctc togacctgac agcgggaagag 840

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gttgataaaa tcacggagct gggctctggaa catgaaccgc tgcgcctgta ctggaataaa 900
 ttgtatggca aatataacta cgccgcccag aaagtgtaat ga 942

<210> 298
 <211> 313
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 298
 Met Ser Phe His Gln Glu Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
 1 5 10 15
 Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Ala Trp Tyr Lys Ser Glu
 20 25 30
 Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Leu Val Tyr
 35 40 45
 Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Ile Tyr
 50 55 60
 Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
 65 70 75 80
 Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
 85 90 95
 Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
 100 105 110
 Thr Asp Tyr Val Asp Leu Tyr Leu Ile His Ser Pro Leu Val Ser Lys
 115 120 125
 Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
 130 135 140
 Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Thr
 145 150 155 160
 Val Glu Asp Leu Gln Arg Ile Leu Lys Val Ala Glu Val Lys Pro Gln
 165 170 175
 Val Asn Gln Ile Glu Phe Ser Pro Phe Leu Gln Asn Gln Thr Pro Gly
 180 185 190
 Ile Cys Lys Phe Cys Gln Gln His Asp Ile Leu Val Glu Ala Tyr Ser
 195 200 205
 Pro Leu Gly Pro Leu Arg Lys Lys Thr Ala Gln Asp Asp Ser Gln Pro
 210 215 220
 Phe Phe Glu Tyr Val Lys Glu Leu Ser Glu Lys Tyr Asn Lys Thr Glu
 225 230 235 240
 Ala Gln Ile Leu Leu Arg Trp Val Thr Lys Arg Gly Val Leu Pro Val
 245 250 255
 Thr Thr Ser Ser Lys Pro Gln Arg Ile Ser Asp Ala Gln Asn Leu Phe
 260 265 270
 Ser Phe Asp Leu Thr Ala Glu Glu Val Asp Lys Ile Thr Glu Leu Gly
 275 280 285
 Leu Glu His Glu Pro Leu Arg Leu Tyr Trp Asn Lys Leu Tyr Gly Lys
 290 295 300
 Tyr Asn Tyr Ala Ala Gln Lys Val
 305 310

<210> 299
 <211> 942
 <212> DNA
 <213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 299

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atgtcttttc accaagaatt ttccacgctg aacaacggca ataaaatccc ggcgattgcc 60
atcatcgga ctggtacagc gtggtataaa agtgaagaaa ctgacgogac cttctccaat 120
agtctggttg aacaaatcgt gtatgcgttg aaactgcogg ggattatcca cctggacgcc 180
gcggagattt atcgcaccta cccggaagtg ggtaaagcac tgtccctgac cgaaaagcct 240
cgtaacgcga tttttatcac ggataaatat tctccgcaga ttaaaatgag tgactccct 300
gcggacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
attcattccc cgttagtttc gaaggaagtg aatggcttaa gcttagaaga ggcttggaaa 420
gatattggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggttc caatttcaca 480
gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aaactcaggt caaccagatt 540
gagttctctc cgttcctgca aaaccaaaca ccaggcattt gcaaattctg tcaggagcac 600
gatatcctgg tggaaagcata ttctccgctg ggcccgtgc ggaagaaaac cgcgcaggat 660
gacagccaac ctttttttga gtacgtcaaa gaattgagcg aaaaatacaa taaaaccgag 720
gccagatct tactgcgctg ggtcactaaa cgcggtgtgc tgccagttac cacctottca 780
aagcctcagc gcattagcga tgctcagaac ctgttttctc tcgacctgac agcgggaagag 840
gttgataaaa tcacggagct gggctcggaa catgaaccgc tgcgcctgta ctggaataaa 900
ttgtatggca aatataacta cgcgcgccag aaagtgtaat ga 942
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<210> 300

<211> 313

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 300

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Met Ser Phe His Gln Glu Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
1          5          10          15
Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Ala Trp Tyr Lys Ser Glu
20          25          30
Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
35          40          45
Ala Leu Lys Leu Pro Gly Ile Ile His Leu Asp Ala Ala Glu Ile Tyr
50          55          60
Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
65          70          75          80
Arg Asn Ala Ile Phe Ile Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
85          90          95
Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
100         105         110
Thr Asp Tyr Val Asp Leu Tyr Leu Ile His Ser Pro Leu Val Ser Lys
115         120         125
Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
130         135         140
Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Thr
145         150         155         160
Val Glu Asp Leu Gln Arg Ile Leu Lys Val Ala Glu Val Lys Pro Gln
165         170         175
Val Asn Gln Ile Glu Phe Ser Pro Phe Leu Gln Asn Gln Thr Pro Gly
180         185         190
Ile Cys Lys Phe Cys Gln Glu His Asp Ile Leu Val Glu Ala Tyr Ser
195         200         205
Pro Leu Gly Pro Leu Arg Lys Lys Thr Ala Gln Asp Asp Ser Gln Pro
210         215         220
Phe Phe Glu Tyr Val Lys Glu Leu Ser Glu Lys Tyr Asn Lys Thr Glu
225         230         235         240
Ala Gln Ile Leu Leu Arg Trp Val Thr Lys Arg Gly Val Leu Pro Val
```

				245					250					255			
Thr	Thr	Ser	Ser	Lys	Pro	Gln	Arg	Ile	Ser	Asp	Ala	Gln	Asn	Leu	Phe		
			260					265					270				
Ser	Phe	Asp	Leu	Thr	Ala	Glu	Glu	Val	Asp	Lys	Ile	Thr	Glu	Leu	Gly		
		275					280					285					
Leu	Glu	His	Glu	Pro	Leu	Arg	Leu	Tyr	Trp	Asn	Lys	Leu	Tyr	Gly	Lys		
	290					295					300						
Tyr	Asn	Tyr	Ala	Ala	Gln	Lys	Val										
305					310												

<210> 301
 <211> 942
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 301
 atgtcttttc accaagaatt ttccacgctg aacaacggca ataaaatccc ggogattgcc 60
 atcatcgcca ctggtacagc gtggtataaa agtgaagaaa ctgacgcgac cttctccaat 120
 agtctggttg aacaattagt gtatgcgttg aaactgccgg ggattatcca catcgacgcc 180
 gcggagattt atcgcaccta cccggaagtg ggtaaagcac tgtccctgac cgaaaagcct 240
 cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactccct 300
 gcggacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
 attcattccc cgttagtttc gaaggaagtg aatgggttaa gcttagaaga ggcttgga 420
 gatattggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggttc caatttcaca 480
 gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
 gagttctctc cgttcctgca aaaccaaaca ccaggcattt gcaaattctg tcaggagcac 600
 gatatcctgg tgggaagcata ttctccgctg ggcccgctgc ggaagaaaac cgcgcaggat 660
 gacagccaac cattttttga gtacgtcaaa gaattgagcg aaaaatacaa taaaaccgag 720
 gccagatca tcttgcgctg ggtcactaaa cgcggtgtgc tgccagttac cacctcttca 780
 aagcctcagc gcattagcga tgctcagaac ctgttttctc tcgacctgac agcgggaagag 840
 gttgataaaa tcacggagct gggctctggaa catgaaccgc tcgcctgta ctggaataaa 900
 ttgtatggca aatataacta cgccgccag aaagtgtaat ga 942

<210> 302
 <211> 313
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 302
 Met Ser Phe His Gln Glu Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
 1 5 10 15
 Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Ala Trp Tyr Lys Ser Glu
 20 25 30
 Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Leu Val Tyr
 35 40 45
 Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Ile Tyr
 50 55 60
 Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
 65 70 75 80
 Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
 85 90 95
 Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
 100 105 110

Thr	Asp	Tyr	Val	Asp	Leu	Tyr	Leu	Ile	His	Ser	Pro	Leu	Val	Ser	Lys
	115						120					125			
Glu	Val	Asn	Gly	Leu	Ser	Leu	Glu	Glu	Ala	Trp	Lys	Asp	Met	Glu	Gln
	130						135				140				
Leu	Tyr	Lys	Ser	Gly	Lys	Ala	Lys	Asn	Ile	Gly	Val	Ser	Asn	Phe	Thr
	145				150					155					160
Val	Glu	Asp	Leu	Gln	Arg	Ile	Leu	Lys	Val	Ala	Glu	Val	Lys	Pro	Gln
			165					170						175	
Val	Asn	Gln	Ile	Glu	Phe	Ser	Pro	Phe	Leu	Gln	Asn	Gln	Thr	Pro	Gly
			180					185					190		
Ile	Cys	Lys	Phe	Cys	Gln	Glu	His	Asp	Ile	Leu	Val	Glu	Ala	Tyr	Ser
	195						200					205			
Pro	Leu	Gly	Pro	Leu	Arg	Lys	Lys	Thr	Ala	Gln	Asp	Asp	Ser	Gln	Pro
	210					215					220				
Phe	Phe	Glu	Tyr	Val	Lys	Glu	Leu	Ser	Glu	Lys	Tyr	Asn	Lys	Thr	Glu
	225				230					235					240
Ala	Gln	Ile	Ile	Leu	Arg	Trp	Val	Thr	Lys	Arg	Gly	Val	Leu	Pro	Val
			245					250						255	
Thr	Thr	Ser	Ser	Lys	Pro	Gln	Arg	Ile	Ser	Asp	Ala	Gln	Asn	Leu	Phe
			260					265					270		
Ser	Phe	Asp	Leu	Thr	Ala	Glu	Glu	Val	Asp	Lys	Ile	Thr	Glu	Leu	Gly
	275						280					285			
Leu	Glu	His	Glu	Pro	Leu	Arg	Leu	Tyr	Trp	Asn	Lys	Leu	Tyr	Gly	Lys
	290					295					300				
Tyr	Asn	Tyr	Ala	Ala	Gln	Lys	Val								
305					310										

<210> 303
 <211> 942
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 303
 atgtcttttc accaagaatt ttccacgctg aacaaaggca ataaaatccc ggcgattgcc 60
 atcatcgga ctggtacagc gtggtataaa agtgaagaaa ctgacgcgac cttctccaat 120
 agtctggttg aacaaatcgt gtatgcgttg aaactgcggg ggattatcca catcgacgcc 180
 gcggagattt atcgcaccta ccoggaagtg ggtaaagcac tgtccctgac cgaaaagcct 240
 cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag cgactcccct 300
 gcggacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
 attcattccc cgttagtctc gaaggaagtg aatggcttaa gcttagaaga ggcttggaaa 420
 gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggttc caatttcaca 480
 gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
 gagttctctc cgttcctgca aaaccaaaca ccaggcattt gcaaattctg tcaggagcac 600
 gatatcctgg tggaagcata ttctccgctg ggcccgtgac ggaagaaaac cgcgcaggat 660
 gacagccaac cattttttga gtacgtcaaa gaattgagcg aaaaatacaa taaatccgag 720
 gccagatca tctgcgctg ggtcactaaa cgcgggtgtg tgccagttac cacctcttca 780
 aagcctcagc gcattagcga tgctcagaac atcttttctc tcgacctgac agcgggaagag 840
 gttgataaaa tcacggagct gggtctggaa catgaaccgc tgcgcctgta ctggaataaa 900
 ttgtatggca aatataacta cgccgccag aaagtgtaat ga 942

<210> 304
 <211> 313
 <212> PRT
 <213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 304

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Met Ser Phe His Gln Glu Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
1      5      10      15
Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Ala Trp Tyr Lys Ser Glu
20      25      30
Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
35      40      45
Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Ile Tyr
50      55      60
Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
65      70      75      80
Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
85      90      95
Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
100     105     110
Thr Asp Tyr Val Asp Leu Tyr Leu Ile His Ser Pro Leu Val Ser Lys
115     120     125
Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
130     135     140
Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Thr
145     150     155     160
Val Glu Asp Leu Gln Arg Ile Leu Lys Val Ala Glu Val Lys Pro Gln
165     170     175
Val Asn Gln Ile Glu Phe Ser Pro Phe Leu Gln Asn Gln Thr Pro Gly
180     185     190
Ile Cys Lys Phe Cys Gln Glu His Asp Ile Leu Val Glu Ala Tyr Ser
195     200     205
Pro Leu Gly Pro Leu Arg Lys Lys Thr Ala Gln Asp Asp Ser Gln Pro
210     215     220
Phe Phe Glu Tyr Val Lys Glu Leu Ser Glu Lys Tyr Asn Lys Ser Glu
225     230     235     240
Ala Gln Ile Ile Leu Arg Trp Val Thr Lys Arg Gly Val Leu Pro Val
245     250     255
Thr Thr Ser Ser Lys Pro Gln Arg Ile Ser Asp Ala Gln Asn Ile Phe
260     265     270
Ser Phe Asp Leu Thr Ala Glu Glu Val Asp Lys Ile Thr Glu Leu Gly
275     280     285
Leu Glu His Glu Pro Leu Arg Leu Tyr Trp Asn Lys Leu Tyr Gly Lys
290     295     300
Tyr Asn Tyr Ala Ala Gln Lys Val
305      310
```

<210> 305

<211> 942

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 305

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atgtcttttc accaagaatt ttccacgctg aacaacggca ataaaatccc ggcgattgcc 60
atcatcgga ctggtacagc gtggtataaa agtgaagaaa ctgacgcgac cttctccaat 120
agtctggttg aacaattagt gtatgcgttg aaactgccgg ggattatcca cctggacgcc 180
gcggagattt atcgcaccta cccggaagtg ggtaaagcac tgtccctgac cgaaaagcct 240
cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactcccct 300
gcggacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
attcattccc cgtagtttgc gaaggaagtg aatggcttaa gcttagaaga ggcttgga 420
```

```

gatatggagg agttatacaa aagtggtaaa gctaaaaaca tcgggggtttc caatttcaca 480
gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
gagttctctc cgttcctgca aaaccaaaca ccaggcattt gcaaattctg tcaggagcac 600
gatatcctgg tggaagcata ttctccgctg ggcccgtctg ggaagaaaac cgcgcaggat 660
gacagccaac cattttttga gtacgtcaaa gaattgagcg aaaaatacaa taaatccgag 720
gccagatca tctgctgctg ggtcactaaa cgcggtgtgc tgccagttac cacctcttca 780
aagcctcagc gcattagcga tgctcagaac ctgttttctt tcgacctgac agcgggaagag 840
gttgataaaa tcacggagct gggctctggaa catgaaccgc tcgcgctgta ctggaataaa 900
ttgtatggca aatataacta cgccaccag aaagtgtaat ga 942

```

<210> 306

<211> 313

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 306

```

Met Ser Phe His Gln Glu Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
1      5      10      15
Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Ala Trp Tyr Lys Ser Glu
20     25     30
Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Leu Val Tyr
35     40     45
Ala Leu Lys Leu Pro Gly Ile Ile His Leu Asp Ala Ala Glu Ile Tyr
50     55     60
Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
65     70     75     80
Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
85     90     95
Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
100    105    110
Thr Asp Tyr Val Asp Leu Tyr Leu Ile His Ser Pro Leu Val Ser Lys
115    120    125
Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Glu
130    135    140
Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Thr
145    150    155    160
Val Glu Asp Leu Gln Arg Ile Leu Lys Val Ala Glu Val Lys Pro Gln
165    170    175
Val Asn Gln Ile Glu Phe Ser Pro Phe Leu Gln Asn Gln Thr Pro Gly
180    185    190
Ile Cys Lys Phe Cys Gln Glu His Asp Ile Leu Val Glu Ala Tyr Ser
195    200    205
Pro Leu Gly Pro Leu Arg Lys Lys Thr Ala Gln Asp Asp Ser Gln Pro
210    215    220
Phe Phe Glu Tyr Val Lys Glu Leu Ser Glu Lys Tyr Asn Lys Ser Glu
225    230    235    240
Ala Gln Ile Ile Leu Arg Trp Val Thr Lys Arg Gly Val Leu Pro Val
245    250    255
Thr Thr Ser Ser Lys Pro Gln Arg Ile Ser Asp Ala Gln Asn Leu Phe
260    265    270
Ser Phe Asp Leu Thr Ala Glu Glu Val Asp Lys Ile Thr Glu Leu Gly
275    280    285
Leu Glu His Glu Pro Leu Arg Leu Tyr Trp Asn Lys Leu Tyr Gly Lys
290    295    300
Tyr Asn Tyr Ala Thr Gln Lys Val
305    310

```

<210> 307
<211> 942
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 307
atgtcttttc accaagaatt ttccacgctg aacaacggca ataaaatccc ggcgattgcc 60
atcatcggca ctggtacagc gtggtataaa agtgaagaaa ctgacgcgac ctctccaat 120
agtctggttg aacaaatcgt gtatgcgttg aaactgcgag ggattatoca catcgacgcc 180
gcggagattt atcgcaccta cccggaagtg ggtaaagcac tgtccctgac cgaaaagcct 240
cgtaacgcga tttttctgac ggataaatat tctcgcaga ttaaaatgag tgactccct 300
gcggacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
attcattccc cgttagtttc gaaggaagtg aatggcttaa gcttagaaga ggcttgaaa 420
gatatggagg agttatacaa aagtggtaaa gctaaaaaca tcgggggttc caatttcaca 480
gtggaagacc tggaaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
gagttctctc cgttcctgca aaaccaaaaca ccaggcattt gcaaattctg tcagcaacac 600
gatatcctgg tggaaagcata ttctcgcgtg ggcccgctgc ggaagaaaac cgcgcaggat 660
gacagccaac cattttttga gtacgtcaaa gaattgagcg aaaaatacaa taaaaccgag 720
gccagatct tactgcgctg ggctactaaa cgcggtgtgc tgccagttac cacctcttca 780
aagcctcagc gcattagcga tgcacagaac ctgttttctc tcgacctgac agcgggaagag 840
gttgataaaa tcacggagct gggctctggaa catgaaccgc tgcgcctgta ctggaataaa 900
ttgtatggca aacataacta cgccgccag aaagtgtaat ga 942

<210> 308
<211> 313
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 308
Met Ser Phe His Gln Glu Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
1 5 10 15
Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Ala Trp Tyr Lys Ser Glu
20 25 30
Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
35 40 45
Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Ile Tyr
50 55 60
Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
65 70 75 80
Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
85 90 95
Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
100 105 110
Thr Asp Tyr Val Asp Leu Tyr Leu Ile His Ser Pro Leu Val Ser Lys
115 120 125
Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Glu
130 135 140
Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Thr
145 150 155 160
Val Glu Asp Leu Glu Arg Ile Leu Lys Val Ala Glu Val Lys Pro Gln
165 170 175
Val Asn Gln Ile Glu Phe Ser Pro Phe Leu Gln Asn Gln Thr Pro Gly
180 185 190

Ile	Cys	Lys	Phe	Cys	Gln	Gln	His	Asp	Ile	Leu	Val	Glu	Ala	Tyr	Ser		
	195						200					205					
Pro	Leu	Gly	Pro	Leu	Arg	Lys	Lys	Thr	Ala	Gln	Asp	Asp	Ser	Gln	Pro		
	210					215					220						
Phe	Phe	Glu	Tyr	Val	Lys	Glu	Leu	Ser	Glu	Lys	Tyr	Asn	Lys	Thr	Glu		
225					230					235					240		
Ala	Gln	Ile	Leu	Leu	Arg	Trp	Val	Thr	Lys	Arg	Gly	Val	Leu	Pro	Val		
			245						250						255		
Thr	Thr	Ser	Ser	Lys	Pro	Gln	Arg	Ile	Ser	Asp	Ala	Gln	Asn	Leu	Phe		
			260					265						270			
Ser	Phe	Asp	Leu	Thr	Ala	Glu	Glu	Val	Asp	Lys	Ile	Thr	Glu	Leu	Gly		
		275					280					285					
Leu	Glu	His	Glu	Pro	Leu	Arg	Leu	Tyr	Trp	Asn	Lys	Leu	Tyr	Gly	Lys		
	290					295					300						
His	Asn	Tyr	Ala	Ala	Gln	Lys	Val										
305					310												

<210> 309
 <211> 942
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 309
 atgtcttttc accaagaatt ttccacgctg aacaacggca ataaaatccc ggcgattgcc 60
 atcatcgcca ctggtacagc gtggtataaa agtgaagaaa ctgacgogac cttotccaat 120
 accctggttg aacaattagt gtatgcgttg aaactgcggg ggattatcca catcgacgcc 180
 gcggagattt atcgcacota ccggaagtgc ggtaaagcac tgtccctgac cgaaaagcct 240
 cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactccoct 300
 gcggacgggc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
 attcattccc cgttagtttc gaaggaagtgc aatggcttaa gcttagaaga ggcttggaag 420
 gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggtttc caatttcaca 480
 gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
 gagttctctc cgttcctgca aaaccaaaca ccaggcattt gcaaattctg tcaggagcac 600
 gatatcctgg tggaagcata ttctccgctg ggcccgctgc ggaagaaaac cgcgcaggat 660
 gacagccaac cattttttga gtacgtcaaa gaattgagcg aaaaatacaa taaatccgag 720
 gccagatca tctgcgctg ggtcactaaa cgoggtgtgc tgccagttac cacctottca 780
 aagcctcagc gcattagcga tgctcagaac ctgttttctc tcgacctgac agcggaagag 840
 gttgataaaa tcacggagct gggtctggaa catgaaccgc tgcgcctgta ctggaataaa 900
 ttgtatggca aatataacta cgccgccagc aaagtataat ga 942

<210> 310
 <211> 313
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 310
 Met Ser Phe His Gln Glu Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
 1 5 10 15
 Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Ala Trp Tyr Lys Ser Glu
 20 25 30
 Glu Thr Asp Ala Thr Phe Ser Asn Thr Leu Val Glu Gln Leu Val Tyr
 35 40 45
 Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Ile Tyr

50	55	60
Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro		
65	70	75
Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met		80
	85	90
Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly		95
	100	105
Thr Asp Tyr Val Asp Leu Tyr Leu Ile His Ser Pro Leu Val Ser Lys		110
	115	120
Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln		125
	130	135
Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Thr		140
145	150	155
Val Glu Asp Leu Gln Arg Ile Leu Lys Val Ala Glu Val Lys Pro Gln		160
	165	170
Val Asn Gln Ile Glu Phe Ser Pro Phe Leu Gln Asn Gln Thr Pro Gly		175
	180	185
Ile Cys Lys Phe Cys Gln Glu His Asp Ile Leu Val Glu Ala Tyr Ser		190
	195	200
Pro Leu Gly Pro Leu Arg Lys Lys Thr Ala Gln Asp Asp Ser Gln Pro		205
	210	215
Phe Phe Glu Tyr Val Lys Glu Leu Ser Glu Lys Tyr Asn Lys Ser Glu		220
225	230	235
Ala Gln Ile Ile Leu Arg Trp Val Thr Lys Arg Gly Val Leu Pro Val		240
	245	250
Thr Thr Ser Ser Lys Pro Gln Arg Ile Ser Asp Ala Gln Asn Leu Phe		255
	260	265
Ser Phe Asp Leu Thr Ala Glu Glu Val Asp Lys Ile Thr Glu Leu Gly		270
	275	280
Leu Glu His Glu Pro Leu Arg Leu Tyr Trp Asn Lys Leu Tyr Gly Lys		285
	290	295
Tyr Asn Tyr Ala Ala Gln Lys Val		300
305	310	

<210> 311
 <211> 942
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 311
 atgtcttttc accaagaatt ttacacgctg aacaacggca ataaaatccc ggcgattgcc 60
 atcatcggca ctggtacagc gtggtataaa agtgaagaaa ctgacgogac cttctccaat 120
 accctggttg aacaattagt gtatgcgttg aaactgccgg ggattatoca catcgacgcc 180
 gcgagatttt atcgcaccta cccggaagtg ggtaaagcac tgtccctgac cgaaaagcct 240
 cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactcccct 300
 gcggacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
 attcattccc cgttagtttc gaaggaagtg aatggcttaa gcttagaaga ggcttgga 420
 gatattggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggtttc caatttcaca 480
 gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
 gagttctctc cgttcctgca aaaccaaaca ccaggcattt gcaaatctctg tcaggagcac 600
 gatatcctgg tggaagcata ttctecgcta ggccogctgc ggaagaaaac cgcgcaggat 660
 gacagccaac cattttttga gtacgtcaaa gaattgagcg aaaaatacaa taaatccgag 720
 gccagatca tcctgcgctg ggtcactaaa cgcggtgtgc tgccagttac cacctcttca 780
 aagcctcagc gcattagcga tgctcagaac ctgttttctt tcgacotgac agcggaagag 840
 gttgataaaa tcacggagct gggctctggaa catgaacgcg tcgcgctgta ctggaataaa 900
 ttgtatggca aatataacta cgccgcccag aaagtgtaat ga 942

<210> 312
 <211> 313
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 312
 Met Ser Phe His Gln Glu Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
 1 5 10 15
 Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Ala Trp Tyr Lys Ser Glu
 20 25 30
 Glu Thr Asp Ala Thr Phe Ser Asn Thr Leu Val Glu Gln Leu Val Tyr
 35 40 45
 Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Ile Tyr
 50 55 60
 Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
 65 70 75 80
 Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
 85 90 95
 Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
 100 105 110
 Thr Asp Tyr Val Asp Leu Tyr Leu Ile His Ser Pro Leu Val Ser Lys
 115 120 125
 Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
 130 135 140
 Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Thr
 145 150 155 160
 Val Glu Asp Leu Gln Arg Ile Leu Lys Val Ala Glu Val Lys Pro Gln
 165 170 175
 Val Asn Gln Ile Glu Phe Ser Pro Phe Leu Gln Asn Gln Thr Pro Gly
 180 185 190
 Ile Cys Lys Phe Cys Gln Glu His Asp Ile Leu Val Glu Ala Tyr Ser
 195 200 205
 Pro Leu Gly Pro Leu Arg Lys Lys Thr Ala Gln Asp Asp Ser Gln Pro
 210 215 220
 Phe Phe Glu Tyr Val Lys Glu Leu Ser Glu Lys Tyr Asn Lys Ser Glu
 225 230 235 240
 Ala Gln Ile Ile Leu Arg Trp Val Thr Lys Arg Gly Val Leu Pro Val
 245 250 255
 Thr Thr Ser Ser Lys Pro Gln Arg Ile Ser Asp Ala Gln Asn Leu Phe
 260 265 270
 Ser Phe Asp Leu Thr Ala Glu Glu Val Asp Lys Ile Thr Glu Leu Gly
 275 280 285
 Leu Glu His Glu Pro Leu Arg Leu Tyr Trp Asn Lys Leu Tyr Gly Lys
 290 295 300
 Tyr Asn Tyr Ala Ala Gln Lys Val
 305 310

<210> 313
 <211> 942
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 313

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atgtcttttc accaagaatt tttcacgctg aacaacggca ataaaaatccc ggcgattgcc 60
atcatcggca ctggtacagc gtggtataaa cccgaagaaa ctgacgcgac cttctccaat 120
agtctggttg aacaattagt gtatgcgttg aaactgcogg ggattatcca catcgacgcc 180
gcggagatth atcgcaccta cccggaagtg ggtaaagcac tgtccctgac cgaaaagcct 240
cgtaacgcga tttttatcac ggataaatat tctccgcaga ttaaaatgag cgactccccct 300
goggacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
attcattccc cgttagtthc gaaggaagtg aatggcttaa gcttagaaga ggcttggaag 420
gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggtttc caatttcaca 480
gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
gagttctctc cgttcctgca aaaccaaaca ccaggcattt gcaaattctg tcaggagcac 600
gatatcctgg tggaaagcata ttctccgcta ggcccgtgc ggaagaaaac cgcgcaggat 660
gacagccaac ctttttttga gtacgtcaaa gaattgagcg aaaaatacaa taaaacogag 720
gcccagatca tcttgcgctg ggctactaaa cgcggtgtgc tgccagttac cacctcttca 780
aagcctcagc gcattagcga tgctcagaac ctgttttctt tcgacctgac agcgggaagag 840
gttgataaaa tcacggagct gggctctggaa catgaaccgc tgcgcctgta ctggaataaa 900
ttgtatggca aatataacta cgccgccagc aaagtataat ga 942

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<210> 314

<211> 313

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 314

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Met Ser Phe His Gln Glu Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
1          5          10          15
Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Ala Trp Tyr Lys Pro Glu
20        25        30
Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Leu Val Tyr
35        40        45
Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Ile Tyr
50        55        60
Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
65        70        75        80
Arg Asn Ala Ile Phe Ile Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
85        90        95
Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
100       105       110
Thr Asp Tyr Val Asp Leu Tyr Leu Ile His Ser Pro Leu Val Ser Lys
115       120       125
Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
130       135       140
Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Thr
145       150       155       160
Val Glu Asp Leu Gln Arg Ile Leu Lys Val Ala Glu Val Lys Pro Gln
165       170       175
Val Asn Gln Ile Glu Phe Ser Pro Phe Leu Gln Asn Gln Thr Pro Gly
180       185       190
Ile Cys Lys Phe Cys Gln Glu His Asp Ile Leu Val Glu Ala Tyr Ser
195       200       205
Pro Leu Gly Pro Leu Arg Lys Lys Thr Ala Gln Asp Asp Ser Gln Pro
210       215       220
Phe Phe Glu Tyr Val Lys Glu Leu Ser Glu Lys Tyr Asn Lys Thr Glu
225       230       235       240
Ala Gln Ile Ile Leu Arg Trp Val Thr Lys Arg Gly Val Leu Pro Val
245       250       255
Thr Thr Ser Ser Lys Pro Gln Arg Ile Ser Asp Ala Gln Asn Leu Phe
260       265       270

```


Ser Phe Asp Leu Thr Ala Glu Glu Val Asp Lys Ile Thr Glu Leu Gly
 275 280 285
 Leu Glu His Glu Pro Leu Arg Leu Tyr Trp Asn Lys Leu Tyr Gly Lys
 290 295 300
 Tyr Asn Tyr Ala Ala Gln Lys Val
 305 310

<210> 315
 <211> 942
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 315
 atgtcttttc accaacagtt tttcacgctg aacaacggca ataaaatccc ggcgattgcc 60
 atcatcgga ctggtacagc gtggtataaa cccgaagaaa ctgaacgcac cttctccaat 120
 agtctgggtg aacaaatcgt gtatgcgttg aaactgccgg ggattatoca catcgacgcc 180
 gcggagtggg atcgcaccta cccggaagtg ggtaaagcac tgtccctgac cgaaaagcct 240
 cgtaacgcga tttttctgac ggataaatat tctcgcgaga ttaaaatgag tgactccccct 300
 gcggacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
 attcattccc cgttagtttc gaaggaagtg aatggcttaa gcttagaaga ggcttggaaa 420
 gatattggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggttc caatttcaca 480
 gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
 gatttctctc cgttcctgca aaaccaaaca ccaggcattt gcaaattctg tcaggagcac 600
 gatatcctgg tggaagcata ttctcgcgtg ggcccgctgc ggaagaaaac cgcgcaggat 660
 gacagccaac cattttttga gtacgtcaaa gaattgagcg aaaaatacaa taaatccgag 720
 gccagatca tcttcgcgtg ggtaactaaa cgcgggtgtg tgccagttac cacctottca 780
 aagcctcagc gcattagoga tgctcagaac ctgttttctt tcgacctgac agcgggaagag 840
 gttgataaaa tcacggagct ggggtctggaa catgaacgc tgccgctgta ctggaataaa 900
 ttgtatggca aatataacta cgccgccag aaagtgtaat ga 942

<210> 316
 <211> 313
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 316
 Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
 1 5 10 15
 Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Ala Trp Tyr Lys Pro Glu
 20 25 30
 Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
 35 40 45
 Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Trp Tyr
 50 55 60
 Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
 65 70 75 80
 Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
 85 90 95
 Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
 100 105 110
 Thr Asp Tyr Val Asp Leu Tyr Leu Ile His Ser Pro Leu Val Ser Lys
 115 120 125
 Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln

130		135		140
Leu Tyr Lys Ser Gly	Lys Ala Lys Asn Ile Gly	Val Ser Asn Phe Thr		
145	150	155		160
Val Glu Asp Leu Gln Arg	Ile Leu Lys Val Ala Glu	Val Lys Pro Gln		
	165	170		175
Val Asn Gln Ile Glu Phe	Ser Pro Phe Leu Gln	Asn Gln Thr Pro Gly		
	180	185		190
Ile Cys Lys Phe Cys Gln	Glu His Asp Ile Leu	Val Glu Ala Tyr Ser		
	195	200		205
Pro Leu Gly Pro Leu Arg	Lys Lys Thr Ala Gln	Asp Asp Ser Gln Pro		
	210	215		220
Phe Phe Glu Tyr Val Lys	Glu Leu Ser Glu Lys	Tyr Asn Lys Ser Glu		
225	230	235		240
Ala Gln Ile Ile Leu Arg	Trp Val Thr Lys Arg	Gly Val Leu Pro Val		
	245	250		255
Thr Thr Ser Ser Lys Pro	Gln Arg Ile Ser Asp	Ala Gln Asn Leu Phe		
	260	265		270
Ser Phe Asp Leu Thr Ala	Glu Glu Val Asp Lys	Ile Thr Glu Leu Gly		
	275	280		285
Leu Glu His Glu Pro Leu	Arg Leu Tyr Trp Asn	Lys Leu Tyr Gly Lys		
	290	295		300
Tyr Asn Tyr Ala Ala Gln	Lys Val			
305	310			

<210> 317

<211> 942

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 317

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atgtcttttc accaacagtt ttacacgctg aacaacggca ataaaatccc ggcgattgcc 60
atcatcggca ctggtacagc gtggtataaa cccgaagaaa ctgacgogac cttctccaat 120
agtctggttg aacaaatcgt gtatgcgttg aaactgccgg ggattatoca catcgacgcc 180
gcggagtggg atcgcaccta cccggaagtg ggtaaagcac tgtccctgac cgaagagcct 240
cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactccctc 300
gcggacggtc tggattttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
attcattccc cgttagtttc gaaggaagtg aatggcttaa gcttagaaga ggcttggaaa 420
gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggttc caatttcaca 480
gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
gagttctctc cgttcctgca aaaccaaaca ccaggcattt gcaaattctg tcaggagcac 600
gatatcctgg tggaagcata ttctccgctg ggcccgctgc ggaagaaaac cgcgcaggat 660
gacagccaac ctttttttga gtacgtcaaa gaattgagcg aaaaatacaa taaatccgag 720
gccagatca tcttgcgctg ggtaactaaa cgcgggtgtgc tgccagttac cacctcttca 780
aagcctcagc gcattagcga tgctcagaac ctgttttctc tcgacctgac agcgggaagag 840
gttgataaaa tcacggagct gggctctggaa catgaaccgc tgcgcctgta ctggaataaa 900
ttgtatggca aatataacta cgccgccagc aaagtgtaat ga 942

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<210> 318

<211> 313

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 318

Met	Ser	Phe	His	Gln	Gln	Phe	Phe	Thr	Leu	Asn	Asn	Gly	Asn	Lys	Ile	
1				5					10					15		
Pro	Ala	Ile	Ala	Ile	Ile	Gly	Thr	Gly	Thr	Ala	Trp	Tyr	Lys	Pro	Glu	
			20					25					30			
Glu	Thr	Asp	Ala	Thr	Phe	Ser	Asn	Ser	Leu	Val	Glu	Gln	Ile	Val	Tyr	
		35					40					45				
Ala	Leu	Lys	Leu	Pro	Gly	Ile	Ile	His	Ile	Asp	Ala	Ala	Glu	Trp	Tyr	
	50					55				60						
Arg	Thr	Tyr	Pro	Glu	Val	Gly	Lys	Ala	Leu	Ser	Leu	Thr	Glu	Lys	Pro	
65					70					75					80	
Arg	Asn	Ala	Ile	Phe	Leu	Thr	Asp	Lys	Tyr	Ser	Pro	Gln	Ile	Lys	Met	
				85					90					95		
Ser	Asp	Ser	Pro	Ala	Asp	Gly	Leu	Asp	Leu	Ala	Leu	Lys	Lys	Met	Gly	
			100					105					110			
Thr	Asp	Tyr	Val	Asp	Leu	Tyr	Leu	Ile	His	Ser	Pro	Leu	Val	Ser	Lys	
	115						120						125			
Glu	Val	Asn	Gly	Leu	Ser	Leu	Glu	Glu	Ala	Trp	Lys	Asp	Met	Glu	Gln	
	130					135					140					
Leu	Tyr	Lys	Ser	Gly	Lys	Ala	Lys	Asn	Ile	Gly	Val	Ser	Asn	Phe	Thr	
145					150					155					160	
Val	Glu	Asp	Leu	Gln	Arg	Ile	Leu	Lys	Val	Ala	Glu	Val	Lys	Pro	Gln	
				165					170					175		
Val	Asn	Gln	Ile	Glu	Phe	Ser	Pro	Phe	Leu	Gln	Asn	Gln	Thr	Pro	Gly	
		180						185					190			
Ile	Cys	Lys	Phe	Cys	Gln	Glu	His	Asp	Ile	Leu	Val	Glu	Ala	Tyr	Ser	
	195						200					205				
Pro	Leu	Gly	Pro	Leu	Arg	Lys	Lys	Thr	Ala	Gln	Asp	Asp	Ser	Gln	Pro	
	210					215					220					
Phe	Phe	Glu	Tyr	Val	Lys	Glu	Leu	Ser	Glu	Lys	Tyr	Asn	Lys	Ser	Glu	
225					230					235					240	
Ala	Gln	Ile	Ile	Leu	Arg	Trp	Val	Thr	Lys	Arg	Gly	Val	Leu	Pro	Val	
				245					250					255		
Thr	Thr	Ser	Ser	Lys	Pro	Gln	Arg	Ile	Ser	Asp	Ala	Gln	Asn	Leu	Phe	
		260						265					270			
Ser	Phe	Asp	Leu	Thr	Ala	Glu	Glu	Val	Asp	Lys	Ile	Thr	Glu	Leu	Gly	
		275					280					285				
Leu	Glu	His	Glu	Pro	Leu	Arg	Leu	Tyr	Trp	Asn	Lys	Leu	Tyr	Gly	Lys	
	290					295					300					
Tyr	Asn	Tyr	Ala	Ala	Gln	Lys	Val									
305					310											

<210> 319

<211> 942

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 319

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atgtcttttc accaacagtt tttcacgctg aacaacggca ataaaatccc ggcgattgcc 60
atcatcggca ctggtacagc gtggtataaa cccgaagaaa ctgacgcgac cttctccaat 120
agtctggttg aacaaatcgt gtatgcgttg aaactgccgg ggattatcca catcgacgcc 180
gcggagattt atcgcaccta cccggaagtg ggtaaagcac tgtccctgac cgaaaagcct 240
cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactccoct 300
gcggacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
attcattccc cgttagtttc gaaggaagtg aatggcttaa gcttagaaga ggcttggaaa 420
gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcggggtttc caatttcaca 480
gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
gagttctctc cgttctctgca aaaccaaaaca ccaggcattt gcaaattctg tcaggagcac 600

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gatatacctgg tggaagcata ttctccgctg ggcccgcgtgc ggaagaaaac cgcgcaggat 660
gacagccaac cattttttga gtacgtcaaa gaattgagcg aaaaatacaa taaatccgag 720
gcccgatca tctgcgctg ggctactaaa cgcggtgtgc tgccagttac caoctottca 780
aagcctcagc gcattagcga tgctcagaac ctgttttctt tgcacctgac agcgggaagag 840
gttgataaaa tcacggagct gggtctggaa catgaaccgc tgcgcctgtg gtggaataaaa 900
ttgtatggca aatataacta cgccgccag aaagtgtaat ga 942

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<210> 320

<211> 313

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 320

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Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
1          5          10          15
Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Ala Trp Tyr Lys Pro Glu
20          25          30
Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
35          40          45
Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Ile Tyr
50          55          60
Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
65          70          75          80
Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
85          90          95
Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
100         105         110
Thr Asp Tyr Val Asp Leu Tyr Leu Ile His Ser Pro Leu Val Ser Lys
115         120         125
Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
130         135         140
Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Thr
145         150         155         160
Val Glu Asp Leu Gln Arg Ile Leu Lys Val Ala Glu Val Lys Pro Gln
165         170         175
Val Asn Gln Ile Glu Phe Ser Pro Phe Leu Gln Asn Gln Thr Pro Gly
180         185         190
Ile Cys Lys Phe Cys Gln Glu His Asp Ile Leu Val Glu Ala Tyr Ser
195         200         205
Pro Leu Gly Pro Leu Arg Lys Lys Thr Ala Gln Asp Asp Ser Gln Pro
210         215         220
Phe Phe Glu Tyr Val Lys Glu Leu Ser Glu Lys Tyr Asn Lys Ser Glu
225         230         235         240
Ala Gln Ile Ile Leu Arg Trp Val Thr Lys Arg Gly Val Leu Pro Val
245         250         255
Thr Thr Ser Ser Lys Pro Gln Arg Ile Ser Asp Ala Gln Asn Leu Phe
260         265         270
Ser Phe Asp Leu Thr Ala Glu Glu Val Asp Lys Ile Thr Glu Leu Gly
275         280         285
Leu Glu His Glu Pro Leu Arg Leu Trp Trp Asn Lys Leu Tyr Gly Lys
290         295         300
Tyr Asn Tyr Ala Ala Gln Lys Val
305          310

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<210> 321

<211> 942

<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 321
atgtcttttc accaacagtt tttcacgctg aacaaaggca ataaaatccc ggcgattgcc 60
atcatcggca ctggtacagc gtggtataaa cccgaagaaa ctgaacgcac cttctocaat 120
agtctggttg aacaaatcgt gtatgcgttg aaactgcggg ggattatcca catcgacgcc 180
gcggagagtt atcgcaccta cccggaagtg ggtaaagcac tgcacctgac cgaaaagcct 240
cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactcccct 300
gcggacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
attcattccc cgtagtttgc gaaggaagtg aatggcttaa gcttagaaga ggcttgaaaa 420
gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggttc caatttcaca 480
gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
gagttctctc cgttcctgca aaaccaaaca ccaggcattt gcaaattctg tcaggagcac 600
gatatcctgg tggaagcata ttctccgctg ggcccgcctgc ggaagaaaac cgcgcaggat 660
gacagccaac cattttttga gtacgtcaaa gaattgagcg aaaaatacaa taaatccgag 720
gccagatca tcctgcgctg ggctactaaa cgcggtgtgc tgccagttac cacctcttca 780
aagcctcagc gcattagcga tgctcagaac ctgttttctt tcgacctgac agcgggaagag 840
gttgataaaa tcacggagct gggctctggaa catgaaccgc tgcgcctgta ctggaataaa 900
aggtatggca aatataacta cgccgccagc aaagtgtaat ga 942

<210> 322
<211> 313
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 322
Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
1 5 10 15
Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Ala Trp Tyr Lys Pro Glu
20 25 30
Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
35 40 45
Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Ile Tyr
50 55 60
Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
65 70 75 80
Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
85 90 95
Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
100 105 110
Thr Asp Tyr Val Asp Leu Tyr Leu Ile His Ser Pro Leu Val Ser Lys
115 120 125
Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
130 135 140
Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Thr
145 150 155 160
Val Glu Asp Leu Gln Arg Ile Leu Lys Val Ala Glu Val Lys Pro Gln
165 170 175
Val Asn Gln Ile Glu Phe Ser Pro Phe Leu Gln Asn Gln Thr Pro Gly
180 185 190
Ile Cys Lys Phe Cys Gln Glu His Asp Ile Leu Val Glu Ala Tyr Ser
195 200 205
Pro Leu Gly Pro Leu Arg Lys Lys Thr Ala Gln Asp Asp Ser Gln Pro

210		215		220
Phe Phe Glu Tyr Val	Lys Glu Leu Ser Glu Lys Tyr Asn Lys Ser Glu			
225	230	235		240
Ala Gln Ile Ile Leu Arg Trp Val Thr	Lys Arg Gly Val Leu Pro Val			
	245	250		255
Thr Thr Ser Ser Lys Pro Gln Arg Ile Ser Asp Ala Gln Asn Leu Phe				
	260	265		270
Ser Phe Asp Leu Thr Ala Glu Glu Val Asp Lys Ile Thr Glu Leu Gly				
	275	280		285
Leu Glu His Glu Pro Leu Arg Leu Tyr Trp Asn Lys Arg Tyr Gly Lys				
	290	295		300
Tyr Asn Tyr Ala Ala Gln Lys Val				
305	310			

<210> 323
 <211> 942
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 323
 atgtcttttc accaacagtt ttccacgctg aacaacggca ataaaatccc ggcgattgcc 60
 atcatcggca ctggtacagc gtggtataaa cccgaagaaa ctgacgcgac cttctccaat 120
 agtctggttg aacaaatcgt gtatgcgttg aaactgccgg ggattatcca catcgacgcc 180
 gcggagattt atcgcaccta cccggaagtg ggtaaagcac tgtccctgac cgaaaagcct 240
 cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactcccct 300
 gcggacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
 attcattccc cgttagtctt gaaggaagtg aatggcttaa gcttagaaga ggcttgga 420
 gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggttt caatttcaca 480
 gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
 gagttctctc cgttcctgca aaaccaaaca ccaggcattt gcaaattctg tcaggagcac 600
 gatatcctgg tggaaagcata ttctccgctg ggcccgtgac ggaagaaaac cgcgcaggat 660
 gacagccaac cattttttga gtacgtcaaa gaattgagcg aaaaatacaa taaatccgag 720
 gccagatca tcttgcgctg ggctactaaa cgcgggtgtg tgccagttac cactcttca 780
 aagcctcagc gcattagcga tgcctcagaac ctgttttctt tcgacctgac agcgggaagag 840
 gttgataaaa tcacggagct gggctctggaa catgaacgcg tgogcctgta ctggaataaa 900
 aagtatggca aatataacta cgcgcgccag aaagtgtaat ga 942

<210> 324
 <211> 313
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 324
 Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
 1 5 10 15
 Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Ala Trp Tyr Lys Pro Glu
 20 25 30
 Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
 35 40 45
 Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Ile Tyr
 50 55 60
 Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
 65 70 75 80

Arg	Asn	Ala	Ile	Phe	Leu	Thr	Asp	Lys	Tyr	Ser	Pro	Gln	Ile	Lys	Met	
			85						90					95		
Ser	Asp	Ser	Pro	Ala	Asp	Gly	Leu	Asp	Leu	Ala	Leu	Lys	Lys	Met	Gly	
			100					105					110			
Thr	Asp	Tyr	Val	Asp	Leu	Tyr	Leu	Ile	His	Ser	Pro	Leu	Val	Ser	Lys	
		115					120					125				
Glu	Val	Asn	Gly	Leu	Ser	Leu	Glu	Glu	Ala	Trp	Lys	Asp	Met	Glu	Gln	
	130					135					140					
Leu	Tyr	Lys	Ser	Gly	Lys	Ala	Lys	Asn	Ile	Gly	Val	Ser	Asn	Phe	Thr	
145					150					155					160	
Val	Glu	Asp	Leu	Gln	Arg	Ile	Leu	Lys	Val	Ala	Glu	Val	Lys	Pro	Gln	
			165					170						175		
Val	Asn	Gln	Ile	Glu	Phe	Ser	Pro	Phe	Leu	Gln	Asn	Gln	Thr	Pro	Gly	
			180					185					190			
Ile	Cys	Lys	Phe	Cys	Gln	Glu	His	Asp	Ile	Leu	Val	Glu	Ala	Tyr	Ser	
	195						200					205				
Pro	Leu	Gly	Pro	Leu	Arg	Lys	Lys	Thr	Ala	Gln	Asp	Asp	Ser	Gln	Pro	
	210					215					220					
Phe	Phe	Glu	Tyr	Val	Lys	Glu	Leu	Ser	Glu	Lys	Tyr	Asn	Lys	Ser	Glu	
225					230					235					240	
Ala	Gln	Ile	Ile	Leu	Arg	Trp	Val	Thr	Lys	Arg	Gly	Val	Leu	Pro	Val	
			245						250					255		
Thr	Thr	Ser	Ser	Lys	Pro	Gln	Arg	Ile	Ser	Asp	Ala	Gln	Asn	Leu	Phe	
		260						265					270			
Ser	Phe	Asp	Leu	Thr	Ala	Glu	Glu	Val	Asp	Lys	Ile	Thr	Glu	Leu	Gly	
	275						280					285				
Leu	Glu	His	Glu	Pro	Leu	Arg	Leu	Tyr	Trp	Asn	Lys	Lys	Tyr	Gly	Lys	
	290					295					300					
Tyr	Asn	Tyr	Ala	Ala	Gln	Lys	Val									
305					310											

<210> 325
 <211> 942
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 325
 atgtcttttc accaacagtt tttaacgctg aacaacggca ataaaatccc ggcgattgcc 60
 atcatcgga ctggtacagc gtggtataaa cccgaagaaa ctgacgcgac cttctccaat 120
 agtctggttg aacaaatcgt gtatgcgttg aaactgcogg ggattatcca catcgacgcc 180
 gcggagtggg atcgcaccta cccggaagtg ggtaaagcac tgtccctgac cgaaaagcct 240
 cgtaacgcga tttttctgac ggataaatat tctcgcgaga ttaaaatgag tgactccct 300
 gcggacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
 attcattccc cgtagtttgc gaaggaagtg aatggcttaa gcttagaaga ggcttgga 420
 gatattggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggttc caatttcaca 480
 gtggaagacc tgcaacgtat cctgaaagtc gotgaagtta aacctcaggt caaccagatt 540
 gagttctctc cgttcctgca aaacaaaaca ccaggcattt gcaaattctg tcaggagcac 600
 gatattcttg tggaagcata ttctccgctg ggcccgctgc ggaagaaaac cgcgcaggat 660
 gacagccaac ctttttttga gtacgtcaaa gaattgagcg aaaaatacaa taaatccgag 720
 gccagatca tcttgccgtg ggctactaaa cgcgggtgtg tgccagttac cactotcca 780
 aagcctcagc gcattagcga tgctcagaac ctgttttctc tcgacctgac agcggagag 840
 gttgataaaa tcacggagct ggtctggaa catgaaccgc tcgcgctgtg gtggaataaa 900
 ttgtatggca aatataacta cgccgccagc aaagtgtaat ga 942

<210> 326
 <211> 313

<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 326
Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
1 5 10 15
Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Ala Trp Tyr Lys Pro Glu
20 25 30
Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
35 40 45
Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Trp Tyr
50 55 60
Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
65 70 75 80
Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
85 90 95
Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
100 105 110
Thr Asp Tyr Val Asp Leu Tyr Leu Ile His Ser Pro Leu Val Ser Lys
115 120 125
Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
130 135 140
Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Thr
145 150 155 160
Val Glu Asp Leu Gln Arg Ile Leu Lys Val Ala Glu Val Lys Pro Gln
165 170 175
Val Asn Gln Ile Glu Phe Ser Pro Phe Leu Gln Asn Gln Thr Pro Gly
180 185 190
Ile Cys Lys Phe Cys Gln Glu His Asp Ile Leu Val Glu Ala Tyr Ser
195 200 205
Pro Leu Gly Pro Leu Arg Lys Lys Thr Ala Gln Asp Asp Ser Gln Pro
210 215 220
Phe Phe Glu Tyr Val Lys Glu Leu Ser Glu Lys Tyr Asn Lys Ser Glu
225 230 235 240
Ala Gln Ile Ile Leu Arg Trp Val Thr Lys Arg Gly Val Leu Pro Val
245 250 255
Thr Thr Ser Ser Lys Pro Gln Arg Ile Ser Asp Ala Gln Asn Leu Phe
260 265 270
Ser Phe Asp Leu Thr Ala Glu Glu Val Asp Lys Ile Thr Glu Leu Gly
275 280 285
Leu Glu His Glu Pro Leu Arg Leu Trp Trp Asn Lys Leu Tyr Gly Lys
290 295 300
Tyr Asn Tyr Ala Ala Gln Lys Val
305 310

<210> 327
<211> 942
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 327
atgtcttttc accaacagtt tttcacgctg aacaacggca ataaaatccc ggcgattgcc 60
atcatcggca ctggtacagc gtggtataaa cccgaagaaa ctgacgcgac cttctccaat 120
agtctggttg aacaaatcgt gtatgcgttg aaactgccgg ggattatcca catcgacgcc 180


```

gcgaggatggg atcgcaccta cccggaagtg ggtaaagcac tgtccctgac cgaaaagcct 240
cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactccct 300
gcggaacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
attcattccc cgtaggttc gaaggaagtg aatggcttaa gcttagaaga ggcttgaaa 420
gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggttc caatttcaca 480
gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
gagttctctc cgttcctgca aaaccaaaca ccaggcattt gcaaattctg tcaggagcac 600
gatatcctgg tggaagcata ttctccgctg ggcccgtgc ggaagaaaac cgcgaggat 660
gacagccaac cattttitga gtacgtcaaa gaattgagcg aaaaatacaa taaatccgag 720
gccagatca tcctgcgctg gggtcactaaa cgcgggtgtgc tgccagttac cacctcttca 780
aagcctcagc gcattagcga tgctcagaac ctgttttctc tcgacctgac agcggaagag 840
gttgataaaa tcacggagct gggtctggaa catgaaccgc tcgcctgtg gtggaataaa 900
aagtatggca aatataacta cgccgccag aaagtgtaat ga 942

```

<210> 328

<211> 313

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 328

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Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
1          5          10          15
Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Ala Trp Tyr Lys Pro Glu
          20          25          30
Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
          35          40          45
Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Trp Tyr
          50          55          60
Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
65          70          75          80
Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
          85          90          95
Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
          100         105         110
Thr Asp Tyr Val Asp Leu Tyr Leu Ile His Ser Pro Leu Val Ser Lys
          115         120         125
Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
          130         135         140
Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Thr
145         150         155         160
Val Glu Asp Leu Gln Arg Ile Leu Lys Val Ala Glu Val Lys Pro Gln
          165         170         175
Val Asn Gln Ile Glu Phe Ser Pro Phe Leu Gln Asn Gln Thr Pro Gly
          180         185         190
Ile Cys Lys Phe Cys Gln Glu His Asp Ile Leu Val Glu Ala Tyr Ser
          195         200         205
Pro Leu Gly Pro Leu Arg Lys Lys Thr Ala Gln Asp Asp Ser Gln Pro
          210         215         220
Phe Phe Glu Tyr Val Lys Glu Leu Ser Glu Lys Tyr Asn Lys Ser Glu
225         230         235         240
Ala Gln Ile Ile Leu Arg Trp Val Thr Lys Arg Gly Val Leu Pro Val
          245         250         255
Thr Thr Ser Ser Lys Pro Gln Arg Ile Ser Asp Ala Gln Asn Leu Phe
          260         265         270
Ser Phe Asp Leu Thr Ala Glu Glu Val Asp Lys Ile Thr Glu Leu Gly
          275         280         285
Leu Glu His Glu Pro Leu Arg Leu Trp Trp Asn Lys Lys Tyr Gly Lys

```

290 295 300
 Tyr Asn Tyr Ala Ala Gln Lys Val
 305 310

<210> 329
 <211> 942
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 329
 atgtcttttc accaagaatt tttcacgctg aacaacggca ataaaatccc ggcgattgcc 60
 atcatcggca ctggtacagc gtggtataaa cccgaagaaa ctgacgcgac cttctccaat 120
 agtctgggtg aacaattagt gtatgcgttg aaactgccgg ggattatcca catcgacgcc 180
 gcggagtggt atcgcaccta cccggaagtg ggtaaagcac tgtccctgac cgaaaagcct 240
 cgtaacgcga tttttatcac ggataaatat tctccgcaga ttaaaatgag cgactccoct 300
 gcggacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
 attcattccc cgttagtttc gaaggaagtg aatggcttaa gottagaaga ggcttggaaa 420
 gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcggggtttc caatttcaca 480
 gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
 gagttctctc cgttcctgca aaaccaaaaca ccaggcattt gcaaattctg tcaggagcac 600
 gatatcctgg tggaagcata ttctccgcta ggcccgtctg ggaagaaaac cgcgcaggat 660
 gacagccaac cattttttga gtacgtcaaa gaattgagcg aaaaatacaa taaaaccgag 720
 gccagatca tcctgcgctg ggtcactaaa cgcggtgtgc tgccagttac cacctcttca 780
 aagcctcagc gcattagcga tgctcagaac ctgttttctc tcgacctgac agcggagag 840
 gttgataaaa tcacggagct gggctctggaa catgaaccgc tgcgcctgta ctggaataaa 900
 ttgtatggca aatataacta cgccgccag aaagtataat ga 942

<210> 330
 <211> 313
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 330
 Met Ser Phe His Gln Glu Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
 1 5 10 15
 Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Ala Trp Tyr Lys Pro Glu
 20 25 30
 Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Leu Val Tyr
 35 40 45
 Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Trp Tyr
 50 55 60
 Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
 65 70 75 80
 Arg Asn Ala Ile Phe Ile Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
 85 90 95
 Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
 100 105 110
 Thr Asp Tyr Val Asp Leu Tyr Leu Ile His Ser Pro Leu Val Ser Lys
 115 120 125
 Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
 130 135 140
 Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Thr
 145 150 155 160

Val	Glu	Asp	Leu	Gln	Arg	Ile	Leu	Lys	Val	Ala	Glu	Val	Lys	Pro	Gln
				165					170					175	
Val	Asn	Gln	Ile	Glu	Phe	Ser	Pro	Phe	Leu	Gln	Asn	Gln	Thr	Pro	Gly
			180					185					190		
Ile	Cys	Lys	Phe	Cys	Gln	Glu	His	Asp	Ile	Leu	Val	Glu	Ala	Tyr	Ser
		195					200					205			
Pro	Leu	Gly	Pro	Leu	Arg	Lys	Lys	Thr	Ala	Gln	Asp	Asp	Ser	Gln	Pro
	210					215					220				
Phe	Phe	Glu	Tyr	Val	Lys	Glu	Leu	Ser	Glu	Lys	Tyr	Asn	Lys	Thr	Glu
225					230					235					240
Ala	Gln	Ile	Ile	Leu	Arg	Trp	Val	Thr	Lys	Arg	Gly	Val	Leu	Pro	Val
			245						250					255	
Thr	Thr	Ser	Ser	Lys	Pro	Gln	Arg	Ile	Ser	Asp	Ala	Gln	Asn	Leu	Phe
			260					265					270		
Ser	Phe	Asp	Leu	Thr	Ala	Glu	Glu	Val	Asp	Lys	Ile	Thr	Glu	Leu	Gly
		275					280					285			
Leu	Glu	His	Glu	Pro	Leu	Arg	Leu	Tyr	Trp	Asn	Lys	Leu	Tyr	Gly	Lys
	290					295					300				
Tyr	Asn	Tyr	Ala	Ala	Gln	Lys	Val								
305					310										

<210> 331
 <211> 942
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 331
 atgtctttt accaacagtt tttcacgctg aacaaoggoa ataaaatccc ggcgattgcc 60
 atcatcgga ctggtacagc gtggtataaa cccgaagaaa ctgacgcgac cttctccaat 120
 agtctggttg aacaaatcgt gtatgcgttg aaactgccgg ggattatcca catcgacgcc 180
 gcggagtggt atcgcaccta cccggaagtg ggtaaagcac tgtccctgac cgaaaagcct 240
 cgtaacgcga tttttctgac ggataaatat tctcgcgaga ttaaaatgag tgactcccct 300
 gcggacggtc tggatttagc attgaagaaa atgggtacag attatggtga tttatatctg 360
 attcattccc cgttagtttc gaaggaagtg aatggcttaa gcttagaaga ggcttgaaa 420
 gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggttc caatttcaca 480
 gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
 gagttctctc cgttcctgca aaaccaaaca ccaggcattt gcaaatctctg tcaggagcac 600
 gatatcctgg tggaagcata ttctcgcgtg ggcccgtctg ggaagaaaac cgcgcaggat 660
 gacagccaac cattttttga gtacgtcaaa gaattgagcg aaaaatacaa taaatccgag 720
 gccagatca tcttgcgctg ggtcactaaa cgcgggtgtg tgccagttac cacctcttca 780
 aagcctcagc gcattagcga tgctcagaac ctgttttctt tcgacctgac agcgggaagag 840
 gttgataaaa tcacggagct gggtctggaa catgaaccgc tgcgcctgtg gtggaataaa 900
 gcgtatggca aatataacta cgccgcccag aaagtgtaat ga 942

<210> 332
 <211> 313
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 332
 Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
 1 5 10 15
 Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Ala Trp Tyr Lys Pro Glu


```

aagcctcagc gcattagcga tgctcagaac ctgttttcct tcgacctgac agcgggaagag 840
gttgataaaa tcacggagct gggctctggaa catgaaccgc tgcgcctgtg gtggaataaa 900
tcgtatggca aatataacta cgccgccag aaagtgtaat ga 942

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<210> 334
 <211> 313
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 334

Met	Ser	Phe	His	Gln	Gln	Phe	Phe	Thr	Leu	Asn	Asn	Gly	Asn	Lys	Ile
1				5					10					15	
Pro	Ala	Ile	Ala	Ile	Ile	Gly	Thr	Gly	Thr	Ala	Trp	Tyr	Lys	Pro	Glu
			20					25					30		
Glu	Thr	Asp	Ala	Thr	Phe	Ser	Asn	Ser	Leu	Val	Glu	Gln	Ile	Val	Tyr
		35					40					45			
Ala	Leu	Lys	Leu	Pro	Gly	Ile	Ile	His	Ile	Asp	Ala	Ala	Glu	Trp	Tyr
	50					55				60					
Arg	Thr	Tyr	Pro	Glu	Val	Gly	Lys	Ala	Leu	Ser	Leu	Thr	Glu	Lys	Pro
65				70					75					80	
Arg	Asn	Ala	Ile	Phe	Leu	Thr	Asp	Lys	Tyr	Ser	Pro	Gln	Ile	Lys	Met
			85					90					95		
Ser	Asp	Ser	Pro	Ala	Asp	Gly	Leu	Asp	Leu	Ala	Leu	Lys	Lys	Met	Gly
			100				105					110			
Thr	Asp	Tyr	Val	Asp	Leu	Tyr	Leu	Ile	His	Ser	Pro	Leu	Val	Ser	Lys
		115				120						125			
Glu	Val	Asn	Gly	Leu	Ser	Leu	Glu	Glu	Ala	Trp	Lys	Asp	Met	Glu	Gln
	130					135					140				
Leu	Tyr	Lys	Ser	Gly	Lys	Ala	Lys	Asn	Ile	Gly	Val	Ser	Asn	Phe	Thr
145				150					155					160	
Val	Glu	Asp	Leu	Gln	Arg	Ile	Leu	Lys	Val	Ala	Glu	Val	Lys	Pro	Gln
			165					170					175		
Val	Asn	Gln	Ile	Glu	Phe	Ser	Pro	Phe	Leu	Gln	Asn	Gln	Thr	Pro	Gly
		180					185					190			
Ile	Cys	Lys	Phe	Cys	Gln	Glu	His	Asp	Ile	Leu	Val	Glu	Ala	Tyr	Ser
	195				200							205			
Pro	Leu	Gly	Pro	Leu	Arg	Lys	Lys	Thr	Ala	Gln	Asp	Asp	Ser	Gln	Pro
	210				215						220				
Phe	Phe	Glu	Tyr	Val	Lys	Glu	Leu	Ser	Glu	Lys	Tyr	Asn	Lys	Ser	Glu
225				230					235					240	
Ala	Gln	Ile	Ile	Leu	Arg	Trp	Val	Thr	Lys	Arg	Gly	Val	Leu	Pro	Val
			245					250					255		
Thr	Thr	Ser	Ser	Lys	Pro	Gln	Arg	Ile	Ser	Asp	Ala	Gln	Asn	Leu	Phe
		260					265					270			
Ser	Phe	Asp	Leu	Thr	Ala	Glu	Glu	Val	Asp	Lys	Ile	Thr	Glu	Leu	Gly
	275					280						285			
Leu	Glu	His	Glu	Pro	Leu	Arg	Leu	Trp	Trp	Asn	Lys	Ser	Tyr	Gly	Lys
	290				295					300					
Tyr	Asn	Tyr	Ala	Ala	Gln	Lys	Val								
305					310										

<210> 335
 <211> 942
 <212> DNA
 <213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 335

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atgtcttttc accaacagtt tttcacgctg aacaacggca ataaaaatccc ggcgattgcc 60
atcatcgcca ctggtacagc gtggtataaa cccgaagaaa ctgacgcgac cttctccaat 120
agtctggttg aacaaatcgt gtatgcgttg aaactgccgg ggattatcca catcgacgcc 180
gcgagagtgt atcgcaccta ccggaagtg ggtaaagcac tgccctgac cgaaaagcct 240
cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactccct 300
gcgacgggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
attcattccc cgttagtttc gaaggaagtg aatggcttaa gcttagaaga ggcttggaaa 420
gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggttc caatttcaca 480
gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
gagttctctc cgttcctgca aaaccaaaca ccaggcattt gcaaattctg tcaggagcac 600
gatatcctgg tggaaagcata ttctccgctg ggcccgtgc ggaagaaaac cgcgaggat 660
gacagccaac ctttttttga gtacgtcaaa gaattgagcg aaaaatacaa taaatccgag 720
gccagatca tctcgctg ggtcactaaa cgcggtgtgc tgccagttac cacctcttca 780
aagcctcagc gcattagcga tgctcagaac ctgttttctc tcgacctgac agcgggaagag 840
gttgataaaa tcacggagct ggtctggaa catgaaccgc tcgcctgtg gtggaataaa 900
gagtatggca aatataacta cgccgccag aaagtgtaat ga 942
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<210> 336

<211> 313

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 336

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Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
1          5          10          15
Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Ala Trp Tyr Lys Pro Glu
20          25          30
Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
35          40          45
Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Trp Tyr
50          55          60
Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
65          70          75          80
Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
85          90          95
Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
100         105         110
Thr Asp Tyr Val Asp Leu Tyr Leu Ile His Ser Pro Leu Val Ser Lys
115         120         125
Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
130         135         140
Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Thr
145         150         155         160
Val Glu Asp Leu Gln Arg Ile Leu Lys Val Ala Glu Val Lys Pro Gln
165         170         175
Val Asn Gln Ile Glu Phe Ser Pro Phe Leu Gln Asn Gln Thr Pro Gly
180         185         190
Ile Cys Lys Phe Cys Gln Glu His Asp Ile Leu Val Glu Ala Tyr Ser
195         200         205
Pro Leu Gly Pro Leu Arg Lys Lys Thr Ala Gln Asp Asp Ser Gln Pro
210         215         220
Phe Phe Glu Tyr Val Lys Glu Leu Ser Glu Lys Tyr Asn Lys Ser Glu
225         230         235         240
```

Ala	Gln	Ile	Ile	Leu	Arg	Trp	Val	Thr	Lys	Arg	Gly	Val	Leu	Pro	Val
				245					250					255	
Thr	Thr	Ser	Ser	Lys	Pro	Gln	Arg	Ile	Ser	Asp	Ala	Gln	Asn	Leu	Phe
			260					265					270		
Ser	Phe	Asp	Leu	Thr	Ala	Glu	Glu	Val	Asp	Lys	Ile	Thr	Glu	Leu	Gly
		275					280					285			
Leu	Glu	His	Glu	Pro	Leu	Arg	Leu	Trp	Trp	Asn	Lys	Glu	Tyr	Gly	Lys
	290					295					300				
Tyr	Asn	Tyr	Ala	Ala	Gln	Lys	Val								
305					310										

<210> 337

<211> 942

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 337

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atgtcttttc accaacagtt tttcacgctg aacaacggca ataaaatccc ggcgattgcc 60
atcatcggca ctggtacagc gtggtataaa cccgaagaaa ctgacgcgac cttctccaat 120
agtctggttg aacaaatcgt gtatgcgttg aaactgccgg ggattatcca catcgacgcc 180
gcgagatggg atcgcaccta cccggaagtg ggtaaagcac tgtccctgac cgaaaagcct 240
cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactccctt 300
gcggacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
attcattccc cgttagtttc gaaggaagtg aatggcttaa gcttagaaga ggcttggaaa 420
gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggttc caatttcaca 480
gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
gagttctctc cgttcctgca aaaccaaaca ccaggcattt gcaaattctg tcaggagcac 600
gatatcctgg tggaagcata ttctccgctg ggcccgtgct ggaagaaaac cgcgcaggat 660
gacagccaac cattttttga gtacgtcaaa gaattgagcg aaaaatacaa taaatccgag 720
gccagatca tcttgccgtg ggctactaaa cgcggtgtgc tgccagttac caoctottca 780
aagcctcagc gcattagcga tgctcagaac ctgttttctt tcgacctgac agcgggaagag 840
gttgataaaa tcacggagct gggctctggaa catgaaccgc tgcgcctgtg gtggaataaa 900
ccttatggca aatataacta cgccgcccag aaagtgtaat ga 942

```

<210> 338

<211> 313

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 338

Met	Ser	Phe	His	Gln	Gln	Phe	Phe	Thr	Leu	Asn	Asn	Gly	Asn	Lys	Ile
1			5						10					15	
Pro	Ala	Ile	Ala	Ile	Ile	Gly	Thr	Gly	Thr	Ala	Trp	Tyr	Lys	Pro	Glu
			20					25					30		
Glu	Thr	Asp	Ala	Thr	Phe	Ser	Asn	Ser	Leu	Val	Glu	Gln	Ile	Val	Tyr
		35					40					45			
Ala	Leu	Lys	Leu	Pro	Gly	Ile	Ile	His	Ile	Asp	Ala	Ala	Glu	Trp	Tyr
	50					55				60					
Arg	Thr	Tyr	Pro	Glu	Val	Gly	Lys	Ala	Leu	Ser	Leu	Thr	Glu	Lys	Pro
65				70					75					80	
Arg	Asn	Ala	Ile	Phe	Leu	Thr	Asp	Lys	Tyr	Ser	Pro	Gln	Ile	Lys	Met
			85					90					95		
Ser	Asp	Ser	Pro	Ala	Asp	Gly	Leu	Asp	Leu	Ala	Leu	Lys	Lys	Met	Gly

<220>

<223> Synthetic Construct

<400> 340

Met	Ser	Phe	His	Gln	Gln	Phe	Phe	Thr	Leu	Asn	Asn	Gly	Asn	Lys	Ile
1			5						10					15	
Pro	Ala	Ile	Ala	Ile	Ile	Gly	Thr	Gly	Thr	Ala	Trp	Tyr	Lys	Pro	Glu
		20						25					30		
Glu	Thr	Asp	Ala	Thr	Phe	Ser	Asn	Ser	Leu	Val	Glu	Gln	Ile	Val	Tyr
		35					40					45			
Ala	Leu	Lys	Leu	Pro	Gly	Ile	Ile	His	Ile	Asp	Ala	Ala	Glu	Trp	Tyr
	50					55				60					
Arg	Thr	Tyr	Pro	Glu	Val	Gly	Lys	Ala	Leu	Ser	Leu	Thr	Glu	Lys	Pro
65				70						75					80
Arg	Asn	Ala	Ile	Phe	Leu	Thr	Asp	Lys	Tyr	Ser	Pro	Gln	Ile	Lys	Met
			85						90					95	
Ser	Asp	Ser	Pro	Ala	Asp	Gly	Leu	Asp	Leu	Ala	Leu	Lys	Lys	Met	Gly
			100					105					110		
Thr	Asp	Tyr	Val	Asp	Leu	Tyr	Leu	Ile	His	Ser	Pro	Leu	Val	Ser	Lys
	115						120					125			
Glu	Val	Asn	Gly	Leu	Ser	Leu	Glu	Glu	Ala	Trp	Lys	Asp	Met	Glu	Gln
	130					135					140				
Leu	Tyr	Lys	Ser	Gly	Lys	Ala	Lys	Asn	Ile	Gly	Val	Ser	Asn	Phe	Thr
145					150					155					160
Val	Glu	Asp	Leu	Gln	Arg	Ile	Leu	Lys	Val	Ala	Glu	Val	Lys	Pro	Gln
			165						170					175	
Val	Asn	Gln	Ile	Glu	Phe	Ser	Pro	Phe	Leu	Gln	Asn	Gln	Thr	Pro	Gly
		180						185					190		
Ile	Cys	Lys	Phe	Cys	Gln	Glu	His	Asp	Ile	Leu	Val	Glu	Ala	Tyr	Ser
	195						200					205			
Pro	Leu	Gly	Pro	Leu	Arg	Lys	Lys	Thr	Ala	Gln	Asp	Asp	Ser	Gln	Pro
	210					215					220				
Phe	Phe	Glu	Tyr	Val	Lys	Glu	Leu	Ser	Glu	Lys	Tyr	Asn	Lys	Ser	Glu
225					230					235					240
Ala	Gln	Ile	Ile	Leu	Arg	Trp	Val	Thr	Lys	Arg	Gly	Val	Leu	Pro	Val
			245						250					255	
Thr	Thr	Ser	Ser	Lys	Pro	Gln	Arg	Ile	Ser	Asp	Ala	Gln	Asn	Leu	Phe
		260						265					270		
Ser	Phe	Asp	Leu	Thr	Ala	Glu	Glu	Val	Asp	Lys	Ile	Thr	Glu	Leu	Gly
		275					280					285			
Leu	Glu	His	Glu	Pro	Leu	Arg	Leu	Trp	Trp	Asn	Lys	Gln	Tyr	Gly	Lys
	290					295					300				
Tyr	Asn	Tyr	Ala	Ala	Gln	Lys	Val								
305					310										

<210> 341

<211> 942

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 341

atgtcttttc	accaacagtt	tttcacgctg	aacaacggca	ataaaaatccc	ggcgattgoc	60
atcatcgcca	ctggtacagc	gtggtataaa	cccgaagaaa	ctgacgcgac	cttctccaat	120
agtctggttg	aacaaatcgt	gtatgcgttg	aaactgocgg	ggattatcca	catcgacgcc	180
gcggagtggg	atcgcaccta	cccggaagtg	ggtaaagcac	tgtccctgac	cgaaaagcct	240
cgtaacgcga	tttttctgac	ggataaatat	tctccgcaga	ttaaaatgag	tgactcccct	300
gcggacggtc	tggatttagc	attgaagaaa	atgggtacag	attatgttga	tttatatctg	360

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attcattccc cgttagtttc gaaggaagtg aatggcttaa gcttagaaga ggcttggaaa 420
gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggtttc caatttcaca 480
gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
gagttctctc cgttcctgca aaaccaaaca ccaggcattt gcaaattctg tcaggagcac 600
gatatcctgg tggaagcata ttctccgctg ggcccgcctgc ggaagaaaac cgcgcaggat 660
gacagccaac cattttttga gtacgtcaaa gaattgagcg aaaaatacaa taaatccgag 720
gccagatca tctgcgctg ggtcactaaa cgcgggtgtgc tgccagttac cacctcttca 780
aagcctcagc gcattagcga tgctcagaac ctgttttcct tcgacctgac agcgggaagag 840
gttgataaaa tcacggagct gggctctggaa catgaaccgc tgcgcctgta ttggaataaa 900
gagtatggca aatataacta cgcgcgccag aaagtgtaat ga 942

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<210> 342

<211> 313

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 342

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Met Ser Phe His Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
1      5      10      15
Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Ala Trp Tyr Lys Pro Glu
20     25     30
Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
35     40     45
Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Trp Tyr
50     55     60
Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
65     70     75     80
Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
85     90     95
Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
100    105    110
Thr Asp Tyr Val Asp Leu Tyr Leu Ile His Ser Pro Leu Val Ser Lys
115    120    125
Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
130    135    140
Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Thr
145    150    155    160
Val Glu Asp Leu Gln Arg Ile Leu Lys Val Ala Glu Val Lys Pro Gln
165    170    175
Val Asn Gln Ile Glu Phe Ser Pro Phe Leu Gln Asn Gln Thr Pro Gly
180    185    190
Ile Cys Lys Phe Cys Gln Glu His Asp Ile Leu Val Glu Ala Tyr Ser
195    200    205
Pro Leu Gly Pro Leu Arg Lys Lys Thr Ala Gln Asp Asp Ser Gln Pro
210    215    220
Phe Phe Glu Tyr Val Lys Glu Leu Ser Glu Lys Tyr Asn Lys Ser Glu
225    230    235    240
Ala Gln Ile Ile Leu Arg Trp Val Thr Lys Arg Gly Val Leu Pro Val
245    250    255
Thr Thr Ser Ser Lys Pro Gln Arg Ile Ser Asp Ala Gln Asn Leu Phe
260    265    270
Ser Phe Asp Leu Thr Ala Glu Glu Val Asp Lys Ile Thr Glu Leu Gly
275    280    285
Leu Glu His Glu Pro Leu Arg Leu Tyr Trp Asn Lys Glu Tyr Gly Lys
290    295    300
Tyr Asn Tyr Ala Ala Gln Lys Val
305    310

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<210> 343
 <211> 942
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 343
 atgtcttttc accaacagtt tttcacgctg aacaacggca ataaaatccc ggogattgcc 60
 atcatcggca ctggtacagc gtggtataaa cccgaagaaa ctgacgcgac cttctccaat 120
 ggtctggttg aacaaatcgt gtatgcgttg aaactgccgg ggattatcca catcgacgcc 180
 gcggagtggt atcgcaccta cccggaagtg ggtaaagcac tgtccctgac cgaaaagcct 240
 cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactccctt 300
 gcggacggctc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
 attcattccc cgttagtctc gaaggaagtg aatggcttaa gcttagaaga ggcttggaag 420
 gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggttc caatttcaca 480
 gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
 gagttctctc cgttcctgca aaaccaaaaca ccaggcattt gcaaattctg tcaggagcac 600
 gatatacttg tggaagcata ttctccgctg ggcccgtctg ggaagaaaac cgcgcaggat 660
 gacagccaac cattttttga gtacgtcaaa gaattgagcg aaaaatacaa taaatccgag 720
 gccagatca tctgcgctg ggtcactaaa cgcggtgtgc tgccagttac cacctcttca 780
 aagcctcagc gcattagcga tgctcagaac ctgttttctt tcgacctgac agcgggaagag 840
 gttgataaaa tcacggagct gggctctggaa catgaaccgc tcgcctgta ctggaataaa 900
 gcgtatggca aatataacta cgcgcccgag aaagtgtaat ga 942

<210> 344
 <211> 313
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 344
 Met Ser Phe His Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
 1 5 10 15
 Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Ala Trp Tyr Lys Pro Glu
 20 25 30
 Glu Thr Asp Ala Thr Phe Ser Asn Gly Leu Val Glu Gln Ile Val Tyr
 35 40 45
 Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Trp Tyr
 50 55 60
 Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
 65 70 75 80
 Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
 85 90 95
 Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
 100 105 110
 Thr Asp Tyr Val Asp Leu Tyr Leu Ile His Ser Pro Leu Val Ser Lys
 115 120 125
 Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
 130 135 140
 Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Thr
 145 150 155 160
 Val Glu Asp Leu Gln Arg Ile Leu Lys Val Ala Glu Val Lys Pro Gln
 165 170 175
 Val Asn Gln Ile Glu Phe Ser Pro Phe Leu Gln Asn Gln Thr Pro Gly

			180					185					190				
Ile	Cys	Lys	Phe	Cys	Gln	Glu	His	Asp	Ile	Leu	Val	Glu	Ala	Tyr	Ser		
		195					200					205					
Pro	Leu	Gly	Pro	Leu	Arg	Lys	Lys	Thr	Ala	Gln	Asp	Asp	Ser	Gln	Pro		
	210					215					220						
Phe	Phe	Glu	Tyr	Val	Lys	Glu	Leu	Ser	Glu	Lys	Tyr	Asn	Lys	Ser	Glu		
225					230					235					240		
Ala	Gln	Ile	Ile	Leu	Arg	Trp	Val	Thr	Lys	Arg	Gly	Val	Leu	Pro	Val		
			245						250					255			
Thr	Thr	Ser	Ser	Lys	Pro	Gln	Arg	Ile	Ser	Asp	Ala	Gln	Asn	Leu	Phe		
		260						265					270				
Ser	Phe	Asp	Leu	Thr	Ala	Glu	Glu	Val	Asp	Lys	Ile	Thr	Glu	Leu	Gly		
		275					280					285					
Leu	Glu	His	Glu	Pro	Leu	Arg	Leu	Tyr	Trp	Asn	Lys	Ala	Tyr	Gly	Lys		
	290					295					300						
Tyr	Asn	Tyr	Ala	Ala	Gln	Lys	Val										
305					310												

<210> 345
 <211> 942
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 345
 atgtcttttc accaacagtt tttcacgctg aacaacggca ataaaatccc ggogattgcc 60
 atcatcgcca ctggtacagc gtggtataaa ccogaagaaa ctgacgogac cttctccaat 120
 agtctggttg aacaaatcgt gtatgcgttg aaactgcggg ggattatcca catcgacgcc 180
 gcggagtggc atcgcaccta ccggaagtg ggtaaagcac tgtccctgac cgaaaagcct 240
 cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactcccct 300
 gcggacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
 attcattccc cgttagtttc gaaggaagtg aatggcttaa gcttagaaga ggcttggaaa 420
 gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggttc caatttcaca 480
 gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
 gagttctctc cgttcctgca aaaccaaaaca ccaggcattt gcaaattctg tcaggagcac 600
 gatatccttg tggaagcata ttctccgctg ggcccgctgc ggaagaaaac cgcgaggat 660
 gacagccaac cattttttga gtacgtcaaa gaattgagcg aaaaatacaa taaatccgag 720
 gccagatca tcttgcgctg ggtcactaaa cgoggtgtgc tgccagttac cacctcttca 780
 aagcctcagc gcattagcga tgctcagaac ctgttttctt tcgacctgac agcgggaagag 840
 gttgataaaa tcacggagct gggtctggaa catgaaccgc tgcgcctgtt ttggaataaa 900
 gagtatggca aatataacta cgccgccag aaagtgtaat ga 942

<210> 346
 <211> 313
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 346
 Met Ser Phe His Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
 1 5 10 15
 Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Ala Trp Tyr Lys Pro Glu
 20 25 30
 Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
 35 40 45

[illegible]

<210> 348
 <211> 313
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 348
 Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
 1 5 10 15
 Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Ala Trp Tyr Lys Pro Glu
 20 25 30
 Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
 35 40 45
 Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Trp Tyr
 50 55 60
 Gly Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
 65 70 75 80
 Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
 85 90 95
 Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
 100 105 110
 Thr Asp Tyr Val Asp Leu Tyr Leu Ile His Ser Pro Leu Val Ser Lys
 115 120 125
 Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
 130 135 140
 Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Thr
 145 150 155 160
 Val Glu Asp Leu Gln Arg Ile Leu Lys Val Ala Glu Val Lys Pro Gln
 165 170 175
 Val Asn Gln Ile Glu Phe Ser Pro Phe Leu Gln Asn Gln Thr Pro Gly
 180 185 190
 Ile Cys Lys Phe Cys Gln Glu His Asp Ile Leu Val Glu Ala Tyr Ser
 195 200 205
 Pro Leu Gly Pro Leu Arg Lys Lys Thr Ala Gln Asp Asp Ser Gln Pro
 210 215 220
 Phe Phe Glu Tyr Val Lys Glu Leu Ser Glu Lys Tyr Asn Lys Ser Glu
 225 230 235 240
 Ala Gln Ile Ile Leu Arg Trp Val Thr Lys Arg Gly Val Leu Pro Val
 245 250 255
 Thr Thr Ser Ser Lys Pro Gln Arg Ile Ser Asp Ala Gln Asn Leu Phe
 260 265 270
 Ser Phe Asp Leu Thr Ala Glu Glu Val Asp Lys Ile Thr Glu Leu Gly
 275 280 285
 Leu Glu His Glu Pro Leu Arg Leu Trp Trp Asn Lys Gln Tyr Gly Lys
 290 295 300
 Tyr Asn Tyr Ala Ala Gln Lys Val
 305 310

<210> 349
 <211> 942
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 349

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atgtcttttc accaacagtt tttcacgctg aacaacggca ataaaatccc ggcgattgcc 60
atcatcgcca ctggtacagc gtggtataaa ccogaagaaa ctgacgcgac cttctccaat 120
agtctggttg aacaaatcgt gtatgcgttg aaactgccgg ggattatcca catcgacgcc 180
gcgagatggg attcgacctt cccggaagtg ggtaaagcac tgtccctgac cgaaaagcct 240
cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactcccct 300
gcgacaggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
attcattccc cgttagtttc gaaggaagtg aatggcttaa gcttagaaga ggcttgaaa 420
gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggttc caatttcaca 480
gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
gagttctctc cgttcctgca aaaccaaaca ccaggcattt gcaaattctg tcaggagcac 600
gatatcctgg tggaaagcata ttctccgctg ggcccgtgct ggaagaaaac cgcgaggat 660
gacagccaac cattttttga gtacgtcaaa gaattgagcg aaaaatacaa taaatccgag 720
gcccagatca tcttgcgctg ggtcactaaa cgcggtgtgc tgccagttac cacctcttca 780
aagcctcagc gcattagcga tgctcagaac ctgttttctt tcgacctgac agcggaagag 840
gttgataaaa tcacggagct gggcctggaa catgaaccgc tgcgcctgtg gtggaataaa 900
cagtatggca aatataacta cgccgccag aaagtgtaat ga 942
```

<210> 350

<211> 313

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 350

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Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
1          5          10          15
Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Ala Trp Tyr Lys Pro Glu
20          25          30
Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
35          40          45
Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Trp Tyr
50          55          60
Ser Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
65          70          75          80
Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
85          90          95
Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
100          105          110
Thr Asp Tyr Val Asp Leu Tyr Leu Ile His Ser Pro Leu Val Ser Lys
115          120          125
Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
130          135          140
Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Thr
145          150          155          160
Val Glu Asp Leu Gln Arg Ile Leu Lys Val Ala Glu Val Lys Pro Gln
165          170          175
Val Asn Gln Ile Glu Phe Ser Pro Phe Leu Gln Asn Gln Thr Pro Gly
180          185          190
Ile Cys Lys Phe Cys Gln Glu His Asp Ile Leu Val Glu Ala Tyr Ser
195          200          205
Pro Leu Gly Pro Leu Arg Lys Lys Thr Ala Gln Asp Asp Ser Gln Pro
210          215          220
Phe Phe Glu Tyr Val Lys Glu Leu Ser Glu Lys Tyr Asn Lys Ser Glu
225          230          235          240
Ala Gln Ile Ile Leu Arg Trp Val Thr Lys Arg Gly Val Leu Pro Val
245          250          255
Thr Thr Ser Ser Lys Pro Gln Arg Ile Ser Asp Ala Gln Asn Leu Phe
```


Glu	Val	Asn	Gly	Leu	Ser	Leu	Glu	Glu	Ala	Trp	Lys	Asp	Met	Glu	Gln
130						135					140				
Leu	Tyr	Lys	Ser	Gly	Lys	Ala	Lys	Asn	Ile	Gly	Val	Ser	Asn	Phe	Thr
145					150					155					160
Val	Glu	Asp	Leu	Gln	Arg	Ile	Leu	Lys	Val	Ala	Glu	Val	Lys	Pro	Gln
			165						170					175	
Val	Asn	Gln	Ile	Glu	Phe	Ser	Pro	Phe	Leu	Gln	Asn	Gln	Thr	Pro	Gly
		180						185					190		
Ile	Cys	Lys	Phe	Cys	Gln	Glu	His	Asp	Ile	Leu	Val	Glu	Ala	Tyr	Ser
	195						200					205			
Pro	Leu	Gly	Pro	Leu	Arg	Lys	Lys	Thr	Ala	Gln	Asp	Asp	Ser	Gln	Pro
	210					215					220				
Phe	Phe	Glu	Tyr	Val	Lys	Glu	Leu	Ser	Glu	Lys	Tyr	Asn	Lys	Ser	Glu
225					230					235					240
Ala	Gln	Ile	Ile	Leu	Arg	Trp	Val	Thr	Lys	Arg	Gly	Val	Leu	Pro	Val
			245						250					255	
Thr	Thr	Ser	Ser	Lys	Pro	Gln	Arg	Ile	Ser	Asp	Ala	Gln	Asn	Leu	Phe
		260						265					270		
Ser	Phe	Asp	Leu	Thr	Ala	Glu	Glu	Val	Asp	Lys	Ile	Thr	Glu	Leu	Gly
	275						280					285			
Leu	Glu	His	Glu	Pro	Leu	Arg	Leu	Trp	Trp	Asn	Lys	Gln	Tyr	Gly	Lys
	290					295					300				
Tyr	Asn	Tyr	Ala	Ala	Gln	Lys	Val								
305					310										

<210> 353
 <211> 943
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 353
 atgtcttttt accaacagtt tttcacgctg aacaacggca ataaaatccc ggcgattgcc 60
 atcatcgga ctggtacagc gtggtataaa ccgaagaaa ctgacgogac cttctccaat 120
 agtctggttg aacaaatcgt gtatgcgttg aaactgccgg ggattatcca catcgacgoc 180
 gcggagtggt atcgcaccta cccggaagtg ggtaaagcac tgtccctgac cgaagagcct 240
 cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactcccct 300
 gcggacgggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
 attcattccc cgtagtttgc gaaggaagtg aatggcttaa gcttagaaga ggcttggaaa 420
 gatattggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggttc caatttcaca 480
 gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
 gagttctctc cgttcctgca aaaccaaaca ccaggcattt gcaaattctg tcaggagcac 600
 gatattcctg tggaagcata ttctccgctg ggcccgctgc ggaagaaaac cgcgcaggat 660
 gacagccaac ctttttttga gtacgtcaaa gaattgagcg aaaaatacaa taaatccgag 720
 gccagatca tctgctgctg ggtcactaaa ccgggtgtgc tgccagttac cacctottca 780
 aagcctcagc gcattagcga tgctcagaac ctgttttctc tcgaactgac agcgggaagag 840
 gttgataaaa tcacggagct gggcctggaa catgaaccgc tgcgcctgtg gtggaataaa 900
 cagtatggca aatataacta cgccgccga gaaagtgtaa tga 943

<210> 354
 <211> 314
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 354

```
Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
1          5          10          15
Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Ala Trp Tyr Lys Pro Glu
20          25          30
Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
35          40          45
Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Trp Tyr
50          55          60
Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
65          70          75          80
Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
85          90          95
Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
100         105         110
Thr Asp Tyr Val Asp Leu Tyr Leu Ile His Ser Pro Leu Val Ser Lys
115         120         125
Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
130         135         140
Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Thr
145         150         155         160
Val Glu Asp Leu Gln Arg Ile Leu Lys Val Ala Glu Val Lys Pro Gln
165         170         175
Val Asn Gln Ile Glu Phe Ser Pro Phe Leu Gln Asn Gln Thr Pro Gly
180         185         190
Ile Cys Lys Phe Cys Gln Glu His Asp Ile Leu Val Glu Ala Tyr Ser
195         200         205
Pro Leu Gly Pro Leu Arg Lys Lys Thr Ala Gln Asp Asp Ser Gln Pro
210         215         220
Phe Phe Glu Tyr Val Lys Glu Leu Ser Glu Lys Tyr Asn Lys Ser Glu
225         230         235         240
Ala Gln Ile Ile Leu Arg Trp Val Thr Lys Arg Gly Val Leu Pro Val
245         250         255
Thr Thr Ser Ser Lys Pro Gln Arg Ile Ser Asp Ala Gln Asn Leu Phe
260         265         270
Ser Phe Asp Leu Thr Ala Glu Glu Val Asp Lys Ile Thr Glu Leu Gly
275         280         285
Leu Glu His Glu Pro Leu Arg Leu Trp Trp Asn Lys Gln Tyr Gly Lys
290         295         300
Tyr Asn Tyr Ala Ala Arg Glu Ser Val Met
305          310
```

<210> 355

<211> 942

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 355

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atgtcttttc accaacagtt ttccacgctg aacaacggca ataaaatccc ggcgattgcc 60
atcatcggca ctggtacagc gtggtataaa cccgaagaaa ctgaacgagac cttctccaat 120
agtctggttg aacaaatcgt gtatgcgttg aaactgcogg ggattatcca catcgacgcc 180
gcgagatggt atcgcaacct cccggaagtg ggtaaagcac tgtccctgac cgaaaagcct 240
cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactcccct 300
gcggacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
attcattccc cgttagtttc gaaggaagtg aatggcttaa gcttagaaga ggcttggaag 420
gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcggggtttc caatttcaca 480
gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
```

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gagttctctc cgttcctgca aaaccaaaca ccaggcattt gcaaattctg tcaggagcac 600
gatatcctgg tggaagcata ttctccgctg ggcccgtgc ggaagaaaac cacgcaggat 660
gacagccaac ctttttttga gtacgtcaaa gaattgagcg aaaaatacaa taaatccgag 720
gcccgatca tcctgcgctg ggtcactaaa cgcgggtgtg tgccagttac cacctcttca 780
aagcctcagc gcattagcga tgctcagaac ctgttttctt tcgacctgac agcggaagag 840
gttgataaaa tcacggagct gggcctggaa catgaaccgc tgcgcctgtg gtggaataaa 900
cagtatggca aatataacta cgccgccag aaagtgtaat ga 942

```

<210> 356

<211> 313

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 356

```

Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
1          5          10          15
Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Ala Trp Tyr Lys Pro Glu
          20          25          30
Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
          35          40          45
Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Trp Tyr
          50          55          60
Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
65          70          75          80
Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
          85          90          95
Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
          100         105         110
Thr Asp Tyr Val Asp Leu Tyr Leu Ile His Ser Pro Leu Val Ser Lys
          115         120         125
Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
          130         135         140
Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Thr
145         150         155         160
Val Glu Asp Leu Gln Arg Ile Leu Lys Val Ala Glu Val Lys Pro Gln
          165         170         175
Val Asn Gln Ile Glu Phe Ser Pro Phe Leu Gln Asn Gln Thr Pro Gly
          180         185         190
Ile Cys Lys Phe Cys Gln Glu His Asp Ile Leu Val Glu Ala Tyr Ser
          195         200         205
Pro Leu Gly Pro Leu Arg Lys Lys Thr Thr Gln Asp Asp Ser Gln Pro
          210         215         220
Phe Phe Glu Tyr Val Lys Glu Leu Ser Glu Lys Tyr Asn Lys Ser Glu
225         230         235         240
Ala Gln Ile Ile Leu Arg Trp Val Thr Lys Arg Gly Val Leu Pro Val
          245         250         255
Thr Thr Ser Ser Lys Pro Gln Arg Ile Ser Asp Ala Gln Asn Leu Phe
          260         265         270
Ser Phe Asp Leu Thr Ala Glu Glu Val Asp Lys Ile Thr Glu Leu Gly
          275         280         285
Leu Glu His Glu Pro Leu Arg Leu Trp Trp Asn Lys Gln Tyr Gly Lys
          290         295         300
Tyr Asn Tyr Ala Ala Gln Lys Val
305          310

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<210> 357

<211> 943
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 357
atgtcttttc accaacagtt tttcacgctg aacaacggca ataaaatccc ggcgattgcc 60
atcatcggca ctggtacagc gtggtataaa cccgaagaaa ctgacgcgac cttctccaat 120
agtctgggtg aacaaatcgt gtatgcgttg aaactgocgg ggattatcca catcgacgcc 180
gcggagtggg atcgcaccta cccggaagtg ggtaaagcac tgtccctgac cgaaaagcct 240
cgtaacgcga tttttctgac ggataaatat tctccgcaga ttaaaatgag tgactcccct 300
gcggacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
attcattccc cgttagtttc gaaggaagtg aatggcttaa gcttagaaga ggcttggaag 420
gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggttc caatttcaca 480
gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
gagttctctc cgttcctgca aaaccaaaca ccaggcattt gcaaattctg tcaggagcac 600
gatatcctgg tgggaagcata ttctccgctg ggcccgtgac ggaagaaaac cgcgcaggat 660
gacagccaac cattttttga gtacgtcaaa gaattgagcg aaaaatacaa taaatccgag 720
goccagatca tcctgcgctg ggtcactaaa cgcggtgtgc tgccagttac cacctcttca 780
aagcctcagc gcattagcga tgctcagaac ctgttttctt tcgacctgac agcgggaagag 840
gttgataaaa tcacggagct gggcctggaa catgaaccgc tgcgccctgtg gtggaataaa 900
cagtatggca aatataacta cgcgcgccca gaaagtgtaa tga 943

<210> 358
<211> 314
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 358
Met Ser Phe His Gln Gln Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
1 5 10 15
Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Ala Trp Tyr Lys Pro Glu
20 25 30
Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Ile Val Tyr
35 40 45
Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Trp Tyr
50 55 60
Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
65 70 75 80
Arg Asn Ala Ile Phe Leu Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
85 90 95
Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
100 105 110
Thr Asp Tyr Val Asp Leu Tyr Leu Ile His Ser Pro Leu Val Ser Lys
115 120 125
Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
130 135 140
Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Thr
145 150 155 160
Val Glu Asp Leu Gln Arg Ile Leu Lys Val Ala Glu Val Lys Pro Gln
165 170 175
Val Asn Gln Ile Glu Phe Ser Pro Phe Leu Gln Asn Gln Thr Pro Gly
180 185 190
Ile Cys Lys Phe Cys Gln Glu His Asp Ile Leu Val Glu Ala Tyr Ser
195 200 205

Pro	Leu	Gly	Pro	Leu	Arg	Lys	Lys	Thr	Ala	Gln	Asp	Asp	Ser	Gln	Pro
210						215					220				
Phe	Phe	Glu	Tyr	Val	Lys	Glu	Leu	Ser	Glu	Lys	Tyr	Asn	Lys	Ser	Glu
225					230					235					240
Ala	Gln	Ile	Ile	Leu	Arg	Trp	Val	Thr	Lys	Arg	Gly	Val	Leu	Pro	Val
				245					250					255	
Thr	Thr	Ser	Ser	Lys	Pro	Gln	Arg	Ile	Ser	Asp	Ala	Gln	Asn	Leu	Phe
			260					265					270		
Ser	Phe	Asp	Leu	Thr	Ala	Glu	Glu	Val	Asp	Lys	Ile	Thr	Glu	Leu	Gly
		275					280					285			
Leu	Glu	His	Glu	Pro	Leu	Arg	Leu	Trp	Trp	Asn	Lys	Gln	Tyr	Gly	Lys
	290					295					300				
Tyr	Asn	Tyr	Ala	Ala	Pro	Glu	Ser	Val	Met						
305					310										

<210> 359

<211> 942

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 359

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atgtcttttc accaagaatt ttccacgctg aacaacggca ataaaatccc ggcgattgcc 60
atcatcggca ctggtacagc gtggtataaa cccgaagaaa ctgacgcgac cttctccaat 120
agtctggttg aacaattagt gtatgcgttg aaactgocgg ggattatoca catcgacgcc 180
gcgagtggtg atcgcaccta cccggaagtg ggtaaagcac tgtccctgac cgaaaagcct 240
cgtaacgcga tttttatcac ggataaatat tctccgcaga ttaaaatgag cgaactccct 300
gcggaacggc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
attcattccc cgttagtttc gaaggaagtg aatggcttaa gcttagaaga ggcttggaaa 420
gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggttc caatttcaca 480
gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
gagttctctc cgttcctgca aaaccaaaca ccaggcattt gcaaattctg tcaggagcac 600
gatatcctgg tggaagcata ttctccgcta ggcccgctgc ggaagaaaac cgcgcaggat 660
gacagccaac cattttttga gtacgtcaaa gaattgagcg aaaaatacaa taaaaccgag 720
gcccagatca tcctgcgctg ggtaactaaa cgcggtgtgc tgccagttac cacctcttca 780
aagcctcagc gcattagcga tgctcagaac ctgttttctc tcgacctgac agcgggaagag 840
gttgataaaa tcacggagct gggctctggaa catgaaccgc tcgcctgtga ctggaataaa 900
gagtatggca aatataacta cgccgccagc aaagtataat ga 942

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<210> 360

<211> 313

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 360

Met	Ser	Phe	His	Gln	Glu	Phe	Phe	Thr	Leu	Asn	Asn	Gly	Asn	Lys	Ile
1			5					10					15		
Pro	Ala	Ile	Ala	Ile	Ile	Gly	Thr	Gly	Thr	Ala	Trp	Tyr	Lys	Pro	Glu
		20					25					30			
Glu	Thr	Asp	Ala	Thr	Phe	Ser	Asn	Ser	Leu	Val	Glu	Gln	Leu	Val	Tyr
	35					40					45				
Ala	Leu	Lys	Leu	Pro	Gly	Ile	Ile	His	Ile	Asp	Ala	Ala	Glu	Trp	Tyr
	50				55				60						
Arg	Thr	Tyr	Pro	Glu	Val	Gly	Lys	Ala	Leu	Ser	Leu	Thr	Glu	Lys	Pro

65					70					75				80
Arg	Asn	Ala	Ile	Phe	Ile	Thr	Asp	Lys	Tyr	Ser	Pro	Gln	Ile	Lys Met
				85					90					95
Ser	Asp	Ser	Pro	Ala	Asp	Gly	Leu	Asp	Leu	Ala	Leu	Lys	Lys	Met Gly
			100					105					110	
Thr	Asp	Tyr	Val	Asp	Leu	Tyr	Leu	Ile	His	Ser	Pro	Leu	Val	Ser Lys
		115					120					125		
Glu	Val	Asn	Gly	Leu	Ser	Leu	Glu	Glu	Ala	Trp	Lys	Asp	Met	Glu Gln
	130					135					140			
Leu	Tyr	Lys	Ser	Gly	Lys	Ala	Lys	Asn	Ile	Gly	Val	Ser	Asn	Phe Thr
145					150					155				160
Val	Glu	Asp	Leu	Gln	Arg	Ile	Leu	Lys	Val	Ala	Glu	Val	Lys	Pro Gln
				165					170					175
Val	Asn	Gln	Ile	Glu	Phe	Ser	Pro	Phe	Leu	Gln	Asn	Gln	Thr	Pro Gly
			180					185					190	
Ile	Cys	Lys	Phe	Cys	Gln	Glu	His	Asp	Ile	Leu	Val	Glu	Ala	Tyr Ser
	195						200					205		
Pro	Leu	Gly	Pro	Leu	Arg	Lys	Lys	Thr	Ala	Gln	Asp	Asp	Ser	Gln Pro
	210					215					220			
Phe	Phe	Glu	Tyr	Val	Lys	Glu	Leu	Ser	Glu	Lys	Tyr	Asn	Lys	Thr Glu
225					230					235				240
Ala	Gln	Ile	Ile	Leu	Arg	Trp	Val	Thr	Lys	Arg	Gly	Val	Leu	Pro Val
				245					250					255
Thr	Thr	Ser	Ser	Lys	Pro	Gln	Arg	Ile	Ser	Asp	Ala	Gln	Asn	Leu Phe
		260						265					270	
Ser	Phe	Asp	Leu	Thr	Ala	Glu	Glu	Val	Asp	Lys	Ile	Thr	Glu	Leu Gly
	275						280					285		
Leu	Glu	His	Glu	Pro	Leu	Arg	Leu	Tyr	Trp	Asn	Lys	Glu	Tyr	Gly Lys
	290					295					300			
Tyr	Asn	Tyr	Ala	Ala	Gln	Lys	Val							
305					310									

<210> 361
 <211> 942
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 361
 atgtcttttc accaagaatt ttccacgctg aacaacggca ataaaatccc ggcgattgcc 60
 atcatcgcca ctggtacagc gtggtataaa cccgaagaaa ctgacgcgac cttctccaat 120
 agtctggttg aacaattagt gtatgcgttg aaactgccgg ggattatcca catcgacgcc 180
 gcggagattt atcgaccta cccggaagtg ggtaaagcac tgtccctgac cgaaaagcct 240
 cgtaacgcga tttttatcac ggataaatat tctccgcaga ttaaaatgag cgactcccct 300
 gcggacggto tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
 attcattccc cgtagtttgc gaaggaagtg aatggcttaa gottagaaga ggcttggaaa 420
 gatattggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggtttc caatttcaca 480
 gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
 gagttctctc cgttcctgca aaaccaaaca ccaggcattt gcaaattctg tcaggagcac 600
 gatattcctg tggaagcata ttctccgcta ggcccgtgct ggaagaaaac cgcgcaggat 660
 gacagccaac ctttttttga gtacgtcaaa gaattgagcg aaaaatacaa taaaaccgag 720
 gccagatca tctctgcgtg ggtcactaaa cgcgggtgtg tgccagttac cactcttca 780
 aagcctcagc gcattagoga tgctcagaac ctgttttcct tcgacctgac agcgggaagag 840
 gttgataaaa tcacggagct gggtctggaa catgaaccgc tgcgcctgtg gtggaataaa 900
 ttgtatggca aatataacta cgccgccagc aaagtataat ga 942

<210> 362

<211> 313
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 362
 Met Ser Phe His Gln Glu Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
 1 5 10 15
 Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Ala Trp Tyr Lys Pro Glu
 20 25 30
 Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Leu Val Tyr
 35 40 45
 Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Ile Tyr
 50 55 60
 Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
 65 70 75 80
 Arg Asn Ala Ile Phe Ile Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
 85 90 95
 Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
 100 105 110
 Thr Asp Tyr Val Asp Leu Tyr Leu Ile His Ser Pro Leu Val Ser Lys
 115 120 125
 Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
 130 135 140
 Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Thr
 145 150 155 160
 Val Glu Asp Leu Gln Arg Ile Leu Lys Val Ala Glu Val Lys Pro Gln
 165 170 175
 Val Asn Gln Ile Glu Phe Ser Pro Phe Leu Gln Asn Gln Thr Pro Gly
 180 185 190
 Ile Cys Lys Phe Cys Gln Glu His Asp Ile Leu Val Glu Ala Tyr Ser
 195 200 205
 Pro Leu Gly Pro Leu Arg Lys Lys Thr Ala Gln Asp Asp Ser Gln Pro
 210 215 220
 Phe Phe Glu Tyr Val Lys Glu Leu Ser Glu Lys Tyr Asn Lys Thr Glu
 225 230 235 240
 Ala Gln Ile Ile Leu Arg Trp Val Thr Lys Arg Gly Val Leu Pro Val
 245 250 255
 Thr Thr Ser Ser Lys Pro Gln Arg Ile Ser Asp Ala Gln Asn Leu Phe
 260 265 270
 Ser Phe Asp Leu Thr Ala Glu Glu Val Asp Lys Ile Thr Glu Leu Gly
 275 280 285
 Leu Glu His Glu Pro Leu Arg Leu Trp Trp Asn Lys Leu Tyr Gly Lys
 290 295 300
 Tyr Asn Tyr Ala Ala Gln Lys Val
 305 310

<210> 363
 <211> 942
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 363
 atgtcttttc accaagaatt tttcacgctg aacaacggca ataaaatccc ggcgattgcc 60
 atcatcggca ctggtacagc gtggtataaa cccgaagaaa ctgacgcgac cttctccaat 120

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agtcctggttg aacaattagt gtatgcgttg aaactgccgg ggattatcca catcgacgcc 180
gcggagtggt atcgcaccta cccggaagtg ggtaaagcac tgtccctgac cgaaaagcct 240
cgtaacgcga tttttatcac ggataaatat tctccgcaga ttaaaatgag cgactccoct 300
gcggacggtc tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
attcatcccc cgttagtttc gaaggaagtg aatggcttaa gcttagaaga ggcttgga 420
gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggttc caatttcaca 480
gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
gagttctctc cgttcctgca aaaccaaaca ccaggcattt gcaaattctg tcaggagcac 600
gatatcctgg tggaagcata ttctccgcta ggcccgtgc ggaagaaaac cgcgcaggat 660
gacagccaac cattttttga gtacgtcaaa gaattgagcg aaaaatacaa taaaaccgag 720
gcccagatca tcctgcgctg ggtcactaaa cgcggtgtgc tgccagttac caoctttca 780
aagcctcagc gcattagcga tgctcagaac ctgttttcct tcgacctgac agcggagag 840
gttgataaaa tcacggagct gggctctgaa catgaaccgc tcgcctgtg gtggaataaa 900
ttgtatggca aatataacta cgcgccag aaagtataat ga 942

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<210> 364

<211> 313

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 364

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Met Ser Phe His Gln Glu Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
1          5          10          15
Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Ala Trp Tyr Lys Pro Glu
          20          25          30
Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Leu Val Tyr
          35          40          45
Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Trp Tyr
          50          55          60
Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
65          70          75          80
Arg Asn Ala Ile Phe Ile Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
          85          90          95
Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
          100          105          110
Thr Asp Tyr Val Asp Leu Tyr Leu Ile His Ser Pro Leu Val Ser Lys
          115          120          125
Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
          130          135          140
Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Thr
145          150          155          160
Val Glu Asp Leu Gln Arg Ile Leu Lys Val Ala Glu Val Lys Pro Gln
          165          170          175
Val Asn Gln Ile Glu Phe Ser Pro Phe Leu Gln Asn Gln Thr Pro Gly
          180          185          190
Ile Cys Lys Phe Cys Gln Glu His Asp Ile Leu Val Glu Ala Tyr Ser
          195          200          205
Pro Leu Gly Pro Leu Arg Lys Lys Thr Ala Gln Asp Asp Ser Gln Pro
          210          215          220
Phe Phe Glu Tyr Val Lys Glu Leu Ser Glu Lys Tyr Asn Lys Thr Glu
225          230          235          240
Ala Gln Ile Ile Leu Arg Trp Val Thr Lys Arg Gly Val Leu Pro Val
          245          250          255
Thr Thr Ser Ser Lys Pro Gln Arg Ile Ser Asp Ala Gln Asn Leu Phe
          260          265          270
Ser Phe Asp Leu Thr Ala Glu Glu Val Asp Lys Ile Thr Glu Leu Gly
          275          280          285

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Leu Glu His Glu Pro Leu Arg Leu Trp Trp Asn Lys Leu Tyr Gly Lys
 290 295 300
 Tyr Asn Tyr Ala Ala Gln Lys Val
 305 310

<210> 365
 <211> 942
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 365
 atgtcttttt accaagaatt tttcacgctg aacaacggca ataaaatccc ggcgattgcc 60
 atcatcgga ctggtacagc gtggtataaa cccgaagaaa ctgacgcgac cttctccaat 120
 agtctggttg aacaattagt gtatgcgttg aaactgccgg ggattatcca catcgacgcc 180
 gcggagtgg atcgcaccta cccggaagtg ggtaaagcac tgtccctgac cgaaaagcct 240
 cgtaacgcga tttttatcac ggataaatat tctccgcaga ttaaatgag cgactccct 300
 gcggacggto tggatttagc attgaagaaa atgggtacag attatgttga tttatatctg 360
 attcattccc cgtagtttc gaaggaagtg aatggcttaa gcttagaaga ggcttgga 420
 gatatggagc agttatacaa aagtggtaaa gctaaaaaca tcgggggttc caatttcaca 480
 gtggaagacc tgcaacgtat cctgaaagtc gctgaagtta aacctcaggt caaccagatt 540
 gagttctctc cgttcctgca aaaccaaaca ccaggcattt gcaaattctg tcaggagcac 600
 gatatcctgg tggaagcata ttctccgcta ggcccgtgc ggaagaaaac cgcgcaggat 660
 gacagccaac cattttttga gtacgtcaaa gaattgagcg aaaaatacaa taaaaccgag 720
 gccagatca tctgcgctg ggtcactaaa cgcggtgtgc tgccagttac cactcttca 780
 aagcctcagc gcattagcga tgctcagaac ctgttttctc tcgacctgac agcggaagag 840
 gttgataaaa tcacggagct ggtcttgaa catgaaccgc tgcgcctgtg gtggaataaa 900
 cagtatggca aatataacta cgccgccag aaagtataat ga 942

<210> 366
 <211> 313
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 366
 Met Ser Phe His Gln Glu Phe Phe Thr Leu Asn Asn Gly Asn Lys Ile
 1 5 10 15
 Pro Ala Ile Ala Ile Ile Gly Thr Gly Thr Ala Trp Tyr Lys Pro Glu
 20 25 30
 Glu Thr Asp Ala Thr Phe Ser Asn Ser Leu Val Glu Gln Leu Val Tyr
 35 40 45
 Ala Leu Lys Leu Pro Gly Ile Ile His Ile Asp Ala Ala Glu Trp Tyr
 50 55 60
 Arg Thr Tyr Pro Glu Val Gly Lys Ala Leu Ser Leu Thr Glu Lys Pro
 65 70 75 80
 Arg Asn Ala Ile Phe Ile Thr Asp Lys Tyr Ser Pro Gln Ile Lys Met
 85 90 95
 Ser Asp Ser Pro Ala Asp Gly Leu Asp Leu Ala Leu Lys Lys Met Gly
 100 105 110
 Thr Asp Tyr Val Asp Leu Tyr Leu Ile His Ser Pro Leu Val Ser Lys
 115 120 125
 Glu Val Asn Gly Leu Ser Leu Glu Glu Ala Trp Lys Asp Met Glu Gln
 130 135 140
 Leu Tyr Lys Ser Gly Lys Ala Lys Asn Ile Gly Val Ser Asn Phe Thr

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