Modified Cpn10 and PRR signalling

Field of the Invention

The present invention relates to modified chaperonin 10 polypeptides, and to nucleic acids encoding the same. The present invention further relates to mutants of chaperonin 10 and to compositions comprising such polypeptides.

Background

Mammalian chaperonin 10 (Cpn10), also known as heat shock protein 10 (Hsp10) and early pregnancy factor (EPF), is typically characterised as a mitochondrial 'molecular chaperone' protein involved in protein folding together with chaperonin 60 (Cpn60), also known as heat shock protein 60 (Hsp60). Cpn10 and Cpn60 are homologues of the bacterial proteins GroES and GroEL respectively. GroES and Cpn10 each oligomerise into seven member rings that bind as a lid onto a barrel-like structure comprising fourteen GroEL or seven Cpn60 molecules respectively, which tether denatured proteins to the complex (Bukau and Horwich, 1998, *Cell* **92**:351-366; Hartl and Hayer-Hartl, 2002, *Science* **295**:1852-1858).

Cpn10 proteins are highly conserved across species. Human Cpn10 is 100% identical to bovine, canine, ovine and porcine Cpn10 and differs from rat Cpn10 at only a single amino acid position. Human Cpn10 shares 38% sequence identity (60% similarity) with GroES from *Escherichia coli*. Cpn10/GroES proteins are dome shaped heptameric rings wherein each monomer is comprised of essentially three different structural regions, a core anti-parallel β-barrel region flanked by a "roof" β-hairpin loop region and a "mobile loop" region. The anti-parallel β-barrel region of each monomer forms the core of a dome and when assembled in the heptamer the β-hairpin loops of each monomer form the roof of the dome. In each monomer, the mobile loop region is at the opposite end of the β-barrel to the roof loops. A section of the anti-parallel β-barrel region forms an inward facing lower rim region of the cavity. This lower rim region contains a number of phylogenetically conserved amino acids including a Tyrosine at position 75 (Y75).

In addition to its intracellular role as a molecular chaperone, Cpn10 is also frequently found at the cell surface (see Belles *et al.*, 1999, *Infect Immun* **67**:4191-4200) and in the extracellular fluid (see Shin *et al.*, 2003, *J Biol Chem* **278**:7607-7616) and is increasingly being recognised as a regulator of the immune response with potential in the treatment of inflammatory disorders. Accordingly, the efficacy and safety of Cpn10 has recently been established in the treatment of

human patients with rheumatoid arthritis (Vanags et al. *Lancet* 2006, 368: 855–863) and psoriasis (Williams et al. Arch. Dermatol. 2008, 144: 683-685).

However the sites within the Cpn10 molecule responsible for mediating this immunomodulatory activity have remained elusive. The present invention relates to the discovery that modification of Cpn10 affects the immunomodulatory activity of Cpn10, in particular its role in binding ligands of pattern recognition receptors (PRRs) such as Toll-like Receptors (TLR), Nucleotide-binding domain LRR-containing family (NLR), RIG-I-like receptors (RLR), DNA-dependent activators of IRF (DAI), C-type Lectin receptors (CLR) or a member of the IFI20X/IFI16 family (e.g. Ifi16, Aim2, MNDA and IFIX).

Summary

According to a first aspect, there is provided an isolated chaperonin 10 polypeptide possessing an increased affinity for a pattern recognition receptor ligand compared to Ala-chaperonin 10 polypeptide.

According to one embodiment, there is provided an isolated Cpn10 polypeptide possessing an increased affinity for a nucleic acid-based PRR ligand compared to Ala-Cpn10 polypeptide (SEQ ID No: 3).

The PRR may be a Toll-like Receptor (TLR), Nucleotide-binding domain LRR-containing family (NLR), RIG-I-like receptor (RLR), DNA-dependent activator of IRF (DAI), C-type Lectin receptor (CLR) or a member of the IFI20X/IFI16 family (e.g. Ifi16, Aim2, MNDA and IFIX)

The TLR may be selected from the group comprising of at least one of TLR3, TLR7, TLR8 or TLR9. In one embodiment the TLR may be TLR9.

The ligand may be an agonist or antagonist. In one embodiment, said polypeptide possesses a greater net positive charge compared to the Ala-Cpn10 polypeptide.

The isolated polypeptide may further comprise an amino acid insertion of glycine (G) at the N terminus compared to wild-type Cpn10 polypeptide. The polypeptide may be naturally-derived, recombinantly produced or synthetically produced. The Cpn10 may be of eukaryotic origin. The polypeptide may be of mammalian origin. The polypeptide may be human Cpn10.

In another embodiment, the isolated polypeptide possesses at least one mutation of the Ala-Cpn10 molecule. The mutation may be an amino acid substitution, addition or deletion or a combination thereof. The substitution may be the replacement of one or more amino acid residues with one or more positively charged residues. In another embodiment, one or more negatively charged residues may be replaced with a neutral or positively charged residue. The mutational addition may be the inclusion of one or more positively charges residues. The mutational deletion may be the removal of one or more negatively charged residues.

In another embodiment, a neutral residue may be replaced with a positively charged residue. The positively charged residue may be arginine (R), lysine (K) or histidine (H). The neutral residue

may be asparagine (N), glutamine (Q), serine (S), threonine (T), glycine (G), alanine (A), valine (V), leucine (L), isoleucine (I), proline (P), phenylalanine (F), tyrosine (Y), tryptophan (W), cysteine (C), methionine (M) or H . Note, Histidine has a pKa ~6.5, therefore it will be ~11% ionised at pH7.4 (eg extracellular milieu) and ~76% ionised at pH6.0 (eg endo-lysosomal compartments containing TLR3, TLR7, TLR8 and TLR9).

In another embodiment, the at least one mutation is located in the N-terminus, β-barrel, mobile loop, roof loop, C-terminus, or any of the three connective loops of the wild-type Cpn10 molecule or any combination thereof.

In yet another embodiment, the polypeptide comprises a mutation at an amino acid position selected from the group consisting of position 1 to 7, 9, 12 to 14, 16, 18 to 42, 44, 46, 50, 52 to 63, 65 to 69, 73 to 79, 81, 83 to 89, 91 to 94, 96, 98, 100 and 101 of the wild-type Cpn10 molecule or any combination thereof.

In a further embodiment, said polypeptide comprises a mutation selected from the group consisting of A1(K, R or H), G2(K, R or H), Q3(K, R or H), A4(K, R or H), F5(K, R or H), R6(K or H), K7(R or H), L9(K, R or H), F12(K, R or H), D13(K, R, H, N, Q, G, A, V, L, I, P, F, Y, W, C, M, S or T), R14 (K or H), L16(K, R or H), E18(K, R, H, N, Q, G, A, V, L, I, P, F, Y, W, C, M, S or T), R19(K or H), S20(K, R or H), A21(K, R or H), A22 (K, R or H), E23(K, R, H, N, Q, G, A, V, L, I, P, F, Y, W, C, M, S or T), T24(K, R or H), V25(K, R or H), T26(K, R or H), R27(K or H), G28(K, R or H), G29(K, R or H), I30(K, R or H), M31(K, R or H), L32(K, R or H), P33(K, R or H), E34(K, R, H, N, Q, G, A, V, L, I, P, F, Y, W, C, M, S or T), K35(R or H), S36(K, R or H), Q37(K, R or H), G38(K, R or H), K39(K , R or H), V40(K, R or H), L41(K, R or H), Q42(K, R or H), T44(K, R or H), V46(K, R or H), S50(K, R or H), S52(K, R or H), K53(R or H), G54(K, R or H), K55(R or H), G56(K, R or H), G57(, K, R or H), E58(K, R, H, N, Q, G, A, V, L, I, P, F, Y, W, C, M, S or T), I59(K, R or H), Q60(K, R or H), P61(K, R or H), V62(K, R or H), S63(K, R or H), K65(R or H), V66(K, R or H), G67(K, R or H), D68(K, R, H, N, Q, G, A, V, L, I, P, F, Y, W, C, M, S or T), K69(R or H), P73(K, R or H), E74(K, R, H, N, Q, G, A, V, L, I, P, F, Y, W, C, M, S or T), Y75(E, GK, K, R or H), G76(K, R or H), G77(K, R or H), T78(K, R or H), K79(R or H), V81(K, R or H), D83(K, R, H, N, Q, G, A, V, L, I, P, F, Y, W, C, M, S or T),D84(K, R, H, N, Q, G, A, V, L, I, P, F, Y, W, C, M, S or T), K85(K , R or H), D86(K, R, H, N, Q, G, A, V, L, I, P, F, Y, W, C, M, S or T), Y87(K, R or H), F88(K, R or H), L89(K, R or H), R91(K or H), D92(K, R, H, N, Q, G, A, V, L, I, P, F, Y, W, C, M, S or T), G93(K, R or H), D94(K, R, H, N, Q, G, A, V, L, I, P, F, Y, W, C, M, S or T), L96(K, R or H), K98(R or H), V100(K, R or H), D101(K, R, H, N, Q, G, A, V, L, I, P, F, Y, W, C, M, S or T), MH-Cpn10, MR-Cpn10, MK-Cpn10, MKK-Cpn10, MKKK-Cpn10, Ala-Cpn10-K21, Ala-Cpn10-KK21, Ala-Cpn10-K39, Ala-Cpn10-KK39, Ala-Cpn10-K57, Ala-Cpn10-KK57, Ala-Cpn10-K76, Ala-Cpn10-KK76, Ala-Cpn10-K85, Ala-Cpn10-KK85, Ala-Cpn10-

K102, Ala-Cpn10-KK102, deltaD13, deltaE18, deltaE23, deltaE34, deltaE58, deltaE68, deltaE74, deltaD83, deltaD84, deltaD86, deltaD92, deltaD94 and deltaD101 or a combination thereof.

In another embodiment, the mutation is located in the N-terminus as defined in Table 2. The mutation may be an insertion. For example, the insertion at the N-terminus is selected from the group consisting of MH, MK, MKK, MKKK and MR as set forth in SEQ ID Nos:307, 313, 316, 319 and 310 respectively.

In addition, the Cpn10 polypeptide may comprise the substitution Q3K or K7R as set forth in SEQ ID Nos.37 or 10 respectively.

In yet another embodiment, the mutation is located in the mobile loop as defined in Table 2. The mutation may be a deletion. The deletion may be E23 or E34 as set forth in SEQ ID Nos: 199 and 202. The mutation may be an insertion. The insertion may be K21 or KK21 as set forth in SEQ ID Nos:322 and 325. The mutation may be a substitution. For example, the substitution is selected from the group consisting of A22K, E23Q, T24K, K27R, G29K, M31K, E34K, E34Q, Q37K as set forth in SEQ ID Nos: 16, 64, 67, 70, 73,76, 79, 265 and 268.

There is also provided herein an isolated Cpn10 oligomer comprising seven Cpn10 monomers wherein two or more monomers are covalently linked to each other. The covalent bond is formed between the C-terminus of one monomer and the N-terminus of an adjacent monomer within the Cpn10 heptamer. The C- and N-termini, used to form a covalent bond, may be lengthed by the addition of one or more amino acids (eg Ala-Cpn10 or Gly-Cpn10), or shortened by the removal of one or more amino acids. For example, the isolated Cpn10 polypeptide is Covalent Cpn10 set forth in SEQ ID NO: 355.

In a further embodiment, each monomer within the covalently bound heptamer may contain one or more mutations selected from the group consisting of A1(K, R or H), G2(K, R or H), Q3(K, R or H), A4(K, R or H), F5(K, R or H), R6(K or H), K7(R or H), L9(K, R or H), F12(K, R or H), D13(K, R, H, N, Q, G, A, V, L, I, P, F, Y, W, C, M, S or T), R14 (K or H),L16(K, R or H), E18(K, R, H, N, Q, G, A, V, L, I, P, F, Y, W, C, M, S or T), R19(K or H), S20(K, R or H), A21(K, R or H), A22 (K, R or H), E23(K, R, H, N, Q, G, A, V, L, I, P, F, Y, W, C, M, S or T), T24(K, R or H), V25(K, R or H), T26(K, R or H), R27(K or H), G28(K, R or H), G29(K, R or H), I30(K, R or H), M31(K, R or H), L32(K, R or H), P33(K, R or H), E34(K, R, H, N, Q, G, A, V, L, I, P, F, Y, W, C, M, S or T), K35(R or H), S36(K, R or H), Q37(K, R or H), G38(K, R or H), K39(K, R or H), V40(K, R or H), L41(K, R or H), Q42(K, R or H), T44(K, R or H), V46(K, R or H), S50(K, R or H), S52(K, R or H), K53(R or H), G54(K, R or H), K55(R or H), G56(K, R or H), G57(K, R or H), E58(K, R, H, N, Q, G, A, V, L, I, P, F, Y, W, C, M, S or T), I59(K, R or H), Q60(K, R or H), P61(K, R or H), V62(K, R or H), S63(K, R or H), K65(R or H), V66(K, R or H), G67(K, R or H), D68(K, R, H, N, Q, G, A, V, L, I, P, F, Y, W, C, M,

S or T), K69(R or H), P73(K, R or H), E74(K, R, H, N, Q, G, A, V, L, I, P, F, Y, W, C, M, S or T), Y75(E, GK, K, R or H), G76(K, R or H), G77(K, R or H), T78(K, R or H), K79(R or H), V81(K, R or H), D83(K, R, H, N, Q, G, A, V, L, I, P, F, Y, W, C, M, S or T),D84(K, R, H, N, Q, G, A, V, L, I, P, F, Y, W, C, M, S or T), K85(K, R or H), D86(K, R, H, N, Q, G, A, V, L, I, P, F, Y, W, C, M, S or T), Y87(K, R or H), F88(K, R or H), L89(K, R or H), R91(K or H), D92(K, R, H, N, Q, G, A, V, L, I, P, F, Y, W, C, M, S or T), G93(K, R or H), D94(K, R, H, N, Q, G, A, V, L, I, P, F, Y, W, C, M, S or T), L96(K, R or H), K98(R or H), V100(K, R or H), D101(K, R, H, N, Q, G, A, V, L, I, P, F, Y, W, C, M, S or T), MH-Cpn10, MR-Cpn10, MK-Cpn10, MKK-Cpn10, MKKK-Cpn10, Ala-Cpn10-K21, Ala-Cpn10-KK21, Ala-Cpn10-K39, Ala-Cpn10-KK39, Ala-Cpn10-K57, Ala-Cpn10-KK57, Ala-Cpn10-K76, Ala-Cpn10-KK76, Ala-Cpn10-K85, Ala-Cpn10-KK85, Ala-Cpn10-K102, Ala-Cpn10-KK102, deltaD13, deltaE18, deltaE23, deltaE34, deltaE58, deltaE68, deltaE74, deltaD83, deltaD84, deltaD86, deltaD92, deltaD94 and deltaD101 or a combination thereof. In another embodiment, the mutation is located in the β-barrel as defined in Table 2. At least one mutation may be a substitution. The substitution may be L9K, F12K, D13K, D13N, E18A, E18K, E18M, E18Q, E18S, E18R, R19K, S20K, L41K, Q42K, T44K, S50K, S50R, V66K, D68K, D68N, K69R, P73K, G77K, T78K, K85R, D86K, D86N, D86R, Y87K, F88K, L89K, D92K, D92N, G93K, D94A, D94K, D94M, D94N, D94R, D94S, L96K, K98R or V100K as set forth in SEQ ID Nos13, 25, 28, 31, 46, 49, 52, 55, 58, 61, 58, 61, 85, 88, 91, 94, 97, 118, 121, 124, 145, 148, 160, 163, 166, 169, 172, 175, 178, 181, 184, 187, 190, 217, 244, 250, 253, 256, 259, 262, 274, 286, 289, 292, 295, 298, 301.

In another embodiment, the mutation is located in the roof loop as defined in Table 2. The mutation may be an insertion. The insertion may be K57 or KK57 as set forth in SEQ ID Nos:334 or 337 The mutation may be a deletion. The deletion may be E58 as set forth in SEQ ID Nos:205. The mutation may be a substitution, for example, the isolated Cpn10 polypeptide is X-Cpn10-K53E, Ala-Cpn10-S52K, G54K, K55R, G56K, E58K, E58Q, Q60K, P61K as set forth in SEQ. ID Nos: 6, 22, 100, 103, 106, 109, 112, 115, 271. In another embodiment, the isolated Cpn10 polypeptide comprises one or more amino acid substitutions in the roof loop at amino acid residue positions 53 and/or 55 of the amino acid sequence of the wild-type Cpn10 polypeptide. For example, the isolated Cpn10 polypeptide may be Ala-Cpn10-K53M,K55M as encoded by the sequence set forth in SEQ. ID No: 8.

In another embodiment, the mutation is located in the connective loop L1 as defined in Table 2. The mutation may be an insertion. The insertion may be K39 or KK39 as set forth in SEQ ID Nos:328 or 331.The mutation may be a substitution. For example, the substitution is selected from the group consisting of K39R or V40K as set forth in SEQ ID Nos: 19 or 82. In yet another embodiment, the mutation is located in connective loop 2 (lower rim region) as defined in Table 2.

The mutation may be an insertion. The insertion may be K76 as set forth in SEQ ID Nos:340. The mutation may be a substitution. The substitution may be X-Cpn10-Y75K as seth forth in SEQ ID No: 130 or Ala-Cpn10-E74K, Y75H, Y75K, Y75R, Y75GK or G76K as set forth in SEQ ID Nos:127, 133, 136, 139, 142, 238 or 277. The mutation may be a deletion. The deletion may be E74 as set forth in SEQ ID Nos:208.

In a further embodiment, the mutation is located in connective loop 3 as defined in Table 2. The mutation may be an insertion. The insertion may be K85 or KK85 as set forth in SEQ ID Nos:343 or 346. The mutation may be a substitution. The substitution may be V81K, D83K, D83N, D84K or D84N as set forth in SEQ ID Nos:151, 154, 157, 280 or 283.. The mutation may be a deletion. The deletion may be D84 as set forth in SEQ ID No:211.

In another embodiment, the mutation is located in the C-terminus as defined in Table 2. The mutation may be an insertion. The insertion may be K102 or KK102 as set forth in SEQ ID Nos:349 or 352. The mutation may be a substitution. The substitution may D101K, D101N or D101R as set forth in SEQ ID Nos:193, 196 or 304.

In another embodiment, the polypeptide may comprise at least two mutations at any position within one or more regions of Cpn10, wherein the regions consist of the N-terminus, β-barrel, mobile loop, roof loop, C-terminus, or any of the three connective loops of the wild-type Cpn10 molecule as defined in Table 2. For example, the Cpn10 polypeptide may comprise Ala-Cpn10-F12K,D92K, E18K,D101K; E34Q,Y75K; Q42K,D101K; T44K,D101K; S50K,D101K; Q60K,T78K; E74K,Y75E;, Y75GK; Y75G,G76K; Y75K,D94K; Y75K,D94N. The polypeptides may comprise amino acid sequences as set forth in SEQ ID Nos. 214, 217, 220, 223, 226, 229, 232, 235, 238, 241, 244, 247.

According to a second aspect, there is provided an isolated nucleic acid encoding a polypeptide as defined above.

In one embodiment, the isolated nucleic acid may comprise a nucleotide sequence selected from the group consisting of SEQ ID Nos. 7, 9, 11, 12, 14, 15, 17, 18, 20, 21, 23, 24, 26, 27, 29, 30, 32, 33, 35, 36, 38, 39, 41, 42, 44, 45, 47, 48, 50, 51, 53, 54, 56, 57, 59, 60, 62, 63, 65, 66, 68, 69, 71, 72, 74, 75, 77, 78, 80, 81, 83, 84, 86, 87, 89, 90, 92, 93, 95, 96, 98, 99, 101, 102, 104, 105, 107, 108, 110, 111, 113, 114, 116, 117, 119, 120, 122, 123, 125, 126, 128, 129, 131, 132, 134, 135, 137, 138, 140, 141, 143, 144, 146, 147, 149, 150, 152, 153, 155, 156, 158, 159, 161, 162, 164, 165, 167, 168, 170, 171, 173, 174, 176, 177, 179, 180, 182, 183, 185, 186, 188, 189, 191, 192, 194, 195, 197, 198, 200, 201, 203, 204, 206, 207, 209, 210, 212, 213, 215, 216, 218, 219, 221, 222, 224, 225, 227, 228, 230, 231, 233, 234, 236, 237, 239, 240, 242, 243, 245, 246, 248, 249, 251, 252, 254, 255, 257, 258, 260, 261, 263, 264, 266, 267, 269, 270, 272, 273, 275, 276,

278, 279, 281, 282, 284, 285 287, 288, 290, 291, 293, 294, 296, 297, 299, 300, 302, 303, 305, 306, 308, 309, 311, 312, 314, 315, 317, 318, 320, 321, 323, 324, 326, 327, 329, 330, 332, 333, 335, 336, 338, 339, 341, 342, 344, 345, 347, 348, 350, 351, 353, 354 or 356.

According to a third aspect, there is provided an expression construct comprising a nucleic acid according to the second aspect, wherein said construct is operably-linked to one or more regulatory sequences.

The nucleic acid may be a codon optimised Cpn10 nucleic acid.

The codon optimised nucleic acid sequence may have one or more nucleotide substitutions that increase the utilisation of transfer RNA pools, exploit more efficient stop codons, remove RNA secondary structures and/or destabilising elements.

According to a fourth aspect, there is provided a host cell expressing a polypeptide as defined above, or comprising a nucleic acid of the second aspect or an expression construct of the third aspect.

According to a fifth aspect, there is provided an antibody that selectively binds to a polypeptide as defined above.

According to one embodiment, there is provided a proinflammatory nucleic acid or immunosuppressive nucleic acid in complex with a polypeptide of the first aspect.

According to one embodiment, there is provided a pharmaceutical composition comprising a polypeptide of the first aspect, a nucleic acid of the second aspect or an

expression construct of the third aspect or an antibody of the fifth aspect.

According to a sixth aspect, there is provided a pharmaceutical composition comprising a polypeptide as defined above either alone or in combination with at least one nucleic acid based pattern recognition receptor ligand, a nucleic acid of the second aspect, an expression construct of the third aspect or an antibody of the fifth aspect or any combination thereof.

According to an embodiment there is provided a method of treating

a subject, including the step of administering to said subject a therapeutically effective amount of a Cpn10 polypeptide of the first aspect or a nucleic acid of the second aspect.

The treatment may modulate the immune response in the subject. The immune response may be modulated via regulation of PRR signalling.

According to another embodiment, there is provided a method for treating or

preventing a disease, disorder or condition in a subject, the method comprising administering to the subject an effective amount of a Cpn10 polypeptide of the first aspect or a nucleic acid of the second aspect.

The disease, disorder or condition may be selected from acute or chronic inflammatory diseases such as, insulin dependent diabetes mellitus, systemic lupus erythematosis, Sjorgren's disease, Graves disease, multiple sclerosis, rheumatoid arthritis, chronic fatigue syndrome, Alzheimer's disease, asthma, allergy, GVHD, artherosclerosis, inflammatory pain, psoriasis, HIV, Chronic immune activation, chronic myositis, scleroderma; or cancers such as, non-small cell lung

carcinoma, renal cell carcinoma, melanoma, non-Hodgkin's lymphoma, colorectal cancer, basal cell carcinoma; or an infectious disease. The infectious disease may be the result of a bacterial, viral or fungal infection.

In one embodiment, chronic immune activation is associated with leakage of bacterial and/or viral products from the gastrointestinal tract into the circulatory system. For example, leakage can occur from the oral cavity, gut or small intestine. Leakage of bacterial or viral products can be caused by an infection or disease such as bacterial infections, viral infections, inflammatory bowel disease and gum disease. An example of viral infection is a HIV or Hepatitis C infection. The bacterial products can comprise LPS or nucleic acids. The viral products can comprise nucleic acids.

In a further embodiment, chronic immune activation involves immunomodulation of TLR signalling through LPS or nucleic acid binding to TLRs. LPS binds to TLR4 whilst nucleic acids can bind to TLR3, 7, 8 or 9.

In a seventh aspect, there is provided the use of an effective amount of a polypeptide as defined above either alone or in combination with at least one nucleic acid based pattern recognition receptor ligand, or a nucleic acid of the second aspect or any combination thereof in the manufacture of a medicament for modulating immune response in the subject, wherein said immune response is modulated via regulation of pattern recognition receptor signalling.

In an eighth aspect, there is provided the use of an effective amount of a polypeptide as defined above either alone or in combination with at least one nucleic acid based pattern recognition receptor ligand, or a nucleic acid of the second aspect or any combination thereof in the manufacture of a medicament for treating or preventing a disease, disorder or condition in a subject, wherein said disease, disorder or condition is selected from: acute or chronic inflammatory diseases such as, insulin dependent diabetes mellitus, systemic lupus erythematosus, Sjogren's disease, Graves disease, multiple sclerosis, rheumatoid arthritis, chronic fatigue syndrome, Alzheimer's disease, asthma, allergy, GVHD1 atherosclerosis, inflammatory pain, psoriasis, HIV, Chronic immune activation, chronic myositis, scleroderma; or cancers such as, non-small cell lung carcinoma, renal cell carcinoma, melanoma, non-Hodgkin's lymphoma, colorectal cancer, basal cell carcinoma; or an infectious disease that may be the result of a bacterial, viral or fungal infection.

In a ninth aspect, there is provided the use of an effective amount of polypeptide as defined above or a nucleic acid of the second aspect or any combination thereof in the manufacture of a medicament for modulating pattern recognition receptor signalling in a subject, or in at least one cell, tissue or organ thereof.

In a tenth aspect, there is provided the use of an effective amount of a polypeptide as defined above or a nucleic acid of the second aspect or any combination thereof in the manufacture of a medicament for modulating the production and/or secretion of one or more immunomodulators in a subject, or at least one cell, tissue or organ thereof.

In an eleventh aspect, there is provided the use of an effective amount of a polypeptide as defined above or a nucleic acid of the second aspect or any combination thereof in the manufacture of a medicament for inhibiting the production and/or secretion of one or more immunomodulators in a subject, or at least one cell, tissue or organ thereof.

According to one embodiment, there is provided a method for modulating PRR signalling in a subject, or in at least one cell, tissue or organ thereof, the method comprising administering a therapeutically effective amount of a Cpn10 polypeptide of the first aspect or a nucleic acid of the second aspect.

According to another embodiment, there is provided a method for modulating the production and/or secretion of one or more immunomodulators in a subject, or at least one cell, tissue or organ thereof, the method comprising administering a therapeutically effective amount of a Cpn10 polypeptide of the first aspect or a nucleic acid of the second aspect.

The polypeptide may modulate signalling from a PRR by binding a PRR ligand. The immunomodulator may be a pro-inflammatory cytokine or chemokine or an anti-inflammatory cytokine or chemokine. The cytokine or chemokine may be selected from TNF-α, IL-1, IL-6, RANTES, IL-10, IL-17, IL-23, TGF-β or a type I interferon. The type I interferon may be IFNα, IFNβ or IFNγ.

According to one embodiment, there is provided a method for inhibiting the production and/or secretion of one or more immunomodulators in a subject, or at least one cell, tissue or organ thereof, the method comprising administering an effective amount of a Cpn10 polypeptide of the first aspect or a nucleic acid of the second aspect.

The polypeptide may modulate signalling from a PRR by binding a PRR ligand. Binding of the polypeptide to a PRR ligand may have an immunomodulatory affect on the cell that posessess the PRR. The cell may be an antigen presenting cell or a T-cell or a B-cell. The antigen presenting cell may be a dendritic cell, macrophage or monocyte.

The immunomodulator may be a pro-inflammatory cytokine or chemokine or an anti-inflammatory cytokine or chemokine. The cytokine or chemokine may be selected from TNF-α, IL-1, IL-6, RANTES, IL-10, IL-17, IL-23, TGF-β or a type I interferon. The type I interferon may be IFNα, IFNβ or IFNγ.

According to one embodiment, there is provided a method of

identifying a compound that binds to a polypeptide of the first aspect, the method comprising the steps of:

(a) contacting a candidate compound with said polypeptide; and

(b) assaying for the formation of a complex between the candidate compound and said polypeptide.

According to a twelfth aspect, there is provided an in vitro method of identifying a compound that binds to a polypeptide as defined above, the method comprising the steps of: (a) contacting a candidate compound with said polypeptide; and (b) assaying for the formation of a complex between the candidate compound and said polypeptide.

The assay for the formation of a complex may be a competitive binding assay, a two-hybrid assay, gel filtration chromatography, AlphaScreen® High Throughput Screening, an electrophoretic mobility shift (gel-shift) assay and/or a plate capture assay.

The assay may be qualitative or quantitative.

According to another embodiment, there is provided a method of

screening for a compound that modulates the activity of a polypeptide of the first aspect, the method comprising the steps of:

(a) contacting said polypeptide with a candidate compound under conditions suitable to enable interaction of said candidate compound to said polypeptide; and

(b) assaying for activity of said polypeptide.

According to a thirteenth aspect, there is provided an in vitro method of screening for a compound that modulates the activity of a polypeptide as defined above, the method comprising the steps of: (a) contacting said polypeptide with a candidate compound under conditions suitable to enable interaction of said candidate compound to said polypeptide; and (b) assaying for activity of said polypeptide.

Assaying for activity of the polypeptide may comprise a step of adding a labelled substrate and measuring a change in the labelled substrate.

According to one embodiment, there is provided a method of

screening for a PRR ligand, the method comprising the steps of:

(a) contacting a polypeptide of the first aspect with a candidate PRR ligand compound under conditions suitable to enable interaction of said candidate compound to said polypeptide; and

(b) assaying for increased affinity of said compound with said polypeptide compared to Ala-Cpn10; and/or

(c) assaying for decreased or increased PRR activation in the presence of the candidate PRR ligand compound and the polypeptide of the first aspect.

According to a fourteenth aspect, there is provided an in vitro method of screening for a pattern recognition receptor ligand, the method comprising the steps of: (a) contacting a polypeptide as defined above with a candidate pattern recognition receptor ligand compound under conditions suitable to enable interaction of said candidate compound to said polypeptide; and (b) assaying for increased affinity of said compound with said polypeptide compared to wild type chaperonin 10; and/or (c) assaying for decreased or increased pattern recognition receptor activation in the presence of the candidate pattern recognition receptor ligand compound and said polypeptide.

According to a fifteenth aspect, there is provided a functional variant, derivative, homologue, analogue or fragment of the polypeptide as defined above.

The disclosure also contemplates variants, derivatives, homologues, analogues and fragments of the isolated Cpn10 polypeptides and polynucleotides according to the above aspects and embodiments.

According to the above aspects and embodiments, the Cpn10 polypeptides and polynucleotides may be derived from any animal, may be generated using recombinant DNA technologies or may be synthetically produced. Cpn10 may be a eukaryotic Cpn10. For example, Cpn10 is human Cpn10.

The wild-type Cpn10 molecule or polypeptide may be acetyl-Cpn10 or X-Cpn10 (SEQ ID No. 1).

According to the above aspects and embodiments the immunomodulatory activity of a Cpn10 polypeptide may involve generation of heptamers of the polypeptide. The heptamers may comprise a mutant or non-mutant polypeptides in any combination.

Definitions

In the context of this specification, the term "comprising" means "including principally, but not necessarily solely". Furthermore, variations of the word "comprising", such as "comprise" and "comprises", have correspondingly varied meanings.

The term "wild-type" as used herein in relation to Cpn10 molecules or polypeptides includes native or non-native forms. For example, native human Cpn10 is acetylated at its N-terminus. The present invention contemplates, within the scope of the term wild-type Cpn10, acetylated or non-acetylated (X-Cpn10) molecules as represented by SEQ ID No. 1.

The term "Ala-Cpn10" refers to human Cpn10 produced in *E. coli* wherein it is produced with an extra N-terminal Alanine residue. The sequence of Ala-Cpn10 is presented as SEQ ID No. 3.

The term "immunomodulator" means a molecular mediator which interacts with the immune system and that plays a role in the activation, inhibition, modulation, maintenance, maturation, suppression or augmentation of an immune response. The immunomodulator may be a pro-inflammatory cytokine or chemokine or an anti-inflammatory cytokine or chemokine. The cytokine or chemokine may be selected from TNF-α, IL-1, IL-6, RANTES, IL-10, IL-17, IL-23, TGF-β or a type I interferon. The type I interferon may be IFNα, IFN β or IFNγ.

The term "Pattern recognition receptors" or PRRs as used herein means several classes of germline-encoded proteins including Toll-like receptors (TLRs), Nucleotide-binding domain LRR-containing family (NLRs), RIG-I-like receptors (RLRs), DNA-dependent activators of IRF (DAIs), C-type Lectin receptors (CLRs) or a member of the IFI20X/IFI16 family (e.g. Ifi16, Aim2, MNDA and IFIX) (see for example Akira et al., Cell 2006, 124: 783-801; Latz, E. and Fitzgerald, K.A. (2008) Nat. Rev. Immunol. Vol. 8, No. 4, Poster). In general, PRRs can be divided into two groups, nucleic acid-based PRRs (that generally reside intracellularly) and cell surface PRRs (that generally

recognise hydrophobic ligands). PRRs are located on various cell types including but not limited to antigen presenting cells (e.g. dendritic cells, monocytes and macrophages),Tcells and B-cells.

The term "Toll-like receptors" or TLRs means receptors which interact with pathogens and initiate the host immune response to infection. In mammals, activation of TLRs by pathogens sets in motion an innate immune inflammatory process that prevents pathogen dissemination and, through TLRs on dendritic cells, directs the development of acquired immunity. The TLRs are encoded by a limited number of genes in the germline, 10 known in humans. These 10 receptors recognize a wide variety of pathogen-derived molecular signatures, including glycolipids such as lipopolysaccharide, proteins such as flagellin, and nucleic acids such as dsRNA. TLRs can be divided into two groups, cell surface TLRs which generally recognize hydrophobic ligands and intracellular TLRs (i.e. TLR-3, TLR-7, TLR-8 and TLR-9) which generally recognize nucleic acid based ligands.

As used herein the terms "modulating", "modulates" and variations thereof refer to increasing or decreasing the level of activity, production, secretion or functioning of a molecule in the presence of a particular modulatory molecule or agent of the invention compared to the level of activity, production, secretion or other functioning thereof in the absence of the modulatory molecule or agent. These terms do not imply quantification of the increase or decrease. The modulation may be of any magnitude sufficient to produce the desired result and may be direct or indirect.

The term "net charge" as used herein refers to the charge of a molecule. Molecules that comprise an amino acid sequence such as proteins, peptides, and polypeptides (e.g. Cpn10 polypeptide) can either be positively or negatively charged. The net charge of a polypeptide at a given pH can be calculated on the basis of the Henderson-Hasselbalch equation (Hasselbalch, K. A., 1917 *Biochemische Zeitschrift* **78**: 112–144) and known pKa values of ionisable amino acid side chains and the N- and C-termini of a polypeptide.

The term "greater net positive charge" as used herein is the increase in positive charge of the molecule over Ala-Cpn10.

The term "mobile loop" is a flexible region of the Cpn10 molecule that comprises 18 amino acid residues. The mobile loop comprises residues A21 to G38 (see Figure 1; residue numbering is based on either acetylated or non-acetylated X-Cpn10 (SEQ ID No. 1) as described herein).

The term "roof loop" is a flexible region of the Cpn10 molecule that comprises 14 amino acid residues. The roof loop comprises residues S52 to V62 (see Figure 1; residue numbering is based on either acetylated or non-acetylated X-Cpn10 (SEQ ID No. 1 as described herein).

"Beta barrel" as described herein is a region of the Cpn10 molecule that comprises five segments, namely 1st, 2nd, 3rd, 4th and 5th segments. 1st segment comprises residues F8 to S20, 2nd segment comprises L41 to G51, 3rd segment comprises S63 to P73, 4th segment comprises G77 to V80 and 5th segment comprises residues K85 to V100 (see Figure 1). Residue numbering is based X-Cpn10 (SEQ ID No. 1) as described herein.

The term "Connective loops" refer to flexible regions of the Cpn10 molecule that connect various loops of the Cpn10 molecule to the Beta barrel, such as the mobile loop and the roof loop. There are three connective loops, 1st, 2nd and 3rd. 1st connective loop comprises residues K39 to V40. 2nd connective loop comprises E74 to G76 and 3rd loop comprises residues V81 to D84 (see Figure 1). Residue numbering is based on X-Cpn10 (SEQ ID No. 1) as described herein.

The term "N-terminus" is a flexible region at the N-terminal of the Cpn10 molecule that comprises residues A1 to K7 (see Figure 1). Residue numbering is based on X-Cpn10 (SEQ ID No. 1) as described herein.

The term "C-terminus" comprises D101 of the Cpn10 molecule (see Figure 1; residue numbering is based on X-Cpn10 (SEQ ID No. 1) as described herein).

The term "amino acid" as used herein means any molecule that contains both amine and carboxyl functional groups.

The term "charged residue" as used herein means any amino acid residue with a side-chain that has the potential to carry a positive or negative charge.

The term "polypeptide" means a polymer made up of amino acids linked together by peptide bonds. The term "polypeptide" may constitute a portion of a full length protein. Further, the term "polypeptide" refers to a polypeptide that may exhibit at least one modification of its amino acid sequence, compared to a wild type Cpn10 molecule. The modification may include chemical modifications such techniques as ubiquitination, labeling (e.g., with radionuclides or various enzymes), covalent polymer attachment such as pegylation (derivatization with polyethylene glycol) and insertion or substitution by chemical synthesis of amino acids such as ornithine, which are naturally occurring in human proteins.

The term "polynucleotide" as used herein refers to a single- or double- stranded polymer of deoxyribonucleotide, ribonucleotide bases or known analogues of natural nucleotides, or mixtures thereof. The term includes reference to the specified sequence as well as to the sequence complimentary thereto, unless otherwise indicated. The terms "polynucleotide" and "nucleic acid" are used interchangeably herein.

The term "CpG" as used herein refers to unmethylated sites within regions of DNA where a cytosine nucleotide occurs next to a guanine nucleotide in linear sequence of bases along its length and is separated by a phosphate, which links the two nucleosides together in DNA. "CpG" is used to distinguish the above meaning from a cytosine base paired to a guanine. Three distinct types of CpG oligodeoxynucleotides have been identified that differ in their capacity to stimulate antigen-presenting cells: CpG-A (human ODN-2216) induces high amounts of interferon-α (IFN-α) and IFN-β in plasmacytoid dendritic cells (PDCs); CpG-B (human ODN-2006 and mouse ODN-1826) induces PDC maturation and is a potent activator of B cells but stimulates only small amounts of IFN-α and IFN-β whereas CpG-C (human ODN-M362) induces B and NK cells and inducing IFN-α production of human peripheral blood mononuclear cells.

The term "isolated" means that the molecule in question has been removed from its natural environment or host, and associated impurities reduced or eliminated such that the molecule in question is the predominant species present (e.g., on a molar basis it is more abundant than any other individual species in the composition/sample). Typically a substantially purified fraction is a composition wherein the object species comprises at least about 30 percent of all macromolecular species present. Generally, a substantially pure composition will comprise more than about 80 to 90 percent of all macromolecular species present in the composition. Most typically, the object species is purified to essential homogeneity (contaminant species cannot be detected in the composition by conventional detection methods) wherein the composition consists essentially of a single macromolecular species.

As used herein the term "substantially" means the majority but not necessarily all, and thus in relation to a modified polypeptide "substantially" lacking a component region of a corresponding wild-type polypeptide, the modified polypeptide may retain a portion of that component region. For example, a modified polypeptide "substantially" lacking a component region of a corresponding wild-type polypeptide may retain approximately 50 percent or less of the sequence of the component region, although typically the component region is rendered structurally and/or functionally inactive by virtue of the proportion of the sequences of the region omitted.

The term "conservative amino acid substitution" as used herein refers to the replacement of one amino acid with another amino acid having similar structural and/or chemical properties. Conservative amino acid substitutions may be made on the basis of similarity in one or more of the following: polarity, charge, solubility, hydrophobicity, hydrophilicity, and/or the amphipathic nature of the residues involved. For example, nonpolar (hydrophobic) amino acids include alanine, leucine, isoleucine, valine, proline, phenylalanine, tyrosine, tryptophan, cysteine and methionine; polar

uncharged amino acids include glycine, serine, threonine, asparagine, and glutamine; polar positively charged (basic) amino acids include arginine, lysine, and histidine; and negatively charged (acidic) amino acids include aspartic acid and glutamic acid. Amino acid "Insertions" or "deletions" are preferably in the range of about 1 to 20 amino acids, more preferably 1 to 10 amino acids. The variation may be experimentally determined by systematically making insertions, deletions, or substitutions of amino acids in a polypeptide molecule using recombinant DNA techniques and assaying the resulting recombinant variants for activity.

As used herein the terms "treatment", "treating" and variations thereof, refer to any and all uses which remedy a disease state or symptoms, prevent the establishment of disease, or otherwise prevent, hinder, retard, or reverse the progression of disease or other undesirable symptoms in any way whatsoever.

As used herein the term "effective amount" includes within its meaning a non-toxic but sufficient amount of an agent or compound to provide the desired therapeutic or prophylactic effect. The exact amount required will vary from subject to subject depending on factors such as the species being treated, the age and general condition of the subject, the severity of the condition being treated, the particular agent being administered and the mode of administration and so forth. Thus, it is not possible to specify an exact "effective amount". However, for any given case, an appropriate "effective amount" may be determined by one of ordinary skill in the art using only routine experimentation.

Brief Description of the Drawings

Figure 1. A. Crystal structure of *E. coli* Cpn10 (GroES) showing various regions of Cpn10. Cpn10 is comprised of seven identical 10kDa subunits. **B.** Amino acid sequences of Cpn10 and GroES are shown. The GroES ribbon structure was created from the X-ray crystal coordinates published by Xu et al. (Nature 1997, 388: 741-750), in this structure the usually disordered mobile loops are perfectly aligned through interaction with GroEL (GroEL was omitted in the diagram).

Figure 2. Sequence alignment of human Cpn10 with Cpn10 homologs from numerous biological kingdoms. Amino acids that are different to human Cpn10 are shaded. The location of the mobile loop and the β-hairpin roof loop are indicated. Boxes (marked *a* to *e*) indicate the predicted boundaries of the 55 residue β-barrel core (Hunt *et al.*, 1997 Cell 90: 361-371). The percentage identity and similarity of the various homologs relative to human Cpn10 are shown. The SwissProt accession number of each protein is given. Calculation of sequence % identity and % similarity to human Cpn10 was performed with NCBI blast (Altschul *et al.*, 1997 Nucleic Acids Res. 25:3389-

3402), NS = no significant similarity found. Isoelectric points (pI) were calculated using the ExPASy proteomics server ProtParam Tool (www.expasy.org/tools/protparam.html).

Figure 3. SDS-PAGE stained with Coomassie brilliant blue reveals that recombinant Cpn10 proteins are >99% pure.

Figure 4. 1µg of TLR3 agonist Poly(I:C) (a synthetic dsRNA analog) was incubated with 50µg of a Cpn10 variant and the indicated salt concentration in 10mM Tris-HCl (pH7.6) for 1hr at 23°C. Samples were resolved in a 1% TAE agarose gel and stained with Ethidium Bromide . Free Cpn10 migrates towards the negative electrode (top of the gel) while free poly(I:C) migrates towards the positive electrode (bottom of the gel), complexes of Cpn10-poly(I:C) retard the movement of both molecules.

Figure 5. 1µg of human ODN-2216 class A (TLR9 agonist; Invivogen) was incubated with 50µg of Cpn10 in 10mM Tris-HCl (pH7.6) and the indicated salt concentration for 15min at 23°C. Samples were resolved in a 1% TAE agarose gel and stained with ethidium bromide. Free Cpn10 migrates towards the negative electrode (top of the gel) while free CpG-ODNs migrate towards the positive electrode (bottom of the gel), complexes of Cpn10-CpG-ODNs retard the movement of both molecules.

Figure 6. 0.5µg of E.coli K12 ssRNA (Invivogen Cat# tlrl-ecrna) (TLR7/8 agonist) was incubated with 50µg of a Cpn10 variant, in 10mM Tris-HCl (pH 7.6) and the indicated salt concentrations (0, 150 and 500mM NaCl) for 30mins at 23°C. Samples were resolved in a 1% TAE agarose gel and stained with Ethidium Bromide. Free Cpn10 migrates towards the negative electrode (top of the gel) while free ssRNA migrate towards the positive electrode (bottom of the gel), complexes of Cpn10- ssRNA retard the movement of both molecules.

Figure 7. Quantitative analysis of Cpn10 binding to CpG oligonucleotides (ODNs). Ala-Cpn10 and Cpn10 mutants were formulated at 1µg/µl in formulation buffer pH7.2 (Invitrogen) and 50µg was adsorbed to triplicate wells of a 96 well plate 16 hr at 4°C. Following the decanting of non-bound protein, the plate was blocked with 1% BSA and 5% sucrose in PBS pH7.2 for 2hr at 23°C. 50µl of 3'-biotin labeled human ODN-2216 class-A, human ODN-2006 class-B, or human ODN-M362 class-C (TLR9 agonists) (Proligo/Sigma) formulated at 0.02 µg/µl in PBS pH 7.2 was added to each well and incubated for 2hr at 23°C. Unbound ligand was removed with five PBS (pH7.2) + 0.05% Tween 20 washes. Bound CpG-ODNs were analysed with a Streptavidin-HRP and TMB detection system at A450nm. The results are the average of three replicates and are normalized to the level of binding of Ala-Cpn10 to each CpG.

Figure 8. Cpn10 modulates CpG-B ODN-induced NFκB activity. RAW264.7 (mouse macrophage) cells were transfected with pNifty NFκB-luciferase reporter plasmid (InvivoGen) using

Genejuice according to the manufacturers instructions (Novogen). 24 hours later cells were trypsinised, counted and 2.5 x 10^5 cells were plated in 1ml of media into each well of a 24 well plate and left to adhere overnight. 100µg of a Cpn10 construct or Formulation buffer control was mixed with 4 µg of CpG-B ODN-1826 (Invivogen) and passed through a centrifugal filter device YM10 (Amicon). The entire flow through volume was added to the RAW264-pNIFty-LUC cells and incubated at 37°C for 5 hours. Cells were washed and subsequently lysed with 100 µl per well of CCLR 1X solution (Promega luciferase lysis buffer), mixed with luciferase substrate following the manufactures instructions and the luciferase counts measured. Figure show NFκB activation levels normalized to Ala-Cpn10 at 100%.

Figure 9. Effect of Cpn10 mutants on Poly (I:C) stimulation. HEK293 cells were transiently transfected with plasmids encoding for TLR3 and pNifty NFkB-luciferase (InvivoGen) using GeneJuice according to the manufacturers instructions (Novogen). 24hours later the transfected cells were trypsinised, counted and 1x10^5 cells were plated in 1ml of media into each well of a 24 well plate and allowed to adhere for 24hrs. Then 100ug of Cpn10, 0.1ug Poly (I:C) (InvivoGen) and 10ul of SUPERase RNAse inhibitor (Ambion) were added to each well for 24hrs. The supernatants were then removed, the cells washed in PBS and lysed with 1x Lysis Buffer (Promega), and assayed for luciferase. Levels of luciferase were normalized to Poly (I:C) alone at 100%. Values represent the mean of triplicate wells.

Detailed Description

Cpn10 is a dome-shaped, heptameric ring of identical 10 kDa subunits (Figure 1). The surface of the dome is hydrophilic and highly charged. Each Cpn10 subunit forms an irregular β-barrel topology with five segments that are joined by several loop structures. Three small connective loops are present and two large loop extensions that protrude from the barrel. The first extension is a β-hairpin loop ("roof loop") that extends towards the centre of the heptamer and forms the roof of the dome-like structure. Intriguingly, whereas the roof of GroES (*E. coli* Cpn10) contains a cluster of negatively charged residues at the tips of the roof loops under physiological conditions, the roof of mammalian Cpn10 contains a positively charged cluster of amino acids at the tips of the roof loops; while a large portion of the roof is missing completely from the bacteriophage Cpn10 (Gp31). The molecule also has another extension that is a flexible 18 amino acid mobile loop that extends from the base of the dome and mediates an interaction with Cpn60. One of the small connection loops, comprised of residues Glu-74, Tyr-75 and Gly-76, extends from the base of the dome and protrudes inwards to form a lower rim region. The amino acid residues in the lower rim region are phylogenetically conserved amongst most eukaryotes.

Without being bound to any mechanism or pathway, the inventors have generated a series of mutations through primarily amino acid substitutions, deletions, additions or combinations thereof which modify the charge of a Cpn10 polypeptide and demonstrated herein that these mutations are effective in modifying the interaction of Cpn10 with one or more PRR ligands, specifically increasing the binding affinity of Cpn10 with the PRR ligand, which indicates an ability to modulate the immune system/response through PRR signalling. Binding of the Cpn10 polypeptide to a PRR ligand may have an immunomodulatory affect on the particular immune cell that posessess the PRR. The cell may be an antigen presenting cell, T-cell or B-cell. The antigen presenting cell may be a dendritic cell, macrophage or monocyte.

Pattern Recognition Receptors (PRRs), including Toll-like receptors (TLRs), Nucleotide-binding domain LRR-containing family (NLR), RIG-I-like receptor (RLR), DNA-dependent activator of IRF (DAI), C-type Lectin receptor (CLR) and the IFI20X/IFI16 family (Ifi16, Aim2, MNDA and IFIX), are the sentinels of the immune system, they act as the first line of defense against invading pathogens, recognising specific pathogenic associated molecular patterns (PAMPS) and initiating an immune response. It appears that PRRs also play a role in many inflammatory syndromes, including sepsis, autoimmune or chronic inflammatory diseases where altered self molecules hyperactivate PRRs leading to the development of a pathological state.

Cpn10 polypeptide mutants

The addition of extra positive charge, through adding positive or removing negative residues generates a Cpn10 molecule which binds significantly stronger (compared to Ala-Cpn10 and X-Cpn10) to nucleic acid-based PRR ligands. Extra positive charge could be added by (1) substituting an existing surface/solution exposed neutral or negative residue for a positive residue, (2) substituting an existing surface/solution exposed negative residue for a neutral residue, (3) introducing an additional surface/solution exposed positive residues (eg lengthen a loop structure or the N-terminus and C-terminus) or (4) deleting an existing surface/solution exposed negative residue (eg shortening a loop structure or the N-terminus and C-terminus). Our results also show that introducing multiple positive charges (eg Ala-Cpn10-Y75K,D94K) may increase the binding potential significantly greater than the individual mutations.

Calculation of Protein Net Charge

The net charge of a polypeptide at a given pH is calculated on the basis of the Henderson-Hasselbalch equation (Hasselbalch, K. A., 1917 *Biochemische Zeitschrift* **78**: 112–144) and known pKa values of ionisable amino acid side chains and the N- and C-termini of a polypeptide. The

Henderson-Hasselbalch equation states that the pH of a solution containing a weak acid/base and its conjugate base/acid is dependent only upon the ratio between the molar concentrations of these two solutes and remains independent of dilution, as shown in the following equations:

Henderson-Hasselbalch equation

the acid equation: $pH = pK_a + \log [A^-]/[HA]$ (used for C-terminus, Asp, Glu, Cys, Tyr)

the base equation: $pH = pK_a + \log [B]/[BH^+]$ (used for N-terminus, Lys, Arg, His)

where $[A^-]$ denotes the molar concentration of the conjugate base of a relevant acid (C-terminus, Asp, Glu, Cys, Tyr) and $[BH^+]$ is the molar concentration of the conjugate acid of a relevant base (N-terminus, Lys, Arg, His). The pKa values of ionisable groups within a polypeptide are well known in the art and can be found in numerous journals and textbooks. Depending on the set of pKa values used, the calculated net charge of a protein will vary slightly, but this does not change the conclusions obtained in this study. The pKa values utilised in Table 3 are N-terminus 8.0, C-terminus 3.1, Lys 10.0, Arg 12.0, His 6.5, Glu 4.4, Asp 4.4, Tyr 10.0 and Cys 8.5 (Stryer, L., 1988 "Biochemistry" textbook 3rd Edition, New York, W.H. Freeman, ISBN 0716719207).

So for a polypeptide with multiple ionisable groups the net charge of that polypeptide may be calculated at a given pH as follows:

1. List all ionizable residues (Cys, Asp, Glu, His, Lys, Arg, Tyr, carboxyl terminus, amino terminus)
2. If the pKa of an ionisable group is ≥ 2 units away from the pH value, the charge can be assigned as 1, 0, -1 without calculation. For example, at pH 7.3 Lysine (pKa 10.0) is going to be 100% protonated and will have an average charge of +1. On the other hand, at pH 7.3 Glutamate (pKa 4.4) and Aspartate (pKa 4.4) will both be 100% deprotonated giving an average charge of -1.
3. Use the Henderson-Hasselbalch equation to calculate the percent ionisation of each ionisable group at the given pH. In Table 3 calculations were made at pH 7.3 and pH7.4 (taken as physiological pH).
4. Multiply the percent ionisation of each ionisable group (z_i) by the total number of individual ionisable groups occuring within a given polypeptide (n_i) to get the total charge contributed by each ionisable group.The net charge (Z) of a polypeptide at a given pH is then provided by the sum of all charges contributed by each ionisable group $Z = \sum n_i z_i$ to arrive at the net charge of that polypeptide at a given pH.

A number of freely available resources exist where this approach to calculating the net charge on a polypeptide has been automated for ease of use. For example Protein Calculator V3.3 (http://www.scripps.edu/~cdputnam/protcalc.html) is a freely available tool to calculate the net charge on a protein based on the amino acid sequence. This tool was used to calculate the net charge of a number of Cpn10 polypetides at physiological pH (taken as 7.3 to 7.4) as in table 3.

Types of Mutations

Cpn10 variants with high affinity for proinflammatory nucleic acids can be generated by adding positive or removing negative residues. The mutations utilised to create Cpn10 variants with high affinity for proinflammatory nucleic acids may be amino acid residue insertion, deletion substitution or addition or a combinations thereof, provided that the mutation results in a Cpn10 variant with higher positive charge at pH 7.4 than Ala-Cpn10.

In one embodiment an existing residue may be substituted for a positively charged residue, a negatively charged residue may be replaced by a neutral residue, an additional positively charged residue may be added, or negatively charged residue may be deleted, for example to any of the regions of the Cpn10 polypeptide defined in figure 1b. The mutation may be made by any means known in the art for example site-direceted mutatgenesis, homologous recombination, transposon mutagenesis or sequence tag mutagenesis. Typically site directed mutagenesis will be used.

One skilled in the art will recognize that any number and type of mutations that result in a Cpn10 variant with a higher positive charge at pH 7.4 and a higher affinity for proinflammatory nucleic acids than Ala-Cpn10 falls within the scope of the invention.

Polypeptides

As disclosed herein the present invention contemplates isolated Cpn10 polypeptides and its increased affinity for a nucleic acid-based PRR ligand, comprising one or more amino acid deletions, additions or substitutions in comparison with Ala-Cpn10.

Cpn10 may be native, naturally-derived, recombinant or synthetic Cpn10. The Cpn10 molecule may be any Cpn10 polypeptide from a eukaryotic organism. By way of example as shown in Figure 2, the Cpn10 may be derived from yeast (e.g. *Saccharomyces cerevisiae*), nematode (e.g. *Caenorhabditis elegans*), frog (e.g. *Xenopus tropicalis*), chicken (e.g. *Gallus gallus*), zebrafish (e.g. *Danio rerio*), fly (e.g. fruit fly such as *Drosphila melanogaster*), plant (e.g. *Arabidopsis thaliana*) or a mammal. The mammalian Cpn10 may be primate, murine, ovine, bovine, canine, feline, porcine or

equine. Alternatively the Cpn10 may be archaeal in origin. In particular embodiments the Cpn10 is human Cpn10.

The present invention also relates to modifications of human Cpn10 polypeptides homologues as disclosed above and encompasses these molecules modified by the addition, deletion, or substitution of one or more amino acid residues herein, and how these modifications can increase the affinity of these Cpn10 polypeptides to a nucleic acid-based PRR ligand. Furthermore, amino acid additions may involve the fusion of a Cpn10 polypeptide or fragment thereof with a second polypeptide or peptide, such as a polyhistidine tag, maltose binding protein fusion, glutathione S transferase fusion, green fluorescent protein fusion, or the addition of an epitope tag such as FLAG, c-myc or hexahistidine tag. The Cpn10 polypeptide may or may not include the initiating methionine at the N-terminus. For example, human Cpn10 may comprise at the N-terminus an additional GSM tripeptide, see for example WO 95/15338, the disclosure of which is incorporated herein by reference, or an additional alanine (A; SEQ ID Nos.3-5) or an additional glycine. The present invention also contemplates the use of polynucleotides encoding such modified forms of Cpn10. In the case of Cpn10 polypeptides of the invention based on, or substantially derived from human Cpn10, such polypeptides may comprise the N-terminal sequence AGQAFRKFL, MAGQ, AGQ or AAGQ and optionally including one or more modifications as described above.

The term "variant" as used herein refers to substantially similar sequences. Generally, polypeptide sequence variants possess qualitative biological activity in common. Further, these polypeptide sequence variants may share at least 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98% or 99% sequence identity. Also included within the meaning of the term "variant" are homologues of polypeptides of the invention. A homologue is typically a polypeptide from a different species but sharing substantially the same biological function or activity as the corresponding polypeptide disclosed herein.

Further, the term "variant" also includes analogues of the polypeptides of the invention, wherein the term "analogue" means a polypeptide which is a derivative of a polypeptide of the invention, which derivative comprises addition, deletion, substitution of one or more amino acids, such that the polypeptide retains substantially the same function.

The present invention also contemplates fragments of the polypeptides disclosed herein. The term "fragment" refers to a polypeptide molecule that encodes a constituent or is a constituent of a polypeptide of the invention or variant thereof. Typically the fragment possesses qualitative biological activity in common with the polypeptide of which it is a constituent. The peptide fragment

may be between about 5 to about 150 amino acids in length, between about 5 to about 100 amino acids in length, between about 5 to about 50 amino acids in length, or between about 5 to about 25 amino acids in length. Alternatively, the peptide fragment may be between about 5 to about 15 amino acids in length.

Cpn10 polypeptides modified at the N- and/or C-terminus by the addition, deletion or substitution of one or more amino acid residues as described above also fall within the scope of the present invention.

Optimisation of Cpn10 cDNA sequence

The present invention utilises optimised Cpn10 cDNA sequences to increase the use of abundant transfer RNA (tRNA) pools for the production of Cpn10 polypeptide. It is known that tRNA pools provide specific codons encoding specific amino acids for the translation of a protein from a messenger RNA. Furthermore, it is also known that some tRNA pools are more abundant than others. This can result in lower abundance tRNA pools being depleted resulting lower yields and/or tRNA substitution generating mutations when a large amount of protein is produced from certain expression systems.

In relation to this invention specific Cpn10 variants were found that were susceptible to this. For example, during over-expression of Cpn10 in *E. coli*, the rare glycine (Gly) GGA tRNA, used for Gly39, is depleted and may be substituted by the very common glutamate/glutamic acid (Glu) GAA tRNA.

Accordingly, an optimised sequence using optimised codons at any number of positions may be constructed. In particular, the specific optimization of glycine and arginine residues G3, G29, G39, G50, G55, G58, G68, G77, G98, R8, R16, R21 and R93 resulted in wild-type cDNA expression levels but a significant decrease of variant levels while maintaining overall yield of Cpn10.

In addition, Cpn10 variants may be generated due to ribosomes reading through the cellular TGA stop codon. In that regard the TGA stop codon may be optimised by changing it to a TAA stop codon to eliminate this problem.

Production of Cpn10

In accordance with the present invention Cpn10 polypeptides may be produced using standard techniques of recombinant DNA and molecular biology that are well known to those skilled in the art. Guidance may be obtained, for example, from standard texts such as Sambrook *et al.*,

Molecular Cloning : A Laboratory Manual, Cold Spring Harbor, New York, 1989 and Ausubel *et al.*, *Current Protocols in Molecular Biology*, Greene Publ. Assoc. and Wiley-Intersciences, 1992. Methods described in Morton *et al.*, 2000 (*Immunol Cell Biol* **78**:603-607), Ryan *et al.*, 1995 (*J Biol Chem* **270**:22037-22043) and Johnson *et al.*, 2005 (*J Biol Chem* **280**:4037-4047) are examples of suitable purification methods for Cpn10 polypeptides, although the skilled addressee will appreciate that the present invention is not limited by the method of purification or production used and any other method may be used to produce Cpn10 for use in accordance with the methods and compositions of the present invention.

Cpn10 polypeptides and peptide fragments for use in accordance with the present invention may be obtained using standard recombinant nucleic acid techniques or may be synthesized, for example using conventional liquid or solid phase synthesis techniques. Cpn10 peptides may be produced by digestion of a polypeptide with one or more proteinases such as endoLys-C, endoArg-C, endoGlu-C and staphylococcus V8-protease. The digested peptide fragments can be purified by, for example, high performance liquid chromatographic (HPLC) techniques.

The purification of Cpn10 polypeptides of the invention may be scaled-up for large-scale production purposes. For example, as described herein the present inventors have developed a bioprocess for the production of large (gram) quantities of highly pure, clinical grade Cpn10 polypeptides.

Cpn10 polypeptides of the present invention, as well as fragments and variants thereof, may also be synthesised by standard methods of liquid or solid phase chemistry well known to those of ordinary skill in the art. For example such molecules may be synthesised following the solid phase chemistry procedures of Steward and Young (Steward, J. M. & Young, J. D., Solid Phase Peptide Synthesis. (2nd Edn.) Pierce Chemical Co., Illinois, USA (1984).

In general, such a synthesis method comprises the sequential addition of one or more amino acids or suitably protected amino acids to a growing peptide chain. Typically, either the amino or carboxyl group of the first amino acid is protected by a suitable protecting group. The protected amino acid is then either attached to an inert solid support or utilised in solution by adding the next amino acid in the sequence having the complimentary (amino or carboxyl) group suitably protected and under conditions suitable for forming the amide linkage. The protecting group is then removed from this newly added amino acid residue and the next (protected) amino acid is added, and so forth. After all the desired amino acids have been linked, any remaining protecting groups, and if necessary any solid support, is removed sequentially or concurrently to produce the final polypeptide.

Amino acid changes in Cpn10 polypeptides may be effected by techniques well known to those persons skilled in the relevant art. For example, amino acid changes may be effected by nucleotide replacement techniques which include the addition, deletion or substitution of nucleotides (conservative and/or non-conservative), under the proviso that the proper reading frame is maintained. Exemplary techniques include random mutagenesis, site-directed mutagenesis, oligonucleotide-mediated or polynucleotide-mediated mutagenesis, deletion of selected region(s) through the use of existing or engineered restriction enzyme sites, and the polymerase chain reaction.

The generation of immunomodulatory activity by the Cpn10 polypeptides of the invention may involve the formation of heptamers of the Cpn10 polypeptides. Testing of immunomodulatory activity for the purposes of the present invention may be via any one of a number of techniques known to those of skill in the art. As exemplified herein immunomodulatory activity of Cpn10 polypeptides may be determined by measuring the ability of the polypeptide to modulate signalling from the Toll-like receptor TLR-3, for example using an NF-κB-luciferase reporter cell line, and typically in the presence of a TLR-3 agonist such as poly(I:C). Other TLRs such as TLR-7, 8 and 9 are also tested as described herein. Alternatively or in addition, immunomodulatory activity may be determined using other assays *in vitro, ex vivo* or *in vivo*, for example via measurement of the production of cytokines in cells such as peripheral blood mononuclear cells, competitive binding assay, a two-hybrid assay, a filter assay, an electrophoretic mobility shift (gel-shift) assay, a plate capture assay or any combination of assays that enables one to measure immunomodulatory activity.

Polynucleotides

Embodiments of the present invention provide isolated polynucleotides encoding Cpn10 polypeptides as described above, and variants and fragments of such polynucleotides. Non-limiting examples of polynucleotides that are contemplated within the scope of the invention are represented herein as SEQ ID No's 7, 9, 11, 12, 14, 15, 17, 18, 20, 21, 23, 24, 26, 27, 29, 30, 32, 33, 35, 36, 38, 39, 41,42, 44, 45, 47, 48, 50, 51, 53, 54, 56, 57, 59, 60, 62, 63, 65, 66, 68, 69, 71, 72, 74, 75, 77, 78, 80, 81, 83, 84, 86, 87, 89, 90, 92, 93, 95, 96, 98, 99, 101, 102, 104, 105, 107, 108, 110, 111, 113, 114, 116, 117, 119, 120, 122, 123, 125, 126, 128, 129, 131, 132, 134, 135, 137, 138, 140, 141, 143, 144, 146, 147, 149, 150, 152, 153, 155, 156, 158, 159, 161, 162, 164, 165, 167, 168, 170, 171, 173, 174, 176, 177, 179, 180, 182, 183, 185, 186, 188, 189, 191,. 192, 194, 195, 197, 198, 200, 201, 203, 204, 206, 207, 209, 210, 212, 213, 215, 216, 218, 219, 221, 222, 224, 225, 227, 228, 230, 231, 233, 234, 236, 237, 239, 240, 242, 243, 245, 246, 248, 249, 251, 252, 254, 255, 257, 258, 260, 261, 263, 264, 266, 267, 269, 270, 272, 273, 275, 276, 278,

279, 281, 282, 284, 285 287, 288, 290, 291, 293, 294, 296, 297, 299, 300, 302, 303, 305, 306, 308, 309, 311, 312, 314, 315, 317, 318, 320, 321, 323, 324, 326, 327, 329, 330, 332, 333, 335, 336, 338, 339, 341, 342, 344, 345, 347, 348, 350, 351, 353, 354 or 356.

As for polypeptides discussed above, the term "variant" as used herein refers to substantially similar sequences. Generally, polynucleotide sequence variants encode polypeptides which possess qualitative biological activity in common. Further, these polynucleotide sequence variants may share at least 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98% or 99% sequence identity. Also included within the meaning of the term "variant" are homologues of polynucleotides of the invention. A homologue is typically a polynucleotide from a different species but sharing substantially the same activity.

Fragments of polynucleotides of the invention are also contemplated. The term "fragment" refers to a nucleic acid molecule that encodes a constituent or is a constituent of a polynucleotide of the invention. Fragments of a polynucleotide, do not necessarily need to encode polypeptides which retain biological activity. Rather the fragment may, for example, be useful as a hybridization probe or PCR primer. The fragment may be derived from a polynucleotide of the invention or alternatively may be synthesized by some other means, for example chemical synthesis. Polynucleotides of the invention and fragments thereof may also be used in the production of antisense molecules using techniques known to those skilled in the art.

Accordingly, the present invention contemplates oligonucleotides and fragments based on the sequences of the polynucleotides of the invention for use as primers and probes. Oligonucleotides are short stretches of nucleotide residues suitable for use in nucleic acid amplification reactions such as PCR, typically being at least about 10 nucleotides to about 50 nucleotides in length, more typically about 15 to about 30 nucleotides in length. Probes are nucleotide sequences of variable length, for example between about 10 nucleotides and several thousand nucleotides, for use in detection of homologous sequences, typically by hybridization. The level of homology (sequence identity) between sequences will largely be determined by the stringency of hybridization conditions. In particular the nucleotide sequence used as a probe may hybridize to a homologue or other variant of a polynucleotide disclosed herein under conditions of low stringency, medium stringency or high stringency. Low stringency hybridization conditions may correspond to hybridization performed at 50°C in 2 x SSC. There are numerous conditions and factors, well known to those skilled in the art, which may be employed to alter the stringency of hybridization. For instance, the length and nature (DNA, RNA, base composition) of the nucleic acid to be hybridized to a specified nucleic acid; concentration of salts and other components, such as the presence or absence of formamide, dextran sulfate, polyethylene glycol etc; and altering the

temperature of the hybridization and/or washing steps. For example, a hybridization filter may be washed twice for 30 minutes in 2 X SSC, 0.5% SDS and at least 55°C (low stringency), at least 60°C (medium stringency), at least 65°C (medium/ high stringency), at least 70°C (high stringency) or at least 75°C (very high stringency).

In particular embodiments, polynucleotides of the invention may be cloned into a vector. The vector may be a plasmid vector, a viral vector, or any other suitable vehicle adapted for the insertion of foreign sequences, their introduction into eukaryotic cells and the expression of the introduced sequences. Typically the vector is a eukaryotic expression vector and may include expression control and processing sequences such as a promoter, an enhancer, ribosome binding sites, polyadenylation signals and transcription termination sequences.

Antibodies

The present invention provides antibodies that selectively bind to the Cpn10 polypeptides of the present invention, as well as fragments and analogues thereof. Suitable antibodies include, but are not limited to polyclonal, monoclonal, chimeric, humanised, single chain, Fab fragments, and an Fab expression library. Antibodies of the present invention may act as agonists or antagonists of Cpn10 polypeptides, or fragments or analogues thereof.

Antibodies may be prepared from discrete regions or fragments of the Cpn10 polypeptides of the invention, in particular those involved in conferring immunomodulatory activity and/or partner or substrate binding. An antigenic Cpn10 polypeptide contains at least about 5, and preferably at least about 10, amino acids.

Methods for the generation of suitable antibodies will be readily appreciated by those skilled in the art. For example, an anti-Cpn10 monoclonal antibody, typically containing Fab portions, may be prepared using the hybridoma technology described in Antibodies-A Laboratory Manual, Harlow and Lane, eds., Cold Spring Harbor Laboratory, N.Y. (1988).

In the preparation of monoclonal antibodies directed toward Cpn10 polypeptides of the invention, fragments or analogues thereof, any technique that provides for the production of antibody molecules by continuous cell lines in culture may be used. These include the hybridoma technique originally developed by Kohler *et al.*, Nature, 256:495-497 (1975), as well as the trioma technique, the human B-cell hybridoma technique [Kozbor *et al.*, Immunology Today, 4:72 (1983)], and the EBV-hybridoma technique to produce human monoclonal antibodies [Cole *et al.*, in Monoclonal Antibodies and Cancer Therapy, pp. 77-96, Alan R. Liss, Inc., (1985)]. Immortal, antibody-producing cell lines can be created by techniques other than fusion, such as direct transformation of B lymphocytes with oncogenic DNA, or transfection with Epstein-Barr virus. See,

e.g., M. Schreier *et al.*, "Hybridoma Techniques" (1980); Hammerling *et al.*, "Monoclonal Antibodies and T-cell Hybridomas" (1981); Kennett *et al.*, "Monoclonal Antibodies" (1980).

In summary, a means of producing a hybridoma from which the monoclonal antibody is produced, a myeloma or other self-perpetuating cell line is fused with lymphocytes obtained from the spleen of a mammal hyperimmunised with a recognition factor-binding portion thereof, or recognition factor, or an origin-specific DNA-binding portion thereof. Hybridomas producing a monoclonal antibody useful in practicing this invention are identified by their ability to immunoreact with the present recognition factor and their ability to inhibit specified transcriptional activity in target cells.

A monoclonal antibody useful in practicing the present invention can be produced by initiating a monoclonal hybridoma culture comprising a nutrient medium containing a hybridoma that secretes antibody molecules of the appropriate antigen specificity. The culture is maintained under conditions and for a time period sufficient for the hybridoma to secrete the antibody molecules into the medium. The antibody-containing medium is then collected. The antibody molecules can then be further isolated by well-known techniques.

Similarly, there are various procedures known in the art which may be used for the production of polyclonal antibodies to Cpn10 polypeptides of the invention, or fragments or analogues thereof. For the production of Cpn10 polyclonal antibody, various host animals can be immunized by injection with a Cpn10 polypeptide, or a fragment or analogue thereof, including but not limited to rabbits, mice, rats, sheep, goats, etc. Further, the Cpn10 polypeptide or fragment or analogue thereof can be conjugated to an immunogenic carrier, e.g., bovine serum albumin (BSA) or keyhole limpet hemocyanin (KLH). Also, various adjuvants may be used to increase the immunological response, including but not limited to Freund's (complete and incomplete), mineral gels such as aluminium hydroxide, surface active substances such as lysolecithin, pluronic polyols, polyanions, peptides, oil emulsions, keyhole limpet hemocyanins, dinitrophenol, and potentially useful human adjuvants such as BCG (bacille Calmette-Guerin) and *Corynebacterium parvum*.

Screening for the desired antibody can also be accomplished by a variety of techniques known in the art. Assays for immunospecific binding of antibodies may include, but are not limited to, radioimmunoassays, ELISAs (enzyme-linked immunosorbent assay), sandwich immunoassays, immunoradiometric assays, gel diffusion precipitation reactions, immunodiffusion assays, in situ immunoassays, Western blots, precipitation reactions, agglutination assays, complement fixation assays, immunofluorescence assays, protein A assays, and immunoelectrophoresis assays, and the like (see, for example, Ausubel *et al.*, eds, 1994, Current Protocols in Molecular Biology, Vol. 1, John Wiley & Sons, Inc., New York). Antibody binding may be detected by virtue of a detectable

label on the primary anti-Cpn10 antibody. Alternatively, the anti-Cpn10 antibody may be detected by virtue of its binding with a secondary antibody or reagent which is appropriately labelled. A variety of methods are known in the art for detecting binding in an immunoassay and are within the scope of the present invention.

Antibodies of the present invention can be used in diagnostic methods and kits that are well known to those of ordinary skill in the art to detect qualitatively or quantify Cpn10 in a body fluid or tissue, or alternatively antibodies may be used in methods and compositions for the treatment of various diseases, disorders and conditions.

The antibody (or fragment thereof) raised against a Cpn10 polypeptide of the invention or a fragment or analogue thereof has binding affinity for Cpn10. Preferably, the antibody (or fragment thereof) has binding affinity or avidity greater than about 10^5 M^{-1}, more preferably greater than about 10^6 M^{-1}, more preferably still greater than about 10^7 M^{-1} and most preferably greater than about 10^8 M^{-1}.

In terms of obtaining a suitable amount of an antibody according to the present invention, one may manufacture the antibody(s) using batch fermentation with serum free medium. After fermentation the antibody may be purified via a multistep procedure incorporating chromatography and viral inactivation/removal steps. For instance, the antibody may be first separated by Protein A affinity chromatography and then treated with solvent/detergent to inactivate any lipid enveloped viruses. Further purification, typically by anion and cation exchange chromatography may be used to remove residual proteins, solvents/detergents and nucleic acids. The purified antibody may be further purified and formulated into 0.9% saline using gel filtration columns. The formulated bulk preparation may then be sterilised and viral filtered and dispensed.

Agonists and antagonists

Using the methods described above, an agent may be identified that is an agonist of a polypeptide of the invention or a variant or fragment thereof. Agents which are agonists enhance one or more of the biological activities of the polypeptide. Alternatively, the methods described above may identify an agent that is an antagonist of a polypeptide of the invention or a variant or fragment thereof. Agents which are antagonists retard one or more of the biological activities of the polypeptide. Agonists enhance one or more of the biological activities of a molecule, such as Cpn10 polypeptides as described herein, whilst antagonists retard one or more of the biological activities of the polypeptides. In one example, an agonist of a polypeptide of the invention may be an immunosuppressive nucleic acid. This nucleic acid may bind a polypeptide of the present invention in a complex. In another example, an antagonist of a polypeptide of the invention may be

a proinflammatory nucleic acid. This nucleic acid may also bind a polypeptide of the present invention in a complex.Such potential modulators of the activity of the polypeptides of the invention may be generated for screening by the above methods by a number of techniques known to those skilled in the art. For example, methods such as X-ray crystallography and nuclear magnetic resonance spectroscopy may be used to model the structure of polypeptide of the invention or a variant or fragment thereof, thus facilitating the design of potential modulating agents using computer-based modeling. Various forms of combinatorial chemistry may also be used to generate putative modulators. Using the screeing methods as described below, an agent may be identified that is an agonist or antagonist of a polypeptide of the invention or a variant or fragment thereof. Antibodies, low molecular weight peptides, nucleic acids and non-proteinaceous organic molecules are examples of such agents that may act as agonists or antagonists of a polypeptide of the invention or a variant or fragment thereof.

Screening

Compounds which bind, or otherwise interact with the polypeptides and polynucleotides of the invention, and specifically compounds which modulate their activity, may be identified by a variety of suitable methods. Non limiting methods include the two-hybrid method, co-immunoprecipitation, affinity purification, mass spectroscopy, tandem affinity purification, phage display, label transfer, DNA microarrays/gene coexpression and protein microarrays.

Cpn10 polypeptides of the invention and appropriate fragments and variants can be used in high-throughput screens to assay candidate compounds for the ability to bind to, or otherwise interact with Cpn10. Such candidate compounds could be proinflammatory nucleic acids or immunosuppressive nucleic acids which form a complex with a polypeptide, fragment or variants of the polypeptide as described herein. Candidate compounds can be proteins.

These candidate compounds can be further screened against functional Cpn10 to determine the effect of the compound on Cpn10 activity. The polypeptides and polynucleotides of the present invention, and fragments and analogues thereof are useful for the screening and identification of compounds and agents that interact with these molecules. In particular, desirable compounds are those that modulate the activity of these polypeptides and polynucleotides. Such compounds may exert a modulatory effect by activating, stimulating, increasing, inhibiting or preventing expression or activity of the polypeptides and/or polynucleotides. Suitable compounds may exert their effect by virtue of either a direct (for example binding) or indirect interaction .As described herein, there are methods of screening for a compound that may modulate the activity of, or otherwise interact with, Cpn10 polypeptides of the invention. These compounds may be identified by a variety of suitable

methods. Interaction and/or binding may be determined using standard competitive binding assays, such as gel-shift assays and plate bound assays described within, or two-hybrid assay systems.

For example, the two-hybrid assay is a yeast-based genetic assay system (Fields and Song, 1989) typically used for detecting protein-protein interactions. Briefly, this assay takes advantage of the multi-domain nature of transcriptional activators. For example, the DNA-binding domain of a known transcriptional activator may be fused to a Cpn10 polypeptide of the invention, or fragment or variant thereof, and the activation domain of the transcriptional activator fused to a candidate protein. Interaction between the candidate protein and the Cpn10 polypeptide , or fragment or variant thereof, will bring the DNA-binding and activation domains of the transcriptional activator into close proximity. Interaction can thus be detected by virtue of transcription of a specific reporter gene activated by the transcriptional activator.

Alternatively, affinity chromatography may be used to identify binding partners of Cpn10. For example, a Cpn10 polypeptide of the invention, or fragment or variant thereof, may be immobilised on a support (such as sepharose) and cell lysates passed over the column. Proteins binding to the immobilised Cpn10 polypeptide, fragment or variant can then be eluted from the column and identified. Initially such proteins may be identified by N-terminal amino acid sequencing for example.

In a modification of the above technique, a fusion protein may be generated by fusing a Cpn10 polypeptide, fragment or variant to a detectable tag, such as alkaline phosphatase, and using a modified form of immunoprecipitation as described by Flanagan and Leder (1990).

Methods for detecting compounds that modulate Cpn10 activity may involve combining a Cpn10 polypeptide with a candidate compound and a suitable labelled substrate and monitoring the effect of the compound on Cpn10 by changes in the substrate (may be determined as a function of time). Suitable labelled substrates include those labelled for colourimetric, radiometric, fluorimetric or fluorescent resonance energy transfer (FRET) based methods, for example.

For example, co-immunoprecipation may be used to to determine whether a candidate agent or plurality of candidate agents interacts or binds with polypeptide of the invention or a variant or fragment thereof. Using this technique, cyanotoxic organisms, cyanobacteria and/or dinoflagellates may be lysed under nondenaturing conditions suitable for the preservation of protein-protein interactions. The resulting solution can then be incubated with an antibody specific for a polypeptide of the invention or a variant or fragment thereof and immunoprecipitated from the bulk solution, for example by capture with an antibody-binding protein attached to a solid support. Immunoprecipitation of the polypeptide of the invention or a variant or fragment thereof by this method facilitates the co-immunoprecipation of an agent associated with that protein. The

identification an associated agent can be established using a number of methods known in the art, including but not limited to SDS-PAGE, western blotting, and mass spectrometry.

Alternatively, the phage display method may be used to to determine whether a candidate agent or plurality of candidate agents interacts or binds with a polypeptide of the invention or a variant or fragment thereof. Phage display is a test to screen for protein interactions by integrating multiple genes from a gene bank into phage. Under this method, recombinant DNA techniques are used to express numerous genes as fusions with the coat protein of a bacteriophage such the peptide or protein product of each gene is displayed on the surface of the viral particle. A whole library of phage-displayed peptides or protein products of interest can be produced in this way. The resulting libraries of phage-displayed peptides or protein products may then be screened for the ability to bind a polypeptide of the invention or a variant or fragment thereof. DNA extracted from interacting phage contains the sequences of interacting proteins.

Alternatively, affinity chromatography may be used to to determine whether a candidate agent or plurality of candidate agents interacts or binds with a polypeptide of the invention or a variant or fragment thereof. For example, a polypeptide of the invention or a variant or fragment thereof, may be immobilised on a support (such as sepharose) and cell lysates passed over the column. Proteins binding to the immobilised polypeptide of the invention or a variant or fragment thereof, may then be eluted from the column and identified, for example by N-terminal amino acid sequencing.

The present invention also contemplates compounds which may exert their modulatory effect on polypeptides of the invention by altering expression of the polypeptide. In this case, such compounds may be identified by comparing the level of expression of the polypeptide in the presence of a candidate compound with the level of expression in the absence of the candidate compound.

In the context of antibodies, screening for the desired antibody can also be accomplished by a variety of techniques known in the art. Assays for immunospecific binding of antibodies may include, but are not limited to, radioimmunoassays, ELISAs (enzyme-linked immunosorbent assay), sandwich immunoassays, immunoradiometric assays, gel diffusion precipitation reactions, immunodiffusion assays, in situ immunoassays, Western blots, precipitation reactions, agglutination assays, complement fixation assays, immunofluorescence assays, protein A assays, and immunoelectrophoresis assays, and the like (see, for example, Ausubel *et al.*, Current Protocols in Molecular Biology, Vol. 1, John Wiley & Sons, Inc., New York (1994)). Antibody binding may be detected by virtue of a detectable label on the primary antibody. Alternatively, the antibody may be

detected by virtue of its binding with a secondary antibody or reagent which is appropriately labelled. A variety of methods are known in the art for detecting binding in an immunoassay and are included in the scope of the present invention.

It will be appreciated that the methods described above are merely examples of the types of methods that may be utilised to identify agents that are capable of interacting with, or modulating the activity of polypeptides of the invention or variants or fragments thereof. Other suitable methods will be known by persons skilled in the art and are within the scope of this invention.

Compositions and routes of administration

Cpn10 polypeptides and polynucleotides of the invention may be useful as therapeutic agents. These molecules find use, for example, in treating or preventing a disease or condition in a subject, by administering a therapeutically effective amount of such a molecule to the subject. Typically such diseases and conditions are amenable to treatment by modulation of the immune response in the subject. By way of example, such diseases and conditions may include acute or chronic inflammatory diseases such as insulin dependent diabetes mellitus, systemic lupus erythematosis, Sjorgren's disease, Graves disease, multiple sclerosis, rheumatoid arthritis, chronic fatigue syndrome, Alzheimer's disease, asthma, allergy, multiple sclerosis, GVHD, artherosclerosis, inflammatory pain, psoriasis, HIV, chronic immune activation, chronic myositis, scleroderma. The disease may also be a cancer such as, non-small cell lung carcinoma, renal cell carcinoma, melanoma, non-Hodgkin's lymphoma, colorectal cancer, basal cell carcinoma. The disease may be an infectious disease.

The infectious disease may result from a bacterial, viral, or fungal infection. Chronic immune activation is associated with leakage of bacterial (e.g. LPS) and/or viral products (e.g. nucleic acids) from the gastrointestinal tract into the circulatory system. For example, leakage can occur from the oral cavity, gut or small intestine. Leakage of bacterial or viral products can be caused by an infection or disease such as bacterial infections, viral infections, inflammatory bowel disease and gum disease. An example of viral infection is a HIV or Hepatitis C infection.

Chronic immune activation involves immunomodulation of TLR signalling through LPS or nucleic acid binding to TLRs. LPS can bind to TLR2 or TLR4 whilst nucleic acids can bind to TLR3, 7, 8 or 9.

Accordingly, pharmaceutically useful compositions comprising Cpn10 polypeptides and polynucleotides for use in treating or preventing diseases and conditions are contemplated herein.

Agonists and antagonists of Cpn10 polypeptides of the invention, including anti-Cpn10 antibodies, may also be useful as therapeutic agents. Accordingly, the present invention also

contemplates methods of treatment using such agonists and antagonists and pharmaceutical compositions comprising the same.

In general, suitable compositions for use in accordance with the methods of the present invention may be prepared according to methods and procedures that are known to those of ordinary skill in the art and accordingly may include a pharmaceutically acceptable carrier, diluent and/or adjuvant.

Compositions may be administered by standard routes. In general, the compositions may be administered by the parenteral (e.g., intravenous, intraspinal, subcutaneous or intramuscular), oral or topical route. Administration may be systemic, regional or local. The particular route of administration to be used in any given circumstance will depend on a number of factors, including the nature of the condition to be treated, the severity and extent of the condition, the required dosage of the particular compound to be delivered and the potential side-effects of the compound.

In general, suitable compositions may be prepared according to methods which are known to those of ordinary skill in the art and may include a pharmaceutically acceptable diluent, adjuvant and/or excipient. The diluents, adjuvants and excipients must be "acceptable" in terms of being compatible with the other ingredients of the composition, and not deleterious to the recipient thereof.

Examples of pharmaceutically acceptable carriers or diluents are demineralised or distilled water; saline solution; vegetable based oils such as peanut oil, safflower oil, olive oil, cottonseed oil, maize oil, sesame oils such as peanut oil, safflower oil, olive oil, cottonseed oil, maize oil, sesame oil, arachis oil or coconut oil; silicone oils, including polysiloxanes, such as methyl polysiloxane, phenyl polysiloxane and methylphenyl polysolpoxane; volatile silicones; mineral oils such as liquid paraffin, soft paraffin or squalane; cellulose derivatives such as methyl cellulose, ethyl cellulose, carboxymethylcellulose, sodium carboxymethylcellulose or hydroxypropylmethylcellulose; lower alkanols, for example ethanol or iso-propanol; lower aralkanols; lower polyalkylene glycols or lower alkylene glycols, for example polyethylene glycol, polypropylene glycol, ethylene glycol, propylene glycol, 1,3-butylene glycol or glycerin; fatty acid esters such as isopropyl palmitate, isopropyl myristate or ethyl oleate; polyvinylpyrridone; agar; carrageenan; gum tragacanth or gum acacia, and petroleum jelly. Typically, the carrier or carriers will form from 10% to 99.9% by weight of the compositions.

The compositions of the invention may be in a form suitable for administration by injection, in the form of a formulation suitable for oral ingestion (such as capsules, tablets, caplets, elixirs, for example), in the form of an ointment, cream or lotion suitable for topical administration, in a form suitable for delivery as an eye drop, in an aerosol form suitable for administration by inhalation, such

as by intranasal inhalation or oral inhalation, in a form suitable for parenteral administration, that is, subcutaneous, intramuscular or intravenous injection.

For administration as an injectable solution or suspension, non-toxic parenterally acceptable diluents or carriers can include, Ringer's solution, isotonic saline, phosphate buffered saline, ethanol and 1,2 propylene glycol.

Some examples of suitable carriers, diluents, excipients and adjuvants for oral use include peanut oil, liquid paraffin, sodium carboxymethylcellulose, methylcellulose, sodium alginate, gum acacia, gum tragacanth, dextrose, sucrose, sorbitol, mannitol, gelatine and lecithin. In addition these oral formulations may contain suitable flavouring and colourings agents. When used in capsule form the capsules may be coated with compounds such as glyceryl monostearate or glyceryl distearate which delay disintegration.

Adjuvants typically include emollients, emulsifiers, thickening agents, preservatives, bactericides and buffering agents.

Solid forms for oral administration may contain binders acceptable in human and veterinary pharmaceutical practice, sweeteners, disintegrating agents, diluents, flavourings, coating agents, preservatives, lubricants and/or time delay agents. Suitable binders include gum acacia, gelatine, corn starch, gum tragacanth, sodium alginate, carboxymethylcellulose or polyethylene glycol. Suitable sweeteners include sucrose, lactose, glucose, aspartame or saccharine. Suitable disintegrating agents include corn starch, methylcellulose, polyvinylpyrrolidone, guar gum, xanthan gum, bentonite, alginic acid or agar. Suitable diluents include lactose, sorbitol, mannitol, dextrose, kaolin, cellulose, calcium carbonate, calcium silicate or dicalcium phosphate. Suitable flavouring agents include peppermint oil, oil of wintergreen, cherry, orange or raspberry flavouring. Suitable coating agents include polymers or copolymers of acrylic acid and/or methacrylic acid and/or their esters, waxes, fatty alcohols, zein, shellac or gluten. Suitable preservatives include sodium benzoate, vitamin E, alpha-tocopherol, ascorbic acid, methyl paraben, propyl paraben or sodium bisulphite. Suitable lubricants include magnesium stearate, stearic acid, sodium oleate, sodium chloride or talc. Suitable time delay agents include glyceryl monostearate or glyceryl distearate.

Liquid forms for oral administration may contain, in addition to the above agents, a liquid carrier. Suitable liquid carriers include water, oils such as olive oil, peanut oil, sesame oil, sunflower oil, safflower oil, arachis oil, coconut oil, liquid paraffin, ethylene glycol, propylene glycol, polyethylene glycol, ethanol, propanol, isopropanol, glycerol, fatty alcohols, triglycerides or mixtures thereof.

Suspensions for oral administration may further comprise dispersing agents and/or suspending agents. Suitable suspending agents include sodium carboxymethylcellulose,

methylcellulose, hydroxypropylmethyl-cellulose, poly-vinyl-pyrrolidone, sodium alginate or acetyl alcohol. Suitable dispersing agents include lecithin, polyoxyethylene esters of fatty acids such as stearic acid, polyoxyethylene sorbitol mono- or di-oleate, -stearate or -laurate, polyoxyethylene sorbitan mono- or di-oleate, -stearate or -laurate and the like.

The emulsions for oral administration may further comprise one or more emulsifying agents. Suitable emulsifying agents include dispersing agents as exemplified above or natural gums such as guar gum, gum acacia or gum tragacanth.

Methods for preparing parenterally administrable compositions are apparent to those skilled in the art, and are described in more detail in, for example, Remington's Pharmaceutical Science, 15th ed., Mack Publishing Company, Easton, Pa., hereby incorporated by reference herein.

The topical formulations of the present invention, comprise an active ingredient together with one or more acceptable carriers, and optionally any other therapeutic ingredients. Formulations suitable for topical administration include liquid or semi-liquid preparations suitable for penetration through the skin to the site of where treatment is required, such as liniments, lotions, creams, ointments or pastes, and drops suitable for administration to the eye, ear or nose.

Drops according to the present invention may comprise sterile aqueous or oily solutions or suspensions. These may be prepared by dissolving the active ingredient in an aqueous solution of a bactericidal and/or fungicidal agent and/or any other suitable preservative, and optionally including a surface active agent. The resulting solution may then be clarified by filtration, transferred to a suitable container and sterilised. Sterilisation may be achieved by: autoclaving or maintaining at 90°C-100°C for half an hour, or by filtration, followed by transfer to a container by an aseptic technique. Examples of bactericidal and fungicidal agents suitable for inclusion in the drops are phenylmercuric nitrate or acetate (0.002%), benzalkonium chloride (0.01%) and chlorhexidine acetate (0.01%). Suitable solvents for the preparation of an oily solution include glycerol, diluted alcohol and propylene glycol.

Lotions according to the present invention include those suitable for application to the skin or eye. An eye lotion may comprise a sterile aqueous solution optionally containing a bactericide and may be prepared by methods similar to those described above in relation to the preparation of drops. Lotions or liniments for application to the skin may also include an agent to hasten drying and to cool the skin, such as an alcohol or acetone, and/or a moisturiser such as glycerol, or oil such as castor oil or arachis oil.

Creams, ointments or pastes according to the present invention are semi-solid formulations of the active ingredient for external application. They may be made by mixing the active ingredient in finely-divided or powdered form, alone or in solution or suspension in an aqueous or non-aqueous

fluid, with a greasy or non-greasy basis. The basis may comprise hydrocarbons such as hard, soft or liquid paraffin, glycerol, beeswax, a metallic soap; a mucilage; an oil of natural origin such as almond, corn, arachis, castor or olive oil; wool fat or its derivatives, or a fatty acid such as stearic or oleic acid together with an alcohol such as propylene glycol or macrogols.

The composition may incorporate any suitable surfactant such as an anionic, cationic or non-ionic surfactant such as sorbitan esters or polyoxyethylene derivatives thereof. Suspending agents such as natural gums, cellulose derivatives or inorganic materials such as silicaceous silicas, and other ingredients such as lanolin, may also be included.

The compositions may also be administered in the form of liposomes. Liposomes are generally derived from phospholipids or other lipid substances, and are formed by mono- or multi-lamellar hydrated liquid crystals that are dispersed in an aqueous medium. Any non-toxic, physiologically acceptable and metabolisable lipid capable of forming liposomes can be used. The compositions in liposome form may contain stabilisers, preservatives, excipients and the like. The preferred lipids are the phospholipids and the phosphatidyl cholines (lecithins), both natural and synthetic. Methods to form liposomes are known in the art, and in relation to this specific reference is made to: Prescott, Ed., Methods in Cell Biology, Volume XIV, Academic Press, New York, N.Y. (1976), p. 33 *et seq.*, the contents of which is incorporated herein by reference.

The compositions may be conjugated to an array of polyethylene glycol (PEG) derivatives. The addition of PEG to proteins (PEGylation) is a well established method for decreasing the plasma clearance rates of proteins, thereby increasing their efficacy (Nucci *et al.*, 1991, *Adv. Drug Del. Rev.* **6**:133). Additional benefits of PEGylation may include, greater stability of proteins, decreased immunogenicity, enhanced solubility and decreased susceptibility to proteolysis (Sheffield W. 2001, *Curr Drug Targets Cardiovasc Haematol Disord.* **1**:1-22). PEG molecules contain the basic repeating structure of -(OCH_3CH_2)n-OH and are classified into groups according to their molecular weight. PEG derivatives are conjugated to proteins to increase their hydrodynamic radius and in general, their increase in half-life is directly related to the size of the PEG chain attached (Sheffield W. 2001, *Curr Drug Targets Cardiovasc Haematol Disord.* **1**:1-22).

The compositions may also be administered in the form of microparticles. Biodegradable microparticles formed from polylactide (PLA), polylactide-co-glycolide (PLGA), and epsilon-caprolactone (ε-caprolactone) have been extensively used as drug carriers to increase plasma half life and thereby prolong efficacy (R. Kumar, M., 2000, *J Pharm Pharmaceut Sci.* **3**(2) 234-258). Microparticles have been formulated for the delivery of a range of drug candidates including vaccines, antibiotics, and DNA. Moreover, these formulations have been developed for various delivery routes including parenteral subcutaneous injection, intravenous injection and inhalation.

The compositions may incorporate a controlled release matrix that is composed of sucrose acetate isobutyrate (SAIB) and organic solvent or organic solvents mixture. Polymer additives may be added to the vehicle as a release modifier to further increase the viscosity and slow down the release rate. SAIB is a well known food additive. It is a very hydrophobic, fully esterified sucrose derivative, at a nominal ratio of six isobutyrate to two acetate groups. As a mixed ester, SAIB does not crystallize but exists as a clear viscous liquid. Mixing SAIB with a pharmaceutically accepted organic solvent such as ethanol or benzyl alcohol decreases the viscosity of the mixture sufficiently to allow for injection. An active pharmaceutical ingredient may be added to the SAIB delivery vehicle to form SAIB solution or suspension formulations. When the formulation is injected subcutaneously, the solvent diffuses from the matrix allowing the SAIB-drug or SAIB-drug-polymer mixtures to set up as an in situ forming depot.

For the purposes of the present invention molecules and agents may be administered to subjects as compositions either therapeutically or preventively. In a therapeutic application, compositions are administered to a patient already suffering from a disease, in an amount sufficient to cure or at least partially arrest the disease and its complications. The composition should provide a quantity of the molecule or agent sufficient to effectively treat the patient.

Embodiments of the invention also contemplate the administration of a polynucleotide encoding Cpn10. In such situations the polynucleotide is typically operably linked to a promoter such that the appropriate polypeptide sequence is produced following administration of the polynucleotide to the subject. The polynucleotide may be administered to subjects in a vector. The vector may be a plasmid vector, a viral vector, or any other suitable vehicle adapted for the insertion of foreign sequences, their introduction into eukaryotic cells and the expression of the introduced sequences. Typically the vector is a eukaryotic expression vector and may include expression control and processing sequences such as a promoter, an enhancer, ribosome binding sites, polyadenylation signals and transcription termination sequences. The nucleic acid construct to be administered may comprise naked DNA or may be in the form of a composition, together with one or more pharmaceutically acceptable carriers.

Those skilled in the art will appreciate that in accordance with the methods of the present invention Cpn10 polypeptides of the invention may be administered alone or in conjunction with one or more additional agents. For example, a Cpn10 polypeptide of the invention may be administered together with one or more agonists capable of stimulating a TLR receptor such as TLR-3. Additionally, the present invention contemplates combination therapy using Cpn10 polypeptides of the invention in conjunction with other therapeutic approaches to the treatment of diseases and disorders. For example, Cpn10 polypeptides may be useful in the treatment of viral diseases which

are responsive to therapy with Type I interferons such as IFNβ or IFN1β and Cpn10 polypeptides of the invention may be used in conjunction with IFNβ in the treatment of autoimmune diseases such as multiple sclerosis.

For such combination therapies, each component of the combination therapy may be administered at the same time, or sequentially in any order, or at different times, so as to provide the desired effect. Alternatively, the components may be formulated together in a single dosage unit as a combination product. When administered separately, it may be preferred for the components to be administered by the same route of administration, although it is not necessary for this to be so.

Dosages

The therapeutically effective dose level for any particular patient will depend upon a variety of factors including: the disorder being treated and the severity of the disorder; activity of the molecule or agent employed; the composition employed; the age, body weight, general health, sex and diet of the patient; the time of administration; the route of administration; the rate of sequestration of the molecule or agent; the duration of the treatment; drugs used in combination or coincidental with the treatment, together with other related factors well known in medicine.

One skilled in the art would be able, by routine experimentation, to determine an effective, non-toxic amount of agent or compound which would be required to treat applicable diseases and conditions.

Generally, an effective dosage is expected to be in the range of about 0.0001mg to about 100mg per kg body weight bi weekly; typically, about 0.001mg to about 75mg per kg body weight bi weekly; about 0.01mg to about 50mg per kg body weight bi weekly; about 0.05mg to about 50mg per kg body weight bi weekly; about 0.1mg to about 10mg per kg body weight per bi weekly; approximately 0.1mg per kg body weight bi weekly. Also contemplated herein is administration of the dosage on a weekly or tri weekly basis.

Alternatively, an effective dosage may be about 25 to 150mg per patient bi weekly. Generally, an effective dosage is expected to be in the range of about 2.5 to about 750mg per patient bi weekly, preferably about 10 to about 350mg per patient bi weekly, more preferably about 25 to 150mg per patient bi weekly, even more preferably about 25 to 200mg weekly.

Typically, in therapeutic applications, the treatment would be for the duration of the disease state.

Further, it will be apparent to one of ordinary skill in the art that the optimal quantity and spacing of individual dosages will be determined by the nature and extent of the disease state being

treated, the form, route and site of administration, and the nature of the particular individual being treated. Also, such optimum conditions can be determined by conventional techniques.

It will also be apparent to one of ordinary skill in the art that the optimal course of treatment, such as, the number of doses of the composition given per day for a defined number of days, can be ascertained by those skilled in the art using conventional course of treatment determination tests.

The present invention will now be described with reference to specific examples, which should not be construed, in any way, as limiting the scope of the invention.

Examples

Example 1: Production of Cpn10 polypeptides

To further define the production process of Cpn10 polypeptides of the invention, the following non-limiting example is provided.

Firstly, a heat-inducible expression plasmid encoding human Cpn10 with or without modification was transformed into the *E. coli* strain XL1-Blue (Stratagene), and a master cell bank was established from a single selected clone.

Cpn10 was then produced in *E. coli* essentially as described by Ryan *et al.* (1995, *J Biol Chem* **270**: 22037-22043). In addition, the material that did not bind Macro-Prep High Q (BioRad) was further purified by S-Sepharose and then Gel-Filtration (Superdex 200, Amersham Biosciences). Purified Cpn10 in a 50 mM Tris-HCl (pH 7.6) and 150 mM NaCl buffer, was filtered through an Acrodisc with a 0.2 mm Mustang E membrane according to the manufacturer's instructions (Pall Corporation, Ann Arbor, MI. Cat No. MSTG5E3) to remove residual endotoxins and was stored at -70°C. The purity of Cpn10, such as various Cpn10 mutant polypeptides as shown in Figure 3, for example, was determined to be >99% by Coomassie brilliant staining on SDS-PAGE. Aliquots were thawed once prior to use.

Example 2: Molecular Chaperone activities of Cpn10 proteins

To examine the importance of the various amino acid residues, their potential charge, and the location of these residues in relation to chaperone activity, the inventors tested the Cpn10 polypeptides (see Table 1) that contain one or more mutations and with or without an extra N-terminal Alanine (Ala) residue for their ability to act as a molecular chaperones and fold proteins in conjunction with E.coli GroEL. This was determined by assaying for rhodanese refolding *in vitro* utilising a method adapted from Weber F. and Hayer-Hartl M.K. (Chaperonin Protocols, Ed Schneider C., Humana Press Inc. , 2000, p117-126).

Native bovine rhodanese (30 μM, SIGMA) was denatured in 20 mM MOPS-KOH (pH7.5), 100 mM KCl and 20 mM $MgCl_2$ (buffer A) containing 5M Guanidine HCl and 8 mM DTT then subsequently diluted (75-fold) from denaturant into buffer A containing GroEL (400 nM), such that the final concentration of rhodanese was 400 nM. GroEL rapidly and stably binds denatured rhodanese (D-Rho) whereas in buffer alone, D-Rho mis-folds and aggregates (ie inefficient spontaneous refolding). The addition of Cpn10 and ATP (20.1 mM) to preformed, stable complexes of GroEL-bound rhodanese permits efficient refolding to proceed. In the absence of Cpn10, the addition of ATP causes D-Rho to cycle on and off GroEL in a folding incompetent manner leading eventually to misfolding and aggregation (this reaction serves as a suitable assay blank). Each folding reaction has a total volume of 290 μL, at specific time points (ie 0, 15, 30, 45, 60, 75, 90 mins) 30μL aliquots are removed and combined with 70μL of rhodanese activity assay mixture (57.1 mM KH_2PO_4 (pH7.5), 71.4 mM EDTA, 71.4 mM Na thiosulfate and 71.4 mM KCN) for 6 min. Prior to the initiation of refolding reactions with ATP, a 30 μL aliquot is taken as a T=0 min of refolding time point. EDTA within the rhodanese activity assay mixture chelates Mg^{2+} ions, which prevents GroEL binding ATP, the result is an immediate stopping of the folding reaction. Subsequently, rhodanese activity is stopped after 6 min by the addition of 50 μL of 15% (v/v) formaldehyde (final concentration 5% v/v).

Rhodanese catalyses the formation of thiocyanide ('Rhodanid') from thiosulfate and cyanide. Thiocyanide is easily detected colourimetrically (Absorbance 450nm) by the formation of its red iron complex in the presence of Ferric Nitrate. Rhodanese activity measurements (150 μL) are developed by the addition of 150 μL of Ferric Nitrate reagent (164.5 mM ferric nitrate and 9.2 % v/v nitric acid). Rhodanese activity measurements are read at A450nm in 96 well microplates.

A typical rhodanese folding reaction follow an exponential incline in rhodanese activity (ie folded rhodanese) with time to a maximum yield of folded rhodanese. At constant amounts of GroEL (400nM) and rhodanese (400nM), a linear relationship is observed (between rhodanese activity and time) with increasing amounts of Cpn10 until an equal molar concentration of Cpn10 (7mer) to GroEL (14mer) is reached (ie 400 nM). At concentrations of Cpn10 above 400 nM, the increase in rhodanese activity rapidly reaches a maximum. The assay consists of five standards (in duplicate) and test samples (in duplicate). The concentrations of Cpn10 standards are 0 nM, 140 nM, 250 nM, 280 nM and 350 nM. Rhodanese activity (ie Cpn10 activity) measurements from the 30, 45, 60, 75 and 90 min time points are averaged. The 0 nM Cpn10 standard serves as a suitable measurement of the assays' background activity; therefore the absorbance value for the 0nM Cpn10 standard is subtracted from all other calculated absorbance values (or activity values). Following background correction, the absorbance value for the 280 nM Cpn10 standard is

nominated as 100% activity and all other absorbance values are converted to a relative % activity based on the 100% standard. Outlier data points are removed by comparison of duplicate measurements, >30% deviation between duplicates is considered unacceptable. Utilizing the acceptable data, a linear calibration curve is generated with five standard concentrations 0 nM Cpn10 (0 % Activity), 140 nM Cpn10 (50 % Activity), 250 nM Cpn10 (89.3 % Activity), 280 nM Cpn10 (100 % Activity) and 350 nM Cpn10 (125 % Activity). Rhodanese activity (e,g, Ala-Cpn10 activity) is plotted against Ala-Cpn10 concentration. For correction of assay bias, the percentage activity values from the test samples are recalculated using the equation generated from the linear calibration curve.

Concentrations of chaperonins (GroEL and Cpn10) are calculated using the oligomeric molecular weights (MW) of the proteins while rhodanese is calculated using the monomeric MW; e.g. *E. coli* GroEL 14 mer (SwissProt P0A6F5) = 800,766.4 g/mol, Human Ala-Cpn10 7 mer (SwissProt P61604) = 76,100.5 g/mol, Human X-Cpn10-Y75K 7 mer = 75,358.5 g/mol, Human Ala-Cpn10-Y75K 7 mer = 75,855.5 g/mol and Bovine rhodanese 1 mer (SwisProt P00586) = 33,164.6 g/mol.

As shown in the table 1 below, the activities of the numerous Cpn10 proteins were determined from a Ala-Cpn10 standard curve linear equation. All reactions were done in duplicate.

Table 1: Chaperonin 10 activity

Cpn10 Protein SEQ ID		Chaperone Activity (% of Ala-Cpn10)
1	X-Cpn10	89.7
3	Ala-Cpn10	100
6	X-Cpn10-K53E	96.7
8	Ala-Cpn10-K53M,K55M	102.3
10	Ala-Cpn10-K7R	113.5
25	Ala-Cpn10-K69R	105.8
37	Ala-Cpn10-Q3K	97.6
58	Ala-Cpn10-E18R	100.5
88	Ala-Cpn10-Q42K	109.7
91	Ala-Cpn10-T44K	106.3
94	Ala-Cpn10-S50K	108.6
121	Ala-Cpn10-D68K	6.2
130	X-Cpn10-Y75K	90.9
133	Ala- Cpn10-Y75H	81.1
136	Ala- Cpn10-Y75K	81.3
139	Ala- Cpn10-Y75R	92.3
181	Ala- Cpn10-D94K	97.4
193	Ala-Cpn10-D101K	103.3
217	Ala-Cpn10-E18K,D101K	97.2
220	Ala-Cpn10-E34Q,Y75K	91.5
223	Ala-Cpn10-Q42K,D101K	97.6
226	Ala-Cpn10-T44K,D101K	92.6
229	Ala-Cpn10-S50K,D101K	101.1
238	Ala- Cpn10-Y75GK	63.0
241	Ala- Cpn10-Y75G,G76K	62.0
244	Ala- Cpn10-Y75K,D94K	69.6
253	Ala-Cpn10-E18A	97.9
256	Ala-Cpn10-E18M	99.0
259	Ala-Cpn10-E18Q	99.0
262	Ala-Cpn10-E18S	93.5
274	Ala-Cpn10-D68N	81.8
280	Ala-Cpn10-D83N	98.1
283	Ala-Cpn10-D84N	95.8
298	Ala-Cpn10-D94N	88.2
304	Ala-Cpn10-D101N	104.3
307	MH-Cpn10	96.7
310	MR-Cpn10	103.6
313	MK-Cpn10	88.6
316	MKK-Cpn10	95.9
319	MKKK-Cpn10	98.8
328	Ala-Cpn10-K39	113.4
331	Ala-Cpn10-KK39	90.1
343	Ala-Cpn10-K85	63.1
346	Ala-Cpn10-KK85	35.7
349	Ala-Cpn10-K102	115.5
352	Ala-Cpn10-KK102	95.9
355	Covalent Cpn10	81.6

Example 3: Cpn10 mutants bind to poly(I:C), CpG-ODNs and RNA

TLRs are expressed both extra- and intracellularly, those on the cell surface (TLR1, TLR2, TLR4, TLR5, TLR6, TLR10 and TLR11) generally recognize hydrophobic ligands while those in intracellular compartments (TLR3, TLR7, TLR8 and TLR9) generally recognize negatively charged nucleic acid based ligands (Akira et al. 2006, 124: 783-801).

As described herein, the inventors have shown that Ala-Cpn10 binds negatively charged nucleic acid based TLR ligands, these include poly(I:C) (TLR3 agonists) as shown in Figure 4, several classes of unmethylated single-stranded CpG-oligonucleotides (ODN) as shown in Figures 5 and 7 (human ODN-2216 class A, human ODN-2006 class B, human ODN-M362 class C; all TLR9 agonists) and *E.coli* K12 ssRNA (TLR7/8 ligand) as shown in Figure 6.

As described below, the inventors have additionally shown that a number of mutants bind more tightly to poly(I:C) (Fig. 4), CpG-ODNs (Fig. 5) and ssRNA (Fig.6) than Ala-Cpn10.

In relation to Fig 4, mutants such as Ala-Cpn10-E18A, Ala-Cpn10-E34Q, Ala-Cpn10-D68N, Ala-Cpn10-D83N, Ala-Cpn10-D94N, Ala-Cpn10-Y75R, Ala-Cpn10-E18K,D101K, Ala-Cpn10-E34Q,Y75K, Ala-Cpn10-Q42,D101K, Ala-Cpn10-T44K,D101K, Ala-Cpn10-S50K,D101K, Ala-Cpn10-E74K,Y75E, Ala-Cpn10-Y75G,G76K, Ala-Cpn10-Y75GK, Ala-Cpn10-Y75K,D94K, Ala-Cpn10-Q3K, Ala-Cpn10-S50K, Ala-Cpn10-D68K, Ala-Cpn10-D94K, Ala-Cpn10-D101K, , Covalent-Cpn10, MR-Cpn10 and MKKK-Cpn10 bind polyI:C more tightly than Ala-Cpn10. Furthermore, several mutants such as X-Cpn10-Y75K and Ala-Cpn10-Y75K bind so tightly to TLR3 agonist poly(I:C) that it cannot be fully released with 500mM NaCl, unlike Ala-Cpn10 which is dissociated at 150mM NaCl (Fig. 4). Intriguingly, at low NaCl concentrations many Cpn10 variants bind the long polymers of poly(I:C) in manner that sequesters them from ethidium bromide intercalation (Fig. 4), possibly indicating that several Cpn10 heptamers bind a single poly(I:C) chain. Several mutants including Ala-Cpn10-Y75K, Ala-Cpn10-KK21, Ala-Cpn10-D94N and Ala-Cpn10-Y75K,D94K also sequester bound poly(I:C) from ethidium bromide intercalation at low salt concentrations but at ≥150 mM the binding site is opened enough for ethidium bromide intercalation without escape of the bound poly(I:C).

Like the interaction with poly(I:C), an unstable complex of X-Cpn10 and Ala-Cpn10 with the TLR9 agonist CpG-class A was observed at physiological salt concentrations (~150mM) (Fig. 5). In contrast, the inventors observed that like the interaction with poly(I:C) a significantly stronger association was formed between several Cpn10 variants and CpG-class A (Fig. 4 and 5). In fact, the complexes with CpG-class A were mostly resistant to dissociation at 500mM NaCl (Fig. 5). In

regards to the TLR7 and TLR8 agonist *E.coli* K12 ssRNA, experiments also show a stronger association was formed with many Cpn10 variants such as Ala-Cpn10-Y75K, Ala-Cpn10-KK21, Ala-Cpn10-D94N and Ala-Cpn10-Y75K,D94K compared with Ala-Cpn10 (Fig. 6). At 150mM NaCl Ala-Cpn10 and X-Cpn10 are completely dissociated from ssRNA. However, several mutants remain firmly bound in the presence of 500 mM NaCl.

Example 4: Quantitative analysis of Cpn10 binding to CpG oligonucleotides (ODNs)

To determine the amount of binding of the Cpn10 mutants to ODNs, the mutants were formulated at 10µg/µl in PBS pH7.2 (Invitrogen) and 50µg was adsorbed to triplicate wells of a 96 well plate 16 hr at 4°C. Following the decanting of non-bound protein, the plate was blocked with 1% BSA and 5% sucrose in PBS pH7.2 for 2hr at 23°C. 50µl of 3'-biotin labeled human ODN-2216 class-A, human ODN-2006 class-B, or human ODN-M362 class-C (TLR9 agonists) (Proligo/Sigma) formulated at 0.01 µg/µl in PBS pH 7.2 was added to each well and incubated for 2hr at 23°C. Unbound ligand was removed with five PBS (pH7.2) + 0.05% Tween 20 washes. Bound CpG-ODNs were analysed with a Streptavidin-HRP and TMB detection system at A450nm.

In Figure 7 a quantitative analysis at physiological salt concentrations (~150mM) highlights the significantly stronger interaction of CpG-classes A, B and C with a number of mutants compared to Ala-Cpn10.

Cpn10 mutants containing positive substitutions (Q3K, E18K, Q42K, T44K, S50K, D86K and D101K) were made and tested had significantly improved affinities for CpG-ODN classess-A\B\C compared to Ala-Cpn10.

All of the negative to neutral substitutions studied (E18Q, E18A, E18S, E18M, D68N, D83N and D101N) had significantly improved affinities for CpG-ODN classess-A\B\C compared to Ala-Cpn10.

With regard to the multiple positive substitution Cpn10 mutants, quantitative analysis of binding to CpG-ODN classess-A\B\C confirmed that all have significantly improved affintity, such as Ala-Cpn10-Y75K,D94K and Ala-Cpn10-E34Q,Y75K compared to Ala-Cpn10(Figure 7).

All of the positive insertions (lengthening) Cpn10 mutants studied, for example MK-Cpn10 and Ala-Cpn10-K85, had significantly improved affinities for \CpG-ODN classes-A/B/C compared to Ala-Cpn10.

Example 5: Cpn10 modulates CpG-B ODN-induced NFκB activity.

In order to establish whether high affinity binding of PRR ligands could be correlated with increased immunomodulatory activity, several cell based assays were developed to assess the abilities of various Cpn10 mutants to sequestor proinflammatory nucleic acids and thereby reduced the level of PRR signaling. Firstly, high affinity binders compared to Ala-Cpn10 and X-Cpn10 where incubated with CpG-ODN class B and the unbound PRR ligand was used to stimulate NFκB in mouse macrophages (RAW264 cells).

RAW264.7 (mouse macrophage) cells were stably transfected with an NFκB-luciferase reporter plasmid (pNIFty2-LUC; Invivogen). RAW264-pNIFty2-LUC cells were plated out and left to adhere overnight. 100µg of a Cpn10 construct or Formulation buffer control was mixed with 4 µg of CpG-B ODN-1826 (Invivogen) and passed through a centrifugal filter device YM10 (Amicon). The entire flow through volume was added to the RAW264-pNIFty2-LUC cells and incubated at 37°C for 5 hours. Cells were washed and subsequently lysed with 100 µl per well of CCLR 1X solution (Promega luciferase lysis buffer), mixed with luciferase substrate following the manufactures instructions and the luciferase counts measured.The level of activation of TLR9 for Ala-Cpn10 was assigned the value of 100%.

Figure 8 shows a tight correlation between high affintiy binders and reduced NFκB levels compared to Ala-Cpn10. It can be seen from Figure 8 that isolated Cpn10 polypeptides comprising one or more amino acid substitutions, deletions and/or additions such as Ala-Cpn10-Y75K, Ala-Cpn10-E18A, , Ala-Cpn10-Y75K,D94K, Ala-Cpn10-E34Q,Y75K, Ala-Cpn10-Q3K, Ala-Cpn10-E18K,D101K and MKK-Cpn10 result in lower levels of activation of TLR9 than for Ala-Cpn10.

Example 6: Cpn10 mutants inhibit poly(I:C)-induced NFκB production through TLR-3 in HEK293 cells

HEK293 cells were transiently transfected with TLR3 and the pNIFTY-NFκB luciferase reporter gene. 24 hours post transfection cells were plated out into 24 well plates at 1 x 10^5 and left to adhere overnight. Cells were then stimulated for 18 hours with 0.1 ug poly(I:C) in the presence or absence of 100ug the Cpn10 mutants and 10ul of SUPERase RNAse inhibitor (Ambion) as a competition assay (Fig. 9). Poly(I:C) and Cpn10 were mixed together at the required concentrations for 30 mins before being added to the cells. Three replicates of each condition were tested. 18 hours post stimulation cells were lysed and luciferase counts were measured.

Luciferase counts were normalized to poly(I:C) alone, which was given the value of 100%. When the cells were stimulated with poly(I:C), Ala-Cpn10 was able to reduce the level of luciferase (ie NFκB) by 22%. Several of the mutants, Ala-Cpn10-Y75K, X-Cpn10-Y75K, Ala-Cpn10-D94K,Ala-Cpn10-Y75GK, Ala-Cpn10-E18K,D101K and Ala-Cpn10-E34Q,Y75K show significant modulation

of Poly(I:C) induced TLR3, with Ala-Cpn10-Y75K reducing signalling by 53%, X-Cpn10-Y75K reducing signalling by 71% and Ala-Cpn10-D94K reducing signalling by 82%, for example (fig. 9). This indicates that most of the Cpn10 mutants have the ability to modulate the immune system, particularly, when involving TLR3 signalling.

Example 7: Panel of Mutants

In applying the above methods and tests, the inventors produced a number of Cpn10 polypeptides with various mutations to assess the importance of various amino acid residues (e.g. such as charge and positioning in the Cpn10 molecule) in their ability to have an increased binding to a PRR ligand, such as poly(I:C) and several classes of ODNs compared to such Cpn10 molecules as X-Cpn10 and Ala-Cpn10.

The inventors have substituted at least one of amino acid residue in each of the N-terminus, β-barrel, mobile loop, roof loop, C-terminus and connective loops of the Cpn10 molecule as shown in the Table 1. The inventors have either replaced a neutral amino acid residue with a positively charged residue, replaced a negatively charged amino acid residue with a neutral or positively charged residue, positively charged residue with another positively charged residue, inserted positively charged residues, or deleted negatively charged residues.

Table 2: Panel of Cpn10 Mutations

Region of Mutation	Residue number (residues with surface exposed side-chains)	Amino acid	*Mutation(s)*
N-terminus	1	A	K, R, H
	2	G	K, R, H
	3	Q	K, R, H
	4	A	K, R, H
	5	F	K, R, H
	6	R	K, H
	7	K	R, H
β-barrel (β-1)	9	L	K, R, H
	12	F	K, R, H
	13	D	K, R, H, G, A, V, L, I, P,

			F, Y, W, C, M, S, T, N, Q
	14	R	K, H
	16	L	K, R, H
	18	E	K, R, H, G, A, V, L, I, P, F, Y, W, C, M, S, T, N, Q
	19	R	K, H
	20	S	K, R, H
Mobile loop	21	A	K, R, H
	22	A	K, R, H
	23	E	K, R, H, G, A, V, L, I, P, F, Y, W, C, M, S, T, N, Q
	24	T	K, R, H
	25	V	K, R, H
	26	T	K, R, H
	27	R	K, H
	28	G	K, R, H
	29	G	K, R, H
	30	I	K, R, H
	31	M	K, R, H
	32	L	K, R, H
	33	P	K, R, H
	34	E	K, R, H, G, A, V, L, I, P, F, Y, W, C, M, S, T, N, Q
	35	K	R, H
	36	S	K, R, H
	37	Q	K, R, H
	38	G	K, R, H
Connective loop 1 (L-1)	39	K	R, H
	40	V	K, R, H
β-barrei (β-2)	41	L	K, R, H
	42	Q	K, R, H
	44	T	K, R, H
	46	V	K, R, H

	50	S	K, R, H
Roof loop	52	S	K, R, H
	53	K	R, H
	54	G	K, R, H
	55	K	R, H
	56	G	K, R, H
	57	G	K, R, H
	58	E	K, R, H, G, A, V, L, I, P, F, Y, W, C, M, S, T, N, Q
	59	I	K, R, H
	60	Q	K, R, H
	61	P	K, R, H
	62	V	K, R, H
β-barrel (β-3)	63	S	K, R, H
	65	K	R, H
	66	V	K, R, H
	67	G	K, R, H
	68	D	K, R, H, G, A, V, L, I, P, F, Y, W, C, M, S, T, N, Q
	69	K	R, H
	73	P	K, R, H
Connective loop 2 (L-2)	74	E	K, R, H, G, A, V, L, I, P, F, Y, W, C, M, S, T, N, Q G
	75	Y	G, GK, K, R, H, D, E,Q
	76	G	K, R, H, D, E, N ,Q, S, T
β-barrel (β-4)	77	G	K, R, H
	78	T	K, R, H
	79	K	R, H
Connective loop 3 (L-3)	81	V	K, R, H
	83	D	K, R, H, G, A, V, L, I, P, F, Y, W, C, M, S, T, N, Q
	84	D	K, R, H, G, A, V, L, I, P,

			F, Y, W, C, M, S, T, N, Q
β-barrel (β-5)	85	K	R, H
	86	D	K, R, H, G, A, V, L, I, P, F, Y, W, C, M, S, T, N, Q
	87	Y	K, R, H
	88	F	K, R, H
	89	L	K, R, H
	91	R	K, H
	92	D	K, R, H, G, A, V, L, I, P, F, Y, W, C, M, S, T, N, Q
	93	G	K, R, H
	94	D	K, R, H, G, A, V, L, I, P, F, Y, W, C, M, S, T, N, Q,
	96	L	K, R, H
	98	K	R, H
	100	V	K, R, H
C-terminus	101	D	K, R, H, G, A, V, L, I, P, F, Y, W, C, M, S, T, N, Q

In addition to single substitution mutations, the inventors have produced Cpn10 polypeptides with any combination of two or more of the above mutations such as double mutants (e.g. Ala-Cpn10-F12K,D92K, Ala-Cpn10-E18K,D101K, Ala-Cpn10-E34Q,Y75K, Ala-Cpn10-Q42K,D101K, Ala-Cpn10-T44K,D101K, Ala-Cpn10-S50K,D101K, Ala-Cpn10-Q60K,T78K, Ala-Cpn10-E74K,Y75E, Ala-Cpn10-Y75GK, Ala-Cpn10-Y75G,G76K, Ala-Cpn10-Y75K,D94K and Ala-Cpn10-Y75K,D94N. Furthermore, the inventors have produced positive insertion (lengthening) and negative deletion (removal) Cpn10 variants (e.g. MH-Cpn10, MR-Cpn10, MK-Cpn10, MKK-Cpn10, MKKK-Cpn10, Ala-Cpn10-K21, Ala-Cpn10-KK21, Ala-Cpn10-K39, Ala-Cpn10-KK39, Ala-Cpn10-K57, Ala-Cpn10-KK57, Ala-Cpn10-K76, Ala-Cpn10-KK76, Ala-Cpn10-K85, Ala-Cpn10-KK85, Ala-Cpn10-K102, Ala-Cpn10-KK102, deltaD13, deltaE18, deltaE23, deltaE34, deltaE58, deltaE68, deltaE74, deltaD83, deltaD84, deltaD86, deltaD92, deltaD94 and deltaD101).

It is contemplated herein that any combination of the above mutations that results in the creation of additional double mutants, triple mutants, and so on, are within the scope of the invention.

Example 8: Calculation of net charge of Cpn10 polypeptides

Calculation of Protein Net Charge

As described above the net charge of a polypeptide at a given pH is calculated on the basis of the Henderson-Hasselbalch equation (Hasselbalch, K. A., 1917 *Biochemische Zeitschrift* **78**: 112–144) and known pKa values of ionisable amino acid side chains and the N- and C-termini of a polypeptide. The pKa values utilised in Table 3 are N-terminus 8.0, C-terminus 3.1, Lys 10.0, Arg 12.0, His 6.5, Glu 4.4, Asp 4.4, Tyr 10.0 and Cys 8.5 (Stryer, L., 1988 "Biochemistry" textbook 3rd Edition, New York, W.H. Freeman, ISBN 0716719207). Using the method described above the net charge of Cpn10 variants was calculated at pH 7.3 and pH7.4 (taken as physiological pH) as shown in Table 3.

Table 3: Calculated Net Charge values of Cpn10 Variants.

Cpn10 Protein SEQ ID		Net Charge at pH7.3	Net Charge at pH7.4
1	X-Cpn10	1.8	1.8
3	Ala-Cpn10	1.8	1.8
6	X-Cpn10-K53E	-0.2	-0.2
8	Ala-Cpn10-K53M,K55M	-0.2	-0.2
10	Ala-Cpn10-K7R	1.8	1.8
13	Ala-Cpn10-R19K	1.8	1.8
16	Ala-Cpn10-K27R	1.8	1.8
19	Ala-Cpn10-K39R	1.8	1.8
22	Ala-Cpn10-K55R	1.8	1.8
25	Ala-Cpn10-K69R	1.8	1.8
28	Ala-Cpn10-K85R	1.8	1.8
31	Ala-Cpn10-K98R	1.8	1.8
34	Ala-Cpn10-A1K	2.8	2.8
37	Ala-Cpn10-Q3K	2.8	2.8
40	Ala-Cpn10-Q3R	2.8	2.8
43	Ala-Cpn10-F5K	2.8	2.8
46	Ala-Cpn10-L9K	2.8	2.8
49	Ala-Cpn10-F12K	2.8	2.8
52	Ala-Cpn10-D13K	3.8	3.8
55	Ala-Cpn10-E18K	3.8	3.8
58	Ala-Cpn10-E18R	3.8	3.8
61	Ala-Cpn10-S20K	2.8	2.8
64	Ala-Cpn10-A22K	2.8	2.8
67	Ala-Cpn10-T24K	2.8	2.8
70	Ala-Cpn10-G29K	2.8	2.8
73	Ala-Cpn10-M31K	2.8	2.8
76	Ala-Cpn10-E34K	3.8	3.8
79	Ala-Cpn10-Q37K	2.8	2.8
82	Ala-Cpn10-V40K	2.8	2.8
85	Ala-Cpn10-L41K	2.8	2.8
88	Ala-Cpn10-Q42K	2.8	2.8
91	Ala-Cpn10-T44K	2.8	2.8
94	Ala-Cpn10-S50K	2.8	2.8

97	Ala-Cpn10-S50R	2.8	2.8
100	Ala-Cpn10-S52K	2.8	2.8
103	Ala-Cpn10-G54K	2.8	2.8
106	Ala-Cpn10-G56K	2.8	2.8
109	Ala-Cpn10-E58K	3.8	3.8
112	Ala-Cpn10-Q60K	2.8	2.8
115	Ala-Cpn10-P61K	2.8	2.8
118	Ala-Cpn10-V66K	2.8	2.8
121	Ala-Cpn10-D68K	3.8	3.8
124	Ala-Cpn10-P73K	2.8	2.8
127	Ala-Cpn10-E74K	3.8	3.8
130	X-Cpn10-Y75K	2.8	2.8
133	Ala- Cpn10-Y75H	2.0	1.9
136	Ala- Cpn10-Y75K	2.8	2.8
139	Ala- Cpn10-Y75R	2.8	2.8
142	Ala- Cpn10-G76K	2.8	2.8
145	Ala- Cpn10-G77K	2.8	2.8
148	Ala- Cpn10-T78K	2.8	2.8
151	Ala- Cpn10-V81K	2.8	2.8
154	Ala- Cpn10-D83K	3.8	3.8
157	Ala- Cpn10-D84K	3.8	3.8
160	Ala- Cpn10-D86K	3.8	3.8
163	Ala- Cpn10-D86R	3.8	3.8
166	Ala- Cpn10-Y87K	2.8	2.8
169	Ala- Cpn10-F88K	2.8	2.8
172	Ala- Cpn10-L89K	2.8	2.8
175	Ala- Cpn10-D92K	3.8	3.8
178	Ala- Cpn10-G93K	2.8	2.8
181	Ala- Cpn10-D94K	3.8	3.8
184	Ala- Cpn10-D94R	3.8	3.8
187	Ala- Cpn10-L96K	2.8	2.8
190	Ala- Cpn10-V100K	2.8	2.8
193	Ala-Cpn10-D101K	3.8	3.8
196	Ala- Cpn10-D101R	3.8	3.8
199	Ala- Cpn10-ΔE23	2.8	2.8
202	Ala- Cpn10-ΔE34	2.8	2.8
205	Ala- Cpn10-ΔE58	2.8	2.8
208	Ala- Cpn10-ΔE74	2.8	2.8
211	Ala- Cpn10-ΔD84	2.8	2.8
214	Ala- Cpn10-F12K,D92K	4.8	4.8
217	Ala-Cpn10-E18K,D101K	5.8	5.8
220	Ala-Cpn10-E34Q,Y75K	3.8	3.8
223	Ala-Cpn10-Q42K,D101K	4.8	4.8
226	Ala-Cpn10-T44K,D101K	4.8	4.8
229	Ala-Cpn10-S50K,D101K	4.8	4.8
232	Ala-Cpn10-Q60K,T78K	3.8	3.8
235	Ala-Cpn10-E74K,Y75E	2.8	2.8
238	Ala- Cpn10-Y75GK	2.8	2.8
241	Ala- Cpn10-Y75G,G76K	2.8	2.8
244	Ala- Cpn10-Y75K,D94K	4.8	4.8
247	Ala-Cpn10-Y75K,D94N	3.8	3.8
250	Ala-Cpn10-D13N	2.8	2.8
253	Ala-Cpn10-E18A	2.8	2.8
256	Ala-Cpn10-E18M	2.8	2.8
259	Ala-Cpn10-E18Q	2.8	2.8
262	Ala-Cpn10-E18S	2.8	2.8
265	Ala-Cpn10-E23Q	2.8	2.8

268	Ala-Cpn10-E34Q	2.8	2.8
271	Ala-Cpn10-E58Q	2.8	2.8
274	Ala-Cpn10-D68N	2.8	2.8
277	Ala-Cpn10-E74Q	2.8	2.8
280	Ala-Cpn10-D83N	2.8	2.8
283	Ala-Cpn10-D84N	2.8	2.8
286	Ala-Cpn10-D86N	2.8	2.8
289	Ala-Cpn10-D92N	2.8	2.8
292	Ala-Cpn10-D94A	2.8	2.8
295	Ala-Cpn10-D94M	2.8	2.8
298	Ala-Cpn10-D94N	2.8	2.8
301	Ala-Cpn10-D94S	2.8	2.8
304	Ala-Cpn10-D101N	2.8	2.8
307	MH-Cpn10	2.0	1.9
310	MR-Cpn10	2.8	2.8
313	MK-Cpn10	2.8	2.8
316	MKK-Cpn10	3.8	3.8
319	MKKK-Cpn10	4.8	4.8
322	Ala-Cpn10-K21	2.8	2.8
325	Ala-Cpn10-KK21	3.8	3.8
328	Ala-Cpn10-K39	2.8	2.8
331	Ala-Cpn10-KK39	3.8	3.8
334	Ala-Cpn10-K57	2.8	2.8
337	Ala-Cpn10-KK57	3.8	3.8
340	Ala-Cpn10-K76	2.8	2.8
343	Ala-Cpn10-K85	2.8	2.8
346	Ala-Cpn10-KK85	3.8	3.8
349	Ala-Cpn10-K102	2.8	2.8
352	Ala-Cpn10-KK102	3.8	3.8
355	Covalent Cpn10	(13.8÷7) 2.0	(13.6÷7) 1.9

Net Charge values were calculated at physiological pH (pH 7.3 to 7.4) using the Protein Calculator V3.3 tool (http://www.scripps.edu/~cdputnam/protcalc.html).

Example 9: Summary

The inventors have previously discovered that Cpn10 modulates several Pathogen Recognition Receptors (PRRs) and have recently shown its efficacy and safety in the treatment of human patients with rheumatoid arthritis (Vanags et al. *Lancet* 2006; 368: 855–863) and psoriasis (Williams et al. *Arch. Dermatol.* 2008; 144: 683-685) . The inventors now show that variants of Cpn10 binds specifically to several nucleic acid-based PRR ligands.

The addition of extra positive charge, through adding positive or removing negative residues generates a Cpn10 molecule which binds significantly stronger (compared to Ala-Cpn10 and X-Cpn10) to nucleic acid-based PRR ligands. Extra positive charge could be added by (1) substituting an existing surface/solution exposed neutral or negative residue for a positive residue, (2) substituting an existing surface/solution exposed negative residue for a neutral residue, (3) introducing an additional surface/solution exposed positive residues (eg lengthen a loop structure or the N-terminus and C-terminus) or (4) deleting an existing surface/solution exposed negative

residue (eg shortening a loop structure or the N-terminus and C-terminus). Our results also show that introducing multiple positive charges (eg Ala-Cpn10-F12K,D92N; E18K,D101K; E34Q,Y75K; Q42K,D101K; T44K,D101K; S50K,D101K; Q60K,T78K; E74K,Y75E; Y75GK; Y75G,G76K; Y75K,D94K; Y75K,D94N) may increase the binding potential significantly greater than the individual mutations.

The effect of substituting pre-existing neutral and negative residues with either Lysine (K) or Arginine (R) residues was examined. All of the positive substitutions studied (A1K, Q3K, Q3R, F5K, D13K, E18K, E18R, S20K, A22K, T24K, G29K, M31K, E34K, Q37K, V40K, L41K, Q42K, T44K, S50K, S50R, S52K, G54K, G56K, E58K, Q60K, P61K, V66K, D68K, P73K, E74K, Y75K, Y75H, Y75R, G76K, G77K, T78K, V81K, D83K, D84L, D86K, D86R, Y87K, F88K, L89K, D92K, G93K, D94K, D94R, L96K, V100K, D101K and D101R; SEQ ID Nos: 34-45 and 52-198) had significantly improved affinities for poly(I:C), E.coli K12 ssRNA and several CpG-ODN classess-A\B\C compared to Ala-Cpn10 (Figures 4 to 9).

The effect of substituting pre-existing negative residues (ie E and D) with neutral residues (eg N, Q, G, A, V, L, I, P, F, Y, W, C, M, S, T, H) was also examined. Again, all of the negative to neutral substitutions studied (D13N, E18A, E18M, E18Q, E18S, E23Q, E34Q, E58Q, D68N, E74Q, D83N, D84N, D86N, D92N, D94A, D94M, D94N, D94S and D101N; SEQ ID Nos: 250-306) had significantly improved affinities for poly(I:C), E.coli K12 ssRNA and several CpG-ODN classess-A\B\C compared to Ala-Cpn10 (Figures 4 to 9).

To examine whether the addition of multiple positive charges would provide tigher binding, several variants were prepared (ieg E18K/D101K, Q42K/D101K, T44K/D101K and S50K/D101K; SEQ ID Nos: 217-231). As expected, high affintiy binding was observed to all nucleic acid-based PRR ligands (Figures 4 to 9). As outlined above positive charge can be added to Cpn10 by replacement of existing neutral or negative residues with positive residues (K,R,H) and negative residues with neutral residues. Another way to add positive charge is to insert positive residue (K,R,H) at positions in Cpn10 that would tolerate such structural changes. Each Cpn10 subunit is formed from 101 amino acid which folds into a discontinuous β-barrel structure connected by 3 small loops and 2 larger β-hairpin turn loops (Figure 1). The β-barrel structure provides all of the subunit-subunit interactions and the Cpn10 heptamer's stability. Lengthening segments of the β-barrel would probably lead to structural instability. In comparison lengthening the N-terminus, C-terminus or several connective loops would probably tolerate such structural changes better. In agreement with this prediction, several Cpn10 homologous have naturally extended segments (Figure 2). For example, Bacteriophage T4 Cpn10 (Gp31) has a significantly lengthened mobile loop and L-3 loop. Mosquito, Fly and Mycobacterial Cpn10 have lengthened roof loops while

numerous Cpn10s contain longer N- and C-termini. Positive residues were successfully inserted into each of the 5 connective loops (ie L-1, L-2, L-3, mobile loop and roof loop), the N-terminus and C-terminus as shown in Table 4.

Table 4. Positive insertion (lengthening) Cpn10 variants

SEQ ID #	Mutant	Site of Lengthening
307	MH-Cpn10	N-terminus
310	MR-Cpn10	N-terminus
313	MK-Cpn10	N-terminus
316	MKK-Cpn10	N-terminus
319	MKKK-Cpn10	N-terminus
322	Ala-Cpn10-K21	mobile loop
325	Ala-Cpn10-KK21	mobile loop
328	Ala-Cpn10-K39	L1 connection loop
331	Ala-Cpn10-KK39	L1 connection loop
334	Ala-Cpn10-K57	roof loop
337	Ala-Cpn10-KK57	roof loop
340	Ala-Cpn10-K76	L2 connection loop
343	Ala-Cpn10-K85	L3 connection loop
346	Ala-Cpn10-KK85	L3 connection loop
349	Ala-Cpn10-K102	C-terminus
352	Ala-Cpn10-KK102	C-terminus

All of the positive insertion (lengthening) Cpn10 variants studied had significantly improved affinities for poly(I:C) and several CpG-ODN classess-A\B\C compared to Ala-Cpn10 (Figures 4 to 9; SEQ ID Nos: 307-354).

All Cpn10 variants with a single positive addition interact with E.coli K12 ssRNA and display higher affinities compared to Ala-Cpn10. Similarly, Cpn10 variants with multiple positive additions

(ie E18K/D101K, Q42K/D101K, T44K/D101K, S50K/D101K, MKK-Cpn10, MKKK-Cpn10, Ala-Cpn10-KK39, Ala-Cpn10-KK85 and Ala-Cpn10-KK102) have an improved affinity for E.coli K12 ssRNA compared to Ala-Cpn10 (Figure 6). Net positive charge can be increased by substituting negative residues with neutral or positive residues. Another possibility is to remove the negative residues completely. As discussed above, numerous Cpn10 homologous have naturally extended and also shortened connective loops (ie L-1, L-2, L-3, mobile loop and roof loop). Removal of negative residues at positions 23, 34, 58, 74 and 84 (SEQ ID Nos: 199-213) demonstrates that these Cpn10 variants have increased affinity for nucleic acid based PRR ligands. Negative residues D68, D84 and D101 could also be deleted without compromising the structural integrity of Cpn10 and that these variants are envisaged to also be high affinity binders.

In order to establish whether high affinity binding of PRR ligands could be correlated with increased immunomodulatory activity, several cell based assays were developed to assess the abilities of various Cpn10 mutants to sequestor proinflammatory nucleic acids and thereby reduced the level of PRR signaling. Firstly, high affinity binders compared to Ala-Cpn10 were incubated with CpG-ODN class B and the unbound PRR ligand was used to stimulate NFκB in mouse macrophages (RAW264 cells). Figure 8 shows a tight correlation between high affinity binders and reduced NFκB levels compared to Ala-Cpn10. Likewise, mutants with compromised affinities for PRR ligands, such as X-Cpn10-K53E and Ala-Cpn10-K53M,K55M, had an increased level of NFκB activation compared to Ala-Cpn10. In order to test the biological activities of high affinity binders on cells, Cpn10 variants were next assessed for their abilities to reduce proinflammatory NFκB activation (from HEK cells expressing TLR3) when stimulated with poly(I:C). In this system the high affinity binders (eg Ala-Cpn10-D101K) generally showed significantly improved ability to inhibit NFκB activation compared to Ala-Cpn10 (Figures 7 + 9). Replacement of a positively charged residue with another positively charged residue (eg K7R, R19K, K27R, K39R, K55R, K69R, K85R and K98R; SEQ ID Nos: 10-33) has no significant effect on the ability of such Cpn10 variants to bind pro-inflammatory nucleic acids compared to Ala-Cpn10 (Figure. 8).

It is demonstrated herein that the isolated Cpn10 polypeptides with the mutations described above and throughout the specification possess an increased affinity for nucleic acid-based PRR ligands, in particular the TLR-3 agonist poly(I:C), TLR7 and TLR8 agonist E.coli ssRNA and TLR9 agonists unmethylated CpG-oligonucleotides (ODNs) (ODN-2216 class A, ODN-2006 class B and ODN-M362 class C). It is also demonstrated herein that these Cpn10 polypeptides inhibit poly(I:C) and CpG induced NFkB activation

Conclusions

The data contained herein reveals that the Cpn10 mutants as listed under Example 8 with an increased affinity for nucleic acid-based ligands of PRRs can be generated by adding positively charged or deleting negatively charged residues, by substituting negatively charged residues for neutral or positively charged residues or by substituting neutral residues for positively charged residues within the Cpn10 molecule. For example, the inventors have identified that Ala-Cpn10-Y75K, as well as many other Cpn10 mutants, had significantly improved affinity for poly(I:C), CpG-ODN classess-A\B\C and E.coli K12 ssRNA compared to Ala-Cpn10 (Figures 4 to 7) which can be attributed to increasing the net positive charge of the Cpn10 molecule through amino acid substitutions, deletions, and/or insertions.

Furthermore, the inventors have found that high affinity binding to nucleic acid-based ligands of PRRs can be achieved by introducing positive charge at several locations within the Cpn10 molecule. The increased affinity of the polypeptides of the invention to a nucleic acid-based PRR ligand is indicative of increased immunomodulatory activity.

1. An isolated chaperonin 10 polypeptide possessing an increased affinity for a pattern recognition receptor ligand compared to Ala-chaperonin 10 polypeptide.

2. The polypeptide of claim 1, wherein said pattern recognition receptor ligand modulates the signalling of pattern recognition receptors selected from the group consisting of a Toll-like Receptor (TLR), Nucleotide-binding domain LRR-containing family (NLR), a RIG-I-like receptor (RLR), a DNA-dependent activator of IRF (DAI), a C-type Lectin receptor (CLR) or a member of the IFI20X/IFI16 family (e.g. Ifi16, Aim2, MNDA and IFIX).

3. The polypeptide of claim 2, wherein said TLR is selected from the group consisting of at least one of TLR3, TLR7, TLR8 or TLR9.

4. The polypeptide of any one of claims 1 to 3, wherein said polypeptide possesses a greater net positive charge compared to the Ala-chaperonin 10 polypeptide.

5. The polypeptide of claim 4, wherein said polypeptide possesses at least one mutation of Ala-chaperonin 10 molecule wherein said mutation is an amino acid substitution, addition or deletion.

6. The polypeptide of claim 5, wherein said mutation is the replacement of one or more amino acid residues with one or more positively charged residues or neutral residues.

7. The polypeptide of claim 5, wherein said mutation is the replacement of one or more amino acid residues with one or more neutral residues.

8. The polypeptide of claim 6, wherein said positively charged residue is selected from the group comprising an arginine (R), lysine (K) and histidine (H).

9. The polypeptide of claim 7, wherein said neutral residue is selected from the group comprising asparagine (N), glutamine (Q), serine (S), threonine (T), glycine (G), alanine (A), valine (V), leucine (L), isoleucine (I), proline (P), phenylalanine (F), tyrosine (Y), tryptophan (W), cysteine (C), methionine (M) and histidine (H).

10. The polypeptide of any one of claims 6 to 9, wherein said mutation is a mutation in either the mobile loop, or the roof loop, or at a position wherein a residue has an exposed free side chain either within the inner surface or the outer surface of the chaperonin 10 molecule, or a combination thereof.

11. The polypeptide of any one of claims 5 to 10, wherein said polypeptide comprises a mutation at an amino acid position selected from the group consisting of position 1-7, 9, 12-14, 16, 18-42, 44, 46, 50, 52-63, 65-69, 73-79, 81, 83-89, 91 to 94, and 96, 98, 100, 101 of said wild-type chaperonin 10 molecule or a combination thereof.

12. The polypeptide of any one of claims 1 to 11, wherein said polypeptide comprises a mutation selected from the group consisting of A1(K, R or H), G2(K, R or H), Q3(K, R or H), A4(K, R or H), F5(K, R or H), R6(K or H), K7(R or H), L9(K, R or H), F12(K, R or H), D13(K, R, H, N, Q, G, A, V, L, I, P, F, Y, W, C, M, S or T), R14 (K or H), L16(K, R or H), E18(K, R, H, N, Q, G, A, V, L, I,

P, F, Y, W, C, M, S or T), R19(K or H), S20(K, R or H), A21(K, R or H), A22 (K, R or H), E23(K, R, H, N, Q, G, A, V, L, I, P, F, Y, W, C, M, S or T), T24(K, R or H), V25(K, R or H), 726(K, R or H), R27(K or H), G28(K, R or H), G29(K, R or H), 130(K, R or H), M31(K, R or H), L32(K, R or H), P33(K, R or H), E34(K, R, H, N, Q, G, A, V, L, I, P, F, Y, W, C, M, S or T), K35(R or H), S36(K, R or H), Q37(K, R or. H), G38(K, R or H), K39(K, R or H), V40(K, R or H), L41(K, R or H), Q42(K, R or H), T44(K, R or H), V46(K, R or H), S50(K, R or H), S52(K, R or H), K53(R or H), G54(K, R or H), K55(R or H), G56(K, R or H), G57(K, R or H), E58(K, R, H, N, Q, G, A, V, L, I, P, F, Y, W, C, M, S or T), 159(K, R or H), Q60(K, R or H), P61(K, R or H), V62(K, R or H), S63(K, R or H), K65(R or H), V66(K, R or H), G67(K, R or H), D68(K, R, H, N, Q, G, A, V, L, I, P, F, Y, W, C, M, S or T), K69(R or H), P73(K, R or H), E74(K, R, H, N, Q, G, A, V, L, I, P, F, Y, W, C, M, S or T), Y75(GK, K, R, H, E), G76(K, R or H), G77(K, R or H), T78(K, R or H), K79(R or H), V81(K, R or H), D83(K, R, H, N, Q, G, A, V, L, I, P, F, Y, W, C, M, S or T), D84(K, R, H, N, Q, G, A, V, L, I, P, F, Y, W, C, M, S or T), K85(K, R or H), D86(K, R, H, N, Q, G, A, V, L, I, P, F, Y, W, C, M, S or T), Y87(K, R or H), F88(K, R or H), L89(K, R or H), R91(K or H), D92(K, R, H, N, Q, G, A, V, L, 1, P, F, Y, W, C, M, S or T), G93(K,. R or H), D94(K, R, H, N, Q, G, A, V, L, I, P, F, Y, W, C, M, S or T), L96(K, R or H), K98(R or H), V100(K, R or H), D101(K, R, H, N, Q, G, A, V, L, I, P, F, Y, W, C, M, S or T), MH-chaperonin 10, MR-chaperonin 10, MK-chaperonin 10, MKK-chaperonin 10, MKKK-chaperonin 10, Ala- chaperonin 10-K21, Ala-chaperonin 10-KK21, Ala-chaperonin 10-K39, Ala- chaperonin 10-KK39, Ala-chaperonin 10-K57, Ala-chaperonin 10-KK57, Ala-chaperonin 10-K76, Ala-chaperonin 10-KK76, Ala-chaperonin 10-K85, Ala- chaperonin 10-KK85, Ala-chaperonin 10-K102, Ala-chaperonin 10-KK102, deltaD13, deltaE18, deltaE23, deltaE34, deltaE58, deltaE68, deltaE74, deltaD83, deltaD84, deltaD86, deltaD92, deltaD94 and deltaD101 or a combination thereof.

13. The polypeptide of any one of claims 1 to 12, wherein said polypeptide comprises a combination of two or more said mutations.

14. The polypeptide of claim 13, wherein said polypeptide comprises mutations selected from the group consisting of F12K,D92K; E18K,D101K; E34Q,Y75K; Q42K,D101K; T44K,D101K; S50K,D101K; Q60K,T78K; E74K,Y75E; Y75GK; Y75G,G76K; Y75K,D94K and Y75K,D94N.

15. The polypeptide of any one of claims 1 to 14, wherein said polypeptide lacks, or substantially lacks, the N-terminus, the mobile loop, the hairpin roof loop or a combination thereof.

16. The polypeptide of any of claims 1 to 15, wherein said polypeptide comprises an amino acid sequence selected from the group consisting of SEQ ID NOs 34, 37, 40, 43, 46, 49, 52, 55, 58, 61, 64, 67, 70, 73, 76, 79, 82, 85, 88, 91, 94, 97, 100, 103, 106, 109, 112, 115, 118, 121, 124, 127, 130, 133, 136, 139, 142, 145, 148, 151, 154, 157, 160, 163, 166, 169, 172, 175, 178, 181, 184, 187, 190, 193, 196, 199, 202, 205, 208, 211, 217, 220, 223, 226, 229, 232, 235, 238, 241, 244, 247, 250, 253, 256, 259, 262, 271, 274, 277, 280, 283, 286, 289, 292, 295, 298, 301, 304, 307, 310, 313, 316, 319, 322, 325, 328, 331, 334, 337, 340, 343, 346, 349, 352 or 355.

17. The polypeptide of any one of claims 1 to 15 wherein said polypeptide is human chaperonin 10.

18. An isolated nucleic acid encoding a polypeptide according to any one of claims 1 to 17.

19. An expression construct comprising a nucleic acid according to claim 18, wherein said construct is operably-linked to one or more regulatory sequences.

20. A host cell expressing a polypeptide according to any one of claims 1 to 17, or comprising a nucleic acid according to claim 18 or an expression construct according to claim 19.

21. An antibody that selectively binds to a polypeptide according to any one of claims 1 to 17.

22. A pharmaceutical composition comprising a polypeptide according to any one of claims 1 to 17 either alone or in combination with at least one nucleic acid based pattern recognition receptor ligand, a nucleic acid according to claim 18, an expression construct according to claim 19 or an antibody according to claim 21 or any combination thereof.

23. Use of an effective amount of a polypeptide according to any one of claims 1 to 17 either alone or in combination with at least one nucleic acid based pattern recognition receptor ligand, or a nucleic acid according to claim 18 or any combination thereof in the manufacture of a medicament for modulating

immune response in the subject, wherein said immune response is modulated via regulation of pattern recognition receptor signalling.

24. Use of an effective amount of a polypeptide according to any one of claims 1 to 17 either alone or in combination with at least one nucleic acid based pattern recognition receptor ligand, or a nucleic acid according to claim 18 or any combination thereof in the manufacture of a medicament for treating or preventing a disease, disorder or condition in a subject,

wherein said disease, disorder or condition is selected from: acute or chronic inflammatory diseases such as, insulin dependent diabetes mellitus, systemic lupus erythematosus, Sjogren's disease, Graves disease, multiple sclerosis, rheumatoid arthritis, chronic fatigue syndrome, Alzheimer's disease, asthma, allergy, GVHD1 atherosclerosis, inflammatory pain, psoriasis, HIV, Chronic immune activation, chronic myositis, scleroderma; or cancers such as, non-small cell lung carcinoma, renal cell carcinoma, melanoma, non-Hodgkin's lymphoma, colorectal cancer, basal cell carcinoma; or an infectious disease that may be the result of a bacterial, viral or fungal infection.

25. Use of an effective amount of a polypeptide according to any one of claims 1 to 17 or a nucleic acid according to claim 18 or any combination thereof in the manufacture of a medicament for modulating pattern recognition receptor signalling in a subject, or in at least one cell, tissue or organ thereof.

26. Use of an effective amount of a polypeptide according to any one of claims 1 to 17 or a nucleic acid according to claim 18 or any combination thereof in the manufacture of a medicament for modulating the production and/or secretion of one or more immunomodulators in a subject, or at least one cell, tissue or organ thereof.

27. Use of an effective amount of a polypeptide according to any one of claims 1 to 17 or a nucleic acid according to claim 18 or any combination thereof in the manufacture of a medicament for inhibiting the production and/or secretion of one or more immunomodulators in a subject, or at least one cell, tissue or organ thereof.

28. The use of claim 26 or 27, wherein said immunomodulator is a pro-inflammatory cytokine or chemokine or an anti-inflammatory cytokine or chemokine, wherein said cytokine or chemokine is selected from TNF-α, IL-1α/β, IL-6, IL-10, IL-12, IL-17, IL-18, IL-23, RANTES, TGF-β or a type I interferon which may be IFN-α, IFN-β or IFN-γ.

29. An in vitro method of identifying a compound that binds to a polypeptide according to any one of claims 1 to 17, the method comprising the steps of:
(a) contacting a candidate compound with said polypeptide; and
(b) assaying for the formation of a complex between the candidate compound and said polypeptide.

30. The method of claim 29, wherein said assay is selected from the group comprising competitive binding assay, gel filtration chromatography, a two-hybrid assay, an electrophoretic mobility shift (gel-shift) assay and a plate capture assay.

31. An in vitro method of screening for a compound that modulates the activity of a polypeptide according to any one of claims 1 to 17, the method comprising the steps of:
(a) contacting said polypeptide with a candidate compound under conditions suitable to enable interaction of said candidate compound to said polypeptide; and
(b) assaying for activity of said polypeptide.

32. An in vitro method of screening for a pattern recognition receptor ligand, the method comprising the steps of:

(a) contacting a polypeptide according to any one of claims 1 to 17 with a candidate pattern recognition receptor ligand compound under conditions suitable to enable interaction of said candidate compound to said polypeptide; and

(b) assaying for increased affinity of said compound with said polypeptide compared to wild type chaperonin 10; and/or

(c) assaying for decreased or increased pattern recognition receptor activation in the presence of the candidate pattern recognition receptor ligand compound and said polypeptide.

33. A functional variant, derivative, homologue, analogue or fragment of the polypeptide according to any one of claims 1 to 17.

SEQUENCE LISTING

<110> CBio Limited

<120> Modified Cpn10 and PRR Signalling
<130> 875371C
<160> 356
<170> PatentIn version 3.5

<210> 1
<211> 101
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 produced in E.coli without N-terminal acetylation (X-Cpn10)
<400> 1
Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val Leu
1 5 10 15
Val Glu Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile Met Leu
20 25 30
Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val Ala Val 35
40 45
Gly Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln Pro Val Ser Val
50 55 60
Lys Val Gly Asp Lys Val Leu Leu Pro Glu Tyr Gly Gly Thr Lys Val
65 70 75 80
Val Leu Asp Asp Lys Asp Tyr Phe Leu Phe Arg Asp Gly Asp Ile Leu
85 90 95
Gly Lys Tyr Val Asp 100

<210> 2
<211> 309
<212> DNA
<213> Artificial Sequence
<220>
<223> Native cDNA (GenBank X75821; GI:509780)
<400> 2
atggcaggac aagcgtttag aaagtttctt ccactctttg accgagtatt ggttgaaagg
60
agtgctgctg aaactgtaac caaaggaggc attatgcttc cagaaaaatc tcaaggaaaa
120
gtattgcaag caacagtagt cgctgttgga tcgggttcta aaggaaaggg tggagagatt
180
caaccagtta gcgtgaaagt tggagataaa gttcttctcc cagaatatgg aggcaccaaa
240
gtagttctag atgacaagga ttatttccta tttagagatg gtgacattct tggaaagtac
300
gtagactga
309

<210> 3
<211> 102
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 produced in E.coli without the N-terminal acetylation. This protein contains an extra N-term Alanine Ala-Cpn10)
<400> 3
Ala Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val
1 5 10 15

Leu Val Glu Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile Met
20 25 30
Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val Ala 35
40 45
Val Gly Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln Pro Val Ser
50 55 60
Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu Tyr Gly Gly Thr Lys
65 70 75 80
Val Val Leu Asp Asp Lys Asp Tyr Phe Leu Phe Arg Asp Gly Asp Ile
85 90 95
Leu Gly Lys Tyr Val Asp 100

<210> 4
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA)
<400> 4
atggcagcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttgaa
60
aggagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccagaaaa atctcaagga
120
aaagtattgc aagcaacagt agtcgctgtt ggatcgggtt ctaaaggaaa gggtggagag
180
attcaaccag ttagcgtgaa agttggagat aaagttcttc tcccagaata tggaggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttagag atggtgacat tcttggaaag
300
tacgtagact ga
312

<210> 5
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA Ala-Cpn10
<400> 5
atggcagcag gccaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttgaa
60
cgcagtgctg ctgaaactgt aaccaaaggt ggcattatgc ttccagaaaa atctcaaggc
120
aaagtattgc aagcaacagt agtcgctgtt ggctcgggtt ctaaaggtaa gggtggcgag
180
attcaaccag ttagcgtgaa agttggcgat aaagttcttc tcccagaata tggtggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttcgtg atggtgacat tcttggcaag
300
tacgtagact aa
312

<210> 6
<211> 101
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 mutant with residue K53 changed to E53, this mutation changes a unique positive charge in the roof loops to a negative charge (X-Cpn10-K53E)
<400> 6

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

<210> 7
<211> 309
<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and with Lys (K) residue 53 changed to Glu (E)
<400> 7
atggcaggac aagcgtttag aaagtttctt ccactctttg accgagtatt ggttgaaagg
60
agtgctgctg aaactgtaac caaaggaggc attatgcttc cagaaaaatc tcaaggaaaa
120
gtattgcaag caacagtagt cgctgttgga tcgggttctg aaggaaaggg tggagagatt
180
caaccagtta gcgtgaaagt tggagataaa gttcttctcc cagaatatgg aggcaccaaa
240
gtagttctag atgacaagga ttatttccta tttagagatg gtgacattct tggaaagtac
300
gtagactga
309

<210> 8
<211> 102
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 mutant with residues K53 and K55 changed to M53 and M55 respectively, these mutations remove a unique cluster of positive charge at the tips of the roof loops. This construct contains an extra N-terminal Alanine residue
<400> 8
Ala Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val
1 5 10 15
Leu Val Glu Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile Met
20 25 30
Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val Ala 35
40 45
Val Gly Ser Gly Ser Met Gly Met Gly Gly Glu Ile Gln Pro Val Ser
50 55 60
Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu Tyr Gly Gly Thr Lys
65 70 75 80
Val Val Leu Asp Asp Lys Asp Tyr Phe Leu Phe Arg Asp Gly Asp Ile
85 90 95
Leu Gly Lys Tyr Val Asp 100

<210> 9
<211> 312

<212> DNA
<213> Artificial Sequence
<220>
<223> Native cDNA with extra N-terminal Alanine codon (GCA) and K53M,K55M mutations
<400> 9
atggcagcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttgaa
60
aggagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccagaaaa atctcaagga
120
aaagtattgc aagcaacagt agtcgctgtt ggatcgggtt ctatgggaat gggtggagag
180
attcaaccag ttagcgtgaa agttggagat aaagttcttc tcccagaata tggaggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttagag atggtgacat tcttggaaag
300
tacgtagact ga
312

<210> 10
<211> 102
<212> PRT
<213> Human
<220>
<221> MISC_FEATURE
<222> (8)..(8)
<223> where X is anyone of the following amino acids: Lys, Arg or His
<400> 10
Ala Ala Gly Gln Ala Phe Arg Xaa Phe Leu Pro Leu Phe Asp Arg Val
1 5 10 15
Leu Val Glu Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile Met
20 25 30
Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val Ala 35
40 45
Val Gly Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln Pro Val Ser
50 55 60
Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu Tyr Gly Gly Thr Lys
65 70 75 80
Val Val Leu Asp Asp Lys Asp Tyr Phe Leu Phe Arg Asp Gly Asp Ile
85 90 95
Leu Gly Lys Tyr Val Asp 100

<210> 11
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and K7R substitution
<400> 11
atggcagcag gacaagcgtt tagacgcttt cttccactct ttgaccgagt attggttgaa
60
aggagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccagaaaa atctcaagga
120
aaagtattgc aagcaacagt agtcgctgtt ggatcgggtt ctaaaggaaa gggtggagag
180
attcaaccag ttagcgtgaa agttggagat aaagttcttc tcccagaata tggaggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttagag atggtgacat tcttggaaag
300

tacgtagact ga
312

<210> 12
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA of Ala-Cpn10-K7R
<400> 12
atggcagcag gccaagcgtt tcgccgcttt cttccactct ttgaccgtgt attggttgaa
60
cgcagtgctg ctgaaactgt aaccaaaggt ggcattatgc ttccagaaaa atctcaaggc
120
aaagtattgc aagcaacagt agtcgctgtt ggctcgggtt ctaaaggtaa gggtggcgag
180
attcaaccag ttagcgtgaa agttggcgat aaagttcttc tcccagaata tggtggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttcgtg atggtgacat tcttggcaag
300
tacgtagact aa
312

<210> 13
<211> 102
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 with residue Arginine (K) 19 changed to Lysine (R)
19. This construct contains an extra N-terminal Alanine residue(Ala-
Cpn10-R19K)
<220>
<221> MISC_FEATURE
<222> (20)..(20)
<223> where X is anyone of the following amino acids: Lys, Arg or
His
<400> 13
Ala Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val
1 5 10 15
Leu Val Glu Xaa Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile Met
20 25 30
Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val Ala 35
40 45
Val Gly Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln Pro Val Ser
50 55 60
Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu Tyr Gly Gly Thr Lys
65 70 75 80
Val Val Leu Asp Asp Lys Asp Tyr Phe Leu Phe Arg Asp Gly Asp Ile
85 90 95
Leu Gly Lys Tyr Val Asp 100

<210> 14
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA)
and R19K substitution
<400> 14
atggcagcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttgaa
60

aaaagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccagaaaa atctcaagga
120
aaagtattgc aagcaacagt agtcgctgtt ggatcgggtt ctaaaggaaa gggtggagag
180
attcaaccag ttagcgtgaa agttggagat aaagttcttc tcccagaata tggaggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttagag atggtgacat tcttggaaag
300
tacgtagact ga
312

<210> 15
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA of Ala-Cpn10-R19K (Gly, Arg and stop codons are optimised in the cDNA)
<400> 15
atggcagcag gccaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttgaa
60
aaaagtgctg ctgaaactgt aaccaaaggt ggcattatgc ttccagaaaa atctcaaggc
120
aaagtattgc aagcaacagt agtcgctgtt ggctcgggtt ctaaaggtaa gggtggcgag
180
attcaaccag ttagcgtgaa agttggcgat aaagttcttc tcccagaata tggtggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttcgtg atggtgacat tcttggcaag
300
tacgtagact aa
312

<210> 16
<211> 102
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 with residue Lysine (K) 27 changed to Arginine (R) 27. This construct contains an extra N-terminal Alanine residue (Ala-Cpn10-K27R)
<220>
<221> MISC_FEATURE
<222> (28)..(28)
<223> where X is anyone of the following amino acids: Lys, Arg or His
<400> 16
Ala Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val
1 5 10 15
Leu Val Glu Arg Ser Ala Ala Glu Thr Val Thr Xaa Gly Gly Ile Met
20 25 30
Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val Ala 35
40 45
Val Gly Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln Pro Val Ser
50 55 60
Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu Tyr Gly Gly Thr Lys
65 70 75 80
Val Val Leu Asp Asp Lys Asp Tyr Phe Leu Phe Arg Asp Gly Asp Ile
85 90 95
Leu Gly Lys Tyr Val Asp 100

<210> 17

<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and K27R substitution
<400> 17
atggcagcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttgaa
60
aggagtgctg ctgaaactgt aacccgcgga ggcattatgc ttccagaaaa atctcaagga
120
aaagtattgc aagcaacagt agtcgctgtt ggatcgggtt ctaaaggaaa gggtggagag
180
attcaaccag ttagcgtgaa agttggagat aaagttcttc tcccagaata tggaggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttagag atggtgacat tcttggaaag
300
tacgtagact ga
312

<210> 18
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA of Ala-Cpn10-K27R (Gly, Arg and stop codons are optimised in the cDNA)
<400> 18
atggcagcag gccaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttgaa
60
cgcagtgctg ctgaaactgt aacccgcggt ggcattatgc ttccagaaaa atctcaaggc
120
aaagtattgc aagcaacagt agtcgctgtt ggctcgggtt ctaaaggtaa gggtggcgag
180
attcaaccag ttagcgtgaa agttggcgat aaagttcttc tcccagaata tggtggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttcgtg atggtgacat tcttggcaag
300
tacgtagact aa
312

<210> 19
<211> 102
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 with residue Lysine (K) 39 changed to Arginine (R) 39. This construct contains an extra N-terminal Alanine residue(Ala-Cpn10-K39R)
<220>
<221> MISC_FEATURE
<222> (40)..(40)
<223> where X is anyone of the following amino acids: Lys, Arg or His
<400> 19
Ala Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val
1 5 10 15
Leu Val Glu Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile Met
20 25 30
Leu Pro Glu Lys Ser Gln Gly Xaa Val Leu Gln Ala Thr Val Val Ala 35
40 45

Val Gly Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln Pro Val Ser
50 55 60
Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu Tyr Gly Gly Thr Lys
65 70 75 80
Val Val Leu Asp Asp Lys Asp Tyr Phe Leu Phe Arg Asp Gly Asp Ile
85 90 95
Leu Gly Lys Tyr Val Asp 100

<210> 20
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and K39R substitution
<400> 20
atggcagcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttgaa
60
aggagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccagaaaa atctcaagga
120
cgtgtattgc aagcaacagt agtcgctgtt ggatcgggtt ctaaaggaaa gggtggagag
180
attcaaccag ttagcgtgaa agttggagat aaagttcttc tcccagaata tggaggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttagag atggtgacat tcttggaaag
300
tacgtagact ga
312

<210> 21
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA of Ala-Cpn10-K39R (Gly, Arg and stop codons are optimised in the cDNA)
<400> 21
atggcagcag gccaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttgaa
60
cgcagtgctg ctgaaactgt aaccaaaggt ggcattatgc ttccagaaaa atctcaaggc
120
cgtgtattgc aagcaacagt agtcgctgtt ggctcgggtt ctaaaggtaa gggtggcgag
180
attcaaccag ttagcgtgaa agttggcgat aaagttcttc tcccagaata tggtggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttcgtg atggtgacat tcttggcaag
300
tacgtagact aa
312
<210> 22
<211> 102
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 with residue Lysine (K) 55 changed to Arginine (R) 55. This construct contains an extra N-terminal Alanine residue (Ala-Cpn10-K55R)
<220>
<221> MISC_FEATURE
<222> (56)..(56)

<223> where X is anyone of the following amino acids: Lys, Arg or His
<400> 22
Ala Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val
1 5 10 15
Leu Val Glu Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile Met
20 25 30
Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val Ala 35
40 45
Val Gly Ser Gly Ser Lys Gly Xaa Gly Gly Glu Ile Gln Pro Val Ser
50 55 60
Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu Tyr Gly Gly Thr Lys
65 70 75 80
Val Val Leu Asp Asp Lys Asp Tyr Phe Leu Phe Arg Asp Gly Asp Ile
85 90 95
Leu Gly Lys Tyr Val Asp 100

<210> 23
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and K55R substitution
<400> 23
atggcagcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttgaa
60
aggagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccagaaaa atctcaagga
120
aaagtattgc aagcaacagt agtcgctgtt ggatcgggtt ctaaaggacg cggtggagag
180
attcaaccag ttagcgtgaa agttggagat aaagttcttc tcccagaata tggaggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttagag atggtgacat tcttggaaag
300
tacgtagact ga
312

<210> 24
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA of Ala-Cpn10-K55R (Gly, Arg and stop codons are optimised in the cDNA)
<400> 24
atggcagcag gccaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttgaa
60
cgcagtgctg ctgaaactgt aaccaaaggt ggcattatgc ttccagaaaa atctcaaggc
120
aaagtattgc aagcaacagt agtcgctgtt ggctcgggtt ctaaaggtcg cggtggcgag
180
attcaaccag ttagcgtgaa agttggcgat aaagttcttc tcccagaata tggtggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttcgtg atggtgacat tcttggcaag
300
tacgtagact aa
312

<210> 25
<211> 102

<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 with residue Lysine (K) 69 changed to Arginine (R) 69. This construct contains an extra N-terminal Alanine residue (Ala-Cpn10-K69R)
<220>
<221> MISC_FEATURE
<222> (70)..(70)
<223> where X is anyone of the following amino acids: Lys, Arg or His
<400> 25
Ala Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val
1 5 10 15
Leu Val Glu Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile Met
20 25 30
Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val Ala 35
40 45
Val Gly Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln Pro Val Ser
50 55 60
Val Lys Val Gly Asp Xaa Val Leu Leu Pro Glu Tyr Gly Gly Thr Lys
65 70 75 80
Val Val Leu Asp Asp Lys Asp Tyr Phe Leu Phe Arg Asp Gly Asp Ile
85 90 95
Leu Gly Lys Tyr Val Asp 100

<210> 26
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and K69R substitution
<400> 26
atggcagcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttgaa
60
aggagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccagaaaa atctcaagga
120
aaagtattgc aagcaacagt agtcgctgtt ggatcgggtt ctaaaggaaa gggtggagag
180
attcaaccag ttagcgtgaa agttggagat cgcgttcttc tcccagaata tggaggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttagag atggtgacat tcttggaaag
300
tacgtagact ga
312
<210> 27
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA of Ala-Cpn10-K69R (Gly, Arg and stop codons are optimised in the cDNA)
<400> 27
atggcagcag gccaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttgaa
60
cgcagtgctg ctgaaactgt aaccaaaggt ggcattatgc ttccagaaaa atctcaaggc
120
aaagtattgc aagcaacagt agtcgctgtt ggctcgggtt ctaaaggtaa gggtggcgag
180

attcaaccag ttagcgtgaa agttggcgat cgcgttcttc tcccagaata tggtggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttcgtg atggtgacat tcttggcaag
300
tacgtagact aa
312

<210> 28
<211> 102
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 with residue to Lysine (K) 85 changed to Arginine (R) 85. This construct contains an extra N-terminal Alanine residue (Ala-Cpn10-K85R)
<220>
<221> MISC_FEATURE
<222> (86)..(86)
<223> where X is anyone of the following amino acids: Lys, Arg or His
<400> 28
Ala Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val
1 5 10 15
Leu Val Glu Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile Met
20 25 30
Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val Ala 35
40 45
Val Gly Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln Pro Val Ser
50 55 60
Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu Tyr Gly Gly Thr Lys
65 70 75 80
Val Val Leu Asp Asp Xaa Asp Tyr Phe Leu Phe Arg Asp Gly Asp Ile
85 90 95
Leu Gly Lys Tyr Val Asp 100

<210> 29
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and K85R substitution
<400> 29
atggcagcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttgaa
60
aggagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccagaaaa atctcaagga
120
aaagtattgc aagcaacagt agtcgctgtt ggatcgggtt ctaaaggaaa gggtggagag
180
attcaaccag ttagcgtgaa agttggagat aaagttcttc tcccagaata tggaggcacc
240
aaagtagttc tagatgaccg cgattatttc ctatttagag atggtgacat tcttggaaag
300
tacgtagact ga
312

<210> 30
<211> 312
<212> DNA
<213> Artificial Sequence
<220>

<223> Optimised cDNA Ala-Cpn10-K85R (Gly, Arg and stop codons are optimised in the cDNA)
<400> 30
atggcagcag gccaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttgaa
60
cgcagtgctg ctgaaactgt aaccaaaggt ggcattatgc ttccagaaaa atctcaaggc
120
aaagtattgc aagcaacagt agtcgctgtt ggctcgggtt ctaaaggtaa gggtggcgag
180
attcaaccag ttagcgtgaa agttggcgat aaagttcttc tcccagaata tggtggcacc
240
aaagtagttc tagatgaccg cgattatttc ctatttcgtg atggtgacat tcttggcaag
300
tacgtagact aa
312

<210> 31
<211> 102
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 with residue to Lysine (K) 98 changed to Arginine (R) 98. This construct contains an extra N-terminal Alanine residue (Ala-Cpn10-K98R)
<220>
<221> MISC_FEATURE
<222> (99)..(99)
<223> where X is anyone of the following amino acids: Lys, Arg or His
<400> 31
Ala Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val
1 5 10 15
Leu Val Glu Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile Met
20 25 30
Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val Ala 35
40 45
Val Gly Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln Pro Val Ser
50 55 60
Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu Tyr Gly Gly Thr Lys
65 70 75 80
Val Val Leu Asp Asp Lys Asp Tyr Phe Leu Phe Arg Asp Gly Asp Ile
85 90 95
Leu Gly Xaa Tyr Val Asp 100

<210> 32
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and K98R substitution
<400> 32
atggcagcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttgaa
60
aggagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccagaaaa atctcaagga
120
aaagtattgc aagcaacagt agtcgctgtt ggatcgggtt ctaaaggaaa gggtggagag
180
attcaaccag ttagcgtgaa agttggagat aaagttcttc tcccagaata tggaggcacc
240

aaagtagttc tagatgacaa ggattatttc ctatttagag atggtgacat tcttggacgc
300
tacgtagact ga
312

<210> 33
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA Ala-Cpn10-K98R (Gly, Arg and stop codons are optimised in the cDNA)
<400> 33
atggcagcag gccaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttgaa
60
cgcagtgctg ctgaaactgt aaccaaaggt ggcattatgc ttccagaaaa atctcaaggc
120
aaagtattgc aagcaacagt agtcgctgtt ggctcgggtt ctaaaggtaa gggtggcgag
180
attcaaccag ttagcgtgaa agttggcgat aaagttcttc tcccagaata tggtggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttcgtg atggtgacat tcttggccgc
300
tacgtagact aa
312

<210> 34
<211> 102
<212> PRT
<213> Human
<220>
<221> MISC_FEATURE
<222> (2)..(2)
<223> where X is anyone of the following amino acids: Lys, Arg or His
<400> 34
Ala Xaa Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val
1 5 10 15
Leu Val Glu Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile Met
20 25 30
Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val Ala 35
40 45
Val Gly Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln Pro Val Ser
50 55 60
Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu Tyr Gly Gly Thr Lys
65 70 75 80
Val Val Leu Asp Asp Lys Asp Tyr Phe Leu Phe Arg Asp Gly Asp Ile
85 90 95
Leu Gly Lys Tyr Val Asp 100

<210> 35
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and A1K substitution
<400> 35
atggcaaaag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttgaa
60

aggagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccagaaaa atctcaagga
120
aaagtattgc aagcaacagt agtcgctgtt ggatcgggtt ctaaaggaaa gggtggagag
180
attcaaccag ttagcgtgaa agttggagat aaagttcttc tcccagaata tggaggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttagag atggtgacat tcttggaaag
300
tacgtagact ga
312

<210> 36
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA Ala-Cpn10-A1K (Gly, Arg and stop codons are optimised in the cDNA)
<400> 36
atggcaaaag gccaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttgaa
60
cgcagtgctg ctgaaactgt aaccaaaggt ggcattatgc ttccagaaaa atctcaaggc
120
aaagtattgc aagcaacagt agtcgctgtt ggctcgggtt ctaaaggtaa gggtggcgag
180
attcaaccag ttagcgtgaa agttggcgat aaagttcttc tcccagaata tggtggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttcgtg atggtgacat tcttggcaag
300
tacgtagact aa
312

<210> 37
<211> 102
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 with the N-terminal residue Glutamine Q3 changed to Lysine K3. This construct also contains an extra N-terminal Alanine (A) residue (Ala-Cpn10-Q3K)
<220>
<221> MISC_FEATURE
<222> (4)..(4)
<223> where X is anyone of the following amino acids: Lys, Arg or His
<400> 37
Ala Ala Gly Xaa Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val
1 5 10 15
Leu Val Glu Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile Met
20 25 30
Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val Ala 35
40 45
Val Gly Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln Pro Val Ser
50 55 60
Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu Tyr Gly Gly Thr Lys
65 70 75 80
Val Val Leu Asp Asp Lys Asp Tyr Phe Leu Phe Arg Asp Gly Asp Ile
85 90 95
Leu Gly Lys Tyr Val Asp 100

<210> 38

<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Native cDNA with an extra N-terminal Alanine codon (GCA) and Q3K substitution
<400> 38
atggcagcag gaaaagcgtt tagaaagttt cttccactct ttgaccgagt attggttgaa
60
aggagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccagaaaa atctcaagga
120
aaagtattgc aagcaacagt agtcgctgtt ggatcgggtt ctaaaggaaa gggtggagag
180
attcaaccag ttagcgtgaa agttggagat aaagttcttc tcccagaata tggaggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttagag atggtgacat tcttggaaag
300
tacgtagact ga
312

<210> 39
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA Ala-Cpn10-Q3K (Gly, Arg and stop codons are optimised in the cDNA)
<400> 39
atggcagcag gcaaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttgaa
60
cgcagtgctg ctgaaactgt aaccaaaggt ggcattatgc ttccagaaaa atctcaaggc
120
aaagtattgc aagcaacagt agtcgctgtt ggctcgggtt ctaaaggtaa gggtggcgag
180
attcaaccag ttagcgtgaa agttggcgat aaagttcttc tcccagaata tggtggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttcgtg atggtgacat tcttggcaag
300
tacgtagact aa
312

<210> 40
<211> 102
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 with the N-terminal residue Glutamine Q3 changed to Arginine R3. This construct also contains an extra N-terminal Alanine (A) residue (Ala-Cpn10-Q3R)
<400> 40
Ala Ala Gly Arg Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val
1 5 10 15
Leu Val Glu Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile Met
20 25 30
Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val Ala 35
40 45
Val Gly Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln Pro Val Ser
50 55 60
Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu Tyr Gly Gly Thr Lys
65 70 75 80

Val Val Leu Asp Asp Lys Asp Tyr Phe Leu Phe Arg Asp Gly Asp Ile
85 90 95
Leu Gly Lys Tyr Val Asp 100

<210> 41
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Native cDNA Ala-Cpn10-Q3R
<400> 41
atggcagcag gacgcgcgtt tagaaagttt cttccactct ttgaccgagt attggttgaa
60
aggagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccagaaaa atctcaagga
120
aaagtattgc aagcaacagt agtcgctgtt ggatcgggtt ctaaaggaaa gggtggagag
180
attcaaccag ttagcgtgaa agttggagat aaagttcttc tcccagaata tggaggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttagag atggtgacat tcttggaaag
300
tacgtagact ga
312

<210> 42
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA Ala-Cpn10-Q3R
<400> 42
atggcagcag gccgcgcgtt tcgcaagttt cttccactct ttgaccgtgt attggttgaa
60
cgcagtgctg ctgaaactgt aaccaaaggt ggcattatgc ttccagaaaa atctcaaggc
120
aaagtattgc aagcaacagt agtcgctgtt ggctcgggtt ctaaaggtaa gggtggcgag
180
attcaaccag ttagcgtgaa agttggcgat aaagttcttc tcccagaata tggtggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttcgtg atggtgacat tcttggcaag
300
tacgtagact aa
312

<210> 43
<211> 102
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 with residue Phenylalanine (F) 5 changed to Lysine (K) 5. This construct contains an extra N-terminal Alanine residue (Ala-Cpn10-F5K)
<220>
<221> MISC_FEATURE
<222> (6)..(6)
<223> where X is anyone of the following amino acids: Lys, Arg or His
<400> 43
Ala Ala Gly Gln Ala Xaa Arg Lys Phe Leu Pro Leu Phe Asp Arg Val
1 5 10 15

Leu Val Glu Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile Met
20 25 30
Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val Ala 35
40 45
Val Gly Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln Pro Val Ser
50 55 60
Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu Tyr Gly Gly Thr Lys
65 70 75 80
Val Val Leu Asp Asp Lys Asp Tyr Phe Leu Phe Arg Asp Gly Asp Ile
85 90 95
Leu Gly Lys Tyr Val Asp 100

<210> 44
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and F5K substitution
<400> 44
atggcagcag gacaagcgaa aagaaagttt cttccactct ttgaccgagt attggttgaa
60
aggagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccagaaaa atctcaagga
120
aaagtattgc aagcaacagt agtcgctgtt ggatcgggtt ctaaaggaaa gggtggagag
180
attcaaccag ttagcgtgaa agttggagat aaagttcttc tcccagaata tggaggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttagag atggtgacat tcttggaaag
300
tacgtagact ga
312

<210> 45
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA Ala-Cpn10-F5K (Gly, Arg and stop codons are optimised in the cDNA)
<400> 45
atggcagcag gccaagcgaa acgcaagttt cttccactct ttgaccgtgt attggttgaa
60
cgcagtgctg ctgaaactgt aaccaaaggt ggcattatgc ttccagaaaa atctcaaggc
120
aaagtattgc aagcaacagt agtcgctgtt ggctcgggtt ctaaaggtaa gggtggcgag
180
attcaaccag ttagcgtgaa agttggcgat aaagttcttc tcccagaata tggtggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttcgtg atggtgacat tcttggcaag
300
tacgtagact aa
312

<210> 46
<211> 102
<212> PRT
<213> Artificial Sequence
<220>

<223> Human Cpn10 with residue Leucine (L) 9 changed to Lysine (K) 9. This construct contains an extra N-terminal Alanine residue (Ala-Cpn10-L9K)
<220>
<221> MISC_FEATURE
<222> (10)..(10)
<223> where X is anyone of the following amino acids: Lys, Arg or His
<400> 46
Ala Ala Gly Gln Ala Phe Arg Lys Phe Xaa Pro Leu Phe Asp Arg Val
1 5 10 15
Leu Val Glu Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile Met
20 25 30
Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val Ala 35
40 45
Val Gly Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln Pro Val Ser
50 55 60
Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu Tyr Gly Gly Thr Lys
65 70 75 80
Val Val Leu Asp Asp Lys Asp Tyr Phe Leu Phe Arg Asp Gly Asp Ile
85 90 95
Leu Gly Lys Tyr Val Asp 100

<210> 47
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and L9K substitution
<400> 47
atggcagcag gacaagcgtt tagaaagttt aaaccactct ttgaccgagt attggttgaa
60
aggagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccagaaaa atctcaagga
120
aaagtattgc aagcaacagt agtcgctgtt ggatcgggtt ctaaaggaaa gggtggagag
180
attcaaccag ttagcgtgaa agttggagat aaagttcttc tcccagaata tggaggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttagag atggtgacat tcttggaaag
300
tacgtagact ga
312

<210> 48
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA Ala-Cpn10-L9K (Gly, Arg and stop codons are optimised in the cDNA)
<400> 48
atggcagcag gccaagcgtt tcgcaagttt aaaccactct ttgaccgtgt attggttgaa
60
cgcagtgctg ctgaaactgt aaccaaaggt ggcattatgc ttccagaaaa atctcaaggc
120
aaagtattgc aagcaacagt agtcgctgtt ggctcgggtt ctaaaggtaa gggtggcgag
180
attcaaccag ttagcgtgaa agttggcgat aaagttcttc tcccagaata tggtggcacc
240

aaagtagttc tagatgacaa ggattatttc ctatttcgtg atggtgacat tcttggcaag
300
tacgtagact aa
312

<210> 49
<211> 102
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 with residue Phenylalanine (F) 12 changed to Lysine (K) 9. This construct contains an extra N-terminal Alanine residue (Ala-Cpn10-F12K)
<220>
<221> MISC_FEATURE
<222> (13)..(13)
<223> where X is anyone of the following amino acids: Lys, Arg or His
<400> 49
Ala Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Xaa Asp Arg Val
1 5 10 15
Leu Val Glu Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile Met
20 25 30
Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val Ala 35
40 45
Val Gly Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln Pro Val Ser
50 55 60
Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu Tyr Gly Gly Thr Lys
65 70 75 80
Val Val Leu Asp Asp Lys Asp Tyr Phe Leu Phe Arg Asp Gly Asp Ile
85 90 95
Leu Gly Lys Tyr Val Asp 100

<210> 50
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and F12K substitution
<400> 50
atggcagcag gacaagcgtt tagaaagttt cttccactca aggaccgagt attggttgaa
60
aggagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccagaaaa atctcaagga
120
aaagtattgc aagcaacagt agtcgctgtt ggatcgggtt ctaaaggaaa gggtggagag
180
attcaaccag ttagcgtgaa agttggagat aaagttcttc tcccagaata tggaggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttagag atggtgacat tcttggaaag
300
tacgtagact ga
312

<210> 51
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA Ala-Cpn10-F12K (Gly, Arg and stop codons are optimised in the cDNA)

<400> 51
atggcagcag gccaagcgtt tcgcaagttt cttccactca aggaccgtgt attggttgaa
60
cgcagtgctg ctgaaactgt aaccaaaggt ggcattatgc ttccagaaaa atctcaaggc
120
aaagtattgc aagcaacagt agtcgctgtt ggctcgggtt ctaaaggtaa gggtggcgag
180
attcaaccag ttagcgtgaa agttggcgat aaagttcttc tcccagaata tggtggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttcgtg atggtgacat tcttggcaag
300
tacgtagact aa
312

<210> 52
<211> 102
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 with residue Phenylalanine (F) 12 changed to Lysine (K) 9. This construct contains an extra N-terminal Alanine residue (Ala-Cpn10-D13K
<220>
<221> MISC_FEATURE
<222> (14)..(14)
<223> where Z is anyone of the following amino acids: Lys, Arg, His, Gly, Ala, Val, Leu, Ile, Pro, Phe, Tyr, Trp, Cys, Met, Ser, Thr, Asn, Gln
<400> 52
Ala Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Glx Arg Val
1 5 10 15
Leu Val Glu Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile Met
20 25 30
Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val Ala 35
40 45
Val Gly Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln Pro Val Ser
50 55 60
Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu Tyr Gly Gly Thr Lys
65 70 75 80
Val Val Leu Asp Asp Lys Asp Tyr Phe Leu Phe Arg Asp Gly Asp Ile
85 90 95
Leu Gly Lys Tyr Val Asp 100

<210> 53
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and D13K substitution
<400> 53
atggcagcag gacaagcgtt tagaaagttt cttccactct ttaaacgagt attggttgaa
60
aggagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccagaaaa atctcaagga
120
aaagtattgc aagcaacagt agtcgctgtt ggatcgggtt ctaaaggaaa gggtggagag
180
attcaaccag ttagcgtgaa agttggagat aaagttcttc tcccagaata tggaggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttagag atggtgacat tcttggaaag
300

tacgtagact ga
312

<210> 54
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA Ala-Cpn10-D13K (Gly, Arg and stop codons are optimised in the cDNA)
<400> 54
atggcagcag gccaagcgtt tcgcaagttt cttccactct ttaaacgtgt attggttgaa
60
cgcagtgctg ctgaaactgt aaccaaaggt ggcattatgc ttccagaaaa atctcaaggc
120
aaagtattgc aagcaacagt agtcgctgtt ggctcgggtt ctaaaggtaa gggtggcgag
180
attcaaccag ttagcgtgaa agttggcgat aaagttcttc tcccagaata tggtggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttcgtg atggtgacat tcttggcaag
300
tacgtagact aa
312

<210> 55
<211> 102
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 with residue Glutamate (E) 18 changed to Lysine (K) 18. This construct contains an extra N-terminal Alanine residue (Ala-Cpn10-E18K)
<220>
<221> MISC_FEATURE
<222> (19)..(19)
<223> where Z is anyone of the following amino acids: Lys, Arg, His, Gly, Ala, Val, Leu, Ile, Pro, Phe, Tyr, Trp, Cys, Met, Ser, Thr, Asn, Gln
<400> 55
Ala Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val
1 5 10 15
Leu Val Glx Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile Met
20 25 30
Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val Ala 35
40 45
Val Gly Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln Pro Val Ser
50 55 60
Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu Tyr Gly Gly Thr Lys
65 70 75 80
Val Val Leu Asp Asp Lys Asp Tyr Phe Leu Phe Arg Asp Gly Asp Ile
85 90 95
Leu Gly Lys Tyr Val Asp 100

<210> 56
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and E18K substitution
<400> 56

atggcagcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttaaa
60
aggagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccagaaaa atctcaagga
120
aaagtattgc aagcaacagt agtcgctgtt ggatcgggtt ctaaaggaaa gggtggagag
180
attcaaccag ttagcgtgaa agttggagat aaagttcttc tcccagaata tggaggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttagag atggtgacat tcttggaaag
300
tacgtagact ga
312

<210> 57
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA of Ala-Cpn10-E18K (Gly, Arg and stop codons are optimised in the cDNA)
<400> 57
atggcagcag gccaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttaaa
60
cgcagtgctg ctgaaactgt aaccaaaggt ggcattatgc ttccagaaaa atctcaaggc
120
aaagtattgc aagcaacagt agtcgctgtt ggctcgggtt ctaaaggtaa gggtggcgag
180
attcaaccag ttagcgtgaa agttggcgat aaagttcttc tcccagaata tggtggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttcgtg atggtgacat tcttggcaag
300
tacgtagact aa
312

<210> 58
<211> 102
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 with residue Glutamic Acid (Q) 18 changed to Arginine (R) 18. This construct contains an extra N-terminal Alanine residue (Ala-Cpn10-E18R)
<400> 58
Ala Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val
1 5 10 15
Leu Val Arg Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile Met
20 25 30
Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val Ala 35
40 45
Val Gly Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln Pro Val Ser
50 55 60
Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu Tyr Gly Gly Thr Lys
65 70 75 80
Val Val Leu Asp Asp Lys Asp Tyr Phe Leu Phe Arg Asp Gly Asp Ile
85 90 95
Leu Gly Lys Tyr Val Asp 100

<210> 59
<211> 312
<212> DNA
<213> Artificial Sequence

<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and E18R substitution
<400> 59
atggcagcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttcgc
60
aggagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccagaaaa atctcaagga
120
aaagtattgc aagcaacagt agtcgctgtt ggatcgggtt ctaaaggaaa gggtggagag
180
attcaaccag ttagcgtgaa agttggagat aaagttcttc tcccagaata tggaggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttagag atggtgacat tcttggaaag
300
tacgtagact ga
312

<210> 60
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA of Ala-Cpn10-E18R (Gly, Arg and stop codons are optimised in the cDNA)
<400> 60
atggcagcag gccaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttcgc
60
cgcagtgctg ctgaaactgt aaccaaaggt ggcattatgc ttccagaaaa atctcaaggc
120
aaagtattgc aagcaacagt agtcgctgtt ggctcgggtt ctaaaggtaa gggtggcgag
180
attcaaccag ttagcgtgaa agttggcgat aaagttcttc tcccagaata tggtggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttcgtg atggtgacat tcttggcaag
300
tacgtagact aa
312

<210> 61
<211> 102
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 with residue Serine (S) 20 changed to Lysine (K) 20. This construct contains an extra N-terminal Alanine residue (Ala-Cpn10-S20K)
<220>
<221> MISC_FEATURE
<222> (21)..(21)
<223> where X is anyone of the following amino acids: Lys, Arg or His
<400> 61
Ala Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val
1 5 10 15
Leu Val Glu Arg Xaa Ala Ala Glu Thr Val Thr Lys Gly Gly Ile Met
20 25 30
Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val Ala 35
40 45
Val Gly Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln Pro Val Ser
50 55 60
Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu Tyr Gly Gly Thr Lys

65 70 75 80
Val Val Leu Asp Asp Lys Asp Tyr Phe Leu Phe Arg Asp Gly Asp Ile
85 90 95
Leu Gly Lys Tyr Val Asp 100

<210> 62
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and S20K substitution
<400> 62
atggcagcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttgaa
60
aggaaagctg ctgaaactgt aaccaaagga ggcattatgc ttccagaaaa atctcaagga
120
aaagtattgc aagcaacagt agtcgctgtt ggatcgggtt ctaaaggaaa gggtggagag
180
attcaaccag ttagcgtgaa agttggagat aaagttcttc tcccagaata tggaggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttagag atggtgacat tcttggaaag
300
tacgtagact ga
312

<210> 63
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA Ala-Cpn10-S20K (Gly, Arg and stop codons are optimised in the cDNA)
<400> 63
atggcagcag gccaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttgaa
60
cgcaaagctg ctgaaactgt aaccaaaggt ggcattatgc ttccagaaaa atctcaaggc
120
aaagtattgc aagcaacagt agtcgctgtt ggctcgggtt ctaaaggtaa gggtggcgag
180
attcaaccag ttagcgtgaa agttggcgat aaagttcttc tcccagaata tggtggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttcgtg atggtgacat tcttggcaag
300
tacgtagact aa
312

<210> 64
<211> 102
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 with residue Alanine (A) 22 changed to Lysine (K) 22. This construct contains an extra N-terminal Alanine residue (Ala-Cpn10-A22K)
<220>
<221> MISC_FEATURE
<222> (23)..(23)
<223> where X is anyone of the following amino acids: Lys, Arg or His
<400> 64

Ala Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val
1 5 10 15
Leu Val Glu Arg Ser Ala Xaa Glu Thr Val Thr Lys Gly Gly Ile Met
20 25 30
Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val Ala 35
40 45
Val Gly Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln Pro Val Ser
50 55 60
Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu Tyr Gly Gly Thr Lys
65 70 75 80
Val Val Leu Asp Asp Lys Asp Tyr Phe Leu Phe Arg Asp Gly Asp Ile
85 90 95
Leu Gly Lys Tyr Val Asp 100

<210> 65
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and A22K
<400> 65
atggcagcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttgaa
60
aggagtgcta aagaaactgt aaccaaagga ggcattatgc ttccagaaaa atctcaagga
120
aaagtattgc aagcaacagt agtcgctgtt ggatcgggtt ctaaaggaaa gggtggagag
180
attcaaccag ttagcgtgaa agttggagat aaagttcttc tcccagaata tggaggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttagag atggtgacat tcttggaaag
300
tacgtagact ga
312

<210> 66
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA Ala-Cpn10-A22K (Gly, Arg and stop codons are optimised in the cDNA)
<400> 66
atggcagcag gccaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttgaa
60
cgcagtgcta aagaaactgt aaccaaaggt ggcattatgc ttccagaaaa atctcaaggc
120
aaagtattgc aagcaacagt agtcgctgtt ggctcgggtt ctaaaggtaa gggtggcgag
180
attcaaccag ttagcgtgaa agttggcgat aaagttcttc tcccagaata tggtggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttcgtg atggtgacat tcttggcaag
300
tacgtagact aa
312

<210> 67
<211> 102
<212> PRT
<213> Artificial Sequence
<220>

<223> Human Cpn10 with residue Threonine (T) 24 changed to Lysine (K) 24. This construct contains an extra N-terminal Alanine residue (Ala-Cpn10-T24K)
<220>
<221> MISC_FEATURE
<222> (25)..(25)
<223> where X is anyone of the following amino acids: Lys, Arg or His
<400> 67
Ala Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val
1 5 10 15
Leu Val Glu Arg Ser Ala Ala Glu Xaa Val Thr Lys Gly Gly Ile Met
20 25 30
Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val Ala 35
40 45
Val Gly Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln Pro Val Ser
50 55 60
Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu Tyr Gly Gly Thr Lys
65 70 75 80
Val Val Leu Asp Asp Lys Asp Tyr Phe Leu Phe Arg Asp Gly Asp Ile
85 90 95
Leu Gly Lys Tyr Val Asp 100

<210> 68
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and T24K substitution
<400> 68
atggcagcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttgaa
60
aggagtgctg ctgaaaaagt aaccaaagga ggcattatgc ttccagaaaa atctcaagga
120
aaagtattgc aagcaacagt agtcgctgtt ggatcgggtt ctaaaggaaa gggtggagag
180
attcaaccag ttagcgtgaa agttggagat aaagttcttc tcccagaata tggaggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttagag atggtgacat tcttggaaag
300
tacgtagact ga
312

<210> 69
<211> 311
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA Ala-Cpn10-T24K (Gly, Arg and stop codons are optimised in the cDNA)
<400> 69
atggcagcag gccaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttgaa
60
cgcagtgctg ctgaaaaagt aaccaaaggt ggcattatgc ttccagaaaa atctcaaggc
120
aaagtattgc aagcaacagt agtcgctgtt ggctcgggtt ctaaaggtaa gggtggcgag
180
attcaaccag ttagcgtgaa agttggcgat aaagttcttc tcccagaata tggtggcacc
240

aaagtagttc tagatgacaa ggattatttc ctatttcgtg atggtgacat tcttggcaag
300
tacgtagact a
311

<210> 70
<211> 102
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 with residue Glycine (G) 29 changed to Lysine (K) 29. This construct contains an extra N-terminal Alanine residue (Ala-Cpn10-G29K)
<220>
<221> MISC_FEATURE
<222> (30)..(30)
<223> where X is anyone of the following amino acids: Lys, Arg or His
<400> 70
Ala Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val
1 5 10 15
Leu Val Glu Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Xaa Ile Met
20 25 30
Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val Ala 35
40 45
Val Gly Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln Pro Val Ser
50 55 60
Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu Tyr Gly Gly Thr Lys
65 70 75 80
Val Val Leu Asp Asp Lys Asp Tyr Phe Leu Phe Arg Asp Gly Asp Ile
85 90 95
Leu Gly Lys Tyr Val Asp 100

<210> 71
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and G29K substitution
<400> 71
atggcagcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttgaa
60
aggagtgctg ctgaaactgt aaccaaagga aaaattatgc ttccagaaaa atctcaagga
120
aaagtattgc aagcaacagt agtcgctgtt ggatcgggtt ctaaaggaaa gggtggagag
180
attcaaccag ttagcgtgaa agttggagat aaagttcttc tcccagaata tggaggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttagag atggtgacat tcttggaaag
300
tacgtagact ga
312

<210> 72
<211> 311
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA Ala-Cpn10-G29K (Gly, Arg and stop codons are optimised in the cDNA)

<400> 72
atggcagcag gccaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttgaa
60
cgcagtgctg ctgaaactgt aaccaaaggt aaaattatgc ttccagaaaa atctcaaggc
120
aaagtattgc aagcaacagt agtcgctgtt ggctcgggtt ctaaaggtaa gggtggcgag
180
attcaaccag ttagcgtgaa agttggcgat aaagttcttc tcccagaata tggtggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttcgtg atggtgacat tcttggcaag
300
tacgtagact a
311

<210> 73
<211> 102
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 with residue Methionine (M) 31 changed to Lysine (K) 31. This construct contains an extra N-terminal Alanine residue (Ala-Cpn10-M31K)
<220>
<221> MISC_FEATURE
<222> (32)..(32)
<223> where X is anyone of the following amino acids: Lys, Arg or His
<400> 73
Ala Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val
1 5 10 15
Leu Val Glu Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile Xaa
20 25 30
Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val Ala 35
40 45
Val Gly Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln Pro Val Ser
50 55 60
Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu Tyr Gly Gly Thr Lys
65 70 75 80
Val Val Leu Asp Asp Lys Asp Tyr Phe Leu Phe Arg Asp Gly Asp Ile
85 90 95
Leu Gly Lys Tyr Val Asp 100

<210> 74
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and M31K substitution
<400> 74
atggcagcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttgaa
60
aggagtgctg ctgaaactgt aaccaaagga ggcattaaac ttccagaaaa atctcaagga
120
aaagtattgc aagcaacagt agtcgctgtt ggatcgggtt ctaaaggaaa gggtggagag
180
attcaaccag ttagcgtgaa agttggagat aaagttcttc tcccagaata tggaggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttagag atggtgacat tcttggaaag
300

tacgtagact ga
312

<210> 75
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA Ala-Cpn10-M31K (Gly, Arg and stop codons are optimised in the cDNA)
<400> 75
atggcagcag gccaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttgaa
60
cgcagtgctg ctgaaactgt aaccaaaggt ggcattaaac ttccagaaaa atctcaaggc
120
aaagtattgc aagcaacagt agtcgctgtt ggctcgggtt ctaaaggtaa gggtggcgag
180
attcaaccag ttagcgtgaa agttggcgat aaagttcttc tcccagaata tggtggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttcgtg atggtgacat tcttggcaag
300
tacgtagact aa
312

<210> 76
<211> 102
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 with residue Glutamic Acid (E) 34 changed to Lysine (K) 34. This construct contains an extra N-terminal Alanine residue (Ala-Cpn10-E34K)
<220>
<221> MISC_FEATURE
<222> (35)..(35)
<223> where X is anyone of the following amino acids: Lys, Arg or His
<220>
<221> MISC_FEATURE
<222> (35)..(35)
<223> where Z is anyone of the following amino acids: Lys, Arg, His, Gly, Ala, Val, Leu, Ile, Pro, Phe, Tyr, Trp, Cys, Met, Ser, Thr, Asn, Gln
<400> 76
Ala Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val
1 5 10 15
Leu Val Glu Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile Met
20 25 30
Leu Pro Glx Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val Ala 35
40 45
Val Gly Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln Pro Val Ser
50 55 60
Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu Tyr Gly Gly Thr Lys
65 70 75 80
Val Val Leu Asp Asp Lys Asp Tyr Phe Leu Phe Arg Asp Gly Asp Ile
85 90 95
Leu Gly Lys Tyr Val Asp 100

<210> 77
<211> 312
<212> DNA

<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and E34K substitution
<400> 77
atggcagcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttgaa
60
aggagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccaaaaaa atctcaagga
120
aaagtattgc aagcaacagt agtcgctgtt ggatcgggtt ctaaaggaaa gggtggagag
180
attcaaccag ttagcgtgaa agttggagat aaagttcttc tcccagaata tggaggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttagag atggtgacat tcttggaaag
300
tacgtagact ga
312

<210> 78
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA Ala-Cpn10-E34K (Gly, Arg and stop codons are optimised in the cDNA)
<400> 78
atggcagcag gccaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttgaa
60
cgcagtgctg ctgaaactgt aaccaaaggt ggcattatgc ttccaaaaaa atctcaaggc
120
aaagtattgc aagcaacagt agtcgctgtt ggctcgggtt ctaaaggtaa gggtggcgag
180
attcaaccag ttagcgtgaa agttggcgat aaagttcttc tcccagaata tggtggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttcgtg atggtgacat tcttggcaag
300
tacgtagact aa
312

<210> 79
<211> 102
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 with residue Glutamine (Q) 37 changed to Lysine (K) 37. This construct contains an extra N-terminal Alanine residue (Ala-Cpn10-Q37K)
<220>
<221> MISC_FEATURE
<222> (37)..(37)
<223> where X is anyone of the following amino acids: Lys, Arg or His
<220>
<221> misc_feature
<222> (38)..(38)
<223> Xaa can be any naturally occurring amino acid
<400> 79
Ala Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val
1 5 10 15
Leu Val Glu Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile Met
20 25 30

Leu Pro Glu Lys Ser Xaa Gly Lys Val Leu Gln Ala Thr Val Val Ala 35
40 45
Val Gly Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln Pro Val Ser
50 55 60
Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu Tyr Gly Gly Thr Lys
65 70 75 80
Val Val Leu Asp Asp Lys Asp Tyr Phe Leu Phe Arg Asp Gly Asp Ile
85 90 95
Leu Gly Lys Tyr Val Asp 100

<210> 80
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and Q37K substitution
<400> 80
atggcagcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttgaa
60
aggagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccagaaaa atctaaagga
120
aaagtattgc aagcaacagt agtcgctgtt ggatcgggtt ctaaaggaaa gggtggagag
180
attcaaccag ttagcgtgaa agttggagat aaagttcttc tcccagaata tggaggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttagag atggtgacat tcttggaaag
300
tacgtagact ga
312

<210> 81
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA Ala-Cpn10-Q37K (Gly, Arg and stop codons are optimised in the cDNA)
<400> 81
atggcagcag gccaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttgaa
60
cgcagtgctg ctgaaactgt aaccaaaggt ggcattatgc ttccagaaaa atctaaaggc
120
aaagtattgc aagcaacagt agtcgctgtt ggctcgggtt ctaaaggtaa gggtggcgag
180
attcaaccag ttagcgtgaa agttggcgat aaagttcttc tcccagaata tggtggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttcgtg atggtgacat tcttggcaag
300
tacgtagact aa
312

<210> 82
<211> 102
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 with residue Valine (V) 40 changed to Lysine (K) 40. This construct contains an extra N-terminal Alanine residue (Ala-Cpn10-V40K
<220>

<221> misc_feature
<222> (40)..(40)
<223> Xaa can be any naturally occurring amino acid
<220>
<221> MISC_FEATURE
<222> (41)..(41)
<223> where X is anyone of the following amino acids: Lys, Arg or His
<400> 82

```
Ala Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val
1               5                  10                  15
Leu Val Glu Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile Met
20                  25                  30
Leu Pro Glu Lys Ser Gln Gly Xaa Lys Leu Gln Ala Thr Val Val Ala   35
40                  45
Val Gly Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln Pro Val Ser
    50                  55                  60
Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu Tyr Gly Gly Thr Lys
65                  70                  75                  80
Val Val Leu Asp Asp Lys Asp Tyr Phe Leu Phe Arg Asp Gly Asp Ile
85                  90                  95
Leu Gly Lys Tyr Val Asp       100
```

<210> 83
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and V40K substitution
<400> 83

```
atggcagcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttgaa
60
aggagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccagaaaa atctcaagga
120
aaaaaattgc aagcaacagt agtcgctgtt ggatcgggtt ctaaaggaaa gggtggagag
180
attcaaccag ttagcgtgaa agttggagat aaagttcttc tcccagaata tggaggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttagag atggtgacat tcttggaaag
300
tacgtagact ga
312
```

<210> 84
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA Ala-Cpn10-V40K (Gly, Arg and stop codons are optimised in the cDNA)
<400> 84

```
atggcagcag gccaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttgaa
60
cgcagtgctg ctgaaactgt aaccaaaggt ggcattatgc ttccagaaaa atctcaaggc
120
aaaaaattgc aagcaacagt agtcgctgtt ggctcgggtt ctaaaggtaa gggtggcgag
180
attcaaccag ttagcgtgaa agttggcgat aaagttcttc tcccagaata tggtggcacc
240
```

aaagtagttc tagatgacaa ggattatttc ctatttcgtg atggtgacat tcttggcaag
300
tacgtagact aa
312

<210> 85
<211> 102
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 with residue Leucine (L) 41 changed to Lysine (K) 41. This construct contains an extra N-terminal Alanine residue (Ala-Cpn10-L41K)
<220>
<221> MISC_FEATURE
<222> (42)..(42)
<223> where X is anyone of the following amino acids: Lys, Arg or His
<400> 85
Ala Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val
1 5 10 15
Leu Val Glu Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile Met
20 25 30
Leu Pro Glu Lys Ser Gln Gly Lys Val Xaa Gln Ala Thr Val Val Ala 35
40 45
Val Gly Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln Pro Val Ser
50 55 60
Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu Tyr Gly Gly Thr Lys
65 70 75 80
Val Val Leu Asp Asp Lys Asp Tyr Phe Leu Phe Arg Asp Gly Asp Ile
85 90 95
Leu Gly Lys Tyr Val Asp 100

<210> 86
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and L41K substitution
<400> 86
atggcagcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttgaa
60
aggagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccagaaaa atctcaagga
120
aaagtaaaac aagcaacagt agtcgctgtt ggatcgggtt ctaaaggaaa gggtggagag
180
attcaaccag ttagcgtgaa agttggagat aaagttcttc tcccagaata tggaggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttagag atggtgacat tcttggaaag
300
tacgtagact ga
312

<210> 87
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA Ala-Cpn10-L41K (Gly, Arg and stop codons are optimised in the cDNA)

<400> 87
atggcagcag gccaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttgaa
60
cgcagtgctg ctgaaactgt aaccaaaggt ggcattatgc ttccagaaaa atctcaaggc
120
aaagtaaaac aagcaacagt agtcgctgtt ggctcgggtt ctaaaggtaa gggtggcgag
180
attcaaccag ttagcgtgaa agttggcgat aaagttcttc tcccagaata tggtggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttcgtg atggtgacat tcttggcaag
300
tacgtagact aa
312

<210> 88
<211> 102
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 with residue Glutamine (Q) 42 changed to Lysine (K) 42. This construct contains an extra N-terminal Alanine residue (Ala-Cpn10-Q42K)
<220>
<221> MISC_FEATURE
<222> (43)..(43)
<223> where X is anyone of the following amino acids: Lys, Arg or His
<400> 88
Ala Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val
1 5 10 15
Leu Val Glu Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile Met
20 25 30
Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Xaa Ala Thr Val Val Ala 35
40 45
Val Gly Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln Pro Val Ser
50 55 60
Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu Tyr Gly Gly Thr Lys
65 70 75 80
Val Val Leu Asp Asp Lys Asp Tyr Phe Leu Phe Arg Asp Gly Asp Ile
85 90 95
Leu Gly Lys Tyr Val Asp 100

<210> 89
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and Q42K substitution
<400> 89
atggcagcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttgaa
60
aggagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccagaaaa atctcaagga
120
aaagtattga aagcaacagt agtcgctgtt ggatcgggtt ctaaaggaaa gggtggagag
180
attcaaccag ttagcgtgaa agttggagat aaagttcttc tcccagaata tggaggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttagag atggtgacat tcttggaaag
300

tacgtagact ga
312

<210> 90
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA of Ala-Cpn10-Q42K (Gly, Arg and stop codons are optimised in the cDNA)
<400> 90
atggcagcag gccaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttgaa
60
cgcagtgctg ctgaaactgt aaccaaaggt ggcattatgc ttccagaaaa atctcaaggc
120
aaagtattga aagcaacagt agtcgctgtt ggctcgggtt ctaaaggtaa gggtggcgag
180
attcaaccag ttagcgtgaa agttggcgat aaagttcttc tcccagaata tggtggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttcgtg atggtgacat tcttggcaag
300
tacgtagact aa
312

<210> 91
<211> 102
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 with residue Threonine (T) 44 changed to Lysine (K) 44. This construct contains an extra N-terminal Alanine residue (Ala-Cpn10-T44K)
<220>
<221> MISC_FEATURE
<222> (45)..(45)
<223> where X is anyone of the following amino acids: Lys, Arg or His
<400> 91
Ala Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val
1 5 10 15
Leu Val Glu Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile Met
20 25 30
Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Xaa Val Val Ala 35
40 45
Val Gly Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln Pro Val Ser
50 55 60
Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu Tyr Gly Gly Thr Lys
65 70 75 80
Val Val Leu Asp Asp Lys Asp Tyr Phe Leu Phe Arg Asp Gly Asp Ile
85 90 95
Leu Gly Lys Tyr Val Asp 100

<210> 92
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and T44K substitution
<400> 92

atggcagcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttgaa
60
aggagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccagaaaa atctcaagga
120
aaagtattgc aagcaaaagt agtcgctgtt ggatcgggtt ctaaaggaaa gggtggagag
180
attcaaccag ttagcgtgaa agttggagat aaagttcttc tcccagaata tggaggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttagag atggtgacat tcttggaaag
300
tacgtagact ga
312

<210> 93
<211> 311
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA of Ala-Cpn10-T44K (Gly, Arg and stop codons are optimised in the cDNA)
<400> 93
atggcagcag gccaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttgaa
60
cgcagtgctg ctgaaactgt aaccaaaggt ggcattatgc ttccagaaaa atctcaaggc
120
aaagtattgc aagcaaaagt agtcgctgtt ggctcgggtt ctaaaggtaa gggtggcgag
180
attcaaccag ttagcgtgaa agttggcgat aaagttcttc tcccagaata tggtggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttcgtg atggtgacat tcttggcaag
300
tacgtagact a
311

<210> 94
<211> 102
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 with residue Serine (S) 50 changed to Lysine (K) 50. This construct contains an extra N-terminal Alanine residue (Ala-Cpn10-S50K)
<220>
<221> MISC_FEATURE
<222> (51)..(51)
<223> where X is anyone of the following amino acids: Lys, Arg or His
<400> 94
Ala Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val
1 5 10 15
Leu Val Glu Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile Met
20 25 30
Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val Ala 35
40 45
Val Gly Xaa Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln Pro Val Ser
50 55 60
Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu Tyr Gly Gly Thr Lys
65 70 75 80
Val Val Leu Asp Asp Lys Asp Tyr Phe Leu Phe Arg Asp Gly Asp Ile
85 90 95
Leu Gly Lys Tyr Val Asp 100

<210> 95
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and S50K substitution
<400> 95
atggcagcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttgaa
60
aggagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccagaaaa atctcaagga
120
aaagtattgc aagcaacagt agtcgctgtt ggaaaaggtt ctaaaggaaa gggtggagag
180
attcaaccag ttagcgtgaa agttggagat aaagttcttc tcccagaata tggaggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttagag atggtgacat tcttggaaag
300
tacgtagact ga
312

<210> 96
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA of Ala-Cpn10-S50K (Gly, Arg and stop codons are optimised in the cDNA)
<400> 96
atggcagcag gccaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttgaa
60
cgcagtgctg ctgaaactgt aaccaaaggt ggcattatgc ttccagaaaa atctcaaggc
120
aaagtattgc aagcaacagt agtcgctgtt ggcaaaggtt ctaaaggtaa gggtggcgag
180
attcaaccag ttagcgtgaa agttggcgat aaagttcttc tcccagaata tggtggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttcgtg atggtgacat tcttggcaag
300
tacgtagact aa
312

<210> 97
<211> 102
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 with residue Serine (S) 50 changed to Arginine (R) 50. This construct contains an extra N-terminal Alanine residue (Ala-Cpn10-S50R)
<400> 97
Ala Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val
1 5 10 15
Leu Val Glu Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile Met
20 25 30
Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val Ala 35
40 45
Val Gly Arg Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln Pro Val Ser
50 55 60
Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu Tyr Gly Gly Thr Lys

65 70 75 80
Val Val Leu Asp Asp Lys Asp Tyr Phe Leu Phe Arg Asp Gly Asp Ile
85 90 95
Leu Gly Lys Tyr Val Asp 100

<210> 98
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and S50R substitution
<400> 98
atggcagcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttgaa
60
aggagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccagaaaa atctcaagga
120
aaagtattgc aagcaacagt agtcgctgtt ggacgcggtt ctaaaggaaa gggtggagag
180
attcaaccag ttagcgtgaa agttggagat aaagttcttc tcccagaata tggaggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttagag atggtgacat tcttggaaag
300
tacgtagact ga
312

<210> 99
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA of Ala-Cpn10-S50R (Gly, Arg and stop codons are optimised in the cDNA)
<400> 99
atggcagcag gccaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttgaa
60
cgcagtgctg ctgaaactgt aaccaaaggt ggcattatgc ttccagaaaa atctcaaggc
120
aaagtattgc aagcaacagt agtcgctgtt ggccgcggtt ctaaaggtaa gggtggcgag
180
attcaaccag ttagcgtgaa agttggcgat aaagttcttc tcccagaata tggtggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttcgtg atggtgacat tcttggcaag
300
tacgtagact aa
312

<210> 100
<211> 102
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 with residue Serine (S) 52 changed to Lysine (L) 52. This construct contains an extra N-terminal Alanine residue (Ala-Cpn10-S52K)
<220>
<221> MISC_FEATURE
<222> (53)..(53)
<223> where X is anyone of the following amino acids: Lys, Arg or His
<400> 100

Ala Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val
1 5 10 15
Leu Val Glu Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile Met
20 25 30
Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val Ala 35
40 45
Val Gly Ser Gly Xaa Lys Gly Lys Gly Gly Glu Ile Gln Pro Val Ser
50 55 60
Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu Tyr Gly Gly Thr Lys
65 70 75 80
Val Val Leu Asp Asp Lys Asp Tyr Phe Leu Phe Arg Asp Gly Asp Ile
85 90 95
Leu Gly Lys Tyr Val Asp 100

<210> 101
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and S52K substitution
<400> 101
atggcagcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttgaa
60
aggagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccagaaaa atctcaagga
120
aaagtattgc aagcaacagt agtcgctgtt ggatcgggta aaaaaggaaa gggtggagag
180
attcaaccag ttagcgtgaa agttggagat aaagttcttc tcccagaata tggaggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttagag atggtgacat tcttggaaag
300
tacgtagact ga
312

<210> 102
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA of Ala-Cpn10-S52K (Gly, Arg and stop codons are optimised in the cDNA)
<400> 102
atggcagcag gccaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttgaa
60
cgcagtgctg ctgaaactgt aaccaaaggt ggcattatgc ttccagaaaa atctcaaggc
120
aaagtattgc aagcaacagt agtcgctgtt ggctcgggta aaaaaggtaa gggtggcgag
180
attcaaccag ttagcgtgaa agttggcgat aaagttcttc tcccagaata tggtggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttcgtg atggtgacat tcttggcaag
300
tacgtagact aa
312

<210> 103
<211> 102
<212> PRT
<213> Artificial Sequence
<220>

<223> Human Cpn10 with residue Glycine (G) 54 changed to Lysine (L) 54. This construct contains an extra N-terminal Alanine residue (Ala-Cpn10-G54K)
<220>
<221> MISC_FEATURE
<222> (55)..(55)
<223> where X is anyone of the following amino acids: Lys, Arg or His
<400> 103
Ala Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val
1 5 10 15
Leu Val Glu Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile Met
20 25 30
Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val Ala 35
40 45
Val Gly Ser Gly Ser Lys Xaa Lys Gly Gly Glu Ile Gln Pro Val Ser
50 55 60
Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu Tyr Gly Gly Thr Lys
65 70 75 80
Val Val Leu Asp Asp Lys Asp Tyr Phe Leu Phe Arg Asp Gly Asp Ile
85 90 95
Leu Gly Lys Tyr Val Asp 100

<210> 104
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and G54K substitution
<400> 104
atggcagcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttgaa
60
aggagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccagaaaa atctcaagga
120
aaagtattgc aagcaacagt agtcgctgtt ggatcgggtt ctaaaaagaa gggtggagag
180
attcaaccag ttagcgtgaa agttggagat aaagttcttc tcccagaata tggaggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttagag atggtgacat tcttggaaag
300
tacgtagact ga
312

<210> 105
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA of Ala-Cpn10-G54K (Gly, Arg and stop codons are optimised in the cDNA)
<400> 105
atggcagcag gccaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttgaa
60
cgcagtgctg ctgaaactgt aaccaaaggt ggcattatgc ttccagaaaa atctcaaggc
120
aaagtattgc aagcaacagt agtcgctgtt ggctcgggtt ctaaaaagaa gggtggcgag
180
attcaaccag ttagcgtgaa agttggcgat aaagttcttc tcccagaata tggtggcacc
240

aaagtagttc tagatgacaa ggattatttc ctatttcgtg atggtgacat tcttggcaag
300
tacgtagact aa
312

<210> 106
<211> 102
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 with residue Glycine (G) 56 changed to Lysine (L) 56. This construct contains an extra N-terminal Alanine residue (Ala-Cpn10-G56K)
<220>
<221> MISC_FEATURE
<222> (57)..(57)
<223> where X is anyone of the following amino acids: Lys, Arg or His
<400> 106
Ala Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val
1 5 10 15
Leu Val Glu Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile Met
20 25 30
Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val Ala 35
40 45
Val Gly Ser Gly Ser Lys Gly Lys Xaa Gly Glu Ile Gln Pro Val Ser
50 55 60
Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu Tyr Gly Gly Thr Lys
65 70 75 80
Val Val Leu Asp Asp Lys Asp Tyr Phe Leu Phe Arg Asp Gly Asp Ile
85 90 95
Leu Gly Lys Tyr Val Asp 100

<210> 107
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and G56K substitution
<400> 107
atggcagcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttgaa
60
aggagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccagaaaa atctcaagga
120
aaagtattgc aagcaacagt agtcgctgtt ggatcgggtt ctaaaggaaa gaaaggagag
180
attcaaccag ttagcgtgaa agttggagat aaagttcttc tcccagaata tggaggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttagag atggtgacat tcttggaaag
300
tacgtagact ga
312

<210> 108
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA of Ala-Cpn10-G56K (Gly, Arg and stop codons are optimised in the cDNA)

<400> 108
atggcagcag gccaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttgaa
60
cgcagtgctg ctgaaactgt aaccaaaggt ggcattatgc ttccagaaaa atctcaaggc
120
aaagtattgc aagcaacagt agtcgctgtt ggctcgggtt ctaaaggtaa gaaaggcgag
180
attcaaccag ttagcgtgaa agttggcgat aaagttcttc tcccagaata tggtggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttcgtg atggtgacat tcttggcaag
300
tacgtagact aa
312

<210> 109
<211> 102
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 with residue Glutamic Acid (E) 58 changed to Lysine (L) 58. This construct contains an extra N-terminal Alanine residue (Ala-Cpn10-E58K)
<220>
<221> MISC_FEATURE
<222> (59)..(59)
<223> where Z is anyone of the following amino acids: Lys, Arg, His, Gly, Ala, Val, Leu, Ile, Pro, Phe, Tyr, Trp, Cys, Met, Ser, Thr, Asn, Gln
<400> 109
Ala Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val
1 5 10 15
Leu Val Glu Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile Met
20 25 30
Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val Ala 35
40 45
Val Gly Ser Gly Ser Lys Gly Lys Gly Gly Glx Ile Gln Pro Val Ser
50 55 60
Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu Tyr Gly Gly Thr Lys
65 70 75 80
Val Val Leu Asp Asp Lys Asp Tyr Phe Leu Phe Arg Asp Gly Asp Ile
85 90 95
Leu Gly Lys Tyr Val Asp 100

<210> 110
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and E58K substitution
<400> 110
atggcagcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttgaa
60
aggagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccagaaaa atctcaagga
120
aaagtattgc aagcaacagt agtcgctgtt ggatcgggtt ctaaaggaaa gggtggaaaa
180
attcaaccag ttagcgtgaa agttggagat aaagttcttc tcccagaata tggaggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttagag atggtgacat tcttggaaag
300

tacgtagact ga
312

<210> 111
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA of Ala-Cpn10-E58K (Gly, Arg and stop codons are optimised in the cDNA)
<400> 111
atggcagcag gccaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttgaa
60
cgcagtgctg ctgaaactgt aaccaaaggt ggcattatgc ttccagaaaa atctcaaggc
120
aaagtattgc aagcaacagt agtcgctgtt ggctcgggtt ctaaaggtaa gggtggcaaa
180
attcaaccag ttagcgtgaa agttggcgat aaagttcttc tcccagaata tggtggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttcgtg atggtgacat tcttggcaag
300
tacgtagact aa
312

<210> 112
<211> 102
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 with residue Glutamine (Q) 60 changed to Lysine (L) 60. This construct contains an extra N-terminal Alanine residue (Ala-Cpn10-Q60K)
<220>
<221> MISC_FEATURE
<222> (61)..(61)
<400> 112
Ala Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val
1 5 10 15
Leu Val Glu Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile Met
20 25 30
Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val Ala 35
40 45
Val Gly Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile Xaa Pro Val Ser
50 55 60
Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu Tyr Gly Gly Thr Lys
65 70 75 80
Val Val Leu Asp Asp Lys Asp Tyr Phe Leu Phe Arg Asp Gly Asp Ile
85 90 95
Leu Gly Lys Tyr Val Asp
100

<210> 113
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and Q60K substitution
<400> 113
atggcagcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttgaa
60

aggagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccagaaaa atctcaagga
120
aaagtattgc aagcaacagt agtcgctgtt ggatcgggtt ctaaaggaaa gggtggagag
180
attaaaccag ttagcgtgaa agttggagat aaagttcttc tcccagaata tggaggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttagag atggtgacat tcttggaaag
300
tacgtagact ga
312

<210> 114
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA of Ala-Cpn10-Q60K (Gly, Arg and stop codons are optimised in the cDNA)
<400> 114
atggcagcag gccaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttgaa
60
cgcagtgctg ctgaaactgt aaccaaaggt ggcattatgc ttccagaaaa atctcaaggc
120
aaagtattgc aagcaacagt agtcgctgtt ggctcgggtt ctaaaggtaa gggtggcgag
180
attaaaccag ttagcgtgaa agttggcgat aaagttcttc tcccagaata tggtggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttcgtg atggtgacat tcttggcaag
300
tacgtagact aa
312

<210> 115
<211> 102
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 with residue Proline (P) 61 changed to Lysine (L) 61. This construct contains an extra N-terminal Alanine residue (Ala-Cpn10-P61K)
<220>
<221> MISC_FEATURE
<222> (62)..(62)
<223> where X is anyone of the following amino acids: Lys, Arg or His
<400> 115
Ala Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val
1 5 10 15
Leu Val Glu Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile Met
20 25 30
Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val Ala 35
40 45
Val Gly Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln Xaa Val Ser
50 55 60
Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu Tyr Gly Gly Thr Lys
65 70 75 80
Val Val Leu Asp Asp Lys Asp Tyr Phe Leu Phe Arg Asp Gly Asp Ile
85 90 95
Leu Gly Lys Tyr Val Asp 100

<210> 116

<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and P61K substitution
<400> 116
atggcagcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttgaa
60
aggagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccagaaaa atctcaagga
120
aaagtattgc aagcaacagt agtcgctgtt ggatcgggtt ctaaaggaaa gggtggagag
180
attcaaaaag ttagcgtgaa agttggagat aaagttcttc tcccagaata tggaggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttagag atggtgacat tcttggaaag
300
tacgtagact ga
312

<210> 117
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA of Ala-Cpn10-P61K (Gly, Arg and stop codons are optimised in the cDNA)
<400> 117
atggcagcag gccaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttgaa
60
cgcagtgctg ctgaaactgt aaccaaaggt ggcattatgc ttccagaaaa atctcaaggc
120
aaagtattgc aagcaacagt agtcgctgtt ggctcgggtt ctaaaggtaa gggtggcgag
180
attcaaaaag ttagcgtgaa agttggcgat aaagttcttc tcccagaata tggtggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttcgtg atggtgacat tcttggcaag
300
tacgtagact aa
312

<210> 118
<211> 102
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 with residue Valine (V) 66 changed to Lysine (K) 66. This construct contains an extra N-terminal Alanine residue (Ala-Cpn10-V66K)
<220>
<221> MISC_FEATURE
<222> (67)..(67)
<223> where X is anyone of the following amino acids: Lys, Arg or His
<400> 118
Ala Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val
1 5 10 15
Leu Val Glu Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile Met
20 25 30
Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val Ala 35
40 45

Val Gly Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln Pro Val Ser
50 55 60
Val Lys Xaa Gly Asp Lys Val Leu Leu Pro Glu Tyr Gly Gly Thr Lys
65 70 75 80
Val Val Leu Asp Asp Lys Asp Tyr Phe Leu Phe Arg Asp Gly Asp Ile
85 90 95
Leu Gly Lys Tyr Val Asp 100

<210> 119
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and V66K substitution
<400> 119
atggcagcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttgaa
60
aggagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccagaaaa atctcaagga
120
aaagtattgc aagcaacagt agtcgctgtt ggatcgggtt ctaaaggaaa gggtggagag
180
attcaaccag ttagcgtgaa aaaaggagat aaagttcttc tcccagaata tggaggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttagag atggtgacat tcttggaaag
300
tacgtagact ga
312

<210> 120
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA Ala-Cpn10-V66K (Gly, Arg and stop codons are optimised in the cDNA)
<400> 120
atggcagcag gccaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttgaa
60
cgcagtgctg ctgaaactgt aaccaaaggt ggcattatgc ttccagaaaa atctcaaggc
120
aaagtattgc aagcaacagt agtcgctgtt ggctcgggtt ctaaaggtaa gggtggcgag
180
attcaaccag ttagcgtgaa aaaaggcgat aaagttcttc tcccagaata tggtggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttcgtg atggtgacat tcttggcaag
300
tacgtagact aa
312

<210> 121
<211> 102
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 with residue Aspartic Acid (D) 68 changed to Lysine (K) 68. This construct contains an extra N-terminal Alanine residue (Ala-Cpn10-D68K)
<220>
<221> MISC_FEATURE
<222> (69)..(69)

<223> where Z is anyone of the following amino acids: Lys, Arg, His, Gly, Ala, Val, Leu, Ile, Pro, Phe, Tyr, Trp, Cys, Met, Ser, Thr, Asn or Gln

<400> 121

Ala Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val
1 5 10 15
Leu Val Glu Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile Met
20 25 30
Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val Ala 35
40 45
Val Gly Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln Pro Val Ser
50 55 60
Val Lys Val Gly Glx Lys Val Leu Leu Pro Glu Tyr Gly Gly Thr Lys
65 70 75 80
Val Val Leu Asp Asp Lys Asp Tyr Phe Leu Phe Arg Asp Gly Asp Ile
85 90 95
Leu Gly Lys Tyr Val Asp 100

<210> 122
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and D68K substitution

<400> 122

atggcagcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttgaa
60
aggagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccagaaaa atctcaagga
120
aaagtattgc aagcaacagt agtcgctgtt ggatcgggtt ctaaaggaaa gggtggagag
180
attcaaccag ttagcgtgaa agttggaaag aaagttcttc tcccagaata tggaggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttagag atggtgacat tcttggaaag
300
tacgtagact ga
312

<210> 123
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA of Ala-Cpn10-D68K (Gly, Arg and stop codons are optimised in the cDNA)

<400> 123

atggcagcag gccaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttgaa
60
cgcagtgctg ctgaaactgt aaccaaaggt ggcattatgc ttccagaaaa atctcaaggc
120
aaagtattgc aagcaacagt agtcgctgtt ggctcgggtt ctaaaggtaa gggtggcgag
180
attcaaccag ttagcgtgaa agttggcaag aaagttcttc tcccagaata tggtggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttcgtg atggtgacat tcttggcaag
300
tacgtagact aa
312

<210> 124

<211> 102
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 with residue Proline (P) 73 changed to Lysine (K) 73. This construct contains an extra N-terminal Alanine residue (Ala-Cpn10-P73K)
<220>
<221> MISC_FEATURE
<222> (74)..(74)
<223> where X is anyone of the following amino acids: Lys, Arg or His
<400> 124
Ala Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val
1 5 10 15
Leu Val Glu Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile Met
20 25 30
Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val Ala 35
40 45
Val Gly Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln Pro Val Ser
50 55 60
Val Lys Val Gly Asp Lys Val Leu Leu Xaa Glu Tyr Gly Gly Thr Lys
65 70 75 80
Val Val Leu Asp Asp Lys Asp Tyr Phe Leu Phe Arg Asp Gly Asp Ile
85 90 95
Leu Gly Lys Tyr Val Asp 100

<210> 125
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and P73K substitution
<400> 125
atggcagcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttgaa
60
aggagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccagaaaa atctcaagga
120
aaagtattgc aagcaacagt agtcgctgtt ggatcgggtt ctaaaggaaa gggtggagag
180
attcaaccag ttagcgtgaa agttggagat aaagttcttc tcaaagaata tggaggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttagag atggtgacat tcttggaaag
300
tacgtagact ga
312

<210> 126
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA Ala-Cpn10-P73K (Gly, Arg and stop codons are optimised in the cDNA)
<400> 126
atggcagcag gccaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttgaa
60
cgcagtgctg ctgaaactgt aaccaaaggt ggcattatgc ttccagaaaa atctcaaggc
120

aaagtattgc aagcaacagt agtcgctgtt ggctcgggtt ctaaaggtaa gggtggcgag
180
attcaaccag ttagcgtgaa agttggcgat aaagttcttc tcaaagaata tggtggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttcgtg atggtgacat tcttggcaag
300
tacgtagact aa
312

<210> 127
<211> 102
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 with residue Glutamic Acid (E) 73 changed to Lysine (K) 73. This construct contains an extra N-terminal Alanine residue (Ala-Cpn10-E74K)
<220>
<221> MISC_FEATURE
<222> (75)..(75)
<223> where Z is anyone of the following amino acids: Lys, Arg, His, Gly, Ala, Val, Leu, Ile, Pro, Phe, Tyr, Trp, Cys, Met, Ser, Thr, Asn or Gln
<400> 127
Ala Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val
1 5 10 15
Leu Val Glu Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile Met
20 25 30
Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val Ala 35
40 45
Val Gly Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln Pro Val Ser
50 55 60
Val Lys Val Gly Asp Lys Val Leu Leu Pro Glx Tyr Gly Gly Thr Lys
65 70 75 80
Val Val Leu Asp Asp Lys Asp Tyr Phe Leu Phe Arg Asp Gly Asp Ile
85 90 95
Leu Gly Lys Tyr Val Asp 100

<210> 128
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and E74K substitution
<400> 128
atggcagcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttgaa
60
aggagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccagaaaa atctcaagga
120
aaagtattgc aagcaacagt agtcgctgtt ggatcgggtt ctaaaggaaa gggtggagag
180
attcaaccag ttagcgtgaa agttggagat aaagttcttc tcccaaaata tggaggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttagag atggtgacat tcttggaaag
300
tacgtagact ga
312

<210> 129
<211> 312

<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA Ala-Cpn10-E74K (Gly, Arg and stop codons are optimised in the cDNA)
<400> 129
atggcagcag gccaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttgaa
60
cgcagtgctg ctgaaactgt aaccaaaggt ggcattatgc ttccagaaaa atctcaaggc
120
aaagtattgc aagcaacagt agtcgctgtt ggctcgggtt ctaaaggtaa gggtggcgag
180
attcaaccag ttagcgtgaa agttggcgat aaagttcttc tcccaaaata tggtggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttcgtg atggtgacat tcttggcaag
300
tacgtagact aa
312

<210> 130
<211> 101
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 with residue Tyrosine (Y) 75 changed to Lysine (K) 75. (X-Cpn10-Y75K)
<220>
<221> MISC_FEATURE
<222> (75)..(75)
<223> where X is anyone of the following amino acids: Lys, Arg or His
<400> 130
Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val Leu
1 5 10 15
Val Glu Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile Met Leu
20 25 30
Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val Ala Val 35
40 45
Gly Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln Pro Val Ser Val
50 55 60
Lys Val Gly Asp Lys Val Leu Leu Pro Glu Lys Gly Gly Thr Lys Val
65 70 75 80
Val Leu Asp Asp Lys Asp Tyr Phe Leu Phe Arg Asp Gly Asp Ile Leu
85 90 95
Gly Lys Tyr Val Asp 100

<210> 131
<211> 309
<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an Y75K substitution:
<400> 131
atggcaggac aagcgtttag aaagtttctt ccactctttg accgagtatt ggttgaaagg
60
agtgctgctg aaactgtaac caaaggaggc attatgcttc cagaaaaatc tcaaggaaaa
120
gtattgcaag caacagtagt cgctgttgga tcgggttcta aaggaaaggg tggagagatt
180
caaccagtta gcgtgaaagt tggagataaa gttcttctcc cagaaaaagg aggcaccaaa
240

gtagttctag atgacaagga ttatttccta tttagagatg gtgacattct tggaaagtac
300
gtagactga
309

<210> 132
<211> 309
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA X-Cpn10-Y75K (Gly, Arg and stop codons are optimised in the cDNA)
<400> 132
atggcaggcc aagcgtttcg caagtttctt ccactctttg accgtgtatt ggttgaacgc
60
agtgctgctg aaactgtaac caaaggtggc attatgcttc cagaaaaatc tcaaggcaaa
120
gtattgcaag caacagtagt cgctgttggc tcgggttcta aaggtaaggg tggcgagatt
180
caaccagtta gcgtgaaagt tggcgataaa gttcttctcc cagaaaaagg tggcaccaaa
240
gtagttctag atgacaagga ttatttccta tttcgtgatg gtgacattct tggcaagtac
300
gtagactaa
309

<210> 133
<211> 102
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 mutant where residue Y75 is changed to H75, in addition this construct contains an extra N-terminal Alanine residue (Ala-Cpn10-Y75H)
<400> 133
Ala Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val
1 5 10 15
Leu Val Glu Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile Met
20 25 30
Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val Ala 35
40 45
Val Gly Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln Pro Val Ser
50 55 60
Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu His Gly Gly Thr Lys
65 70 75 80
Val Val Leu Asp Asp Lys Asp Tyr Phe Leu Phe Arg Asp Gly Asp Ile
85 90 95
Leu Gly Lys Tyr Val Asp 100

<210> 134
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and Y75H substitution
<400> 134
atggcagcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttgaa
60
aggagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccagaaaa atctcaagga
120

aaagtattgc aagcaacagt agtcgctgtt ggatcgggtt ctaaaggaaa gggtggagag
180
attcaaccag ttagcgtgaa agttggagat aaagttcttc tcccagaaca cggaggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttagag atggtgacat tcttggaaag
300
tacgtagact ga
312

<210> 135
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA Ala-Cpn10-Y75H (Gly, Arg and stop codons are optimised in the cDNA)
<400> 135
atggcagcag gccaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttgaa
60
cgcagtgctg ctgaaactgt aaccaaaggt ggcattatgc ttccagaaaa atctcaaggc
120
aaagtattgc aagcaacagt agtcgctgtt ggctcgggtt ctaaaggtaa gggtggcgag
180
attcaaccag ttagcgtgaa agttggcgat aaagttcttc tcccagaaca cggtggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttcgtg atggtgacat tcttggcaag
300
tacgtagact aa
312

<210> 136
<211> 102
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 with residue Tyrosine (Y) 75 changed to Lysine (K) 75. This construct contains an extra N-terminal Alanine residue (Ala-Cpn10-Y75K)
<400> 136
Ala Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val
1 5 10 15
Leu Val Glu Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile Met
20 25 30
Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val Ala 35
40 45
Val Gly Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln Pro Val Ser
50 55 60
Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu Lys Gly Gly Thr Lys
65 70 75 80
Val Val Leu Asp Asp Lys Asp Tyr Phe Leu Phe Arg Asp Gly Asp Ile
85 90 95
Leu Gly Lys Tyr Val Asp 100

<210> 137
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and Y75K substitution
<400> 137

atggcagcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttgaa
60
aggagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccagaaaa atctcaagga
120
aaagtattgc aagcaacagt agtcgctgtt ggatcgggtt ctaaaggaaa gggtggagag
180
attcaaccag ttagcgtgaa agttggagat aaagttcttc tcccagaaaa aggaggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttagag atggtgacat tcttggaaag
300
tacgtagact ga
312

<210> 138
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA Ala-Cpn10-Y75K (Gly, Arg and stop codons are optimised in the cDNA)
<400> 138
atggcagcag gccaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttgaa
60
cgcagtgctg ctgaaactgt aaccaaaggt ggcattatgc ttccagaaaa atctcaaggc
120
aaagtattgc aagcaacagt agtcgctgtt ggctcgggtt ctaaaggtaa gggtggcgag
180
attcaaccag ttagcgtgaa agttggcgat aaagttcttc tcccagaaaa aggtggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttcgtg atggtgacat tcttggcaag
300
tacgtagact aa
312

<210> 139
<211> 102
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 mutant where residue Y75 is changed to R75. This mutation introduces extra postive charge under the dome, in addition this construct contains an extra N-terminal Alanine residue (Ala-Cpn10-Y75R)
<400> 139
Ala Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val
1 5 10 15
Leu Val Glu Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile Met
20 25 30
Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val Ala 35
40 45
Val Gly Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln Pro Val Ser
50 55 60
Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu Arg Gly Gly Thr Lys
65 70 75 80
Val Val Leu Asp Asp Lys Asp Tyr Phe Leu Phe Arg Asp Gly Asp Ile
85 90 95
Leu Gly Lys Tyr Val Asp 100

<210> 140
<211> 312
<212> DNA

<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and Y75R substitution
<400> 140
atggcagcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttgaa
60
aggagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccagaaaa atctcaagga
120
aaagtattgc aagcaacagt agtcgctgtt ggatcgggtt ctaaaggaaa gggtggagag
180
attcaaccag ttagcgtgaa agttggagat aaagttcttc tcccagaacg cggaggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttagag atggtgacat tcttggaaag
300
tacgtagact ga
312

<210> 141
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA Ala-Cpn10-Y75R (Gly, Arg and stop codons are optimised in the cDNA)
<400> 141
atggcagcag gccaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttgaa
60
cgcagtgctg ctgaaactgt aaccaaaggt ggcattatgc ttccagaaaa atctcaaggc
120
aaagtattgc aagcaacagt agtcgctgtt ggctcgggtt ctaaaggtaa gggtggcgag
180
attcaaccag ttagcgtgaa agttggcgat aaagttcttc tcccagaacg cggtggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttcgtg atggtgacat tcttggcaag
300
tacgtagact aa
312

<210> 142
<211> 102
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 with residue Glycine (G) 76 changed to Lysine (K) 76. This construct contains an extra N-terminal Alanine residue (Ala-Cpn10-G76K)
<220>
<221> MISC_FEATURE
<222> (77)..(77)
<223> where X is anyone of the following amino acids: Lys, Arg or His
<400> 142
Ala Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val
1 5 10 15
Leu Val Glu Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile Met
20 25 30
Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val Ala 35
40 45
Val Gly Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln Pro Val Ser
50 55 60

Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu Tyr Xaa Gly Thr Lys
65 70 75 80
Val Val Leu Asp Asp Lys Asp Tyr Phe Leu Phe Arg Asp Gly Asp Ile
85 90 95
Leu Gly Lys Tyr Val Asp 100

<210> 143
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and G76K substitution
<400> 143
atggcagcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttgaa
60
aggagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccagaaaa atctcaagga
120
aaagtattgc aagcaacagt agtcgctgtt ggatcgggtt ctaaaggaaa gggtggagag
180
attcaaccag ttagcgtgaa agttggagat aaagttcttc tcccagaata taaaggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttagag atggtgacat tcttggaaag
300
tacgtagact ga
312

<210> 144
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA Ala-Cpn10-G76K (Gly, Arg and stop codons are optimised in the cDNA)
<400> 144
atggcagcag gccaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttgaa
60
cgcagtgctg ctgaaactgt aaccaaaggt ggcattatgc ttccagaaaa atctcaaggc
120
aaagtattgc aagcaacagt agtcgctgtt ggctcgggtt ctaaaggtaa gggtggcgag
180
attcaaccag ttagcgtgaa agttggcgat aaagttcttc tcccagaata taaaggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttcgtg atggtgacat tcttggcaag
300
tacgtagact aa
312

<210> 145
<211> 102
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 with residue Glycine (G) 77 changed to Lysine (K) 77. This construct contains an extra N-terminal Alanine residue (Ala-Cpn10-G77K)
<220>
<221> MISC_FEATURE
<222> (78)..(78)
<223> where X is anyone of the following amino acids: Lys, Arg or His

<400> 145
Ala Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val
1 5 10 15
Leu Val Glu Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile Met
20 25 30
Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val Ala 35
40 45
Val Gly Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln Pro Val Ser
50 55 60
Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu Tyr Gly Xaa Thr Lys
65 70 75 80
Val Val Leu Asp Asp Lys Asp Tyr Phe Leu Phe Arg Asp Gly Asp Ile
85 90 95
Leu Gly Lys Tyr Val Asp 100

<210> 146
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and G77K substitution
<400> 146
atggcagcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttgaa
60
aggagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccagaaaa atctcaagga
120
aaagtattgc aagcaacagt agtcgctgtt ggatcgggtt ctaaaggaaa gggtggagag
180
attcaaccag ttagcgtgaa agttggagat aaagttcttc tcccagaata tggaaaaacc
240
aaagtagttc tagatgacaa ggattatttc ctatttagag atggtgacat tcttggaaag
300
tacgtagact ga
312

<210> 147
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA Ala-Cpn10-G77K (Gly, Arg and stop codons are optimised in the cDNA)
<400> 147
atggcagcag gccaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttgaa
60
cgcagtgctg ctgaaactgt aaccaaaggt ggcattatgc ttccagaaaa atctcaaggc
120
aaagtattgc aagcaacagt agtcgctgtt ggctcgggtt ctaaaggtaa gggtggcgag
180
attcaaccag ttagcgtgaa agttggcgat aaagttcttc tcccagaata tggtaaaacc
240
aaagtagttc tagatgacaa ggattatttc ctatttcgtg atggtgacat tcttggcaag
300
tacgtagact aa
312

<210> 148
<211> 102
<212> PRT
<213> Artificial Sequence

<220>
<223> Human Cpn10 with residue Threonine (T) 78changed to Lysine (K) 78. This construct contains an extra N-terminal Alanine residue (Ala-Cpn10-T78K)
<220>
<221> MISC_FEATURE
<222> (79)..(79)
<223> where X is anyone of the following amino acids: Lys, Arg or His
<400> 148
Ala Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val
1 5 10 15
Leu Val Glu Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile Met
20 25 30
Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val Ala 35
40 45
Val Gly Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln Pro Val Ser
50 55 60
Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu Tyr Gly Gly Xaa Lys
65 70 75 80
Val Val Leu Asp Asp Lys Asp Tyr Phe Leu Phe Arg Asp Gly Asp Ile
85 90 95
Leu Gly Lys Tyr Val Asp 100

<210> 149
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and T78K substitution
<400> 149
atggcagcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttgaa
60
aggagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccagaaaa atctcaagga
120
aaagtattgc aagcaacagt agtcgctgtt ggatcgggtt ctaaaggaaa gggtggagag
180
attcaaccag ttagcgtgaa agttggagat aaagttcttc tcccagaata tggaggcaaa
240
aaagtagttc tagatgacaa ggattatttc ctatttagag atggtgacat tcttggaaag
300
tacgtagact ga
312

<210> 150
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA Ala-Cpn10-T78K (Gly, Arg and stop codons are optimised in the cDNA)
<400> 150
atggcagcag gccaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttgaa
60
cgcagtgctg ctgaaactgt aaccaaaggt ggcattatgc ttccagaaaa atctcaaggc
120
aaagtattgc aagcaacagt agtcgctgtt ggctcgggtt ctaaaggtaa gggtggcgag
180
attcaaccag ttagcgtgaa agttggcgat aaagttcttc tcccagaata tggtggcaaa
240

aaagtagttc tagatgacaa ggattatttc ctatttcgtg atggtgacat tcttggcaag
300
tacgtagact aa
312

<210> 151
<211> 102
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 with residue Valine (V) 81 changed to Lysine (K) 81. This construct contains an extra N-terminal Alanine residue (Ala-Cpn10-V81K)
<220>
<221> MISC_FEATURE
<222> (82)..(82)
<223> where X is anyone of the following amino acids: Lys, Arg or His
<400> 151
Ala Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val
1 5 10 15
Leu Val Glu Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile Met
20 25 30
Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val Ala 35
40 45
Val Gly Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln Pro Val Ser
50 55 60
Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu Tyr Gly Gly Thr Lys
65 70 75 80
Val Xaa Leu Asp Asp Lys Asp Tyr Phe Leu Phe Arg Asp Gly Asp Ile
85 90 95
Leu Gly Lys Tyr Val Asp 100

<210> 152
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and V81K substitution
<400> 152
atggcagcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttgaa
60
aggagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccagaaaa atctcaagga
120
aaagtattgc aagcaacagt agtcgctgtt ggatcgggtt ctaaaggaaa gggtggagag
180
attcaaccag ttagcgtgaa agttggagat aaagttcttc tcccagaata tggaggcacc
240
aaagtaaaac tagatgacaa ggattatttc ctatttagag atggtgacat tcttggaaag
300
tacgtagact ga
312

<210> 153
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA Ala-Cpn10- V81K (Gly, Arg and stop codons are optimised in the cDNA)

<400> 153
atggcagcag gccaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttgaa
60
cgcagtgctg ctgaaactgt aaccaaaggt ggcattatgc ttccagaaaa atctcaaggc
120
aaagtattgc aagcaacagt agtcgctgtt ggctcgggtt ctaaaggtaa gggtggcgag
180
attcaaccag ttagcgtgaa agttggcgat aaagttcttc tcccagaata tggtggcacc
240
aaagtaaaac tagatgacaa ggattatttc ctatttcgtg atggtgacat tcttggcaag
300
tacgtagact aa
312

<210> 154
<211> 102
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 with residue Aspartate (D) 83 changed to Lysine (K) 83. This construct contains an extra N-terminal Alanine residue (Ala-Cpn10-D83K)
<220>
<221> MISC_FEATURE
<222> (84)..(84)
<223> where Z is anyone of the following amino acids: Lys, Arg, His, Gly, Ala, Val, Leu, Ile, Pro, Phe, Tyr, Trp, Cys, Met, Ser, Thr, Asn, Gln
<400> 154
Ala Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val
1 5 10 15
Leu Val Glu Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile Met
20 25 30
Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val Ala 35
40 45
Val Gly Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln Pro Val Ser
50 55 60
Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu Tyr Gly Gly Thr Lys
65 70 75 80
Val Val Leu Glx Asp Lys Asp Tyr Phe Leu Phe Arg Asp Gly Asp Ile
85 90 95
Leu Gly Lys Tyr Val Asp 100

<210> 155
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and D83K substitution
<400> 155
atggcagcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttgaa
60
aggagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccagaaaa atctcaagga
120
aaagtattgc aagcaacagt agtcgctgtt ggatcgggtt ctaaaggaaa gggtggagag
180
attcaaccag ttagcgtgaa agttggagat aaagttcttc tcccagaata tggaggcacc
240
aaagtagttc taaaagacaa ggattatttc ctatttagag atggtgacat tcttggaaag
300

tacgtagact ga
312

<210> 156
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA Ala-Cpn10- D83K (Gly, Arg and stop codons are optimised in the cDNA)
<400> 156
atggcagcag gccaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttgaa
60
cgcagtgctg ctgaaactgt aaccaaaggt ggcattatgc ttccagaaaa atctcaaggc
120
aaagtattgc aagcaacagt agtcgctgtt ggctcgggtt ctaaaggtaa gggtggcgag
180
attcaaccag ttagcgtgaa agttggcgat aaagttcttc tcccagaata tggtggcacc
240
aaagtagttc taaaagacaa ggattatttc ctatttcgtg atggtgacat tcttggcaag
300
tacgtagact aa
312

<210> 157
<211> 102
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 with residue Aspartate (D) 84 changed to Lysine (K) 84. This construct contains an extra N-terminal Alanine residue (Ala-Cpn10-D84K)
<220>
<221> MISC_FEATURE
<222> (85)..(85)
<223> where Z is anyone of the following amino acids: Lys, Arg, His, Gly, Ala, Val, Leu, Ile, Pro, Phe, Tyr, Trp, Cys, Met, Ser, Thr, Asn, Gln
<400> 157
Ala Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val
1 5 10 15
Leu Val Glu Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile Met
20 25 30
Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val Ala 35
40 45
Val Gly Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln Pro Val Ser
50 55 60
Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu Tyr Gly Gly Thr Lys
65 70 75 80
Val Val Leu Asp Glx Lys Asp Tyr Phe Leu Phe Arg Asp Gly Asp Ile
85 90 95
Leu Gly Lys Tyr Val Asp 100

<210> 158
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and D84K substitution
<400> 158

atggcagcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttgaa
60
aggagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccagaaaa atctcaagga
120
aaagtattgc aagcaacagt agtcgctgtt ggatcgggtt ctaaaggaaa gggtggagag
180
attcaaccag ttagcgtgaa agttggagat aaagttcttc tcccagaata tggaggcacc
240
aaagtagttc tagataaaaa ggattatttc ctatttagag atggtgacat tcttggaaag
300
tacgtagact ga
312

<210> 159
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA Ala-Cpn10- D84K (Gly, Arg and stop codons are optimised in the cDNA)
<400> 159
atggcagcag gccaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttgaa
60
cgcagtgctg ctgaaactgt aaccaaaggt ggcattatgc ttccagaaaa atctcaaggc
120
aaagtattgc aagcaacagt agtcgctgtt ggctcgggtt ctaaaggtaa gggtggcgag
180
attcaaccag ttagcgtgaa agttggcgat aaagttcttc tcccagaata tggtggcacc
240
aaagtagttc tagataaaaa ggattatttc ctatttcgtg atggtgacat tcttggcaag
300
tacgtagact aa
312

<210> 160
<211> 102
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 with residue Aspartate (D) 86 changed to Lysine (K) 86. This construct contains an extra N-terminal Alanine residue (Ala-Cpn10-D86K)
<220>
<221> MISC_FEATURE
<222> (87)..(87)
<223> where X is anyone of the following amino acids: Lys, Arg or His
<400> 160
Ala Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val
1 5 10 15
Leu Val Glu Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile Met
20 25 30
Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val Ala 35
40 45
Val Gly Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln Pro Val Ser
50 55 60
Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu Tyr Gly Gly Thr Lys
65 70 75 80
Val Val Leu Asp Asp Lys Xaa Tyr Phe Leu Phe Arg Asp Gly Asp Ile
85 90 95
Leu Gly Lys Tyr Val Asp 100

<210> 161
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and D86K substitution
<400> 161
atggcagcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttgaa
60
aggagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccagaaaa atctcaagga
120
aaagtattgc aagcaacagt agtcgctgtt ggatcgggtt ctaaaggaaa gggtggagag
180
attcaaccag ttagcgtgaa agttggagat aaagttcttc tcccagaata tggaggcacc
240
aaagtagttc tagatgacaa gaaatatttc ctatttagag atggtgacat tcttggaaag
300
tacgtagact ga
312

<210> 162
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA Ala-Cpn10- D86K (Gly, Arg and stop codons are optimised in the cDNA)
<400> 162
atggcagcag gccaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttgaa
60
cgcagtgctg ctgaaactgt aaccaaaggt ggcattatgc ttccagaaaa atctcaaggc
120
aaagtattgc aagcaacagt agtcgctgtt ggctcgggtt ctaaaggtaa gggtggcgag
180
attcaaccag ttagcgtgaa agttggcgat aaagttcttc tcccagaata tggtggcacc
240
aaagtagttc tagatgacaa gaaatatttc ctatttcgtg atggtgacat tcttggcaag
300
tacgtagact aa
312

<210> 163
<211> 102
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 with residue Aspartate (D) 86 changed to Arginine (R) 86. This construct contains an extra N-terminal Alanine residue (Ala-Cpn10-D86R)
<400> 163
Ala Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val
1 5 10 15
Leu Val Glu Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile Met
20 25 30
Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val Ala 35
40 45
Val Gly Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln Pro Val Ser
50 55 60
Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu Tyr Gly Gly Thr Lys

65 70 75 80
Val Val Leu Asp Asp Lys Arg Tyr Phe Leu Phe Arg Asp Gly Asp Ile
85 90 95
Leu Gly Lys Tyr Val Asp 100

<210> 164
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and D86R substitution
<400> 164
atggcagcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttgaa
60
aggagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccagaaaa atctcaagga
120
aaagtattgc aagcaacagt agtcgctgtt ggatcgggtt ctaaaggaaa gggtggagag
180
attcaaccag ttagcgtgaa agttggagat aaagttcttc tcccagaata tggaggcacc
240
aaagtagttc tagatgacaa gcgctatttc ctatttagag atggtgacat tcttggaaag
300
tacgtagact ga
312

<210> 165
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA Ala-Cpn10- D86R (Gly, Arg and stop codons are optimised in the cDNA)
<400> 165
atggcagcag gccaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttgaa
60
cgcagtgctg ctgaaactgt aaccaaaggt ggcattatgc ttccagaaaa atctcaaggc
120
aaagtattgc aagcaacagt agtcgctgtt ggctcgggtt ctaaaggtaa gggtggcgag
180
attcaaccag ttagcgtgaa agttggcgat aaagttcttc tcccagaata tggtggcacc
240
aaagtagttc tagatgacaa gcgctatttc ctatttcgtg atggtgacat tcttggcaag
300
tacgtagact aa
312

<210> 166
<211> 102
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 with residue Tyrosine (Y) 87 changed to Lysine (K) 87. This construct contains an extra N-terminal Alanine residue (Ala-Cpn10-Y87K)
<220>
<221> MISC_FEATURE
<222> (88)..(88)
<223> where X is anyone of the following amino acids: Lys, Arg or His
<400> 166

Ala Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val
1 5 10 15
Leu Val Glu Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile Met
20 25 30
Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val Ala 35
40 45
Val Gly Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln Pro Val Ser
50 55 60
Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu Tyr Gly Gly Thr Lys
65 70 75 80
Val Val Leu Asp Asp Lys Asp Xaa Phe Leu Phe Arg Asp Gly Asp Ile
85 90 95
Leu Gly Lys Tyr Val Asp 100

<210> 167
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and Y87K substitution
<400> 167
atggcagcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttgaa
60
aggagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccagaaaa atctcaagga
120
aaagtattgc aagcaacagt agtcgctgtt ggatcgggtt ctaaaggaaa gggtggagag
180
attcaaccag ttagcgtgaa agttggagat aaagttcttc tcccagaata tggaggcacc
240
aaagtagttc tagatgacaa ggataaattc ctatttagag atggtgacat tcttggaaag
300
tacgtagact ga
312

<210> 168
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA Ala-Cpn10-Y87K (Gly, Arg and stop codons are optimised in the cDNA)
<400> 168
atggcagcag gccaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttgaa
60
cgcagtgctg ctgaaactgt aaccaaaggt ggcattatgc ttccagaaaa atctcaaggc
120
aaagtattgc aagcaacagt agtcgctgtt ggctcgggtt ctaaaggtaa gggtggcgag
180
attcaaccag ttagcgtgaa agttggcgat aaagttcttc tcccagaata tggtggcacc
240
aaagtagttc tagatgacaa ggataaattc ctatttcgtg atggtgacat tcttggcaag
300
tacgtagact aa
312

<210> 169
<211> 102
<212> PRT
<213> Artificial Sequence
<220>

<223> Human Cpn10 with residue Phenylalanine (F) 88 changed to Lysine (K) 88. This construct contains an extra N-terminal Alanine residue (Ala-Cpn10-F88K
<220>
<221> MISC_FEATURE
<222> (89)..(89)
<223> where X is anyone of the following amino acids: Lys, Arg or His
<400> 169
Ala Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val
1 5 10 15
Leu Val Glu Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile Met
20 25 30
Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val Ala 35
40 45
Val Gly Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln Pro Val Ser
50 55 60
Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu Tyr Gly Gly Thr Lys
65 70 75 80
Val Val Leu Asp Asp Lys Asp Tyr Xaa Leu Phe Arg Asp Gly Asp Ile
85 90 95
Leu Gly Lys Tyr Val Asp 100

<210> 170
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and F88K substitution
<400> 170
atggcagcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttgaa
60
aggagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccagaaaa atctcaagga
120
aaagtattgc aagcaacagt agtcgctgtt ggatcgggtt ctaaaggaaa gggtggagag
180
attcaaccag ttagcgtgaa agttggagat aaagttcttc tcccagaata tggaggcacc
240
aaagtagttc tagatgacaa ggattataaa ctatttagag atggtgacat tcttggaaag
300
tacgtagact ga
312

<210> 171
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA Ala-Cpn10-F88K (Gly, Arg and stop codons are optimised in the cDNA)
<400> 171
atggcagcag gccaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttgaa
60
cgcagtgctg ctgaaactgt aaccaaaggt ggcattatgc ttccagaaaa atctcaaggc
120
aaagtattgc aagcaacagt agtcgctgtt ggctcgggtt ctaaaggtaa gggtggcgag
180
attcaaccag ttagcgtgaa agttggcgat aaagttcttc tcccagaata tggtggcacc
240

aaagtagttc tagatgacaa ggattataaa ctatttcgtg atggtgacat tcttggcaag
300
tacgtagact aa
312

<210> 172
<211> 102
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 with residue Leucine (L) 89 changed to Lysine (K) 89. This construct contains an extra N-terminal Alanine residue (Ala-Cpn10-L89K)
<220>
<221> MISC_FEATURE
<222> (90)..(90)
<223> where X is anyone of the following amino acids: Lys, Arg or His
<400> 172
Ala Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val
1 5 10 15
Leu Val Glu Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile Met
20 25 30
Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val Ala 35
40 45
Val Gly Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln Pro Val Ser
50 55 60
Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu Tyr Gly Gly Thr Lys
65 70 75 80
Val Val Leu Asp Asp Lys Asp Tyr Phe Xaa Phe Arg Asp Gly Asp Ile
85 90 95
Leu Gly Lys Tyr Val Asp 100

<210> 173
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and L89K substitution
<400> 173
atggcagcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttgaa
60
aggagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccagaaaa atctcaagga
120
aaagtattgc aagcaacagt agtcgctgtt ggatcgggtt ctaaaggaaa gggtggagag
180
attcaaccag ttagcgtgaa agttggagat aaagttcttc tcccagaata tggaggcacc
240
aaagtagttc tagatgacaa ggattatttc aaatttagag atggtgacat tcttggaaag
300
tacgtagact ga
312

<210> 174
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA Ala-Cpn10-L89K (Gly, Arg and stop codons are optimised in the cDNA)

<400> 174
atggcagcag gccaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttgaa
60
cgcagtgctg ctgaaactgt aaccaaaggt ggcattatgc ttccagaaaa atctcaaggc
120
aaagtattgc aagcaacagt agtcgctgtt ggctcgggtt ctaaaggtaa gggtggcgag
180
attcaaccag ttagcgtgaa agttggcgat aaagttcttc tcccagaata tggtggcacc
240
aaagtagttc tagatgacaa ggattatttc aaatttcgtg atggtgacat tcttggcaag
300
tacgtagact aa
312

<210> 175
<211> 102
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 with residue to Aspartic Acid (D) 92 changed to Lysine (K) 92. This construct contains an extra N-terminal Alanine residue (Ala-Cpn10-D92K
<220>
<221> MISC_FEATURE
<222> (93)..(93)
<223> where Z is anyone of the following amino acids: Lys, Arg, His, Gly, Ala, Val, Leu, Ile, Pro, Phe, Tyr, Trp, Cys, Met, Ser, Thr, Asn, Gln
<400> 175
Ala Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val
1 5 10 15
Leu Val Glu Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile Met
20 25 30
Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val Ala 35
40 45
Val Gly Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln Pro Val Ser
50 55 60
Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu Tyr Gly Gly Thr Lys
65 70 75 80
Val Val Leu Asp Asp Lys Asp Tyr Phe Leu Phe Arg Glx Gly Asp Ile
85 90 95
Leu Gly Lys Tyr Val Asp 100

<210> 176
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and D92K substitution
<400> 176
atggcagcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttgaa
60
aggagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccagaaaa atctcaagga
120
aaagtattgc aagcaacagt agtcgctgtt ggatcgggtt ctaaaggaaa gggtggagag
180
attcaaccag ttagcgtgaa agttggagat aaagttcttc tcccagaata tggaggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttagaa aaggtgacat tcttggaaag
300

tacgtagact ga
312

<210> 177
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA Ala-Cpn10-D92K (Gly, Arg and stop codons are optimised in the cDNA)
<400> 177
atggcagcag gccaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttgaa
60
cgcagtgctg ctgaaactgt aaccaaaggt ggcattatgc ttccagaaaa atctcaaggc
120
aaagtattgc aagcaacagt agtcgctgtt ggctcgggtt ctaaaggtaa gggtggcgag
180
attcaaccag ttagcgtgaa agttggcgat aaagttcttc tcccagaata tggtggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttcgta aaggtgacat tcttggcaag
300
tacgtagact aa
312

<210> 178
<211> 102
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 with residue to Glycine (G) 93 changed to Lysine (K) 93. This construct contains an extra N-terminal Alanine residue (Ala-Cpn10-G93K
<220>
<221> misc_feature
<222> (84)..(84)
<223> Xaa can be any naturally occurring amino acid
<220>
<221> MISC_FEATURE
<222> (94)..(94)
<223> where X is anyone of the following amino acids: Lys, Arg or His
<400> 178
Ala Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val
1 5 10 15
Leu Val Glu Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile Met
20 25 30
Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val Ala 35
40 45
Val Gly Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln Pro Val Ser
50 55 60
Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu Tyr Gly Gly Thr Lys
65 70 75 80
Val Val Leu Xaa Asp Lys Asp Tyr Phe Leu Phe Arg Asp Xaa Asp Ile
85 90 95
Leu Gly Lys Tyr Val Asp 100

<210> 179
<211> 312
<212> DNA
<213> Artificial Sequence
<220>

<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and G93K substitution
<400> 179
atggcagcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttgaa
60
aggagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccagaaaa atctcaagga
120
aaagtattgc aagcaacagt agtcgctgtt ggatcgggtt ctaaaggaaa gggtggagag
180
attcaaccag ttagcgtgaa agttggagat aaagttcttc tcccagaata tggaggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttagag ataaagacat tcttggaaag
300
tacgtagact ga
312

<210> 180
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA Ala-Cpn10-G93K (Gly, Arg and stop codons are optimised in the cDNA)
<400> 180
atggcagcag gccaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttgaa
60
cgcagtgctg ctgaaactgt aaccaaaggt ggcattatgc ttccagaaaa atctcaaggc
120
aaagtattgc aagcaacagt agtcgctgtt ggctcgggtt ctaaaggtaa gggtggcgag
180
attcaaccag ttagcgtgaa agttggcgat aaagttcttc tcccagaata tggtggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttcgtg ataaagacat tcttggcaag
300
tacgtagact aa
312

<210> 181
<211> 101
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 with residue to Aspartic Acid (D) 94 changed to Lysine (K) 94. This construct contains an extra N-terminal Alanine residue (Ala-Cpn10-D94K)
<220>
<221> MISC_FEATURE
<222> (95)..(95)
<223> where Z is anyone of the following amino acids: Lys, Arg, His, Gly, Ala, Val, Leu, Ile, Pro, Phe, Tyr, Trp, Cys, Met, Ser, Thr, Asn or Gln
<400> 181
Ala Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val
1 5 10 15
Leu Val Glu Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile Met
20 25 30
Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val Ala 35
40 45
Val Gly Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln Pro Val Ser
50 55 60
Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu Tyr Gly Gly Thr Lys

65 70 75 80
Val Val Leu Asp Asp Lys Asp Tyr Phe Leu Phe Arg Asp Gly Glx Leu
85 90 95
Gly Lys Tyr Val Asp 100

<210> 182
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and D94K substitution
<400> 182
atggcagcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttgaa
60
aggagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccagaaaa atctcaagga
120
aaagtattgc aagcaacagt agtcgctgtt ggatcgggtt ctaaaggaaa gggtggagag
180
attcaaccag ttagcgtgaa agttggagat aaagttcttc tcccagaata tggaggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttagag atggtaaaat tcttggaaag
300
tacgtagact ga
312

<210> 183
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA Ala-Cpn10-D94K (Gly, Arg and stop codons are optimised in the cDNA)
<400> 183
atggcagcag gccaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttgaa
60
cgcagtgctg ctgaaactgt aaccaaaggt ggcattatgc ttccagaaaa atctcaaggc
120
aaagtattgc aagcaacagt agtcgctgtt ggctcgggtt ctaaaggtaa gggtggcgag
180
attcaaccag ttagcgtgaa agttggcgat aaagttcttc tcccagaata tggtggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttcgtg atggtaaaat tcttggcaag
300
tacgtagact aa
312

<210> 184
<211> 102
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 with residue to Aspartic Acid (D) 94 changed to Arginine (R) 94. This construct contains an extra N-terminal Alanine residue (Ala-Cpn10-D94R)
<400> 184
Ala Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val
1 5 10 15
Leu Val Glu Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile Met
20 25 30

Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val Ala 35
40 45
Val Gly Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln Pro Val Ser
50 55 60
Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu Tyr Gly Gly Thr Lys
65 70 75 80
Val Val Leu Asp Asp Lys Asp Tyr Phe Leu Phe Arg Asp Gly Arg Ile
85 90 95
Leu Gly Lys Tyr Val Asp 100

<210> 185
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and D94R substitution
<400> 185
atggcagcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttgaa
60
aggagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccagaaaa atctcaagga
120
aaagtattgc aagcaacagt agtcgctgtt ggatcgggtt ctaaaggaaa gggtggagag
180
attcaaccag ttagcgtgaa agttggagat aaagttcttc tcccagaata tggaggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttagag atggtcgcat tcttggaaag
300
tacgtagact ga
312

<210> 186
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA Ala-Cpn10-D94R (Gly, Arg and stop codons are optimised in the cDNA)
<400> 186
atggcagcag gccaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttgaa
60
cgcagtgctg ctgaaactgt aaccaaaggt ggcattatgc ttccagaaaa atctcaaggc
120
aaagtattgc aagcaacagt agtcgctgtt ggctcgggtt ctaaaggtaa gggtggcgag
180
attcaaccag ttagcgtgaa agttggcgat aaagttcttc tcccagaata tggtggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttcgtg atggtcgcat tcttggcaag
300
tacgtagact aa
312

<210> 187
<211> 102
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 with residue to Leucine (L) 96 changed to Lysine (K) 96. This construct contains an extra N-terminal Alanine residue (Ala-Cpn10-L96K)
<220>

<221> MISC_FEATURE
<222> (97)..(97)
<223> where X is anyone of the following amino acids: Lys, Arg or His
<400> 187
Ala Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val
1 5 10 15
Leu Val Glu Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile Met
20 25 30
Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val Ala 35
40 45
Val Gly Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln Pro Val Ser
50 55 60
Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu Tyr Gly Gly Thr Lys
65 70 75 80
Val Val Leu Asp Asp Lys Asp Tyr Phe Leu Phe Arg Asp Gly Asp Ile
85 90 95
Xaa Gly Lys Tyr Val Asp 100

<210> 188
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and L96K substitution
<400> 188
atggcagcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttgaa
60
aggagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccagaaaa atctcaagga
120
aaagtattgc aagcaacagt agtcgctgtt ggatcgggtt ctaaaggaaa gggtggagag
180
attcaaccag ttagcgtgaa agttggagat aaagttcttc tcccagaata tggaggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttagag atggtgacat taaaggaaag
300
tacgtagact ga
312

<210> 189
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA Ala-Cpn10-L96K (Gly, Arg and stop codons are optimised in the cDNA)
<400> 189
atggcagcag gccaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttgaa
60
cgcagtgctg ctgaaactgt aaccaaaggt ggcattatgc ttccagaaaa atctcaaggc
120
aaagtattgc aagcaacagt agtcgctgtt ggctcgggtt ctaaaggtaa gggtggcgag
180
attcaaccag ttagcgtgaa agttggcgat aaagttcttc tcccagaata tggtggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttcgtg atggtgacat taaaggcaag
300
tacgtagact aa
312

<210> 190
<211> 102
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 with residue Valine (V) 100 changed to Lysine (K) 100. This construct contains an extra N-terminal Alanine residue (Ala-Cpn10-V100K)
<220>
<221> MISC_FEATURE
<222> (101)..(101)
<223> where X is anyone of the following amino acids: Lys, Arg or His
<400> 190
Ala Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val
1 5 10 15
Leu Val Glu Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile Met
20 25 30
Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val Ala 35
40 45
Val Gly Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln Pro Val Ser
50 55 60
Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu Tyr Gly Gly Thr Lys
65 70 75 80
Val Val Leu Asp Asp Lys Asp Tyr Phe Leu Phe Arg Asp Gly Asp Ile
85 90 95
Leu Gly Lys Tyr Xaa Asp 100

<210> 191
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and V100K substitution
<400> 191
atggcagcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttgaa
60
aggagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccagaaaa atctcaagga
120
aaagtattgc aagcaacagt agtcgctgtt ggatcgggtt ctaaaggaaa gggtggagag
180
attcaaccag ttagcgtgaa agttggagat aaagttcttc tcccagaata tggaggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttagag atggtgacat tcttggaaag
300
tacaaagact ga
312

<210> 192
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA Ala-Cpn10-V100K (Gly, Arg and stop codons are optimised in the cDNA)
<400> 192
atggcagcag gccaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttgaa
60

cgcagtgctg ctgaaactgt aaccaaaggt ggcattatgc ttccagaaaa atctcaaggc
120
aaagtattgc aagcaacagt agtcgctgtt ggctcgggtt ctaaaggtaa gggtggcgag
180
attcaaccag ttagcgtgaa agttggcgat aaagttcttc tcccagaata tggtggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttcgtg atggtgacat tcttggcaag
300
tacaaagact aa
312

<210> 193
<211> 102
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 with residue Aspartate (D) 101 changed to Lysine (K) 101. This construct contains an extra N-terminal Alanine residue (Ala-Cpn10-D101K)
<220>
<221> MISC_FEATURE
<222> (102)..(102)
<223> where X is anyone of the following amino acids: Lys, Arg or His
<400> 193
Ala Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val
1 5 10 15
Leu Val Glu Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile Met
20 25 30
Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val Ala 35
40 45
Val Gly Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln Pro Val Ser
50 55 60
Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu Tyr Gly Gly Thr Lys
65 70 75 80
Val Val Leu Asp Asp Lys Asp Tyr Phe Leu Phe Arg Asp Gly Asp Ile
85 90 95
Leu Gly Lys Tyr Val Xaa 100

<210> 194
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and D101K substitution
<400> 194
atggcagcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttgaa
60
aggagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccagaaaa atctcaagga
120
aaagtattgc aagcaacagt agtcgctgtt ggatcgggtt ctaaaggaaa gggtggagag
180
attcaaccag ttagcgtgaa agttggagat aaagttcttc tcccagaata tggaggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttagag atggtgacat tcttggaaag
300
tacgtaaaat ga
312

<210> 195

<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA of Ala-Cpn10-D101K (Gly, Arg and stop codons are optimised in the cDNA)
<400> 195
atggcagcag gccaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttgaa
60
cgcagtgctg ctgaaactgt aaccaaaggt ggcattatgc ttccagaaaa atctcaaggc
120
aaagtattgc aagcaacagt agtcgctgtt ggctcgggtt ctaaaggtaa gggtggcgag
180
attcaaccag ttagcgtgaa agttggcgat aaagttcttc tcccagaata tggtggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttcgtg atggtgacat tcttggcaag
300
tacgtaaaat aa
312

<210> 196
<211> 102
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 with residue to Aspartic Acid (D) 101 changed to Arginine (R) 101. This construct contains an extra N-terminal Alanine residue (Ala-Cpn10-D101R
<220>
<221> MISC_FEATURE
<222> (102)..(102)
<223> where Z is anyone of the following amino acids: Lys, Arg, His, Gly, Ala, Val, Leu, Ile, Pro, Phe, Tyr, Trp, Cys, Met, Ser, Thr, Asn or Gln
<400> 196
Ala Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val
1 5 10 15
Leu Val Glu Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile Met
20 25 30
Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val Ala 35
40 45
Val Gly Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln Pro Val Ser
50 55 60
Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu Tyr Gly Gly Thr Lys
65 70 75 80
Val Val Leu Asp Asp Lys Asp Tyr Phe Leu Phe Arg Asp Gly Asp Ile
85 90 95
Leu Gly Lys Tyr Val Glx 100

<210> 197
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and D101R substitution
<400> 197
atggcagcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttgaa
60
aggagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccagaaaa atctcaagga
120

aaagtattgc aagcaacagt agtcgctgtt ggatcgggtt ctaaaggaaa gggtggagag
180
attcaaccag ttagcgtgaa agttggagat aaagttcttc tcccagaata tggaggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttagag atggtgacat tcttggaaag
300
tacgtacgct ga
312

<210> 198
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA Ala-Cpn10-D101R (Gly, Arg and stop codons are optimised in the cDNA)
<400> 198
atggcagcag gccaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttgaa
60
cgcagtgctg ctgaaactgt aaccaaaggt ggcattatgc ttccagaaaa atctcaaggc
120
aaagtattgc aagcaacagt agtcgctgtt ggctcgggtt ctaaaggtaa gggtggcgag
180
attcaaccag ttagcgtgaa agttggcgat aaagttcttc tcccagaata tggtggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttcgtg atggtgacat tcttggcaag
300
tacgtacgct aa
312

<210> 199
<211> 101
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 with Glutamic Acid E23 removed. This construct also contains an extra N-terminal Alanine (A) residue (Ala-Cpn10-deltaE23
<400> 199
Ala Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val
1 5 10 15
Leu Val Glu Arg Ser Ala Ala Thr Val Thr Lys Gly Gly Ile Met Leu
20 25 30
Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val Ala Val 35
40 45
Gly Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln Pro Val Ser Val
50 55 60
Lys Val Gly Asp Lys Val Leu Leu Pro Glu Tyr Gly Gly Thr Lys Val
65 70 75 80
Val Leu Asp Asp Lys Asp Tyr Phe Leu Phe Arg Asp Gly Asp Ile Leu
85 90 95
Gly Lys Tyr Val Asp 100
<210> 200
<211> 309
<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and E23 removed
<400> 200

atggcagcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttgaa
60
aggagtgctg ctactgtaac caaaggaggc attatgcttc cagaaaaatc tcaaggaaaa
120
gtattgcaag caacagtagt cgctgttgga tcgggttcta aaggaaaggg tggagagatt
180
caaccagtta gcgtgaaagt tggagataaa gttcttctcc cagaatatgg aggcaccaaa
240
gtagttctag atgacaagga ttatttccta tttagagatg gtgacattct tggaaagtac
300
gtagactga
309

<210> 201
<211> 309
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA of Ala-Cpn10- ?E23 (Gly, Arg and stop codons are optimised in the cDNA)
<400> 201
atggcagcag gccaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttgaa
60
cgcagtgctg ctactgtaac caaaggtggc attatgcttc cagaaaaatc tcaaggcaaa
120
gtattgcaag caacagtagt cgctgttggc tcgggttcta aaggtaaggg tggcgagatt
180
caaccagtta gcgtgaaagt tggcgataaa gttcttctcc cagaatatgg tggcaccaaa
240
gtagttctag atgacaagga ttatttccta tttcgtgatg gtgacattct tggcaagtac
300
gtagactaa
309

<210> 202
<211> 101
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 with Glutamic Acid E34 removed. This construct also contains an extra N-terminal Alanine (A) residue (Ala-Cpn10-deltaE34)
<400> 202

Ala	Ala	Gly	Gln	Ala	Phe	Arg	Lys	Phe	Leu	Pro	Leu	Phe	Asp	Arg	Val
1				5				10						15	
Leu	Val	Glu	Arg	Ser	Ala	Ala	Glu	Thr	Val	Thr	Lys	Gly	Gly	Ile	Met
20				25				30							
Leu	Pro	Lys	Ser	Gln	Gly	Lys	Val	Leu	Gln	Ala	Thr	Val	Val	Ala	Val
40				45											
Gly	Ser	Gly	Ser	Lys	Gly	Lys	Gly	Gly	Glu	Ile	Gln	Pro	Val	Ser	Val
	50					55					60				
Lys	Val	Gly	Asp	Lys	Val	Leu	Leu	Pro	Glu	Tyr	Gly	Gly	Thr	Lys	Val
65				70					75					80	
Val	Leu	Asp	Asp	Lys	Asp	Tyr	Phe	Leu	Phe	Arg	Asp	Gly	Asp	Ile	Leu
85				90					95						
Gly	Lys	Tyr	Val	Asp				100							

<210> 203
<211> 309
<212> DNA
<213> Artificial Sequence

<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and E34 removed
<400> 203
atggcagcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttgaa
60
aggagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccaaaatc tcaaggaaaa
120
gtattgcaag caacagtagt cgctgttgga tcgggttcta aaggaaaggg tggagagatt
180
caaccagtta gcgtgaaagt tggagataaa gttcttctcc cagaatatgg aggcaccaaa
240
gtagttctag atgacaagga ttatttccta tttagagatg gtgacattct tggaaagtac
300
gtagactga
309

<210> 204
<211> 309
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA of Ala-Cpn10- ?E34 (Gly, Arg and stop codons are optimised in the cDNA)
<400> 204
atggcagcag gccaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttgaa
60
cgcagtgctg ctgaaactgt aaccaaaggt ggcattatgc ttccaaaatc tcaaggcaaa
120
gtattgcaag caacagtagt cgctgttggc tcgggttcta aaggtaaggg tggcgagatt
180
caaccagtta gcgtgaaagt tggcgataaa gttcttctcc cagaatatgg tggcaccaaa
240
gtagttctag atgacaagga ttatttccta tttcgtgatg gtgacattct tggcaagtac
300
gtagactaa
309

<210> 205
<211> 101
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 with Glutamic Acid E58 removed. This construct also contains an extra N-terminal Alanine (A) residue (Ala-Cpn10-deltaE58)
<400> 205
Ala Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val
1 5 10 15
Leu Val Glu Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile Met
20 25 30
Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val Ala 35
40 45
Val Gly Ser Gly Ser Lys Gly Lys Gly Gly Ile Gln Pro Val Ser Val
50 55 60
Lys Val Gly Asp Lys Val Leu Leu Pro Glu Tyr Gly Gly Thr Lys Val
65 70 75 80
Val Leu Asp Asp Lys Asp Tyr Phe Leu Phe Arg Asp Gly Asp Ile Leu
85 90 95
Gly Lys Tyr Val Asp 100
<210> 206

<211> 309
<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and E58 removed
<400> 206
atggcagcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttgaa
60
aggagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccagaaaa atctcaagga
120
aaagtattgc aagcaacagt agtcgctgtt ggatcgggtt ctaaaggaaa gggtggaatt
180
caaccagtta gcgtgaaagt tggagataaa gttcttctcc cagaatatgg aggcaccaaa
240
gtagttctag atgacaagga ttatttccta tttagagatg gtgacattct tggaaagtac
300
gtagactga
309

<210> 207
<211> 309
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA of Ala-Cpn10- ?E58 (Gly, Arg and stop codons are optimised in the cDNA)
<400> 207
atggcagcag gccaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttgaa
60
cgcagtgctg ctgaaactgt aaccaaaggt ggcattatgc ttccagaaaa atctcaaggc
120
aaagtattgc aagcaacagt agtcgctgtt ggctcgggtt ctaaaggtaa gggtggcatt
180
caaccagtta gcgtgaaagt tggcgataaa gttcttctcc cagaatatgg tggcaccaaa
240
gtagttctag atgacaagga ttatttccta tttcgtgatg gtgacattct tggcaagtac
300
gtagactaa
309

<210> 208
<211> 101
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 with Glutamic Acid E74 removed. This construct also contains an extra N-terminal Alanine (A) residue (Ala-Cpn10-deltaE74)
<400> 208

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

35

Val Leu Asp Asp Lys Asp Tyr Phe Leu Phe Arg Asp Gly Asp Ile Leu
85 90 95
Gly Lys Tyr Val Asp 100

<210> 209
<211> 309
<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and E74 removed
<400> 209
atggcagcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttgaa
60
aggagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccagaaaa atctcaagga
120
aaagtattgc aagcaacagt agtcgctgtt ggatcgggtt ctaaaggaaa gggtggagag
180
attcaaccag ttagcgtgaa agttggagat aaagttcttc tcccatatgg aggcaccaaa
240
gtagttctag atgacaagga ttatttccta tttagagatg gtgacattct tggaaagtac
300
gtagactga
309

<210> 210
<211> 309
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA of Ala-Cpn10- ?E74 (Gly, Arg and stop codons are optimised in the cDNA)
<400> 210
atggcagcag gccaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttgaa
60
cgcagtgctg ctgaaactgt aaccaaaggt ggcattatgc ttccagaaaa atctcaaggc
120
aaagtattgc aagcaacagt agtcgctgtt ggctcgggtt ctaaaggtaa gggtggcgag
180
attcaaccag ttagcgtgaa agttggcgat aaagttcttc tcccatatgg tggcaccaaa
240
gtagttctag atgacaagga ttatttccta tttcgtgatg gtgacattct tggcaagtac
300
gtagactaa
309

<210> 211
<211> 101
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 with Aspartic Acid D84 removed. This construct also contains an extra N-terminal Alanine (A) residue (Ala-Cpn10-deltaD84)
<400> 211
Ala Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val
1 5 10 15
Leu Val Glu Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile Met
20 25 30
Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val Ala 35
40 45

Val Gly Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln Pro Val Ser
50 55 60
Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu Tyr Gly Gly Thr Lys
65 70 75 80
Val Val Leu Asp Lys Asp Tyr Phe Leu Phe Arg Asp Gly Asp Ile Leu
85 90 95
Gly Lys Tyr Val Asp 100

<210> 212
<211> 309
<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and D84 removed
<400> 212
atggcagcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttgaa
60
aggagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccagaaaa atctcaagga
120
aaagtattgc aagcaacagt agtcgctgtt ggatcgggtt ctaaaggaaa gggtggagag
180
attcaaccag ttagcgtgaa agttggagat aaagttcttc tcccagaata tggaggcacc
240
aaagtagttc tagataagga ttatttccta tttagagatg gtgacattct tggaaagtac
300
gtagactga
309

<210> 213
<211> 309
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA of Ala-Cpn10- ?D84 (Gly, Arg and stop codons are optimised in the cDNA)
<400> 213
atggcagcag gccaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttgaa
60
cgcagtgctg ctgaaactgt aaccaaaggt ggcattatgc ttccagaaaa atctcaaggc
120
aaagtattgc aagcaacagt agtcgctgtt ggctcgggtt ctaaaggtaa gggtggcgag
180
attcaaccag ttagcgtgaa agttggcgat aaagttcttc tcccagaata tggtggcacc
240
aaagtagttc tagataagga ttatttccta tttcgtgatg gtgacattct tggcaagtac
300
gtagactaa
309

<210> 214
<211> 102
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 with residue Phenylalanine (F) 12 changed to Lysine (K) 18 and residue Aspartate (D) 92 changed to Lysine (K) 92. This construct contains an extra N-terminal Alanine residue (Ala-Cpn10-F12K,D92K)
<220>
<221> MISC_FEATURE

<222> (13)..(13)
<223> where X is anyone of the following amino acids: Lys, Arg or His
<220>
<221> MISC_FEATURE
<222> (93)..(93)
<223> where Z is anyone of the following amino acids: Lys, Arg, His, Gly, Ala, Val, Leu, Ile, Pro, Phe, Tyr, Trp, Cys, Met, Ser, Thr, Asn or Gln
<400> 214
Ala Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Xaa Asp Arg Val
1 5 10 15
Leu Val Glu Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile Met
20 25 30
Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val Ala 35
40 45
Val Gly Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln Pro Val Ser
50 55 60
Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu Tyr Gly Gly Thr Lys
65 70 75 80
Val Val Leu Asp Asp Lys Asp Tyr Phe Leu Phe Arg Glx Gly Asp Ile
85 90 95
Leu Gly Lys Tyr Val Asp 100

<210> 215
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and F12K,D92K substitutions
<400> 215
atggcagcag gacaagcgtt tagaaagttt cttccactca aagaccgagt attggttgaa
60
aggagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccagaaaa atctcaagga
120
aaagtattgc aagcaacagt agtcgctgtt ggatcgggtt ctaaaggaaa gggtggagag
180
attcaaccag ttagcgtgaa agttggagat aaagttcttc tcccagaata tggaggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttagaa aaggtgacat tcttggaaag
300
tacgtagact ga
312

<210> 216
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA of Ala-Cpn10-F12K,D92K (Gly, Arg and stop codons are optimised in the cDNA)
<400> 216
atggcagcag gccaagcgtt tcgcaagttt cttccactca aagaccgtgt attggttgaa
60
cgcagtgctg ctgaaactgt aaccaaaggt ggcattatgc ttccagaaaa atctcaaggc
120
aaagtattgc aagcaacagt agtcgctgtt ggctcgggtt ctaaaggtaa gggtggcgag
180
attcaaccag ttagcgtgaa agttggcgat aaagttcttc tcccagaata tggtggcacc
240

aaagtagttc tagatgacaa ggattatttc ctatttcgta aaggtgacat tcttggcaag
300
tacgtagact aa
312

<210> 217
<211> 102
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 with residue Glutamate (E) 18 changed to Lysine (K) 18 and residue Aspartate (D) 101 changed to Lysine (K) 101. This construct contains an extra N-terminal Alanine residue (Ala-Cpn10-E18K,D101K)
<220>
<221> MISC_FEATURE
<222> (19)..(19)
<223> where Z is anyone of the following amino acids: Lys, Arg, His, Gly, Ala, Val, Leu, Ile, Pro, Phe, Tyr, Trp, Cys, Met, Ser, Thr, Asn or Gln
<220>
<221> MISC_FEATURE
<222> (102)..(102)
<223> where Z is anyone of the following amino acids: Lys, Arg, His, Gly, Ala, Val, Leu, Ile, Pro, Phe, Tyr, Trp, Cys, Met, Ser, Thr, Asn or Gln
<400> 217
Ala Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val
1 5 10 15
Leu Val Lys Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile Met
20 25 30
Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val Ala 35
40 45
Val Gly Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln Pro Val Ser
50 55 60
Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu Tyr Gly Gly Thr Lys
65 70 75 80
Val Val Leu Asp Asp Lys Asp Tyr Phe Leu Phe Arg Asp Gly Asp Ile
85 90 95
Leu Gly Lys Tyr Val Lys 100

<210> 218
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and E18K,D101K substitutions
<400> 218
atggcagcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttaaa
60
aggagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccagaaaa atctcaagga
120
aaagtattgc aagcaacagt agtcgctgtt ggatcgggtt ctaaaggaaa gggtggagag
180
attcaaccag ttagcgtgaa agttggagat aaagttcttc tcccagaata tggaggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttagag atggtgacat tcttggaaag
300
tacgtaaaat ga
312

<210> 219
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA of Ala-Cpn10-E18K,D101K (Gly, Arg and stop codons are optimised in the cDNA)
<400> 219
atggcagcag gccaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttaaa 60
cgcagtgctg ctgaaactgt aaccaaaggt ggcattatgc ttccagaaaa atctcaaggc 120
aaagtattgc aagcaacagt agtcgctgtt ggctcgggtt ctaaaggtaa gggtggcgag 180
attcaaccag ttagcgtgaa agttggcgat aaagttcttc tcccagaata tggtggcacc 240
aaagtagttc tagatgacaa ggattatttc ctatttcgtg atggtgacat tcttggcaag 300
tacgtaaaat aa
312

<210> 220
<211> 102
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 with residue Glutamic Acid (E) 34 changed to Glutamine (Q)34 and residue Tyrosine (Y) 75 changed to Lysine (K) 75. This construct contains an extra N-terminal Alanine residue (Ala-Cpn10-E34Q,Y75K)
<220>
<221> MISC_FEATURE
<222> (35)..(35)
<223> where Z is anyone of the following amino acids: Lys, Arg, His, Gly, Ala, Val, Leu, Ile, Pro, Phe, Tyr, Trp, Cys, Met, Ser, Thr, Asn or Gln
<220>
<221> MISC_FEATURE
<222> (76)..(76)
<223> where X is anyone of the following amino acids: Lys, Arg or His
<400> 220
Ala Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val
1 5 10 15
Leu Val Glu Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile Met
20 25 30
Leu Pro Gln Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val Ala 35
40 45
Val Gly Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln Pro Val Ser
50 55 60
Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu Lys Gly Gly Thr Lys
65 70 75 80
Val Val Leu Asp Asp Lys Asp Tyr Phe Leu Phe Arg Asp Gly Asp Ile
85 90 95
Leu Gly Lys Tyr Val Asp 100

<210> 221
<211> 312
<212> DNA
<213> Artificial Sequence

<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and E34Q,Y75K substitutions
<400> 221
atggcagcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttgaa
60
aggagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccacaaaa atctcaagga
120
aaagtattgc aagcaacagt agtcgctgtt ggatcgggtt ctaaaggaaa gggtggagag
180
attcaaccag ttagcgtgaa agttggagat aaagttcttc tcccagaaaa aggaggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttagag atggtgacat tcttggaaag
300
tacgtagact ga
312

<210> 222
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA of Ala-Cpn10-E34Q,Y75K (Gly, Arg and stop codons are optimised in the cDNA)
<400> 222
atggcagcag gccaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttgaa
60
cgcagtgctg ctgaaactgt aaccaaaggt ggcattatgc ttccacaaaa atctcaaggc
120
aaagtattgc aagcaacagt agtcgctgtt ggctcgggtt ctaaaggtaa gggtggcgag
180
attcaaccag ttagcgtgaa agttggcgat aaagttcttc tcccagaaaa aggtggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttcgtg atggtgacat tcttggcaag
300
tacgtagact aa
312

<210> 223
<211> 102
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 with residue Glutamine (Q) 42 changed to Lysine (K) 42 and residue Aspartate (D) 101 changed to Lysine (K) 101. This construct contains an extra N-terminal Alanine residue (Ala-Cpn10-Q42K,D101K
<220>
<221> MISC_FEATURE
<222> (43)..(43)
<223> where X is anyone of the following amino acids: Lys, Arg or His
<220>
<221> MISC_FEATURE
<222> (102)..(102)
<223> where Z is anyone of the following amino acids: Lys, Arg, His, Gly, Ala, Val, Leu, Ile, Pro, Phe, Tyr, Trp, Cys, Met, Ser, Thr, Asn or Gln
<400> 223
Ala Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val
1 5 10 15

Leu Val Glu Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile Met
20 25 30
Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Xaa Ala Thr Val Val Ala 35
40 45
Val Gly Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln Pro Val Ser
50 55 60
Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu Tyr Gly Gly Thr Lys
65 70 75 80
Val Val Leu Asp Asp Lys Asp Tyr Phe Leu Phe Arg Asp Gly Asp Ile
85 90 95
Leu Gly Lys Tyr Val Glx 100

<210> 224
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and Q42K,D101K substitutions
<400> 224
atggcagcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttgaa
60
aggagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccagaaaa atctcaagga
120
aaagtattga aagcaacagt agtcgctgtt ggatcgggtt ctaaaggaaa gggtggagag
180
attcaaccag ttagcgtgaa agttggagat aaagttcttc tcccagaata tggaggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttagag atggtgacat tcttggaaag
300
tacgtaaaat ga
312

<210> 225
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA of Ala-Cpn10-Q42K,D101K (Gly, Arg and stop codons are optimised in the cDNA)
<400> 225
atggcagcag gccaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttgaa
60
cgcagtgctg ctgaaactgt aaccaaaggt ggcattatgc ttccagaaaa atctcaaggc
120
aaagtattga aagcaacagt agtcgctgtt ggctcgggtt ctaaaggtaa gggtggcgag
180
attcaaccag ttagcgtgaa agttggcgat aaagttcttc tcccagaata tggtggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttcgtg atggtgacat tcttggcaag
300
tacgtaaaat aa
312

<210> 226
<211> 102
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 with residue Threonine (T) 44 changed to Lysine (K) 44 and residue Aspartate (D) 101 changed to Lysine (K) 101. This

construct contains an extra N-terminal Alanine residue (Ala-Cpn10-T44K,D101K)
<220>
<221> MISC_FEATURE
<222> (45)..(45)
<223> where X is anyone of the following amino acids: Lys, Arg or His
<220>
<221> MISC_FEATURE
<222> (102)..(102)
<223> where Z is anyone of the following amino acids: Lys, Arg, His, Gly, Ala, Val, Leu, Ile, Pro, Phe, Tyr, Trp, Cys, Met, Ser, Thr, Asn or Gln
<400> 226

```
Ala Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val
1               5                  10                  15
Leu Val Glu Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile Met
20                  25                  30
Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Xaa Val Val Ala   35
40                  45
Val Gly Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln Pro Val Ser
    50                  55                  60
Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu Tyr Gly Gly Thr Lys
65                  70                  75                  80
Val Val Leu Asp Asp Lys Asp Tyr Phe Leu Phe Arg Asp Gly Asp Ile
85                  90                  95
Leu Gly Lys Tyr Val Glx       100
```

<210> 227
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and T44K,D101K substitutions
<400> 227

```
atggcagcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttgaa
60
aggagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccagaaaa atctcaagga
120
aaagtattgc aagcaaaagt agtcgctgtt ggatcgggtt ctaaaggaaa gggtggagag
180
attcaaccag ttagcgtgaa agttggagat aaagttcttc tcccagaata tggaggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttagag atggtgacat tcttggaaag
300
tacgtaaaat ga
312
```

<210> 228
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA of Ala-Cpn10-T44K,D101K (Gly, Arg and stop codons are optimised in the cDNA)
<400> 228

```
atggcagcag gccaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttgaa
60
cgcagtgctg ctgaaactgt aaccaaaggt ggcattatgc ttccagaaaa atctcaaggc
120
```

aaagtattgc aagcaaaagt agtcgctgtt ggctcgggtt ctaaaggtaa gggtggcgag
180
attcaaccag ttagcgtgaa agttggcgat aaagttcttc tcccagaata tggtggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttcgtg atggtgacat tcttggcaag
300
tacgtaaaat aa
312

<210> 229
<211> 102
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 with residue Serine (S) 50 changed to Lysine (K) 50 and residue Aspartate (D) 101 changed to Lysine (K) 101. This construct contains an extra N-terminal Alanine residue (Ala-Cpn10-S50K,D101K)
<220>
<221> MISC_FEATURE
<222> (51)..(51)
<223> where X is anyone of the following amino acids: Lys, Arg or His
<220>
<221> MISC_FEATURE
<222> (102)..(102)
<223> where Z is anyone of the following amino acids: Lys, Arg, His, Gly, Ala, Val, Leu, Ile, Pro, Phe, Tyr, Trp, Cys, Met, Ser, Thr, Asn or Gln
<400> 229
Ala Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val
1 5 10 15
Leu Val Glu Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile Met
20 25 30
Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val Ala 35
40 45
Val Gly Xaa Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln Pro Val Ser
50 55 60
Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu Tyr Gly Gly Thr Lys
65 70 75 80
Val Val Leu Asp Asp Lys Asp Tyr Phe Leu Phe Arg Asp Gly Asp Ile
85 90 95
Leu Gly Lys Tyr Val Glx
100

<210> 230
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and S50K,D101K substitutions
<400> 230
atggcagcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttgaa
60
aggagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccagaaaa atctcaagga
120
aaagtattgc aagcaacagt agtcgctgtt ggaaaaggtt ctaaaggaaa gggtggagag
180
attcaaccag ttagcgtgaa agttggagat aaagttcttc tcccagaata tggaggcacc
240

aaagtagttc tagatgacaa ggattatttc ctatttagag atggtgacat tcttggaaag
300
tacgtaaaat ga
312

<210> 231
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA of Ala-Cpn10-S50K,D101K (Gly, Arg and stop codons are optimised in the cDNA)
<400> 231
atggcagcag gccaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttgaa
60
cgcagtgctg ctgaaactgt aaccaaaggt ggcattatgc ttccagaaaa atctcaaggc
120
aaagtattgc aagcaacagt agtcgctgtt ggcaaaggtt ctaaaggtaa gggtggcgag
180
attcaaccag ttagcgtgaa agttggcgat aaagttcttc tcccagaata tggtggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttcgtg atggtgacat tcttggcaag
300
tacgtaaaat aa
312

<210> 232
<211> 102
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 with residue Glutamine (Q) 60 changed to Lysine (K) 60 and residue Threonine (T) 78 changed to Lysine (K) 78. This construct contains an extra N-terminal Alanine residue (Ala-Cpn10-Q60K,T78K
<220>
<221> MISC_FEATURE
<222> (61)..(61)
<223> where X is anyone of the following amino acids: Lys, Arg or His
<220>
<221> MISC_FEATURE
<222> (79)..(79)
<223> where X is anyone of the following amino acids: Lys, Arg or His
<400> 232
Ala Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val
1 5 10 15
Leu Val Glu Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile Met
20 25 30
Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val Ala 35
40 45
Val Gly Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile Xaa Pro Val Ser
50 55 60
Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu Tyr Gly Gly Xaa Lys
65 70 75 80
Val Val Leu Asp Asp Lys Asp Tyr Phe Leu Phe Arg Asp Gly Asp Ile
85 90 95
Leu Gly Lys Tyr Val Asp 100
<210> 233
<211> 312

<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and Q60K,T78K substitutions
<400> 233
atggcagcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttgaa
60
aggagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccagaaaa atctcaagga
120
aaagtattgc aagcaacagt agtcgctgtt ggatcgggtt ctaaaggaaa gggtggagag
180
attaaaccag ttagcgtgaa agttggagat aaagttcttc tcccagaata tggaggcaag
240
aaagtagttc tagatgacaa ggattatttc ctatttagag atggtgacat tcttggaaag
300
tacgtagact ga
312

<210> 234
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA of Ala-Cpn10-Q60K,T78K (Gly, Arg and stop codons are optimised in the cDNA)
<400> 234
atggcagcag gccaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttgaa
60
cgcagtgctg ctgaaactgt aaccaaaggt ggcattatgc ttccagaaaa atctcaaggc
120
aaagtattgc aagcaacagt agtcgctgtt ggctcgggtt ctaaaggtaa gggtggcgag
180
attaaaccag ttagcgtgaa agttggcgat aaagttcttc tcccagaata tggtggcaag
240
aaagtagttc tagatgacaa ggattatttc ctatttcgtg atggtgacat tcttggcaag
300
tacgtagact aa
312

<210> 235
<211> 102
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 with residue Glutamic Acid (E) 74 changed to Lysine (K) 74 and residue Tyrosine (Y) 75 changed to Glutamic Acid (E) 75. This construct contains an extra N-terminal Alanine residue (Ala-Cpn10-E74K,Y75E)
<220>
<221> MISC_FEATURE
<222> (75)..(75)
<223> where Z is anyone of the following amino acids: Lys, Arg, His, Gly, Ala, Val, Leu, Ile, Pro, Phe, Tyr, Trp, Cys, Met, Ser, Thr, Asn or Gln
<400> 235
Ala Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val
1 5 10 15
Leu Val Glu Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile Met
20 25 30

Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val Ala 35
40 45
Val Gly Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln Pro Val Ser
50 55 60
Val Lys Val Gly Asp Lys Val Leu Leu Pro Glx Glu Gly Gly Thr Lys
65 70 75 80
Val Val Leu Asp Asp Lys Asp Tyr Phe Leu Phe Arg Asp Gly Asp Ile
85 90 95
Leu Gly Lys Tyr Val Asp 100

<210> 236
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and E74K,Y75E substitutions
<400> 236
atggcagcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttgaa
60
aggagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccagaaaa atctcaagga
120
aaagtattgc aagcaacagt agtcgctgtt ggatcgggtt ctaaaggaaa gggtggagag
180
attcaaccag ttagcgtgaa agttggagat aaagttcttc tcccaaaaga aggaggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttagag atggtgacat tcttggaaag
300
tacgtagact ga
312

<210> 237
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA of Ala-Cpn10- E74K,Y75E (Gly, Arg and stop codons are optimised in the cDNA)
<400> 237
atggcagcag gccaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttgaa
60
cgcagtgctg ctgaaactgt aaccaaaggt ggcattatgc ttccagaaaa atctcaaggc
120
aaagtattgc aagcaacagt agtcgctgtt ggctcgggtt ctaaaggtaa gggtggcgag
180
attcaaccag ttagcgtgaa agttggcgat aaagttcttc tcccaaaaga aggtggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttcgtg atggtgacat tcttggcaag
300
tacgtagact aa
312

<210> 238
<211> 103
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 with residue Tyrosine (Y) 75 changed to Glycine_Lysine (GK) 75. This construct contains an extra N-terminal Alanine residue (Ala-Cpn10-Y75GK)
<220>

<221> MISC_FEATURE
<222> (77)..(77)
<223> where X is anyone of the following amino acids: Lys, Arg or His
<400> 238
Ala Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val
1 5 10 15
Leu Val Glu Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile Met
20 25 30
Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val Ala 35
40 45
Val Gly Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln Pro Val Ser
50 55 60
Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu Gly Xaa Gly Gly Thr
65 70 75 80
Lys Val Val Leu Asp Asp Lys Asp Tyr Phe Leu Phe Arg Asp Gly Asp
85 90 95
Ile Leu Gly Lys Tyr Val Asp 100

<210> 239
<211> 315
<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and Y75GK substitutions
<400> 239
atggcagcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttgaa
60
aggagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccagaaaa atctcaagga
120
aaagtattgc aagcaacagt agtcgctgtt ggatcgggtt ctaaaggaaa gggtggagag
180
attcaaccag ttagcgtgaa agttggagat aaagttcttc tcccagaagg caaaggaggc
240
accaaagtag ttctagatga caaggattat ttcctattta gagatggtga cattcttgga
300
aagtacgtag actga
315

<210> 240
<211> 315
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA of Ala-Cpn10-Y75GK (Gly, Arg and stop codons are optimised in the cDNA)
<400> 240
atggcagcag gccaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttgaa
60
cgcagtgctg ctgaaactgt aaccaaaggt ggcattatgc ttccagaaaa atctcaaggc
120
aaagtattgc aagcaacagt agtcgctgtt ggctcgggtt ctaaaggtaa gggtggcgag
180
attcaaccag ttagcgtgaa agttggcgat aaagttcttc tcccagaagg caaaggtggc
240
accaaagtag ttctagatga caaggattat ttcctatttc gtgatggtga cattcttggc
300
aagtacgtag actaa
315

<210> 241
<211> 102
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 with residue residue Tyrosine (Y) 75 changed to Glycine (G) 75 and Glycine (G) 76 changed to Lysine (K) 76. This construct contains an extra N-terminal Alanine residue (Ala-Cpn10-Y75G,G76K)
<400> 241
Ala Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val
1 5 10 15
Leu Val Glu Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile Met
20 25 30
Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val Ala 35
40 45
Val Gly Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln Pro Val Ser
50 55 60
Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu Gly Lys Gly Thr Lys
65 70 75 80
Val Val Leu Asp Asp Lys Asp Tyr Phe Leu Phe Arg Asp Gly Asp Ile
85 90 95
Leu Gly Lys Tyr Val Asp 100

<210> 242
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and Y75G,G76K substitutions
<400> 242
atggcagcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttgaa
60
aggagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccagaaaa atctcaagga
120
aaagtattgc aagcaacagt agtcgctgtt ggatcgggtt ctaaaggaaa gggtggagag
180
attcaaccag ttagcgtgaa agttggagat aaagttcttc tcccagaagg taaaggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttagag atggtgacat tcttggaaag
300
tacgtagact ga
312

<210> 243
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA of Ala-Cpn10-Y75G,G76K (Gly, Arg and stop codons are optimised in the cDNA)
<400> 243
atggcagcag gccaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttgaa
60
cgcagtgctg ctgaaactgt aaccaaaggt ggcattatgc ttccagaaaa atctcaaggc
120
aaagtattgc aagcaacagt agtcgctgtt ggctcgggtt ctaaaggtaa gggtggcgag
180
attcaaccag ttagcgtgaa agttggcgat aaagttcttc tcccagaagg taaaggcacc
240

aaagtagttc tagatgacaa ggattatttc ctatttcgtg atggtgacat tcttggcaag
300
tacgtagact aa
312

<210> 244
<211> 102
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 with residue residue Tyrosine (Y) 75 changed to Lysine (K) 75 and Aspartic Acid (D) 94 changed to Lysine (K) 94. This construct contains an extra N-terminal Alanine residue (Ala-Cpn10-Y75K,D94K)
<220>
<221> MISC_FEATURE
<222> (76)..(76)
<223> where X is anyone of the following amino acids: Lys, Arg or His
<220>
<221> MISC_FEATURE
<222> (95)..(95)
<223> where Z is anyone of the following amino acids: Lys, Arg, His, Gly, Ala, Val, Leu, Ile, Pro, Phe, Tyr, Trp, Cys, Met, Ser, Thr, Asn or Gln
<400> 244
Ala Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val
1 5 10 15
Leu Val Glu Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile Met
20 25 30
Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val Ala 35
40 45
Val Gly Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln Pro Val Ser
50 55 60
Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu Xaa Gly Gly Thr Lys
65 70 75 80
Val Val Leu Asp Asp Lys Asp Tyr Phe Leu Phe Arg Asp Gly Glx Ile
85 90 95
Leu Gly Lys Tyr Val Asp 100

<210> 245
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and Y75K,D94K substitutions
<400> 245
atggcagcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttgaa
60
aggagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccagaaaa atctcaagga
120
aaagtattgc aagcaacagt agtcgctgtt ggatcgggtt ctaaaggaaa gggtggagag
180
attcaaccag ttagcgtgaa agttggagat aaagttcttc tcccagaaaa aggaggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttagag atggtaaaat tcttggaaag
300
tacgtagact ga
312

<210> 246
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA of Ala-Cpn10-Y75K,D94K (Gly, Arg and stop codons are optimised in the cDNA)
<400> 246
atggcagcag gccaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttgaa
60
cgcagtgctg ctgaaactgt aaccaaaggt ggcattatgc ttccagaaaa atctcaaggc
120
aaagtattgc aagcaacagt agtcgctgtt ggctcgggtt ctaaaggtaa gggtggcgag
180
attcaaccag ttagcgtgaa agttggcgat aaagttcttc tcccagaaaa aggtggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttcgtg atggtaaaat tcttggcaag
300
tacgtagact aa
312

<210> 247
<211> 102
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 with residue residue Tyrosine (Y) 75 changed to Lysine (K) 75 and Aspartic Acid (D) 94 changed to Lysine (K) 94. This construct contains an extra N-terminal Alanine residue (Ala-Cpn10-Y75K,D94N)
<220>
<221> MISC_FEATURE
<222> (76)..(76)
<223> where X is anyone of the following amino acids: Lys, Arg or His
<220>
<221> MISC_FEATURE
<222> (95)..(95)
<223> where Z is anyone of the following amino acids: Lys, Arg, His, Gly, Ala, Val, Leu, Ile, Pro, Phe, Tyr, Trp, Cys, Met, Ser, Thr, Asn or Gln
<400> 247
Ala Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val
1 5 10 15
Leu Val Glu Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile Met
20 25 30
Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val Ala 35
40 45
Val Gly Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln Pro Val Ser
50 55 60
Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu Xaa Gly Gly Thr Lys
65 70 75 80
Val Val Leu Asp Asp Lys Asp Tyr Phe Leu Phe Arg Asp Gly Glx Ile
85 90 95
Leu Gly Lys Tyr Val Asp 100

<210> 248
<211> 312
<212> DNA
<213> Artificial Sequence
<220>

<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and Y75K,D94N substitutions
<400> 248
atggcagcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttgaa
60
aggagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccagaaaa atctcaagga
120
aaagtattgc aagcaacagt agtcgctgtt ggatcgggtt ctaaaggaaa gggtggagag
180
attcaaccag ttagcgtgaa agttggagat aaagttcttc tcccagaaaa aggaggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttagag atggtaacat tcttggaaag
300
tacgtagact ga
312

<210> 249
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA of Ala-Cpn10-Y75K,D94N (Gly, Arg and stop codons are optimised in the cDNA)
<400> 249
atggcagcag gccaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttgaa
60
cgcagtgctg ctgaaactgt aaccaaaggt ggcattatgc ttccagaaaa atctcaaggc
120
aaagtattgc aagcaacagt agtcgctgtt ggctcgggtt ctaaaggtaa gggtggcgag
180
attcaaccag ttagcgtgaa agttggcgat aaagttcttc tcccagaaaa aggtggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttcgtg atggtaacat tcttggcaag
300
tacgtagact aa
312

<210> 250
<211> 102
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 with residue Aspartic Acid (D) 13 changed to Asparagine (N) 13. This construct contains an extra N-terminal Alanine residue (Ala-Cpn10-D13N)
<220>
<221> MISC_FEATURE
<222> (14)..(14)
<223> where Z is anyone of the following amino acids: Lys, Arg, His, Gly, Ala, Val, Leu, Ile, Pro, Phe, Tyr, Trp, Cys, Met, Ser, Thr, Asn or Gln
<400> 250
Ala Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Glx Arg Val
1 5 10 15
Leu Val Glu Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile Met
20 25 30
Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val Ala 35
40 45
Val Gly Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln Pro Val Ser
50 55 60
Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu Tyr Gly Gly Thr Lys

65 70 75 80
Val Val Leu Asp Asp Lys Asp Tyr Phe Leu Phe Arg Asp Gly Asp Ile
85 90 95
Leu Gly Lys Tyr Val Asp 100

<210> 251
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and D13N substitution
<400> 251
atggcagcag gacaagcgtt tagaaagttt cttccactct ttaaccgagt attggttgaa
60
aggagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccagaaaa atctcaagga
120
aaagtattgc aagcaacagt agtcgctgtt ggatcgggtt ctaaaggaaa gggtggagag
180
attcaaccag ttagcgtgaa agttggagat aaagttcttc tcccagaata tggaggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttagag atggtgacat tcttggaaag
300
tacgtagact ga
312

<210> 252
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA of Ala-Cpn10-D13N (Gly, Arg and stop codons are optimised in the cDNA)
<400> 252
atggcagcag gccaagcgtt tcgcaagttt cttccactct ttaaccgtgt attggttgaa
60
cgcagtgctg ctgaaactgt aaccaaaggt ggcattatgc ttccagaaaa atctcaaggc
120
aaagtattgc aagcaacagt agtcgctgtt ggctcgggtt ctaaaggtaa gggtggcgag
180
attcaaccag ttagcgtgaa agttggcgat aaagttcttc tcccagaata tggtggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttcgtg atggtgacat tcttggcaag
300
tacgtagact aa
312

<210> 253
<211> 102
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 with residue Glutamate (E) 18 changed to Alanine (A) 18. This construct contains an extra N-terminal Alanine residue (Ala-Cpn10-E18A)
<220>
<221> MISC_FEATURE
<222> (19)..(19)
<223> where Z is anyone of the following amino acids: Lys, Arg, His, Gly, Ala, Val, Leu, Ile, Pro, Phe, Tyr, Trp, Cys, Met, Ser, Thr, Asn or Gln

<400> 253
Ala Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val
1 5 10 15
Leu Val Glx Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile Met
20 25 30
Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val Ala 35
40 45
Val Gly Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln Pro Val Ser
50 55 60
Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu Tyr Gly Gly Thr Lys
65 70 75 80
Val Val Leu Asp Asp Lys Asp Tyr Phe Leu Phe Arg Asp Gly Asp Ile
85 90 95
Leu Gly Lys Tyr Val Asp 100

<210> 254
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and E18A substitution
<400> 254
atggcagcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttgcg
60
aggagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccagaaaa atctcaagga
120
aaagtattgc aagcaacagt agtcgctgtt ggatcgggtt ctaaaggaaa gggtggagag
180
attcaaccag ttagcgtgaa agttggagat aaagttcttc tcccagaata tggaggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttagag atggtgacat tcttggaaag
300
tacgtagact ga
312

<210> 255
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA of Ala-Cpn10-E18A (Gly, Arg and stop codons are optimised in the cDNA)
<400> 255
atggcagcag gccaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttgcg
60
cgcagtgctg ctgaaactgt aaccaaaggt ggcattatgc ttccagaaaa atctcaaggc
120
aaagtattgc aagcaacagt agtcgctgtt ggctcgggtt ctaaaggtaa gggtggcgag
180
attcaaccag ttagcgtgaa agttggcgat aaagttcttc tcccagaata tggtggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttcgtg atggtgacat tcttggcaag
300
tacgtagact aa
312

<210> 256
<211> 102
<212> PRT
<213> Artificial Sequence

<220>
<223> Human Cpn10 with residue Glutamate (E) 18 changed to Methionine (M) 18. This construct contains an extra N-terminal Alanine residue (Ala-Cpn10-E18M)
<400> 256
Ala Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val
1 5 10 15
Leu Val Met Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile Met
20 25 30
Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val Ala 35
40 45
Val Gly Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln Pro Val Ser
50 55 60
Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu Tyr Gly Gly Thr Lys
65 70 75 80
Val Val Leu Asp Asp Lys Asp Tyr Phe Leu Phe Arg Asp Gly Asp Ile
85 90 95
Leu Gly Lys Tyr Val Asp 100

<210> 257
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and E18M substitution
<400> 257
atggcagcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttatg
60
aggagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccagaaaa atctcaagga
120
aaagtattgc aagcaacagt agtcgctgtt ggatcgggtt ctaaaggaaa gggtggagag
180
attcaaccag ttagcgtgaa agttggagat aaagttcttc tcccagaata tggaggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttagag atggtgacat tcttggaaag
300
tacgtagact ga
312

<210> 258
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA of Ala-Cpn10-E18M (Gly, Arg and stop codons are optimised in the cDNA)
<400> 258
atggcagcag gccaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttatg
60
cgcagtgctg ctgaaactgt aaccaaaggt ggcattatgc ttccagaaaa atctcaaggc
120
aaagtattgc aagcaacagt agtcgctgtt ggctcgggtt ctaaaggtaa gggtggcgag
180
attcaaccag ttagcgtgaa agttggcgat aaagttcttc tcccagaata tggtggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttcgtg atggtgacat tcttggcaag
300
tacgtagact aa
312
<210> 259

<211> 102
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 with residue Glutamate (E) 18 changed to Glutamine (Q) 18. This construct contains an extra N-terminal Alanine residue (Ala-Cpn10-E18Q
<400> 259
Ala Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val
1 5 10 15
Leu Val Gln Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile Met
20 25 30
Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val Ala 35
40 45
Val Gly Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln Pro Val Ser
50 55 60
Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu Tyr Gly Gly Thr Lys
65 70 75 80
Val Val Leu Asp Asp Lys Asp Tyr Phe Leu Phe Arg Asp Gly Asp Ile
85 90 95
Leu Gly Lys Tyr Val Asp 100

<210> 260
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and E18Q substitution
<400> 260
atggcagcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttcag
60
aggagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccagaaaa atctcaagga
120
aaagtattgc aagcaacagt agtcgctgtt ggatcgggtt ctaaaggaaa gggtggagag
180
attcaaccag ttagcgtgaa agttggagat aaagttcttc tcccagaata tggaggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttagag atggtgacat tcttggaaag
300
tacgtagact ga
312

<210> 261
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA of Ala-Cpn10-E18Q (Gly, Arg and stop codons are optimised in the cDNA)
<400> 261
atggcagcag gccaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttcag
60
cgcagtgctg ctgaaactgt aaccaaaggt ggcattatgc ttccagaaaa atctcaaggc
120
aaagtattgc aagcaacagt agtcgctgtt ggctcgggtt ctaaaggtaa gggtggcgag
180
attcaaccag ttagcgtgaa agttggcgat aaagttcttc tcccagaata tggtggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttcgtg atggtgacat tcttggcaag
300

tacgtagact aa
312

<210> 262
<211> 102
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 with residue Glutamate (E) 18 changed to Serine (S) 18. This construct contains an extra N-terminal Alanine residue (Ala-Cpn10-E18S)
<400> 262
Ala Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val
1 5 10 15
Leu Val Ser Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile Met
20 25 30
Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val Ala 35
40 45
Val Gly Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln Pro Val Ser
50 55 60
Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu Tyr Gly Gly Thr Lys
65 70 75 80
Val Val Leu Asp Asp Lys Asp Tyr Phe Leu Phe Arg Asp Gly Asp Ile
85 90 95
Leu Gly Lys Tyr Val Asp 100

<210> 263
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and E18S substitution
<400> 263
atggcagcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttagc
60
aggagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccagaaaa atctcaagga
120
aaagtattgc aagcaacagt agtcgctgtt ggatcgggtt ctaaaggaaa gggtggagag
180
attcaaccag ttagcgtgaa agttggagat aaagttcttc tcccagaata tggaggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttagag atggtgacat tcttggaaag
300
tacgtagact ga
312

<210> 264
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA of Ala-Cpn10-E18S (Gly, Arg and stop codons are optimised in the cDNA)
<400> 264
atggcagcag gccaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttagc
60
cgcagtgctg ctgaaactgt aaccaaaggt ggcattatgc ttccagaaaa atctcaaggc
120
aaagtattgc aagcaacagt agtcgctgtt ggctcgggtt ctaaaggtaa gggtggcgag
180

attcaaccag ttagcgtgaa agttggcgat aaagttcttc tcccagaata tggtggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttcgtg atggtgacat tcttggcaag
300
tacgtagact aa
312

<210> 265
<211> 102
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 with residue Glutamate (E) 23 changed to Glutamine (Q) 23. This construct contains an extra N-terminal Alanine residue (Ala-Cpn10-E23Q)
<400> 265
Ala Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val
1 5 10 15
Leu Val Glu Arg Ser Ala Ala Gln Thr Val Thr Lys Gly Gly Ile Met
20 25 30
Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val Ala 35
40 45
Val Gly Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln Pro Val Ser
50 55 60
Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu Tyr Gly Gly Thr Lys
65 70 75 80
Val Val Leu Asp Asp Lys Asp Tyr Phe Leu Phe Arg Asp Gly Asp Ile
85 90 95
Leu Gly Lys Tyr Val Asp 100

<210> 266
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and E23Q substitution
<400> 266
atggcagcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttgaa
60
aggagtgctg ctcagactgt aaccaaagga ggcattatgc ttccagaaaa atctcaagga
120
aaagtattgc aagcaacagt agtcgctgtt ggatcgggtt ctaaaggaaa gggtggagag
180
attcaaccag ttagcgtgaa agttggagat aaagttcttc tcccagaata tggaggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttagag atggtgacat tcttggaaag
300
tacgtagact ga
312

<210> 267
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA of Ala-Cpn10-E23Q (Gly, Arg and stop codons are optimised in the cDNA)
<400> 267
atggcagcag gccaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttgaa
60

cgcagtgctg ctcagactgt aaccaaaggt ggcattatgc ttccagaaaa atctcaaggc
120
aaagtattgc aagcaacagt agtcgctgtt ggctcgggtt ctaaaggtaa gggtggcgag
180
attcaaccag ttagcgtgaa agttggcgat aaagttcttc tcccagaata tggtggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttcgtg atggtgacat tcttggcaag
300
tacgtagact aa
312

<210> 268
<211> 102
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 with residue Glutamate (E) 34 changed to Glutamine (Q) 34. This construct contains an extra N-terminal Alanine residue (Ala-Cpn10-E34Q)
<220>
<221> MISC_FEATURE
<222> (35)..(35)
<223> where Z is anyone of the following amino acids: Lys, Arg, His, Gly, Ala, Val, Leu, Ile, Pro, Phe, Tyr, Trp, Cys, Met, Ser, Thr, Asn or Gln
<400> 268
Ala Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val
1 5 10 15
Leu Val Glu Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile Met
20 25 30
Leu Pro Glx Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val Ala 35
40 45
Val Gly Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln Pro Val Ser
50 55 60
Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu Tyr Gly Gly Thr Lys
65 70 75 80
Val Val Leu Asp Asp Lys Asp Tyr Phe Leu Phe Arg Asp Gly Asp Ile
85 90 95
Leu Gly Lys Tyr Val Asp 100

<210> 269
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and E34Q substitution
<400> 269
atggcagcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttgaa
60
aggagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccacagaa atctcaagga
120
aaagtattgc aagcaacagt agtcgctgtt ggatcgggtt ctaaaggaaa gggtggagag
180
attcaaccag ttagcgtgaa agttggagat aaagttcttc tcccagaata tggaggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttagag atggtgacat tcttggaaag
300
tacgtagact ga
312

<210> 270
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA of Ala-Cpn10-E34Q (Gly, Arg and stop codons are optimised in the cDNA)
<400> 270
atggcagcag gccaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttgaa
60
cgcagtgctg ctgaaactgt aaccaaaggt ggcattatgc ttccacagaa atctcaaggc
120
aaagtattgc aagcaacagt agtcgctgtt ggctcgggtt ctaaaggtaa gggtggcgag
180
attcaaccag ttagcgtgaa agttggcgat aaagttcttc tcccagaata tggtggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttcgtg atggtgacat tcttggcaag
300
tacgtagact aa
312

<210> 271
<211> 102
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 with residue Glutamate (E) 58 changed to Glutamine (Q) 58. This construct contains an extra N-terminal Alanine residue (Ala-Cpn10-E58Q)
<220>
<221> MISC_FEATURE
<222> (59)..(59)
<223> where Z is anyone of the following amino acids: Lys, Arg, His, Gly, Ala, Val, Leu, Ile, Pro, Phe, Tyr, Trp, Cys, Met, Ser, Thr, Asn or Gln
<400> 271
Ala Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val
1 5 10 15
Leu Val Glu Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile Met
20 25 30
Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val Ala 35
40 45
Val Gly Ser Gly Ser Lys Gly Lys Gly Gly Glx Ile Gln Pro Val Ser
50 55 60
Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu Tyr Gly Gly Thr Lys
65 70 75 80
Val Val Leu Asp Asp Lys Asp Tyr Phe Leu Phe Arg Asp Gly Asp Ile
85 90 95
Leu Gly Lys Tyr Val Asp 100

<210> 272
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and E58Q substitution
<400> 272
atggcagcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttgaa
60

aggagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccagaaaa atctcaagga
120
aaagtattgc aagcaacagt agtcgctgtt ggatcgggtt ctaaaggaaa gggtggacag
180
attcaaccag ttagcgtgaa agttggagat aaagttcttc tcccagaata tggaggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttagag atggtgacat tcttggaaag
300
tacgtagact ga
312

<210> 273
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA of Ala-Cpn10-E58Q (Gly, Arg and stop codons are optimised in the cDNA)
<400> 273
atggcagcag gccaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttgaa
60
cgcagtgctg ctgaaactgt aaccaaaggt ggcattatgc ttccagaaaa atctcaaggc
120
aaagtattgc aagcaacagt agtcgctgtt ggctcgggtt ctaaaggtaa gggtggccag
180
attcaaccag ttagcgtgaa agttggcgat aaagttcttc tcccagaata tggtggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttcgtg atggtgacat tcttggcaag
300
tacgtagact aa
312

<210> 274
<211> 102
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 with residue Aspartate (D) 68 changed to Asparagine (N) 68. This construct contains an extra N-terminal Alanine residue (Ala-Cpn10-D68N)
<220>
<221> MISC_FEATURE
<222> (69)..(69)
<223> where Z is anyone of the following amino acids: Lys, Arg, His, Gly, Ala, Val, Leu, Ile, Pro, Phe, Tyr, Trp, Cys, Met, Ser, Thr, Asn or Gln
<400> 274
Ala Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val
1 5 10 15
Leu Val Glu Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile Met
20 25 30
Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val Ala 35
40 45
Val Gly Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln Pro Val Ser
50 55 60
Val Lys Val Gly Glx Lys Val Leu Leu Pro Glu Tyr Gly Gly Thr Lys
65 70 75 80
Val Val Leu Asp Asp Lys Asp Tyr Phe Leu Phe Arg Asp Gly Asp Ile
85 90 95
Leu Gly Lys Tyr Val Asp 100

<210> 275
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and D68N substitution
<400> 275
atggcagcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttgaa
60
aggagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccagaaaa atctcaagga
120
aaagtattgc aagcaacagt agtcgctgtt ggatcgggtt ctaaaggaaa gggtggagag
180
attcaaccag ttagcgtgaa agttggaaac aaagttcttc tcccagaata tggaggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttagag atggtgacat tcttggaaag
300
tacgtagact ga
312

<210> 276
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA of Ala-Cpn10-D68N (Gly, Arg and stop codons are optimised in the cDNA)
<400> 276
atggcagcag gccaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttgaa
60
cgcagtgctg ctgaaactgt aaccaaaggt ggcattatgc ttccagaaaa atctcaaggc
120
aaagtattgc aagcaacagt agtcgctgtt ggctcgggtt ctaaaggtaa gggtggcgag
180
attcaaccag ttagcgtgaa agttggcaac aaagttcttc tcccagaata tggtggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttcgtg atggtgacat tcttggcaag
300
tacgtagact aa
312

<210> 277
<211> 102
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 with residue Glutamate (E) 74 changed to Glutamine (Q) 74. This construct contains an extra N-terminal Alanine residue (Ala-Cpn10-E74Q)
<220>
<221> MISC_FEATURE
<222> (75)..(75)
<223> where Z is anyone of the following amino acids: Lys, Arg, His, Gly, Ala, Val, Leu, Ile, Pro, Phe, Tyr, Trp, Cys, Met, Ser, Thr, Asn or Gln
<400> 277
Ala Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val
1 5 10 15
Leu Val Glu Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile Met
20 25 30

Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val Ala 35
40 45
Val Gly Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln Pro Val Ser
50 55 60
Val Lys Val Gly Asp Lys Val Leu Leu Pro Glx Tyr Gly Gly Thr Lys
65 70 75 80
Val Val Leu Asp Asp Lys Asp Tyr Phe Leu Phe Arg Asp Gly Asp Ile
85 90 95
Leu Gly Lys Tyr Val Asp 100

<210> 278
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and E74Q substitution
<400> 278
atggcagcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttgaa
60
aggagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccagaaaa atctcaagga
120
aaagtattgc aagcaacagt agtcgctgtt ggatcgggtt ctaaaggaaa gggtggagag
180
attcaaccag ttagcgtgaa agttggagat aaagttcttc tcccacagta tggaggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttagag atggtgacat tcttggaaag
300
tacgtagact ga
312

<210> 279
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA of Ala-Cpn10-E74Q (Gly, Arg and stop codons are optimised in the cDNA)
<400> 279
atggcagcag gccaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttgaa
60
cgcagtgctg ctgaaactgt aaccaaaggt ggcattatgc ttccagaaaa atctcaaggc
120
aaagtattgc aagcaacagt agtcgctgtt ggctcgggtt ctaaaggtaa gggtggcgag
180
attcaaccag ttagcgtgaa agttggcgat aaagttcttc tcccacagta tggtggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttcgtg atggtgacat tcttggcaag
300
tacgtagact aa
312

<210> 280
<211> 102
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 with residue Aspartate (D) 83 changed to Asparagine (N) 83. This construct contains an extra N-terminal Alanine residue (Ala-Cpn10-D83N)
<220>

<221> MISC_FEATURE
<222> (84)..(84)
<223> where Z is anyone of the following amino acids: Lys, Arg, His, Gly, Ala, Val, Leu, Ile, Pro, Phe, Tyr, Trp, Cys, Met, Ser, Thr, Asn or Gln
<400> 280
Ala Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val
1 5 10 15
Leu Val Glu Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile Met
20 25 30
Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val Ala 35
40 45
Val Gly Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln Pro Val Ser
50 55 60
Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu Tyr Gly Gly Thr Lys
65 70 75 80
Val Val Leu Glx Asp Lys Asp Tyr Phe Leu Phe Arg Asp Gly Asp Ile
85 90 95
Leu Gly Lys Tyr Val Asp 100

<210> 281
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and D83N substitution
<400> 281
atggcagcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttgaa
60
aggagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccagaaaa atctcaagga
120
aaagtattgc aagcaacagt agtcgctgtt ggatcgggtt ctaaaggaaa gggtggagag
180
attcaaccag ttagcgtgaa agttggagat aaagttcttc tcccagaata tggaggcacc
240
aaagtagttc taaacgacaa ggattatttc ctatttagag atggtgacat tcttggaaag
300
tacgtagact ga
312

<210> 282
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA of Ala-Cpn10-D83N (Gly, Arg and stop codons are optimised in the cDNA)
<400> 282
atggcagcag gccaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttgaa
60
cgcagtgctg ctgaaactgt aaccaaaggt ggcattatgc ttccagaaaa atctcaaggc
120
aaagtattgc aagcaacagt agtcgctgtt ggctcgggtt ctaaaggtaa gggtggcgag
180
attcaaccag ttagcgtgaa agttggcgat aaagttcttc tcccagaata tggtggcacc
240
aaagtagttc taaacgacaa ggattatttc ctatttcgtg atggtgacat tcttggcaag
300
tacgtagact aa
312

<210> 283
<211> 102
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 with residue Aspartate (D) 84 changed to Asparagine (N) 84 This construct contains an extra N-terminal Alanine residue (Ala-Cpn10-D84N)
<220>
<221> MISC_FEATURE
<222> (85)..(85)
<223> where Z is anyone of the following amino acids: Lys, Arg, His, Gly, Ala, Val, Leu, Ile, Pro, Phe, Tyr, Trp, Cys, Met, Ser, Thr, Asn or Gln
<400> 283
Ala Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val
1 5 10 15
Leu Val Glu Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile Met
20 25 30
Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val Ala 35
40 45
Val Gly Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln Pro Val Ser
50 55 60
Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu Tyr Gly Gly Thr Lys
65 70 75 80
Val Val Leu Asp Glx Lys Asp Tyr Phe Leu Phe Arg Asp Gly Asp Ile
85 90 95
Leu Gly Lys Tyr Val Asp 100

<210> 284
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and D84N substitution
<400> 284
atggcagcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttgaa
60
aggagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccagaaaa atctcaagga
120
aaagtattgc aagcaacagt agtcgctgtt ggatcgggtt ctaaaggaaa gggtggagag
180
attcaaccag ttagcgtgaa agttggagat aaagttcttc tcccagaata tggaggcacc
240
aaagtagttc tagataacaa ggattatttc ctatttagag atggtgacat tcttggaaag
300
tacgtagact ga
312

<210> 285
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA of Ala-Cpn10-D84N (Gly, Arg and stop codons are optimised in the cDNA)
<400> 285
atggcagcag gccaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttgaa
60

cgcagtgctg ctgaaactgt aaccaaaggt ggcattatgc ttccagaaaa atctcaaggc
120
aaagtattgc aagcaacagt agtcgctgtt ggctcgggtt ctaaaggtaa gggtggcgag
180
attcaaccag ttagcgtgaa agttggcgat aaagttcttc tcccagaata tggtggcacc
240
aaagtagttc tagataacaa ggattatttc ctatttcgtg atggtgacat tcttggcaag
300
tacgtagact aa
312

<210> 286
<211> 102
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 with residue Aspartate (D) 86 changed to Asparagine (N) 86 This construct contains an extra N-terminal Alanine residue (Ala-Cpn10-D86N)
<220>
<221> MISC_FEATURE
<222> (87)..(87)
<223> where Z is anyone of the following amino acids: Lys, Arg, His, Gly, Ala, Val, Leu, Ile, Pro, Phe, Tyr, Trp, Cys, Met, Ser, Thr, Asn or Gln
<400> 286
Ala Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val
1 5 10 15
Leu Val Glu Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile Met
20 25 30
Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val Ala 35
40 45
Val Gly Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln Pro Val Ser
50 55 60
Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu Tyr Gly Gly Thr Lys
65 70 75 80
Val Val Leu Asp Asp Lys Glx Tyr Phe Leu Phe Arg Asp Gly Asp Ile
85 90 95
Leu Gly Lys Tyr Val Asp 100

<210> 287
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and D86N substitution
<400> 287
atggcagcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttgaa
60
aggagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccagaaaa atctcaagga
120
aaagtattgc aagcaacagt agtcgctgtt ggatcgggtt ctaaaggaaa gggtggagag
180
attcaaccag ttagcgtgaa agttggagat aaagttcttc tcccagaata tggaggcacc
240
aaagtagttc tagatgacaa gaactatttc ctatttagag atggtgacat tcttggaaag
300
tacgtagact ga
312

<210> 288
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA of Ala-Cpn10-D86N (Gly, Arg and stop codons are optimised in the cDNA)
<400> 288
atggcagcag gccaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttgaa
60
cgcagtgctg ctgaaactgt aaccaaaggt ggcattatgc ttccagaaaa atctcaaggc
120
aaagtattgc aagcaacagt agtcgctgtt ggctcgggtt ctaaaggtaa gggtggcgag
180
attcaaccag ttagcgtgaa agttggcgat aaagttcttc tcccagaata tggtggcacc
240
aaagtagttc tagatgacaa gaactatttc ctatttcgtg atggtgacat tcttggcaag
300
tacgtagact aa
312

<210> 289
<211> 102
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 with residue Aspartate (D) 92 changed to Asparagine (N) 92 This construct contains an extra N-terminal Alanine residue (Ala-Cpn10-D92N)
<220>
<221> MISC_FEATURE
<222> (93)..(93)
<223> where Z is anyone of the following amino acids: Lys, Arg, His, Gly, Ala, Val, Leu, Ile, Pro, Phe, Tyr, Trp, Cys, Met, Ser, Thr, Asn or Gln
<400> 289
Ala Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val
1 5 10 15
Leu Val Glu Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile Met
20 25 30
Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val Ala 35
40 45
Val Gly Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln Pro Val Ser
50 55 60
Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu Tyr Gly Gly Thr Lys
65 70 75 80
Val Val Leu Asp Asp Lys Asp Tyr Phe Leu Phe Arg Glx Gly Asp Ile
85 90 95
Leu Gly Lys Tyr Val Asp 100

<210> 290
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and D92N substitution
<400> 290
atggcagcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttgaa
60

aggagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccagaaaa atctcaagga
120
aaagtattgc aagcaacagt agtcgctgtt ggatcgggtt ctaaaggaaa gggtggagag
180
attcaaccag ttagcgtgaa agttggagat aaagttcttc tcccagaata tggaggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttagaa acggtgacat tcttggaaag
300
tacgtagact ga
312

<210> 291
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA of Ala-Cpn10-D92N (Gly, Arg and stop codons are optimised in the cDNA)
<400> 291
atggcagcag gccaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttgaa
60
cgcagtgctg ctgaaactgt aaccaaaggt ggcattatgc ttccagaaaa atctcaaggc
120
aaagtattgc aagcaacagt agtcgctgtt ggctcgggtt ctaaaggtaa gggtggcgag
180
attcaaccag ttagcgtgaa agttggcgat aaagttcttc tcccagaata tggtggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttcgta acggtgacat tcttggcaag
300
tacgtagact aa
312

<210> 292
<211> 102
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 with residue Aspartate (D) 94 changed to Alanine (A) 94 This construct contains an extra N-terminal Alanine residue (Ala-Cpn10-D94A)
<220>
<221> MISC_FEATURE
<222> (94)..(94)
<223> where Z is anyone of the following amino acids: Lys, Arg, His, Gly, Ala, Val, Leu, Ile, Pro, Phe, Tyr, Trp, Cys, Met, Ser, Thr, Asn or Gln
<400> 292

Ala	Ala	Gly	Gln	Ala	Phe	Arg	Lys	Phe	Leu	Pro	Leu	Phe	Asp	Arg	Val
1				5				10					15		
Leu	Val	Glu	Arg	Ser	Ala	Ala	Glu	Thr	Val	Thr	Lys	Gly	Gly	Ile	Met
20				25				30							
Leu	Pro	Glu	Lys	Ser	Gln	Gly	Lys	Val	Leu	Gln	Ala	Thr	Val	Val	Ala
40				45											
Val	Gly	Ser	Gly	Ser	Lys	Gly	Lys	Gly	Gly	Glu	Ile	Gln	Pro	Val	Ser
	50					55					60				
Val	Lys	Val	Gly	Asp	Lys	Val	Leu	Leu	Pro	Glu	Tyr	Gly	Gly	Thr	Lys
65				70				75					80		
Val	Val	Leu	Asp	Asp	Lys	Asp	Tyr	Phe	Leu	Phe	Arg	Asp	Gly	Glx	Ile
85				90				95							
Leu	Gly	Lys	Tyr	Val	Asp			100							

<210> 293
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and D94A substitution
<400> 293
atggcagcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttgaa
60
aggagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccagaaaa atctcaagga
120
aaagtattgc aagcaacagt agtcgctgtt ggatcgggtt ctaaaggaaa gggtggagag
180
attcaaccag ttagcgtgaa agttggagat aaagttcttc tcccagaata tggaggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttagag atggtgcgat tcttggaaag
300
tacgtagact ga
312

<210> 294
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA of Ala-Cpn10-D94A (Gly, Arg and stop codons are optimised in the cDNA)
<400> 294
atggcagcag gccaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttgaa
60
cgcagtgctg ctgaaactgt aaccaaaggt ggcattatgc ttccagaaaa atctcaaggc
120
aaagtattgc aagcaacagt agtcgctgtt ggctcgggtt ctaaaggtaa gggtggcgag
180
attcaaccag ttagcgtgaa agttggcgat aaagttcttc tcccagaata tggtggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttcgtg atggtgcgat tcttggcaag
300
tacgtagact aa
312

<210> 295
<211> 102
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 with residue Aspartate (D) 94 changed to Methionine (M) 94 This construct contains an extra N-terminal Alanine residue (Ala-Cpn10-D94M)
<400> 295
Ala Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val
1 5 10 15
Leu Val Glu Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile Met
20 25 30
Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val Ala 35
40 45
Val Gly Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln Pro Val Ser
50 55 60
Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu Tyr Gly Gly Thr Lys
65 70 75 80

Val Val Leu Asp Asp Lys Asp Tyr Phe Leu Phe Arg Asp Gly Met Ile
85 90 95
Leu Gly Lys Tyr Val Asp 100

<210> 296
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and D94M substitution
<400> 296
atggcagcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttgaa
60
aggagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccagaaaa atctcaagga
120
aaagtattgc aagcaacagt agtcgctgtt ggatcgggtt ctaaaggaaa gggtggagag
180
attcaaccag ttagcgtgaa agttggagat aaagttcttc tcccagaata tggaggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttagag atggtatgat tcttggaaag
300
tacgtagact ga
312

<210> 297
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA of Ala-Cpn10-D94M (Gly, Arg and stop codons are optimised in the cDNA)
<400> 297
atggcagcag gccaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttgaa
60
cgcagtgctg ctgaaactgt aaccaaaggt ggcattatgc ttccagaaaa atctcaaggc
120
aaagtattgc aagcaacagt agtcgctgtt ggctcgggtt ctaaaggtaa gggtggcgag
180
attcaaccag ttagcgtgaa agttggcgat aaagttcttc tcccagaata tggtggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttcgtg atggtatgat tcttggcaag
300
tacgtagact aa
312

<210> 298
<211> 102
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 with residue Aspartate (D) 94 changed to Asparagine (N) 94 This construct contains an extra N-terminal Alanine residue (Ala-Cpn10-D94N)
<400> 298
Ala Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val
1 5 10 15
Leu Val Glu Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile Met
20 25 30
Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val Ala 35
40 45

Val Gly Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln Pro Val Ser
50 55 60
Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu Tyr Gly Gly Thr Lys
65 70 75 80
Val Val Leu Asp Asp Lys Asp Tyr Phe Leu Phe Arg Asp Gly Asn Ile
85 90 95
Leu Gly Lys Tyr Val Asp 100

<210> 299
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and D94N substitution
<400> 299
atggcagcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttgaa
60
aggagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccagaaaa atctcaagga
120
aaagtattgc aagcaacagt agtcgctgtt ggatcgggtt ctaaaggaaa gggtggagag
180
attcaaccag ttagcgtgaa agttggagat aaagttcttc tcccagaata tggaggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttagag atggtaacat tcttggaaag
300
tacgtagact ga
312

<210> 300
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA of Ala-Cpn10-D94N (Gly, Arg and stop codons are optimised in the cDNA)
<400> 300
atggcagcag gccaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttgaa
60
cgcagtgctg ctgaaactgt aaccaaaggt ggcattatgc ttccagaaaa atctcaaggc
120
aaagtattgc aagcaacagt agtcgctgtt ggctcgggtt ctaaaggtaa gggtggcgag
180
attcaaccag ttagcgtgaa agttggcgat aaagttcttc tcccagaata tggtggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttcgtg atggtaacat tcttggcaag
300
tacgtagact aa
312

<210> 301
<211> 102
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 with residue Aspartate (D) 94 changed to Serine (S) 94 This construct contains an extra N-terminal Alanine residue (Ala-Cpn10-D94S)
<400> 301
Ala Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val
1 5 10 15

Leu Val Glu Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile Met
20 25 30
Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val Ala 35
40 45
Val Gly Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln Pro Val Ser
50 55 60
Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu Tyr Gly Gly Thr Lys
65 70 75 80
Val Val Leu Asp Asp Lys Asp Tyr Phe Leu Phe Arg Asp Gly Ser Ile
85 90 95
Leu Gly Lys Tyr Val Asp 100

<210> 302
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and D94S substitution
<400> 302
atggcagcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttgaa
60
aggagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccagaaaa atctcaagga
120
aaagtattgc aagcaacagt agtcgctgtt ggatcgggtt ctaaaggaaa gggtggagag
180
attcaaccag ttagcgtgaa agttggagat aaagttcttc tcccagaata tggaggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttagag atggtagcat tcttggaaag
300
tacgtagact ga
312

<210> 303
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA of Ala-Cpn10-D94S (Gly, Arg and stop codons are optimised in the cDNA)
<400> 303
atggcagcag gccaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttgaa
60
cgcagtgctg ctgaaactgt aaccaaaggt ggcattatgc ttccagaaaa atctcaaggc
120
aaagtattgc aagcaacagt agtcgctgtt ggctcgggtt ctaaaggtaa gggtggcgag
180
attcaaccag ttagcgtgaa agttggcgat aaagttcttc tcccagaata tggtggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttcgtg atggtagcat tcttggcaag
300
tacgtagact aa
312

<210> 304
<211> 102
<212> PRT
<213> Artificial Sequence
<220>

<223> Human Cpn10 with residue Aspartate (D) 101 changed to Asparagine (N) 101. This construct contains an extra N-terminal Alanine residue (Ala-Cpn10-D101N)
<220>
<221> MISC_FEATURE
<222> (101)..(101)
<223> where Z is anyone of the following amino acids: Lys, Arg, His, Gly, Ala, Val, Leu, Ile, Pro, Phe, Tyr, Trp, Cys, Met, Ser, Thr, Asn or Gln
<400> 304
Ala Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val
1 5 10 15
Leu Val Glu Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile Met
20 25 30
Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val Ala 35
40 45
Val Gly Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln Pro Val Ser
50 55 60
Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu Tyr Gly Gly Thr Lys
65 70 75 80
Val Val Leu Asp Asp Lys Asp Tyr Phe Leu Phe Arg Asp Gly Asp Ile
85 90 95
Leu Gly Lys Tyr Val Glx 100

<210> 305
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and D101N substitution
<400> 305
atggcagcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttgaa
60
aggagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccagaaaa atctcaagga
120
aaagtattgc aagcaacagt agtcgctgtt ggatcgggtt ctaaaggaaa gggtggagag
180
attcaaccag ttagcgtgaa agttggagat aaagttcttc tcccagaata tggaggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttagag atggtgacat tcttggaaag
300
tacgtaaact ga
312

<210> 306
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA of Ala-Cpn10-D101N (Gly, Arg and stop codons are optimised in the cDNA)
<400> 306
atggcagcag gccaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttgaa
60
cgcagtgctg ctgaaactgt aaccaaaggt ggcattatgc ttccagaaaa atctcaaggc
120
aaagtattgc aagcaacagt agtcgctgtt ggctcgggtt ctaaaggtaa gggtggcgag
180
attcaaccag ttagcgtgaa agttggcgat aaagttcttc tcccagaata tggtggcacc
240

aaagtagttc tagatgacaa ggattatttc ctatttcgtg atggtgacat tcttggcaag
300
tacgtaaact aa
312

<210> 307
<211> 103
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 with an additional N-terminal Histidine (H) residue. The initiation Methionine (M) is not removed from this protein (MH-Cpn10)
<400> 307
Met His Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg
1 5 10 15
Val Leu Val Glu Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile
20 25 30
Met Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val 35
40 45
Ala Val Gly Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln Pro Val
50 55 60
Ser Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu Tyr Gly Gly Thr
65 70 75 80
Lys Val Val Leu Asp Asp Lys Asp Tyr Phe Leu Phe Arg Asp Gly Asp
85 90 95
Ile Leu Gly Lys Tyr Val Asp
100

<210> 308
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Histidine (H) codon.
<400> 308
atgcatgcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttgaa
60
aggagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccagaaaa atctcaagga
120
aaagtattgc aagcaacagt agtcgctgtt ggatcgggtt ctaaaggaaa gggtggagag
180
attcaaccag ttagcgtgaa agttggagat aaagttcttc tcccagaata tggaggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttagag atggtgacat tcttggaaag
300
tacgtagact ga
312

<210> 309
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised Cpn10 cDNA with an extra N-terminal Histidine (H) codon (Gly, Arg and stop codons are optimised in the cDNA).
<400> 309
atgcatgcag gccaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttgaa
60
cgcagtgctg ctgaaactgt aaccaaaggt ggcattatgc ttccagaaaa atctcaaggc
120

aaagtattgc aagcaacagt agtcgctgtt ggctcgggtt ctaaaggtaa gggtggcgag
180
attcaaccag ttagcgtgaa agttggcgat aaagttcttc tcccagaata tggtggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttcgtg atggtgacat tcttggcaag
300
tacgtagact aa
312

<210> 310
<211> 103
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 with an additional N-terminal Arginine (R) residue inserted. The initiation Methionine (M) is not removed from this protein (MR-Cpn10)
<400> 310
Met Arg Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg
1 5 10 15
Val Leu Val Glu Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile
20 25 30
Met Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val 35
40 45
Ala Val Gly Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln Pro Val
50 55 60
Ser Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu Tyr Gly Gly Thr
65 70 75 80
Lys Val Val Leu Asp Asp Lys Asp Tyr Phe Leu Phe Arg Asp Gly Asp
85 90 95
Ile Leu Gly Lys Tyr Val Asp 100

<210> 311
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Arginine (R) codon
<400> 311
atgcgcgcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttgaa
60
aggagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccagaaaa atctcaagga
120
aaagtattgc aagcaacagt agtcgctgtt ggatcgggtt ctaaaggaaa gggtggagag
180
attcaaccag ttagcgtgaa agttggagat aaagttcttc tcccagaata tggaggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttagag atggtgacat tcttggaaag
300
tacgtagact ga
312

<210> 312
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised Cpn10 cDNA with an extra N-terminal Arginine (R) codon (Gly, Arg and stop codons are optimised in the cDNA)
<400> 312

atgcgcgcag gccaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttgaa
60
cgcagtgctg ctgaaactgt aaccaaaggt ggcattatgc ttccagaaaa atctcaaggc
120
aaagtattgc aagcaacagt agtcgctgtt ggctcgggtt ctaaaggtaa gggtggcgag
180
attcaaccag ttagcgtgaa agttggcgat aaagttcttc tcccagaata tggtggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttcgtg atggtgacat tcttggcaag
300
tacgtagact aa
312

<210> 313
<211> 103
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 with an additional N-terminal Lysine (K) residue inserted. The initiation Methionine (M) is not removed from this protein (MK-Cpn10)
<400> 313
Met Lys Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg
1 5 10 15
Val Leu Val Glu Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile
20 25 30
Met Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val 35
40 45
Ala Val Gly Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln Pro Val
50 55 60
Ser Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu Tyr Gly Gly Thr
65 70 75 80
Lys Val Val Leu Asp Asp Lys Asp Tyr Phe Leu Phe Arg Asp Gly Asp
85 90 95
Ile Leu Gly Lys Tyr Val Asp 100

<210> 314
<211> 312
<212> DNA
<213> Artificial Sequence
<220>
<223> Native cDNA with an extra N-terminal Lysine (AAA) codon
<400> 314
atgaaagcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttgaa
60
aggagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccagaaaa atctcaagga
120
aaagtattgc aagcaacagt agtcgctgtt ggatcgggtt ctaaaggaaa gggtggagag
180
attcaaccag ttagcgtgaa agttggagat aaagttcttc tcccagaata tggaggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttagag atggtgacat tcttggaaag
300
tacgtagact ga
312
<210> 315
<211> 312
<212> DNA
<213> Artificial Sequence
<220>

<223> Optimised cDNA with an extra N-terminal Lysine (AAA) codon (Gly, Arg and stop codons are optimised in the cDNA)
<400> 315
atgaaagcag gccaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttgaa 60
cgcagtgctg ctgaaactgt aaccaaaggt ggcattatgc ttccagaaaa atctcaaggc 120
aaagtattgc aagcaacagt agtcgctgtt ggctcgggtt ctaaaggtaa gggtggcgag 180
attcaaccag ttagcgtgaa agttggcgat aaagttcttc tcccagaata tggtggcacc 240
aaagtagttc tagatgacaa ggattatttc ctatttcgtg atggtgacat tcttggcaag 300
tacgtagact aa 312

<210> 316
<211> 104
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 with two additional N-terminal Lysine (K) residues inserted. The initiation Methionine (M) is not removed from this protein (MKK-Cpn10
<220>
<221> MISC_FEATURE
<222> (2)..(3)
<223> where K is anyone of the following amino acids: Lys, Arg or His
<400> 316
Met Lys Lys Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp
1 5 10 15
Arg Val Leu Val Glu Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly
20 25 30
Ile Met Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val 35
40 45
Val Ala Val Gly Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln Pro
50 55 60
Val Ser Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu Tyr Gly Gly
65 70 75 80
Thr Lys Val Val Leu Asp Asp Lys Asp Tyr Phe Leu Phe Arg Asp Gly
85 90 95
Asp Ile Leu Gly Lys Tyr Val Asp 100

<210> 317
<211> 315
<212> DNA
<213> Artificial Sequence
<220>
<223> Native cDNA with two extra N-terminal Lysine (AAA) codons
<400> 317
atgaaaaaag caggacaagc gtttagaaag tttcttccac tctttgaccg agtattggtt 60
gaaaggagtg ctgctgaaac tgtaaccaaa ggaggcatta tgcttccaga aaaatctcaa 120
ggaaaagtat tgcaagcaac agtagtcgct gttggatcgg gttctaaagg aaagggtgga 180
gagattcaac cagttagcgt gaaagttgga gataaagttc ttctcccaga atatggaggc 240
accaaagtag ttctagatga caaggattat ttcctattta gagatggtga cattcttgga 300

aagtacgtag actga
315

<210> 318
<211> 315
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA with two extra N-terminal Lysine (AAA) codons (Gly, Arg and stop codons are optimised in the cDNA)
<400> 318
atgaaaaaag caggccaagc gtttcgcaag tttcttccac tctttgaccg tgtattggtt
60
gaacgcagtg ctgctgaaac tgtaaccaaa ggtggcatta tgcttccaga aaaatctcaa
120
ggcaaagtat tgcaagcaac agtagtcgct gttggctcgg gttctaaagg taagggtggc
180
gagattcaac cagttagcgt gaaagttggc gataaagttc ttctcccaga atatggtggc
240
accaaagtag ttctagatga caaggattat ttcctatttc gtgatggtga cattcttggc
300
aagtacgtag actaa
315

<210> 319
<211> 105
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 with three additional N-terminal Lysine (K) residues inserted. The initiation Methionine (M) is not removed from this protein (MKKK-Cpn10)
<220>
<221> MISC_FEATURE
<222> (2)..(4)
<223> where K is anyone of the following amino acids: Lys, Arg or His
<400> 319
Met Lys Lys Lys Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe
1 5 10 15
Asp Arg Val Leu Val Glu Arg Ser Ala Ala Glu Thr Val Thr Lys Gly
20 25 30
Gly Ile Met Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr 35
40 45
Val Val Ala Val Gly Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln
50 55 60
Pro Val Ser Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu Tyr Gly
65 70 75 80
Gly Thr Lys Val Val Leu Asp Asp Lys Asp Tyr Phe Leu Phe Arg Asp
85 90 95
Gly Asp Ile Leu Gly Lys Tyr Val Asp 100 105

<210> 320
<211> 318
<212> DNA
<213> Artificial Sequence
<220>
<223> Native cDNA with three extra N-terminal Lysine codons
<400> 320
atgaaaaaga aagcaggaca agcgtttaga aagtttcttc cactctttga ccgagtattg
60

gttgaaagga gtgctgctga aactgtaacc aaaggaggca ttatgcttcc agaaaaatct
120
caaggaaaag tattgcaagc aacagtagtc gctgttggat cgggttctaa aggaaagggt
180
ggagagattc aaccagttag cgtgaaagtt ggagataaag ttcttctccc agaatatgga
240
ggcaccaaag tagttctaga tgacaaggat tatttcctat ttagagatgg tgacattctt
300
ggaaagtacg tagactga
318

<210> 321
<211> 318
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA with three extra N-terminal Lysine codons
(Gly, Arg and stop codons are optimised in the cDNA)
<400> 321
atgaaaaaga aagcaggcca agcgtttcgc aagtttcttc cactctttga ccgtgtattg
60
gttgaacgca gtgctgctga aactgtaacc aaaggtggca ttatgcttcc agaaaaatct
120
caaggcaaag tattgcaagc aacagtagtc gctgttggct cgggttctaa aggtaagggt
180
ggcgagattc aaccagttag cgtgaaagtt ggcgataaag ttcttctccc agaatatggt
240
ggcaccaaag tagttctaga tgacaaggat tatttcctat ttcgtgatgg tgacattctt
300
ggcaagtacg tagactaa
318

<210> 322
<211> 103
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 with a Lysine (K) residue inserted at position 21
(ie mobile loop). This construct contains an extra N-terminal Alanine
residue. (Ala-Cpn10-K21)
<220>
<221> MISC_FEATURE
<222> (22)..(22)
<223> where K is anyone of the following amino acids: Lys, Arg or
His
<400> 322
Ala Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val
1 5 10 15
Leu Val Glu Arg Ser Lys Ala Ala Glu Thr Val Thr Lys Gly Gly Ile
20 25 30
Met Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val 35
40 45
Ala Val Gly Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln Pro Val
50 55 60
Ser Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu Tyr Gly Gly Thr
65 70 75 80
Lys Val Val Leu Asp Asp Lys Asp Tyr Phe Leu Phe Arg Asp Gly Asp
85 90 95
Ile Leu Gly Lys Tyr Val Asp 100

<210> 323

<211> 315
<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and K21 insertion
<400> 323
atggcagcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttgaa
60
aggagtaaag ctgctgaaac tgtaaccaaa ggaggcatta tgcttccaga aaaatctcaa
120
ggaaaagtat tgcaagcaac agtagtcgct gttggatcgg gttctaaagg aaagggtgga
180
gagattcaac cagttagcgt gaaagttgga gataaagttc ttctcccaga atatggaggc
240
accaaagtag ttctagatga caaggattat ttcctattta gagatggtga cattcttgga
300
aagtacgtag actga
315

<210> 324
<211> 315
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA of Ala-Cpn10-K21 (Gly, Arg and stop codons are optimised in the cDNA)
<400> 324
atggcagcag gccaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttgaa
60
cgcagtaaag ctgctgaaac tgtaaccaaa ggtggcatta tgcttccaga aaaatctcaa
120
ggcaaagtat tgcaagcaac agtagtcgct gttggctcgg gttctaaagg taagggtggc
180
gagattcaac cagttagcgt gaaagttggc gataaagttc ttctcccaga atatggtggc
240
accaaagtag ttctagatga caaggattat ttcctatttc gtgatggtga cattcttggc
300
aagtacgtag actaa
315

<210> 325
<211> 104
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 with two Lysine (K) residues inserted at position 21 (ie mobile loop). This construct contains an extra N-terminal Alanine residue. (Ala-Cpn10-KK21)
<220>
<221> MISC_FEATURE
<222> (22)..(23)
<223> where K is anyone of the following amino acids: Lys, Arg or His
<400> 325
Ala Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val
1 5 10 15
Leu Val Glu Arg Ser Lys Lys Ala Ala Glu Thr Val Thr Lys Gly Gly
20 25 30
Ile Met Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val 35
40 45

Val Ala Val Gly Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln Pro
50 55 60
Val Ser Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu Tyr Gly Gly
65 70 75 80
Thr Lys Val Val Leu Asp Asp Lys Asp Tyr Phe Leu Phe Arg Asp Gly
85 90 95
Asp Ile Leu Gly Lys Tyr Val Asp 100

<210> 326
<211> 318
<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and KK21 insertion
<400> 326
atggcagcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttgaa
60
aggagtaaaa aagctgctga aactgtaacc aaaggaggca ttatgcttcc agaaaaatct
120
caaggaaaag tattgcaagc aacagtagtc gctgttggat cgggttctaa aggaaagggt
180
ggagagattc aaccagttag cgtgaaagtt ggagataaag ttcttctccc agaatatgga
240
ggcaccaaag tagttctaga tgacaaggat tatttcctat ttagagatgg tgacattctt
300
ggaaagtacg tagactga
318

<210> 327
<211> 318
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA of Ala-Cpn10-KK21 (Gly, Arg and stop codons are optimised in the cDNA)
<400> 327
atggcagcag gccaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttgaa
60
cgcagtaaaa aagctgctga aactgtaacc aaaggtggca ttatgcttcc agaaaaatct
120
caaggcaaag tattgcaagc aacagtagtc gctgttggct cgggttctaa aggtaagggt
180
ggcgagattc aaccagttag cgtgaaagtt ggcgataaag ttcttctccc agaatatggt
240
ggcaccaaag tagttctaga tgacaaggat tatttcctat ttcgtgatgg tgacattctt
300
ggcaagtacg tagactaa
318

<210> 328
<211> 103
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 with a Lysine (K) residue inserted at position 39 (ie L1 connection loop). This construct contains an extra N-terminal Alanine residue. (Ala-Cpn10-K39)
<220>
<221> MISC_FEATURE
<222> (40)..(40)

<223> where K is anyone of the following amino acids: Lys, Arg or His

<400> 328

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

<210> 329
<211> 315
<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and K39 insertion

<400> 329

atggcagcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttgaa
60
aggagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccagaaaa atctcaagga
120
aagaaagtat tgcaagcaac agtagtcgct gttggatcgg gttctaaagg aaagggtgga
180
gagattcaac cagttagcgt gaaagttgga gataaagttc ttctcccaga atatggaggc
240
accaaagtag ttctagatga caaggattat ttcctattta gagatggtga cattcttgga
300
aagtacgtag actga
315

<210> 330
<211> 315
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA of Ala-Cpn10-K39 (Gly, Arg and stop codons are optimised in the cDNA)

<400> 330

atggcagcag gccaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttgaa
60
cgcagtgctg ctgaaactgt aaccaaaggt ggcattatgc ttccagaaaa atctcaaggc
120
aagaaagtat tgcaagcaac agtagtcgct gttggctcgg gttctaaagg taagggtggc
180
gagattcaac cagttagcgt gaaagttggc gataaagttc ttctcccaga atatggtggc
240
accaaagtag ttctagatga caaggattat ttcctatttc gtgatggtga cattcttggc
300
aagtacgtag actaa
315

<210> 331
<211> 104

<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 with two Lysine (K) residues inserted at position 39 (ie L1 connection loop). This construct contains an extra N-terminal Alanine residue. (Ala-Cpn10-KK39)
<220>
<221> MISC_FEATURE
<222> (40)..(41)
<223> where K is anyone of the following amino acids: Lys, Arg or His
<400> 331
Ala Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val
1 5 10 15
Leu Val Glu Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile Met
20 25 30
Leu Pro Glu Lys Ser Gln Gly Lys Lys Lys Val Leu Gln Ala Thr Val 35
40 45
Val Ala Val Gly Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln Pro
50 55 60
Val Ser Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu Tyr Gly Gly
65 70 75 80
Thr Lys Val Val Leu Asp Asp Lys Asp Tyr Phe Leu Phe Arg Asp Gly
85 90 95
Asp Ile Leu Gly Lys Tyr Val Asp
100

<210> 332
<211> 318
<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and KK39 insertion
<400> 332
atggcagcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttgaa
60
aggagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccagaaaa atctcaagga
120
aaaaagaaag tattgcaagc aacagtagtc gctgttggat cgggttctaa aggaaagggt
180
ggagagattc aaccagttag cgtgaaagtt ggagataaag ttcttctccc agaatatgga
240
ggcaccaaag tagttctaga tgacaaggat tatttcctat ttagagatgg tgacattctt
300
ggaaagtacg tagactga
318

<210> 333
<211> 318
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA of Ala-Cpn10-KK39 (Gly, Arg and stop codons are optimised in the cDNA)
<400> 333
atggcagcag gccaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttgaa
60
cgcagtgctg ctgaaactgt aaccaaaggt ggcattatgc ttccagaaaa atctcaaggc
120
aaaaagaaag tattgcaagc aacagtagtc gctgttggct cgggttctaa aggtaagggt
180

ggcgagattc aaccagttag cgtgaaagtt ggcgataaag ttcttctccc agaatatggt
240
ggcaccaaag tagttctaga tgacaaggat tatttcctat ttcgtgatgg tgacattctt
300
ggcaagtacg tagactaa
318

<210> 334
<211> 103
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 with a Lysine (K) residue inserted at position 57 (ie roof loop). This construct contains an extra N-terminal Alanine residue. (Ala-Cpn10-K57)
<220>
<221> MISC_FEATURE
<222> (58)..(58)
<223> where K is anyone of the following amino acids: Lys, Arg or His
<400> 334
Ala Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val
1 5 10 15
Leu Val Glu Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile Met
20 25 30
Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val Ala 35
40 45
Val Gly Ser Gly Ser Lys Gly Lys Gly Lys Gly Glu Ile Gln Pro Val
50 55 60
Ser Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu Tyr Gly Gly Thr
65 70 75 80
Lys Val Val Leu Asp Asp Lys Asp Tyr Phe Leu Phe Arg Asp Gly Asp
85 90 95
Ile Leu Gly Lys Tyr Val Asp 100

<210> 335
<211> 315
<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and K57 insertion
<400> 335
atggcagcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttgaa
60
aggagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccagaaaa atctcaagga
120
aaagtattgc aagcaacagt agtcgctgtt ggatcgggtt ctaaaggaaa gggtaaagga
180
gagattcaac cagttagcgt gaaagttgga gataaagttc ttctcccaga atatggaggc
240
accaaagtag ttctagatga caaggattat ttcctattta gagatggtga cattcttgga
300
aagtacgtag actga
315

<210> 336
<211> 315
<212> DNA
<213> Artificial Sequence
<220>

<223> Optimised cDNA of Ala-Cpn10-K57 (Gly, Arg and stop codons are optimised in the cDNA)
<400> 336
atggcagcag gccaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttgaa
60
cgcagtgctg ctgaaactgt aaccaaaggt ggcattatgc ttccagaaaa atctcaaggc
120
aaagtattgc aagcaacagt agtcgctgtt ggctcgggtt ctaaaggtaa gggtaaaggc
180
gagattcaac cagttagcgt gaaagttggc gataaagttc ttctcccaga atatggtggc
240
accaaagtag ttctagatga caaggattat ttcctatttc gtgatggtga cattcttggc
300
aagtacgtag actaa
315

<210> 337
<211> 104
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 with two Lysine (K) residues inserted at position 57 (ie roof loop). This construct contains an extra N-terminal Alanine residue. (Ala-Cpn10-KK57)
<220>
<221> MISC_FEATURE
<222> (58)..(59)
<223> where K is anyone of the following amino acids: Lys, Arg or His
<400> 337
Ala Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val
1 5 10 15
Leu Val Glu Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile Met
20 25 30
Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val Ala 35
40 45
Val Gly Ser Gly Ser Lys Gly Lys Gly Lys Lys Gly Glu Ile Gln Pro
50 55 60
Val Ser Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu Tyr Gly Gly
65 70 75 80
Thr Lys Val Val Leu Asp Asp Lys Asp Tyr Phe Leu Phe Arg Asp Gly
85 90 95
Asp Ile Leu Gly Lys Tyr Val Asp 100

<210> 338
<211> 318
<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and KK57 insertion
<400> 338
atggcagcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttgaa
60
aggagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccagaaaa atctcaagga
120
aaagtattgc aagcaacagt agtcgctgtt ggatcgggtt ctaaaggaaa gggtaagaaa
180
ggagagattc aaccagttag cgtgaaagtt ggagataaag ttcttctccc agaatatgga
240

ggcaccaaag tagttctaga tgacaaggat tatttcctat ttagagatgg tgacattctt
300
ggaaagtacg tagactga
318

<210> 339
<211> 318
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA of Ala-Cpn10-KK57 (Gly, Arg and stop codons are optimised in the cDNA)
<400> 339
atggcagcag gccaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttgaa
60
cgcagtgctg ctgaaactgt aaccaaaggt ggcattatgc ttccagaaaa atctcaaggc
120
aaagtattgc aagcaacagt agtcgctgtt ggctcgggtt ctaaaggtaa gggtaagaaa
180
ggcgagattc aaccagttag cgtgaaagtt ggcgataaag ttcttctccc agaatatggt
240
ggcaccaaag tagttctaga tgacaaggat tatttcctat ttcgtgatgg tgacattctt
300
ggcaagtacg tagactaa
318

<210> 340
<211> 103
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 with a Lysine (K) residue inserted at position 76 (ie L2 connection loop). This construct contains an extra N-terminal Alanine residue. (Ala-Cpn10-K76)
<220>
<221> MISC_FEATURE
<222> (77)..(77)
<223> where K is anyone of the following amino acids: Lys, Arg or His
<400> 340
Ala Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val
1 5 10 15
Leu Val Glu Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile Met
20 25 30
Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val Ala 35
40 45
Val Gly Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln Pro Val Ser
50 55 60
Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu Tyr Lys Gly Gly Thr
65 70 75 80
Lys Val Val Leu Asp Asp Lys Asp Tyr Phe Leu Phe Arg Asp Gly Asp
85 90 95
Ile Leu Gly Lys Tyr Val Asp 100

<210> 341
<211> 315
<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and K76 insertion

<400> 341
atggcagcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttgaa
60
aggagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccagaaaa atctcaagga
120
aaagtattgc aagcaacagt agtcgctgtt ggatcgggtt ctaaaggaaa gggtggagag
180
attcaaccag ttagcgtgaa agttggagat aaagttcttc tcccagaata taaaggaggc
240
accaaagtag ttctagatga caaggattat ttcctattta gagatggtga cattcttgga
300
aagtacgtag actga
315

<210> 342
<211> 315
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA of Ala-Cpn10-K76 (Gly, Arg and stop codons are optimised in the cDNA)
<400> 342
atggcagcag gccaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttgaa
60
cgcagtgctg ctgaaactgt aaccaaaggt ggcattatgc ttccagaaaa atctcaaggc
120
aaagtattgc aagcaacagt agtcgctgtt ggctcgggtt ctaaaggtaa gggtggcgag
180
attcaaccag ttagcgtgaa agttggcgat aaagttcttc tcccagaata taaaggtggc
240
accaaagtag ttctagatga caaggattat ttcctatttc gtgatggtga cattcttggc
300
aagtacgtag actaa
315

<210> 343
<211> 103
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 with a Lysine (K) residue inserted at position 85 (ie L3 connection loop). This construct contains an extra N-terminal Alanine residue. (Ala-Cpn10-K85)
<220>
<221> MISC_FEATURE
<222> (86)..(86)
<223> where K is anyone of the following amino acids: Lys, Arg or His
<400> 343
Ala Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val
1 5 10 15
Leu Val Glu Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile Met
20 25 30
Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val Ala 35
40 45
Val Gly Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln Pro Val Ser
50 55 60
Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu Tyr Gly Gly Thr Lys
65 70 75 80
Val Val Leu Asp Asp Lys Lys Asp Tyr Phe Leu Phe Arg Asp Gly Asp
85 90 95

Ile Leu Gly Lys Tyr Val Asp 100

<210> 344
<211> 315
<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and K85 insertion
<400> 344
atggcagcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttgaa
60
aggagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccagaaaa atctcaagga
120
aaagtattgc aagcaacagt agtcgctgtt ggatcgggtt ctaaaggaaa gggtggagag
180
attcaaccag ttagcgtgaa agttggagat aaagttcttc tcccagaata tggaggcacc
240
aaagtagttc tagatgacaa aaaggattat ttcctattta gagatggtga cattcttgga
300
aagtacgtag actga
315

<210> 345
<211> 315
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA of Ala-Cpn10-K85 (Gly, Arg and stop codons are optimised in the cDNA)
<400> 345
atggcagcag gccaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttgaa
60
cgcagtgctg ctgaaactgt aaccaaaggt ggcattatgc ttccagaaaa atctcaaggc
120
aaagtattgc aagcaacagt agtcgctgtt ggctcgggtt ctaaaggtaa gggtggcgag
180
attcaaccag ttagcgtgaa agttggcgat aaagttcttc tcccagaata tggtggcacc
240
aaagtagttc tagatgacaa aaaggattat ttcctatttc gtgatggtga cattcttggc
300
aagtacgtag actaa
315

<210> 346
<211> 104
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 with two Lysine (K) residues inserted at position 85 (ie L3 connection loop). This construct contains an extra N-terminal Alanine residue. (Ala-Cpn10-KK85)
<220>
<221> MISC_FEATURE
<222> (86)..(87)
<223> where K is anyone of the following amino acids: Lys, Arg or His
<400> 346
Ala Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val
1 5 10 15

Leu Val Glu Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile Met
20 25 30
Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val Ala 35
40 45
Val Gly Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln Pro Val Ser
50 55 60
Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu Tyr Gly Gly Thr Lys
65 70 75 80
Val Val Leu Asp Asp Lys Lys Lys Asp Tyr Phe Leu Phe Arg Asp Gly
85 90 95
Asp Ile Leu Gly Lys Tyr Val Asp 100

<210> 347
<211> 318
<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and KK85 insertion
<400> 347
atggcagcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttgaa
60
aggagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccagaaaa atctcaagga
120
aaagtattgc aagcaacagt agtcgctgtt ggatcgggtt ctaaaggaaa gggtggagag
180
attcaaccag ttagcgtgaa agttggagat aaagttcttc tcccagaata tggaggcacc
240
aaagtagttc tagatgacaa gaaaaaggat tatttcctat ttagagatgg tgacattctt
300
ggaaagtacg tagactga
318

<210> 348
<211> 318
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA of Ala-Cpn10-KK85 (Gly, Arg and stop codons are optimised in the cDNA)
<400> 348
atggcagcag gccaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttgaa
60
cgcagtgctg ctgaaactgt aaccaaaggt ggcattatgc ttccagaaaa atctcaaggc
120
aaagtattgc aagcaacagt agtcgctgtt ggctcgggtt ctaaaggtaa gggtggcgag
180
attcaaccag ttagcgtgaa agttggcgat aaagttcttc tcccagaata tggtggcacc
240
aaagtagttc tagatgacaa gaaaaaggat tatttcctat ttcgtgatgg tgacattctt
300
ggcaagtacg tagactaa
318

<210> 349
<211> 103
<212> PRT
<213> Artificial Sequence
<220>

<223> Human Cpn10 with a Lysine (K) residue inserted at position 102 (ie the C-terminus). This construct contains an extra N-terminal Alanine residue. (Ala-Cpn10-K102)
<220>
<221> MISC_FEATURE
<222> (103)..(103)
<223> where K is anyone of the following amino acids: Lys, Arg or His
<400> 349
Ala Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val
1 5 10 15
Leu Val Glu Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile Met
20 25 30
Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val Ala 35
40 45
Val Gly Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln Pro Val Ser
50 55 60
Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu Tyr Gly Gly Thr Lys
65 70 75 80
Val Val Leu Asp Asp Lys Asp Tyr Phe Leu Phe Arg Asp Gly Asp Ile
85 90 95
Leu Gly Lys Tyr Val Asp Lys 100

<210> 350
<211> 315
<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and K102 insertion
<400> 350
atggcagcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttgaa
60
aggagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccagaaaa atctcaagga
120
aaagtattgc aagcaacagt agtcgctgtt ggatcgggtt ctaaaggaaa gggtggagag
180
attcaaccag ttagcgtgaa agttggagat aaagttcttc tcccagaata tggaggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttagag atggtgacat tcttggaaag
300
tacgtagaca aatga
315

<210> 351
<211> 315
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA of Ala-Cpn10-K102 (Gly, Arg and stop codons are optimised in the cDNA)
<400> 351
atggcagcag gccaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttgaa
60
cgcagtgctg ctgaaactgt aaccaaaggt ggcattatgc ttccagaaaa atctcaaggc
120
aaagtattgc aagcaacagt agtcgctgtt ggctcgggtt ctaaaggtaa gggtggcgag
180
attcaaccag ttagcgtgaa agttggcgat aaagttcttc tcccagaata tggtggcacc
240

aaagtagttc tagatgacaa ggattatttc ctatttcgtg atggtgacat tcttggcaag
300
tacgtagaca aataa
315

<210> 352
<211> 104
<212> PRT
<213> Artificial Sequence
<220>
<223> Human Cpn10 with two Lysine (K) residues inserted at position 102 (ie the C-terminus). This construct contains an extra N-terminal Alanine residue. (Ala-Cpn10-KK102)
<220>
<221> MISC_FEATURE
<222> (103)..(104)
<223> where K is anyone of the following amino acids: Lys, Arg or His
<400> 352
Ala Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val
1 5 10 15
Leu Val Glu Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile Met
20 25 30
Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val Ala 35
40 45
Val Gly Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln Pro Val Ser
50 55 60
Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu Tyr Gly Gly Thr Lys
65 70 75 80
Val Val Leu Asp Asp Lys Asp Tyr Phe Leu Phe Arg Asp Gly Asp Ile
85 90 95
Leu Gly Lys Tyr Val Asp Lys Lys 100

<210> 353
<211> 318
<212> DNA
<213> Artificial Sequence
<220>
<223> Native Cpn10 cDNA with an extra N-terminal Alanine codon (GCA) and KK102 insertion
<400> 353
atggcagcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttgaa
60
aggagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccagaaaa atctcaagga
120
aaagtattgc aagcaacagt agtcgctgtt ggatcgggtt ctaaaggaaa gggtggagag
180
attcaaccag ttagcgtgaa agttggagat aaagttcttc tcccagaata tggaggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttagag atggtgacat tcttggaaag
300
tacgtagaca agaaatga
318

<210> 354
<211> 318
<212> DNA
<213> Artificial Sequence
<220>
<223> Optimised cDNA of Ala-Cpn10-KK102 (Gly, Arg and stop codons are optimised in the cDNA)

<400> 354
atggcagcag gccaagcgtt tcgcaagttt cttccactct ttgaccgtgt attggttgaa
60
cgcagtgctg ctgaaactgt aaccaaaggt ggcattatgc ttccagaaaa atctcaaggc
120
aaagtattgc aagcaacagt agtcgctgtt ggctcgggtt ctaaaggtaa gggtggcgag
180
attcaaccag ttagcgtgaa agttggcgat aaagttcttc tcccagaata tggtggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttcgtg atggtgacat tcttggcaag
300
tacgtagaca agaaataa
318

<210> 355
<211> 715
<212> PRT
<213> Artificial Sequence
<220>
<223> Seven Cpn10 cDNA subunits joined through a Glycine (G) spacer. The 1st Cpn10 has the extra N-terminal alanine (A) however this extra alanine has been removed from the remaining six Cpn10 genes. There is an extra isoleucine (I) residue on the final
<400> 355
Ala Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val
1 5 10 15
Leu Val Glu Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile Met
20 25 30
Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val Ala 35
40 45
Val Gly Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln Pro Val Ser
50 55 60
Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu Tyr Gly Gly Thr Lys
65 70 75 80
Val Val Leu Asp Asp Lys Asp Tyr Phe Leu Phe Arg Asp Gly Asp Ile
85 90 95
Leu Gly Lys Tyr Val Asp Gly Ala Gly Gln Ala Phe Arg Lys Phe Leu
100 105 110
Pro Leu Phe Asp Arg Val Leu Val Glu Arg Ser Ala Ala Glu Thr Val 115
120 125
Thr Lys Gly Gly Ile Met Leu Pro Glu Lys Ser Gln Gly Lys Val Leu
130 135 140
Gln Ala Thr Val Val Ala Val Gly Ser Gly Ser Lys Gly Lys Gly Gly
145 150 155 160
Glu Ile Gln Pro Val Ser Val Lys Val Gly Asp Lys Val Leu Leu Pro
165 170 175
Glu Tyr Gly Gly Thr Lys Val Val Leu Asp Asp Lys Asp Tyr Phe Leu
180 185 190
Phe Arg Asp Gly Asp Ile Leu Gly Lys Tyr Val Asp Gly Ala Gly Gln 195
200 205
Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val Leu Val Glu Arg
210 215 220
Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile Met Leu Pro Glu Lys
225 230 235 240
Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val Ala Val Gly Ser Gly
245 250 255
Ser Lys Gly Lys Gly Gly Glu Ile Gln Pro Val Ser Val Lys Val Gly
260 265 270
Asp Lys Val Leu Leu Pro Glu Tyr Gly Gly Thr Lys Val Val Leu Asp 275
280 285
Asp Lys Asp Tyr Phe Leu Phe Arg Asp Gly Asp Ile Leu Gly Lys Tyr

290 295 300
Val Asp Gly Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp
305 310 315 320
Arg Val Leu Val Glu Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly
325 330 335
Ile Met Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val
340 345 350
Val Ala Val Gly Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln Pro 355
360 365
Val Ser Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu Tyr Gly Gly
370 375 380
Thr Lys Val Val Leu Asp Asp Lys Asp Tyr Phe Leu Phe Arg Asp Gly
385 390 395 400
Asp Ile Leu Gly Lys Tyr Val Asp Gly Ala Gly Gln Ala Phe Arg Lys
405 410 415
Phe Leu Pro Leu Phe Asp Arg Val Leu Val Glu Arg Ser Ala Ala Glu
420 425 430
Thr Val Thr Lys Gly Gly Ile Met Leu Pro Glu Lys Ser Gln Gly Lys 435
440 445
Val Leu Gln Ala Thr Val Val Ala Val Gly Ser Gly Ser Lys Gly Lys
450 455 460
Gly Gly Glu Ile Gln Pro Val Ser Val Lys Val Gly Asp Lys Val Leu
465 470 475 480
Leu Pro Glu Tyr Gly Gly Thr Lys Val Val Leu Asp Asp Lys Asp Tyr
485 490 495
Phe Leu Phe Arg Asp Gly Asp Ile Leu Gly Lys Tyr Val Asp Gly Ala
500 505 510
Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu Phe Asp Arg Val Leu Val 515
520 525
Glu Arg Ser Ala Ala Glu Thr Val Thr Lys Gly Gly Ile Met Leu Pro
530 535 540
Glu Lys Ser Gln Gly Lys Val Leu Gln Ala Thr Val Val Ala Val Gly
545 550 555 560
Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile Gln Pro Val Ser Val Lys
565 570 575
Val Gly Asp Lys Val Leu Leu Pro Glu Tyr Gly Gly Thr Lys Val Val
580 585 590
Leu Asp Asp Lys Asp Tyr Phe Leu Phe Arg Asp Gly Asp Ile Leu Gly 595
600 605
Lys Tyr Val Asp Gly Ala Gly Gln Ala Phe Arg Lys Phe Leu Pro Leu
610 615 620
Phe Asp Arg Val Leu Val Glu Arg Ser Ala Ala Glu Thr Val Thr Lys
625 630 635 640
Gly Gly Ile Met Leu Pro Glu Lys Ser Gln Gly Lys Val Leu Gln Ala
645 650 655
Thr Val Val Ala Val Gly Ser Gly Ser Lys Gly Lys Gly Gly Glu Ile
660 665 670
Gln Pro Val Ser Val Lys Val Gly Asp Lys Val Leu Leu Pro Glu Tyr 675
680 685
Gly Gly Thr Lys Val Val Leu Asp Asp Lys Asp Tyr Phe Leu Phe Arg
690 695 700
Asp Gly Asp Ile Leu Gly Lys Tyr Val Asp Ile
705 710 715

<210> 356
<211> 2151
<212> DNA
<213> Artificial Sequence
<220>
<223> cDNA of Covalent Cpn10. Seven Cpn10 cDNA subunits joined through a Glycine (G) spacer. The 1st Cpn10 has the extra N-

terminal alanine (A) however this extra alanine has been removed from the remaining six Cpn10 genes. There is an extra isoleucine (I)

<400> 356

atggcagcag gacaagcgtt tagaaagttt cttccactct ttgaccgagt attggttgaa
60
aggagtgctg ctgaaactgt aaccaaagga ggcattatgc ttccagaaaa atctcaagga
120
aaagtattgc aagcaacagt agtcgctgtt ggatcgggtt ctaaaggaaa gggtggagag
180
attcaaccag ttagcgtgaa agttggagat aaagttcttc tcccagaata tggaggcacc
240
aaagtagttc tagatgacaa ggattatttc ctatttagag atggtgacat tcttggaaag
300
tacgtagatg gcgcaggaca agcgtttaga aagtttcttc cactctttga ccgagtattg
360
gttgaaagga gtgctgctga aactgtaacc aaaggaggca ttatgcttcc agaaaaatct
420
caaggaaaag tattgcaagc aacagtagtc gctgttggat cgggttctaa aggaaagggt
480
ggagagattc aaccagttag cgtgaaagtt ggagataaag ttcttctccc agaatatgga
540
ggcaccaaag tagttctaga tgacaaggat tatttcctat ttagagatgg tgacattctt
600
ggaaagtacg tagatggcgc aggacaagcg tttagaaagt ttcttccact ctttgaccga
660
gtattggttg aaaggagtgc tgctgaaact gtaaccaaag gaggcattat gcttccagaa
720
aaatctcaag gaaaagtatt gcaagcaaca gtagtcgctg ttggatcggg ttctaaagga
780
aagggtggag agattcaacc agttagcgtg aaagttggag ataaagttct tctcccagaa
840
tatggaggca ccaaagtagt tctagatgac aaggattatt tcctatttag agatggtgac
900
attcttggaa agtacgtaga tggcgcagga caagcgttta gaaagtttct tccactcttt
960
gaccgagtat tggttgaaag gagtgctgct gaaactgtaa ccaaaggagg cattatgctt
1020
ccagaaaaat ctcaaggaaa agtattgcaa gcaacagtag tcgctgttgg atcgggttct
1080
aaaggaaagg gtggagagat tcaaccagtt agcgtgaaag ttggagataa agttcttctc
1140
ccagaatatg gaggcaccaa agtagttcta gatgacaagg attatttcct atttagagat
1200
ggtgacattc ttggaaagta cgtagatggc gcaggacaag cgtttagaaa gtttcttcca
1260
ctctttgacc gagtattggt tgaaaggagt gctgctgaaa ctgtaaccaa aggaggcatt
1320
atgcttccag aaaaatctca aggaaaagta ttgcaagcaa cagtagtcgc tgttggatcg
1380
ggttctaaag gaaagggtgg agagattcaa ccagttagcg tgaaagttgg agataaagtt
1440
cttctcccag aatatggagg caccaaagta gttctagatg acaaggatta tttcctattt
1500
agagatggtg acattcttgg aaagtacgta gatggcgcag gacaagcgtt tagaaagttt
1560
cttccactct ttgaccgagt attggttgaa aggagtgctg ctgaaactgt aaccaaagga
1620
ggcattatgc ttccagaaaa atctcaagga aaagtattgc aagcaacagt agtcgctgtt
1680
ggatcgggtt ctaaaggaaa gggtggagag attcaaccag ttagcgtgaa agttggagat
1740

aaagttcttc tcccagaata tggaggcacc aaagtagttc tagatgacaa ggattatttc
1800
ctatttagag atggtgacat tcttggaaag tacgtagatg gcgcaggaca agcgtttaga
1860
aagtttcttc cactctttga ccgagtattg gttgaaagga gtgctgctga aactgtaacc
1920
aaaggaggca ttatgcttcc agaaaaatct caaggaaaag tattgcaagc aacagtagtc
1980
gctgttggat cgggttctaa aggaaagggt ggagagattc aaccagttag cgtgaaagtt
2040
ggagataaag ttcttctccc agaatatgga ggcaccaaag tagttctaga tgacaaggat
2100
tatttcctat ttagagatgg tgacattctt ggaaagtacg tagatatcta g
2151