

METHODS AND SYSTEMS FOR SELECTIVE FLUORINATION OF ORGANIC MOLECULES

By Rudi Fasan and Frances Arnold

CROSS REFERENCE TO RELATED APPLICATIONS

[0001] This application claims priority to U.S. Provisional Application Serial No. 60/835,613 filed on August 4, 2006, the disclosure of which is incorporated herein by reference in its entirety.

TECHNICAL FIELD

[0002] The present disclosure generally relates to the fields of synthetic organic chemistry and pharmaceutical chemistry. In particular, the present disclosure relates to methods and systems for the selective fluorination of organic molecules.

BACKGROUND

[0003] The importance of fluorine in altering the physicochemical properties of organic molecules and its exploitation in medicinal chemistry has been highlighted in recent reviews (Bohm, Banner et al. 2004). Although similar in size to hydrogen, H→F substitutions can cause dramatic effects on several properties of organic molecules, including the lipophilicity, dipole moment, and pKa thereof. In addition, fluorine substitutions can dramatically alter the reactivity of the fluorinated site as well as that of neighboring functional groups.

[0004] In particular, in medicinal chemistry, there is a growing interest towards incorporating fluorine atoms in building blocks, lead compounds and drugs in that this may increase by many-fold the chances of turning these molecules into marketable drugs. Several studies have shown that potent drugs can be obtained through fluorination of much less active precursors. Some representative examples include anticholesterolemic Ezetimib (Clader 2004), anticancer CF3-taxanes (Ojima 2004), fluoro-steroids, and antibacterial fluoroquinolones.

[0005] The improved pharmacological properties of fluoro-containing drugs are often due to their improved pharmacokinetic properties (biodistribution, clearance), and enhanced metabolic stability (Park, Kitteringham et al. 2001). Primary metabolism of drugs in humans generally occurs through P450-dependent systems, and the introduction of fluorine atoms at or near the sites of metabolic attack has often proven successful in increasing the half-life of a compound (Bohm, Banner et al. 2004). A comprehensive review covering the influence of fluorination on drug metabolism (especially P450-dependent) is presented (Park, Kitteringham et al. 2001).

[0006] In other cases, the introduction of fluorine substituents leads to improvements in the pharmacological properties as a result of enhanced binding affinity of the molecule to biological receptors. Examples of the effect of fluorine on binding affinity are provided by recent results in the preparation of NK1 antagonists (Swain and Rupniak 1999), 5HT1D agonists (van Niel, Collins et al. 1999), and PTB1B antagonists (Burke, Ye et al. 1996).

[0007] Over the past years, fluorination has been covering an increasingly important role in drug discovery, as exemplified by the development of fluorinated derivatives of the anticancer drugs paclitaxel and docetaxel (Ojima 2004).

[0008] However, only a handful of organofluorine compounds occur in nature and even those only in very small amounts (Harper and O'Hagan 1994). Consequently, any fluorine-containing substance selected for research, pharmaceutical, or agrochemical application has to be man-made.

[0009] Despite a few reports on the application of molecular fluorine (F₂) for direct fluorination of organic compounds (Chambers, Skinner et al. 1996; Chambers, Hutchinson et al. 2000), this method typically suffers from poor selectivity and requires handling of a highly toxic and gaseous reagent. Several chemical strategies have been developed over the past decades to afford selective fluorination of organic compounds under friendlier conditions. These have been recently reviewed by Togni (Togni, Mezzetti et al. 2001), Cahard (Ma and Cahard 2004), Sodeoka (Hamashima and Sodeoka 2006), and Gouverneur (Bobbio and Gouverneur 2006). These strategies involve catalytic as well as non-catalytic methods. The latter comprise substrate-controlled fluorination methods, which generally make use of a

chiral auxiliary, and reagent-controlled fluorination methods, which generally make use of chiral electrophilic N-F or nucleophilic fluorinating reagents.

[0010] These fluorination methods, however, need several chemical steps to prepare the chiral substrates (Davis and Han 1992; Enders, Potthoff et al. 1997) or the chiral reagents (Davis, Zhou et al. 1998; Taylor, Kotoris et al. 1999; Nyffeler, Duron et al. 2005) and have an applicability restricted to reactive C-H bonds (Cahard, Audouard et al. 2000; Shibata, Suzuki et al. 2000; Kim and Park 2002; Beeson and MacMillan 2005; Marigo, Fielenbach et al. 2005) in specific classes of compounds such as aldehydes (Beeson and MacMillan 2005; Marigo, Fielenbach et al. 2005) or di-carbonyls (Hintermann and Togni 2000; Ma and Cahard 2004; Shibata, Ishimaru et al. 2004; Hamashima and Sodeoka 2006).

[0011] Despite much progress in the field of organofluorine chemistry, the number of available methods for direct or indirect asymmetric synthesis of organofluorine compounds remains limited and additional tools are desirable. In particular, a general method to afford mono- or poly-fluorination of organic compounds at reactive and unreactive sites of their molecular scaffold is desirable.

SUMMARY

[0012] Provided herein are methods and systems for the selective fluorination of a target site of an organic molecule, which include the activation and subsequent fluorination of the target site. In the methods and systems herein disclosed, the target site is an oxidizable carbon atom of the organic molecule, the activation is performed by introducing an oxygen-containing functional group on the target site, and the fluorination of the activated site is performed by replacing the functional group introduced on the target site with fluorine. The introduction of the oxygen-containing functional group and the replacement of the functional group with a fluorine can be performed by suitable agents

[0013] According to an embodiment, a method for fluorinating an organic molecule is disclosed, the method comprising providing an organic molecule comprising a target site; providing an oxidizing agent that oxidizes the organic molecule by introducing an oxygen containing functional group on the target site, contacting the oxidizing agent with the organic molecule for a time and under condition to allow introduction of the oxygen-containing functional group on the target site thus providing an oxygenated organic molecule, providing

a fluorinating agent and contacting the fluorinating agent with the oxygenated organic molecule, for a time and under condition to allow replacement of the oxygen-containing functional group with fluorine.

[0013a] According to a first aspect, there is provided a method for fluorinating an organic molecule, the method comprising providing an organic molecule comprising a target site; providing an oxygenase enzyme that oxidizes the target site by introduction of an oxygen-containing functional group; contacting the oxygenase enzyme with the organic molecule for a time and under condition to allow introduction of the oxygen-containing functional group on the target site thus providing an oxidized organic molecule; providing a fluorinating agent and contacting the fluorinating agent with the oxidized organic molecule, for a time and under condition to allow replacement of the oxygen-containing functional group with fluorine.

[0014] According to another embodiment, a system for the fluorination of an organic molecule is disclosed, the system comprising an oxidizing agent for introducing an oxygen-containing functional group in an organic molecule and a fluorinating agent for replacing the oxygen-containing functional group in the organic molecule with fluorine or a fluorine group. An oxygen-providing compound and/or fluorine-providing compound can also be included in the system.

[0015] A first advantage of the methods and systems herein disclosed is to allow the fluorination of organic molecules in one or more specific and predetermined target sites, including one or more target sites of interest, thus allowing a regioselective mono- and poly-fluorination.

[0016] A second advantage of the methods and systems herein disclosed is to allow introduction of fluorine in a fluorine unreactive site of a molecule, i.e. a site that, in absence of the oxygen-containing functional group is unlikely to undergo a chemical transformation such as a fluorination, as long as said site is oxidizable.

[0017] A third advantage of the methods and systems herein disclosed is that by using a suitable agent, in particular a suitable oxidizing agent, it is possible to control the chirality of the final product and therefore produce a product molecule having a desired chirality (stereoselective fluorination).

[0018] A fourth advantage of the methods and systems herein disclosed is that the methods and system can provide fluorinated compounds wherein the fluorine is introduced in a predetermined site expected to be associated with a biological activity, which are therefore candidate compounds to be screened for the activity.

[0019] According to an embodiment, a method for the identification of a molecule having a biological activity is disclosed, the method comprising, providing an organic molecule comprising a target site; providing an oxidizing agent, contacting the oxidizing agent with the organic molecule for a time and under condition to allow introduction of an

oxygen-containing functional group on the target site thus providing an oxygenated organic molecule, providing a fluorinating agent; contacting the fluorinating agent with the oxygenated organic molecule, for a time and under condition to allow replacement of the oxygen-containing functional group with fluorine and testing the fluorinated organic molecule for the biological activity.

[0020] According to another embodiment, a system for identifying a molecule having a biological activity is disclosed. The system comprises an oxidizing agent capable of introducing an oxygen-containing functional group in a target site of an organic molecule, a fluorinating agent capable of replacing the oxygen-containing functional group in the organic molecule with fluorine, and an agent for testing the biological activity. An oxygen-providing agent and/or fluorine-providing-agent can also be included in the system.

[0021] A further advantage of the methods and systems for the identification of a molecule having a biological activity is the possibility to produce a broad spectrum of molecules that in view of the selected insertion of fluorine, already constitute promising candidates, thus shortening and improving the selection process.

[0022] An additional advantage of the methods and systems for the identification of a molecule having a biological activity is the possibility to confer new activities to a molecule that is already biologically active and/or to improve the biological activity of the original molecule by selective insertion of fluorine.

[0023] A still further advantage of the methods and systems of the identification of a molecule having a biological activity, is the possibility to derive molecules that have a biological activity that is pharmacologically relevant, or to improve the pharmacologically activity of a molecule that is already pharmacologically active. This in view of the known ability of fluorine to improve the pharmacological profile of drugs.

[0024] The details of one or more embodiments of the disclosure are set forth in the accompanying drawings and the description below. Other features, objects, and advantages will be apparent from the description and drawings, and from the claims.

BRIEF DESCRIPTION OF THE DRAWINGS

[0025] The accompanying drawings, which are incorporated into and constitute a part of this specification, illustrate one or more embodiments of the present disclosure and, together with the detailed description, serve to explain the principles and implementations of the disclosure.

[0026] In the drawings:

[0027] Figure 1 is a schematic representation of the methods and systems for the selective fluorination of an organic molecule A according to an embodiment of herein disclosed;

[0028] Figure 2 is a schematic representation of methods and systems for stereoselective fluorination of an organic molecule A according to an embodiment of what herein disclosed (chemo-enzymatic strategy), illustrated in comparison with methods and systems of the art (chemical strategy);

[0029] Figure 3 is a graphic representation of the crystal structure of a P450 heme domain; helixes D, L, I and E in the domain are also indicated; the heme prosthetic group in the domain is indicated as "heme"; the cysteine in the heme-ligand loop is displayed in spheres (black).

[0030] Figure 4 is a schematic representation of methods and system for identifying a molecule having a biological activity according to an embodiment disclosed in the present specification;

[0031] Figure 5, illustrates exemplary results from the screening of a subset of pre-selected oxygenases for the identification of a suitable oxidizing agent for the selective activation of the organic molecule dihydrojasnone. Panel A) is a diagram showing the conversion ratios for the reaction of activation of dihydrojasnone with wild-type P450_{BM3} and variants thereof, as determined by GC analysis; Panel B) is a diagram showing the product distribution obtained with wild-type P450_{BM3} and variants thereof in the reaction of activation of dihydrojasnone, as determined by GC analysis. Cpd 1 to cpd 9 indicate activated products 1 to 9;

[0032] Figure 6, illustrates exemplary results from the screening of a subset of pre-selected oxygenases for the identification of a suitable oxidizing agent for the selective

activation of the organic molecule Menthofuran; Panel A) is a diagram showing the conversion ratios for the reaction of activation of menthofuran with wild-type P450_{BM3} and variants thereof, as determined by GC analysis. Panel B) is a diagram showing the product distribution obtained with wild-type P450_{BM3} and variants thereof in the reaction of activation of menthofuran, as determined by GC analysis. Cpd 1 to cpd 10 indicate activated products 1 to 10;

[0033] Figure 7 illustrates exemplary results from the screening of a subset of pre-selected oxygenases for the identification of a suitable oxydizing agent for the selective activation of the organic molecule dihydro-4-methoxymethyl-2-methyl-5-phenyl-2-oxazoline (MMPO). In particular, Panel (A) is a diagram showing the results from HTS screening of oxydizing agent pool using colorimetric reagent Purpald; Panel (B) is a diagram showing the results from the re-screen of the positive hits identified with colorimetric HTS, where the regioselectivity of each oxygenase is determined by GC analysis (MMPOH is dihydro-4-hydroxymethyl-2-methyl-5-phenyl-2-oxazoline, that is the desired activated product); Panel (C) is a diagram showing the conversion ratios for the activation reactions of MMPO with each of the tested oxydizing agents, as determined by GC analysis; and

[0034] Figure 8 shows a diagram illustrating the time course for whole-cell activation of the organic molecule dihydrojasnone (DHJ) using batch culture of var3-expressing *E. coli* DH5 α cells (0.5 L). The consumption of substrate (DHJ) and the accumulation of the desired activated product (oxDHJ) were monitored over time by GC analysis of aliquots of the cell culture.

DETAILED DESCRIPTION

[0035] Methods and systems for the selective fluorination of a predetermined target site of an organic molecule are herein disclosed. In these methods and systems, the predetermined target site is first activated by an oxydizing agent that introduces an oxygen-containing functional group in the target site; and then fluorinated by a fluorinating agent that replaces the oxygen-containing functional group with fluorine or a fluorine group. In particular, activation and fluorination of an organic molecule can be performed as schematically illustrated in Figures 1 and 2, Figure 2 also showing activation and fluorination

of an organic molecule performed according to some embodiments herein disclosed, in comparison with chemical methods and systems of the art.

[0036] The term "target site" as used herein refers to an oxidizable C atom, i.e. a C atom in the organic molecule that bears an oxidizable bond. Examples of oxidizable bonds include but are not limited to a C-H bond, a C-C double bond, and a C-X bond, single or double, where X is an heteroatom independently selected from the group consisting of B (boron), O, (oxygen), P (phosphorous), N (nitrogen), S (sulphur), Si (silicium), Se (selenium), F (fluorine), Cl (chlorine), Br (bromine), and I (iodine).

[0037] The terms "activate" and "activation" as used herein with reference to a target site indicate a chemical reaction resulting in an enhanced reactivity of the C atom that forms the site, so that said C atom acquires or improves its ability to undergo a chemical transformation, more specifically a fluorination reaction. For example, the insertion of an oxygen atom in a target site bearing a C-H bond and resulting in the formation of a hydroxyl group (C-OH) on the site activates the target site for a deoxofluorination reaction. A further example is the insertion of an oxygen atom in a target site bearing a C=C double bond and resulting in the formation of an epoxy group activates the site for a ring-opening fluorination reaction. Accordingly, the wording "activated site" as used herein refers to a C atom of an organic molecule that, following activation, has acquired or improved its ability to undergo a chemical transformation and in particular a fluorination reaction when contacted with a fluorine.

[0038] The term "contact" as used herein with reference to interactions of chemical units indicates that the chemical units are at a distance that allows short range non-covalent interactions (such as Van der Waals forces, hydrogen bonding, hydrophobic interactions, electrostatic interactions, dipole-dipole interactions) to dominate the interaction of the chemical units. For example, when an oxygenase enzyme is 'contacted' with a target molecule, the enzyme is allowed to interact with and bind to the organic molecule through non-covalent interactions so that a reaction between the enzyme and the target molecule can occur.

[0039] The wording "chemical unit" identifies single atoms as well as groups of atoms connected by a chemical bond. Exemplary chemical units herein described include, but

are not limited to fluorine atom, chemical groups such as oxygen-containing chemical group and fluorine-containing groups, organic molecules or portions thereof including target sites, chemical agents, including oxydizing agents and fluorinating agents.

[0040] The term "agent" as used herein refers to a chemical unit that is capable to cause a chemical reaction specified in the identifier accompanying the term. Accordingly, an "oxydizing agent" is an agent capable of causing an oxygenation reaction of a suitable substrate and a "fluorinating agent" is an agent capable of causing a fluorination reaction of a suitable substrate. An oxygenation reaction is a chemical reaction in which one or more oxygen atoms are inserted into one or more pre-existing chemical bonds of said substrate. A fluorination reaction is a chemical reaction in which a substituent connected to an atom in said substrate is substituted for fluorine.

[0041] The term "introducing" as used herein with reference to the interaction between two chemical units, such as a functional groups and a target site, indicates a reaction resulting in the formation of a bond between the two chemical units, e.g. the functional group and the target site.

[0042] The term "functional group" as used herein refers to a chemical unit within a molecule that is responsible for a characteristic chemical reaction of that molecule. An "oxygen-containing functional group" is a functional group that comprises an oxygen atom. Exemplary oxygen-containing functional groups include but are not limited to a hydroxyl group (—OH), ether group (—OR), carbonyl oxygen (=O), hydroperoxy group (—OOH), and peroxy group (—OOR).

[0043] The terms "replace" and "replacement" as used herein with reference to chemical units indicates formation of a chemical bond between the chemical units in place of a pre-existing bond in at least one of said chemical unit. In particular, replacing an oxygen-containing functional group on the target site with a fluorine or fluorine group indicates the formation of a bond between the target site and the fluorine or fluorine group in place of the bond between the target site and the oxygen-containing functional group.

[0044] Any organic molecule that includes at least one target site, i.e. at least one oxidizable C atom, and is a substrate of at least one oxydizing agent, can be used as an organic molecule to be fluorinated according to the methods and systems herein disclosed.

[0045] In some embodiments, the oxidizing agent is an enzyme such as an oxygenase or oxidizing enzymes that is able to introduce an oxygen-containing functional group in the target site of the organic molecule using an oxygen source such as molecular oxygen (O_2), hydrogen peroxide (H_2O_2), a hydroperoxide ($R-OOH$), or a peroxide ($R-O-O-R'$), including the oxidoreductases with an Enzyme Classification (EC) number typically corresponding to EC 1.13 or EC 1.14. Suitable oxygenases for the systems and methods herein described include but are not limited to monooxygenases, dioxygenases, peroxygenases, and peroxidases. In particular, monooxygenases and peroxygenase can be used to introduce on the target site an oxygen-containing functional group that comprises one oxygen atom, dioxygenases can be used to introduce on the target site an oxygen-containing functional group that comprises two oxygen atoms, and peroxidases can be used to introduce on the target site an oxygen-containing functional group that comprises one or two oxygen atoms.

[0046] In some embodiments, the oxygenases are wild-type oxygenases and in some embodiments the oxygenase is a mutant or variant. An oxygenase is wild-type if it has the structure and function of an oxygenase as it exists in nature. An oxygenase is a mutant or variant if it has been mutated from the oxygenase as it exists in nature and provides an oxygenase enzymatic activity.

[0047] In some embodiments, the variant oxygenase provides an enhanced oxygenase enzymatic activity compared to the corresponding wild-type oxygenase. In some embodiments, the variant oxygenases maintain the binding specificity of the corresponding wild-type oxygenase, in other embodiments the variant oxygenases disclosed herein are instead bindingly distinguishable from the corresponding wild-type and bindingly distinguishable from another. The wording "bindingly distinguishable" as used herein with reference to molecules, indicates molecules that are distinguishable based on their ability to specifically bind to, and are thereby defined as complementary to a specific molecule. Accordingly, a first oxygenase is bindingly distinguishable from a second oxygenase if the first oxygenase specifically binds and is thereby defined as complementary to a first substrate and the second oxygenase specifically binds and is thereby defined as complementary to a second substrate, with the first substrate distinct from the second substrate. In some embodiments, the variant oxygenase herein disclosed, has an increased enzyme half-time in

vivo, a reduced antigenicity, and/or an increased storage stability when compared to the corresponding wild-type oxygenase.

[0048] In some embodiments, the oxygenase is a heme-containing oxygenase or a variant thereof. The wording "heme" or "heme domain" as used herein refers to an amino acid sequence within an oxygenase, which is capable of binding an iron-complexing structure such as a porphyrin. Compounds of iron are typically complexed in a porphyrin (tetrapyrrole) ring that may differ in side chain composition. Heme groups can be the prosthetic groups of cytochromes and are found in most oxygen carrier proteins. Exemplary heme domains include that of P450_{BM3} as well as truncated or mutated versions of these that retain the capability to bind the iron-complexing structure. A skilled person can identify the heme domain of a specific protein using methods known in the art. Exemplary organic molecules that can be oxidized by heme-containing oxygenases include C₅-C₂₂ alkanes, fatty acids, steroids, terpenes, aromatic hydrocarbons, polyketides, prostaglandins, terpenes, statins, amino acids, flavonoids, and stilbenes.

[0049] In particular, in some embodiments the "heme-containing oxygenase" is a cytochrome P450 enzyme (herein also indicates as CYPs or P450s) or a variant thereof. The wording "P450 enzymes" indicates a group of heme-containing oxygenases that share a common overall fold and topology despite less than 20% sequence identity across the corresponding gene superfamily (Denisov, Makris et al. 2005). In particular, the P450 enzymes share a conserved P450 structural core, which binds to the heme group and comprises a P450 signature sequence. The conserved P450 structural core is formed by a four-helix bundle composed of three parallel helices (usually labeled D, L, and I), and one antiparallel helix (usually labeled as helix E) (Presnell and Cohen 1989) and by a Cys heme-ligand loop which includes a conserved cysteine that binds to the heme group and the P450 signature. In particular, the conserved cysteine that binds to the heme group is the proximal or "fifth" ligand to the heme iron and the relevant ligand group (a thiolate) is the origin of the characteristic name giving 450-nm Soret absorbance observed for the ferrous-CO complex (Pylypenko and Schlichting 2004). The P450 signature sequence is the sequence indicated in the enclosed sequence listing as SEQ ID NO:1. Figure 3 is a representation of the P450 structural core of bacterial P450_{BM3}. In the illustration of Figure 3, the prosthetic heme group ("heme") is located between the distal I helix ("helix I") and proximal L helix ("helix L") and

is bound to the adjacent Cys heme-ligand loop containing the P450 signature sequence SEQ ID NO: 1. Helices D and E are also indicated in [Figure 3](#).

[0050] P450 enzymes are known to be involved in metabolism of exogenous and endogenous compounds. In particular, P450 enzymes can act as terminal oxidases in multicomponent electron transfer chains, called here P450-containing systems. Reactions catalyzed by cytochrome P450 enzymes include hydroxylation, epoxidation, N-dealkylation, O-dealkylation, S-oxidation and other less common transformations. The most common reaction catalyzed by P450 enzymes is the monooxygenase reaction using molecular oxygen (O_2), where one atom of oxygen is inserted into a substrate while the other is reduced to water.

[0051] P450 monooxygenases can catalyze the monooxygenation of a variety of structurally diverse substrates. Exemplary substrates, that can be oxidized by naturally-occurring P450s include C_5 - C_{22} alkanes, cyclic alkanes, cyclic alkenes, alkane derivatives, alkene derivatives, C_{10} - C_{20} fatty acids, steroids, terpenes, aromatic hydrocarbons, natural products and natural product analogues such as polyketides, prostaglandins, thromboxanes, leukotrienes, anthraquinones, tetracyclines, anthracenes, polyenes, statins, amino acids, flavonoids, stilbenes, alkaloids (e.g. lysine-derived, nicotinic acid-derived, tyrosine-derived, tryptophan-derived, anthranilic acid-derived, histidine-derived, purine-derived alkaloids), beta-lactams, aminoglycosides, polymyxins, quinolones, synthetic derivatives such as aromatic heterocyclic derivatives (e.g. phenyl-, pyrimidine-, pyridine-, piperidine-, pyrrole-, furan-, triazol-, thiophene-, pyrazole-, imidazole-, tetrazole-, oxazole-, isoxazole-, thiazole-, isothiazole-, pyran-, pyridazine-, pyrazine-, piperazine-, thiazine-, and oxazine-derivatives), and the like.

[0052] Naturally-occurring P450 monooxygenases have been also mutated in their primary sequence to favor their activity towards other non-native substrates such as short-chain fatty acids, 8- and 12-pNCA, indole, aniline, *p*-nitrophenol, polycyclic hydrocarbons (e.g. indole, naphthalene), styrene, medium- and short-chain alkanes, alkenes (e.g. cyclohexene, 1-hexene, styrene, benzene), quinoline, steroid derivatives, and various drugs (e.g. chlorzoxazone, propranolol, amodiaquine, dextromethorphan, acetaminophen, ifosfamide, cyclophosphamide, benzphetamine, buspirone, MDMA).

[0053] P450 monooxygenases suitable in the methods and systems herein disclosed include cytochrome P450 monooxygenases (EC 1.14.14.1) from different sources (bacterial, fungi, yeast, plant, mammalian, and human), and variants thereof. Exemplary P450 monooxygenases suitable in the methods and systems herein disclosed include members of CYP102A subfamily (e.g. CYP102A1, CYP102A2, CYP102A3, CYP102A5), members of CYP101A subfamily (e.g. CYP101A1), members of CYP102E subfamily (e.g. CYP102E1), members of CYP1A subfamily (e.g. CYP1A1, CYP1A2), members of CYP2A subfamily (e.g. CYP2A3, CYP2A4, CYP2A5, CYP2A6, CYP2A12, CYP2A13), members of CYP1B subfamily (e.g. CYP1B1), members of CYP2B subfamily (e.g. CYP2B6), members of CYP2C subfamily (e.g. CYP2C8, CYP2C9, CYP2C10, CYP2C18, CYP2C19) members of CYP2D subfamily (e.g. CYP2D6), members of CYP3A subfamily (e.g. CYP3A4, CYP3A5, CYP3A7, CYP3A43), members of CYP107A subfamily (e.g. CYP107A1), and members of CYP153 family (e.g. CYP153A1, CYP153A2, CYP153A6, CYP153A7, CYP153A8, CYP153A11, CYP153D3, and CYP153D2, (van Beilen and Funhoff 2007)). Exemplary organic molecules oxidizable by P450 monooxygenases include C₅-C₂₂ alkanes, cyclic alkanes, cyclic alkenes, alkane derivatives, alkene derivatives, C₁₀-C₂₀ fatty acids, steroids, terpenes, aromatic hydrocarbons, natural products and natural product analogues such as polyketides, prostaglandins, thromboxanes, leukotrienes, anthraquinones, tetracyclines, anthracyclines, polyenes, statins, amino acids, flavonoids, stilbenes, alkaloids (e.g. lysine-derived, nicotinic acid-derived, tyrosine-derived, tryptophan-derived, anthranilic acid-derived, histidine-derived, purine-derived, alkaloids), beta-lactams, aminoglycosides, polymyxins, quinolones, synthetic derivatives such as aromatic heterocyclic derivatives (e.g. phenyl-, pyrimidine-, pyridine-, piperidine-, pyrrole-, furan-, triazol-, thiophene-, pyrazole-, imidazole-, tetrazole-, oxazole-, isoxazole-, thiazole-, isothiazole-, pyran-, pyridazine-, pyrazine-, piperazine-, thiazine-, and oxazine-derivatives), and the like.

[0054] Other exemplary P450 monooxygenases suitable in the methods and systems herein disclosed include CYP106A2, CYP2F1, CYP2J2, CYP2R1, CYP2S1, CYP2U1, CYP2W1, CYP4A11, CYP4A22, CYP4B1, CYP4F2, CYP4F3, CYP4F8, CYP4F11, CYP4F12, CYP4F22, CYP4V2, CYP4X1, CYP4Z1, CYP5A1, CYP7A1, CYP7B1, CYP8A1, CYP8B1, CYP11A1, CYP11B1, CYP11B2, CYP17A1, CYP19A1, CYP20A1, CYP21A2, CYP24A1, CYP26A1, CYP26B1, CYP26C1, CYP27A1, CYP27C1, CYP39A1, CYP46A1, CYP51A1.

[0055] In particular, in some embodiments P450 monooxygenases suitable in the methods and systems herein disclosed include CYP102A1 (also called P450_{BM3}) from *Bacillus megaterium* (SEQ ID NO: 2), CYP102A2 from *Bacillus subtilis* (SEQ ID NO: 3), CYP102A3 from *Bacillus subtilis* (SEQ ID NO: 4), CYP102A5 from *Bacillus cereus* (SEQ ID NO: 5), CYP102E1 from *Ralstonia metallidurans* (SEQ ID NO: 6), CYP102A6 from *Bradyrhizobium japonicum* (SEQ ID NO: 7), CYP101A1 (also called P450cam) from *Pseudomonas putida* (SEQ ID NO: 8), CYP106A2 (also called P450meg) from *Bacillus megaterium* (SEQ ID NO: 9), CYP153A6 (SEQ ID NO: 54), CYP153A7 (SEQ ID NO: 55), CYP153A8 (SEQ ID NO: 56), CYP153A11 (SEQ ID NO: 57), CYP153D2 (SEQ ID NO: 58), CYP153D3 (SEQ ID NO: 59), P450cin from *Citrobacter braktii* (SEQ ID NO: 10), P450terp from *Pseudomonas* sp. (SEQ ID NO: 11), P450eryF from *Saccharopolyspora erythraea* (SEQ ID NO: 12), CYP1A2 (SEQ ID NO: 13), CYP2C8 (SEQ ID NO: 14), CYP2C9 (SEQ ID NO: 15), CYP2C19 (SEQ ID NO: 16), CYP2D6 (SEQ ID NO: 17), CYP2E1 (SEQ ID NO: 18), CYP2F1 (SEQ ID NO: 19), CYP3A4 (SEQ ID NO: 20), CYP153-AlkB_{Burk} from *Alcanivorax borkumensis* (SEQ ID NO: 60), CYP153-EB104 from *Acinetobacter* sp. EB104 (SEQ ID NO: 61), CYP153-OC4 from *Acinetobacter* sp. OC4 (SEQ ID NO: 62), and variants thereof. Exemplary organic molecules that can be oxidized by these P450 monooxygenases include branched and linear C₁₀-C₂₀ fatty acids, C₆-C₂₀ alkanes, cyclic alkanes, cyclic alkenes, alkane derivatives, alkene derivatives, steroids, terpenes, aromatic hydrocarbons, natural products and natural product analogues such as polyketides, prostaglandins, thromboxanes, leukotrienes, anthraquinones, tetracyclines, anthracenes, polyenes, statins, amino acids, flavonoids, stilbenes, alkaloids (e.g. lysine-derived, nicotinic acid-derived, tyrosine-derived, tryptophan-derived, anthranilic acid-derived, histidine-derived, purine-derived alkaloids), beta-lactams, aminoglycosides, polymyxins, quinolones, synthetic derivatives such as aromatic heterocyclic derivatives (e.g. phenyl-, pyrimidine-, pyridine-, piperidine-, pyrrole-, furan-, triazol-, thiophene-, pyrazole-, imidazole-, tetrazole-, oxazole-, isoxazole-, thiazole-, isothiazole-, pyran-, pyridazine-, pyrazine-, piperazine-, thiazine-, and oxazine-derivatives), and the like.

[0056] In particular, in some embodiments P450 monooxygenases suitable for the methods and systems herein disclosed include CYP102A1 (SEQ ID NO: 2) and variants thereof, wherein none, one or more of the amino acids that are located within 50 Å from the heme iron are mutated to any other of the natural amino acids or mutated to an unnatural

amino acid or modified in some way so to alter the properties of the enzyme. Examples of amino acid positions that can be modified in CYP102A1 to produce a P450 monooxygenase suitable in the methods and systems herein disclosed include without limitations: 25, 26, 42, 47, 51, 52, 58, 74, 75, 78, 81, 82, 87, 88, 90, 94, 96, 102, 106, 107, 108, 118, 135, 138, 142, 145, 152, 172, 173, 175, 178, 180, 181, 184, 185, 188, 197, 199, 205, 214, 226, 231, 236, 237, 239, 252, 255, 260, 263, 264, 265, 268, 273, 274, 275, 290, 295, 306, 324, 328, 354, 366, 398, 401, 430, 433, 434, 437, 438, 442, 443, 444, and 446.

[0057] In particular, in some embodiments, P450 monooxygenases suitable in the methods and system herein disclosed are selected from the group consisting of CYP102A1 (SEQ ID NO:2) and variants thereof including CYP102A1var1 (SEQ ID NO: 21), CYP102A1var2 (SEQ ID NO: 22), CYP102A1var3 (SEQ ID NO: 23), CYP102A1var3-2 (SEQ ID NO:24), CYP102A1var3-3(SEQ ID NO: 25), CYP102A1var3-4(SEQ ID NO: 26), CYP102A1var3-5(SEQ ID NO: 27), CYP102A1var3-6(SEQ ID NO: 28), CYP102A1var3-7(SEQ ID NO: 29), CYP102A1var3-8(SEQ ID NO: 30), CYP102A1var3-9(SEQ ID NO: 31); CYP102A1var3-10(SEQ ID NO: 32), CYP102A1var3-11(SEQ ID NO: 33), CYP102A1var3-12(SEQ ID NO: 34), CYP102A1var3-13(SEQ ID NO: 35), CYP102A1var3-14(SEQ ID NO: 36), CYP102A1var3-15(SEQ ID NO: 37), CYP102A1var3-16(SEQ ID NO: 38), CYP102A1var3-17(SEQ ID NO: 39), CYP102A1var3-18(SEQ ID NO: 40), CYP102A1var3-19(SEQ ID NO: 41), CYP102A1var3-20 (SEQ ID NO: 42) CYP102A1var3-21(SEQ ID NO: 43), CYP102A1var3-22 (SEQ ID NO: 44), CYP102A1var3-23 (SEQ ID NO: 45), CYP102A1var4 (SEQ ID NO: 46) CYP102A1var5 (SEQ ID NO:47), CYP102A1var6 (SEQ ID NO: 48), CYP102A1var7 (SEQ ID NO: 49), CYP102A1var8 (SEQ ID NO:50), CYP102A1var9 (SEQ ID NO: 51), CYP102A1var9-1 (SEQ ID NO: 52)

[0058] The above variants are illustrated in particular in the following Table 1 wherein the respective sequences reporting in the enclosed Sequence Listing and the mutations of each variant with respect to the wild type (SEQ ID NO: 2) are listed.

Table 1

Name	Sequence	Mutation(s) with respect to CYP102A1
CYP102A1	SEQ ID NO:2	--
CYP102A1var1	SEQ ID NO: 21	V78A, H138Y, T175I, V178I, A184V, H236Q, E252G, R255S, A290V, A295T, L353V

Table 1

Name	Sequence	Mutation(s) with respect to CYP102A1
CYP102A1var2	SEQ ID NO: 22	V78A, T175I, A184V, F205C, S226R, H236Q, E252G, R255S, A290V, L353V
CYP102A1var3	SEQ ID NO: 23	R47C, V78A, K94I, P142S, T175I, A184V, F205C, S226R, H236Q, E252G, R255S, A290V, L353V
CYP102A1var3-2	SEQ ID NO: 24	V78A, F81P, A82L, F87A, P142S, T175I, A180T, A184V, A197V, F205C, S226R, H236Q, E252G, R255S, A290V, L353V
CYP102A1var3-3	SEQ ID NO: 25	V78A, F81C, A82P, F87A, P142S, T175I, A180T, A184V, A197V, F205C, S226R, H236Q, E252G, R255S, A290V, L353V
CYP102A1var3-4	SEQ ID NO: 26	V78A, F81W, A82I, F87A, P142S, T175I, A180T, A184V, A197V, F205C, S226R, H236Q, E252G, R255S, A290V, L353V
CYP102A1var3-5	SEQ ID NO: 27	V78A, A82G, F87V, P142S, T175I, A184V, F205C, S226R, H236Q, E252G, R255S, A290V, A328V, L353V
CYP102A1var3-6	SEQ ID NO: 28	R47C, V78A, F87I, K94I, P142S, T175I, A184V, F205C, S226R, H236Q, E252G, R255S, A290V, L353V
CYP102A1var3-7	SEQ ID NO: 29	R47C, V78A, F87A, K94I, P142S, T175I, A184V, F205C, S226R, H236Q, E252G, R255S, A290V, L353V
CYP102A1var3-8	SEQ ID NO: 30	R47C, V78A, A82L, K94I, P142S, T175I, A184V, F205C, S226R, H236Q, E252G, R255S, A290V, L353V
CYP102A1var3-9	SEQ ID NO: 31	R47C, V78T, A82G, F87V, K94I, P142S, T175I, A184V, F205C, S226R, H236Q, E252G, R255S, A290V, A328L, L353V
CYP102A1var3-10	SEQ ID NO: 32	R47C, L52I, V78F, A82S, K94I, P142S, T175I, A184V, F205C, S226R, H236Q, E252G, R255S, A290V, A328F, I366V, L353V, E464G, I710T
CYP102A1var3-11	SEQ ID NO: 33	R47C, L52I, V78F, A82S, K94I, P142S, T175I, A184V, F205C, S226R, H236Q, E252G, R255S, A290V, A328L, K349N, L353V, I366V, E464G, I710T

Table 1

Name	Sequence	Mutation(s) with respect to CYP102A1
CYP102A1var3-12	SEQ ID NO: 34	R47C, L52I, V78F, A82S, K94I, P142S, T175I, A184V, L188P, F205C, S226R, H236Q, E252G, R255S, A290V, A328L, I366V, L353V, E464G, I710T
CYP102A1var3-13	SEQ ID NO: 35	R47C, V78T, A82G, K94I, P142S, T175I, A184V, F205C, S226R, H236Q, E252G, R255S, A290V, A328L, L353V
CYP102A1var3-14	SEQ ID NO: 36	V78A, A82V, F81R, F87A, P142S, T175I, A180T, A184V, A197V, F205C, S226R, H236Q, E252G, R255S, A290V, L353V
CYP102A1var3-15	SEQ ID NO: 37	V78A, F81W, A82S, F87A, P142S, T175I, A184V, A197V, F205C, S226R, H236Q, E252G, R255S, A290V, L353V
CYP102A1var3-16	SEQ ID NO: 38	R47C, V78F, A82S, K94I, P142S, T175I, A184V, F205C, S226R, H236Q, E252G, R255S, A290V, A328F, L353V, E464G, I710T
CYP102A1var3-17	SEQ ID NO: 39	V78A, F81V, A82T, F87A, P142S, T175I, A180T, A184V, A197V, F205C, S226R, H236Q, E252G, R255S, A290V, L353V
CYP102A1var3-18	SEQ ID NO: 40	R47C, L52I, V78F, A82S, K94I, P142S, T175I, A184V, L188P, F205C, S226R, H236Q, E252G, R255S, A290V, A328F, I366V, L353V, E464G, I710T
CYP102A1var3-19	SEQ ID NO: 41	R47C, L52I, A74S, V78F, A82S, K94I, P142S, T175I, L188P, F205C, S226R, H236Q, E252G, R255S, A290V, A328F, I366V, L353V, E464G, I710T
CYP102A1var3-20	SEQ ID NO: 42	R47C, V78A, A82V, K94I, P142S, T175I, A184V, F205C, S226R, H236Q, E252G, R255S, A290V, A328V, L353V
CYP102A1var3-21	SEQ ID NO: 43	R47C, V78A, F87V, K94I, P142S, T175I, A184V, F205C, S226R, H236Q, E252G, R255S, I263A, A290V, L353V
CYP102A1var3-22	SEQ ID NO: 44	R47C, V78A, A82F, K94I, P142S, T175I, A184V, F205C, S226R, I263A, H236Q, E252G, R255S, A290V, A328V, L353V

Table 1

Name	Sequence	Mutation(s) with respect to CYP102A1
CYP102A1var3-23	SEQ ID NO: 45	R47C, V78A, K94I, P142S, T175I, A184V, F205C, S226R, H236Q, E252G, R255S, A290V, A328V, L353V
CYP102A1var4	SEQ ID NO: 46	F87A
CYP102A1var5	SEQ ID NO: 47	F87V
CYP102A1var6	SEQ ID NO: 48	F87V, L188Q
CYP102A1var7	SEQ ID NO: 49	A74G, F87V, L188Q
CYP102A1var8	SEQ ID NO: 50	R47L, F87V, L188Q
CYP102A1var9	SEQ ID NO: 51	F87A, T235A, R471A, E494K, S1024E
CYP102A1var9-1	SEQ ID NO: 52	F87A, A184K, T235A, R471A, E494K, S1024E

[0059] In some embodiments, the P450 monooxygenases listed in Table 1 are provided as oxygenating agents for the methods and systems herein disclosed, wherein the organic molecules, include branched and linear C₆-C₂₀ fatty acids, C₂-C₂₀ alkanes, cyclic alkanes, cyclic alkenes, alkane derivatives, alkene derivatives, steroids, terpenes, aromatic hydrocarbons, prostaglandines, aromatic heterocyclic derivatives such as phenyl-, pyrimidine-, pyridine-, piperidine-, pyrrole-, furan-, triazol-, thiophene-, pyrazole-, imidazole-, tetrazole-, oxazole-, isoxazole-, thiazole-, isothiazole-, pyran-, pyridazine-, pyrazine-, piperazine-, thiazine-, and oxazine-derivatives.

[0060] In some embodiments P450 monooxygenases suitable in the methods and systems herein disclosed include CYP102A2 from *Bacillus subtilis* (SEQ ID NO: 3), and variants thereof, wherein none, one or more of the amino acids that are located within 50 Å from the heme iron are mutated to any other of the natural amino acids or mutated to an unnatural amino acid or modified in some way so to alter the properties of the enzyme.

[0061] In particular, in some embodiments, P450 monooxygenases suitable in the methods and system herein disclosed are selected from the group consisting of CYP102A2 (SEQ ID NO:3) and variants thereof including CYP102A2var1 (SEQ ID NO:63). The above variants are illustrated in particular in the following Table 2 wherein the mutations of each variant with respect to the wild type (SEQ ID NO: 3) are listed.

Table 2

Name	Sequence	Mutation(s) with respect to CYP101A1
CYP102A2	SEQ ID NO:3	--
CYP102A2var1	SEQ ID NO: 63	F88A

[0062] In some embodiments P450 monooxygenases suitable for the methods and systems herein disclosed include CYP102A3 from *Bacillus subtilis* (SEQ ID NO: 4), and variants thereof, wherein none, one or more of the amino acids that are located within 50 Å from the heme iron are mutated to any other of the natural aminoacids or mutated to an unnatural amino acid or modified in some way so to alter the properties of the enzyme.

[0063] In particular, in some embodiments P450 monooxygenases suitable in the methods and systems herein disclosed are selected from the group consisting of CYP102A3 (SEQ ID NO:4) and variants thereof including CYP102A3var1 (SEQ ID NO: 64). The above variants are illustrated in particular in the following Table 3 wherein the mutations of each variant with respect to the wild type (SEQ ID NO: 4) are listed.

Table 3

Name	Sequence	Mutation(s) with respect to CYP101A1
CYP102A3	SEQ ID NO:4	--
CYP102A3var1	SEQ ID NO: 64	F88A

[0064] In particular, in some embodiments P450 monooxygenases suitable in the methods and systems herein disclosed include CYP101A1 (also called P450cam) from *Pseudomonas putida* (SEQ ID NO: 8) and variants thereof, wherein none, one or more of the amino acids that are located within 50 Å from the heme iron are mutated to any other of the natural aminoacids or mutated to an unnatural amino acid or modified in some way so to alter the properties of the enzyme.

[0065] In particular, in some embodiments, P450 monooxygenases suitable in the methods and system herein disclosed are selected from the group consisting of CYP101A1 (SEQ ID NO:8) and variants thereof including CYP101A1var1 (SEQ ID NO:65), CYP101A1var2 (SEQ ID NO:66), CYP101A1var2-1 (SEQ ID NO:67), CYP101A1var2-2 (SEQ ID NO:68), and CYP101A1 var2-3 (SEQ ID NO:69).

[0066] The above variants are illustrated in particular in the following Table 4 wherein the mutations of each variant with respect to the wild type (SEQ ID NO: 8) are listed.

Table 4

Name	Sequence	Mutation(s) with respect to CYP101A1
CYP101A1	SEQ ID NO:8	--
CYP101A1var1	SEQ ID NO: 65	Y96A
CYP101A1var2	SEQ ID NO: 66	Y96F
CYP101A1var2-1	SEQ ID NO: 67	Y96F, F87W
CYP101A1var2-2	SEQ ID NO: 68	Y96F, V247L
CYP101A1var2-3	SEQ ID NO: 69	F87W, Y96F, V247L

[0067] In some embodiments, the P450 enzyme is included in a P450-containing system, a system including a P450 enzyme and one or more proteins that deliver one or more electrons to the heme iron in the P450 enzyme. Natural P450-containing systems occur according to the following general schemes:

[0068] CYP reductase (CPR)/cytochrome b5 (cyb5)/P450 systems: typically employed by eukaryotic microsomal (i.e., not mitochondrial) CYPs, they involve the reduction of cytochrome P450 reductase (variously CPR, POR, or CYPOR) by NADPH, and the transfer of reducing power as electrons to the CYP. Cytochrome b5 (cyb5) can also contribute reducing power to this system after being reduced by cytochrome b5 reductase (CYB5R);

[0069] Ferredoxin Reductase (FdxR) or Putidaredoxin Reductase (PdxR)/Ferredoxin (Fdx) or Putidaredoxin (Pdx)/P450 systems, typically employed by mitochondrial and some bacterial CYPs. Reducing electrons from a soluble cofactor, typically NADPH or NADH, are transferred through the reductase to electron carrier, Fdx or Pdx, and transferred from the electron carrier to the P450 component;

[0070] P450-CPR fusion systems, where the CYP domain is naturally fused to the electron donating partners. An example of these systems is represented by cytochrome P450_{BM3} (CYP102A1) from the soil bacterium *Bacillus megaterium*;

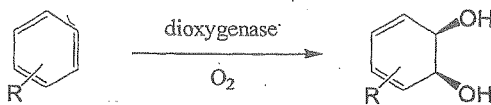
[0071] CYB5R / cyb5 / P450 systems, where both electrons required by the CYP derive from cytochrome b5;

[0072] FMN / Fd / P450 systems, where a FMN-domain-containing reductase is fused to the CYP. This type of system was originally found in *Rhodococcus sp*;

[0073] P450 only systems, which do not require external reducing power. These include CYP5 (thromboxane synthase), CYP8, prostacyclin synthase, and CYP74A (allene oxide synthase).

[0074] In some embodiments, the oxidizing agent is a non-heme containing monooxygenases i.e. a monooxygenases that is able to function without a heme prosthetic group. These monooxygenases include but are not limited to flavin monooxygenases, pterin-dependent non-heme monooxygenases, non-heme diiron monooxygenases, and diiron hydroxylases. In these enzymes, oxygen activation occurs at a site in the enzyme's structural fold that is covalently or non-covalently bound to a flavin cofactor, a pterin cofactor, or a diiron cluster. Examples of non-heme containing monooxygenases include but are not limited to ω -hydroxylases (*n*-octane ω -hydroxylase, *n*-decane ω -hydroxylases, 9- α -hydroxylase, and AlkB), styrene monooxygenase, butane monooxygenases, propane monooxygenases, and methane monooxygenases. Non-heme containing monooxygenases catalyze the monooxygenation of a variety of structurally diverse substrates. Exemplary substrates accepted by progesterone 9- α -hydroxylase from *Nocardia* sp. include steroid derivatives. Exemplary substrates accepted by non-heme monooxygenases such as integral membrane di-iron alkane hydroxylases (e.g. AlkB), soluble di-iron methane monooxygenases (sMMO), di-iron propane monooxygenases, di-iron butane monooxygenases, membrane-bound copper-containing methane monooxygenases, styrene monooxygenase, xylene monooxygenase include C₁-C₂₄ linear and branched alkanes, alkenes, and aromatic hydrocarbons.

[0075] In some embodiments, the oxidizing agent is a dioxygenase or a variant thereof and in particular a dioxygenase involved in the catabolism of aromatic hydrocarbons. Dioxygenases are a class of oxygenase enzymes that incorporate both atoms of molecular oxygen (O₂) onto the substrate according to the general scheme of reaction:



[0076] Dioxygenases are metalloprotein and activation of molecular oxygen is carried out in a site within the structural fold of the enzyme that is covalently or non-covalently bound to one or more metal atoms. The metal is typically iron, manganese, or copper. Example of dioxygenases are catechol dioxygenases, toluene dioxygenases, biphenyl dioxygenases. Catechol dioxygenases catalyze the oxidative cleavage of catechols and have different substrate specificities, including catechol 1,2-dioxygenase (EC 1.13.11.1), catechol 2,3-dioxygenase (EC 1.13.11.2), and protocatechuate 3,4-dioxygenase (EC 1.13.11.3). Toluene dioxygenase and biphenyl dioxygenases are involved in the natural degradation of aromatic compounds and typically introduce two oxygen atoms across a double bond in aromatic or non-aromatic compounds. Dioxygenases, e.g. toluene dioxygenase, can be engineered to accept substrates for which the wild-type enzyme shows only basal or no activity, e.g. 4-picoline (Sakamoto, Joern et al. 2001). Potentially suitable substrates for dioxygenase enzymes include but are not restricted to substituted or non-substituted monocyclic, polycyclic, and heterocyclic aromatic compounds. On these substrates, the dioxygenase can introduce one or more *cis* dihydrodiol functional group.

[0077] In some embodiments, the oxidizing agent is a peroxygenase. Natural peroxygenases are heme-dependent oxidases that are distinct from cytochrome P450 enzymes and peroxidases and that accept only peroxides, in particular hydrogen peroxide, as the source of oxidant. Natural peroxygenases are typically membrane-bound and can catalyze hydroxylation reactions of aromatics, sulfoxidations of xenobiotics, or epoxidations of unsaturated fatty acids. In contrast to cytochrome P450 monooxygenases, peroxygenases' activity does not require any cofactor such as NAD(P)H and does not use molecular oxygen. Examples are the plant peroxygenase (PXG) (Hanano, Burcklen et al. 2006), soybean peroxygenase (Blee, Wilcox et al. 1993), and oat seed peroxygenase.

[0078] In some embodiments, the peroxygenase is a cytochrome P450s can also use peroxides as oxygen donors. This constitutes the so-called 'peroxide shunt pathway' and the enzyme does not need a reductase and NAD(P)H to carry out catalysis. Normally, this peroxide-driven reaction in P450s is not significant. However, mutations in the heme domain

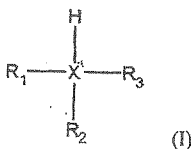
of P450 enzymes can enhance their latent peroxygenase activity, as in the case of P450cam (Joo, Lin et al. 1999) and P450_{BM3} (Cirino and Arnold 2003). Using three engineered P450 enzymes, namely CYP102A1, CYP102A2 and CYP102A3, that are capable of peroxygenase activity, a library of ~ 6000 members peroxygenase chimeras was created by site-directed recombination (Otey, Landwehr et al. 2006).

[0079] Naturally-occurring P450 peroxygenases also exist. P450_{BSP} (CYP152A1) and P450_{SPα} (CYP152B1), recently isolated from *Bacillus subtilis* and *Sphingomonas paucimobilis* (Matsunaga, Sumimoto et al. 2002; Matsunaga, Yamada et al. 2002), efficiently utilize H₂O₂ to hydroxylate fatty acids, prevalently in α and β positions.

[0080] Exemplary peroxygenases suitable in the methods and system herein disclosed include but are not limited to natural heme-containing peroxygenases, natural P450 peroxygenases, engineered P450s with peroxygenase activity, and P450 peroxygenase chimeras described in more details in the work of Arnold and co-workers (Otey, Landwehr et al. 2006). These peroxygenases show activity on a variety of substrates including fatty acids, 8- and 12-pNCA, indole, aniline, *p*-nitrophenol, heterocyclic derivatives (e.g. chlorzoxazone, bupirone), statins, naphthyl derivatives.

[0081] Other suitable oxidizing agents for the systems and methods herein disclosed are peroxidases (EC number 1.11.1.x). Sequences of the peroxidase enzymes identified so far can be found in the PeroxiBase database. Peroxidases typically catalyze a reaction of the form: ROOR' + electron donor (2 e⁻) + 2H⁺ → ROH + R'OH. For most peroxidases the optimal oxygen providing compound is hydrogen peroxide, but others are more active with organic hydroperoxides such as lipid peroxides. Peroxidases can contain a heme cofactor in their active sites, or redox-active cysteine or selenocysteine residues. The nature of the electron donor is very dependent on the structure of the enzyme. For example, horseradish peroxidase can use a variety of organic compounds as electron donors and acceptors. Horseradish peroxidase has an accessible active site and many compounds can reach the site of the reaction. In contrast, cytochrome *c* peroxidase has a much more restricted active site, and the electron-donating compounds are very specific. Glutathione peroxidase is a peroxidase found in humans, which contains selenocysteine. It uses glutathione as an electron donor and is active with both hydrogen peroxide and organic hydroperoxide substrates.

[0082] In some embodiments the organic molecule has the structure of formula (I)



in which X = C atom is the target site, and R₁, R₂, and R₃ are independently selected from the group consisting of hydrogen, aliphatic, aryl, substituted aliphatic, substituted aryl, heteroatom-containing aliphatic, heteroatom-containing aryl, substituted heteroatom-containing aliphatic, substituted heteroatom-containing aryl, alkoxy, aryloxy, and functional groups (FG) or are taken together to form a ring, such that the carbon atom is a secondary or tertiary carbon atom.

[0083] The term "aliphatic" is used in the conventional sense to refer to an open-chain or cyclic, linear or branched, saturated or unsaturated hydrocarbon group, including but not limited to alkyl group, alkenyl group and alkynyl groups. The term "heteroatom-containing aliphatic" as used herein refer to an aliphatic moiety where at least one carbon atom is replaced with a heteroatom.

[0084] The term "alkyl" and "alkyl group" as used herein refers to a linear, branched, or cyclic saturated hydrocarbon typically containing 1 to 24 carbon atoms, preferably 1 to 12 carbon atoms, such as methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, t-butyl, octyl, decyl and the like. The term "heteroatom-containing alkyl" as used herein refers to an alkyl moiety where at least one carbon atom is replaced with a heteroatom, e.g. oxygen, nitrogen, sulphur, phosphorus, or silicon, and typically oxygen, nitrogen, or sulphur.

[0085] The term "alkenyl" and "alkenyl group" as used herein refers to a linear, branched, or cyclic hydrocarbon group of 2 to 24 carbon atoms, preferably of 2 to 12 carbon atoms, containing at least one double bond, such as ethenyl, n-propenyl, isopropenyl, n-butenyl, isobutenyl, octenyl, decenyl, and the like. The term "heteroatom-containing alkenyl" as used herein refer to an alkenyl moiety where at least one carbon atom is replaced with a heteroatom.

[0086] The term "alkynyl" and "alkynyl group" as used herein refers to a linear, branched, or cyclic hydrocarbon group of 2 to 24 carbon atoms, preferably of 2 to 12 carbon atoms, containing at least one triple bond, such as ethynyl, n-propynyl, and the like. The term "heteroatom-containing alkynyl" as used herein refer to an alkynyl moiety where at least one carbon atom is replaced with a heteroatom.

[0087] The term "aryl" and "aryl group" as used herein refers to an aromatic substituent containing a single aromatic or multiple aromatic rings that are fused together, directly linked, or indirectly linked (such as linked through a methylene or an ethylene moiety). Preferred aryl groups contain 5 to 24 carbon atoms, and particularly preferred aryl groups contain 5 to 14 carbon atoms. The term "heteroatom-containing aryl" as used herein refer to an aryl moiety where at least one carbon atom is replaced with a heteroatom.

[0088] The term "alkoxy" and "alkoxy group" as used herein refers to an aliphatic group or a heteroatom-containing aliphatic group bound through a single, terminal ether linkage. Preferred aryl alkoxy groups contain 1 to 24 carbon atoms, and particularly preferred alkoxy groups contain 1 to 14 carbon atoms.

[0089] The term "aryloxy" and "aryloxy group" as used herein refers to an aryl group or a heteroatom-containing aryl group bound through a single, terminal ether linkage. Preferred aryloxy groups contain 5 to 24 carbon atoms, and particularly preferred aryloxy groups contain 5 to 14 carbon atoms.

[0090] The terms "halo" and "halogen" are used in the conventional sense to refer to a fluoro, chloro, bromo or iodo substituent.

[0091] By "substituted" it is intended that in the alkyl, alkenyl, alkynyl, aryl, or other moiety, at least one hydrogen atom is replaced with one or more non-hydrogen atoms. Examples of such substituents include, without limitation: functional groups referred to herein as "FG", such as alkoxy, aryloxy, alkyl, heteroatom-containing alkyl, alkenyl, heteroatom-containing alkenyl, alkynyl, heteroatom-containing alkynyl, aryl, heteroatom-containing aryl, alkoxy, heteroatom-containing alkoxy, aryloxy, heteroatom-containing aryloxy, halo, hydroxyl ($-\text{OH}$), sulfhydryl ($-\text{SH}$), substituted sulfhydryl, carbonyl ($-\text{CO}-$), thiocarbonyl, ($-\text{CS}-$), carboxy ($-\text{COOH}$), amino ($-\text{NH}_2$), substituted amino, nitro ($-\text{NO}_2$), nitroso ($-\text{NO}$), sulfo ($-\text{SO}_2-\text{OH}$), cyano ($-\text{C}\equiv\text{N}$), cyanato ($-\text{O}-\text{C}\equiv\text{N}$).

thiocyanato ($-\text{S}-\text{C}\equiv\text{N}$), formyl ($-\text{CO}-\text{H}$), thioformyl ($-\text{CS}-\text{H}$), phosphono ($-\text{P}(\text{O})(\text{OH})_2$), substituted phosphono, and phospho ($-\text{PO}_2$).

[0092] In particular, the substituents R_1 , R_2 and R_3 of formula I can be independently selected from hydrogen, $\text{C}_1\text{-C}_{24}$ alkyl, $\text{C}_1\text{-C}_{24}$ substituted alkyl, $\text{C}_1\text{-C}_{24}$ substituted heteroatom-containing alkyl, $\text{C}_1\text{-C}_{24}$ substituted heteroatom-containing alkyl, $\text{C}_2\text{-C}_{24}$ alkenyl, $\text{C}_2\text{-C}_{24}$ substituted alkenyl, $\text{C}_2\text{-C}_{24}$ substituted heteroatom-containing alkenyl, $\text{C}_2\text{-C}_{24}$ substituted heteroatom-containing alkenyl, $\text{C}_5\text{-C}_{24}$ aryl, $\text{C}_5\text{-C}_{24}$ substituted aryl, $\text{C}_5\text{-C}_{24}$ substituted heteroatom-containing aryl, $\text{C}_5\text{-C}_{24}$ substituted heteroatom-containing aryl, $\text{C}_1\text{-C}_{24}$ alkoxy, $\text{C}_5\text{-C}_{24}$ aryloxy, carbonyl, thiocarbonyl, and carboxy. More in particular, R_1 , R_2 and R_3 of formula I can be independently selected from hydrogen, $\text{C}_1\text{-C}_{12}$ alkyl, $\text{C}_1\text{-C}_{12}$ substituted alkyl, $\text{C}_1\text{-C}_{12}$ substituted heteroatom-containing alkyl, $\text{C}_1\text{-C}_{12}$ substituted heteroatom-containing alkyl, $\text{C}_2\text{-C}_{12}$ alkenyl, $\text{C}_2\text{-C}_{12}$ substituted alkenyl, $\text{C}_2\text{-C}_{12}$ substituted heteroatom-containing alkenyl, $\text{C}_2\text{-C}_{12}$ substituted heteroatom-containing alkenyl, $\text{C}_5\text{-C}_{14}$ aryl, $\text{C}_5\text{-C}_{14}$ substituted aryl, $\text{C}_5\text{-C}_{14}$ substituted heteroatom-containing aryl, $\text{C}_5\text{-C}_{14}$ substituted heteroatom-containing aryl, $\text{C}_2\text{-C}_{14}$ alkoxy, $\text{C}_5\text{-C}_{14}$ aryloxy, carbonyl, thiocarbonyl, and carboxy.

[0093] Oxidizing agents known or expected to react with the target site of a compound of Formula (I) include but are not limited to oxygenases or variants thereof.

[0094] In some embodiments, the oxygenase can be a non-heme monooxygenase or a variant thereof, a heme-containing monooxygenase or a variant thereof, a peroxxygenase or a variant thereof, such as any of the heme-containing monooxygenase, non heme -containing monooxygenases and peroxxygenases herein disclosed. In particular, the oxygenase can be any of the P450 monooxygenases and P450 peroxxygenases herein disclosed.

[0095] In some embodiments, the oxygenase or variant thereof can be butane monooxygenase, CYP102A1 (SEQ ID NO:2), CYP102A1var4 (SEQ ID NO:46), CYP102A1var8 (SEQ ID NO: 50), CYP102A1var1 (SEQ ID NO:21), CYP102A1var2 (SEQ ID NO:22), CYP102A1var3 (SEQ ID NO:23), CYP102A1var3-20 (SEQ ID NO:42), CYP102A1var3-2 (SEQ ID NO:44), CYP102A1var3-3 (SEQ ID NO:25), CYP102A1var3-4 (SEQ ID NO:26), CYP102A1var3-5 (SEQ ID NO:27), CYP102A1var3-7 (SEQ ID NO:29), CYP102A1var3-8 (SEQ ID NO:30), CYP102A1var3-9 (SEQ ID NO:31), CYP102A1var3-11

(SEQ ID NO:33), CYP102A1var3-13 (SEQ ID NO:35), CYP102A1var3-14 (SEQ ID NO:36), CYP102A1var3-15 (SEQ ID NO:37), CYP101A1 (SEQ ID NO:8), CYP101A1var1 (SEQ ID NO: 65), CYP101A1var2-3 (SEQ ID NO:69), CYP102A2(SEQ ID NO:3), CYP102A2var1 (SEQ ID NO:63), CYP102A3(SEQ ID NO:4), CYP102A3var1 (SEQ ID NO:64) and CYP153A6 (SEQ ID NO:54), CYP153A7 (SEQ ID NO:55), CYP153A8 (SEQ ID NO:56), CYP153A11 (SEQ ID NO:57), CYP153D2(SEQ ID NO:58); and/or CYP106A2(SEQ ID NO:9). In particular, in those embodiments at least one of said oxygenases or variants thereof is expected to activate the target site by introducing an oxygen-containing functional group in the form of a hydroxyl group. In these embodiments, the final products resulting from the application of the systems and methods herein disclosed can be $(R_1R_2R_3CF)$, $(R_1R_2CF_2)$, $(R_1R_3CF_2)$, or $(R_2R_3CF_2)$.

[0096] In some embodiments of the methods and systems herein disclosed wherein the organic molecule is a compound of Formula (I), in which $R_1 = H$, $-CH_3$ or $=O$, and/or R_2 and R_3 are connected together through 4, 5, 6, or 7-methylene moiety to form a ring, the oxidizing agent can be an oxygenase, such as a P450 monooxygenase, and in particular CYP102A1var1 (SEQ ID NO:21), CYP102A1var2 (SEQ ID NO:22), CYP102A1var3 (SEQ ID NO:23), CYP102A1var3-7 (SEQ ID NO:29), CYP101A1 (SEQ ID NO:8), CYP101A1var1 (SEQ ID NO:65), and/or CYP101A1var2-3 (SEQ ID NO:69), and is expected to activate the target site of the corresponding compound of Formula (I) by introducing an oxygen-containing functional group in the form of a hydroxyl group.

[0097] In some embodiments of the methods and systems herein disclosed wherein the organic molecule is a compound of Formula (I), in which $R_1 = H$, $R_2 = -Me$, $-Et$, $-Pr$, or $-iPr$, and/or $R_3 = -(CH_2)_nCOOH$ with n between 9 and 15, the oxidizing agent can be an oxygenase such as a P450 monooxygenase, in particular CYP102A1 (SEQ ID NO:2), CYP102A1var4 (SEQ ID NO:46), CYP102A1var5 (SEQ ID NO:47), CYP102A2 (SEQ ID NO:3), CYP102A2var1 (SEQ ID NO:63), CYP102A3 (SEQ ID NO:4), and/or CYP102A3var1 (SEQ ID NO:64), which is expected to activate the target site by introducing an oxygen-containing functional group in the form of a hydroxyl group.

[0098] In some embodiments of the methods and systems herein disclosed wherein the organic molecule is a compound of Formula (I), in which $R_1 = R_2 = -Me$, $R_3 = -CH_2-o$ -substituted-Ph, activation can be performed by reacting the organic molecule with an

oxygenase, such as a P450 monooxygenase, including CYP102A1 (SEQIDNO:2), CYP102A1var3-4 (SEQIDNO:26), CYP102A1var3-14 (SEQIDNO:36), CYP102A1var3-15 (SEQIDNO:37), CYP102A1var3-3 (SEQIDNO:25), CYP102A1var3-2 (SEQIDNO:24), CYP102A1var3 (SEQIDNO:23), CYP102A1var3-9 (SEQIDNO:31), CYP102A1var1 (SEQIDNO:21), and/or CYP102A1var2 (SEQ ID NO:22), which introduce an hydroxyl group in the target site, as exemplified in Examples 11 and illustrated in corresponding scheme 11.

[0099] In some embodiments of the methods and systems herein disclosed wherein the organic molecule is a compound of Formula (I), in which $R_1 = R_2 = H$, activation can be performed by reacting the organic molecule with an oxygenase such as a P450 monooxygenase, including CYP153A6 (SEQIDNO:54), CYP153A7 (SEQIDNO:55), CYP153A8 (SEQIDNO:56), CYP153A11 (SEQIDNO:57), CYP153D2 (SEQIDNO:58), and/or CYP153D3 (SEQIDNO:59), which are expected to introduce an hydroxyl group on the target site.

[00100] In some embodiments of the methods and systems herein disclosed wherein the organic molecule is a compound of Formula (I), in which $R_3 = n\text{-C}_6\text{-C}_{10}$ alkyl (e.g. linear $\text{C}_6\text{-C}_{10}$ alkanes), activation can be performed by an oxygenase such as a butane monooxygenase, which is expected to introduce an hydroxyl group on the target site.

[00101] In some embodiments of the methods and systems herein disclosed wherein the organic molecule is a compound of Formula (I), in which $R_3 = \text{cyclohexenyl}$ (e.g. limonene), the oxidating agent can be an oxygenase, such as a P450 monooxygenase including CYP153A6 (SEQIDNO:54), CYP153A7 (SEQIDNO:55), CYP153A8 (SEQIDNO:56), CYP153A11 (SEQIDNO:57), CYP153D2 (SEQIDNO:58), and/or CYP153D3 (SEQIDNO:59) which are expected to introduce an hydroxyl group on the target site.

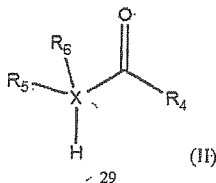
[00102] In some embodiments of the methods and systems herein disclosed wherein the organic molecule is a compound of Formula (I), in which $R_3 = n\text{-C}_7$, the oxidating agent can be a monooxygenase such as a P450 monooxygenases including CYP102A1var3-13 (SEQ ID NO: 35), which is expected to introduce an hydroxyl group on the target site.

[00103] In some embodiments of the methods and systems herein disclosed wherein the organic molecule is a compound of Formula (I), in which $R_1 = H$, R_2 and R_3 are connected through n methylene moieties, activation can be performed by reacting the substrate with monooxygenases such as P450 monooxygenases including CYP102A1var1 (SEQ ID NO: 21), CYP102A1var2 (SEQ ID NO: 22), CYP102A1var3-20 (SEQ ID NO: 42). In particular, when $n = 5$, as in the case of cyclopentanecarboxylic acid derivatives, the compound of formula (I) can be activated with methods and systems herein disclosed wherein the oxidating agent is a monooxygenase CYP102A1var8 (SEQ ID NO: 50). When instead $n = 6$, as in the case of camphor, cyclohexane and cyclohexene, the compound of formula (I) can be activated with methods and systems herein disclosed wherein the oxidating agent is a monooxygenase, such as a P450 monooxygenase including CYP101A1 (SEQ ID NO: 8), CYP153A6 (SEQ ID NO: 54), CYP153A7 (SEQ ID NO: 55), CYP153A8 (SEQ ID NO: 56), CYP153A11 (SEQ ID NO: 57), CYP153D3 (SEQ ID NO: 59) or CYP153D2 (SEQ ID NO: 58). In those embodiments, activation is known or expected to result in the introduction of a hydroxyl group in the target site.

[00104] In some embodiments of the methods and systems herein disclosed wherein the organic molecule is a compound of Formula (I), wherein $R_1 = H$, R_2 and R_3 are connected through 5 or 6 methylene moieties, so to form a polycyclic unsaturated system, such as in steroids, activation can be performed by reacting the substrate with a monooxygenase such as a P450 monooxygenase including CYP106A2 (SEQ ID NO: 9), and the activation is expected to result in the introduction of an hydroxyl group in the target site.

[00105] In the compound of formula I, wherein $R_1 = H$, $R_2 = -CH_2COOH$, $R_3 = n$ -dodecyl, activation can be performed by reacting the substrate with peroxygenase P450_{BSB} (CYP152A1) (SEQ ID NO: 70), resulting in the introduction of a hydroxyl group in the target site.

[00106] In some embodiments, the organic molecule has the structure of formula (II)



in which X is the target site C atom, and R₄, R₅, and R₆ are independently selected from the group consisting of hydrogen, aliphatic, aryl, substituted aliphatic, substituted aryl, heteroatom-containing aliphatic, heteroatom-containing aryl, substituted heteroatom-containing aliphatic, substituted heteroatom-containing aryl, alkoxy, aryloxy, and functional groups (FG) or are taken together to form a ring, such that the carbon atom is a secondary or tertiary carbon atom.

[00107] In particular, the substituents R₄, R₅ and R₆ of Formula (II) can be independently selected from hydrogen, C₁-C₂₄ alkyl, C₁-C₂₄ substituted alkyl, C₁-C₂₄ substituted heteroatom-containing alkyl, C₁-C₂₄ substituted heteroatom-containing alkyl, C₂-C₂₄ alkenyl, C₂-C₂₄ substituted alkenyl, C₂-C₂₄ substituted heteroatom-containing alkenyl, C₂-C₂₄ substituted heteroatom-containing alkenyl, C₅-C₂₄ aryl, C₅-C₂₄ substituted aryl, C₅-C₂₄ substituted heteroatom-containing aryl, C₅-C₂₄ substituted heteroatom-containing aryl, C₁-C₂₄ alkoxy, C₅-C₂₄ aryloxy, carbonyl, thiocarbonyl, carboxy, sulfhydryl, amino, substituted amino. More in particular, R₄ can be independently selected from hydrogen, C₂-C₁₄ alkoxy, C₅-C₁₄ aryloxy, amino, substituted amino, sulfhydryl, substituted sulfhydryl, C₁-C₁₂ alkyl, C₁-C₁₂ substituted alkyl, C₁-C₁₂ substituted heteroatom-containing alkyl, C₁-C₁₂ substituted heteroatom-containing alkyl, C₂-C₁₂ alkenyl, C₂-C₁₂ substituted alkenyl, C₂-C₁₂ substituted heteroatom-containing alkenyl, C₂-C₁₂ substituted heteroatom-containing alkenyl, C₅-C₁₄ aryl, C₅-C₁₄ substituted aryl, C₅-C₁₄ substituted heteroatom-containing aryl, and C₅-C₁₄ substituted heteroatom-containing aryl, while R₅ and R₆ are independently selected from hydrogen, C₁-C₁₂ alkyl, C₁-C₁₂ substituted alkyl, C₁-C₁₂ substituted heteroatom-containing alkyl, C₁-C₁₂ substituted heteroatom-containing alkyl, C₂-C₁₂ alkenyl, C₂-C₁₂ substituted alkenyl, C₂-C₁₂ substituted heteroatom-containing alkenyl, C₂-C₁₂ substituted heteroatom-containing alkenyl, C₅-C₁₄ aryl, C₅-C₁₄ substituted aryl, C₅-C₁₄ substituted heteroatom-containing aryl, C₅-C₁₄ substituted heteroatom-containing aryl, C₂-C₁₄ alkoxy, C₅-C₁₄ aryloxy, carbonyl, thiocarbonyl, and carboxy.

[00108] Oxidizing agents known or expected to react with the target site of a compound of Formula (II) include but are not limited to oxygenases or variants thereof.

[00109] In some embodiments, the oxygenase can be a non-heme monooxygenase or a variant thereof, a heme-containing monooxygenase or a variant thereof, a peroxxygenase or a variant thereof, such as any of the heme-containing monooxygenase, non heme-containing

monooxygenases and peroxxygenases herein disclosed. In-particular, the oxygenase can be any of the P450 monooxygenases and P450 peroxxygenases herein disclosed.

[00110] In some embodiments, the oxygenase or variant thereof can be a P450 monooxygenase or peroxxygenase including CYP102A1 (SEQ ID NO:2), CYP102A1var4 (SEQ ID NO:46), CYP102A1var8 (SEQ ID NO:50), CYP102A1var1 (SEQ ID NO:21), CYP102A1var2 (SEQ ID NO:22), CYP102A1var3 (SEQ ID NO:23), CYP102A1var3-7 (SEQ ID NO:9), CYP102A1var3-5 (SEQ ID NO:27), CYP102A1var3-9 (SEQ ID NO:31), CYP102A1var3-14 (SEQ ID NO:36), CYP102A1var3-15 (SEQ ID NO:37), CYP102A1var3-17 (SEQ ID NO:39), CYP101A1 (SEQ ID NO:8), CYP101A1(Y96F), CYP101A1var2-1 (SEQ ID NO:67), CYP101A1var1 (SEQ ID NO:65), CYP101A1var2-2 (SEQ ID NO:68), CYP1A2 (SEQ ID NO:13), CYP2C9 (SEQ ID NO:15), CYP2C19 (SEQ ID NO:16), CYP2D6 (SEQ ID NO:17), CYP2E1 (SEQ ID NO:18), CYP3A4 (SEQ ID NO:20), P450_{BSP} (CYP152A1) (SEQ ID NO:70) and/or P450_{SPX} (CYP152B1). In particular, in those embodiments at least one of said oxygenases or variants thereof is expected to activate the target site of a compound of Formula (II) by introducing an oxygen-containing functional group in the form of a hydroxyl group. In these embodiments, the final products resulting from the application of the systems and methods herein disclosed can be (R₅R₆CF—(CO)—R₄), (R₅CF₂—(CO)—R₄), or (R₆CF₂—(CO)—R₄).

[00111] In some embodiments of the methods and systems herein disclosed wherein the organic molecule is a compound of Formula (II) with R₄ = —OH, the oxydizing agent can be a peroxxygenase, such as a P450_{BSP} (CYP152A1) (SEQ ID NO:70) and/or a peroxxygenase P450_{SPX} (CYP152B1), which are most expected activate the target site, in particular by introducing an oxygen-containing functional group in the form of a hydroxyl group.

[00112] In some embodiments of the methods and systems herein disclosed wherein the organic molecule is a compound of Formula (II), with R₄ = —OR, and R = a C₁-C₆ alkyl, the oxydizing agent can be an oxygenase, and in particular a P450 oxygenase such as CYP102A1(F87A), CYP102A1var3 (SEQ ID NO: 23), CYP102A1var3-7 (SEQ ID NO: 29), CYP102A1var3-14 (SEQ ID NO: 36), CYP102A1var3-15 (SEQ ID NO: 37), and/or CYP102A1var3-5 (SEQ ID NO: 27), which are most expected to activate the target site, in

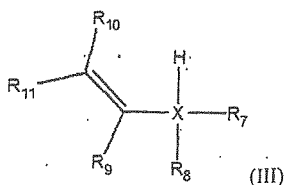
particular by introducing an oxygen-containing functional group in the form of a hydroxyl group.

[00113] In some embodiments of the methods and systems herein disclosed wherein the organic molecule is a compound of Formula (II), in which R_4 is —OMe, —OEt, —OPr, —OBu, —OtBu, R_5 is hydrogen, and R_6 is benzyl, *o*-chloro-phenyl, *p*-chloro-phenyl, or *m*-chloro-phenyl, *o*-methyl-phenyl, *p*-methyl-phenyl, or *m*-methyl-phenyl, *o*-methoxy-phenyl, *p*-methoxy-phenyl, or *m*-methoxy-phenyl, the activation can be performed by reacting the substrate with oxygenase CYP102A1var4 (SEQ ID NO: 46), CYP102A1var3 (SEQ ID NO: 23), and CYP102A1var3-7 (SEQ ID NO: 29), as illustrated in Examples 1, 2, 3 and 4 and corresponding schemes 1, 2, 3, and 4.

[00114] In some embodiments of the methods and systems herein disclosed wherein the organic molecule is a compound of Formula (II), in which R_4 is —OH, R_5 is hydrogen, and R_6 is a linear C_{12-16} alkyl chain, (for example a myristic acid), the activation can be performed by reacting the substrate with peroxygenases P450_{BSP} (CYP152A1) and P450_{SPA} (CYP152B1), resulting in the introduction of an hydroxy group in the target site.

[00115] In some embodiments of the methods and systems herein disclosed wherein the organic molecule is a compound of Formula (II), in which R_5 is —Me, and R_5 and R_6 are connected through a 6-methylene ring, (for example a α -thujone), the activation can be performed by reacting the substrate with monooxygenases CYP101A1 (SEQ ID NO: 8), CYP102A1 (SEQ ID NO: 2), CYP1A2 (SEQ ID NO: 13), CYP2C9 (SEQ ID NO: 14), CYP2C19 (SEQ ID NO: 16), CYP2D6 (SEQ ID NO: 17), CYP2E1 (SEQ ID NO: 18), and CYP3A4 (SEQ ID NO: 20), resulting in the introduction of an hydroxyl group in the target site.

[00116] In some embodiments, the organic molecule has the structure of formula (III)



in which X is the target site C atom, and R₇, R₈, R₉, R₁₀ and R₁₁ are independently selected from the group consisting of hydrogen, aliphatic, aryl, substituted aliphatic, substituted aryl, heteroatom-containing aliphatic, heteroatom-containing aryl, substituted heteroatom-containing aliphatic, substituted heteroatom-containing aryl, alkoxy, aryloxy, and functional groups (FG) or are taken together to form a ring, such that the carbon atom is a secondary or tertiary carbon atom.

[00117] In particular, the substituents R₇, R₈, R₉, R₁₀, and R₁₁ of Formula (III) can be independently selected from hydrogen, C₁-C₂₄ alkyl, C₁-C₂₄ substituted alkyl, C₁-C₂₄ substituted heteroatom-containing alkyl, C₁-C₂₄ substituted heteroatom-containing aryl, C₂-C₂₄ alkenyl, C₂-C₂₄ substituted alkenyl, C₂-C₂₄ substituted heteroatom-containing alkenyl, C₂-C₂₄ substituted heteroatom-containing alkenyl, C₅-C₂₄ aryl, C₅-C₂₄ substituted aryl, C₅-C₂₄ substituted heteroatom-containing aryl, C₅-C₂₄ substituted heteroatom-containing aryl, C₁-C₂₄ alkoxy, C₅-C₂₄ aryloxy, carbonyl, thiocarbonyl, and carboxy. More in particular, R₇, R₈, R₉, R₁₀, and R₁₁ are independently selected from hydrogen, C₁-C₁₂ alkyl, C₁-C₁₂ substituted alkyl, C₁-C₁₂ substituted heteroatom-containing alkyl, C₁-C₁₂ substituted heteroatom-containing aryl, C₂-C₁₂ alkenyl, C₂-C₁₂ substituted alkenyl, C₂-C₁₂ substituted heteroatom-containing alkenyl, C₂-C₁₂ substituted heteroatom-containing alkenyl, C₅-C₁₄ aryl, C₅-C₁₄ substituted aryl, C₅-C₁₄ substituted heteroatom-containing aryl, C₅-C₁₄ substituted heteroatom-containing aryl, C₂-C₁₄ alkoxy, C₅-C₁₄ aryloxy, carbonyl, thiocarbonyl, and carboxy.

[00118] Oxydizing agents known or expected to react with the target site of a compound of Formula (III) include but are not limited to oxygenases or variants thereof.

[00119] In some embodiments, the oxygenase can be a non-heme monooxygenase or a variant thereof, a heme-containing monooxygenase or a variant thereof, a peroxxygenase or a variant thereof, such as any of the heme-containing monooxygenase, non heme -containing monooxygenases and peroxxygenases herein disclosed. In particular, the oxygenase can be any of the P450 monooxygenases and P450 peroxxygenases herein disclosed.

[00120] In some embodiments, the oxygenase or variant thereof can be a P450 oxygenase including CYP102A1var1 (SEQ ID NO:21), CYP102A1var2 (SEQ ID NO:22), CYP102A1var3 (SEQ ID NO:23), CYP102A1var3-2 (SEQ ID NO:24), CYP102A1var3-6 (SEQ ID NO:28), CYP102A1var3-5 (SEQ ID NO:27), CYP102A1var3-8 (SEQ ID NO:30),

CYP102A1var3-9(SEQ ID NO:31), CYP102A1var3-11(SEQ ID NO:33), CYP102A1var3-17(SEQ ID NO:39), CYP102A1var5(SEQ ID NO:47), CYP102A1var6 (SEQ ID NO:48), CYP102A1var7(SEQ ID NO:49), CYP102A1var8(SEQ ID NO:50), CYP101A1var1(SEQ ID NO:65), CYP101A1var2-1(SEQ ID NO:67), CYP101A1var2-3(SEQ ID NO:69), CYP2C19(SEQ ID NO:16) and/or CYP2D6 (SEQ ID NO:17). In particular, in those embodiments at least one of said oxygenases or variants thereof is expected to activate the target site of a compound of Formula III by introducing an oxygen-containing functional group in the form of a hydroxyl group. In these embodiments, the final products resulting from the application of the systems and methods herein disclosed can be $(R_7R_8CF-C(R_9)=CR_{10}R_{11})_2$, $(R_7CF_2-C(R_9)=CR_{10}R_{11})$ or $(R_8CF_2-C(R_9)=CR_{10}R_{11})$.

[00121] In some embodiments of the methods and systems herein disclosed wherein the organic molecule is a compound of Formula (III) in which $R_7 = H$, $R_9 = -CH_3$, $R_{10} = -n-C_5H_{11}$, and R_8 and R_{11} are linked to form a substituted 5-member ring, activation can be performed by reacting the substrate with oxygenases such as CYP102A1var2 (SEQ ID NO:22), CYP102A1var3 (SEQ ID NO:23), CYP102A1var3-2(SEQ ID NO:24), CYP102A1var3-6 (SEQ ID NO:28), CYP102A1var3-5(SEQ ID NO:27), CYP102A1var3-8(SEQ ID NO:30), CYP102A1var3-9 (SEQ ID NO:31), resulting in the introduction of an hydroxyl group in the target site as illustrated in Examples 5 and corresponding scheme 5.

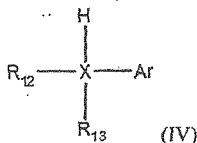
[00122] In some embodiments of the methods and systems herein disclosed wherein the organic molecule is a compound of Formula (III), in which $R_7 = H$, $R_9 = H$, $R_{10} = -CH_3$, R_8 and R_{11} are linked to form a substituted 6-member ring, activation can be performed by reacting the substrate with oxygenase CYP101A1var2-3(SEQ ID NO:69), resulting in the introduction of an hydroxyl group in the target site as in the case of α -pinene.

[00123] In some embodiments of the methods and systems herein disclosed wherein the organic molecule is a compound of Formula (III), in which $R_7 = R_8 = R_{10} = H$, R_9 and R_{11} are connected through a substituted 5-member ring, activation can be performed by reacting the organic molecule with an oxygenase such as CYP102A1var3-2 (SEQ ID NO:24), resulting in the introduction of an hydroxyl group in the target site as illustrated by Example 6 and corresponding scheme 6.

[00124] In some embodiments of the methods and systems herein disclosed wherein the organic molecule is a compound of Formula (III), in which $R_{10} = R_{11} = -CH_3$, $R_8 = R_9 = H$, and $R_7 =$ substituted C_5 alkenyl, activation can be performed by reacting the substrate with oxygenases such as CYP2C19 (SEQ ID NO:16) and CYP2D6 (SEQ ID NO:17), as in the case of linalool.

[00125] In some embodiments of the methods and systems herein disclosed wherein the organic molecule is a compound of Formula (II), in which $R_7 = H$, R_9 and R_{11} are linked together to form a 6-membered aromatic ring, R_7 and R_{10} are linked together to form a 5-carbon cyclic alkenyl, activation can be performed by reacting the substrate with oxygenases CYP102A1var5 (SEQ ID NO:47), CYP102A1var6 (SEQ ID NO:48), and/or CYP102A1var7 (SEQ ID NO:49), resulting in the introduction of an hydroxyl group in the target site as in the case of acenaphthene.

[00126] In some embodiments, the organic molecule has the structure of formula (IV)



in which the C is the target site, Ar can be a C_5 - C_{24} aryl, C_5 - C_{24} substituted aryl, C_5 - C_{24} substituted heteroatom-containing aryl or C_5 - C_{24} substituted heteroatom-containing aryl, while R_{12} and R_{13} are independently selected from the group consisting of hydrogen, aliphatic, aryl, substituted aliphatic, substituted aryl, heteroatom-containing aliphatic, heteroatom-containing aryl, substituted heteroatom-containing aliphatic, substituted heteroatom-containing aryl, alkoxy, aryloxy, and functional groups (FG) or are taken together to form a ring, such that the carbon atom is a secondary or tertiary carbon atom.

[00127] In particular, the substituent Ar of Formula (IV) can be C_5 - C_{14} aryl, C_5 - C_{14} substituted aryl, C_5 - C_{14} substituted heteroatom-containing aryl, or C_5 - C_{14} substituted heteroatom-containing aryl, while R_{12} and R_{13} are independently selected from hydrogen, C_1 - C_{12} alkyl, C_1 - C_{12} substituted alkyl, C_1 - C_{12} substituted heteroatom-containing alkyl, C_1 - C_{12} substituted heteroatom-containing alkyl, C_2 - C_{12} alkenyl, C_2 - C_{12} substituted alkenyl, C_2 - C_{12} substituted heteroatom-containing alkenyl, C_2 - C_{12} substituted heteroatom-containing alkenyl,

C₅-C₁₄ aryl, C₅-C₁₄ substituted aryl, C₅-C₁₄ substituted heteroatom-containing aryl, C₅-C₁₄ substituted heteroatom-containing aryl, C₂-C₁₄ alkoxy, C₅-C₁₄ aryloxy, carbonyl, thiocarbonyl, and carboxy.

[00128] Oxidizing agents known or expected to react with the target site of a compound of Formula (IV) include but are not limited to oxygenases or variants thereof.

[00129] In some embodiments, the oxygenase can be a non-heme monooxygenase or a variant thereof, a heme-containing monooxygenase or a variant thereof, a peroxxygenase or a variant thereof, such as any of the heme-containing monooxygenase, non heme-containing monooxygenases and peroxxygenases herein disclosed. In particular, the oxygenase can be any of the P450 monooxygenases and P450 peroxxygenases herein disclosed.

[00130] In some embodiments, the oxygenase or variant thereof can be such as CYP102A1 (SEQ ID NO:2), CYP102A1var4(SEQ ID NO:46), CYP102A1var5(SEQ ID NO:47), CYP102A1var6(SEQ ID NO:48), CYP102A1var7 (SEQ ID NO:49), CYP102A1var1(SEQ ID NO:21), CYP102A1var2(SEQ ID NO:22), CYP102A1var3(SEQ ID NO:23), CYP102A1var3-2(SEQ ID NO:24), CYP102A1var3-3(SEQ ID NO:25), CYP102A1var3-4(SEQ ID NO:26), CYP102A1var3-5(SEQ ID NO:27), CYP102A1var3-7(SEQ ID NO:29), CYP102A1var3-8(SEQ ID NO:30), CYP102A1var3-9 (SEQ ID NO:31), CYP102A1var3-17(SEQ ID NO:39), CYP102A1var8(SEQ ID NO:50), CYP101A1var2-1(SEQ ID NO:67), and/or CYP101A1var2-3(SEQ ID NO:69). In particular, in those embodiments at least one of said oxygenases or variants thereof is expected to activate the target site of a compound of Formula IV by introducing an oxygen-containing functional group in the form of a hydroxyl group. In these embodiments, the final products resulting from the application of the systems and methods herein disclosed can be R₁₂R₁₃ArC—F, R₁₂ArCF₂, or R₁₃ArCF₂.

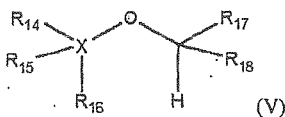
[00131] In some embodiments of the methods and systems herein disclosed wherein the organic molecule is a compound of Formula (IV), in which Ar = para-substituted phenyl R₁₃ = H, R₁₂ = —iPr, activation can be performed by reacting the organic molecule with an oxygenase such as a P450 monooxygenase including CYP102A1 (SEQ ID NO:2) and CYP102A1var5 (SEQ ID NO:47), which results in the introduction of an hydroxyl group in the target site as illustrated in Examples 10 and corresponding scheme 10.

[00132] In some embodiments of the methods and systems herein disclosed wherein the organic molecule is a compound of Formula (IV), in which Ar = para- or ortho or meta substituted phenyl (where substituent is halo, —CH₃, or —OCH₃), R₁₂ = H, R₁₃ = —COOR, where R is C₁-C₆ n-alkyl, activation can be performed by reacting the substrate with oxygenase CYP102A1var5 (SEQ ID NO:47), CYP102A1var3 (SEQ ID NO:23), and CYP102A1var3-7 (SEQ ID NO:29), as illustrated in Examples 1, 2, 3 and 4 and corresponding schemes 1, 2, 3, and 4.

[00133] In some embodiments of the methods and systems herein disclosed wherein the organic molecule is a compound of Formula (IV), in which R₁₂ = H, Ar is ortho substituted phenyl, R₁₃ is linked to Ar through a phenyl moiety, activation can be performed by reacting the substrate with oxygenases CYP102A1var6 (SEQ ID NO:48) and CYP102A1var8 (SEQ ID NO:50), resulting in the introduction of an hydroxyl group in the target site as in the case of fluorene.

[00134] In some embodiments of the methods and systems herein disclosed wherein the organic molecule is a compound of Formula (IV), in which R₁₂ = H, Ar is ortho substituted phenyl, R₁₃ is linked to Ar through a 2-methylene bridge, activation can be performed by reacting the substrate with oxygenase CYP102A1var5 (SEQ ID NO:47), resulting in the introduction of an hydroxyl group in the target site as in the case of indan.

[00135] In some embodiments the organic molecule has the structure of formula (V),



in which X is the target site C atom, R₁₄, R₁₅, R₁₆, R₁₇, R₁₈ are independently selected from the group consisting of hydrogen, aliphatic, aryl, substituted aliphatic, substituted aryl, heteroatom-containing aliphatic, heteroatom-containing aryl, substituted heteroatom-containing aliphatic, substituted heteroatom-containing aryl, alkoxy, aryloxy, and functional groups (FG) or are taken together to form a ring, such that the carbon atom is a secondary or tertiary carbon atom.

[00136] In particular, the substituents R_{14} , R_{15} , R_{16} , R_{17} , and R_{18} of Formula (V) can be independently selected from hydrogen, C_1 - C_{24} alkyl, C_1 - C_{24} substituted alkyl, C_1 - C_{24} substituted heteroatom-containing alkyl, C_1 - C_{24} substituted heteroatom-containing alkyl, C_2 - C_{24} alkenyl, C_2 - C_{24} substituted alkenyl, C_2 - C_{24} substituted heteroatom-containing alkenyl, C_2 - C_{24} substituted heteroatom-containing alkenyl, C_5 - C_{24} aryl, C_5 - C_{24} substituted aryl, C_5 - C_{24} substituted heteroatom-containing aryl, C_5 - C_{24} substituted heteroatom-containing aryl, carbonyl, thiocarbonyl, and carboxy. More in particular, R_{14} , R_{15} , R_{16} , R_{17} , and R_{18} are independently selected from hydrogen, C_1 - C_{12} alkyl, C_1 - C_{12} substituted alkyl, C_1 - C_{12} substituted heteroatom-containing alkyl, C_1 - C_{12} substituted heteroatom-containing alkyl, C_2 - C_{12} alkenyl, C_2 - C_{12} substituted alkenyl, C_2 - C_{12} substituted heteroatom-containing alkenyl, C_2 - C_{12} substituted heteroatom-containing alkenyl, C_5 - C_{14} aryl, C_5 - C_{14} substituted aryl, C_5 - C_{14} substituted heteroatom-containing aryl, C_5 - C_{14} substituted heteroatom-containing aryl, C_2 - C_{14} alkoxy, C_5 - C_{14} aryloxy, carbonyl, and carboxy.

[00137] Oxidizing agents known or expected to react with the target site of a compound of Formula (V) include but are not limited to oxygenases or variants thereof.

[00138] In some embodiments, the oxygenase can be a non-heme monooxygenase or a variant thereof, a heme-containing monooxygenase or a variant thereof, a peroxxygenase or a variant thereof, such as any of the heme-containing monooxygenase, non heme -containing monooxygenases and peroxxygenases herein disclosed. In particular, the oxygenase can be any of the P450 monooxygenases and P450 peroxxygenases herein disclosed.

[00139] In some embodiments, the oxygenase or variant thereof can be CYP102A1var8 (SEQ ID NO:50), CYP102A1var3-2 (SEQ ID NO:24), CYP102A1var3-3 (SEQ ID NO:25), CYP102A1var3-5 (SEQ ID NO:27), CYP102A1var3-6 (SEQ ID NO:28), CYP102A1var3-9 (SEQ ID NO:31), CYP102A1var3-11 (SEQ ID NO:33), CYP102A1var3-16 (SEQ ID NO:38), CYP102A1var3-19 (SEQ ID NO:41), CYP102A1var3-18 (SEQ ID NO:40), CYP102A1var3-2 (SEQ ID NO:24), CYP102A1var3-3 (SEQ ID NO:25), CYP102A1var3-14 (SEQ ID NO:36), CYP102A1var3-15 (SEQ ID NO:37), CYP102A1var3-17 (SEQ ID NO:39), CYP102A1var3-9 (SEQ ID NO:31), CYP101A1var2-3 (SEQ ID NO:69), and/or CYP3A4 (SEQ ID NO:20). In particular, in those embodiments, at least one of said oxygenases or variants thereof is expected to activate a compound of Formula V by affording a hydroxyl group at the target site. In these embodiments, the final product

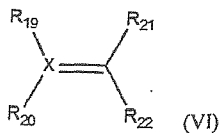
resulting from the application of the systems and methods herein disclosed can be $R_{14}R_{15}R_{16}C-F$.

[00140] In some embodiments of the methods and systems herein disclosed wherein the organic molecule is a compound of Formula (V), in which R_{14} , R_{15} , R_{17} , R_{18} are hydrogen, and R_{16} is 2-methyl-5-phenyl-4,5-dihydrooxazolyl, activation can be performed by reacting the substrate with oxygenases CYP102A1var3-5 (SEQ ID NO:27), CYP102A1var3-6 (SEQ ID NO:28), CYP102A1var3-11 (SEQ ID NO:33), CYP102A1var3-16 (SEQ ID NO:38), CYP102A1var3-19 (SEQ ID NO:41), CYP102A1var3-18 (SEQ ID NO:40), resulting in a hydroxyl group at the target site as illustrated in Examples 12 and corresponding scheme 12.

[00141] In some embodiments of the methods and systems herein disclosed wherein the organic molecule is a compound of Formula (V), in which R_{14} , R_{15} , R_{17} , R_{18} are hydrogen, and R_{16} is 2,3,4,5-tetramethoxy-tetrahydro-2H-pyranyl, activation can be performed by reacting the substrate with oxygenases such as CYP102A1var3-2 (SEQ ID NO:24), CYP102A1var3-3 (SEQ ID NO:25), CYP102A1var3-14 (SEQ ID NO:36), CYP102A1var3-15 (SEQ ID NO:37), CYP102A1var3-17 (SEQ ID NO:39), CYP102A1var3-9 (SEQ ID NO:31), resulting in a hydroxyl group at the target site as illustrated in Examples 13 and corresponding scheme 13.

[00142] In some embodiments of the methods and systems herein disclosed wherein the organic molecule is a compound of Formula (V), in which $R_{14} = CN$, $R_{15} = 6$ -dimethylamino-naphtyl, $R_{16} = R_{17} = H$, $R_{18} = H$, or hydrogen, activation can be performed by reacting the substrate with oxygenases such as CYP102A1var8 (SEQ ID NO:50) and CYP3A4 (SEQ ID NO:20), as in the case of α cyano-naphtyl ethers.

[00143] In some embodiments the organic molecule has the structure of formula (VI)



in which X is the target site C atom, and R_{19} , R_{20} , R_{21} , R_{22} are independently selected from the group consisting of hydrogen, aliphatic, aryl, substituted aliphatic, substituted aryl,

heteroatom-containing aliphatic, heteroatom-containing aryl, substituted heteroatom-containing aliphatic, substituted heteroatom-containing aryl, and functional groups (FG) or are taken together to form a ring representing in this case a cycloalkenyl, substituted cycloalkenyl, heteroatom-containing cycloalkenyl, or a substituted heteroatom-containing cycloalkenyl derivative.

[00144] In particular, the substituents R₁₉, R₂₀, R₂₁ and R₂₂ of formula VI are independently selected from hydrogen, C₁-C₂₄ alkyl, C₁-C₂₄ substituted alkyl, C₁-C₂₄ substituted heteroatom-containing alkyl, C₁-C₂₄ substituted heteroatom-containing alkyl, C₂-C₂₄ alkenyl, C₂-C₂₄ substituted alkenyl, C₂-C₂₄ substituted heteroatom-containing alkenyl, C₂-C₂₄ substituted heteroatom-containing alkenyl, C₅-C₂₄ aryl, C₅-C₂₄ substituted aryl, C₅-C₂₄ substituted heteroatom-containing aryl, C₅-C₂₄ substituted heteroatom-containing aryl, carbonyl, thiocarbonyl, carboxy, and substituted amino. More in particular, R₁₉, R₂₀, R₂₁ and R₂₂ are independently selected from hydrogen, C₁-C₁₂ alkyl, C₁-C₁₂ substituted alkyl, C₁-C₁₂ substituted heteroatom-containing alkyl, C₁-C₁₂ substituted heteroatom-containing alkyl, C₂-C₁₂ alkenyl, C₂-C₁₂ substituted alkenyl, C₂-C₁₂ substituted heteroatom-containing alkenyl, C₂-C₁₂ substituted heteroatom-containing alkenyl, C₅-C₁₄ aryl, C₅-C₁₄ substituted aryl, C₅-C₁₄ substituted heteroatom-containing aryl, C₅-C₁₄ substituted heteroatom-containing aryl, carbonyl, and carboxy.

[00145] Oxydizing agents known or expected to react with the target site of a compound of Formula (VI) include but are not limited to oxygenases or variants thereof.

[00146] In some embodiments, the oxygenase can be a non-heme monooxygenase or a variant thereof, a heme-containing monooxygenase or a variant thereof, a peroxxygenase or a variant thereof, such as any of the heme-containing monooxygenase, non heme -containing monooxygenases and peroxxygenases herein disclosed. In particular, the oxygenase can be any of the P450 monooxygenases and P450 peroxxygenases herein disclosed.

[00147] In some embodiments, the oxygenase or variant thereof can be CYP102A1 (SEQ ID NO:2), CYP102A1var1 (SEQ ID NO:21), CYP102A1var2 (SEQ ID NO:22), CYP102A1var3 (SEQ ID NO:23), CYP102A1var3-18 (SEQ ID NO:40), CYP102A1var5 (SEQ ID NO:47), CYP102A1var4 (SEQ ID NO:46), CYP102A1var3-21 (SEQ ID NO:43), CYP102A1var3-22 (SEQ ID NO:44), CYP102A1var3-23 (SEQ ID NO:45), CYP102A1var9

(SEQ ID NO:51); CYP102A1var9-1 (SEQ ID NO:52), and/or toluene dioxygenase. In particular, in those embodiments at least one of said oxygenases or variants thereof is expected to activate a compound of Formula VI by introducing an oxygen-containing functional group in the form of an epoxy group. In these embodiments, the final products resulting from the application of the systems and methods herein disclosed can be $(R_{19}R_{20}C(OH)-CFR_{21}R_{22})$, $(R_{19}R_{20}CF-C(OH)R_{21}R_{22})$, or $(R_{19}R_{20}CF-CFR_{21}R_{22})$.

[00148] Additional oxydizing agents that are expected to react with the target site of a compound of Formula (VI) include but are not limited to dioxygenases such as toluene dioxygenase. More specifically, dioxydizing agents are expected to activate a compound of Formula (VI) by introducing an oxygen-containing functional group in the form of a vicinal diol. In these embodiments, the final products resulting from the application of the systems and methods herein disclosed can be $(R_{19}R_{20}C(OH)-CFR_{21}R_{22})$, $(R_{19}R_{20}CF-C(OH)R_{21}R_{22})$, or $(R_{19}R_{20}CF-CFR_{21}R_{22})$.

[00149] In some embodiments of the methods and systems herein disclosed wherein the organic molecule is a compound of Formula (VI), in which $R_{19} = R_{20} = R_{21} = H$, $R_{22} = n$ -butyl, activation through epoxidation can be performed by reacting the substrate with oxygenases such as CYP102A1var1 (SEQ ID NO; 21), CYP102A1var3-21 (SEQ ID NO; 43), CYP102A1var3-22 (SEQ ID NO; 44), CYP102A1var3-23 (SEQ ID NO; 45), resulting in the introduction of an epoxide functional group at the target site as in the case of 1-hexene.

[00150] In some embodiments of the methods and systems herein disclosed wherein the organic molecule is a compound of Formula (VI), in which $R_{19} = R_{20} = R_{21} = H$, $R_{22} =$ phenyl, activation through epoxidation can be performed by reacting the substrate with oxygenases var1, CYP1A2 (SEQ ID NO; 13), CYP102A1var9 (SEQ ID NO; 51) or CYP102A1var9-1 (SEQ ID NO; 52), resulting in the introduction of an epoxide functional group at the target site as in the case of styrene.

[00151] In some embodiments of the methods and systems herein disclosed wherein the organic molecule is a compound of Formula (VI), in which $R_{19} = R_{21} = H$, R_{21} and R_{22} are connected together through 4 methylene units so to form a 6-membered ring, activation through epoxidation can be performed by reacting the substrate with oxygenases of CYP153 family, such as CYP153A6 (SEQ ID NO; 54), CYP153A7 (SEQ ID NO; 55), CYP153A8

(SEQ ID NO; 56), CYP153A11 (SEQ ID NO; 57), CYP153D2 (SEQ ID NO; 58), resulting in the introduction of an epoxide functional group at the target site as in the case of cyclohexene.

[00152] In some embodiments of the methods and systems herein disclosed wherein the organic molecule is a compound of Formula (VI), in which $R_{20} = R_{21} = H$, $R_{19} = n$ -pentyl, $R_{22} = C_{10}$ -alkenyl, activation through epoxidation can be performed by reacting the substrate with oxygenases CYP102A1 (SEQ ID NO; 2), resulting in the introduction of an epoxide functional group at the target site as in the case of linolenic acid.

[00153] In some embodiments of the methods and systems herein disclosed wherein the organic molecule is a compound of Formula (VI), in which $R_{19} = R_{21} = H$, R_{20} and R_{22} are linked together to form a 6-membered substituted or non-substituted aromatic ring, activation can be performed by reacting the substrate with toluene dioxygenase, resulting in the introduction of an oxygen-containing functional group in the form of a vicinal diol. In those embodiments, the oxygen-containing functional group will have the form of an epoxy group ($C(O)=C$), that is an oxygen atom joined by single bonds to two adjacent carbon atoms so to form a three-membered ring.

[00154] In some embodiments, the oxidating agent suitable to activate an organic molecule including a target site with the methods and systems herein disclosed can be identified by (a) providing the organic molecule, (b) providing an oxydizing agent, (c) contacting the oxydizing agent with the organic molecule for a time and under condition to allow the introduction of an oxygen-containing functional group on the target site; (d) detecting the oxygen-containing functional group on the target site of the organic molecule resulting from step c), and repeating steps (a) to (d) until an oxygen containing functional group is detected on the target site. In particular, one or more oxidating agents can be provided under step b) of the method herein disclosed.

[00155] In particular, in embodiments wherein the organic molecule is a molecule of formula (I), (II), (III), and (IV), detecting the oxygen-containing functional group on the target site can be performed by: e) isolating of the organic molecule resulting from step c), for example by a separation method or a combination of separation methods, including but not limited to extraction, chromatography, distillation, precipitation, sublimation, and

crystallization; and f) characterizing the isolated organic molecule resulting from step c) to identify the oxygen containing functional group, for example by a characterization method or a combination of methods, including but not limited to spectroscopic or spectrometric technique, preferably a combination of two or more spectroscopic or spectrometric techniques, including UV-VIS spectroscopy, fluorescence spectroscopy, IR spectroscopy, ^1H -NMR, ^{13}C -NMR, 2D-NMR, 3D-NMR, GC-MS, LC-MS, and MS-MS.

[00156] In particular, in embodiments wherein the organic molecule is a molecule of formula (V), detecting the oxygen-containing functional group on the target site can be performed by monitoring the removal of the $-\text{CHR}_{17}\text{R}_{18}$ moiety associated with the introduction of an oxygen containing functional group in the target site. In those embodiments, monitoring the removal of the $-\text{CHR}_{17}\text{R}_{18}$ moiety, can be performed by g) contacting the organic molecule resulting from step c) with a reagent that can react with an aldehyde ($\text{R}-\text{CHO}$), a ketone ($\text{R}-\text{C}(\text{O})-\text{R}$), a dicarbonyl ($\text{R}-\text{C}(\text{O})-\text{C}(\text{O})-\text{R}$), or a glyoxal ($\text{R}-\text{C}(\text{O})-\text{CHO}$) functional group; and h) detecting the formation of an adduct or a complex between an aldehyde, ketone, dicarbonyl, or glyoxal in the organic molecule, the aldehyde, ketone, dicarbonyl, or glyoxal resulting from the removal of the $-\text{CHR}_4\text{R}_5$ moiety.

[00157] Detecting the formation of an adduct or complex can be performed by spectroscopic (colorimetric, fluorimetric) or chromatographic methods and additional methods identifiable by a skilled person upon reading of the present disclosure.

[00158] Reagents that can react with an aldehyde, ketone, dicarbonyl, or glyoxal and suitable for the methods and systems described herein include but are not limited to 4-amino-3-hydrazino-5-mercapto-1,2,4-triazole-4-amino-5-hydrazino-1,2,4-triazole-3-thiol (Purpald), (pentafluorobenzyl)-hydroxylamine, *p*-nitrophenyl-hydrazine, 2,4-dinitrophenyl-hydrazine, 3-methylbenzothiazolin-2-one hydrazone, diethyl acetonedicarboxylate and ammonia, cyclohexane-1,3-dione and ammonia, *m*-phenylenediamine, *p*-aminophenol, 3,5-diaminobenzoic acid, *p*-dimethylamino-aniline, *m*-dinitrobenzene, *o*-phenylenediamine, and the like.

[00159] In some embodiments, a plurality of oxidating agents can be provided to identify a suitable oxidating agent in the methods and systems herein disclosed. In particular, in some of those embodiments wherein the organic molecule is an organic molecule of

general formula (I), (II), (III), (IV) and (V) a pool of oxydizing agents, for example a library of engineered P450s, e.g. in a 96-well plate, can be provided. In particular, in embodiments wherein the organic molecule is an organic molecule of general formula (I), (II), (III) and (IV), isolating the organic molecule resulting from step c) can be performed by extracting the reaction mixture with organic solvent and characterizing the oxygen containing functional group in the organic molecule can be performed by GC analysis of the extraction solution. In some of those embodiments, selected mixtures of oxydizing agent; and co-reagents (e.g. cofactors, oxygen) which gave rise to the largest amount of activated products for a given organic molecule, can be repeated at a larger scale. The activated products can be subsequently isolated by suitable technique including liquid chromatography and identified by ^1H -, ^{13}C -NMR, and MS and additional techniques identifiable by a skilled person. Examples of those embodiments is provided in the Examples section and illustrated in Figures 5 and 6.

[00160] In embodiments wherein the organic molecule is an organic molecule of general formula (V) wherein R_1 is 2-methyl-5-phenyl-4,5-dihydrooxazolyl and $\text{R}_2=\text{R}_3=\text{R}_4=\text{R}_5=\text{H}$, upon contacting a library of engineered P450 monooxygenases (oxydizing agents) the oxygen containing functional group can be detected using colorimetric reagent (e.g. Purpald) and measuring the change in absorbance (e.g. at 550 nm on a microtiter plate reader). In embodiments wherein the organic molecule is an organic molecule of general formula (V) wherein R_1 is 2,3,4,5-tetramethoxytetrahydro-2H-pyranyl and $\text{R}_2=\text{R}_3=\text{R}_4=\text{R}_5=\text{H}$ upon contacting a library of engineered P450 monooxygenases, the oxygen containing functional group can also using colorimetric reagent (e.g. Purpald) and measuring the change in absorbance (e.g. at 550 nm on a microtiter plate reader).

[00161] In some embodiments, the isolated and characterized organic molecule that includes the oxygen-containing functional group at the target site can be used as authentic standard for high-throughput screening of other, more suitable oxydizing agents, or improvement of reaction conditions for the activation reaction. In exemplary embodiments, high-throughput screening can be carried out performing the activation reaction in a multi-well plate, typically a 96-well or 384-well plate, each well containing the candidate organic molecule, the oxydizing agent, and the co-reagents (e.g. cofactors, oxygen) required for the reaction to proceed, and detecting the activation of the target site using one of the following techniques, UV-VIS spectroscopy, fluorimetry, IR, LC, GC, GC-MS, LC-MS, or a

combination thereof, according to the nature and properties of the candidate organic molecule and the activated product.

[00162] In some embodiments, an oxygenase that oxidizes a pre-determined organic molecule in a target site is provided by (i) providing a candidate oxygenase, (j) mutating the candidate oxygenase to generate a mutant or variant oxygenase, (k) contacting the variant oxygenase with the pre-determined organic molecule for a time and under condition to allow detection of an oxygen containing functional group on the target site, (l) detecting the introduction of the oxygen containing functional group on the target site and repeating steps (i) to (l) until formation of an oxygen containing functional group is detected.

[00163] In some embodiments, mutating the candidate oxygenase can be performed by laboratory evolutionary methods and/or rational design methods, using one or a combination of techniques such as random mutagenesis, site-saturation mutagenesis, site-directed mutagenesis, DNA shuffling, DNA recombination, and additional techniques identifiable by a skilled person. In particular, mutating a candidate oxygenase can be performed by targeting one or more of the amino acid residues comprised in the oxygenase's nucleotidic or amino acidic primary sequence to provide a mutant or variant polynucleotide or polypeptide.

[00164] In general, the term "mutant" or "variant" as used herein with reference to a molecule such as polynucleotide or polypeptide, indicates that has been mutated from the molecule as it exists in nature. In particular, the term "mutate" and "mutation" as used herein indicates any modification of a nucleic acid and/or polypeptide which results in an altered nucleic acid or polypeptide. Mutations include any process or mechanism resulting in a mutant protein, enzyme, polynucleotide, gene, or cell. This includes any mutation in which a polynucleotide or polypeptide sequence is altered, as well as any detectable change in a cell wherein the mutant polynucleotide or polypeptide is expressed arising from such a mutation. Typically, a mutation occurs in a polynucleotide or gene sequence, by point mutations, deletions, or insertions of single or multiple nucleotide residues. A mutation in a polynucleotide includes mutations arising within a protein-encoding region of a gene as well as mutations in regions outside of a protein-encoding sequence, such as; but not limited to, regulatory or promoter sequences. A mutation in a coding polynucleotide such as a gene can be "silent", i.e., not reflected in an amino acid alteration upon expression, leading to a "sequence-conservative" variant of the gene. A mutation in a polypeptide includes but is not

limited to mutation in the polypeptide sequence and mutation resulting in a modified amino acid. Non-limiting examples of a modified amino acid include a glycosylated amino acid, a sulfated amino acid, a prenylated (e.g., farnesylated, geranylgeranylated) amino acid, an acetylated amino acid, an acylated amino acid, a PEGylated amino acid, a biotinylated amino acid, a carboxylated amino acid, a phosphorylated amino acid, and the like. References adequate to guide one of skill in the modification of amino acids are replete throughout the literature. Example protocols are found in Walker (1998) Protein Protocols on CD-ROM (Humana Press, Towata, N.J.).

[00165] A mutant or engineered protein or enzyme is usually, although not necessarily, expressed from a mutant polynucleotide or gene. Engineered cells can be obtained by introduction of an engineered gene or part of it in the cell. The terms "engineered cell", "mutant cell" or "recombinant cell" as used herein refer to a cell that has been altered or derived, or is in some way different or changed, from a parent cell, including a wild-type cell. The term "recombinant" as used herein with reference to a cell in alternative to "wild-type" or "native", indicates a cell that has been engineered to modify the genotype and/or the phenotype of the cell as found in nature, e.g., by modifying the polynucleotides and/or polypeptides expressed in the cell as it exists in nature. A "wild-type cell" refers instead to a cell which has not been engineered and displays the genotype and phenotype of said cell as found in nature.

[00166] The term "engineer" refers to any manipulation of a molecule or cell that result in a detectable change in the molecule or cell, wherein the manipulation includes but is not limited to inserting a polynucleotide and/or polypeptide heterologous to the cell and mutating a polynucleotide and/or polypeptide native to the cell. Engineered cells can also be obtained by modification of the cell's genetic material, lipid distribution, or protein content. In addition to recombinant production, the enzymes may be produced by direct peptide synthesis using solid-phase techniques, such as Solid-Phase Peptide Synthesis. Peptide synthesis may be performed using manual techniques or by automation. Automated synthesis may be achieved, for example, using Applied Biosystems 431A Peptide Synthesizer (Perkin Elmer, Foster City, Calif.) in accordance with the instructions provided by the manufacturer.

[00167] Variants of naturally-occurring sequences can be generated by site-directed mutagenesis (Botstein and Shortle 1985; Smith 1985; Carter 1986; Dale and Felix 1996; Ling

and Robinson 1997), mutagenesis using uracil containing templates (Kunkel, Roberts et al. 1987; Bass, Sorrells et al. 1988), oligonucleotide-directed mutagenesis (Zoller and Smith 1983; Zoller and Smith 1987; Zoller 1992), phosphorothioate-modified DNA mutagenesis (Taylor, Schmidt et al. 1985; Nakamaye and Eckstein 1986; Sayers, Schmidt et al. 1988), mutagenesis using gapped duplex DNA (Kramer, Drutsa et al. 1984; Kramer and Fritz 1987), point mismatch, mutagenesis using repair-deficient host strains, deletion mutagenesis (Eghtedarzadeh and Henikoff 1986), restriction-selection and restriction-purification (Braxton and Wells 1991), mutagenesis by total gene synthesis (Nambiar, Stackhouse et al. 1984; Grundstrom, Zenke et al. 1985; Wells, Vasser et al. 1985)], double-strand break repair (Mandecki 1986), and the like. Additional details on many of the above methods can be found in *Methods in Enzymology* Volume 154, which also describes useful controls for trouble-shooting problems with various mutagenesis methods.

[00168] Additional details regarding the methods to generate variants of naturally-occurring sequences can be found in the following U.S. patents, PCT publications, and EPO publications: U.S. Pat. No. 5,605,793 to Stemmer (Feb. 25, 1997), "Methods for In vitro Recombination;" U.S. Pat. No. 5,811,238 to Stemmer et al. (Sep. 22, 1998) "Methods for Generating Polynucleotides having Desired Characteristics by Iterative Selection and Recombination;" U.S. Pat. No. 5,830,721 to Stemmer et al. (Nov. 3, 1998), "DNA Mutagenesis by Random Fragmentation and Reassembly;" U.S. Pat. No. 5,834,252 to Stemmer, et al. (Nov. 10, 1998) "End-Complementary Polymerase Reaction;" U.S. Pat. No. 5,837,458 to Minshull, et al. (Nov. 17, 1998), "Methods and Compositions for Cellular and Metabolic Engineering;" WO 95/22625, Stemmer and Cramer, "Mutagenesis by Random Fragmentation and Reassembly;" WO 96/33207 by Stemmer and Lipschutz "End Complementary Polymerase Chain Reaction;" WO 97/20078 by Stemmer and Cramer "Methods for Generating Polynucleotides having Desired Characteristics by Iterative Selection and Recombination;" WO 97/35966 by Minshull and Stemmer, "Methods and Compositions for Cellular and Metabolic Engineering;" WO 99/41402 by Punnonen et al. "Targeting of Genetic Vaccine Vectors;" WO 99/41383 by Punnonen et al. "Antigen Library Immunization;" WO 99/41369 by Punnonen et al. "Genetic Vaccine Vector Engineering;" WO 99/41368 by Punnonen et al. "Optimization of Immunomodulatory Properties of Genetic Vaccines;" EP 752008 by Stemmer and Cramer, "DNA Mutagenesis by Random Fragmentation and Reassembly;" EP 0932670 by Stemmer "Evolving Cellular DNA Uptake

by Recursive Sequence Recombination;" WO 99/23107 by Stemmer et al., "Modification of Virus Tropism and Host Range by Viral Genome Shuffling;" WO 99/21979 by Apt et al., "Human Papillomavirus Vectors;" WO 98/31837 by del Cardayre et al. "Evolution of Whole Cells and Organisms by Recursive Sequence Recombination;" WO 98/27230 by Patten and Stemmer, "Methods and Compositions for Polypeptide Engineering;" WO 98/13487 by Stemmer et al., "Methods for Optimization of Gene Therapy by Recursive Sequence Shuffling and Selection;" WO 00/00632, "Methods for Generating Highly Diverse Libraries;" WO 00/09679, "Methods for Obtaining in vitro Recombined Polynucleotide Sequence Banks and Resulting Sequences;" WO 98/42832 by Arnold et al., "Recombination of Polynucleotide Sequences Using Random or Defined Primers;" WO 99/29902 by Arnold et al., "Method for Creating Polynucleotide and Polypeptide Sequences;" WO 98/41653 by Vind, "An in vitro Method for Construction of a DNA Library;" WO 98/41622 by Borchert et al., "Method for Constructing a Library Using DNA Shuffling;" WO 98/42727 by Pati and Zarling, "Sequence Alterations using Homologous Recombination;" WO 00/18906 by Patten et al., "Shuffling of Codon-Altered Genes;" WO 00/04190 by del Cardayre et al. "Evolution of Whole Cells and Organisms by Recursive Recombination;" WO 00/42561 by Crameri et al., "Oligonucleotide Mediated Nucleic Acid Recombination;" WO 00/42559 by Selifonov and Stemmer "Methods of Populating Data Structures for Use in Evolutionary Simulations;" WO 00/42560 by Selifonov et al., "Methods for Making Character Strings, Polynucleotides & Polypeptides Having Desired Characteristics;" WO 01/23401 by Welch et al., "Use of Codon-Varied Oligonucleotide Synthesis for Synthetic Shuffling;" and WO 01/64864 "Single-Stranded Nucleic Acid Template-Mediated Recombination and Nucleic Acid Fragment Isolation" by Affholter.

[00169] In particular, in some embodiments, site-directed mutagenesis can be performed on predetermined residues of the oxygenase. These predetermined sites can be identified using the crystal structure of said oxydizing agent if available or a crystal structure of a homologous protein that shares at least 20% sequence identity with said oxydizing agent and an alignment of the polynucleotide or amino acid sequences of the oxydizing agent and its homologous protein. The predetermined sites are chosen among the amino acid residues that are found within 50 Å, preferably within 35 Å from the oxygen-activating site of said oxydizing agent. For example, when a cytochrome P450 monooxygenase is to be used as the oxydizing agent, the predetermined site are chosen among the amino acid residues that are

found within 50 Å, preferably within 35 Å from the heme iron. Mutagenesis of the predetermined sites can be performed changing one, two or three of the nucleotides in the codon that encodes for each of the predetermined amino acids. Mutagenesis of the predetermined sites can be performed in the described way so that each of the predetermined amino acid is mutated to any of the other 19 natural amino acids. Substitution of the predetermined sites with unnatural amino acids can be performed using methods established *in vivo* (Wang, Xie et al. 2006), *in vitro* (Shimizu, Kuruma et al. 2006), semisynthetic (Schwarzer and Cole 2005) or synthetic methods (Camarero and Mitchell 2005) for incorporation of unnatural amino acids into polypeptides.

[00170] In still further embodiments, libraries of engineered variants can be obtained by laboratory evolutionary methods and/or rational design methods, using one or a combination of techniques such as random mutagenesis, site-saturation mutagenesis, site-directed mutagenesis, DNA shuffling, DNA recombination, and the like and targeting one or more of the amino acid residues, one at a time or simultaneously, comprised in the oxidizing agent's amino acid sequence. Said libraries can be arrayed on multi-well plates and screened for activity on the target molecule using a colorimetric, fluorimetric, enzymatic, or luminescence assay and the like. For example a method for making libraries for directed evolution to obtain P450s with new or altered properties is recombination, or chimeragenesis, in which portions of homologous P450s are swapped to form functional chimeras, can be used. Recombining equivalent segments of homologous proteins generates variants in which every amino acid substitution has already proven to be successful in one of the parents. Therefore, the amino acid mutations made in this way are less disruptive, on average, than random mutations. A structure-based algorithm, such as SCHEMA, can be used to identify fragments of proteins that can be recombined to minimize disruptive interactions that would prevent the protein from folding into its active form.

[00171] In some embodiments, activation of a target site in an organic molecule can be performed in a whole-cell system. To prepare the whole-cell system, the encoding sequence of the oxidizing agent can be introduced into a host cell using a suitable vector, such as a plasmid, a cosmid, a phage, a virus, a bacterial artificial chromosome (BAC), a yeast artificial chromosome (YAC), or the like, into which the said sequence of the disclosure has been inserted, in a forward or reverse orientation. In some embodiments, the construct further comprises regulatory sequences, including, for example, a promoter linked to the sequence.

Large numbers of suitable vectors and promoters are known to those of skill in the art, and are commercially available.

[00172] Accordingly, in other embodiments, vectors that include a nucleic acid molecule of the disclosure are provided. In other embodiments, host cells transfected with a nucleic acid molecule of the disclosure, or a vector that includes a nucleic acid molecule of the disclosure, are provided. Host cells include eucaryotic cells such as yeast cells, insect cells, or animal cells. Host cells also include procaryotic cells such as bacterial cells.

[00173] In other embodiments, methods for producing a cell that converts a target molecule into a pre-determined oxygenated derivative are provided. Such methods generally include: (a) transforming a cell with an isolated nucleic acid molecule encoding a polypeptide comprising an amino acid sequence set forth in SEQ ID NO: 2 to SEQ ID NO: 70; (b) transforming a cell with an isolated nucleic acid molecule encoding a polypeptide of the disclosure; or (c) transforming a cell with an isolated nucleic acid molecule of the disclosure.

[00174] The terms "vector", "vector construct" and "expression vector" as used herein refer to a vehicle by which a DNA or RNA sequence (e.g. a foreign gene) can be introduced into a host cell, so as to transform the host and promote expression (e.g. transcription and translation) of the introduced sequence. Vectors typically comprise the DNA of a transmissible agent, into which foreign DNA encoding a protein is inserted by restriction enzyme technology. A common type of vector is a "plasmid", which generally is a self-contained molecule of double-stranded DNA that can readily accept additional (foreign) DNA and which can readily introduced into a suitable host cell. A large number of vectors, including plasmid and fungal vectors, have been described for replication and/or expression in a variety of eukaryotic and prokaryotic hosts. Non-limiting examples include pKK plasmids (Clontech), pUC plasmids, pET plasmids (Novagen, Inc., Madison, Wis.), pRSET or pREP plasmids (Invitrogen, San Diego, Calif.), or pMAL plasmids (New England Biolabs, Beverly, Mass.), and many appropriate host cells, using methods disclosed or cited herein or otherwise known to those skilled in the relevant art. Recombinant cloning vectors will often include one or more replication systems for cloning or expression, one or more markers for selection in the host, e.g., antibiotic resistance, and one or more expression cassettes.

[00175] The terms "express" and "expression" refers to allowing or causing the information in a gene or DNA sequence to become manifest, for example producing a protein by activating the cellular functions involved in transcription and translation of a corresponding gene or DNA sequence. A DNA sequence is expressed in or by a cell to form an "expression product" such as a protein. The expression product itself, e.g. the resulting protein, may also be said to be "expressed" by the cell. A polynucleotide or polypeptide is expressed recombinantly, for example, when it is expressed or produced in a foreign host cell under the control of a foreign or native promoter, or in a native host cell under the control of a foreign promoter.

[00176] Polynucleotides provided herein can be incorporated into any one of a variety of expression vectors suitable for expressing a polypeptide. Suitable vectors include chromosomal, nonchromosomal and synthetic DNA sequences, e.g., derivatives of SV40; bacterial plasmids; phage DNA; baculovirus; yeast plasmids; vectors derived from combinations of plasmids and phage DNA, viral DNA such as vaccinia, adenovirus, fowl pox virus, pseudorabies, adenovirus, adeno-associated viruses, retroviruses and many others. Any vector that transduces genetic material into a cell, and, if replication is desired, which is replicable and viable in the relevant host can be used.

[00177] Vectors can be employed to transform an appropriate host to permit the host to express a protein or polypeptide. Examples of appropriate expression hosts include: bacterial cells, such as *E. coli*, *B. subtilis*, *Streptomyces*, and *Salmonella typhimurium*; fungal cells, such as *Saccharomyces cerevisiae*, *Pichia pastoris*, and *Neurospora crassa*; insect cells such as *Drosophila* and *Spodoptera frugiperda*; mammalian cells such as CHO, COS, BHK, HEK 293 or Bowes melanoma; or plant cells or explants, etc.

[00178] In bacterial systems, a number of expression vectors may be selected, depending upon the use intended for the oxydizing polypeptide. For example, such vectors include, but are not limited to, multifunctional *E. coli* cloning and expression vectors such as BLUESCRIPT (Stratagene), in which the oxydizing agent-encoding sequence may be ligated into the vector in-frame with sequences for the amino-terminal Met and the subsequent 7 residues of beta-galactosidase so that a hybrid protein is produced; pIN vectors; pET vectors; and the like.

[00179] Similarly, in the yeast *Saccharomyces cerevisiae* a number of vectors containing constitutive or inducible promoters such as alpha factor, alcohol oxidase and PGH may be used for production of the oxydizing agent.

[00180] In some embodiments, the activation of the target site in an organic molecule by an oxidating agent can be performed using an immobilized oxydizing agent. Immobilization of the oxydizing agent can be carried out through covalent attachment or physical adsorption to a support, entrapment in a matrix, encapsulation, cross-linking of oxydizing agent's crystals or aggregates and the like. Several immobilization techniques are known (Bornscheuer 2003; Cao 2005). The type of immobilization and matrix that preserves activity often depends on the nature and physical-chemical properties of the oxydizing agent.

[00181] In any of the above mentioned embodiments, the oxygen-containing functional group introduced on a target site of any of the above molecules is then replaced by fluorine.

[00182] In some embodiments, the fluorination is performed by deoxofluorination of the oxygenated organic molecule.

[00183] The terms "deoxofluorination" and "deoxofluorination reaction" as used herein refer to a chemical reaction where an oxygen-containing chemical unit is replaced with fluorine. Accordingly, the terms "deoxofluorinating agent", "deoxofluorinating agent", and "deoxofluorination agent" as used herein refer to a chemical agent that is able to carry out a deoxofluorination reaction. The term "reagent" as used herein is equivalent to the term "agent".

[00184] In some embodiments, the fluorination can be performed by ring-opening fluorination of the oxygenated organic molecule.

[00185] The terms "ring-opening fluorination" and "ring-opening fluorination reaction" as used herein refer to a chemical reaction where an epoxide is reacted with a nucleophile, specifically fluoride (F^-) to afford a fluorohydrin ($-CFR_1-C(OH)R_2-$) or a vicinal difluoride ($-CR_1F-CR_2F-$) containing derivative. Accordingly, the terms "ring-opening fluorination agent" and "ring-opening fluorinating agent" as used herein refer to a chemical agent that is able to carry out a ring-opening fluorination reaction.

[00186] In particular, the deoxofluorination reaction can be performed using commercially available, deoxofluorinating agents such as sulfur tetrachloride (SF_4), DAST (diethylaminosulfur trifluoride, (Middleton 1975), U.S. Patent 3,914,265; U.S. Patent 3,976,691), Deoxo-Fluor (*bis*-(2-methoxyethyl)-aminosulfur trifluoride, (Lal, Pez et al. 1999), U.S. Patent 6,222,064), DFI (2,2-difluoro-1,3-dimethylimidazolidine, (Hayashi, Sonoda et al. 2002), U.S. Patent 6,632,949), or analogues and derivatives thereof. Other deoxofluorinating agents include XeF_2 , SiF_4 , and SeF_4 . The deoxofluorination reaction can be performed in the presence or in the absence of additional chemical agents that facilitate or enable the deoxofluorination to occur. These additional agents include but are not limited to hydrogen fluoride (HF), Lewis acids, fluoride salts (e.g. CsF, KF, NaF, LiF, BF_3), crown-ethers, ionic liquids and the like.

[00187] In particular, the ring-opening fluorination reaction can be performed using nucleophilic fluoride-containing agents including without limitations metal fluorides (e.g. CsF, KF, NaF, LiF, AgF, BF_3), potassium hydrogen difluoride (KHF_2), $\text{Bu}_4\text{NH}_2\text{F}_3$, $\text{R}_3\text{N}\cdot\text{nHF}$, $\text{Bu}_4\text{NF}\cdot\text{nHF}$, Py-9 HF (Olah's reagent), and the like. The ring-opening fluorination reaction can be performed in the presence or in the absence of additional chemical agents that facilitate or enable the deoxofluorination to occur. These additional agents include but are not limited to hydrogen fluoride (HF), Lewis acids, fluoride salts (e.g. CsF, KF, NaF, LiF), crown-ethers, ionic liquids and the like

[00188] Exemplary fluorinations of an organic molecule containing an oxygen-containing group include but are not limited to conversion of a hydroxyl group to a fluoride, a carboxylic acid group to a carbonyl fluoride, an aldehyde group to a *gem*-difluoride, a keto group to a *gem*-difluoride, an epoxide group to a fluorohydrin (also called *vic*-fluoro-alcohol), an epoxide group to a *vic*-difluoride.

[00189] Exemplary products produced by methods and systems herein disclosed comprise fluorinated derivatives of organic molecules which include 2-aryl-acetate esters, dihydrojasnone, menthofuran, guaïol, permethylated mannopyranoside, methyl 2-(4'-(2''-methylpropyl)phenyl)propanoate and a 5-phenyl-2-oxazoline.

[00190] Specifically, the methods and systems herein disclosed have been applied to produce methyl 2-fluoro-2-phenylacetate, ethyl 2-fluoro-2-phenylacetate, propyl 2-(3-

chlorophenyl)-2-fluoroacetate, propyl 2-fluoro-*o*-tolylacetate, and propyl 2-fluoro-*p*-tolylacetate starting from corresponding 2-aryl-acetate esters; 4-fluoro-3-methyl-2-pentylcyclopent-2-enone, 4,4-difluoro-3-methyl-2-pentylcyclopent-2-enone, and 3-(fluoromethyl)-2-pentylcyclopent-2-enone, starting from dihydrojasnone; methyl 2-(4'-(1''-fluoro-2''-methylpropyl)phenyl)propanoate and methyl 2-(4'-(2''-fluoro-2''-methylpropyl)phenyl)propanoate, starting from methyl 2-(4'-(2''-methylpropyl)phenyl)propanoate; 6-fluoro-menthofuran-2-ol from menthofuran; 2-((3S,5S,8S)-4-fluoro-3,8-dimethyl-1,2,3,4,5,6,7,8-octahydroazulen-5-yl)propan-2-ol from (-)-guaioi; 6-fluoro-6-deoxy-1,2,3,4-tetramethyl-mannopyranoside starting from 1,2,3,4,6-pentamethyl-mannopyranoside; (4R,5S)-4-(fluoromethyl)-2-methyl-5-phenyl-4,5-dihydrooxazole, starting from (4S,5S)-4-(methoxymethyl)-2-methyl-5-phenyl-4,5-dihydrooxazole.

[00191] More specifically, the methods and systems herein disclosed have been applied to fluorinate a target site, namely a C carbon atom, in a highly regioselective manner despite the presence of other similar moieties in the molecule, as in the case of 1,2,3,4,6-pentamethyl-mannopyranoside.

[00192] Even more specifically, the methods and systems herein disclosed have been applied to fluorinate target organic molecules, namely 2-aryl-acetate esters, in a highly stereoselective manner, leading to the formation of the (R)-fluoro enantiomer in considerable excess over the (S)-fluoro enantiomer.

[00193] The above mentioned fluorinated products are or can be associated with a biological activity or can be used for the synthesis of chemical compounds that are or can be associated with a biological activity.

[00194] 2-fluoro-2-phenylacetate derivatives find potential applications in the synthesis of prodrugs, in particular in the preparation of ester-type anticancer prodrugs with different susceptibility to hydrolysis, which can be useful in selective targeting of cancer cells (Yamazaki; Yusa et al. 1996). 2-(4'-(2''-methylpropyl)phenyl)propionate also known as ibuprofen is a marketed drug of the class non-steroidal anti-inflammatory drugs (NSAIDs). This drug has ample application in the treatment of arthritis, primary dysmenorrhoea, fever, and as an analgesic, especially in the presence of inflammation process. Ibuprofen exerts its

analgesic, antipyretic, and anti-inflammatory activity through inhibition of cyclooxygenase (COX-2), thus inhibiting prostaglandin synthesis. More recently, ibuprofen was found to be useful in the prophylaxis of Alzheimer's disease (AD) (Townsend and Pratico 2005). The anti-AD activity of ibuprofen is presumably due to its ability to lower the levels of amyloid-beta (A β) peptides, in particular the longer, highly amyloidogenic isoform A β 42, which are believed to be the central disease-causing agents in Alzheimer's disease (AD). There is therefore a growing interest towards the discovery of A β 42-lowering compounds with improved potency and brain permeability (Leuchtenberger, Beher et al. 2006). Unlike other NSAIDs, ibuprofen was also found to be useful in protection against Parkinson's disease, although the underlying mechanism is not yet known (Casper, Yaparalvi et al. 2000).

[00195] Dihydrojasmonone incorporates a cyclopentenone structural unit. The cyclopentanone and cyclopentenone scaffolds are present in a wide range of important natural products such as jasmonoids, cyclopentanoid antibiotic, and prostaglandins. This type of compound has a broad spectrum of biological activities and important application in medicinal chemistry as well as in the perfume and cosmetic industry, and agriculture. Despite their relatively simple structures, the synthesis of these scaffolds is not trivial (Mikolajczyk, Mikina et al. 1999). Therefore, novel routes for functionalization (and specifically in the context of the disclosure, fluorination) of these scaffolds and compounds incorporating these scaffolds would be highly desirable.

[00196] Guaiol is a sesquiterpene alcohol having the guaiane skeleton, found in many medicinal plants. The essential oils of *Salvia lanigera* and *Helicta longifoliata*, which both contain guaiol as a major component, were found to possess pronounced antibacterial activity (De-Moura, Simionatto et al. 2002). Structural modification of naturally-occurring bioactive substances by conventional chemical methods is very difficult and often not feasible. Accessible methods to produce derivatives of these natural products (and specifically in the context of this disclosure, fluorinated derivatives) would be highly desirable.

[00197] Furans and 2-(5H)-furanones are attractive building blocks being present in a large number of natural products that display a wide range of biological activities, and being present in a number of drugs with biologically relevant properties, such as antifungal, antibacterial and anti-inflammatory activities (Knight 1994; De Souza 2005). Many methods

are available for their synthesis. However, strategies for post-synthetic functionalization (and specifically in the context of the disclosure, fluorination) of these scaffolds and compounds incorporating these scaffolds would be highly desirable.

[00198] Embodiments, wherein methods for selective fluorination of protected hydroxyl groups in the form of $R_1-O-CHR_2R_3$ are performed where the resulting product is R_1-F is expected to expand our current synthetic capabilities and facilitate the synthesis of fluorinated compounds that bear multiple hydroxyl functional groups as well as the synthesis of compounds that incorporate chemical units or structural features that are incompatible with the currently available methods for protection/deprotection of hydroxyl groups (Green and Wuts 1999). The protection of hydroxyl groups with alkyl groups different from methoxymethyl (MOM), tetrahydropyranyl (THP), allyl, and benzyl (Bn) is rarely used in practice, if ever, due to the requirement of harsh chemical reagents and conditions for their removal (e.g. strong Lewis acids in the case of a methoxy group). These chemical reagents are poorly chemoselective, reacting with any nucleophilic group of the molecule. Chemical methods for regioselective substitution, and more specifically fluorination, of a single protected hydroxyl functional group in the presence of multiple identically protected hydroxyl groups are not available.

[00199] In some embodiments, activation and fluorination of the organic molecules can be performed as it follows.

[00200] The activation reaction can be carried out in aqueous solvent containing variable amounts of organic solvents to facilitate dissolution of the organic molecule in the mixture. The co-solvents include but are not limited to alcohols, acetonitrile, dimethyl sulfoxide, dimethylformamide, acetone. The one or more oxidizing agents can be present as free in solution or inside a cell where its expression has been achieved using a plasmid vector or other strategies as described earlier. The reaction can be carried out in batch, semicontinuously or continuously, in air or using devices to flow air or oxygen through the solution, at autogeneous pressure or higher. The reaction temperature will generally be in the range of 0°C and 100°C, depending on the nature and stability of the biocatalysts and substrates, preferably in the range of about 4°C and 30°C. The amount of biocatalyst is generally in the range of about 0.01 mole % to 10 mole %, preferably in the range of about 0.05 mole % to 1 mole %. The cofactor (NADPH) can be added directly, regenerated using

an enzyme-coupled system (typically dehydrogenase-based), or provided by the host cell. Reducing equivalent to the biocatalysts can be provided through the use of an electrode or chemical reagents. Superoxide dismutase, catalase or other reactive oxygen species-scavenging agents, can be used to prevent biocatalyst inactivation and improve the yields of the activation reaction. Glycerol, bovine serum albumine or other stabilizing agents can be used to prevent biocatalyst aggregation and improve the yields of the activation reaction.

[00201] After the activation reaction, the activated products may or may not be isolated through any of the following methods or combination thereof: extraction, distillation, precipitation, sublimation, chromatography, crystallization with optional seeding and/or co-crystallization aids.

[00202] The activated products are then contacted with the fluorinating agent in the presence or the absence of an organic solvent under inert atmosphere. The activated products can be reacted in the form of isolated compound, purified compound, partially-purified mixtures or crude mixtures. No particular restriction is imposed upon the solvent of the reaction as long as the solvent does not react with the fluorination reagent, enzymatic product, or reaction product.

[00203] Solvents that can be used in the fluorination reaction include, but are not restricted to, dichloromethane, pyridine, acetonitrile, chloroform, ethylene dichloride, 1,2-dimethoxyethane, diethylene glycol dimethyl ether, N-methylpyrrolidone, dimethylformamide, and 1,3-dimethyl-2-imidazolidinone, preferably dichloromethane or pyridine. The reaction temperature will generally be in the range of -80°C to 150°C, preferably in the range of about -78°C and 30°C. The amount of the fluorination reagent is preferably 1 equivalent or more for oxygen atom introduced in the molecular scaffold of the organic molecule during the enzymatic reaction. After completion of the reaction, the fluorinated products are isolated through any of the following methods or combination thereof: extraction, distillation, precipitation, sublimation, chromatography, crystallization with optional seeding and/or co-crystallization aids.

[00204] An advantage of the methods and systems is the possibility to perform fluorination of predetermined target sites in a candidate organic molecule. A further advantage is that subjecting the activated product or the fluorinated derivative to the action of

the same oxydizing agent used for its preparation or another oxydizing agent, polyfluorination of the molecule, at the same or another predetermined target site can be achieved. A further advantage is that the mono- and/or poly fluorination of predetermined target sites in a candidate organic molecule can be carried out under mild conditions (room temperature and pressure), with limited use of hazardous chemical and toxic solvents, in a chemoselective, regioselective, and stereoselective manner.

[00205] An additional advantage of the methods and systems herein disclosed is the possibility to carry out fluorination of nonreactive sites of a candidate organic molecule, that is sites that would could not be easily functionalized using chemical reagents or would react only after or concurrently to other, more reactive sites of the molecule.

[00206] A further advantage of the methods and systems herein disclosed is the possibility to produce fluorinated derivatives of candidate organic molecules with an established or potentially relevant biological activity in only two steps. This "post-synthetic" transformation represents a considerable advantage compared to synthesis of the same derivative or derivatives starting from fluorine-containing building blocks which may or may not be available, thus requiring numerous additional synthetic steps. For example, the described methyl 2-(4'-(1''-fluoro-2''-methylpropyl)phenyl)propanoate, methyl 2-(4'-(2''-fluoro-2''-methylpropyl)phenyl)propanoate, and methyl 2-(4'-(1'',1''-difluoro-2''-methylpropyl)phenyl)propanoate prepared according to the methods and systems herein disclosed could be conceivably synthesized using (1-fluoro-2-methylpropyl)benzyl, (2-fluoro-2-methylpropyl)benzyl, (1,1-difluoro-2-methylpropyl)benzyl derivatives, which however are not commercially available and therefore need to be prepared from raw material through several chemical steps.

[00207] A further advantage of the methods and systems herein disclosed is the possibility to produce fluorinated derivatives of a candidate organic molecule at a preparative scale, obtaining from a minimum of 10 up to hundreds milligrams of the final fluorinated product with overall yields (after isolation) of up to 80%. These quantities and yields enable the evaluation of the biological, pharmacological, and pharmacokinetic properties of said products as well as their use in further synthesis of more complex molecules.

[00208] An additional advantage of the methods and systems herein disclosed is the possibility to substitute protected hydroxyl groups in the form of $R_1-O-CH(R_2)R_3$ for fluorine. A further advantage is that the substitution of protected hydroxyl group for fluorine can be carried out under mild conditions (room temperature and pressure), with limited use of hazardous chemical and toxic solvents, in a chemoselective and regioselective manner.

[00209] Classes of molecules that can be potentially obtained using the methods and systems herein disclosed include but are not limited to α -fluoro acid derivatives, fluoro-alkyl derivatives, fluoro-allyl derivatives, fluorohydrins, *vic*- and *gem*-difluoride derivatives.

[00210] Classes of molecules that can be potentially obtained in enantiopure form using the methods and systems herein disclosed include but are not limited to α -fluoro acid derivatives, fluoro-alkyl derivatives, fluoro-allyl derivatives, and fluorohydrins.

[00211] In general, the methods and systems herein disclosed, in contrast to previously known synthetic methods, provide a simple, environmentally benign, two-step procedure for regio- and stereospecific incorporation of fluorine in a wide variety of organic compounds both at reactive and non-reactive sites of their molecular scaffold. Particularly, it will be appreciated that methods and systems herein disclosed procedure gives access to organofluorine derivatives, whose preparation through alternative routes would require many more synthetic steps and much higher amounts of toxic reagents and organic solvents.

[00212] Accordingly, the methods and systems herein disclosed have utility in the field of organic chemistry for preparation of fluorinated building blocks and in medicinal chemistry for the preparation or discovery of fluorinated derivatives of drugs, drug-like molecules, drug precursors, and chemical building blocks with altered or improved physical, chemical, pharmacokinetic, or pharmacological properties.

[00213] In particular, in some embodiment of the methods and systems herein disclosed, the organic molecules are pre-selected among molecules of interest, such as drugs, drug precursors, lead compounds, and synthetic building blocks. The term "drug" as used herein refer to a synthetic or non-synthetic chemical entity with established biological and/or pharmacological activity, which is used to treat a disease, cure a disfunction, or alter in some way a physiological or non-physiological function of a living organism. Lists of drugs can be easily found in online databases such as www.accessdata.fda.gov, www.drugs.com,

www.rxlist.com, and the like. The term "drug precursor" as used herein refers to a synthetic or non-synthetic chemical entity which can be converted into a drug through a chemical or biochemical transformation. The conversion of a drug precursor into a drug can also occur after administration, in which case the drug precursor is typically referred to as "prodrug". Accordingly, any synthetic or semi-synthetic intermediate in the preparation of a drug can be considered a drug precursor. The term "lead compound" as used herein refers to a synthetic or non-synthetic chemical entity that has pharmacological or biological activity and whose chemical structure is used as a starting point for chemical modifications in order to improve potency, selectivity, or pharmacokinetic parameters. Lead compounds are often found in high-throughput screenings ("hits") or are secondary metabolites from natural sources. Reports on the discovery and/or identification of lead compounds for various applications are widespread in the scientific literature and in particular in specialized journals such as *Journal of medicinal chemistry*, *Bioorganic & medicinal chemistry*, *Current medicinal chemistry*, *Current topics in medicinal chemistry*, *European Journal of Medicinal Chemistry*, *Mini reviews in medicinal chemistry*, and the like. The term "synthetic building blocks" as used herein refer to any synthetic or non-synthetic chemical entity that is used for the preparation of a structurally more complex molecule.

[00214] Upon fluorination of the target site of the pre-selected molecule, the fluorinated organic molecules produced can be further used in the synthesis of more complex molecules, or, in addition, or in alternative, being tested for biological activities.

[00215] In particular, in any embodiment, wherein identification of a an organic molecule having a predetermined biological activity is desired, the methods and systems herein disclosed further comprise testing the fluorinated organic molecule for the desired biological activity. Testing can in particular be performed by screening the products of the reaction by the methods and systems illustrated in [Figure 4](#) in form of mixture or as isolated compound for altered or improved metabolic stability, biological activity, pharmacological potency, and pharmacokinetic properties.

[00216] The wording "biological activity" as used herein refers to any activity that can affect the status of a biological molecule or biological entity. A biological molecule can be a protein or a polynucleotide. A biological entity can be a cell, an organ, or a living organism.

The wording "pharmacological activity" as used herein refers to any activity that can affect and, generally but not necessarily, improve the status of a living organism.

[00217] In embodiments where identification of a molecule having pharmacological activity is desired, use of P450 as oxydizing agents is particularly preferred, since Phase I drug metabolism in humans is mainly dependent on P450s. In this connection, one clear advantage of the methods and systems herein disclosed is that they allow for protection through fluorination of sites in the molecule that are sensitive to P450 hydroxylation attack.

[00218] A further advantage of the methods and systems herein described for the identification of a molecule having biological activity compared to corresponding strategies known in the art for producing fluorinated drugs (which mainly rely on the use of fluorinated building blocks), is that the methods herein disclosed can be carried out post-synthetically. As a consequence, the method herein disclosed can be broadly applied to produce oxygenated/fluorinated derivatives starting from marketed drugs, drugs in advanced testing phase, lead compounds, or screening hits.

[00219] Additionally, a pre-selection of organic molecules of interest and/or related fluorinated products can be made on the basis of the ability of fluorine atoms to improve dramatically the pharmacological profile of drugs. In particular, this can be done in view of several studies have shown that potent drugs can be obtained through fluorination of much less active precursors. Anticholesterolemic Ezetimib (Clader 2004), anticancer CF₃-taxanes (Ojima 2004), fluoro-steroids, and antibacterial fluoroquinolones are only some representative examples. The improved pharmacological properties of fluoro-containing drugs are due mainly to enhanced metabolic stability (Park, Kitteringham et al. 2001). Primary metabolism of drugs in humans generally occurs through P450-dependent systems, and the introduction of fluorine atoms at or near the sites of metabolic attack has often proven successful in increasing the half-life of a compound (Bohm, Banner et al. 2004).

[00220] In some cases, the introduction of fluorine substituents leads to improvements in the pharmacological properties as a result of enhanced binding affinity of the molecule to biological receptors. Examples of the effect of fluorine on binding affinity are provided by recent results in the preparation of NK1 antagonists (Swain and Rupniak 1999), 5HT_{1D} agonists (van Niel, Collins et al. 1999), and PTB1B antagonists (Burke, Ye et al. 1996).

[00221] Accordingly, with the methods and system herein disclosed production of various oxygenated/fluorinated products was expected starting from a given drug or a drug-like molecule, for example a 'lead' compound identified in a drug-discovery program.

[00222] In an embodiment of the methods and systems, an array of oxygenases (P450 monooxygenases, non-heme iron monooxygenases, dioxygenases and peroxygenases) can be used to produce various mono- and poly-oxygenated compounds. Some of these products can be isolated and subjected to fluorination, e.g. deoxo-fluorination, where all or a subset of the introduced oxygen-containing functional groups are substituted for fluorine. The resulting products can then be separated and tested for improved biological properties.

EXAMPLES

[00223] The present disclosure is further illustrated in the following examples, which are provided by way of illustration and are not intended to be limiting.

[00224] The following experiments have been carried out to perform chemo-enzymatic fluorination approach according to embodiments of the methods and systems herein disclosed.

[00225] First, a set of organic molecules has been selected, from which potentially useful fluorinated products can be obtained.

[00226] These compounds include: (a) 2-aryl acetic acid derivatives, as demonstrative examples of useful synthetic blocks, for example in the preparation of prodrugs with different susceptibility to hydrolysis. With the systems and methods herein described, stereoselective fluorination of the alpha position of these target molecules was achieved, affording 2-fluoro-2-aryl acetic acid derivatives in considerable enantiomeric excess; (b) ibuprofen methyl ester, as demonstrative example of a marketed drug, of which more potent and BBB(blood-brain-barrier)-penetrating derivatives are sought after for treatment of Alzheimer's and Parkinson's diseases. With the systems and methods herein described, regioselective fluorination of weakly reactive sites of this target molecule was achieved, affording various C—F derivatives; (c) dihydrojasnone, menthofuran, and guaicol, as demonstrative examples of various molecular scaffolds that are present in several natural, synthetic, and semisynthetic biologically active molecules. With the systems and methods herein described, regioselective

fluorination of weakly reactive sites of these target molecules was achieved, affording various C—F derivatives; (d) dihydro-4-methoxymethyl-2-methyl-5-phenyl-2-oxazoline, as demonstrative example for chemoselective substitution of methoxygroup for fluorine. With the systems and methods herein described, fluorination of the methoxy protected group in the target molecules was achieved, affording a demethoxy-fluoro derivative; (e) permethylated mannopyranoside as demonstrative example for regioselective substitution of a specific methoxy group for fluorine in the presence of several other identical groups in the molecule. With the systems and methods herein described, regioselective fluorination of the methoxy protected group in position 6 of the target molecule was achieved, affording a 6-demethoxy-fluoro derivative.

[00227] A pool of oxydizing agents, comprising wild-type P450_{BM3} (CYP102A1), variants of wild-type P450_{BM3} carrying one or more mutations at the positions 25, 26, 42, 47, 51, 52, 58, 64, 74, 75, 78, 81, 82, 87, 88, 90, 94, 96, 102, 106, 107, 108, 118, 135, 138, 142, 143, 145, 152, 172, 173, 175, 178, 180, 181, 184, 185, 188, 197, 199, 205, 214, 226, 231, 236, 237, 239, 252, 255, 260, 263, 264, 265, 267, 268, 273, 274, 275, 290, 295, 306, 324, 328, 354, 366, 398, 401, 430, 433, 434, 437, 438, 442, 443, 444, and 446, and a selection of the most active P450 chimera peroxygenases and monooxygenases from the libraries described in Otey *et al.* (Otey, Landwehr *et al.* 2006) and Landwehr *et al.* (Landwehr, Carbone *et al.* 2007) were arrayed on 96-well plates. Arrays were prepared by growing recombinant *E. coli* transformed with an expression plasmid encoding for the P450 sequence, inducing protein expression with IPTG, and preparing a cell lysate.

[00228] The activation reaction of the pre-selected organic molecules ibuprofen methyl ester, menthofuran, dihydrojasnone, and guaiol with the pool of pre-selected oxydizing agents was tested at a 1-mL scale dissolving the organic molecule in phosphate buffer (1% ethanol) at a final concentration of 2 mM. The oxydizing agent was then added to the solution at a final concentration of about 200-400 nM. The reaction was started by adding NADPH and a glucose-6-phosphate dehydrogenase cofactor regeneration system to the mixture. After 20 hrs incubation at room temperature, the reactions were extracted with chloroform and analyzed by gas chromatography. Total conversion ratios were calculated including in the experiment a sample containing no enzyme and adding an internal standard to the samples. The 20-30% most promising oxydizing agents were re-tested at a larger scale (3 mL) to identify false positives and determine regioselectivity and product distribution. Exemplary

results from the screening of the pool of P450s on dihydrojasnone and menthofuran are reported on Figure 5 and 6.

[00229] A group of about 5 to 10 most interesting oxydizing agents were then selected based on the results from the re-screen, in particular based on their regioselectivity, conversion efficiency, or ability to produce "rare" activated product. Using the selected oxydizing agents, conditions for the activation reaction were optimized, testing different co-solvents (e.g. ethanol, ethylacetate), additives (e.g. BSA, glycerol), ROS(Reactive oxygen species) scavengers (e.g. SOD, catalase), temperature, and target molecule:oxydizing agent ratios. Once optimized, the activation reaction was scaled up to 100-300 mL reaction scale, where the oxydizing agent concentration typically ranged from 0.5 to 15 μ M, the target molecule concentration from 5 to 20 mM, and a cofactor regeneration system was used. The co-solvent was usually ethanol, typically at a final concentration of 0.5% to 2%.

[00230] Large scale reactions were incubated under stirring at room temperature for a period of time of up to 56 hours, during which target molecule conversion was monitored by extracting small aliquots of the reaction mixture and analyzing them by gas chromatography.

[00231] As the desired amount of activated product was produced, the reaction mixture was extracted with an organic solvent, typically chloroform, and the activated product was isolated by silica gel chromatography using hexane:ethyl acetate gradient. Purified products were identified using GC-MS, ^1H -, and ^{13}C -NMR.

[00232] Once the product with the activated target site was identified, the activated product was subjected to fluorination using the deoxo-fluorinating agent DAST in dichloromethane. Different reaction conditions were typically tested to optimize yield and possibly achieve quantitative conversion. During these tests, the conversion of the activated product to the corresponding fluorinated derivative was typically monitored by GC-MS.

[00233] After the fluorination reaction, the fluorinated product was isolated by silica gel chromatography using a hexane:ethyl acetate gradient. The identity of the purified product was confirmed by GC-MS, HR-MS, ^1H -, ^{13}C -, and ^{19}F -NMR.

[00234] The pool of pre-selected oxydizing agents and other selected variants from mutagenesis libraries of var3-10—i.e. libraries where positions 74, 82, 87, 88, and 328

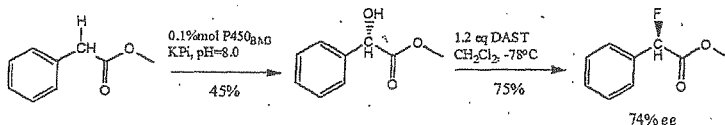
position of var3-10 were subjected to saturation mutagenesis— were screened for activity towards activation of the pre-selected organic molecules dihydro-4-methoxymethyl-2-methyl-5-phenyl-2-oxazoline (MMPO) and 1,2,3,4,6-pentamethyl mannopyranoside using a colorimetric assay on a 96-well plate format. In the case of MMPO, for example, different oxydizing agents were arrayed on a 96-well plate, each well containing about 150 μ L phosphate buffer and about 1 μ M oxydizing agent. The target molecule was added to the solution from an ethanol stock to a final concentration of 2 mM (and 1% ethanol). After addition of 1 mM NADPH, the reaction mixture was incubated for 30 minutes at room temperature. After incubation, MMPO activation activity was determined using the colorimetric reagent Purpald (Sigma), which reacts with formaldehyde and serves in this case to detect the demethylation of the methoxy group in the target molecule. Positive 'hits' were re-tested on a 1-mL scale using 1 mM MMPO, 0.5 μ M oxydizing agent, 1 mM NADPH, and a cofactor regeneration system. After incubation at room temperature, the reaction mixtures were extracted with chloroform and analyzed by gas chromatography. In this way, the regioselectivity and conversion efficiency of each oxydizing agent was established. The identity of the activated product was also confirmed by GC-MS. Most promising oxydizing agents, that is those showing highest regioselectivity and/or conversion efficiency, were used for scale-up tests and for producing larger quantities of activated product for the fluorination reaction as described above. Representative results from the screening of the P450 pool for MMPO activation activity are reported on [Figure 7](#).

[00235] The activation of the target molecule dihydrojasnone was also carried out using a whole-cell system ([Figure 8](#)). Specifically, the whole-cell system consisted of *E. coli* DH5a cells transformed with a pCWqri vector that contains the sequence for var3. The whole-cell activation reaction was carried out growing a 0.5 L culture of the recombinant cells in TB medium, inducing the intracellular expression of var3 during mid-log phase by adding 0.5 mM IPTG, and growing the cells at 30°C for further 12 hours. After that, 15 mL dodecane were added to the culture. Dihydrojasnone was then added to the culture at a final concentration of 30 mM. Formation of the activated product and consumption of the target molecule were monitored by gas chromatography for up to 36 hours. Conversion ratio at the end of the 36 hours amounted to ~ 10%. Higher conversion ratios (>90-95%) were achieved *in vitro* with the same variant using a cofactor regeneration system. The lower efficiency of the whole-cell system in the case of dihydrojasnone may be attributed to potential toxicity of

this molecule or its activated product to the cells as well as their low membrane permeability. Nevertheless, this experiment demonstrates that the activation of the target molecule for the scope of the systems and methods herein described can also be performed using a whole-cell, especially in cases where the chemo-physical properties of the candidate molecule may make this option more favorable.

[00236] Chemical reagents, substrates and solvents were purchased from Sigma, Aldrich, and Fluka. Silica gel chromatography purifications were carried out using AMD Silica Gel 60 230-400 mesh. Gas chromatography (GC) analyses were carried out using a Shimadzu GC-17A gas chromatograph, a FID detector, and an Agilent HP5 column (30 m x 0.32 mm x 0.1 μ m film). Chiral GC analyses were carried out using a Shimadzu GC-17A gas chromatograph, a FID detector, and an Agilent CyclosilB column (30 m x 0.52 mm x 0.25 μ m film). GC-MS analyses were carried out on a Hewlett-Packard 5970B MSD with 5890 GC and a DB-5 capillary column. ^1H , ^{13}C , and ^{19}F NMR spectra were recorded on a Varian Mercury 300 spectrometer (300 MHz, 75 MHz, and 282 MHz, respectively), and are internally referenced to residual protio solvent signal. Data for ^1H NMR are reported in the conventional form: chemical shift (δ ppm), multiplicity (s=singlet, d=doublet, t=triplet, q=quartet, m=multiplet, br=broad), coupling constant (Hz), integration, and assignment). Data for ^{13}C NMR are reported in the terms of chemical shift (δ ppm). Data for ^{19}F NMR are reported in the terms of chemical shift (δ ppm) and multiplicity. High-resolution mass spectra were obtained with a JEOL JMS-600H High Resolution Mass Spectrometer at the California Institute of Technology Mass Spectral facility.

Example 1 – Stereoselective fluorination of methyl 2-phenyl acetate.

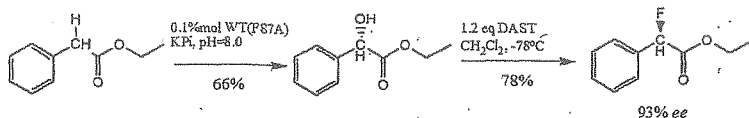


Scheme 1.

[00237] Methyl 2-phenyl acetate was subjected to selective fluorination of the target site C (alpha position) according to the systems and methods herein disclosed and, more specifically, according to the general procedure described above.

[00238] Experimental description: 90 mg methyl 2-phenyl acetate were dissolved in 500 μ L ethanol and added to 240 mL potassium phosphate buffer pH 8.0. P450_{BM3} was added to the mixture at a final concentration of 2 μ M. The mixture was split in 4 mL aliquots into 15 mL scintillation vials equipped with a stir bar. 500 μ L of a 5 mM NADPH solution were added to each vial and stirred for 2 minutes. 500 μ L of a cofactor regeneration solution containing 300 mM glucose-6-phosphate and 10 units/mL glucose-6-phosphate dehydrogenase were then added to each vial. The resulting mixtures were stirred at room temperature. After 4 hours, the reaction mixtures were joined together and extracted with chloroform (3x 100 mL). The organic phase was then dried over magnesium sulfate (MgSO₄) and evaporated in vacuo. Purification of the resulting oil by silica gel chromatography (5% ethyl acetate : 95% hexane) afforded the activated product ((S)-methyl 2-hydroxy-2-phenylacetate, 40.5 mg). 40 mg (0.24 mmol) of activated product were dissolved in 2 mL dry dichloromethane (CH₂Cl₂) and a catalytic amount (4 drops) of ethanol was added to the solution. The solution was cooled to -78°C (dry ice) and added with 41 μ L DAST (0.29 mmol). The reaction was stirred in dry ice for 12 hours. The reaction mixture was then added with 5 mL saturated sodium bicarbonate (NaHCO₃) and extracted with dichloromethane (3x 15 mL). The organic phase was then dried over magnesium sulfate (MgSO₄) and evaporated in vacuo. Purification of the resulting oil by silica gel chromatography (5% ethyl acetate : 95% hexane) afforded the fluorinated product ((R)-methyl 2-fluoro-2-phenylacetate) (30 mg, 75% yield, pale yellow oil) in 74% ee, as determined by chiral GC analysis. ¹H-NMR (300 MHz, CDCl₃): δ 3.75 (s, 3H, -OCH₃), δ 5.77 (d, J= 48 Hz, 1H, -CHF), δ 7.37-7.46 (m, 5H); ¹³C-NMR (75 MHz, CDCl₃): 52.8, 89.5 (d, J= 184.5 Hz), 126.8, 126.9, 129.0, δ 129.9, δ 134.4 (d, J= 34.5 Hz), δ 169.0. ¹⁹F-NMR (282 MHz, CDCl₃): δ -180.29 (d, J= 48.7 Hz). HRMS (EI+): exact mass calculated for C₉H₉FO₂ requires m/z 168.0587, found 168.0594.

Example 2 – Stereoselective fluorination of ethyl 2-phenyl acetate.



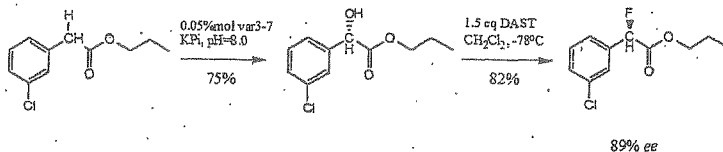
Scheme 2.

[00239] Ethyl 2-phenyl acetate was subjected to selective fluorination of the target site C (alpha position) according to the systems and methods herein disclosed and, more specifically, according to the general procedure described above.

[00240] Experimental description: 100 mg ethyl 2-phenyl acetate were dissolved in 500 μL ethanol and added to 250 mL potassium phosphate buffer pH 8.0. WT(F87A) was added to the mixture at a final concentration of 2 μM . The mixture was split in 4 mL aliquots into 15 mL scintillation vials equipped with a stir bar. 500 μL of a 5 mM NADPH solution were added to each vial and stirred for 2 minutes. 500 μL of a cofactor regeneration solution containing 300 mM glucose-6-phosphate and 10 units/mL glucose-6-phosphate dehydrogenase were then added to each vial. The resulting mixtures were stirred at room temperature. After 3 hours, the reaction mixtures were joined together and extracted with chloroform (3x 100 mL). The organic phase was then dried over magnesium sulfate (MgSO_4) and evaporated in vacuo. Purification of the resulting oil by silica gel chromatography (5% ethyl acetate : 95% hexane) afforded the activated product ((S)-ethyl 2-hydroxy-2-phenylacetate, 66 mg). 66 mg (0.36 mmol) of activated product were dissolved in 2 mL dry dichloromethane (CH_2Cl_2) and a catalytic amount (4 drops) of ethanol was added to the solution. The solution was cooled to -78°C (dry ice) and added with 61 μL DAST (0.43 mmol). The reaction was stirred in dry ice for 12 hours. The reaction mixture was then added with 5 mL saturated sodium bicarbonate (NaHCO_3) and extracted with dichloromethane (3x 15 mL). The organic phase was then dried over magnesium sulfate (MgSO_4) and evaporated in vacuo. Purification of the resulting oil by silica gel chromatography (5% ethyl acetate : 95% hexane) afforded the fluorinated product ((R)-ethyl 2-fluoro-2-phenylacetate) (51 mg, 78% yield, pale yellow oil) in 93% ee, as determined by chiral GC analysis. $^1\text{H-NMR}$ (300 MHz, CDCl_3): δ 1.24 (t, J = 7.2 Hz, 3H, $-\text{CH}_3$), δ 4.16-4.27 (m, 2H, $-\text{OCH}_2$), δ 5.75 (d, J = 48 Hz, 1H, $-\text{CHF}$), δ 7.37-7.46 (m, 5H); $^{13}\text{C-NMR}$ (75 MHz, CDCl_3): 14.2, 62.0, 81.2, 89.6 (d, J = 184.5 Hz), 126.8, 126.9, 128.9, 129.8, 134.4 (d, J = 34.5 Hz), δ 169.0. $^{19}\text{F-NMR}$

(282 MHz, CDCl_3): δ -180.27 (d, J = 48.7 Hz). HRMS (EI+): exact mass calculated for $\text{C}_{10}\text{H}_{11}\text{FO}_2$ requires m/z 182.0743, found 182.0750.

Example 3 – Stereoselective fluorination of propyl 2-(3-chlorophenyl)acetate.



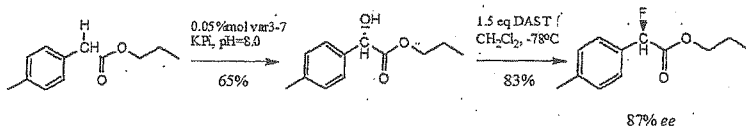
Scheme 3.

[00241] Propyl 2-(3-chlorophenyl)acetate was subjected to selective fluorination of the target site C (alpha position) according to the systems and methods herein disclosed and, more specifically, according to the general procedure described above.

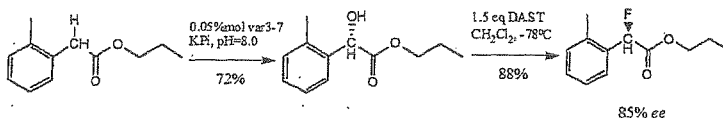
[00242] Experimental description: 95 mg propyl 2-(3-chlorophenyl)acetate were dissolved in 500 μL ethanol and added to 250 mL potassium phosphate buffer pH 8.0. Var3-7 was added to the mixture at a final concentration of 1 μM . The mixture was split in 4 mL aliquots into 15 mL scintillation vials equipped with a stir bar. 500 μL of a 5 mM NADPH solution were added to each vial and stirred for 2 minutes. 500 μL of a cofactor regeneration solution containing 300 mM glucose-6-phosphate and 10 units/mL glucose-6-phosphate dehydrogenase were then added to each vial. The resulting mixtures were stirred at room temperature. After 4 hours, the reaction mixtures were joined together and extracted with chloroform (3x 100 mL). The organic phase was then dried over magnesium sulfate (MgSO_4) and evaporated in vacuo. Purification of the resulting oil by silica gel chromatography (5% ethyl acetate : 95% hexane) afforded the activated product ((S)-propyl 2-hydroxy-2-(3-chlorophenyl)acetate, 71 mg). 70 mg (0.3 mmol) of activated product were dissolved in 2 mL dry dichloromethane (CH_2Cl_2) and a catalytic amount (4 drops) of ethanol was added to the solution. The solution was cooled to -78°C (dry ice) and added with 64 μL DAST (0.45 mmol). The reaction was stirred in dry ice for 12 hours. The reaction mixture was then added with 5 mL saturated sodium bicarbonate (NaHCO_3) and extracted with dichloromethane (3x 15 mL). The organic phase was then dried over magnesium sulfate (MgSO_4) and evaporated in vacuo. Purification of the resulting oil by silica gel chromatography (5% ethyl acetate :

95% hexane) afforded the fluorinated product ((R)-propyl 2-fluoro-2-(3-chlorophenyl)acetate) (57 mg, 82% yield, colorless oil) in 89% ee, as determined by chiral GC analysis. $^1\text{H-NMR}$ (300 MHz, CDCl_3): δ 0.85 (t, J = 7Hz, 3H, $-\text{CH}_3$), δ 1.56-1.68 (m, 2H, CH_2), δ 4.12 (t, J = 6Hz, 2H, $-\text{OCH}_2$), δ 5.72 (d, J = 48Hz, 1H, $-\text{CHF}$), δ 7.32 (br, 3H), δ 7.44 (br, 1H); $^{13}\text{C-NMR}$ (75 MHz, CDCl_3): 10.3, 21.9, 67.7, δ 88.7 (d, J = 186.5Hz), 124.8, 126.9, 129.9, 130.3, 134.9. $^{19}\text{F-NMR}$ (282 MHz, CDCl_3): δ -182.8 (d, J = 48.7Hz). HRMS (EI+): exact mass calculated for $\text{C}_{11}\text{H}_{12}\text{ClFO}_2$ requires m/z 230.0510, found 230.0502.

Example 4 – Stereoselective fluorination of propyl 2-(4-methylphenyl)acetate and propyl 2-(2-methylphenyl)acetate.



Scheme 4-1.



Scheme 4-2.

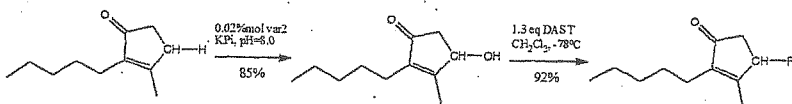
[00243] Propyl 2-(4-methylphenyl)acetate and propyl 2-(2-methylphenyl)acetate were subjected to selective fluorination of the target site C (alpha position) according to the systems and methods herein disclosed and, more specifically, according to the general procedure described above.

[00244] Experimental description: stereoselective activation and fluorination of 2-(4-methylphenyl)acetate and propyl 2-(2-methylphenyl)acetate were carried out starting from 100 mg substrate according to the experimental protocol described in Example 3. The fluorinated product (R)-propyl 2-fluoro-2-(4-methylphenyl)acetate was obtained in 87% ee (54 mg, colorless oil). $^1\text{H-NMR}$ (300 MHz, CDCl_3): δ 0.84-0.91 (m, 3H, $-\text{CH}_3$), δ 1.57-1.68

(m, 2H, CH₂), δ 2.37 (s, 3H, -CH₃), δ 4.08-4.16 (m, 2H, -OCH₂), δ 5.75 (d, J = 48Hz, 1H, -CHF), δ 7.18-7.27 (m, 2H), δ 7.27-7.44 (m, 2H); ¹³C-NMR (75 MHz, CDCl₃): 10.40, 19.41, 22.08, 67.47, 126.57, 131.10. ¹⁹F-NMR (282 MHz, CDCl₃): δ -178.5 (d, J = 48.7Hz). HRMS (EI+): exact mass calculated for C₁₂H₁₅FO₂ requires m/z 210.1056, found 210.1062. The fluorinated product (R)-propyl 2-fluoro-2-(2-methylphenyl)acetate was obtained in 87% ee (54 mg, colorless oil). ¹H-NMR (300 MHz, CDCl₃): δ 0.83 (t, J = 7.5Hz, 3H, -CH₃), δ 1.52-1.68 (m, 2H, CH₂), δ 2.43 (s, 3H, -CH₃), δ 4.12 (m, 2H, -OCH₂), δ 5.96 (d, J = 48Hz, 1H, -CHF), δ 7.16-7.30 (m, 4H); ¹³C-NMR (75 MHz, CDCl₃): 10.3, 19.3, 22.0, 29.9, 67.4, 87.4 (d, J = 183Hz), δ 126.5, δ 127.5, δ 129.8, δ 131.0. ¹⁹F-NMR (282 MHz, CDCl₃): δ -180.1 (d, J = 48.7Hz). HRMS (EI+): exact mass calculated for C₁₂H₁₅FO₂ requires m/z 210.1056, found 210.1070.

[00245] Examples 1, 2, 3, and 4 illustrate the application of the systems and methods of the disclosure for stereoselective fluorination of a chemical building block, exemplified by 2-aryl acetic acid derivatives (Schemes 1-4).

Example 5 – Regioselective fluorination of 3-methyl-2-pentylcyclopent-2-enone (dihydrojasmane) in position 4.



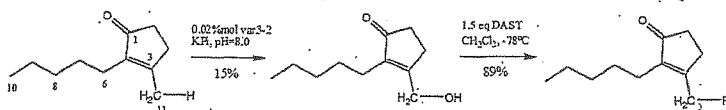
Scheme 5.

[00246] Dihydrojasmane was subjected to selective fluorination of the target site C (position 4) according to the systems and methods herein disclosed and, more specifically, according to the general procedure described above.

[00247] Experimental description: 270 μ L dihydrojasmane were dissolved in 1.2 mL ethanol and added to 150 mL potassium phosphate buffer pH 8.0. Var2 was added to the mixture at a final concentration of 2 μ M. The mixture was split in 4.8 mL aliquots into 15 mL scintillation vials equipped with a stir bar. 600 μ L 10 mM NADPH in KPi buffer were added

to each vial and stirred for 2 minutes. 600 μ L cofactor regeneration solution containing 500 mM glucose-6-phosphate and 10 units/mL glucose-6-phosphate dehydrogenase were then added to each vial. The resulting mixtures were stirred at room temperature. After 36 hours, the reaction mixtures were joined together and extracted with chloroform (3x 50 mL). The organic phase was then dried over magnesium sulfate (MgSO_4) and evaporated in vacuo. Purification of the resulting oil by silica gel chromatography (0-30% ethyl acetate/hexane) afforded the activated product (4-hydroxy-3-methyl-2-pentylcyclopent-2-enone, 222 mg). 210 mg (1.15 mmol) of activated product were dissolved in 2 mL dry dichloromethane (CH_2Cl_2) and a catalytic amount (4 drops) of ethanol was added to the solution. The solution was cooled to -78°C (dry ice) and added with 215 μ L DAST (1.5 mmol). The reaction was stirred in dry ice for 12 hours. The reaction mixture was then added with 5 mL saturated sodium bicarbonate (NaHCO_3) and extracted with dichloromethane (3x 15 mL). The organic phase was then dried over magnesium sulfate (MgSO_4) and evaporated in vacuo. Purification of the resulting oil by silica gel chromatography (0-30% ethyl acetate/hexane) afforded the fluorinated product, 4-fluoro-3-methyl-2-pentylcyclopent-2-enone (193 mg, 92% yield, yellow oil). ^1H -NMR (300 MHz, CDCl_3): δ 0.88 (t, J = 6.6 Hz, 3H, CH_3), δ 1.25-1.40 (m, 6H, CH_2), δ 2.10 (d, J = 2.1 Hz, 2H, CH_3), δ 2.20 (t, J = 7.1 Hz, 2H), δ 2.44-2.60 (m, 1H), δ 2.70-2.82 (m, 1H), δ 5.47 (dd, J = 54.2 Hz, J = 5.8, 1H); ^{13}C -NMR (75 MHz, CDCl_3): δ 13.7, 14.2, 22.6, 23.1, 27.9, 29.9, 31.9, 41.4 (d, J = 19.6 Hz), δ 91.2 (d, J = 174 Hz); ^{19}F -NMR (282 MHz, CDCl_3): δ -179.08 (ddd, J = 51.88 Hz, J = 21.43 Hz, J = 9.3 Hz). HRMS (EI $^+$): exact mass calculated for $\text{C}_{11}\text{H}_{17}\text{FO}$ requires m/z 184.1263, found 184.1255.

Example 6 – Regioselective fluorination of 3-methyl-2-pentylcyclopent-2-enone (dihydrojasmonone) in position 11.



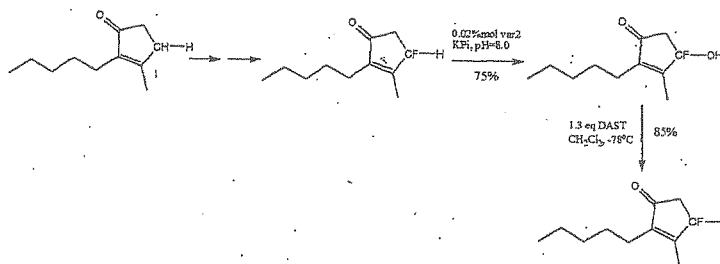
Scheme 6.

[00248] Dihydrojasmonone was subjected to selective fluorination of the target site C (position 11) according to the systems and methods herein disclosed and, more specifically, according to the general procedure described above.

[00249] Experimental description: 240 μ L dihydrojasmonone were dissolved in 1.1 mL ethanol and added to 130 mL potassium phosphate buffer pH 8.0. Var2 was added to the mixture at a final concentration of 2 μ M. The mixture was split in 4.8 mL aliquots into 15 mL scintillation vials equipped with a stir bar. 600 μ L 10 mM NADPH in KPi buffer were added to each vial and stirred for 2 minutes. 600 μ L cofactor regeneration solution containing 500 mM glucose-6-phosphate and 10 units/mL glucose-6-phosphate dehydrogenase were then added to each vial. The resulting mixtures were stirred at room temperature. After 36 hours, the reaction mixtures were joined together and extracted with chloroform (3x 50 mL). The organic phase was then dried over magnesium sulfate (MgSO_4) and evaporated in vacuo. Purification of the resulting oil by silica gel chromatography (0-30% ethyl acetate/hexane) afforded the activated product (11-hydroxy-3-methyl-2-pentylcyclopent-2-enone, 35 mg). 30 mg (0.16 mmol) of activated product were dissolved in 2 mL dry dichloromethane (CH_2Cl_2) and a catalytic amount (4 drops) of ethanol was added to the solution. The solution was cooled to -78°C (dry ice) and added with 35 μ L DAST (0.25 mmol). The reaction was stirred in dry ice for 12 hours. The reaction mixture was then added with 5 mL saturated sodium bicarbonate (NaHCO_3) and extracted with dichloromethane (3x 15 mL). The organic phase was then dried over magnesium sulfate (MgSO_4) and evaporated in vacuo. Purification of the resulting oil by silica gel chromatography (0-30% ethyl acetate/hexane) afforded the fluorinated product, 11-fluoro-3-methyl-2-pentylcyclopent-2-enone (27 mg, 89% yield, yellow oil). ^1H -NMR (300 MHz, CDCl_3): δ 0.88 (t, J = 6.6 Hz, 3H, CH_3), δ 1.25-1.40 (m, 6H, CH_2), δ 2.10 (d, J = 2.1 Hz, 2H, CH_3), δ 2.17 (t, J = 7.6 Hz, 2H), δ 2.38-2.44 (m, 1H), δ 2.59-2.64 (m, 1H), δ 5.20 (d, J = 48.8 Hz, 1H); ^{13}C -NMR (75 MHz, CDCl_3): δ 14.3, 22.8, 23.3, 28.4, 31.8, 29.9, 31.9, 34.8, 60.6, 80.3 (d, J = 164 Hz), 87.9; ^{19}F -NMR (282 MHz, CDCl_3): δ -48.80 (d, J = 48.7 Hz). HRMS (EI $^+$): exact mass calculated for $\text{C}_{11}\text{H}_{17}\text{FO}$ requires m/z 184.1263, found 184.1263.

[00250] Examples 5 and 6 illustrate the application of the systems and methods of the disclosure for regioselective fluorination of an organic molecule at weakly reactive sites, exemplified by dihydrojasmonone (Schemes 5 and 6).

Example 7 – Regioselective difluorination of 3-methyl-2-pentylcyclopent-2-enone (dihydrojasmonone) in position 4.



Scheme 7.

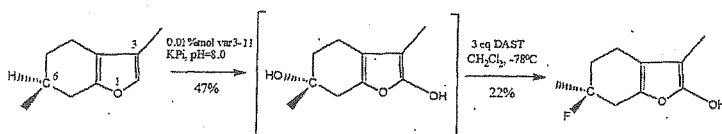
[00251] Dihydrojasmonone was subjected to selective difluorination of the target site C (position 4) according to the systems and methods herein disclosed and, more specifically, according to the general procedure described above.

[00252] Experimental description: 4-fluoro-3-methyl-2-pentylcyclopent-2-enone was obtained according to the experimental described in Example 5. 180 mg 4-fluoro-3-methyl-2-pentylcyclopent-2-enone were dissolved in 900 μL ethanol and added to 120 mL potassium phosphate buffer pH 8.0. Var2 was added to the mixture at a final concentration of 2 μM . The mixture was split in 4.8 mL aliquots into 15 mL scintillation vials equipped with a stir bar. 600 μL 10 mM NADPH in KPi buffer were added to each vial and stirred for 2 minutes. 600 μL cofactor regeneration solution containing 500 mM glucose-6-phosphate, and 10 units/mL glucose-6-phosphate dehydrogenase were then added to each vial. The resulting mixtures were stirred at room temperature. After 36 hours, the reaction mixtures were joined together and extracted with chloroform (3x 50 mL). The organic phase was then dried over magnesium sulfate (MgSO_4) and evaporated in vacuo. Purification of the resulting oil by silica gel chromatography (0-30% ethyl acetate/hexane) afforded the activated product (4-hydroxy-4-fluoro-3-methyl-2-pentylcyclopent-2-enone, 135 mg). 100 mg (0.54 mmol) of activated product were dissolved in 2 mL dry dichloromethane (CH_2Cl_2) and a catalytic amount (4 drops) of ethanol was added to the solution. The solution was cooled to -78°C (dry ice) and added with 100 μL DAST (0.7 mmol). The reaction was stirred in dry ice for 12 hours. The reaction mixture was then added with 5 mL saturated sodium bicarbonate

(NaHCO_3) and extracted with dichloromethane (3x 15 mL). The organic phase was then dried over magnesium sulfate (MgSO_4) and evaporated in vacuo. Purification of the resulting oil by silica gel chromatography (0-30% ethyl acetate/hexane) afforded the fluorinated product, 4,4-difluoro-3-methyl-2-pentylcyclopent-2-enone (85 mg, 85% yield, yellow oil). MS (EI+): m/z 202. Mw for $\text{C}_{11}\text{H}_{16}\text{F}_2\text{O}$: 202.24.

[00253] Example 7 illustrates the application of the systems and methods of the disclosure for regioselective polyfluorination of an organic molecule at a weakly reactive site, exemplified by dihydrojasnone (Scheme 7).

Example 8 – Regioselective fluorination of menthofuran.



Scheme 8.

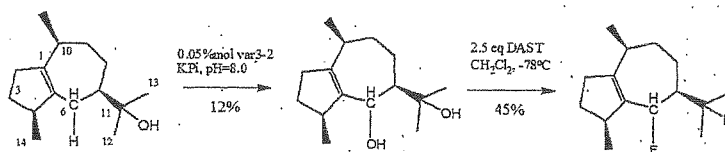
[00254] Menthofuran was subjected to selective fluorination of the target site C (position 6) according to the systems and methods herein disclosed and, more specifically, according to the general procedure described above.

[00255] Experimental description: 112 mg menthofuran were dissolved in 0.6 mL ethanol and added to 125 mL potassium phosphate buffer pH 8.0. Var3-11 was added to the mixture at a final concentration of 0.7 μM . The mixture was split in 4 mL aliquots into 15 mL scintillation vials equipped with a stir bar. 500 μL 10 mM NADPH in KPi buffer were added to each vial and stirred for 2 minutes. 500 μL cofactor regeneration solution containing 500 mM glucose-6-phosphate and 10 units/mL glucose-6-phosphate dehydrogenase were then added to each vial. The resulting mixtures were stirred at room temperature. After 24 hours, the reaction nearly reached completion (95% substrate conversion). The reaction mixtures were joined together and extracted with chloroform (3x 50 mL). The organic phase was then dried over magnesium sulfate (MgSO_4) and evaporated in vacuo. The resulting oil (53 mg) was subjected directly to deoxo-fluorination without purification of the activated product. 53 mg of the activation mixture (~0.32 mmol) were dissolved in 2 mL dry dichloromethane

(CH₂Cl₂) and a catalytic amount (4 drops) of ethanol was added to the solution. The solution was cooled to -78°C (dry ice) and added with 150 µL DAST (1 mmol). The reaction was stirred in dry ice for 16 hours. The reaction mixture was then added with 5 mL saturated sodium bicarbonate (NaHCO₃) and extracted with dichloromethane (3x 15 mL). The organic phase was then dried over magnesium sulfate (MgSO₄) and evaporated in vacuo. Purification of the resulting oil by silica gel chromatography (0-10% ethyl acetate/hexane) afforded the fluorinated product, 6-fluoro-menthofuran-2-ol (12 mg, 22% yield, yellow oil). ¹H-NMR (300 MHz, CDCl₃): δ 1.13 (d, J: 75.6Hz, 3H, —CH₃), δ 1.2-1.3 (m, 2H, —CH₂—), δ 1.84 (s, 3H, —CH₃), 1.95-2.4 (dm, 2H, —CH₂—), 2.4-2.6 (dm, 2H, —CH₂—); ¹³C-NMR (75 MHz, CDCl₃): δ 22.7 (d, J= 209Hz), 43.08, 45.36, 91.7 (d, J= 215Hz), 114.9, 127.1. ¹⁹F-NMR (282 MHz, CDCl₃): δ -114.4 (m). HRMS (EI+): exact mass calculated for C₁₀H₁₃FO₂ requires m/z 184.0909, found 184.0899.

[00256] Example 8 illustrates the application of the systems and methods of the disclosure for regioselective fluorination of an organic molecule at a weakly reactive site, exemplified by menthofuran (Scheme 8).

Example 9 – Regioselective fluorination of (-)-guaiaol.



Scheme 9.

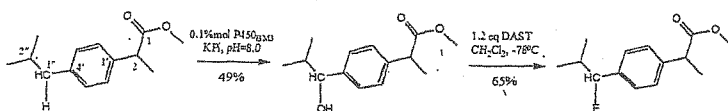
[00257] (-)-Guaiaol was subjected to selective fluorination of the target site C (position 6) according to the systems and methods herein disclosed and, more specifically, according to the general procedure described above.

[00258] Experimental description: 250 mg guaiaol were dissolved in 2 mL ethanol and added to 210 mL potassium phosphate buffer pH 8.0. Var3-2 was added to the mixture at a final concentration of 3 µM. The mixture was split in 4.8 mL aliquots into 15 mL scintillation vials equipped with a stir bar. 600 µL 10 mM NADPH in KPi buffer were added to each vial

and stirred for 2 minutes. 600 μ L cofactor regeneration solution containing 500 mM glucose-6-phosphate and 10 units/mL glucose-6-phosphate dehydrogenase were then added to each vial. The resulting mixtures were stirred at room temperature. After 48 hours, the reaction mixtures were joined together and extracted with chloroform (3x 50 mL). The organic phase was then dried over magnesium sulfate (MgSO_4) and evaporated in vacuo. Purification of the resulting oil by silica gel chromatography (0-30% ethyl acetate/hexane) afforded the activated product (6-hydroxy-guaiol, 30 mg, colorless oil). $^1\text{H-NMR}$ (300 MHz, CDCl_3): δ 1.01 (d, J = 6.9Hz, 3H, $-\text{CH}_3$), δ 1.22 (s, 3H, CH_3), δ 1.28 (s, 3H, CH_3), δ 1.25 (d, J = 9Hz, 3H, CH_3), δ 1.42-1.45 (m, 2H), δ 1.685 (bs, 2H), δ 1.74-1.183 (m, 2H), δ 1.95-2.03 (m, 2H), δ 2.15-2.24 (m, 2H), δ 2.54-2.72 (m, 3H), δ 2.97-3.06 (m, 1H), δ 3.67 (d, J = 9Hz, 1H); $^{13}\text{C-NMR}$ (75 MHz, CDCl_3): δ 11.20, 19.41, 26.08, 28.32, 31.07, 34.13, 35.33, 38.08, 42.42, 48.01, 72.12, 73.15, 178.94. 15 mg of the activated product ($\sim$ 0.06 mmol) were dissolved in 1 mL dry dichloromethane (CH_2Cl_2) and a catalytic amount (3 drops) of ethanol was added to the solution. The solution was cooled to -78°C (dry ice) and added with 18 μ L DAST (0.12 mmol). The reaction was stirred in dry ice for 16 hours. The reaction mixture was then added with 5 mL saturated sodium bicarbonate (NaHCO_3) and extracted with dichloromethane (3x 15 mL). The organic phase was then dried over magnesium sulfate (MgSO_4) and evaporated in vacuo. Purification of the resulting oil by silica gel chromatography (0-30% ethyl acetate/hexane) afforded the fluorinated product, 6-fluoro-guaiol (7 mg, 45% yield, pale yellow oil). MS (EI+): m/z 242. Mw for $\text{C}_{15}\text{H}_{25}\text{FO}$: 242.35.

[00259] Example 9 illustrates the application of the systems and methods of the disclosure for regioselective fluorination of an organic molecule at a weakly reactive site, exemplified by (-)-guaiol (Scheme 9).

Example 10 – Regioselective fluorination of ibuprofen methyl ester (methyl 2-(4'-(2''-methylpropyl)phenyl)propanoate) in 1'' position.

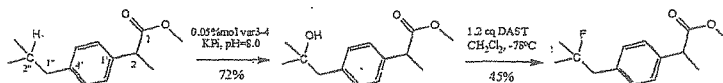


Scheme 10.

[00260] Ibuprofen methyl ester was subjected to selective fluorination of the target site C (position 1'') according to the systems and methods herein disclosed and, more specifically, according to the general procedure described above.

[00261] Experimental description: 150 mg ibuprofen methyl ester were dissolved in 1.4 mL ethanol and added to 150 mL potassium phosphate buffer pH 8.0. P450_{BM3} was added to the mixture at a final concentration of 10 μ M. The mixture was split in 4 mL-aliquots into 15 mL scintillation vials equipped with a stir bar. 500 μ L 10 mM NADPH in KPi buffer were added to each vial and stirred for 2 minutes. 500 μ L cofactor regeneration solution containing 500 mM glucose-6-phosphate and 10 units/mL glucose-6-phosphate dehydrogenase were then added to each vial. The resulting mixtures were stirred at room temperature. After 48 hours, the reaction mixtures were joined together and extracted with chloroform (3x 50 mL). The organic phase was then dried over magnesium sulfate (MgSO₄) and evaporated in vacuo. Purification of the resulting oil by silica gel chromatography (5-40% ethyl acetate/hexane) afforded the activated product (methyl 2-(4'-(1''-hydroxy-2'''-methylpropyl)phenyl)propanoate, 73 mg). 15 mg (0.06 mmol) of activated product were dissolved in 2 mL dry dichloromethane (CH₂Cl₂) and a catalytic amount (4 drops) of ethanol was added to the solution. The solution was cooled to -78°C (dry ice) and added with 11 μ L DAST (0.72 mmol). The reaction was stirred in dry ice for 16 hours. The reaction mixture was then added with 5 mL saturated sodium bicarbonate (NaHCO₃) and extracted with dichloromethane (3x 15 mL). The organic phase was then dried over magnesium sulfate (MgSO₄) and evaporated in vacuo. Purification of the resulting oil by silica gel chromatography (0-30% ethyl acetate/hexane) afforded the fluorinated product, methyl 2-(4'-(1''-fluoro-2'''-methylpropyl)phenyl)propanoate (10 mg, 65% yield, colorless oil). ¹H-NMR (300 MHz, CDCl₃): δ 0.84 (d, J= 6.9Hz, 3H, CH₃), δ 1.01 (d, J= 6.9Hz, 3H, -CH₃), δ 1.49 (d, J= 8.7Hz, 3H, CH₃), δ 2.05-2.08 (m, 1H), δ 3.66 (s, 3H, OCH₃), δ 3.73 (q, J= 7.5Hz, 1H), δ 5.07 (dd, J= 40.0, J= 6.9Hz, 1H, CHF), δ 7.25 (m, 4H); ¹³C-NMR (75 MHz, CDCl₃): δ 15.5, 17.82 (d), 18.54 (d), 34.48 (d, J: 85.7Hz), 45.37, 52.31, 99.3 (d, J= 174Hz), 175.6; ¹⁹F-NMR (282 MHz, CDCl₃): δ -179.8 (m). HRMS (EI+): exact mass calculated for C₁₄H₁₉FO₂ requires m/z 238.1369, found 238.1367.

Example 11 – Regioselective fluorination of ibuprofen methyl ester (methyl 2-(4'-(2''-methylpropyl)phenyl)propanoate) in 2'' position.



Scheme 11.

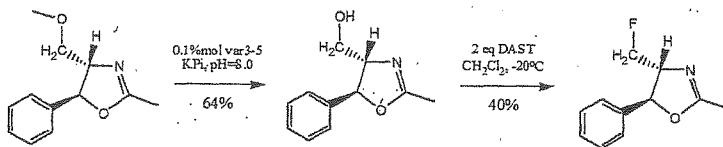
[00262] Ibuprofen methyl ester was subjected to selective fluorination of the target site C (position 2'') according to the systems and methods herein disclosed and, more specifically, according to the general procedure described above.

[00263] Experimental description: 150 mg ibuprofen methyl ester were dissolved in 1.4 mL ethanol and added to 150 mL potassium phosphate buffer pH 8.0. Var3-4 was added to the mixture at a final concentration of 3 μ M. The mixture was split in 4 mL-aliquots into 15 mL scintillation vials equipped with a stir bar. 500 μ L 10 mM NADPH in KPi buffer were added to each vial and stirred for 2 minutes. 500 μ L cofactor regeneration solution containing 500 mM glucose-6-phosphate and 10 units/mL glucose-6-phosphate dehydrogenase were then added to each vial. The resulting mixtures were stirred at room temperature. After 48 hours, the reaction mixtures were joined together and extracted with chloroform (3x 50 mL). The organic phase was then dried over magnesium sulfate (MgSO_4) and evaporated in vacuo. Purification of the resulting oil by silica gel chromatography (5-40% ethyl acetate/hexane) afforded the activated product (methyl 2-(4'-(2''-hydroxy-2''-methylpropyl)phenyl)propanoate, 81 mg). 15 mg (0.06 mmol) of activated product were dissolved in 2 mL dry dichloromethane (CH_2Cl_2) and a catalytic amount (4 drops) of ethanol was added to the solution. The solution was cooled to -78°C (dry ice) and added with 11 μ L DAST (0.72 mmol). The reaction was stirred in dry ice for 16 hours. The reaction mixture was then added with 5 mL saturated sodium bicarbonate (NaHCO_3) and extracted with dichloromethane (3x 15 mL). The organic phase was then dried over magnesium sulfate (MgSO_4) and evaporated in vacuo. Purification of the resulting oil by silica gel chromatography (0-30% ethyl acetate/hexane) afforded the fluorinated product, methyl 2-(4'-(1''-fluoro-2''-methylpropyl)phenyl)propanoate (7 mg, 45% yield, colorless oil). $^1\text{H-NMR}$ (300 MHz, CDCl_3): δ 1.28 (s, 3H, CH_3), δ 1.35 (s, 3H, CH_3), δ 1.48 (d, $J=6.9\text{Hz}$, 3H, CH_3),

δ 2.87 (d, J: 20.4Hz, 2H), δ 3.65 (s, 3H, OCH₃), δ 3.70 (q, J= 7.15Hz, 1H), δ 7.17 (m, 4H); ¹³C-NMR (75 MHz, CDCl₃): δ 18.80, 26.83 (d, J: 24.2Hz), 45.24, 47.37 (d, J: 22.8Hz), 52.25, 129.12 (d, J: 258.8Hz), ca. 130, ca. 132, ca. 139, ca. 173; ¹⁹F-NMR (282 MHz, CDCl₃): δ -137.7 (m). HRMS (EI⁺): exact mass calculated for C₁₄H₁₉FO₂ requires m/z 238.1369, found 238.1370.

[00264] Example 10 and 11 illustrate the application of the systems and methods of the disclosure for regioselective fluorination of an organic molecule at weakly and non-reactive site, such as positions 1'' and 2'' of ibuprofen methyl ester (Schemes 10 and 11).

Example 12— Regioselective fluorination of dihydro-4-methoxymethyl-2-methyl- 5-phenyl-2-oxazoline.



Scheme 12.

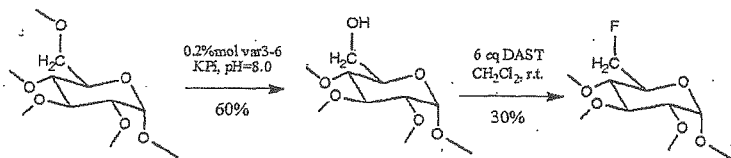
[00265] Dihydro-4-methoxymethyl-2-methyl-5-phenyl-2-oxazoline was subjected to selective fluorination of the target site C atom carrying a methoxy group, according to the systems and methods herein disclosed and, more specifically, according to the general procedure described above.

[00266] Experimental description: 100 mg dihydro-4-methoxymethyl-2-methyl-5-phenyl-2-oxazoline ibuprofen methyl ester were dissolved in 1.2 mL ethanol and added to 160 mL potassium phosphate buffer pH 8.0. Var3-5 was added to the mixture at a final concentration of 3 μ M. The mixture was split in 4 mL-aliquots into 15 mL scintillation vials equipped with a stir bar. 500 μ L 10 mM NADPH in KPi buffer were added to each vial and stirred for 2 minutes. 500 μ L cofactor regeneration solution containing 500 mM glucose-6-phosphate and 10 units/mL glucose-6-phosphate dehydrogenase were then added to each vial. The resulting mixtures were stirred at room temperature. After 48 hours, the reaction mixtures were joined together and extracted with chloroform (3x 50 mL). The organic phase was then dried over

magnesium sulfate (MgSO_4) and evaporated in vacuo. Purification of the resulting oil by silica gel chromatography (20% ethyl acetate/hexane) afforded the activated product (dihydro-4-hydroxymethyl-2-methyl-5-phenyl-2-oxazoline, 64 mg). 30 mg (0.16 mmol) of activated product were dissolved in 2 mL dry dichloromethane (CH_2Cl_2) and a catalytic amount (4 drops) of ethanol was added to the solution. The solution was cooled to -78°C (dry ice) and added with 22 μL DAST (0.32 mmol). The reaction was stirred in dry ice for 2 hours and then at -20°C for 16 hours. The reaction mixture was then added with 5 mL saturated sodium bicarbonate (NaHCO_3) and extracted with dichloromethane (3x 15 mL). The organic phase was then dried over magnesium sulfate (MgSO_4) and evaporated in vacuo. Purification of the resulting oil by silica gel chromatography (20% ethyl acetate/hexane) afforded the fluorinated product, dihydro-4-fluoromethyl-2-methyl-5-phenyl-2-oxazoline (12 mg, 40% yield, colorless oil). $^1\text{H-NMR}$ (300 MHz, CDCl_3): δ 1.59 (s, 3H, CH_3), δ 2.09 (dm, 1H, CH), δ 4.15-4.35 (m, 1H, CH), δ 5.66 (tm, 1H, CH), δ 7.37 (m, 5H, Ph); $^{19}\text{F-NMR}$ (282 MHz, CDCl_3): δ -114.14 (m). HRMS (EI+): exact mass calculated for $\text{C}_{11}\text{H}_{12}\text{FNO}$ requires m/z 193.0903, found 193.0917.

[00267] In another aspect, example 12 illustrates the application of the systems and methods of the disclosure for selective fluorination of an organic molecule at a site carrying a protected hydroxyl group, such as in dihydro-4-methoxymethyl-2-methyl-5-phenyl-2-oxazoline (Scheme 12).

Example 13— Regioselective fluorination of 1,2,3,4,6-pentamethyl- α -D-mannopyranoside.



Scheme 13.

[00268] 1,2,3,4,6-pentamethyl- α -D-mannopyranoside was subjected to regioselective fluorination of the target site C in position 6, according to the systems and methods herein disclosed and, more specifically, according to the general procedure described above.

[00269] Experimental description: 50 mg of 1,2,3,4,6-pentamethyl- α -D-mannopyranoside were dissolved in 0.5 mL ethanol and added to 100 mL potassium phosphate buffer pH 8.0. Var3-6 was added to the mixture at a final concentration of 4 μ M. The mixture was split in 4 mL-aliquots into 15 mL scintillation vials equipped with a stir bar. 500 μ L 10 mM NADPH in KPi buffer were added to each vial and stirred for 2 minutes. 500 μ L cofactor regeneration solution containing 500 mM glucose-6-phosphate and 10 units/mL glucose-6-phosphate dehydrogenase were then added to each vial. The resulting mixtures were stirred at room temperature. After 36 hours, the reaction mixtures were joined together and extracted with chloroform (3x 50 mL). The organic phase was then dried over magnesium sulfate (MgSO_4) and evaporated in vacuo. Purification of the resulting oil by silica gel chromatography (10% ethyl acetate/hexane) afforded the activated product (1,2,3,4-tetramethyl- α -D-mannopyranoside; 30 mg). 15 mg (0.1 mmol) of activated product were dissolved in 2 mL dry dichloromethane (CH_2Cl_2) and a catalytic amount (4 drops) of ethanol was added to the solution. The solution was cooled to -78°C (dry ice) and added with 85 μ L DAST (0.6 mmol). The reaction was stirred in dry ice for 2 hours and then at room temperature for 16 hours. The reaction mixture was then added with 5 mL saturated sodium bicarbonate (NaHCO_3) and extracted with dichloromethane (3x 15 mL). The organic phase was then dried over magnesium sulfate (MgSO_4) and evaporated in vacuo. Purification of the resulting oil by silica gel chromatography (10% ethyl acetate/hexane) afforded the fluorinated product, 6-deoxy-6-fluoro-1,2,3,4-tetramethyl- α -D-mannopyranoside (4.5 mg, 30% yield, colorless oil). $^1\text{H-NMR}$ (300 MHz, CDCl_3): δ 3.35 (s, 3H, OCH_3), 3.48 (s, 6H, OCH_3), 3.53 (s, 3H, OCH_3), 4.0-4.2 (m, 4H), 4.6 (dm, J: 47.5Hz, 2H, CH_2F); $^{13}\text{C-NMR}$ (75 MHz, CDCl_3): δ 55.24, 57.94, 59.24, 61.02, 71.12 (d, J: 18.4Hz), 73.2, 75.5, 82.49 (d, J: 192Hz), 98.26. $^{19}\text{F-NMR}$ (282 MHz, CDCl_3): δ -235.2 (m). ESI-MS: m/z calculated for Mw $\text{C}_{10}\text{H}_{19}\text{FO}_5$: 238.2533, found 238.28.

[00270] In another aspect, example 13 illustrates the application of the systems and methods of the disclosure for regioselective fluorination of an organic molecule at a defined site carrying a protected hydroxyl group in the presence of other identical functional groups, such as in 1,2,3,4,6-pentamethyl- α -D-mannopyranoside (Scheme 13).

[00271] The examples set forth above are provided to give those of ordinary skill in the art a complete disclosure and description of how to make and use the embodiments of the

methods and systems herein disclosed, and are not intended to limit the scope of the disclosure. Modifications of the above-described modes for carrying out the disclosure that are obvious to persons of skill in the art are intended to be within the scope of the following claims. All patents and publications mentioned in the specification are indicative of the levels of skill of those skilled in the art to which the disclosure pertains. All references cited in this disclosure are incorporated by reference to the same extent as if each reference had been incorporated by reference in its entirety individually.

[00272] In summary, a method and system, and in particular a chemo-enzymatic method and system for selectively fluorinating organic molecules on a target site wherein the target site is activated and then fluorinated are present together with a method and system for identifying a molecule having a biological activity. In particular, A chemo-enzymatic method for preparation of selectively fluorinated derivatives of organic compounds with diverse molecular structures is presented together with a system for fluorination of an organic molecule and a method for identification of a molecule having a biological activity.

[00273] It is to be understood that the embodiments are not limited to particular compositions or biological systems, which can, of course, vary. It is also to be understood that the terminology used herein is for the purpose of describing particular embodiments only, and is not intended to be limiting. As used in this specification and the appended claims, the singular forms "a," "an," and "the" include plural referents unless the content clearly dictates otherwise. The term "plurality" includes two or more referents unless the content clearly dictates otherwise. Unless defined otherwise, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which the disclosure pertains. Although any methods and materials similar or equivalent to those described herein can be used in the practice for testing of the disclosure(s), specific examples of appropriate materials and methods are described herein.

[00274] Unless otherwise indicated, the disclosure is not limited to specific molecular structures, substituents, synthetic methods, reaction conditions, or the like, as such may vary. It is also to be understood that the terminology used herein is for the purpose of describe particular embodiments only and is not intended to be limiting.

[00275] The entire disclosure of each document cited (including patents, patent applications, journal articles, abstracts, laboratory manuals, books, or other disclosures) in the Background, Detailed Description, and Examples is hereby incorporated herein by reference. Further, the hard copy of the sequence listing submitted herewith and the corresponding computer readable form are both incorporated herein by reference in their entireties.

[00276] A number of embodiments of the disclosure have been described. Nevertheless, it will be understood that various modifications may be made without departing from the spirit and scope of the disclosure. Accordingly, other embodiments are within the scope of the following claims.

REFERENCES

- Bass, S., V. Sorrells, et al. (1988). "Mutant Trp repressors with new DNA-binding specificities." *Science* 242(4876): 240-5.
- Beeson, T. D. and D. W. C. MacMillan (2005). "Enantioselective organocatalytic alpha-fluorination of aldehydes." *Journal of the American Chemical Society* 127(24): 8826-8828.
- Blee, E., A. L. Wilcox, et al. (1993). "Mechanism of Reaction of Fatty-Acid Hydroperoxides with Soybean Peroxygenase." *Journal of Biological Chemistry* 268(3): 1708-1715.
- Bobbio, C. and V. Gouverneur (2006). "Catalytic asymmetric fluorinations." *Org Biomol Chem* 4(11): 2065-75.
- Bohm, H. J., D. Banner, et al. (2004). "Fluorine in medicinal chemistry." *Chembiochem* 5(5): 637-43.
- Bornscheuer, U. T. (2003). "Immobilizing enzymes: how to create more suitable biocatalysts." *Angew. Chem. Int. Ed. Engl.* 42: 3336-3337.
- Botstein, D. and D. Shortle (1985). "Strategies and applications of in vitro mutagenesis." *Science* 229(4719): 1193-201.
- Braxton, S. and J. A. Wells (1991). "The importance of a distal hydrogen bonding group in stabilizing the transition state in subtilisin BPN'." *J Biol Chem* 266(18): 11797-800.
- Burke, T. R., B. Ye, et al. (1996). "Small molecule interactions with protein-tyrosine phosphatase PTP1B and their use in inhibitor design." *Biochemistry* 35(50): 15989-15996.
- Cahard, D., C. Audouard, et al. (2000). "Design, synthesis, and evaluation of a novel class of enantioselective electrophilic fluorinating agents: N-fluoro ammonium salts of cinchona alkaloids (F-CA-BF4)." *Organic Letters* 2(23): 3699-3701.
- Camarero, J. A. and A. R. Mitchell (2005). "Synthesis of proteins by native chemical ligation using Fmoc-based chemistry." *Protein Pept. Lett.* 12(8): 723-8.
- Cao, L. (2005). "Immobilised enzymes: science or art?" *Curr Opin Chem Biol* 9(2): 217-26.
- Carter, P. (1986). "Site-directed mutagenesis." *Biochem J* 237(1): 1-7.
- Casper, D., U. Yarpalvi, et al. (2000). "Ibuprofen protects dopaminergic neurons against glutamate toxicity in vitro." *Neurosci Lett* 289(3): 201-4.
- Chambers, R. D., J. Hutchinson, et al. (2000). *J. Fluorine Chem.* 102: 169.

- Chambers, R. D., C. J. Skinner, et al. (1996). *J. Chem. Soc., Perkin Trans. I*: 605.
- Cirino, P. C. and F. H. Arnold (2003). "A self-sufficient peroxide-driven hydroxylation biocatalyst." *Angewandte Chemie-International Edition* 42(28): 3299-3301.
- Clader, J. W. (2004). "The discovery of ezetimibe: a view from outside the receptor." *J. Med. Chem.* 47(1): 1-9.
- Dale, S. J. and I. R. Felix (1996). "Oligonucleotide-directed mutagenesis using an improved phosphorothioate approach." *Methods Mol Biol* 57: 55-64.
- Davis, F. A. and W. Han (1992). "Diastereoselective Fluorination of Chiral Imide Enolates Using N-Fluoro-O-Benzenedisulfonimide (Nfobs)." *Tetrahedron Letters* 33(9): 1153-1156.
- Davis, F. A., P. Zhou, et al. (1998). "Asymmetric fluorination of enolates with nonracemic N-fluoro-2,10-camphorsultams." *Journal of Organic Chemistry* 63(7): 2273-2280.
- De-Moura, N. F., E. Simionatto, et al. (2002). "Quinoline Alkaloids, Coumarins and Volatile Constituents of *Helietta longifolia*." *Planta Med.* 68: 631-634.
- De Souza, M. V. N. (2005). "The furan-2(5H)-ones: Recent synthetic methodologies and its application in total synthesis of natural products." *Mini-rev. Org. Chem.* 2(2): 139-145.
- Denisov, I. G., T. M. Makris, et al. (2005). "Structure and chemistry of cytochrome P450." *Chem. Rev.* 105(6): 2253-77.
- Eghedardazadeh, M. K. and S. Henikoff (1986). "Use of oligonucleotides to generate large deletions." *Nucleic Acids Res* 14(12): 5115.
- Enders, D., M. Potthoff, et al. (1997). "Regio- and enantioselective synthesis of alpha-fluoroketones by electrophilic fluorination of alpha-silylketone enolates with N-fluorobenzosulfonimide." *Angewandte Chemie-International Edition in English* 36(21): 2362-2364.
- Green, T. W. and P. G. M. Wuts (1999). *Protective Groups in Organic Synthesis*. New York, Wiley-Interscience.
- Grundstrom, T., W. M. Zenke, et al. (1985). "Oligonucleotide-directed mutagenesis by microscale 'shot-gun' gene synthesis." *Nucleic Acids Res* 13(9): 3305-16.
- Hamashima, Y. and M. Sodeoka (2006). "Enantioselective fluorination reactions catalyzed by chiral palladium complexes." *Synlett*(10): 1467-1478.
- Hanano, A., M. Burcklen, et al. (2006). "Plant seed peroxxygenase is an original heme-oxygenase with an EF-hand calcium binding motif." *Journal of Biological Chemistry* 281(44): 33140-33151.
- Harper, D. B. and D. O'Hagan (1994). "The fluorinated natural products." *Nat' Prod Rep* 11(2): 123-33.
- Hayashi, H., H. Sonoda, et al. (2002). "2,2-difluoro-1,3-dimethylimidazolidine (DFI). A new fluorinating agent." *Chemical Communications*(15): 1618-1619.
- Hintermann, L. and A. Togni (2000). "Catalytic enantioselective fluorination of beta-ketoesters." *Angewandte Chemie-International Edition* 39(23): 4359-+.
- Joo, H., Z. L. Lin, et al. (1999). "Laboratory evolution of peroxide-mediated cytochrome P450 hydroxylation." *Nature* 399(6737): 670-673.
- Kim, D. Y. and E. J. Park (2002). "Catalytic enantioselective fluorination of beta-keto esters by phase-transfer catalysis using chiral quaternary ammonium salts." *Organic Letters* 4(4): 545-547.
- Knight, D. W. (1994). *Contemporary Organic Synthesis* 1: 287.
- Kramer, W., V. Drutsa, et al. (1984). "The gapped duplex DNA approach to oligonucleotide-directed mutation construction." *Nucleic Acids Res* 12(24): 9441-56.

- Kramer, W. and H. J. Fritz (1987). "Oligonucleotide-directed construction of mutations via gapped duplex DNA." Methods Enzymol 154: 350-67.
- Kunkel, T. A., J. D. Roberts, et al. (1987). "Rapid and efficient site-specific mutagenesis without phenotypic selection." Methods Enzymol 154: 367-82.
- Lal, G. S., G. P. Pez, et al. (1999). "Bis(2-methoxyethyl)aminosulfur trichloride: a new broad-spectrum deoxofluorinating agent with enhanced thermal stability." J. Org. Chem. 64: 7048-54.
- Landwehr, M., M. Carbone, et al. (2007). "Diversification of catalytic function in a synthetic family of chimeric cytochrome p450s." Chem Biol 14(3): 269-78.
- Leuchtenberger, S., D. Beher, et al. (2006). "Selective modulation of Abeta42 production in Alzheimer's disease: non-steroidal anti-inflammatory drugs and beyond." Curr Pharm Des 12(33): 4337-55.
- Ling, M. M. and B. H. Robinson. (1997). "Approaches to DNA mutagenesis: an overview." Anal Biochem 254(2): 157-78.
- Ma, J. A. and D. Cahard (2004). "Asymmetric fluorination, trifluoromethylation, and perfluoroalkylation reactions." Chem Rev 104(12): 6119-46.
- Ma, J. A. and D. Cahard (2004). "Copper(II) triflate-bis(oxazoline)-catalysed enantioselective electrophilic fluorination of beta-ketoesters." Tetrahedron-Asymmetry 15(6): 1007-1011.
- Mandecki, W. (1986). "Oligonucleotide-directed double-strand break repair in plasmids of *Escherichia coli*: a method for site-specific mutagenesis." Proc Natl Acad Sci U S A 83(19): 7177-81.
- Marigo, M., D. I. Fielenbach, et al. (2005). "Enantioselective formation of stereogenic carbon-fluorine centers by a simple catalytic method." Angewandte Chemie-International Edition 44(24): 3703-3706.
- Matsunaga, I., T. Sumimoto, et al. (2002). "Functional modulation of a peroxxygenase cytochrome P450: novel insight into the mechanisms of peroxxygenase and peroxidase enzymes." Febs Letters 528(1-3): 90-94.
- Matsunaga, I., A. Yamada, et al. (2002). "Enzymatic reaction of hydrogen peroxide-dependent peroxxygenase cytochrome P450s: kinetic deuterium isotope effects and analyses by resonance Raman spectroscopy." Biochemistry 41(6): 1886-92.
- Middleton, W. J. (1975). "New Fluorinating Reagents - Dialkylaminosulfur Fluorides." Journal of Organic Chemistry 40(5): 574-578.
- Mikolajczyk, M., M. Mikina, et al. (1999). "New phosphonate-mediated syntheses of cyclopentanoids and prostaglandins." Pure Appl. Chem. 71(3): 473-480.
- Nakamaye, K. L. and F. Eckstein (1986). "Inhibition of restriction endonuclease Nci I cleavage by phosphorothioate groups and its application to oligonucleotide-directed mutagenesis." Nucleic Acids Res 14(24): 9679-98.
- Nambiar, K. P., J. Stackhouse, et al. (1984). "Total synthesis and cloning of a gene coding for the ribonuclease S protein." Science 223(4642): 1299-301.
- Nyffeler, P. T., S. G. Duron, et al. (2005). "Selectfluor: Mechanistic insight and applications." Angewandte Chemie-International Edition 44(2): 192-212.
- Ojima, I. (2004). "Use of fluorine in the medicinal chemistry and chemical biology of bioactive compounds—a case study on fluorinated taxane anticancer agents." ChemBiochem 5(5): 628-35.
- Otey, C. R., M. Landwehr, et al. (2006). "Structure-Guided Recombination Creates an Artificial Family of Cytochromes P450." PLoS Biol 4(5): e112.
- Park, B. K., N. R. Kitteringham, et al. (2001). "Metabolism of fluorine-containing drugs." Annu. Rev. Pharmacol. Toxicol. 41: 443-70.

- Presnell, S. R. and F. E. Cohen (1989). Proc. Natl. Acad. Sci. U.S.A. 86: 6592.
- Pylypenko, O. and I. Schlichting (2004). "Structural aspects of ligand binding to and electron transfer in bacterial and fungal P450s." Annu. Rev. Biochem. 73: 991-1018.
- Sakamoto, T., J. M. Joern, et al. (2001). "Laboratory evolution of toluene dioxygenase to accept 4-picoline as a substrate." Applied and Environmental Microbiology 67(9): 3882-+.
- Sayers, J. R., W. Schmidt, et al. (1988). "5'-3' exonucleases in phosphorothioate-based oligonucleotide-directed mutagenesis." Nucleic Acids Res 16(3): 791-802.
- Schwarzer, D. and P. A. Cole (2005). "Protein semisynthesis and expressed protein ligation: chasing a protein's tail." Curr. Opin. Chem. Biol. 9(6): 561-9.
- Shibata, N., T. Ishimaru, et al. (2004). "First enantio-flexible fluorination reaction using metal-bis(oxazoline) complexes." Synlett(10): 1703-1706.
- Shibata, N., E. Suzuki, et al. (2000). "A fundamentally new approach to enantioselective fluorination based on cinchona alkaloid derivatives/selectfluor combination." Journal of the American Chemical Society 122(43): 10728-10729.
- Shimizu, Y., Y. Kuruma, et al. (2006). "Cell-free translation systems for protein engineering." FEBS J. 273(18): 4133-40.
- Smith, M. (1985). "In vitro mutagenesis." Annu Rev Genet 19: 423-62.
- Swain, C. and N. M. J. Rupniak (1999). "Progress in the development of neurokinin antagonists." Annual Reports in Medicinal Chemistry, Vol 34 34: 51-60.
- Taylor, J. W., W. Schmidt, et al. (1985). "The use of phosphorothioate-modified DNA in restriction enzyme reactions to prepare nicked DNA." Nucleic Acids Res 13(24): 8749-64.
- Taylor, S. D., C. C. Kotoris, et al. (1999). "Recent advances in electrophilic fluorination." Tetrahedron 55(43): 12431-12477.
- Togni, A., A. Mezzetti, et al. (2001). "Developing catalytic enantioselective fluorination." Chimia 55(10): 801-805.
- Townsend, K. P. and D. Pratico (2005). "Novel therapeutic opportunities for Alzheimer's disease: focus on nonsteroidal anti-inflammatory drugs." FASEB J 19(12): 1592-601.
- van Beilen, J. B. and E. G. Funhoff (2007). "Alkane hydroxylases involved in microbial alkane degradation." Appl Microbiol Biotechnol 74(1): 13-21.
- van Niel, M. B., I. Collins, et al. (1999). "Fluorination of 3-(3-(piperidin-1-yl)propyl)indoles and 3-(3-(piperazin-1-yl)propyl)indoles gives selective human 5-HT1D receptor ligands with improved pharmacokinetic profiles." Journal of Medicinal Chemistry 42(12): 2087-2104.
- Wang, L., J. Xie, et al. (2006). "Expanding the genetic code." Annu. Rev. Biophys. Biomol. Struct. 35: 225-249.
- Wells, J. A., M. Vasser, et al. (1985). "Cassette mutagenesis: an efficient method for generation of multiple mutations at defined sites." Gene 34(2-3): 315-23.
- Yamazaki, Y., S. Yusa, et al. (1996). "Effect of fluorine substitution of alpha- and beta-hydrogen atoms in ethyl phenylacetate and phenylpropionate on their stereoselective hydrolysis by cultured cancer cells." J. Fluorine Chem. 79(2): 167-171.
- Zoller, M. J. (1992). "New recombinant DNA methodology for protein engineering." Curr Opin Biotechnol 3(4): 348-54.
- Zoller, M. J. and M. Smith (1983). "Oligonucleotide-directed mutagenesis of DNA fragments cloned into M13 vectors." Methods Enzymol 100: 468-500.
- Zoller, M. J. and M. Smith (1987). "Oligonucleotide-directed mutagenesis: a simple method using two oligonucleotide primers and a single-stranded DNA template." Methods Enzymol 154: 329-50.

WHAT IS CLAIMED IS

1. A method for fluorinating an organic molecule, the method comprising

providing an organic molecule comprising a target site;

providing an oxygenase enzyme that oxidizes the target site by introduction of an oxygen-containing functional group;

contacting the oxygenase enzyme with the organic molecule for a time and under condition to allow introduction of the oxygen-containing functional group on the target site thus providing an oxidized organic molecule;

providing a fluorinating agent and

contacting the fluorinating agent with the oxidized organic molecule, for a time and under condition to allow replacement of the oxygen-containing functional group with fluorine.

2. The method of claim 1, wherein the organic molecule is selected from the group consisting of C₅-C₂₂ alkanes, fatty acids, steroids, terpenes, aromatic hydrocarbons, polyketides, prostaglandins, terpenes, statins, amino acids, flavonoids and stilbenes, and wherein the oxygenase is a heme-containing oxygenase or variant thereof.

3. The method of claim 1, wherein the organic molecule is a molecule selected from the group consisting of C₁-C₂₄ linear and branched alkanes, alkenes and aromatic hydrocarbons, and wherein the oxygenase is a non-heme containing monooxygenases or variant thereof.

4. The method of claim 1, wherein the organic molecule is selected from the group consisting of substituted or non-substituted monocyclic, polycyclic and heterocyclic aromatic compounds, and wherein the oxygenase is a dioxygenase or variant thereof.

5. The method of claim 1, wherein the organic molecule is selected from the group consisting of fatty acids, 8- and 12-pNCA, indole, aniline, *p*-nitrophenol, heterocyclic derivatives, statins and naphthyl derivatives, and wherein the oxygenase is a dioxygenase or variant thereof.

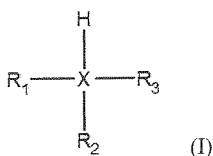
6. The method of claim 2, wherein the organic molecule is selected from the group consisting of C₅-C₂₂ alkanes, cyclic alkanes, cyclic alkenes, alkane derivatives, alkene derivatives, C₁₀-

C₂₀ fatty acids, steroids, terpenes, aromatic hydrocarbons, natural products and natural product analogues including polyketides, prostaglandines, thromboxanes, leukotrienes, anthraquinones, tetracyclines, anthracyclines, polyenes, statins, amino acids, flavonoids, stilbenes, alkaloids including lysine-derived, nicotinic acid-derived, tyrosine-derived, tryptophan-derived, anthranilic acid-derived, histidine-derived, purine-derived alkaloids, beta-lactams, aminoglycosides, polymyxins, quinolones, synthetic derivatives including aromatic heterocyclic derivatives including phenyl-, pyrimidine-, pyridine-, piperidine-, pyrrole-, furan-, triazol-, thiophene-, pyrazole-, imidazole-, tetrazole-, oxazole-, isoxazole-, thiazole-, isothiazole-, pyran-, pyridazine-, pyrazine-, piperazine-, thiazine- and oxazine-derivatives, and wherein the heme-containing oxygenase is a P450 oxygenase or a variant thereof.

7. The method of claim 6, wherein the P450 oxygenase is selected from the group consisting of CYP102A1, CYP102A2, CYP102A3, CYP102A5, , CYP102E1, CYP102A6, CYP101A1, CYP106A2, CYP153A6, CYP153A7, CYP153A8, CYP153A11, CYP153D2, CYP153D3, P450cin, P450terp, P450eryF, CYP1A2, CYP2C8, CYP2C9, CYP2C19, CYP2D6, CYP2E1, CYP2F1, CYP3A4, CYP153-AlkB_{Burk} , CYP153-EB104, CYP153-OC4, P450_{BSP} (CYP152A1), and P450_{SPa} (CYP152B1).

8. The method of claim 7, wherein the variant is a P450 oxygenase having a sequence selected from the group consisting of SEQ ID NO: 21, SEQ ID NO: 22, SEQ ID NO: 23, SEQ ID NO:24, SEQ ID NO: 25, SEQ ID NO: 26, SEQ ID NO: 27, SEQ ID NO: 28, SEQ ID NO: 29, SEQ ID NO: 30, SEQ ID NO: 31, SEQ ID NO: 32, SEQ ID NO: 33, SEQ ID NO: 34, SEQ ID NO: 35, SEQ ID NO: 36, SEQ ID NO: 37, SEQ ID NO: 38, SEQ ID NO: 39, SEQ ID NO: 40, SEQ ID NO: 41, SEQ ID NO: 42, SEQ ID NO: 43, SEQ ID NO: 44, SEQ ID NO: 45, SEQ ID NO: 46, SEQ ID NO:47, SEQ ID NO: 48, SEQ ID NO: 49, SEQ ID NO:50, SEQ ID NO: 51, SEQ ID NO: 52; SEQ ID NO: 63, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO: 67. SEQ ID NO:68 and SEQ ID NO: 69

9. The method of claim 1, wherein the organic molecule has the structure of formula (I)

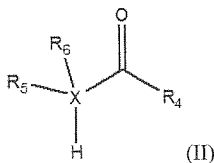


in which X = C atom is the target site, and R₁, R₂, and R₃ are independently selected from the group consisting of hydrogen, aliphatic, aryl, substituted aliphatic, substituted aryl, heteroatom-containing aliphatic, heteroatom-containing aryl, substituted heteroatom-containing aliphatic, substituted heteroatom-containing aryl, alkoxy, aryloxy, and functional groups (FG) or are taken together to form a ring, such that the C atom is a secondary or tertiary carbon atom and the oxidizing agent is an oxygenase or variant thereof.

10. The method of claim 9, wherein the oxygenase is a monooxygenase or a peroxygenase.

11. The method of claim 10, wherein the oxygenase or variant thereof is selected from the group consisting of butane monooxygenase, CYP102A1, CYP101A1, CYP102A2, CYP102A3, and CYP153A6, CYP153A7, CYP153A8, CYP153A11, CYP153D2, CYP106A, and any oxygenase having a sequence selected from the group consisting of SEQ ID NO:46, SEQ ID NO: 50, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:42, SEQ ID NO:44, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO: 65, SEQ ID NO: 69 SEQ ID NO: 62, and SEQ ID NO: 63.

12. The method of claim 1, where the organic molecule has the structure of formula (II)



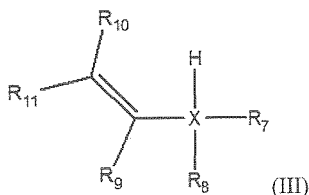
in which X=C is the target site, and R₄, R₅, and R₆ are independently selected from the group consisting of hydrogen, aliphatic, aryl, substituted aliphatic, substituted aryl, heteroatom-containing aliphatic, heteroatom-containing aryl, substituted heteroatom-containing aliphatic, substituted heteroatom-containing aryl, alkoxy, aryloxy, and functional groups (FG) or are taken together to form a ring, such that the C atom is a secondary or tertiary carbon atom and the oxidizing agent is an oxygenase or a variant thereof.

13. The method of claim 8, wherein the oxygenase is a monooxygenase or a peroxygenase.

14. The method of claim 8, wherein the oxygenase or variant thereof is selected from the group consisting of CYP102A1, , CYP101A1, , CYP1A2, CYP2C9, CYP2C19, CYP2D6, CYP2E1, CYP3A4, CYP152A1, CYP152B1, and any oxygenase having a sequence selected

from the group consisting of SEQ ID NO:46, SEQ ID NO:50, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:9, SEQ ID NO:27, SEQ ID NO:31, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:39, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:65, and SEQ ID NO:68.

15. The method of claim 1, wherein the organic molecule has the structure of formula (III)

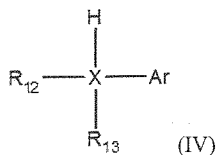


in which X is the target site C atom, and R₇, R₈, R₉, R₁₀ and R₁₁ are independently selected from the group consisting of hydrogen, aliphatic, aryl, substituted aliphatic, substituted aryl, heteroatom-containing aliphatic, heteroatom-containing aryl, substituted heteroatom-containing aliphatic, substituted heteroatom-containing aryl, alkoxy, aryloxy, and functional groups (FG) or are taken together to form a ring, such that the C atom is a secondary or tertiary carbon atom and the oxidizing agent is an oxygenase or a variant thereof.

16. The method of claim 15, wherein the oxygenase wherein the oxygenase is a monooxygenase or a peroxygenase.

17. The method of claim 16, wherein the oxygenase or variant thereof is selected from the group consisting of CYP2C19, CYP2D6, and any oxygenase having a sequence selected from the group consisting of SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:28, SEQ ID NO:27, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:33, SEQ ID NO:39, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:65, SEQ ID NO:67, SEQ ID NO:69.

18. The method of claim 1, wherein the organic molecule has the structure of formula (IV)

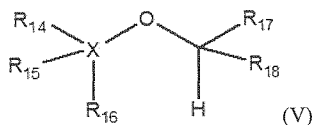


in which X= C is the target site, Ar can be a C₅-C₂₄ aryl, C₅-C₂₄ substituted aryl, C₅-C₂₄ substituted heteroatom-containing aryl or C₅-C₂₄ substituted heteroatom-containing aryl, while R₁₂ and R₁₃ are independently selected from the group consisting of hydrogen, aliphatic, aryl, substituted aliphatic, substituted aryl, heteroatom-containing aliphatic, heteroatom-containing aryl, substituted heteroatom-containing aliphatic, substituted heteroatom-containing aryl, alkoxy, aryloxy and functional groups (FG), or are taken together to form a ring, such that the carbon atom is a secondary or tertiary carbon atom, and the oxydizing agent is an oxygenase or a variant thereof

19. The method of claim 18, wherein the oxygenase is a monooxygenase or a peroxygenase.

20. The method of claim 19, wherein the oxygenase or variant thereof is selected from the group consisting of CYP102A1 and any oxygenase having a sequence selected from the group consisting of SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:39, SEQ ID NO:50, SEQ ID NO: 67, and SEQ ID NO: 69.

21. The method of claim 1, wherein the organic molecule has the structure of formula (V)



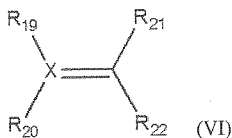
in which X=C is the target site, R₁₄, R₁₅, R₁₆, R₁₇, R₁₈ are independently selected from the group consisting of hydrogen, aliphatic, aryl, substituted aliphatic, substituted aryl, heteroatom-containing aliphatic, heteroatom-containing aryl, substituted heteroatom-containing aliphatic, substituted heteroatom-containing aryl, alkoxy, aryloxy, and functional groups (FG), or are taken together to form a ring, such that the C atom is a secondary or tertiary carbon atom, and the oxydizing agent is an oxygenase or variant thereof.

22. The method of claim 21, wherein the oxygenase is a monooxygenase or a peroxygenase.

23. The method of claim 22, wherein the oxygenase or variant thereof is selected from the group consisting of CYP3A4 and any oxygenase having a sequence selected from the group consisting of SEQ ID NO:50, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:31, SEQ ID NO:33, SEQ ID NO:38, SEQ ID NO:41, SEQ ID NO:40,

SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:39, SEQ ID NO:31 and SEQ ID NO:69.

24. The method of claim 1, wherein the organic molecule has the structure of formula (VI)



in which X is the target site C atom, and R₁₉, R₂₀, R₂₁, R₂₂ are independently selected from the group consisting of hydrogen, aliphatic, aryl, substituted aliphatic, substituted aryl, heteroatom-containing aliphatic, heteroatom-containing aryl, substituted heteroatom-containing aliphatic, substituted heteroatom-containing aryl, and functional groups (FG) or are taken together to form a ring representing a cycloalkenyl, substituted cycloalkenyl, heteroatom-containing cycloalkenyl, or a substituted heteroatom-containing cycloalkenyl derivative, and the oxidizing agent is an oxygenase or variant thereof.

25. The method of claim 24, wherein the oxygenase is a dioxygenase a monooxygenase or a peroxygenase.

26. The method of claim 25, wherein the oxygenase or variant thereof is selected from the group consisting of toluene dioxygenase CYP102A1 and any oxygenase having a sequence selected from the group consisting of SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:40, SEQ ID NO:47, SEQ ID NO:46, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:51, SEQ ID NO:52.

27. The method of claim 1 where the fluorinating agent is a nucleophilic fluorination reagent.

28. The method of claim 27, wherein the fluorinating agent is selected from the group consisting of diethylaminosulfur trifluoride, bis-(2-methoxyethyl)-aminosulfur trifluoride, and 2,2-difluoro-1,3-dimethylimidazolidine (DFI).

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt
SEQUENCE LISTING

<110> California Institute of Technology
Fasan, Rudi
Arnold, Frances H.

<120> Methods and Systems for Selective Fluorination of Organic
Molecules

<130> P008-CIT

<140> To be determined
<141> 2007-08-04

<150> 60/835,613
<151> 2006-08-04

<160> 70

<170> PatentIn version 3.4

<210> 1
<211> 10
<212> PRT
<213> Artificial sequence

<220>
<223> Cytochrome P450 signature sequence

<220>
<221> MISC_FEATURE
<222> (2)..(2)
<223> Xaa can be any amino acid

<220>
<221> MISC_FEATURE
<222> (3)..(3)
<223> Xaa can be any amino acid

<220>
<221> MISC_FEATURE
<222> (5)..(5)
<223> Xaa can be any amino acid

<220>
<221> MISC_FEATURE
<222> (6)..(6)
<223> Xaa can be Histidine or Arginine

<220>
<221> MISC_FEATURE
<222> (7)..(7)
<223> Xaa can be any amino acid

<220>
<221> MISC_FEATURE
<222> (9)..(9)
<223> Xaa can be any amino acid

<400> 1

Phe Xaa Xaa Gly Xaa Xaa Xaa Cys Xaa Gly

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.TXT

1

5

10

<210> 2
 <211> 1048
 <212> PRT
 <213> Bacillus megaterium

<220>
 <221> MISC_FEATURE
 <222> (1)..(1048)
 <223> Cytochrome P450 enzyme CYP102A1

<400> 2

Thr Ile Lys Glu Met Pro Gln Pro Lys Thr Phe Gly Glu Leu Lys Asn
 1 5 10 15

Leu Pro Leu Leu Asn Thr Asp Lys Pro Val Gln Ala Leu Met Lys Ile
 20 25 30

Ala Asp Glu Leu Gly Glu Ile Phe Lys Phe Glu Ala Pro Gly Arg Val
 35 40 45

Thr Arg Tyr Leu Ser Ser Gln Arg Leu Ile Lys Glu Ala Cys Asp Glu
 50 55 60

Ser Arg Phe Asp Lys Asn Leu Ser Gln Ala Leu Lys Phe Val Arg Asp
 65 70 75 80

Phe Ala Gly Asp Gly Leu Phe Thr Ser Trp Thr His Glu Lys Asn Trp
 85 90 95

Lys Lys Ala His Asn Ile Leu Leu Pro Ser Phe Ser Gln Gln Ala Met
 100 105 110

Lys Gly Tyr His Ala Met Met Val Asp Ile Ala Val Gln Leu Val Gln
 115 120 125

Lys Trp Glu Arg Leu Asn Ala Asp Glu His Ile Glu Val Pro Glu Asp
 130 135 140

Met Thr Arg Leu Thr Leu Asp Thr Ile Gly Leu Cys Gly Phe Asn Tyr
 145 150 155 160

Arg Phe Asn Ser Phe Tyr Arg Asp Gln Pro His Pro Phe Ile Thr Ser
 165 170 175

Met Val Arg Ala Leu Asp Glu Ala Met Asn Lys Leu Gln Arg Ala Asn
 180 185 190

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Pro Asp Asp Pro Ala Tyr Asp Glu Asn Lys Arg Gln Phe Gln Glu Asp
195 200 205

Ile Lys Val Met Asn Asp Leu Val Asp Lys Ile Ile Ala Asp Arg Lys
210 215 220

Ala Ser Gly Glu Gln Ser Asp Asp Leu Leu Thr His Met Leu Asn Gly
225 230 235 240

Lys Asp Pro Glu Thr Gly Glu Pro Leu Asp Asp Glu Asn Ile Arg Tyr
245 250 255

Gln Ile Ile Thr Phe Leu Ile Ala Gly His Glu Thr Thr Ser Gly Leu
260 265 270

Leu Ser Phe Ala Leu Tyr Phe Leu Val Lys Asn Pro His Val Leu Gln
275 280 285

Lys Ala Ala Glu Glu Ala Ala Arg Val Leu Val Asp Pro Val Pro Ser
290 295 300

Tyr Lys Gln Val Lys Gln Leu Lys Tyr Val Gly Met Val Leu Asn Glu
305 310 315 320

Ala Leu Arg Leu Trp Pro Thr Ala Pro Ala Phe Ser Leu Tyr Ala Lys
325 330 335

Glu Asp Thr Val Leu Gly Gly Glu Tyr Pro Leu Glu Lys Gly Asp Glu
340 345 350

Leu Met Val Leu Ile Pro Gln Leu His Arg Asp Lys Thr Ile Trp Gly
355 360 365

Asp Asp Val Glu Glu Phe Arg Pro Glu Arg Phe Glu Asn Pro Ser Ala
370 375 380

Ile Pro Gln His Ala Phe Lys Pro Phe Gly Asn Gly Gln Arg Ala Cys
385 390 395 400

Ile Gly Gln Gln Phe Ala Leu His Glu Ala Thr Leu Val Leu Gly Met
405 410 415

Met Leu Lys His Phe Asp Phe Glu Asp His Thr Asn Tyr Glu Leu Asp
420 425 430

Ile Lys Glu Thr Leu Thr Leu Lys Pro Glu Gly Phe Val Val Lys Ala
435 440 445

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Lys Ser Lys Lys Ile Pro Leu Gly Gly Ile Pro Ser Pro Ser Thr Glu
450 455 460

Gln Ser Ala Lys Lys Val Arg Lys Lys Ala Glu Asn Ala His Asn Thr
465 470 475 480

Pro Leu Leu Val Leu Tyr Gly Ser Asn Met Gly Thr Ala Glu Gly Thr
485 490 495

Ala Arg Asp Leu Ala Asp Ile Ala Met Ser Lys Gly Phe Ala Pro Gln
500 505 510

Val Ala Thr Leu Asp Ser His Ala Gly Asn Leu Pro Arg Glu Gly Ala
515 520 525

Val Leu Ile Val Thr Ala Ser Tyr Asn Gly His Pro Pro Asp Asn Ala
530 535 540

Lys Gln Phe Val Asp Trp Leu Asp Gln Ala Ser Ala Asp Glu Val Lys
545 550 555 560

Gly Val Arg Tyr Ser Val Phe Gly Cys Gly Asp Lys Asn Trp Ala Thr
565 570 575

Thr Tyr Gln Lys Val Pro Ala Phe Ile Asp Glu Thr Leu Ala Ala Lys
580 585 590

Gly Ala Glu Asn Ile Ala Asp Arg Gly Glu Ala Asp Ala Ser Asp Asp
595 600 605

Phe Glu Gly Thr Tyr Glu Glu Trp Arg Glu His Met Trp Ser Asp Val
610 615 620

Ala Ala Tyr Phe Asn Leu Asp Ile Glu Asn Ser Glu Asp Asn Lys Ser
625 630 635 640

Thr Leu Ser Leu Gln Phe Val Asp Ser Ala Ala Asp Met Pro Leu Ala
645 650 655

Lys Met His Gly Ala Phe Ser Thr Asn Val Val Ala Ser Lys Glu Leu
660 665 670

Gln Gln Pro Gly Ser Ala Arg Ser Thr Arg His Leu Glu Ile Glu Leu
675 680 685

Pro Lys Glu Ala Ser Tyr Gln Glu Gly Asp His Leu Gly Val Ile Pro
Page 4

Printed: 10/30/2007

SPONSOR

PCT/US2007/017409

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

690

695

P008-CIT_ST25.txt

700

Arg Asn Tyr Glu Gly Ile Val Asn Arg Val Thr Ala Arg Phe Gly Leu
705 710 715 720

Asp Ala Ser Gln Gln Ile Arg Leu Glu Ala Glu Glu Glu Lys Leu Ala
725 730 735

His Leu Pro Leu Ala Lys Thr Val Ser Val Glu Glu Leu Leu Gln Tyr
740 745 750

Val Glu Leu Gln Asp Pro Val Thr Arg Thr Gln Leu Arg Ala Met Ala
755 760 765

Ala Lys Thr Val Cys Pro Pro His Lys Val Glu Leu Glu Ala Leu Leu
770 775 780

Glu Lys Gln Ala Tyr Lys Glu Gln Val Leu Ala Lys Arg Leu Thr Met
785 790 795 800

Leu Glu Leu Leu Glu Lys Tyr Pro Ala Cys Glu Met Lys Phe Ser Glu
805 810 815

Phe Ile Ala Leu Leu Pro Ser Ile Arg Pro Arg Tyr Tyr Ser Ile Ser
820 825 830

Ser Ser Pro Arg Val Asp Glu Lys Gln Ala Ser Ile Thr Val Ser Val
835 840 845

Val Ser Gly Glu Ala Trp Ser Gly Tyr Gly Glu Tyr Lys Gly Ile Ala
850 855 860

Ser Asn Tyr Leu Ala Glu Leu Gln Glu Gly Asp Thr Ile Thr Cys Phe
865 870 875 880

Ile Ser Thr Pro Gln Ser Glu Phe Thr Leu Pro Lys Asp Pro Glu Thr
885 890 895

Pro Leu Ile Met Val Gly Pro Gly Thr Gly Val Ala Pro Phe Arg Gly
900 905 910

Phe Val Gln Ala Arg Lys Gln Leu Lys Glu Gln Gly Gln Ser Leu Gly
915 920 925

Glu Ala His Leu Tyr Phe Gly Cys Arg Ser Pro His Glu Asp Tyr Leu
930 935 940

Title: "Methods and systems for selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Tyr Gln Glu Glu Leu Glu Asn Ala Gln Ser Glu Gly Ile Ile Thr Leu
 945 950 955 960

His Thr Ala Phe Ser Arg Met Pro Asn Gln Pro Lys Thr Tyr Val Gln
 965 970 975

His Val Met Glu Gln Asp Gly Lys Lys Leu Ile Glu Leu Leu Asp Gln
 980 985 990

Gly Ala His Phe Tyr Ile Cys Gly Asp Gly Ser Gln Met Ala Pro Ala
 995 1000 1005

Val Glu Ala Thr Leu Met Lys Ser Tyr Ala Asp Val His Gln Val
 1010 1015 1020

Ser Glu Ala Asp Ala Arg Leu Trp Leu Gln Gln Leu Glu Glu Lys
 1025 1030 1035

Gly Arg Tyr Ala Lys Asp Val Trp Ala Gly
 1040 1045

<210> 3
 <211> 1059
 <212> PRT
 <213> Bacillus subtilis

<220>
 <221> MISC_FEATURE
 <222> (1) (1059)
 <223> Cytochrome P450 enzyme CYP102A2

<400> 3

Lys Glu Thr Ser Pro Ile Pro Gln Pro Lys Thr Phe Gly Pro Leu Gly
 1 5 10 15

Asn Leu Pro Leu Ile Asp Lys Asp Lys Pro Thr Leu Ser Leu Ile Lys
 20 25 30

Leu Ala Glu Glu Gln Gly Pro Ile Phe Gln Ile His Thr Pro Ala Gly
 35 40 45

Thr Thr Ile Val Val Ser Gly His Glu Leu Val Lys Glu Val Cys Asp
 50 55 60

Glu Glu Arg Phe Asp Lys Ser Ile Glu Gly Ala Leu Glu Lys Val Arg
 65 70 75 80

Ala Phe Ser Gly Asp Gly Leu Phe Thr Ser Trp Thr His Glu Pro Asn
 85 90 95

Printed: 10/30/2007

Page: 1

PCT/US2007/017409

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Trp Arg Lys Ala His Asn Ile Leu Met Pro Thr Phe Ser Gln Arg Ala
100 105 110

Met Lys Asp Tyr His Glu Lys Met Val Asp Ile Ala Val Gln Leu Ile
115 120 125

Gln Lys Trp Ala Arg Leu Asn Pro Asn Glu Ala Val Asp Val Pro Gly
130 135 140

Asp Met Thr Arg Leu Thr Leu Asp Thr Ile Gly Leu Cys Gly Phe Asn
145 150 155 160

Tyr Arg Phe Asn Ser Tyr Tyr Arg Glu Thr Pro His Pro Phe Ile Asn
165 170 175

Ser Met Val Arg Ala Leu Asp Glu Ala Met His Gln Met Gln Arg Leu
180 185 190

Asp Val Gln Asp Lys Leu Met Val Arg Thr Lys Arg Gln Phe Arg Tyr
195 200 205

Asp Ile Gln Thr Met Phe Ser Leu Val Asp Ser Ile Ile Ala Glu Arg
210 215 220

Arg Ala Asn Gly Asp Gln Asp Glu Lys Asp Leu Leu Ala Arg Met Leu
225 230 235 240

Asn Val Glu Asp Pro Glu Thr Gly Glu Lys Leu Asp Asp Glu Asn Ile
245 250 255

Arg Phe Gln Ile Ile Thr Phe Leu Ile Ala Gly His Glu Thr Thr Ser
260 265 270

Gly Leu Leu Ser Phe Ala Thr Tyr Phe Leu Leu Lys His Pro Asp Lys
275 280 285

Leu Lys Lys Ala Tyr Glu Glu Val Asp Arg Val Leu Thr Asp Ala Ala
290 295 300

Pro Thr Tyr Lys Gln Val Leu Glu Leu Thr Tyr Ile Arg Met Ile Leu
305 310 315 320

Asn Glu Ser Leu Arg Leu Trp Pro Thr Ala Pro Ala Phe Ser Leu Tyr
325 330 335

Pro Lys Glu Asp Thr Val Ile Gly Gly Lys Phe Pro Ile Thr Thr Asn

08/04/2007

Printed: 10/30/2007

SEQUENCE

PCT/US2007/017409

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EP511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

340

345

350

Asp Arg Ile Ser Val Leu Ile Pro Gln Leu His Arg Asp Arg Asp Ala
355 360 365

Trp Gly Lys Asp Ala Glu Glu Phe Arg Pro Glu Arg Phe Glu His Gln
370 375 380

Asp Gln Val Pro His His Ala Tyr Lys Pro Phe Gly Asn Gly Gln Arg
385 390 395 400

Ala Cys Ile Gly Met Gln Phe Ala Leu His Glu Ala Thr Leu Val Leu
405 410 415

Gly Met Ile Leu Lys Tyr Phe Thr Leu Ile Asp His Glu Asn Tyr Glu
420 425 430

Leu Asp Ile Lys Gln Thr Leu Thr Leu Lys Pro Gly Asp Phe His Ile
435 440 445

Ser Val Gln Ser Arg His Gln Glu Ala Ile His Ala Asp Val Gln Ala
450 455 460

Ala Glu Lys Ala Ala Pro Asp Glu Gln Lys Glu Lys Thr Glu Ala Lys
465 470 475 480

Gly Ala Ser Val Ile Gly Leu Asn Asn Arg Pro Leu Leu Val Leu Tyr
485 490 495

Gly Ser Asp Thr Gly Thr Ala Glu Gly Val Ala Arg Glu Leu Ala Asp
500 505 510

Thr Ala Ser Leu His Gly Val Arg Thr Lys Thr Ala Pro Leu Asn Asp
515 520 525

Arg Ile Gly Lys Leu Pro Lys Glu Gly Ala Val Val Ile Val Thr Ser
530 535 540

Ser Tyr Asn Gly Lys Pro Pro Ser Asn Ala Gly Gln Phe Val Gln Trp
545 550 555 560

Leu Gln Glu Ile Lys Pro Gly Glu Leu Glu Gly Val His Tyr Ala Val
565 570 575

Phe Gly Cys Gly Asp His Asn Trp Ala Ser Thr Tyr Gln Tyr Val Pro
580 585 590

08/04/2007

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Arg Phe Ile Asp Glu Gln Leu Ala Glu Lys Gly Ala Thr Arg Phe Ser
595 600 605

Ala Arg Gly Glu Gly Asp Val Ser Gly Asp Phe Glu Gly Gln Leu Asp
610 615 620

Glu Trp Lys Lys Ser Met Trp Ala Asp Ala Ile Lys Ala Phe Gly Leu
625 630 635 640

Glu Leu Asn Glu Asn Ala Asp Lys Glu Arg Ser Thr Leu Ser Leu Gln
645 650 655

Phe Val Arg Gly Leu Gly Glu Ser Pro Leu Ala Arg Ser Tyr Glu Ala
660 665 670

Ser His Ala Ser Ile Ala Glu Asn Arg Glu Leu Gln Ser Ala Asp Ser
675 680 685

Asp Arg Ser Thr Arg His Ile Glu Ile Ala Leu Pro Pro Asp Val Glu
690 695 700

Tyr Gln Glu Gly Asp His Leu Gly Val Leu Pro Lys Asn Ser Gln Thr
705 710 715 720

Asn Val Ser Arg Ile Leu His Arg Phe Gly Leu Lys Gly Thr Asp Gln
725 730 735

Val Thr Leu Ser Ala Ser Gly Arg Ser Ala Gly His Leu Pro Leu Gly
740 745 750

Arg Pro Val Ser Leu His Asp Leu Leu Ser Tyr Ser Val Glu Val Gln
755 760 765

Glu Ala Ala Thr Arg Ala Gln Ile Arg Glu Leu Ala Ser Phe Thr Val
770 775 780

Cys Pro Pro His Arg Arg Glu Leu Glu Glu Leu Ser Ala Glu Gly Val
785 790 795 800

Tyr Gln Glu Gln Ile Leu Lys Lys Arg Ile Ser Met Leu Asp Leu Leu
805 810 815

Glu Lys Tyr Glu Ala Cys Asp Met Pro Phe Glu Arg Phe Leu Glu Leu
820 825 830

Leu Arg Pro Leu Lys Pro Arg Tyr Tyr Ser Ile Ser Ser Ser Pro Arg
835 840 845

Printed: 10/30/2007

USP015

PCT/US2007/017409

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: BB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Val Asn Pro Arg Gln Ala Ser Ile Thr Val Gly Val Val Arg Gly Pro
850 855 860

Ala Trp Ser Gly Arg Gly Glu Tyr Arg Gly Val Ala Ser Asn Asp Leu
865 870 875 880

Ala Glu Arg Gln Ala Gly Asp Asp Val Val Met Phe Ile Arg Thr Pro
885 890 895

Glu Ser Arg Phe Gln Leu Pro Lys Asp Pro Glu Thr Pro Ile Ile Met
900 905 910

Val Gly Pro Gly Thr Gly Val Ala Pro Phe Arg Gly Phe Leu Gln Ala
915 920 925

Arg Asp Val Leu Lys Arg Glu Gly Lys Thr Leu Gly Glu Ala His Leu
930 935 940

Tyr Phe Gly Cys Arg Asn Asp Arg Asp Phe Ile Tyr Arg Asp Glu Leu
945 950 955 960

Glu Arg Phe Glu Lys Asp Gly Ile Val Thr Val His Thr Ala Phe Ser
965 970 975

Arg Lys Glu Gly Met Pro Lys Thr Tyr Val Gln His Leu Met Ala Asp
980 985 990

Gln Ala Asp Thr Leu Ile Ser Ile Leu Asp Arg Gly Gly Arg Leu Tyr
995 1000 1005

Val Cys Gly Asp Gly Ser Lys Met Ala Pro Asp Val Glu Ala Ala
1010 1015 1020

Leu Gln Lys Ala Tyr Gln Ala Val His Gly Thr Gly Glu Gln Glu
1025 1030 1035

Ala Gln Asn Trp Leu Arg His Leu Gln Asp Thr Gly Met Tyr Ala
1040 1045 1050

Lys Asp Val Trp Ala Gly
1055

<210> 4
<211> 1052
<212> PRT
<213> Bacillus subtilis

08/04/2007

Printed: 10/30/2007

SEQUENCE

PCT/US2007/017409

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

<220>
<221> MISC_FEATURE
<222> (1)...(1052)
<223> Cytochrome P450 enzyme CYP102A3

<400> 4

Lys Gln Ala Ser Ala Ile Pro Gln Pro Lys Thr Tyr Gly Pro Leu Lys
1 5 10 15

Asn Leu Pro His Leu Glu Lys Glu Gln Leu Ser Gln Ser Leu Trp Arg
20 25 30

Ile Ala Asp Glu Leu Gly Pro Ile Phe Arg Phe Asp Phe Pro Gly Val
35 40 45

Ser Ser Val Phe Val Ser Gly His Asn Leu Val Ala Glu Val Cys Asp
50 55 60

Glu Lys Arg Phe Asp Lys Asn Leu Gly Lys Gly Leu Gln Lys Val Arg
65 70 75 80

Glu Phe Gly Gly Asp Gly Leu Phe Thr Ser Trp Thr His Glu Pro Asn
85 90 95

Trp Gln Lys Ala His Arg Ile Leu Leu Pro Ser Phe Ser Gln Lys Ala
100 105 110

Met Lys Gly Tyr His Ser Met Met Leu Asp Ile Ala Thr Gln Leu Ile
115 120 125

Gln Lys Trp Ser Arg Leu Asn Pro Asn Glu Glu Ile Asp Val Ala Asp
130 135 140

Asp Met Thr Arg Leu Thr Leu Asp Thr Ile Gly Leu Cys Gly Phe Asn
145 150 155 160

Tyr Arg Phe Asn Ser Phe Tyr Arg Asp Ser Gln His Pro Phe Ile Thr
165 170 175

Ser Met Leu Arg Ala Leu Lys Glu Ala Met Asn Gln Ser Lys Arg Leu
180 185 190

Gly Leu Gln Asp Lys Met Met Val Lys Thr Lys Leu Gln Phe Gln Lys
195 200 205

Asp Ile Glu Val Met Asn Ser Leu Val Asp Arg Met Ile Ala Glu Arg
210 215 220

Printed: 10/30/2007

SHOULS

PCT/US2007/017409

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EE511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Lys Ala Asn Pro Asp Glu Asn Ile Lys Asp Leu Leu Ser Leu Met Leu
225 230 235 240

Tyr Ala Lys Asp Pro Val Thr Gly Glu Thr Leu Asp Asp Glu Asn Ile
245 250 255

Arg Tyr Gln Ile Ile Thr Phe Leu Ile Ala Gly His Glu Thr Thr Ser
260 265 270

Gly Leu Leu Ser Phe Ala Ile Tyr Cys Leu Leu Thr His Pro Glu Lys
275 280 285

Leu Lys Lys Ala Gln Glu Glu Ala Asp Arg Val Leu Thr Asp Asp Thr
290 295 300

Pro Glu Tyr Lys Gln Ile Gln Gln Leu Lys Tyr Ile Arg Met Val Leu
305 310 315 320

Asn Glu Thr Leu Arg Leu Tyr Pro Thr Ala Pro Ala Phe Ser Leu Tyr
325 330 335

Ala Lys Glu Asp Thr Val Leu Gly Gly Glu Tyr Pro Ile Ser Lys Gly
340 345 350

Gln Pro Val Thr Val Leu Ile Pro Lys Leu His Arg Asp Gln Asn Ala
355 360 365

Trp Gly Pro Asp Ala Glu Asp Phe Arg Pro Glu Arg Phe Glu Asp Pro
370 375 380

Ser Ser Ile Pro His His Ala Tyr Lys Pro Phe Gly Asn Gly Gln Arg
385 390 395 400

Ala Cys Ile Gly Met Gln Phe Ala Leu Gln Glu Ala Thr Met Val Leu
405 410 415

Gly Leu Val Leu Lys His Phe Glu Leu Ile Asn His Thr Gly Tyr Glu
420 425 430

Leu Lys Ile Lys Glu Ala Leu Thr Ile Lys Pro Asp Asp Phe Lys Ile
435 440 445

Thr Val Lys Pro Arg Lys Thr Ala Ala Ile Asn Val Gln Arg Lys Glu
450 455 460

Gln Ala Asp Ile Lys Ala Glu Thr Lys Pro Lys Glu Thr Lys Pro Lys
465 470 475 480

Printed: 10/30/2007

SEQUENCE

PGT/US2007/017409

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

His Gly Thr Pro Leu Leu Val Leu Phe Gly Ser Asn Leu Gly Thr Ala
485 490 495

Glu Gly Ile Ala Gly Glu Leu Ala Ala Gln Gly Arg Gln Met Gly Phe
500 505 510

Thr Ala Glu Thr Ala Pro Leu Asp Asp Tyr Ile Gly Lys Leu Pro Glu
515 520 525

Glu Gly Ala Val Val Ile Val Thr Ala Ser Tyr Asn Gly Ala Pro Pro
530 535 540

Asp Asn Ala Ala Gly Phe Val Glu Trp Leu Lys Glu Leu Glu Glu Gly
545 550 555 560

Gln Leu Lys Gly Val Ser Tyr Ala Val Phe Gly Cys Gly Asn Arg Ser
565 570 575

Trp Ala Ser Thr Tyr Gln Arg Ile Pro Arg Leu Ile Asp Asp Met Met
580 585 590

Lys Ala Lys Gly Ala Ser Arg Leu Thr Ala Ile Gly Glu Gly Asp Ala
595 600 605

Ala Asp Asp Phe Glu Ser His Arg Glu Ser Trp Glu Asn Arg Phe Trp
610 615 620

Lys Glu Thr Met Asp Ala Phe Asp Ile Asn Glu Ile Ala Gln Lys Glu
625 630 635 640

Asp Arg Pro Ser Leu Ser Ile Thr Phe Leu Ser Glu Ala Thr Glu Thr
645 650 655

Pro Val Ala Lys Ala Tyr Gly Ala Phe Glu Gly Ile Val Leu Glu Asn
660 665 670

Arg Glu Leu Gln Thr Ala Ala Ser Thr Arg Ser Thr Arg His Ile Glu
675 680 685

Leu Glu Ile Pro Ala Gly Lys Thr Tyr Lys Glu Gly Asp His Ile Gly
690 695 700

Ile Leu Pro Lys Asn Ser Arg Glu Leu Val Gln Arg Val Leu Ser Arg
705 710 715 720

Phe Gly Leu Gln Ser Asn His Val Ile Lys Val Ser Gly Ser Ala His
725 730 735

Page 13

08/04/2007

Printed: 10/30/2007

PCT/US2007/017409

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EBS11041342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Met Ala His Leu Pro Met Asp Arg Pro Ile Lys Val Val Asp Leu Leu
740 745 750

Ser Ser Tyr Val Glu Leu Gln Glu Pro Ala Ser Arg Leu Gln Leu Arg
755 760 765

Glu Leu Ala Ser Tyr Thr Val Cys Pro Pro His Gln Lys Glu Leu Glu
770 775 780

Gln Leu Val Ser Asp Asp Gly Ile Tyr Lys Glu Gln Val Leu Ala Lys
785 790 795 800

Arg Leu Thr Met Leu Asp Phe Leu Glu Asp Tyr Pro Ala Cys Glu Met
805 810 815

Pro Phe Glu Arg Phe Leu Ala Leu Leu Pro Ser Leu Lys Pro Arg Tyr
820 825 830

Tyr Ser Ile Ser Ser Ser Pro Lys Val His Ala Asn Ile Val Ser Met
835 840 845

Thr Val Gly Val Val Lys Ala Ser Ala Trp Ser Gly Arg Gly Glu Tyr
850 855 860

Arg Gly Val Ala Ser Asn Tyr Leu Ala Glu Leu Asn Thr Gly Asp Ala
865 870 875 880

Ala Ala Cys Phe Ile Arg Thr Pro Gln Ser Gly Phe Gln Met Pro Asn
885 890 895

Asp Pro Glu Thr Pro Met Ile Met Val Gly Pro Gly Thr Gly Ile Ala
900 905 910

Pro Phe Arg Gly Phe Ile Gln Ala Arg Ser Val Leu Lys Lys Glu Gly
915 920 925

Ser Thr Leu Gly Glu Ala Leu Leu Tyr Phe Gly Cys Arg Arg Pro Asp
930 935 940

His Asp Asp Leu Tyr Arg Glu Glu Leu Asp Gln Ala Glu Gln Asp Gly
945 950 955 960

Leu Val Thr Ile Arg Arg Cys Tyr Ser Arg Val Glu Asn Glu Pro Lys
965 970 975

Gly Tyr Val Gln His Leu Leu Lys Gln Asp Thr Gln Lys Leu Met Thr
Page 14

08/04/2007

Printed: 10/30/2007

SEQUENCE

PCT/US2007/017499

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

980

P008-CIT_ST25.txt
985 990

Leu Ile Glu Lys Gly Ala His Ile Tyr Val Cys Gly Asp Gly Ser Gln
995 1000 1005

Met Ala Pro Asp Val Glu Arg Thr Leu Arg Leu Ala Tyr Glu Ala
1010 1015 1020

Glu Lys Ala Ala Ser Gln Glu Glu Ser Ala Val Trp Leu Gln Lys
1025 1030 1035

Leu Gln Asp Gln Arg Arg Tyr Val Lys Asp Val Trp Thr Gly
1040 1045 1050

<210> 5
<211> 1065
<212> PRT
<213> Bacillus cereus

<220>
<221> MISC_FEATURE
<222> (1)...(1065)
<223> Cytochrome P450 enzyme CYP102A5

<400> 5

Met Asp Lys Lys Val Ser Ala Ile Pro Gln Pro Lys Thr Tyr Gly Pro
1 5 10 15

Leu Gly Asn Leu Pro Leu Ile Asp Lys Asp Lys Pro Thr Leu Ser Phe
20 25 30

Ile Lys Ile Ala Glu Glu Tyr Gly Pro Ile Phe Gln Ile Gln Thr Leu
35 40 45

Ser Asp Thr Ile Ile Val Ile Ser Gly His Glu Leu Val Ala Glu Val
50 55 60

Cys Asp Glu Thr Arg Phe Asp Lys Ser Ile Glu Gly Ala Leu Ala Lys
65 70 75 80

Val Arg Ala Phe Ala Gly Asp Gly Leu Phe Thr Ser Glu Thr Gln Glu
85 90 95

Pro Asn Trp Lys Lys Ala His Asn Ile Leu Met Pro Thr Phe Ser Gln
100 105 110

Arg Ala Met Lys Asp Tyr His Ala Met Met Val Asp Ile Ala Val Gln
115 120 125

08/04/2007

Printed: 10/30/2007

8:11:13

PCT/US2007/017409

US2007/017409

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Leu Val Gln Lys Trp Ala Arg Leu Asn Pro Asn Glu Asn Val Asp Val
130 135 140

Pro Glu Asp Met Thr Arg Leu Thr Leu Asp Thr Ile Gly Leu Cys Gly
145 150 155 160

Phe Asn Tyr Arg Phe Asn Ser Phe Tyr Arg Glu Thr Pro His Pro Phe
165 170 175

Ile Thr Ser Met Thr Arg Ala Leu Asp Glu Ala Met His Gln Leu Gln
180 185 190

Arg Leu Asp Ile Glu Asp Lys Leu Met Trp Arg Thr Lys Arg Gln Phe
195 200 205

Gln His Asp Ile Gln Ser Met Phe Ser Leu Val Asp Asn Ile Ile Ala
210 215 220

Glu Arg Lys Ser Ser Gly Asn Gln Glu Glu Asn Asp Leu Leu Ser Arg
225 230 235 240

Met Leu His Val Gln Asp Pro Glu Thr Gly Glu Lys Leu Asp Asp Glu
245 250 255

Asn Ile Arg Phe Gln Ile Ile Thr Phe Leu Ile Ala Gly His Glu Thr
260 265 270

Thr Ser Gly Leu Leu Ser Phe Ala Ile Tyr Phe Leu Leu Lys Asn Pro
275 280 285

Asp Lys Leu Lys Lys Ala Tyr Glu Glu Val Asp Arg Val Leu Thr Asp
290 295 300

Pro Thr Pro Thr Tyr Gln Gln Val Met Lys Leu Lys Tyr Ile Arg Met
305 310 315 320

Ile Leu Asn Glu Ser Leu Arg Leu Trp Pro Thr Ala Pro Ala Phe Ser
325 330 335

Leu Tyr Ala Lys Glu Asp Thr Val Ile Gly Gly Lys Tyr Pro Ile Lys
340 345 350

Lys Gly Glu Asp Arg Ile Ser Val Leu Ile Pro Gln Leu His Arg Asp
355 360 365

Lys Asp Ala Trp Gly Asp Asn Val Glu Glu Phe Gln Pro Glu Arg Phe
370 375 380

Page 16

08/04/2007

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Glu Asp Leu Asp Lys Val Pro His His Ala Tyr Lys Pro Phe Gly Asn
385 390 395 400

Gly Gln Arg Ala Cys Ile Gly Met Gln Phe Ala Leu His Glu Ala Thr
405 410 415

Leu Val Met Gly Met Leu Leu Gln His Phe Glu Phe Ile Asp Tyr Glu
420 425 430

Asp Tyr Gln Leu Asp Val Lys Gln Thr Leu Thr Leu Lys Pro Gly Asp
435 440 445

Phe Lys Ile Arg Ile Val Pro Arg Asn Gln Asn Ile Ser His Thr Thr
450 455 460

Val Leu Ala Pro Thr Glu Glu Lys Leu Lys Asn His Glu Ile Lys Gln
465 470 475 480

Gln Val Gln Lys Thr Pro Ser Ile Ile Gly Ala Asp Asn Leu Ser Leu
485 490 495

Leu Val Leu Tyr Gly Ser Asp Thr Gly Val Ala Glu Gly Ile Ala Arg
500 505 510

Glu Leu Ala Asp Thr Ala Ser Leu Glu Gly Val Gln Thr Glu Val Ala
515 520 525

Ala Leu Asn Asp Arg Ile Gly Ser Leu Pro Lys Glu Gly Ala Val Leu
530 535 540

Ile Val Thr Ser Ser Tyr Asn Gly Lys Pro Pro Ser Asn Ala Gly Gln
545 550 555 560

Phe Val Gln Trp Leu Glu Glu Leu Lys Pro Asp Glu Leu Lys Gly Val
565 570 575

Gln Tyr Ala Val Phe Gly Cys Gly Asp His Asn Trp Ala Ser Thr Tyr
580 585 590

Gln Arg Ile Pro Arg Tyr Ile Asp Glu Gln Met Ala Gln Lys Gly Ala
595 600 605

Thr Arg Phe Ser Thr Arg Gly Glu Ala Asp Ala Ser Gly Asp Phe Glu
610 615 620

Glu Gln Leu Glu Gln Trp Lys Glu Ser Met Trp Ser Asp Ala Met Lys

P008-CIT_ST25.txt

625

630

635

640

Ala Phe Gly Leu Glu Leu Asn Lys Asn Met Glu Lys Glu Arg Ser Thr
645 650 655

Leu Ser Leu Gln Phe Val Ser Arg Leu Gly Gly Ser Pro Leu Ala Arg
660 665 670

Thr Tyr Glu Ala Val Tyr Ala Ser Ile Leu Glu Asn Arg Glu Leu Gln
675 680 685

Ser Ser Ser Ser Glu Arg Ser Thr Arg His Ile Glu Ile Ser Leu Pro
690 695 700

Glu Gly Ala Thr Tyr Lys Glu Gly Asp His Leu Gly Val Leu Pro Ile
705 710 715 720

Asn Ser Glu Lys Asn Val Asn Arg Ile Leu Lys Arg Phe Gly Leu Asn
725 730 735

Gly Lys Asp Gln Val Ile Leu Ser Ala Ser Gly Arg Ser Val Asn His
740 745 750

Ile Pro Leu Asp Ser Pro Val Arg Leu Tyr Asp Leu Leu Ser Tyr Ser
755 760 765

Val Glu Val Gln Glu Ala Ala Thr Arg Ala Gln Ile Arg Glu Met Val
770 775 780

Thr Phe Thr Ala Cys Pro Pro His Lys Lys Glu Leu Glu Ser Leu Leu
785 790 795 800

Glu Asp Gly Val Tyr His Glu Gln Ile Leu Lys Lys Arg Ile Ser Met
805 810 815

Leu Asp Leu Leu Glu Lys Tyr Glu Ala Cys Glu Ile Arg Phe Glu Arg
820 825 830

Phe Leu Glu Leu Leu Pro Ala Leu Lys Pro Arg Tyr Tyr Ser Ile Ser
835 840 845

Ser Ser Pro Leu Ile Ala Gln Asp Arg Leu Ser Ile Thr Val Gly Val
850 855 860

Val Asn Ala Pro Ala Trp Ser Gly Glu Gly Thr Tyr Glu Gly Val Ala
865 870 875 880

Printed: 10/30/2007

SH01157

PCT/US2007/017409

Title: "Methods and Systems for Selective"

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Ser Asn Tyr Leu Ala Gln Arg His Asn Lys Asp Glu Ile Ile Cys Phe
885 890 895

Ile Arg Thr Pro Gln Ser Asn Phe Gln Leu Pro Glu Asn Pro Glu Thr
900 905 910

Pro Ile Ile Met Val Gly Pro Gly Thr Gly Ile Ala Pro Phe Arg Gly
915 920 925

Phe Leu Gln Ala Arg Arg Val Gln Lys Gln Lys Gly Met Asn Leu Gly
930 935 940

Glu Ala His Leu Tyr Phe Gly Cys Arg His Pro Glu Lys Asp Tyr Leu
945 950 955 960

Tyr Arg Thr Glu Leu Glu Asn Asp Glu Arg Asp Gly Leu Ile Ser Leu
965 970 975

His Thr Ala Phe Ser Arg Leu Glu Gly His Pro Lys Thr Tyr Val Gln
980 985 990

His Val Ile Lys Glu Asp Arg Met Asn Leu Ile Ser Leu Leu Asp Asn
995 1000 1005

Gly Ala His Leu Tyr Ile Cys Gly Asp Gly Ser Lys Met Ala Pro
1010 1015 1020

Asp Val Glu Asp Thr Leu Cys Gln Ala Tyr Gln Glu Ile His Glu
1025 1030 1035

Val Ser Glu Gln Glu Ala Arg Asn Trp Leu Asp Arg Leu Gln Asp
1040 1045 1050

Glu Gly Arg Tyr Gly Lys Asp Val Trp Ala Gly Ile
1055 1060 1065

<210> 6
<211> 1063
<212> PRT
<213> Ralstonia metallidurans

<220>
<221> MISC_FEATURE
<222> (1)..(1063)
<223> Cytochrome P450 enzyme CYP102E1

<400> 6

Ser Thr Ala Thr Pro Ala Ala Ala Leu Glu Pro Ile Pro Arg Asp Pro
1 5 10 15

08/04/2007

Printed: 10/30/2007

SEQUENCE

PCT/US2007/017409

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EBS11841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Gly Trp Pro Ile Phe Gly Asn Leu Phe Gln Ile Thr Pro Gly Glu Val
20 25 30

Gly Gln His Leu Leu Ala Arg Ser Arg His His Asp Gly Ile Phe Glu
35 40 45

Leu Asp Phe Ala Gly Lys Arg Val Pro Phe Val Ser Ser Val Ala Leu
50 55 60

Ala Ser Glu Leu Cys Asp Ala Thr Arg Phe Arg Lys Ile Ile Gly Pro
65 70 75 80

Pro Leu Ser Tyr Leu Arg Asp Met Ala Gly Asp Gly Leu Phe Thr Ala
85 90 95

His Ser Asp Glu Pro Asn Trp Gly Cys Ala His Arg Ile Leu Met Pro
100 105 110

Ala Phe Ser Gln Arg Ala Met Lys Ala Tyr Phe Asp Val Met Leu Arg
115 120 125

Val Ala Asn Arg Leu Val Asp Lys Trp Asp Arg Gln Gly Pro Asp Ala
130 135 140

Asp Ile Ala Val Ala Asp Asp Met Thr Arg Leu Thr Leu Asp Thr Ile
145 150 155 160

Ala Leu Ala Gly Phe Gly Tyr Asp Phe Ala Ser Phe Ala Ser Asp Glu
165 170 175

Leu Asp Pro Phe Val Met Ala Met Val Gly Ala Leu Gly Glu Ala Met
180 185 190

Gln Lys Leu Thr Arg Leu Pro Ile Gln Asp Arg Phe Met Gly Arg Ala
195 200 205

His Arg Gln Ala Ala Glu Asp Ile Ala Tyr Met Arg Asn Leu Val Asp
210 215 220

Asp Val Ile Arg Gln Arg Arg Val Ser Pro Thr Ser Gly Met Asp Leu
225 230 235 240

Leu Asn Leu Met Leu Glu Ala Arg Asp Pro Glu Thr Asp Arg Arg Leu
245 250 255

Asp Asp Ala Asn Ile Arg Asn Gln Val Ile Thr Phe Leu Ile Ala Gly
Page 20

08/04/2007

Printed: 10/30/2007

8-0116

PCT/US2007/017409

08/04/2007

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

260

265

270

His Glu Thr Thr Ser Gly Leu Leu Thr Phe Ala Leu Tyr Glu Leu Leu
275 280 285

Arg Asn Pro Gly Val Leu Ala Gln Ala Tyr Ala Glu Val Asp Thr Val
290 295 300

Leu Pro Gly Asp Ala Leu Pro Val Tyr Ala Asp Leu Ala Arg Met Pro
305 310 315 320

Val Leu Asp Arg Val Leu Lys Glu Thr Leu Arg Leu Trp Pro Thr Ala
325 330 335

Pro Ala Phe Ala Val Ala Pro Phe Asp Asp Val Val Leu Gly Gly Arg
340 345 350

Tyr Arg Leu Arg Lys Asp Arg Arg Ile Ser Val Val Leu Thr Ala Leu
355 360 365

His Arg Asp Pro Lys Val Trp Ala Asn Pro Glu Arg Phe Asp Ile Asp
370 375 380

Arg Phe Leu Pro Glu Asn Glu Ala Lys Leu Pro Ala His Ala Tyr Met
385 390 395 400

Pro Phe Gly Gln Gly Glu Arg Ala Cys Ile Gly Arg Gln Phe Ala Leu
405 410 415

Thr Glu Ala Lys Leu Ala Leu Ala Leu Met Leu Arg Asn Phe Ala Phe
420 425 430

Gln Asp Pro His Asp Tyr Gln Phe Arg Leu Lys Glu Thr Leu Thr Ile
435 440 445

Lys Pro Asp Gln Phe Val Leu Arg Val Arg Arg Arg Pro His Glu
450 455 460

Arg Phe Val Thr Arg Gln Ala Ser Gln Ala Val Ala Asp Ala Ala Gln
465 470 475 480

Thr Asp Val Arg Gly His Gly Gln Ala Met Thr Val Leu Cys Ala Ser
485 490 495

Ser Leu Gly Thr Ala Arg Glu Leu Ala Glu Gln Ile His Ala Gly Ala
500 505 510

08/04/2007

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Ile Ala Ala Gly Phe Asp Ala Lys Leu Ala Asp Leu Asp Asp Ala Val
 515 520 525

Gly Val Leu Pro Thr Ser Gly Leu Val Val Val Ala Ala Thr Tyr
 530 535 540

Asn Gly Arg Ala Pro Asp Ser Ala Arg Lys Phe Glu Ala Met Leu Asp
 545 550 555 560

Ala Asp Asp Ala Ser Gly Tyr Arg Ala Asn Gly Met Arg Leu Ala Leu
 565 570 575

Leu Gly Cys Gly Asn Ser Gln Trp Ala Thr Tyr Gln Ala Phe Pro Arg
 580 585 590

Arg Val Phe Asp Phe Phe Ile Thr Ala Gly Ala Val Pro Leu Leu Pro
 595 600 605

Arg Gly Glu Ala Asp Gly Asn Gly Asp Phe Asp Gln Ala Ala Glu Arg
 610 615 620

Trp Leu Ala Gln Leu Trp Gln Ala Leu Gln Ala Asp Gly Ala Gly Thr
 625 630 635 640

Gly Gly Leu Gly Val Asp Val Gln Val Arg Ser Met Ala Ala Ile Arg
 645 650 655

Ala Glu Thr Leu Pro Ala Gly Thr Gln Ala Phe Thr Val Leu Ser Asn
 660 665 670

Asp Glu Leu Val Gly Asp Pro Ser Gly Leu Trp Asp Phe Ser Ile Glu
 675 680 685

Ala Pro Arg Thr Ser Thr Arg Asp Ile Arg Leu Gln Leu Pro Pro Gly
 690 695 700

Ile Thr Tyr Arg Thr Gly Asp His Ile Ala Val Trp Pro Gln Asn Asp
 705 710 715 720

Ala Gln Leu Val Ser Glu Leu Cys Glu Arg Leu Asp Leu Asp Pro Asp
 725 730 735

Ala Gln Ala Thr Ile Ser Ala Pro His Gly Met Gly Arg Gly Leu Pro
 740 745 750

Ile Asp Gln Ala Leu Pro Val Arg Gln Leu Leu Thr His Phe Ile Glu
 755 760 765

Printed: 10/30/2007

SEQUENCE

PCT/US2007/017409

2136

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Leu Gln Asp Val Val Ser Arg Gln Thr Leu Arg Ala Leu Ala Gln Ala
770 775 780

Thr Arg Cys Pro Phe Thr Lys Gln Ser Ile Glu Gln Leu Ala Ser Asp
785 790 795 800

Asp Ala Glu His Gly Tyr Ala Thr Lys Val Val Ala Arg Arg Leu Gly
805 810 815

Ile Leu Asp Val Leu Val Glu His Pro Ala Ile Ala Leu Thr Leu Gln
820 825 830

Glu Leu Leu Ala Cys Thr Val Pro Met Arg Pro Arg Leu Tyr Ser Ile
835 840 845

Ala Ser Ser Pro Leu Val Ser Pro Asp Val Ala Thr Leu Leu Val Gly
850 855 860

Thr Val Cys Ala Pro Ala Leu Ser Gly Arg Gly Gln Phe Arg Gly Val
865 870 875 880

Ala Ser Thr Trp Leu Gln His Leu Pro Pro Gly Ala Arg Val Ser Ala
885 890 895

Ser Ile Arg Thr Pro Asn Pro Pro Phe Ala Pro Asp Pro Asp Pro Ala
900 905 910

Ala Pro Met Leu Leu Ile Gly Pro Gly Thr Gly Ile Ala Pro Phe Arg
915 920 925

Gly Phe Leu Glu Glu Arg Ala Leu Arg Lys Met Ala Gly Asn Ala Val
930 935 940

Thr Pro Ala Gln Leu Tyr Phe Gly Cys Arg His Pro Gln His Asp Trp
945 950 955 960

Leu Tyr Arg Glu Asp Ile Glu Arg Trp Ala Gly Gln Gly Val Val Glu
965 970 975

Val His Pro Ala Tyr Ser Val Val Pro Asp Ala Pro Arg Tyr Val Gln
980 985 990

Asp Leu Leu Trp Gln Arg Arg Glu Gln Val Trp Ala Gln Val Arg Asp
995 1000 1005

Gly Ala Thr Ile Tyr Val Cys Gly Asp Gly Arg Arg Met Ala Pro
1010 1015 1020

Page 23

08/04/2007

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Ala Val Arg Gln Thr Leu Ile Glu Ile Gly Met Ala Gln Gly Gly
1025 1030 1035

Met Thr Asp Lys Ala Ala Ser Asp Trp Phe Gly Gly Leu Val Ala
1040 1045 1050

Gln Gly Arg Tyr Arg Gln Asp Val Phe Asn
1055 1060

<210> 7
<211> 1077
<212> PRT
<213> Bradyrhizobium japonicum

<220>
<221> MISC_FEATURE
<222> (1)..(1077)
<223> Cytochrome P450 enzyme CYP102A6

<400> 7

Ser Ser Lys Asn Arg Leu Asp Pro Ile Pro Gln Pro Pro Thr Lys Pro
1 5 10 15

Val Val Gly Asn Met Leu Ser Leu Asp Ser Ala Ala Pro Val Gln His
20 25 30

Leu Thr Arg Leu Ala Lys Glu Leu Gly Pro Ile Phe Trp Leu Asp Met
35 40 45

Met Gly Ser Pro Ile Val Val Val Ser Gly His Asp Leu Val Asp Glu
50 55 60

Leu Ser Asp Glu Lys Arg Phe Asp Lys Thr Val Arg Gly Ala Leu Arg
65 70 75 80

Arg Val Arg Ala Val Gly Gly Asp Gly Leu Phe Thr Ala Asp Thr Arg
85 90 95

Glu Pro Asn Trp Ser Lys Ala His Asn Ile Leu Leu Gln Pro Phe Gly
100 105 110

Asn Arg Ala Met Gln Ser Tyr His Pro Ser Met Val Asp Ile Ala Glu
115 120 125

Gln Leu Val Gln Lys Trp Glu Arg Leu Asn Ala Asp Asp Glu Ile Asp
130 135 140

Printed: 10/30/2007

80015

PCT/US2007/017409

Title: "Methods and Systems for Selective..."

Inventors: Rudi Faşan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Val Val His Asp Met Thr Ala Leu Thr Leu Asp Thr Ile Gly Leu Cys
145 150 155 160

Gly Phe Asp Tyr Arg Phe Asn Ser Phe Tyr Arg Arg Asp Tyr His Pro
165 170 175

Phe Val Glu Ser Leu Val Arg Ser Leu Glu Thr Ile Met Met Thr Arg
180 185 190

Gly Leu Pro Phe Glu Gln Ile Trp Met Gln Lys Arg Arg Lys Thr Leu
195 200 205

Ala Glu Asp Val Ala Phe Met Asn Lys Met Val Asp Glu Ile Ile Ala
210 215 220

Glu Arg Arg Lys Ser Ala Glu Gly Ile Asp Asp Lys Lys Asp Met Leu
225 230 235 240

Ala Ala Met Met Thr Gly Val Asp Arg Ser Thr Gly Glu Gln Leu Asp
245 250 255

Asp Val Asn Ile Arg Tyr Gln Ile Asn Thr Phe Leu Ile Ala Gly His
260 265 270

Glu Thr Thr Ser Gly Leu Leu Ser Tyr Thr Leu Tyr Ala Leu Leu Lys
275 280 285

His Pro Asp Ile Leu Lys Lys Ala Tyr Asp Glu Val Asp Arg Val Phe
290 295 300

Gly Pro Asp Val Asn Ala Lys Pro Thr Tyr Gln Gln Val Thr Gln Leu
305 310 315 320

Thr Tyr Ile Thr Gln Ile Leu Lys Glu Ala Leu Arg Leu Trp Pro Pro
325 330 335

Ala Pro Ala Tyr Gly Ile Ser Pro Leu Ala Asp Glu Thr Ile Gly Gly
340 345 350

Gly Lys Tyr Lys Leu Arg Lys Gly Thr Phe Ile Thr Ile Leu Val Thr
355 360 365

Ala Leu His Arg Asp Pro Ser Val Trp Gly Pro Asn Pro Asp Ala Phe
370 375 380

Asp Pro Glu Asn Phe Ser Arg Glu Ala Glu Ala Lys Arg Pro Ile Asn
385 390 395 400

08/04/2007

Printed: 10/30/2007

Sheet 13

PCT/US2007/017409

017409-100

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Ala Trp Lys Pro Phe Gly Asn Gly Gln Arg Ala Cys Ile Gly Arg Gly
405 410 415

Phe Ala Met His Glu Ala Ala Leu Ala Leu Gly Met Ile Leu Gln Arg
420 425 430

Phe Lys Leu Ile Asp His Gln Arg Tyr Gln Met His Leu Lys Glu Thr
435 440 445

Leu Thr Met Lys Pro Glu Gly Phe Lys Ile Lys Val Arg Pro Arg Ala
450 455 460

Asp Arg Glu Arg Gly Ala Tyr Gly Gly Pro Val Ala Ala Val Ser Ser
465 470 475 480

Ala Pro Arg Ala Pro Arg Gln Pro Thr Ala Arg Pro Gly His Asn Thr
485 490 495

Pro Met Leu Val Leu Tyr Gly Ser Asn Leu Gly Thr Ala Glu Glu Leu
500 505 510

Ala Thr Arg Met Ala Asp Leu Ala Glu Ile Asn Gly Phe Ala Val His
515 520 525

Leu Gly Ala Leu Asp Glu Tyr Val Gly Lys Leu Pro Gln Glu Gly Gly
530 535 540

Val Leu Ile Ile Cys Ala Ser Tyr Asn Gly Ala Pro Pro Asp Asn Ala
545 550 555 560

Thr Gln Phe Val Lys Trp Leu Gly Ser Asp Leu Pro Lys Asp Ala Phe
565 570 575

Ala Asn Val Arg Tyr Ala Val Phe Gly Cys Gly Asn Ser Asp Trp Ala
580 585 590

Ala Thr Tyr Gln Ser Val Pro Arg Phe Ile Asp Glu Gln Leu Ser Gly
595 600 605

His Gly Ala Arg Ala Val Tyr Pro Arg Gly Glu Gly Asp Ala Arg Ser
610 615 620

Asp Leu Asp Gly Gln Phe Gln Lys Trp Phe Pro Ala Ala Ala Gln Val
625 630 635 640

Ala Thr Lys Glu Phe Gly Ile Asp Trp Asn Phe Thr Arg Thr Ala Glu
645 650 655

03/04/2007

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.TXT

Asp Asp Pro Leu Tyr Ala Ile Glu Pro Val Ala Val Thr Ala Val Asn
660 665 670

Thr Ile Val Ala Gln Gly Gly Ala Val Ala Met Lys Val Leu Val Asn
675 680 685

Asp Glu Leu Gln Asn Lys Ser Gly Ser Asn Pro Ser Glu Arg Ser Thr
690 695 700

Arg His Ile Glu Val Gln Leu Pro Ser Asn Ile Thr Tyr Arg Val Gly
705 710 715 720

Asp His Leu Ser Val Val Pro Arg Asn Asp Pro Thr Leu Val Asp Ser
725 730 735

Val Ala Arg Arg Phe Gly Phe Leu Pro Ala Asp Gln Ile Arg Leu Gln
740 745 750

Val Ala Glu Gly Arg Arg Ala Gln Leu Pro Val Gly Glu Ala Val Ser
755 760 765

Val Gly Arg Leu Leu Ser Glu Phe Val Glu Leu Gln Gln Val Ala Thr
770 775 780

Arg Lys Gln Ile Gln Ile Met Ala Glu His Thr Arg Cys Pro Val Thr
785 790 795 800

Lys Pro Lys Leu Leu Ala Phe Val Gly Glu Glu Ala Glu Pro Ala Glu
805 810 815

Arg Tyr Arg Thr Glu Ile Leu Ala Met Arg Lys Ser Val Tyr Asp Leu
820 825 830

Leu Leu Glu Tyr Pro Ala Cys Glu Leu Pro Phe His Val Tyr Leu Glu
835 840 845

Met Leu Ser Leu Leu Ala Pro Arg Tyr Tyr Ser Ile Ser Ser Ser Pro
850 855 860

Ser Val Asp Pro Ala Arg Cys Ser Ile Thr Val Gly Val Val Glu Gly
865 870 875 880

Pro Ala Ala Ser Gly Arg Gly Val Tyr Lys Gly Ile Cys Ser Asn Tyr
885 890 895

Leu Ala Asn Arg Arg Ala Ser Asp Ala Ile Tyr Ala Thr Val Arg Glu
Page 27

P008-CIT_ST25.txt 900 905 910

Thr Lys Ala Gly Phe Arg Leu Pro Asp Asp Ser Ser Val Pro Ile Ile
915 920 925

Met Ile Gly Pro Gly Thr Gly Leu Ala Pro Phe Arg Gly Phe Leu Gln
930 935 940

Glu Arg Ala Ala Arg Lys Ala Lys Gly Ala Ser Leu Gly Pro Ala Met
945 950 955 960

Leu Phe Phe Gly Cys Arg His Pro Asp Gln Asp Phe Leu Tyr Ala Asp
965 970 975

Glu Leu Lys Ala Leu Ala Ala Ser Gly Val Thr Glu Leu Phe Thr Ala
980 985 990

Phe Ser Arg Ala Asp Gly Pro Lys Thr Tyr Val Gln His Val Leu Ala
995 1000 1005

Ala Gln Lys Asp Lys Val Trp Pro Leu Ile Glu Gln Gly Ala Ile
1010 1015 1020

Ile Tyr Val Cys Gly Asp Gly Gly Gln Met Glu Pro Asp Val Lys
1025 1030 1035

Ala Ala Leu Val Ala Ile Arg His Glu Lys Ser Gly Ser Asp Thr
1040 1045 1050

Ala Thr Ala Ala Arg Trp Ile Glu Glu Met Gly Ala Thr Asn Arg
1055 1060 1065

Tyr Val Leu Asp Val Trp Ala Gly Gly
1070 1075

<210> 8
<211> 415
<212> PRT
<213> Pseudomonas putida

<220>
<221> MISC_FEATURE
<222> (1)..(415)
<223> Cytochrome P450 enzyme CYP101A1

<400> 8

Met Thr Thr Glu Thr Ile Gln Ser Asn Ala Asn Leu Ala Pro Leu Pro
1 5 10 15

Printed: 10/30/2007

810161

PCT/US2007/017409

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Pro His Val Pro Glu His Leu Val Phe Asp Phe Asp Met Tyr Asn Pro
20 25 30

Ser Asn Leu Ser Ala Gly Val Gln Glu Ala Trp Ala Val Leu Gln Glu
35 40 45

Ser Asn Val Pro Asp Leu Val Trp Thr Arg Cys Asn Gly Gly His Trp
50 55 60

Ile Ala Thr Arg Gly Gln Leu Ile Arg Glu Ala Tyr Glu Asp Tyr Arg
65 70 75 80

His Phe Ser Ser Glu Cys Pro Phe Ile Pro Arg Glu Ala Gly Glu Ala
85 90 95

Tyr Asp Phe Ile Pro Thr Ser Met Asp Pro Pro Glu Gln Arg Gln Phe
100 105 110

Arg Ala Leu Ala Asn Gln Val Val Gly Met Pro Val Val Asp Lys Leu
115 120 125

Glu Asn Arg Ile Gln Glu Leu Ala Cys Ser Leu Ile Glu Ser Leu Arg
130 135 140

Pro Gln Gly Gln Cys Asn Phe Thr Glu Asp Tyr Ala Glu Pro Phe Pro
145 150 155 160

Ile Arg Ile Phe Met Leu Leu Ala Gly Leu Pro Glu Glu Asp Ile Pro
165 170 175

His Leu Lys Tyr Leu Thr Asp Gln Met Thr Arg Pro Asp Gly Ser Met
180 185 190

Thr Phe Ala Glu Ala Lys Glu Ala Leu Tyr Asp Tyr Leu Ile Pro Ile
195 200 205

Ile Glu Gln Arg Arg Gln Lys Pro Gly Thr Asp Ala Ile Ser Ile Val
210 215 220

Ala Asn Gly Gln Val Asn Gly Arg Pro Ile Thr Ser Asp Glu Ala Lys
225 230 235 240

Arg Met Cys Gly Leu Leu Leu Val Gly Gly Leu Asp Thr Val Val Asn
245 250 255

Phe Leu Ser Phe Ser Met Glu Phe Leu Ala Lys Ser Pro Glu His Arg
260 265 270

08/04/2007

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Gln Glu Leu Ile Glu Arg Pro Glu Arg Ile Pro Ala Ala Cys Glu Glu
275 280 285

Leu Leu Arg Arg Phe Ser Leu Val Ala Asp Gly Arg Ile Leu Thr Ser
290 295 300

Asp Tyr Glu Phe His Gly Val Gln Leu Lys Lys Gly Asp Gln Ile Leu
305 310 315 320

Leu Pro Gln Met Leu Ser Gly Leu Asp Glu Arg Glu Asn Ala Cys Pro
325 330 335

Met His Val Asp Phe Ser Arg Gln Lys Val Ser His Thr Thr Phe Gly
340 345 350

His Gly Ser His Leu Cys Leu Gly Gln His Leu Ala Arg Arg Glu Ile
355 360 365

Ile Val Thr Leu Lys Glu Trp Leu Thr Arg Ile Pro Asp Phe Ser Ile
370 375 380

Ala Pro Gly Ala Gln Ile Gln His Lys Ser Gly Ile Val Ser Gly Val
385 390 395 400

Gln Ala Leu Pro Leu Val Trp Asp Pro Ala Thr Thr Lys Ala Val
405 410 415

<210> 9

<211> 410

<212> PRT

<213> Bacillus megaterium

<220>

<221> MISC_FEATURE

<222> (1)..(410)

<223> Cytochrome P450 enzyme CYP106A2

<400> 9

Met Lys Glu Val Ile Ala Val Lys Glu Ile Thr Arg Phe Lys Thr Arg
1 5 10 15

Thr Glu Glu Phe Ser Pro Tyr Ala Trp Cys Lys Arg Met Leu Glu Asn
20 25 30

Asp Pro Val Ser Tyr His Glu Gly Thr Asp Thr Trp Asn Val Phe Lys
35 40 45

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Tyr Glu Asp Val Lys Arg Val Leu Ser Asp Tyr Lys His Phe Ser Ser
50 55 60

Val Arg Lys Arg Thr Thr Ile Ser Val Gly Thr Asp Ser Glu Glu Gly
65 70 75 80

Ser Val Pro Glu Lys Ile Gln Ile Thr Glu Ser Asp Pro Pro Asp His
85 90 95

Arg Lys Arg Arg Ser Leu Leu Ala Ala Phe Thr Pro Arg Ser Leu
100 105 110

Gln Asn Trp Glu Pro Arg Ile Gln Glu Ile Ala Asp Glu Leu Ile Gly
115 120 125

Gln Met Asp Gly Gly Thr Glu Ile Asp Ile Val Ala Ser Leu Ala Ser
130 135 140

Pro Leu Pro Ile Ile Val Met Ala Asp Leu Met Gly Val Pro Ser Lys
145 150 155 160

Asp Arg Leu Leu Phe Lys Lys Trp Val Asp Thr Leu Phe Leu Pro Phe
165 170 175

Asp Arg Glu Lys Gln Glu Glu Val Asp Lys Leu Lys Gln Val Ala Ala
180 185 190

Lys Glu Tyr Tyr Gln Tyr Leu Tyr Pro Ile Val Val Gln Lys Arg Leu
195 200 205

Asn Pro Ala Asp Asp Ile Ile Ser Asp Leu Leu Lys Ser Glu Val Asp
210 215 220

Gly Glu Met Phe Thr Asp Asp Glu Val Val Arg Thr Thr Met Leu Ile
225 230 235 240

Leu Gly Ala Gly Val Glu Thr Thr Ser His Leu Leu Ala Asn Ser Phe
245 250 255

Tyr Ser Leu Leu Tyr Asp Asp Lys Glu Val Tyr Gln Glu Leu His Glu
260 265 270

Asn Leu Asp Leu Val Pro Gln Ala Val Glu Glu Met Leu Arg Phe Arg
275 280 285

Phe Asn Leu Ile Lys Leu Asp Arg Thr Val Lys Glu Asp Asn Asp Leu
290 295 300

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Leu Gly Val Glu Leu Lys Glu Gly Asp Ser Val Val Val Trp Met Ser
 305 310 315 320

Ala Ala Asn Met Asp Glu Glu Met Phe Glu Asp Pro Phe Thr Leu Asn
 325 330 335

Ile His Arg Pro Asn Asn Lys Lys His Leu Thr Phe Gly Asn Gly Pro
 340 345 350

His Phe Cys Leu Gly Ala Pro Leu Ala Arg Leu Glu Ala Lys Ile Ala
 355 360 365

Leu Thr Ala Phe Leu Lys Lys Phe Lys His Ile Glu Ala Val Pro Ser
 370 375 380

Phe Gln Leu Glu Glu Asn Leu Thr Asp Ser Ala Thr Gly Gln Thr Leu
 385 390 395 400

Thr Ser Leu Pro Leu Lys Ala Ser Arg Met
 405 410

<210> 10
 <211> 404
 <212> PRT
 <213> Citrobacter braakii

<220>
 <221> MISC_FEATURE
 <222> (1)..(404)
 <223> Cytochrome P450 enzyme P450cin

<400> 10

Met Thr Ala Thr Val Ala Ser Thr Ser Leu Phe Thr Thr Ala Asp His
 1 5 10 15

Tyr His Thr Pro Leu Gly Pro Asp Gly Thr Pro His Ala Phe Phe Glu
 20 25 30

Ala Leu Arg Asp Glu Ala Glu Thr Thr Pro Ile Gly Trp Ser Glu Ala
 35 40 45

Tyr Gly Gly His Trp Val Val Ala Gly Tyr Lys Glu Ile Gln Ala Val
 50 55 60

Ile Gln Asn Thr Lys Ala Phe Ser Asn Lys Gly Val Thr Phe Pro Arg
 65 70 75 80

Tyr Glu Thr Gly Glu Phe Glu Leu Met Met Ala Gly Gln Asp Asp Pro
 Page 32

Printed 10/30/2007

Spotlight

PCT/US2007/017409

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasàn et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

85

P008-CIT_ST25.txt

90

95

Val His Lys Lys Tyr Arg Gln Leu Val Ala Lys Pro Phe Ser Pro Glu
100 105 110

Ala Thr Asp Leu Phe Thr Glu Gln Leu Arg Gln Ser Thr Asn Asp Leu
115 120 125

Ile Asp Ala Arg Ile Glu Leu Gly Glu Gly Asp Ala Ala Thr Trp Leu
130 135 140

Ala Asn Glu Ile Pro Ala Arg Leu Thr Ala Ile Leu Leu Gly Leu Pro
145 150 155 160

Pro Glu Asp Gly Asp Thr Tyr Arg Arg Trp Val Trp Ala Ile Thr His
165 170 175

Val Glu Asn Pro Glu Glu Gly Ala Glu Ile Phe Ala Glu Leu Val Ala
180 185 190

His Ala Arg Thr Leu Ile Ala Glu Arg Arg Thr Asn Pro Gly Asn Asp
195 200 205

Ile Met Ser Arg Val Ile Met Ser Lys Ile Asp Gly Glu Ser Leu Ser
210 215 220

Glu Asp Asp Leu Ile Gly Phe Phe Thr Ile Leu Leu Leu Gly Gly Ile
225 230 235 240

Asp Asn Thr Ala Arg Phe Leu Ser Ser Val Phe Trp Arg Leu Ala Trp
245 250 255

Asp Ile Glu Leu Arg Arg Arg Leu Ile Ala His Pro Glu Leu Ile Pro
260 265 270

Asn Ala Val Asp Glu Leu Leu Arg Phe Tyr Gly Pro Ala Met Val Gly
275 280 285

Arg Leu Val Thr Gln Glu Val Thr Val Gly Asp Ile Thr Met Lys Pro
290 295 300

Gly Gln Thr Ala Met Leu Trp Phe Pro Ile Ala Ser Arg Asp Arg Ser
305 310 315 320

Ala Phe Asp Ser Pro Asp Asn Ile Val Ile Glu Arg Thr Pro Asn Arg
325 330 335

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

His Leu Ser Leu Gly His Gly Ile His Arg Cys Leu Gly Ala His Leu
340 345 350

Ile Arg Val Glu Ala Arg Val Ala Ile Thr Glu Phe Leu Lys Arg Ile
355 360 365

Pro Glu Phe Ser Leu Asp Pro Asn Lys Glu Cys Glu Trp Leu Met Gly
370 375 380

Gln Val Ala Gly Met Leu His Val Pro Ile Ile Phe Pro Lys Gly Lys
385 390 395 400

Arg Leu Ser Glu

<210> 11
<211> 428
<212> PRT
<213> Pseudomonas sp

<220>
<221> MISC_FEATURE
<222> (1)..(428)
<223> Cytochrome P450 enzyme P450terp

<400> 11

Met Asp Ala Arg Ala Thr Ile Pro Glu His Ile Ala Arg Thr Val Ile
1 5 10 15

Leu Pro Gln Gly Tyr Ala Asp Asp Glu Val Ile Tyr Pro Ala Phe Lys
20 25 30

Trp Leu Arg Asp Glu Gln Pro Leu Ala Met Ala His Ile Glu Gly Tyr
35 40 45

Asp Pro Met Trp Ile Ala Thr Lys His Ala Asp Val Met Gln Ile Gly
50 55 60

Lys Gln Pro Gly Leu Phe Ser Asn Ala Glu Gly Ser Glu Ile Leu Tyr
65 70 75 80

Asp Gln Asn Asn Glu Ala Phe Met Arg Ser Ile Ser Gly Gly Cys Pro
85 90 95

His Val Ile Asp Ser Leu Thr Ser Met Asp Pro Pro Thr His Thr Ala
100 105 110

Tyr Arg Gly Leu Thr Leu Asn Trp Phe Gln Pro Ala Ser Ile Arg Lys
115 120 125

Printed: 10/30/2007

PCT/US2007/017409

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Leu Glu Glu Asn Ile Arg Arg Ile Ala Gln Ala Ser Val Gln Arg Leu
130 135 140

Leu Asp Phe Asp Gly Glu Cys Asp Phe Met Thr Asp Cys Ala Leu Tyr
145 150 155 160

Tyr Pro Leu His Val Val Met Thr Ala Leu Gly Val Pro Glu Asp Asp
165 170 175

Glu Pro Leu Met Leu Lys Leu Thr Gln Asp Phe Phe Gly Val His Glu
180 185 190

Pro Asp Glu Gln Ala Val Ala Ala Pro Arg Gln Ser Ala Asp Glu Ala
195 200 205

Ala Arg Arg Phe His Glu Thr Ile Ala Thr Phe Tyr Asp Tyr Phe Asn
210 215 220

Gly Phe Thr Val Asp Arg Arg Ser Cys Pro Lys Asp Asp Val Met Ser
225 230 235 240

Leu Leu Ala Asn Ser Lys Leu Asp Gly Asn Tyr Ile Asp Asp Lys Tyr
245 250 255

Ile Asn Ala Tyr Tyr Val Ala Ile Ala Thr Ala Gly His Asp Thr Thr
260 265 270

Ser Ser Ser Ser Gly Gly Ala Ile Ile Gly Leu Ser Arg Asn Pro Glu
275 280 285

Gln Leu Ala Leu Ala Lys Ser Asp Pro Ala Leu Ile Pro Arg Leu Val
290 295 300

Asp Glu Ala Val Arg Trp Thr Ala Pro Val Lys Ser Phe Met Arg Thr
305 310 315 320

Ala Leu Ala Asp Thr Glu Val Arg Gly Gln Asn Ile Lys Arg Gly Asp
325 330 335

Arg Ile Met Leu Ser Tyr Pro Ser Ala Asn Arg Asp Glu Glu Val Phe
340 345 350

Ser Asn Pro Asp Glu Phe Asp Ile Thr Arg Phe Pro Asn Arg His Leu
355 360 365

Gly Phe Gly Trp Gly Ala His Met Cys Leu Gly Gln His Leu Ala Lys
Page 35

08/04/2007

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

370

375

380

Leu Glu Met Lys Ile Phe Phe Glu Glu Leu Leu Pro Lys Leu Lys Ser
385 390 395 400

Val Glu Leu Ser Gly Pro Pro Arg Leu Val Ala Thr Asn Phe Val Gly
405 410 415

Gly Pro Lys Asn Val Pro Ile Arg Phe Thr Lys Ala
420 425

<210> 12
<211> 404
<212> PRT
<213> Saccharopolyspora erythrae

<220>
<221> MISC_FEATURE
<222> (1)...(404)
<223> Cytochrome P450 enzyme P450eryF

<400> 12

Met Thr Thr Val Pro Asp Leu Glu Ser Asp Ser Phe His Val Asp Trp
1 5 10 15

Tyr Arg Thr Tyr Ala Glu Leu Arg Glu Thr Ala Pro Val Thr Pro Val
20 25 30

Arg Phe Leu Gly Gln Asp Ala Trp Leu Val Thr Gly Tyr Asp Glu Ala
35 40 45

Lys Ala Ala Leu Ser Asp Leu Arg Leu Ser Ser Asp Pro Lys Lys Lys
50 55 60

Tyr Pro Gly Val Glu Val Glu Phe Pro Ala Tyr Leu Gly Phe Pro Glu
65 70 75 80

Asp Val Arg Asn Tyr Phe Ala Thr Asn Met Gly Thr Ser Asp Pro Pro
85 90 95

Thr His Thr Arg Leu Arg Lys Leu Val Ser Gln Glu Phe Thr Val Arg
100 105 110

Arg Val Glu Ala Met Arg Pro Arg Val Glu Gln Ile Thr Ala Glu Leu
115 120 125

Leu Asp Glu Val Gly Asp Ser Gly Val Val Asp Ile Val Asp Arg Phe
130 135 140

P008-CIT_ST25.txt

Ala His Pro Leu Pro Ile Lys Val Ile Cys Glu Leu Leu Gly Val Asp
145 150 155 160

Glu Lys Tyr Arg Gly Glu Phe Gly Arg Trp Ser Ser Glu Ile Leu Val
165 170 175

Met Asp Pro Glu Arg Ala Glu Gln Arg Gly Gln Ala Ala Arg Glu Val
180 185 190

Val Asn Phe Ile Leu Asp Leu Val Glu Arg Arg Arg Thr Glu Pro Gly
195 200 205

Asp Asp Leu Leu Ser Ala Leu Ile Arg Val Gln Asp Asp Asp Asp Gly
210 215 220

Arg Leu Ser Ala Asp Glu Leu Thr Ser Ile Ala Leu Val Leu Leu Leu
225 230 235 240

Ala Gly Phe Glu Ala Ser Val Ser Leu Ile Gly Ile Gly Thr Tyr Leu
245 250 255

Leu Leu Thr His Pro Asp Gln Leu Ala Leu Val Arg Arg Asp Pro Ser
260 265 270

Ala Leu Pro Asn Ala Val Glu Glu Ile Leu Arg Tyr Ile Ala Pro Pro
275 280 285

Glu Thr Thr Thr Arg Phe Ala Ala Glu Glu Val Glu Ile Gly Gly Val
290 295 300

Ala Ile Pro Gln Tyr Ser Thr Val Leu Val Ala Asn Gly Ala Ala Asn
305 310 315 320

Arg Asp Pro Lys Gln Phe Pro Asp Pro His Arg Phe Asp Val Thr Arg
325 330 335

Asp Thr Arg Gly His Leu Ser Phe Gly Gln Gly Ile His Phe Cys Met
340 345 350

Gly Arg Pro Leu Ala Lys Leu Glu Gly Glu Val Ala Leu Arg Ala Leu
355 360 365

Phe Gly Arg Phe Pro Ala Leu Ser Leu Gly Ile Asp Ala Asp Asp Val
370 375 380

Val Trp Arg Arg Ser Leu Leu Leu Arg Gly Ile Asp His Leu Pro Val
385 390 395 400

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Arg Leu Asp Gly

<210> 13
<211> 516
<212> PRT
<213> homo sapiens

<220>
<221> MISC_FEATURE
<222> (1)..(516)
<223> Cytochrome P450 enzyme CYP1A2

<400> 13

Met Ala Leu Ser Gln Ser Val Pro Phe Ser Ala Thr Glu Leu Leu Leu
1 5 10 15

Ala Ser Ala Ile Phe Cys Leu Val Phe Trp Val Leu Lys Gly Leu Arg
20 25 30

Pro Arg Val Pro Lys Gly Leu Lys Ser Pro Pro Glu Pro Trp Gly Trp
35 40 45

Pro Leu Leu Gly His Val Leu Thr Leu Gly Lys Asn Pro His Leu Ala
50 55 60

Leu Ser Arg Met Ser Gln Arg Tyr Gly Asp Val Leu Gln Ile Arg Ile
65 70 75 80

Gly Ser Thr Pro Val Leu Val Leu Ser Arg Leu Asp Thr Ile Arg Gln
85 90 95

Ala Leu Val Arg Gln Gly Asp Asp Phe Lys Gly Arg Pro Asp Leu Tyr
100 105 110

Thr Ser Thr Leu Ile Thr Asp Gly Gln Ser Leu Thr Phe Ser Thr Asp
115 120 125

Ser Gly Pro Val Trp Ala Ala Arg Arg Arg Leu Ala Gln Asn Ala Leu
130 135 140

Asn Thr Phe Ser Ile Ala Ser Asp Pro Ala Ser Ser Ser Ser Cys Tyr
145 150 155 160

Leu Glu Glu His Val Ser Lys Glu Ala Lys Ala Leu Ile Ser Arg Leu
165 170 175

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Gln Glu Leu Met Ala Gly Pro Gly His Phe Asp Pro Tyr Asn Gln Val
180 185 190

Val Val Ser Val Ala Asn Val Ile Gly Ala Met Cys Phe Gly Gln His
195 200 205

Phe Pro Glu Ser Ser Asp Glu Met Leu Ser Leu Val Lys Asn Thr His
210 215 220

Glu Phe Val Glu Thr Ala Ser Ser Gly Asn Pro Leu Asp Phe Phe Pro
225 230 235 240

Ile Leu Arg Tyr Leu Pro Asn Pro Ala Leu Gln Arg Phe Lys Ala Phe
245 250 255

Asn Gln Arg Phe Leu Trp Phe Leu Gln Lys Thr Val Gln Glu His Tyr
260 265 270

Gln Asp Phe Asp Lys Asn Ser Val Arg Asp Ile Thr Gly Ala Leu Phe
275 280 285

Lys His Ser Lys Lys Gly Pro Arg Ala Ser Gly Asn Leu Ile Pro Gln
290 295 300

Glu Lys Ile Val Asn Leu Val Asn Asp Ile Phe Gly Ala Gly Phe Asp
305 310 315 320

Thr Val Thr Thr Ala Ile Ser Trp Ser Leu Met Tyr Leu Val Thr Lys
325 330 335

Pro Glu Ile Gln Arg Lys Ile Gln Lys Glu Leu Asp Thr Val Ile Gly
340 345 350

Arg Glu Arg Arg Pro Arg Leu Ser Asp Arg Pro Gln Leu Pro Tyr Leu
355 360 365

Glu Ala Phe Ile Leu Glu Thr Phe Arg His Ser Ser Phe Leu Pro Phe
370 375 380

Thr Ile Pro His Ser Thr Arg Asp Thr Thr Leu Asn Gly Phe Tyr
385 390 395 400

Ile Pro Lys Lys Cys Cys Val Phe Val Asn Gln Trp Gln Val Asn His
405 410 415

Asp Pro Glu Leu Trp Glu Asp Pro Ser Glu Phe Arg Pro Glu Arg Phe
420 425 430

Title: "Methods and Systems for selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Leu Thr Ala Asp Gly Thr Ala Ile Asn Lys Pro Leu Ser Glu Lys Met
 435 440 445

Met Leu Phe Gly Met Gly Lys Arg Arg Cys Ile Gly Glu Val Leu Ala
 450 455 460

Lys Trp Glu Ile Phe Leu Phe Leu Ala Ile Leu Leu Gln Gln Leu Glu
 465 470 475 480

Phe Ser Val Pro Pro Gly Val Lys Val Asp Leu Thr Pro Ile Tyr Gly
 485 490 495

Leu Thr Met Lys His Ala Arg Cys Glu His Val Gln Ala Arg Leu Arg
 500 505 510

Phe Ser Ile Asn
 515

<210> 14
 <211> 489
 <212> PRT
 <213> homo sapiens

<220>
 <221> MISC_FEATURE
 <222> (1)..(489)
 <223> Cytochrome P450 enzyme CYP2C8

<400> 14

Met Glu Pro Phe Val Val Leu Val Leu Cys Leu Ser Phe Met Leu Leu
 1 5 10 15

Phe Ser Leu Trp Arg Gln Ser Cys Arg Arg Arg Lys Leu Pro Pro Gly
 20 25 30

Pro Thr Pro Leu Pro Ile Ile Gly Asn Met Leu Gln Ile Asp Val Lys
 35 40 45

Asp Ile Cys Lys Ser Phe Thr Asn Phe Ser Lys Val Tyr Gly Pro Val
 50 55 60

Phe Thr Val Tyr Phe Gly Asn Pro Ile Val Val Phe His Gly Tyr Glu
 65 70 75 80

Ala Val Lys Glu Ala Leu Ile Asp Asn Gly Glu Glu Phe Ser Gly Arg
 85 90 95

Gly Asn Ser Pro Ile Ser Gln Arg Ile Thr Lys Gly Leu Gly Ile Ile
 Page 40

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

100

P008-CIT_ST25.txt

105

110

Ser Ser Asn Gly Lys Arg Trp Lys Glu Ile Arg Arg Phe Ser Leu Thr.
115 120 125

Thr Leu Arg Asn Phe Gly Met Gly Lys Arg Ser Ile Glu Asp Arg Val
130 135 140

Gln Glu Glu Ala His Cys Leu Val Glu Glu Leu Arg Lys Thr Lys Ala
145 150 155 160

Ser Pro Cys Asp Pro Thr Phe Ile Leu Gly Cys Ala Pro Cys Asn Val
165 170 175

Ile Cys Ser Val Val Phe Gln Lys Arg Phe Asp Tyr Lys Asp Gln Asn
180 185 190

Phe Leu Thr Leu Met Lys Arg Phe Asn Glu Asn Phe Arg Ile Leu Asn
195 200 205

Ser Pro Trp Ile Gln Val Cys Asn Asn Phe Pro Leu Leu Ile Asp Cys
210 215 220

Phe Pro Gly Thr His Asn Lys Val Leu Lys Asn Val Ala Leu Thr Arg
225 230 235 240

Ser Tyr Ile Arg Glu Lys Val Lys Glu His Gln Ala Ser Leu Asp Val
245 250 255

Asn Asn Pro Arg Asp Phe Ile Asp Cys Phe Leu Ile Lys Met Glu Gln
260 265 270

Glu Lys Asp Asn Gln Lys Ser Glu Phe Asn Ile Glu Asn Leu Val Gly
275 280 285

Thr Val Ala Asp Leu Phe Val Ala Gly Thr Glu Thr Thr Ser Thr Thr
290 295 300

Leu Arg Tyr Gly Leu Leu Leu Leu Lys His Pro Glu Val Thr Ala
305 310 315 320

Lys Val Gln Glu Glu Ile Asp His Val Ile Gly Arg His Arg Ser Pro
325 330 335

Cys Met Gln Asp Arg Ser His Met Pro Tyr Thr Asp Ala Val Val His
340 345 350

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Glu Ile Gln Arg Tyr Ser Asp Leu Val Pro Thr Gly Val Pro His Ala
355 360 365

Val Thr Thr Asp Thr Lys Phe Arg Asn Tyr Leu Ile Pro Lys Gly Thr
370 375 380

Thr Ile Met Ala Leu Leu Thr Ser Val Leu His Asp Asp Lys Glu Phe
385 390 395 400

Pro Asn Pro Asn Ile Phe Asp Pro Gly His Phe Leu Asp Lys Asn Gly
405 410 415

Asn Phe Lys Lys Ser Asp Tyr Phe Met Pro Phe Ser Ala Gly Lys Arg
420 425 430

Ile Cys Ala Gly Glu Gly Leu Ala Arg Met Glu Leu Phe Leu Phe Leu
435 440 445

Thr Thr Ile Leu Gln Asn Phe Asn Leu Lys Ser Val Asp Asp Leu Lys
450 455 460

Asn Leu Asn Thr Thr Ala Val Thr Lys Gly Ile Val Ser Leu Pro Pro
465 470 475 480

Ser Tyr Gln Ile Cys Phe Ile Pro Val
485

<210> 15
<211> 490
<212> PRT
<213> homo sapiens

<220>
<221> MISC_FEATURE
<222> (1) (490)
<223> Cytochrome P450 enzyme CYP2C9

<400> 15

Met Asp Ser Leu Val Val Leu Val Leu Cys Leu Ser Cys Leu Leu Leu
1 5 10 15

Leu Ser Leu Trp Arg Gln Ser Ser Gly Arg Gly Lys Leu Pro Pro Gly
20 25 30

Pro Thr Pro Leu Pro Val Ile Gly Asn Ile Leu Gln Ile Gly Ile Lys
35 40 45

Asp Ile Ser Lys Ser Leu Thr Asn Leu Ser Lys Val Tyr Gly Pro Val
50 55 60

Printed: 10/30/2007

US 0019

PCT/US2007/017409

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Phe Thr Leu Tyr Phe Gly Leu Lys Pro Ile Val Val Leu His Gly Tyr
65 70 75 80

Glu Ala Val Lys Glu Ala Leu Ile Asp Leu Gly Glu Glu Phe Ser Gly
85 90 95

Arg Gly Ile Phe Pro Leu Ala Glu Arg Ala Asn Arg Gly Phe Gly Ile
100 105 110

Val Phe Ser Asn Gly Lys Lys Trp Lys Glu Ile Arg Arg Phe Ser Leu
115 120 125

Met Thr Leu Arg Asn Phe Gly Met Gly Lys Arg Ser Ile Glu Asp Arg
130 135 140

Val Gln Glu Glu Ala Arg Cys Leu Val Glu Glu Leu Arg Lys Thr Lys
145 150 155 160

Ala Ser Pro Cys Asp Pro Thr Phe Ile Leu Gly Cys Ala Pro Cys Asn
165 170 175

Val Ile Cys Ser Ile Ile Phe His Lys Arg Phe Asp Tyr Lys Asp Gln
180 185 190

Gln Phe Leu Asn Leu Met Glu Lys Leu Asn Glu Asn Ile Lys Ile Leu
195 200 205

Ser Ser Pro Trp Ile Gln Ile Cys Asn Asn Phe Ser Pro Ile Ile Asp
210 215 220

Tyr Phe Pro Gly Thr His Asn Lys Leu Leu Lys Asn Val Ala Phe Met
225 230 235 240

Lys Ser Tyr Ile Leu Glu Lys Val Lys Glu His Gln Glu Ser Met Asp
245 250 255

Met Asn Asn Pro Gln Asp Phe Ile Asp Cys Phe Leu Met Lys Met Glu
260 265 270

Lys Glu Lys His Asn Gln Pro Ser Glu Phe Thr Ile Glu Ser Leu Glu
275 280 285

Asn Thr Ala Val Asp Leu Phe Gly Ala Gly Thr Glu Thr Thr Ser Thr
290 295 300

Thr Leu Arg Tyr Ala Leu Leu Leu Leu Lys His Pro Glu Val Thr
Page 43

08/04/2007

Printed: 10/30/2007

SEQUENCE

PCT/US2007/017409

260

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

305

310

P008-CIT_ST25.txt

315

320

Ala Lys Val Gln Glu Glu Ile Glu Arg Val Ile Gly Arg Asn Arg Ser
325 330 335

Pro Cys Met Gln Asp Arg Ser His Met Pro Tyr Thr Asp Ala Val Val
340 345 350

His Glu Val Gln Arg Tyr Ile Asp Leu Leu Pro Thr Ser Leu Pro His
355 360 365

Ala Val Thr Cys Asp Ile Lys Phe Arg Asn Tyr Leu Ile Pro Lys Gly
370 375 380

Thr Thr Ile Leu Ile Ser Leu Thr Ser Val Leu His Asp Asn Lys Glu
385 390 395 400

Phe Pro Asn Pro Glu Met Phe Asp Pro His His Phe Leu Asp Glu Gly
405 410 415

Gly Asn Phe Lys Lys Ser Lys Tyr Phe Met Pro Phe Ser Ala Gly Lys
420 425 430

Arg Ile Cys Val Gly Glu Ala Leu Ala Gly Met Glu Leu Phe Leu Phe
435 440 445

Leu Thr Ser Ile Leu Gln Asn Phe Asn Leu Lys Ser Leu Val Asp Pro
450 455 460

Lys Asn Leu Asp Thr Thr Pro Val Val Asn Gly Phe Ala Ser Val Pro
465 470 475 480

Pro Phe Tyr Gln Leu Cys Phe Ile Pro Val
485 490

<210> 16
<211> 490
<212> PRT
<213> homo sapiens

<220>
<221> MISC_FEATURE
<222> (1)..(490)
<223> Cytochrome P450 enzyme CYP2C19

<400> 16

Met Asp Pro Phe Val Val Leu Val Leu Cys Leu Ser Cys Leu Leu Leu
1 5 10 15

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Leu Ser Ile Trp Arg Gln Ser Ser Gly Arg Gly Lys Leu Pro Pro Gly
20 25 30

Pro Thr Pro Leu Pro Val Ile Gly Asn Ile Leu Gln Ile Asp Ile Lys
35 40 45

Asp Val Ser Lys Ser Leu Thr Asn Leu Ser Lys Ile Tyr Gly Pro Val
50 55 60

Phe Thr Leu Tyr Phe Gly Leu Glu Arg Met Val Val Leu His Gly Tyr
65 70 75 80

Glu Val Val Lys Glu Ala Leu Ile Asp Leu Gly Glu Glu Phe Ser Gly
85 90 95

Arg Gly His Phe Pro Leu Ala Glu Arg Ala Asn Arg Gly Phe Gly Ile
100 105 110

Val Phe Ser Asn Gly Lys Arg Trp Lys Glu Ile Arg Arg Phe Ser Leu
115 120 125

Met Thr Leu Arg Asn Phe Gly Met Gly Lys Arg Ser Ile Glu Asp Arg
130 135 140

Val Gln Glu Glu Ala Arg Cys Leu Val Glu Glu Leu Arg Lys Thr Lys
145 150 155 160

Ala Ser Pro Cys Asp Pro Thr Phe Ile Leu Gly Cys Ala Pro Cys Asn
165 170 175

Val Ile Cys Ser Ile Ile Phe Gln Lys Arg Phe Asp Tyr Lys Asp Gln
180 185 190

Gln Phe Leu Asn Leu Met Glu Lys Leu Asn Glu Asn Ile Arg Ile Val
195 200 205

Ser Thr Pro Trp Ile Gln Ile Cys Asn Asn Phe Pro Thr Ile Ile Asp
210 215 220

Tyr Phe Pro Gly Thr His Asn Lys Leu Leu Lys Asn Leu Ala Phe Met
225 230 235 240

Glu Ser Asp Ile Leu Glu Lys Val Lys Glu His Gln Glu Ser Met Asp
245 250 255

Ile Asn Asn Pro Arg Asp Phe Ile Asp Cys Phe Leu Ile Lys Met Glu
260 265 270

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Lys Glu Lys Gln Asn Gln Gln Ser Glu Phe Thr Ile Glu Asn Leu Val
275 280 285

Ile Thr Ala Ala Asp Leu Leu Gly Ala Gly Thr Glu Thr Thr Ser Thr
290 295 300

Thr Leu Arg Tyr Ala Leu Leu Leu Leu Lys His Pro Glu Val Thr
305 310 315 320

Ala Lys Val Gln Glu Glu Ile Glu Arg Val Ile Gly Arg Asn Arg Ser
325 330 335

Pro Cys Met Gln Asp Arg Gly His Met Pro Tyr Thr Asp Ala Val Val
340 345 350

His Glu Val Gln Arg Tyr Ile Asp Leu Ile Pro Thr Ser Leu Pro His
355 360 365

Ala Val Thr Cys Asp Val Lys Phe Arg Asn Tyr Leu Ile Pro Lys Gly
370 375 380

Thr Thr Ile Leu Thr Ser Leu Thr Ser Val Leu His Asp Asn Lys Glu
385 390 395 400

Phe Pro Asn Pro Glu Met Phe Asp Pro Arg His Phe Leu Asp Glu Gly
405 410 415

Gly Asn Phe Lys Lys Ser Asn Tyr Phe Met Pro Phe Ser Ala Gly Lys
420 425 430

Arg Ile Cys Val Gly Glu Gly Leu Ala Arg Met Glu Leu Phe Leu Phe
435 440 445

Leu Thr Phe Ile Leu Gln Asn Phe Asn Leu Lys Ser Leu Ile Asp Pro
450 455 460

Lys Asp Leu Asp Thr Thr Pro Val Val Asn Gly Phe Ala Ser Val Pro
465 470 475 480

Pro Phe Tyr Gln Leu Cys Phe Ile Pro Val
485 490

<210> 17
<211> 446
<212> PRT
<213> homo sapiens

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

<220>
 <221> MISC_FEATURE
 <222> (1)..(446)
 <223> Cytochrome P450 enzyme CYP2D6

<400> 17

Met Gly Leu Glu Ala Leu Val Pro Leu Ala Val Ile Val Ala Ile Phe
 1 5 10 15

Leu Leu Leu Val Asp Leu Met His Arg Arg Gln Arg Trp Ala Ala Arg
 20 25 30

Tyr Pro Pro Gly Pro Leu Pro Leu Pro Gly Leu Gly Asn Leu Leu His
 35 40 45

Val Asp Phe Gln Asn Thr Pro Tyr Cys Phe Asp Gln Leu Arg Arg Arg
 50 55 60

Phe Gly Asp Val Phe Ser Leu Gln Leu Ala Trp Thr Pro Val Val Val
 65 70 75 80

Leu Asn Gly Leu Ala Ala Val Arg Glu Ala Leu Val Thr His Gly Glu
 85 90 95

Asp Thr Ala Asp Arg Pro Pro Val Pro Ile Thr Gln Ile Leu Gly Phe
 100 105 110

Gly Pro Arg Ser Gln Gly Arg Pro Phe Arg Pro Asn Gly Leu Leu Asp
 115 120 125

Lys Ala Val Ser Asn Val Ile Ala Ser Leu Thr Cys Gly Arg Arg Phe
 130 135 140

Glu Tyr Asp Asp Pro Arg Phe Leu Arg Leu Leu Asp Leu Ala Gln Glu
 145 150 155 160

Gly Leu Lys Glu Glu Ser Gly Phe Leu Arg Glu Val Leu Asn Ala Val
 165 170 175

Pro Val Leu Leu His Ile Pro Ala Leu Ala Gly Lys Val Leu Arg Phe
 180 185 190

Gln Lys Ala Phe Leu Thr Gln Leu Asp Glu Leu Leu Thr Glu His Arg
 195 200 205

Met Thr Trp Asp Pro Ala Gln Pro Pro Arg Asp Leu Thr Glu Ala Phe
 210 215 220

Printed: 10/30/2007

SP0019

PCT/US2007/017409

109

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Leu Ala Glu Met Glu Lys Ala Lys Gly Asn Pro Glu Ser Ser Phe Asn
225 230 235 240

Asp Glu Asn Leu Cys Ile Val Val Ala Asp Leu Phe Ser Ala Gly Met
245 250 255

Val Thr Thr Ser Thr Thr Leu Ala Trp Gly Leu Leu Leu Met Ile Leu
260 265 270

His Pro Asp Val Gln Arg Arg Val Gln Gln Glu Ile Asp Asp Val Ile
275 280 285

Gly Gln Val Arg Arg Pro Glu Met Gly Asp Gln Ala His Met Pro Tyr
290 295 300

Thr Thr Ala Val Ile His Glu Val Gln Arg Phe Gly Asp Ile Val Pro
305 310 315 320

Leu Gly Val Thr His Met Thr Ser Arg Asp Ile Glu Val Gln Gly Phe
325 330 335

Arg Ile Pro Lys Gly Thr Thr Leu Ile Thr Asn Leu Ser Ser Val Leu
340 345 350

Lys Asp Glu Ala Val Trp Glu Lys Pro Phe Arg Phe His Pro Glu His
355 360 365

Phe Leu Asp Ala Gln Gly His Phe Val Lys Pro Glu Ala Phe Leu Pro
370 375 380

Phe Ser Ala Gly Arg Arg Ala Cys Leu Gly Glu Pro Leu Ala Arg Met
385 390 395 400

Glu Leu Phe Leu Phe Phe Thr Ser Leu Leu Gln His Phe Ser Phe Ser
405 410 415

Val Pro Thr Gly Gln Pro Arg Pro Ser His His Gly Val Phe Ala Phe
420 425 430

Leu Val Thr Pro Ser Pro Tyr Glu Leu Cys Ala Val Pro Arg
435 440 445

<210> 18
<211> 493
<212> PRT
<213> homo sapiens

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

<220>

<221> MISC_FEATURE

<222> (1)..(493)

<223> Cytochrome P450-enzyme CYP2E1

<400> 18

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

Printed: 10/30/2007

Sheet 1

PCT/US2007/017409

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Leu His Tyr Leu Pro Gly Ser His Arg Lys Val Ile Lys Asn Val Ala
225 230 235 240

Glu Val Lys Glu Tyr Val Ser Glu Arg Val Lys Glu His His Gln Ser
245 250 255

Leu Asp Pro Asn Cys Pro Arg Asp Leu Thr Asp Cys Leu Leu Val Glu
260 265 270

Met Glu Lys Glu Lys His Ser Ala Glu Arg Leu Tyr Thr Met Asp Gly
275 280 285

Ile Thr Val Thr Val Ala Asp Leu Phe Phe Ala Gly Thr Glu Thr Thr
290 295 300

Ser Thr Thr Leu Arg Tyr Gly Leu Leu Ile Leu Met Lys Tyr Pro Glu
305 310 315 320

Ile Glu Glu Lys Leu His Glu Glu Ile Asp Arg Val Ile Gly Pro Ser
325 330 335

Arg Ile Pro Ala Ile Lys Asp Arg Gln Glu Met Pro Tyr Met Asp Ala
340 345 350

Val Val His Glu Ile Gln Arg Phe Ile Thr Leu Val Pro Ser Asn Leu
355 360 365

Pro His Glu Ala Thr Arg Asp Thr Ile Phe Arg Gly Tyr Leu Ile Pro
370 375 380

Lys Gly Thr Val Val Val Pro Thr Leu Asp Ser Val Leu Tyr Asp Asn
385 390 395 400

Gln Glu Phe Pro Asp Pro Glu Lys Phe Lys Pro Glu His Phe Leu Asn
405 410 415

Glu Asn Gly Lys Phe Lys Tyr Ser Asp Tyr Phe Lys Pro Phe Ser Thr
420 425 430

Gly Lys Arg Val Cys Ala Gly Glu Gly Leu Ala Arg Met Glu Leu Phe
435 440 445

Leu Leu Leu Cys Ala Ile Leu Gln His Phe Asn Leu Lys Pro Leu Val
450 455 460

Asp Pro Lys Asp Ile Asp Leu Ser Pro Ile His Ile Gly Phe Gly Cys
465 470 475 480

Printed: 10/30/2007

SEQUENCE

PCT/US2007/017409

Title: "Methods and Systems for Selective"

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Ile .Pro Pro Arg Tyr Lys Leu Cys Val Ile Pro Arg Ser
485 490

<210> 19
<211> 491
<212> PRT
<213> homo sapiens

<220>
<221> MISC_FEATURE
<222> (1)..(491)
<223> Cytochrome P450 enzyme CYP2F1

<400> 19

Met Asp Ser Ile Ser Thr Ala Ile Leu Leu Leu Leu Ala Leu Val
1 5 10 15

Cys Leu Leu Leu Thr Leu Ser Ser Arg Asp Lys Gly Lys Leu Pro Pro
20 25 30

Gly Pro Arg Pro Leu Ser Ile Leu Gly Asn Leu Leu Leu Leu Cys Ser
35 40 45

Gln Asp Met Leu Thr Ser Leu Thr Lys Leu Ser Lys Glu Tyr Gly Ser
50 55 60

Met Tyr Thr Val His Leu Gly Pro Arg Arg Val Val Val Leu Ser Gly
65 70 75 80

Tyr Gln Ala Val Lys Glu Ala Leu Val Asp Gln Gly Glu Glu Phe Ser
85 90 95

Gly Arg Gly Asp Tyr Pro Ala Phe Phe Asn Phe Thr Lys Gly Asn Gly
100 105 110

Ile Ala Phe Ser Ser Gly Asp Arg Trp Lys Val Leu Arg Gln Phe Ser
115 120 125

Ile Gln Ile Leu Arg Asn Phe Gly Met Gly Lys Arg Ser Ile Glu Glu
130 135 140

Arg Ile Leu Glu Glu Gly Ser Phe Leu Leu Ala Glu Leu Arg Lys Thr
145 150 155 160

Glu Gly Glu Pro Phe Asp Pro Thr Phe Val Leu Ser Arg Ser Val Ser
165 170 175

Asn Ile Ile Cys Ser Val Leu Phe Gly Ser Arg Phe Asp Tyr Asp Asp
Page 51

08/04/2007

Printed: 10/30/2007

SEQUENCE

PCT/US2007/017409

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

180

185

190

Glu Arg Leu Leu Thr Ile Ile Arg Leu Ile Asn Asp Asn Phe Gln Ile
195 200 205

Met Ser Ser Pro Trp Gly Glu Leu Tyr Asp Ile Phe Pro Ser Leu Leu
210 215 220

Asp Trp Val Pro Gly Pro His Gln Arg Ile Phe Gln Asn Phe Lys Cys
225 230 235 240

Leu Arg Asp Leu Ile Ala His Ser Val His Asp His Gln Ala Ser Leu
245 250 255

Asp Pro Arg Ser Pro Arg Asp Phe Ile Gln Cys Phe Leu Thr Lys Met
260 265 270

Ala Glu Glu Lys Gly Asp Pro Leu Ser His Phe His Met Asp Thr Leu
275 280 285

Leu Met Thr Thr His Asn Leu Leu Phe Gly Gly Thr Lys Thr Val Ser
290 295 300

Thr Thr Leu His His Ala Phe Leu Ala Leu Met Lys Tyr Pro Lys Val
305 310 315 320

Gln Ala Arg Val Gln Glu Glu Ile Asp Leu Val Val Gly Arg Ala Arg
325 330 335

Leu Pro Ala Leu Lys Asp Arg Ala Ala Met Pro Tyr Thr Asp Ala Val
340 345 350

Ile His Glu Val Gln Arg Phe Ala Asp Ile Ile Pro Met Asn Leu Pro
355 360 365

His Arg Val Thr Arg Asp Thr Ala Phe Arg Gly Phe Leu Ile Pro Lys
370 375 380

Gly Thr Asp Val Ile Thr Leu Leu Asn Thr Val His Tyr Asp Pro Ser
385 390 395 400

Gln Phe Leu Thr Pro Gln Glu Phe Asn Pro Glu His Phe Leu Asp Ala
405 410 415

Asn Gln Ser Phe Lys Lys Ser Pro Ala Phe Met Pro Phe Ser Ala Gly
420 425 430

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Arg Arg Leu Cys Leu Gly Glu Ser 440
 435 Leu Ala Arg Met Glu Leu Phe Leu 445

Tyr Leu Thr Ala Ile Leu Gln Ser Phe Ser Leu Gln Pro Leu Gly Ala 460
 450 455

Pro Glu Asp Ile Asp Leu Thr Pro Leu Ser Ser Gly Leu Gly Asn Leu 480
 465 470 475

Pro Arg Pro Phe Gln Leu Cys Leu Arg Pro Arg 490
 485

<210> 20
 <211> 503
 <212> PRT
 <213> homo sapiens

<220>
 <221> MISC_FEATURE
 <222> (1)..(503)
 <223> Cytochrome P450 enzyme CYP3A4

<400> 20

Met Ala Leu Ile Pro Asp Leu Ala Met Glu Thr Trp Leu Leu Leu Ala 15
 1 5 10

Val Ser Leu Val Leu Leu Tyr Leu Tyr Gly Thr His Ser His Gly Leu 30
 20 25

Phe Lys Lys Leu Gly Ile Pro Gly Pro Thr Pro Leu Pro Phe Leu Gly 45
 35 40

Asn Ile Leu Ser Tyr His Lys Gly Phe Cys Met Phe Asp Met Glu Cys 60
 50 55

His Lys Lys Tyr Gly Lys Val Trp Gly Phe Tyr Asp Gly Gln Gln Pro 80
 65 70 75

Val Leu Ala Ile Thr Asp Pro Asp Met Ile Lys Thr Val Leu Val Lys 95
 85 90

Glu Cys Tyr Ser Val Phe Thr Asn Arg Arg Pro Phe Gly Pro Val Gly 110
 100 105

Phe Met Lys Ser Ala Ile Ser Ile Ala Glu Asp Glu Glu Trp Lys Arg 125
 115 120

Leu Arg Ser Leu Leu Ser Pro Thr Phe Thr Ser Gly Lys Leu Lys Glu 140
 130 135

Printed: 10/30/2007

167015

PCT/US2007/017409

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Met Val Pro Ile Ile Ala Gln Tyr Gly Asp Val Leu Val Arg Asn Leu
145 150 155 160

Arg Arg Glu Ala Glu Thr Gly Lys Pro Val Thr Leu Lys Asp Val Phe
165 170 175

Gly Ala Tyr Ser Met Asp Val Ile Thr Ser Thr Ser Phe Gly Val Asn
180 185 190

Ile Asp Ser Leu Asn Asn Pro Gln Asp Pro Phe Val Glu Asn Thr Lys
195 200 205

Lys Leu Leu Arg Phe Asp Phe Leu Asp Pro Phe Phe Leu Ser Ile Thr
210 215 220

Val Phe Pro Phe Leu Ile Pro Ile Leu Glu Val Leu Asn Ile Cys Val
225 230 235 240

Phe Pro Arg Glu Val Thr Asn Phe Leu Arg Lys Ser Val Lys Arg Met
245 250 255

Lys Glu Ser Arg Leu Glu Asp Thr Gln Lys His Arg Val Asp Phe Leu
260 265 270

Gln Leu Met Ile Asp Ser Gln Asn Ser Lys Glu Thr Glu Ser His Lys
275 280 285

Ala Leu Ser Asp Leu Glu Leu Val Ala Gln Ser Ile Ile Phe Ile Phe
290 295 300

Ala Gly Tyr Glu Thr Thr Ser Ser Val Leu Ser Phe Ile Met Tyr Glu
305 310 315 320

Leu Ala Thr His Pro Asp Val Gln Gln Lys Leu Gln Glu Glu Ile Asp
325 330 335

Ala Val Leu Pro Asn Lys Ala Pro Pro Thr Tyr Asp Thr Val Leu Gln
340 345 350

Met Glu Tyr Leu Asp Met Val Val Asn Glu Thr Leu Arg Leu Phe Pro
355 360 365

Ile Ala Met Arg Leu Glu Arg Val Cys Lys Lys Asp Val Glu Ile Asn
370 375 380

Gly Met Phe Ile Pro Lys Gly Val Val Val Met Ile Pro Ser Tyr Ala
Page 54

Printed: 10/30/2007

SECRET

PCT/US2007/017409

409

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

385

390

395

400

Leu His Arg Asp Pro Lys Tyr Trp Thr Glu Pro Glu Lys Phe Leu Pro
405 410 415

Glu Arg Phe Ser Lys Lys Asn Lys Asp Asn Ile Asp Pro Tyr Ile Tyr
420 425 430

Thr Pro Phe Gly Ser Gly Pro Arg Asn Cys Ile Gly Met Arg Phe Ala
435 440 445

Leu Met Asn Met Lys Leu Ala Leu Ile Arg Val Leu Gln Asn Phe Ser
450 455 460

Phe Lys Pro Cys Lys Glu Thr Gln Ile Pro Leu Lys Leu Ser Leu Gly
465 470 475 480

Gly Leu Leu Gln Pro Glu Lys Pro Val Val Leu Lys Val Glu Ser Arg
485 490 495

Asp Gly Thr Val Ser Gly Ala
500

<210> 21
<211> 1048
<212> PRT
<213> Artificial sequence

<220>
<223> Cytochrome P450 variant CYP102A1var1

<400> 21

Thr Ile Lys Glu Met Pro Gln Pro Lys Thr Phe Gly Glu Leu Lys Asn
1 5 10 15

Leu Pro Leu Leu Asn Thr Asp Lys Pro Val Gln Ala Leu Met Lys Ile
20 25 30

Ala Asp Glu Leu Gly Glu Ile Phe Lys Phe Glu Ala Pro Gly Arg Val
35 40 45

Thr Arg Tyr Leu Ser Ser Gln Arg Leu Ile Lys Glu Ala Cys Asp Glu
50 55 60

Ser Arg Phe Asp Lys Asn Leu Ser Gln Ala Leu Lys Phe Ala Arg Asp
65 70 75 80

Phe Ala Gly Asp Gly Leu Phe Thr Ser Trp Thr His Glu Lys Asn Trp
85 90 95

Page 55

Printed: 10/30/2007

Sequence

PCT/US2007/017409

Title: "Methods and systems for selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Lys Lys Ala His Asn Ile Leu Leu Pro Ser Phe Ser Gln Gln Ala Met
100 105 110

Lys Gly Tyr His Ala Met Met Val Asp Ile Ala Val Gln Leu Val Gln
115 120 125

Lys Trp Glu Arg Leu Asn Ala Asp Glu Tyr Ile Glu Val Pro Glu Asp
130 135 140

Met Thr Arg Leu Thr Leu Asp Thr Ile Gly Leu Cys Gly Phe Asn Tyr
145 150 155 160

Arg Phe Asn Ser Phe Tyr Arg Asp Gln Pro His Pro Phe Ile Ile Ser
165 170 175

Met Ile Arg Ala Leu Asp Glu Val Met Asn Lys Leu Gln Arg Ala Asn
180 185 190

Pro Asp Asp Pro Ala Tyr Asp Glu Asn Lys Arg Gln Phe Gln Glu Asp
195 200 205

Ile Lys Val Met Asn Asp Leu Val Asp Lys Ile Ile Ala Asp Arg Lys
210 215 220

Ala Ser Gly Glu Gln Ser Asp Asp Leu Leu Thr Gln Met Leu Asn Gly
225 230 235 240

Lys Asp Pro Glu Thr Gly Glu Pro Leu Asp Asp Gly Asn Ile Ser Tyr
245 250 255

Gln Ile Ile Thr Phe Leu Ile Ala Gly His Glu Thr Thr Ser Gly Leu
260 265 270

Leu Ser Phe Ala Leu Tyr Phe Leu Val Lys Asn Pro His Val Leu Gln
275 280 285

Lys Val Ala Glu Glu Ala Thr Arg Val Leu Val Asp Pro Val Pro Ser
290 295 300

Tyr Lys Gln Val Lys Gln Leu Lys Tyr Val Gly Met Val Leu Asn Glu
305 310 315 320

Ala Leu Arg Leu Trp Pro Thr Ala Pro Ala Phe Ser Leu Tyr Ala Lys
325 330 335

Glu Asp Thr Val Leu Gly Gly Glu Tyr Pro Leu Glu Lys Gly Asp Glu
Page 56

Printed: 10/30/2007

SEQUENCE

PCT/US2007/017409

109

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

340

345

350

Val Met Val Leu Ile Pro Gln Leu His Arg Asp Lys Thr Ile Trp Gly
355 360 365

Asp Asp Val Glu Glu Phe Arg Pro Glu Arg Phe Glu Asn Pro Ser Ala
370 375 380

Ile Pro Gln His Ala Phe Lys Pro Phe Gly Asn Gly Gln Arg Ala Cys
385 390 395 400

Ile Gly Gln Gln Phe Ala Leu His Glu Ala Thr Leu Val Leu Gly Met
405 410 415

Met Leu Lys His Phe Asp Phe Glu Asp His Thr Asn Tyr Glu Leu Asp
420 425 430

Ile Lys Glu Thr Leu Thr Leu Lys Pro Glu Gly Phe Val Val Lys Ala
435 440 445

Lys Ser Lys Lys Ile Pro Leu Gly Gly Ile Pro Ser Pro Ser Thr Glu
450 455 460

Gln Ser Ala Lys Lys Val Arg Lys Lys Ala Glu Asn Ala His Asn Thr
465 470 475 480

Pro Leu Leu Val Leu Tyr Gly Ser Asn Met Gly Thr Ala Glu Gly Thr
485 490 495

Ala Arg Asp Leu Ala Asp Ile Ala Met Ser Lys Gly Phe Ala Pro Gln
500 505 510

Val Ala Thr Leu Asp Ser His Ala Gly Asn Leu Pro Arg Glu Gly Ala
515 520 525

Val Leu Ile Val Thr Ala Ser Tyr Asn Gly His Pro Pro Asp Asn Ala
530 535 540

Lys Gln Phe Val Asp Trp Leu Asp Gln Ala Ser Ala Asp Glu Val Lys
545 550 555 560

Gly Val Arg Tyr Ser Val Phe Gly Cys Gly Asp Lys Asn Trp Ala Thr
565 570 575

Thr Tyr Gln Lys Val Pro Ala Phe Ile Asp Glu Thr Leu Ala Ala Lys
580 585 590

Printed: 10/30/2007

SP00151

PCT/US2007/017409

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT:ST25.txt

Gly Ala Glu Asn Ile Ala Asp Arg Gly Glu Ala Asp Ala Ser Asp Asp
595 600 605

Phe Glu Gly Thr Tyr Glu Glu Trp Arg Glu His Met Trp Ser Asp Val
610 615 620

Ala Ala Tyr Phe Asn Leu Asp Ile Glu Asn Ser Glu Asp Asn Lys Ser
625 630 635 640

Thr Leu Ser Leu Gln Phe Val Asp Ser Ala Ala Asp Met Pro Leu Ala
645 650 655

Lys Met His Gly Ala Phe Ser Thr Asn Val Val Ala Ser Lys Glu Leu
660 665 670

Gln Gln Pro Gly Ser Ala Arg Ser Thr Arg His Leu Glu Ile Glu Leu
675 680 685

Pro Lys Glu Ala Ser Tyr Gln Glu Gly Asp His Leu Gly Val Ile Pro
690 695 700

Arg Asn Tyr Glu Gly Ile Val Asn Arg Val Thr Ala Arg Phe Gly Leu
705 710 715 720

Asp Ala Ser Gln Gln Ile Arg Leu Glu Ala Glu Glu Glu Lys Leu Ala
725 730 735

His Leu Pro Leu Ala Lys Thr Val Ser Val Glu Glu Leu Leu Gln Tyr
740 745 750

Val Glu Leu Gln Asp Pro Val Thr Arg Thr Gln Leu Arg Ala Met Ala
755 760 765

Ala Lys Thr Val Cys Pro Pro His Lys Val Glu Leu Glu Ala Leu Leu
770 775 780

Glu Lys Gln Ala Tyr Lys Glu Gln Val Leu Ala Lys Arg Leu Thr Met
785 790 795 800

Leu Glu Leu Leu Glu Lys Tyr Pro Ala Cys Glu Met Lys Phe Ser Glu
805 810 815

Phe Ile Ala Leu Leu Pro Ser Ile Arg Pro Arg Tyr Tyr Ser Ile Ser
820 825 830

Ser Ser Pro Arg Val Asp Glu Lys Gln Ala Ser Ile Thr Val Ser Val
835 840 845

Printed: 10/30/2007

SEQUENCE

PCT/US2007/017409

Title: "Methods and systems for selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Val Ser Gly Glu Ala Trp Ser Gly Tyr Gly Glu Tyr Lys Gly Ile Ala
850 855 860

Ser Asn Tyr Leu Ala Glu Leu Gln Glu Gly Asp Thr Ile Thr Cys Phe
865 870 875 880

Ile Ser Thr Pro Gln Ser Glu Phe Thr Leu Pro Lys Asp Pro Glu Thr
885 890 895

Pro Leu Ile Met Val Gly Pro Gly Thr Gly Val Ala Pro Phe Arg Gly
900 905 910

Phe Val Gln Ala Arg Lys Gln Leu Lys Glu Gln Gly Gln Ser Leu Gly
915 920 925

Glu Ala His Leu Tyr Phe Gly Cys Arg Ser Pro His Glu Asp Tyr Leu
930 935 940

Tyr Gln Glu Glu Leu Glu Asn Ala Gln Ser Glu Gly Ile Ile Thr Leu
945 950 955 960

His Thr Ala Phe Ser Arg Met Pro Asn Gln Pro Lys Thr Tyr Val Gln
965 970 975

His Val Met Glu Gln Asp Gly Lys Lys Leu Ile Glu Leu Leu Asp Gln
980 985 990

Gly Ala His Phe Tyr Ile Cys Gly Asp Gly Ser Gln Met Ala Pro Ala
995 1000 1005

Val Glu Ala Thr Leu Met Lys Ser Tyr Ala Asp Val His Gln Val
1010 1015 1020

Ser Glu Ala Asp Ala Arg Leu Trp Leu Gln Gln Leu Glu Glu Lys
1025 1030 1035

Gly Arg Tyr Ala Lys Asp Val Trp Ala Gly
1040 1045

<210> 22
<211> 1048
<212> PRT
<213> Artificial sequence

<220>
<223> Cytochrome P450 variant CYP102A1var2

<400> 22

Printed: 10/30/2007

Page 60

PCT/US2007/017409

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Thr Ile Lys Glu Met Pro Gln Pro Lys Thr Phe Gly Glu Leu Lys Asn
1 5 10 15

Leu Pro Leu Leu Asn Thr Asp Lys Pro Val Gln Ala Leu Met Lys Ile
20 25 30

Ala Asp Glu Leu Gly Glu Ile Phe Lys Phe Glu Ala Pro Gly Arg Val
35 40 45

Thr Arg Tyr Leu Ser Ser Gln Arg Leu Ile Lys Glu Ala Cys Asp Glu
50 55 60

Ser Arg Phe Asp Lys Asn Leu Ser Gln Ala Leu Lys Ala Val Arg Asp
65 70 75 80

Phe Ala Gly Asp Gly Leu Phe Thr Ser Trp Thr His Glu Lys Asn Trp
85 90 95

Lys Lys Ala His Asn Ile Leu Leu Pro Ser Phe Ser Gln Ala Met
100 105 110

Lys Gly Tyr His Ala Met Met Val Asp Ile Ala Val Gln Leu Val Gln
115 120 125

Lys Trp Glu Arg Leu Asn Ala Asp Glu His Ile Glu Val Pro Glu Asp
130 135 140

Met Thr Arg Leu Thr Leu Asp Thr Ile Gly Leu Cys Gly Phe Asn Tyr
145 150 155 160

Arg Phe Asn Ser Phe Tyr Arg Asp Gln Pro His Pro Phe Ile Ile Ser
165 170 175

Met Val Arg Ala Leu Asp Glu Val Met Asn Lys Leu Gln Arg Ala Asn
180 185 190

Pro Asp Asp Pro Ala Tyr Asp Glu Asn Lys Arg Gln Cys Gln Glu Asp
195 200 205

Ile Lys Val Met Asn Asp Leu Val Asp Lys Ile Ile Ala Asp Arg Lys
210 215 220

Ala Arg Gly Glu Gln Ser Asp Asp Leu Leu Thr Gln Met Leu Asn Gly
225 230 235 240

Lys Asp Pro Glu Thr Gly Glu Pro Leu Asp Asp Gly Asn Ile Ser Tyr
245 250 255

Printed: 10/30/2007

8:30:51

PCT/US2007/017409

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Gln Ile Ile Thr Phe Leu Ile Ala Gly His Glu Thr Thr Ser Gly Leu
260 265 270

Leu Ser Phe Ala Leu Tyr Phe Leu Val Lys Asn Pro His Val Leu Gln
275 280 285

Lys Val Ala Glu Glu Ala Ala Arg Val Leu Val Asp Pro Val Pro Ser
290 295 300

Tyr Lys Gln Val Lys Gln Leu Lys Tyr Val Gly Met Val Leu Asn Glu
305 310 315 320

Ala Leu Arg Leu Trp Pro Thr Ala Pro Ala Phe Ser Leu Tyr Ala Lys
325 330 335

Glu Asp Thr Val Leu Gly Gly Glu Tyr Pro Leu Glu Lys Gly Asp Glu
340 345 350

Val Met Val Leu Ile Pro Gln Leu His Arg Asp Lys Thr Ile Trp Gly
355 360 365

Asp Asp Val Glu Glu Phe Arg Pro Glu Arg Phe Glu Asn Pro Ser Ala
370 375 380

Ile Pro Gln His Ala Phe Lys Pro Phe Gly Asn Gly Gln Arg Ala Cys
385 390 395 400

Ile Gly Gln Gln Phe Ala Leu His Glu Ala Thr Leu Val Leu Gly Met
405 410 415

Met Leu Lys His Phe Asp Phe Glu Asp His Thr Asn Tyr Glu Leu Asp
420 425 430

Ile Lys Glu Thr Leu Thr Leu Lys Pro Glu Gly Phe Val Val Lys Ala
435 440 445

Lys Ser Lys Lys Ile Pro Leu Gly Gly Ile Pro Ser Pro Ser Thr Glu
450 455 460

Gln Ser Ala Lys Lys Val Arg Lys Lys Ala Glu Asn Ala His Asn Thr
465 470 475 480

Pro Leu Leu Val Leu Tyr Gly Ser Asn Met Gly Thr Ala Glu Gly Thr
485 490 495

Ala Arg Asp Leu Ala Asp Ile Ala Met Ser Lys Gly Phe Ala Pro Gln
500 505 510

Printed: 10/30/2007

11/01/01

PCT/US2007/017409

017409

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EP511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Val Ala Thr Leu Asp Ser His Ala Gly Asn Leu Pro Arg Glu Gly Ala
515 520 525

Val Leu Ile Val Thr Ala Ser Tyr Asn Gly His Pro Pro Asp Asn Ala
530 535 540

Lys Gln Phe Val Asp Trp Leu Asp Gln Ala Ser Ala Asp Glu Val Lys
545 550 555 560

Gly Val Arg Tyr Ser Val Phe Gly Cys Gly Asp Lys Asn Trp Ala Thr
565 570 575

Thr Tyr Gln Lys Val Pro Ala Phe Ile Asp Glu Thr Leu Ala Ala Lys
580 585 590

Gly Ala Glu Asn Ile Ala Asp Arg Gly Glu Ala Asp Ala Ser Asp Asp
595 600 605

Phe Glu Gly Thr Tyr Glu Glu Trp Arg Glu His Met Trp Ser Asp Val
610 615 620

Ala Ala Tyr Phe Asn Leu Asp Ile Glu Asn Ser Glu Asp Asn Lys Ser
625 630 635 640

Thr Leu Ser Leu Gln Phe Val Asp Ser Ala Ala Asp Met Pro Leu Ala
645 650 655

Lys Met His Gly Ala Phe Ser Thr Asn Val Val Ala Ser Lys Glu Leu
660 665 670

Gln Gln Pro Gly Ser Ala Arg Ser Thr Arg His Leu Glu Ile Glu Leu
675 680 685

Pro Lys Glu Ala Ser Tyr Gln Glu Gly Asp His Leu Gly Val Ile Pro
690 695 700

Arg Asn Tyr Glu Gly Ile Val Asn Arg Val Thr Ala Arg Phe Gly Leu
705 710 715 720

Asp Ala Ser Gln Gln Ile Arg Leu Glu Ala Glu Glu Glu Lys Leu Ala
725 730 735

His Leu Pro Leu Ala Lys Thr Val Ser Val Glu Glu Leu Leu Gln Tyr
740 745 750

Val Glu Leu Gln Asp Pro Val Thr Arg Thr Gln Leu Arg Ala Met Ala
Page 62

Printed: 10/30/2007

Sheet 1

PCT/US2007/017409

109

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

755

760

765

Ala Lys Thr Val Cys Pro Pro His Lys Val Glu Leu Glu Ala Leu Leu
770 775 780

Glu Lys Gln Ala Tyr Lys Glu Gln Val Leu Ala Lys Arg Leu Thr Met
785 790 795 800

Leu Glu Leu Leu Glu Lys Tyr Pro Ala Cys Glu Met Lys Phe Ser Glu
805 810 815

Phe Ile Ala Leu Leu Pro Ser Ile Arg Pro Arg Tyr Tyr Ser Ile Ser
820 825 830

Ser Ser Pro Arg Val Asp Glu Lys Gln Ala Ser Ile Thr Val Ser Val
835 840 845

Val Ser Gly Glu Ala Trp Ser Gly Tyr Gly Glu Tyr Lys Gly Ile Ala
850 855 860

Ser Asn Tyr Leu Ala Glu Leu Gln Glu Gly Asp Thr Ile Thr Cys Phe
865 870 875 880

Ile Ser Thr Pro Gln Ser Glu Phe Thr Leu Pro Lys Asp Pro Glu Thr
885 890 895

Pro Leu Ile Met Val Gly Pro Gly Thr Gly Val Ala Pro Phe Arg Gly
900 905 910

Phe Val Gln Ala Arg Lys Gln Leu Lys Glu Gln Gly Gln Ser Leu Gly
915 920 925

Glu Ala His Leu Tyr Phe Gly Cys Arg Ser Pro His Glu Asp Tyr Leu
930 935 940

Tyr Gln Glu Glu Leu Glu Asn Ala Gln Ser Glu Gly Ile Ile Thr Leu
945 950 955 960

His Thr Ala Phe Ser Arg Met Pro Asn Gln Pro Lys Thr Tyr Val Gln
965 970 975

His Val Met Glu Gln Asp Gly Lys Lys Leu Ile Glu Leu Leu Asp Gln
980 985 990

Gly Ala His Phe Tyr Ile Cys Gly Asp Gly Ser Gln Met Ala Pro Ala
995 1000 1005

08/04/2007

Printed: 10/30/2007

Sheet 1 of 1

PCT/US2007/017409

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt.

Val Glu Ala Thr Leu Met Lys Ser Tyr Ala Asp Val His Gln Val
1010 1015 1020

Ser Glu Ala Asp Ala Arg Leu Trp Leu Gln Gln Leu Glu Glu Lys
1025 1030 1035

Gly Arg Tyr Ala Lys Asp Val Trp Ala Gly
1040 1045

<210> 23
<211> 1048
<212> PRT
<213> Artificial sequence

<220>
<223> Cytochrome P450 variant CYP102A1var3

<400> 23

Thr Ile Lys Glu Met Pro Gln Pro Lys Thr Phe Gly Glu Leu Lys Asn
1 5 10 15

Leu Pro Leu Leu Asn Thr Asp Lys Pro Val Gln Ala Leu Met Lys Ile
20 25 30

Ala Asp Glu Leu Gly Glu Ile Phe Lys Phe Glu Ala Pro Gly Cys Val
35 40 45

Thr Arg Tyr Leu Ser Ser Gln Arg Leu Ile Lys Glu Ala Cys Asp Glu
50 55 60

Ser Arg Phe Asp Lys Asn Leu Ser Gln Ala Leu Lys Ala Val Arg Asp
65 70 75 80

Phe Ala Gly Asp Gly Leu Phe Thr Ser Trp Thr His Glu Ile Asn Trp
85 90 95

Lys Lys Ala His Asn Ile Leu Leu Pro Ser Phe Ser Gln Gln Ala Met
100 105 110

Lys Gly Tyr His Ala Met Met Val Asp Ile Ala Val Gln Leu Val Gln
115 120 125

Lys Trp Glu Arg Leu Asn Ala Asp Glu His Ile Glu Val Ser Glu Asp
130 135 140

Met Thr Arg Leu Thr Leu Asp Thr Ile Gly Leu Cys Gly Phe Asn Tyr
145 150 155 160

Arg Phe Asn Ser Phe Tyr Arg Asp Gln Pro His Pro Phe Ile Ile Ser
Page 64

Printed: 10/30/2007

Sequence

PCT/US2007/017409

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

165

170

175

Met Val Arg Ala Leu Asp Glu Val Met Asn Lys Leu Gln Arg Ala Asn
180 185 190

Pro Asp Asp Pro Ala Tyr Asp Glu Asn Lys Arg Gln Cys Gln Glu Asp
195 200 205

Ile Lys Val Met Asn Asp Leu Val Asp Lys Ile Ile Ala Asp Arg Lys
210 215 220

Ala Arg Gly Glu Gln Ser Asp Asp Leu Leu Thr Gln Met Leu Asn Gly
225 230 235 240

Lys Asp Pro Glu Thr Gly Glu Pro Leu Asp Asp Gly Asn Ile Ser Tyr
245 250 255

Gln Ile Ile Thr Phe Leu Ile Ala Gly His Glu Thr Thr Ser Gly Leu
260 265 270

Leu Ser Phe Ala Leu Tyr Phe Leu Val Lys Asn Pro His Val Leu Gln
275 280 285

Lys Val Ala Glu Glu Ala Ala Arg Val Leu Val Asp Pro Val Pro Ser
290 295 300

Tyr Lys Gln Val Lys Gln Leu Lys Tyr Val Gly Met Val Leu Asn Glu
305 310 315 320

Ala Leu Arg Leu Trp Pro Thr Ala Pro Ala Phe Ser Leu Tyr Ala Lys
325 330 335

Glu Asp Thr Val Leu Gly Gly Glu Tyr Pro Leu Glu Lys Gly Asp Glu
340 345 350

Val Met Val Leu Ile Pro Gln Leu His Arg Asp Lys Thr Ile Trp Gly
355 360 365

Asp Asp Val Glu Glu Phe Arg Pro Glu Arg Phe Glu Asn Pro Ser Ala
370 375 380

Ile Pro Gln His Ala Phe Lys Pro Phe Gly Asn Gly Gln Arg Ala Cys
385 390 395 400

Ile Gly Gln Gln Phe Ala Leu His Glu Ala Thr Leu Val Leu Gly Met
405 410 415

Printed: 10/30/2007

P008-CIT

PCT/US2007/017409

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Met Leu Lys His Phe Asp Phe Glu Asp His Thr Asn Tyr Glu Leu Asp
420 425 430

Ile Lys Glu Thr Leu Thr Leu Lys Pro Glu Gly Phe Val Val Lys Ala
435 440 445

Lys Ser Lys Lys Ile Pro Leu Gly Gly Ile Pro Ser Pro Ser Thr Glu
450 455 460

Gln Ser Ala Lys Lys Val Arg Lys Lys Ala Glu Asn Ala His Asn Thr
465 470 475 480

Pro Leu Leu Val Leu Tyr Gly Ser Asn Met Gly Thr Ala Glu Gly Thr
485 490 495

Ala Arg Asp Leu Ala Asp Ile Ala Met Ser Lys Gly Phe Ala Pro Gln
500 505 510

Val Ala Thr Leu Asp Ser His Ala Gly Asn Leu Pro Arg Glu Gly Ala
515 520 525

Val Leu Ile Val Thr Ala Ser Tyr Asn Gly His Pro Pro Asp Asn Ala
530 535 540

Lys Gln Phe Val Asp Trp Leu Asp Gln Ala Ser Ala Asp Glu Val Lys
545 550 555 560

Gly Val Arg Tyr Ser Val Phe Gly Cys Gly Asp Lys Asn Trp Ala Thr
565 570 575

Thr Tyr Gln Lys Val Pro Ala Phe Ile Asp Glu Thr Leu Ala Ala Lys
580 585 590

Gly Ala Glu Asn Ile Ala Asp Arg Gly Glu Ala Asp Ala Ser Asp Asp
595 600 605

Phe Glu Gly Thr Tyr Glu Glu Trp Arg Glu His Met Trp Ser Asp Val
610 615 620

Ala Ala Tyr Phe Asn Leu Asp Ile Glu Asn Ser Glu Asp Asn Lys Ser
625 630 635 640

Thr Leu Ser Leu Gln Phe Val Asp Ser Ala Ala Asp Met Pro Leu Ala
645 650 655

Lys Met His Gly Ala Phe Ser Thr Asn Val Val Ala Ser Lys Glu Leu
660 665 670

Printed: 10/30/2007

ST01151

PCT/US2007/017409

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Gln Gln Pro Gly Ser Ala Arg Ser Thr Arg His Leu Glu Ile Glu Leu
675 680 685

Pro Lys Glu Ala Ser Tyr Gln Glu Gly Asp His Leu Gly Val Ile Pro
690 695 700

Arg Asn Tyr Glu Gly Ile Val Asn Arg Val Thr Ala Arg Phe Gly Leu
705 710 715 720

Asp Ala Ser Gln Gln Ile Arg Leu Glu Ala Glu Glu Glu Lys Leu Ala
725 730 735

His Leu Pro Leu Ala Lys Thr Val Ser Val Glu Glu Leu Leu Gln Tyr
740 745 750

Val Glu Leu Gln Asp Pro Val Thr Arg Thr Gln Leu Arg Ala Met Ala
755 760 765

Ala Lys Thr Val Cys Pro Pro His Lys Val Glu Leu Glu Ala Leu Leu
770 775 780

Glu Lys Gln Ala Tyr Lys Glu Gln Val Leu Ala Lys Arg Leu Thr Met
785 790 795 800

Leu Glu Leu Leu Glu Lys Tyr Pro Ala Cys Glu Met Lys Phe Ser Glu
805 810 815

Phe Ile Ala Leu Leu Pro Ser Ile Arg Pro Arg Tyr Tyr Ser Ile Ser
820 825 830

Ser Ser Pro Arg Val Asp Glu Lys Gln Ala Ser Ile Thr Val Ser Val
835 840 845

Val Ser Gly Glu Ala Trp Ser Gly Tyr Gly Glu Tyr Lys Gly Ile Ala
850 855 860

Ser Asn Tyr Leu Ala Glu Leu Gln Glu Gly Asp Thr Ile Thr Cys Phe
865 870 875 880

Ile Ser Thr Pro Gln Ser Glu Phe Thr Leu Pro Lys Asp Pro Glu Thr
885 890 895

Pro Leu Ile Met Val Gly Pro Gly Thr Gly Val Ala Pro Phe Arg Gly
900 905 910

Phe Val Gln Ala Arg Lys Gln Leu Lys Glu Gln Gly Gln Ser Leu Gly
915 920 925

Page 67

Printed: 10/30/2007

SEQUENCE

PCT/US2007/017409

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Glu Ala His Leu Tyr Phe Gly Cys Arg Ser Pro His Glu Asp Tyr Leu
930 935 940

Tyr Gln Glu Glu Leu Glu Asn Ala Gln Ser Glu Gly Ile Ile Thr Leu
945 950 955 960

His Thr Ala Phe Ser Arg Met Pro Asn Gln Pro Lys Thr Tyr Val Gln
965 970 975

His Val Met Glu Gln Asp Gly Lys Lys Leu Ile Glu Leu Leu Asp Gln
980 985 990

Gly Ala His Phe Tyr Ile Cys Gly Asp Gly Ser Gln Met Ala Pro Ala
995 1000 1005

Val Glu Ala Thr Leu Met Lys Ser Tyr Ala Asp Val His Gln Val
1010 1015 1020

Ser Glu Ala Asp Ala Arg Leu Trp Leu Gln Gln Leu Glu Glu Lys
1025 1030 1035

Gly Arg Tyr Ala Lys Asp Val Trp Ala Gly
1040 1045

<210> 24
<211> 1048
<212> PRT
<213> Artificial sequence

<220>
<223> Cytochrome P450 variant CYP102A1var3-2

<400> 24

Thr Ile Lys Glu Met Pro Gln Pro Lys Thr Phe Gly Glu Leu Lys Asn
1 5 10 15

Leu Pro Leu Leu Asn Thr Asp Lys Pro Val Gln Ala Leu Met Lys Ile
20 25 30

Ala Asp Glu Leu Gly Glu Ile Phe Lys Phe Glu Ala Pro Gly Arg Val
35 40 45

Thr Arg Tyr Leu Ser Ser Gln Arg Leu Ile Lys Glu Ala Cys Asp Glu
50 55 60

Ser Arg Phe Asp Lys Asn Leu Ser Gln Ala Leu Lys Ala Val Arg Asp
65 70 75 80

Page 68

Printed: 10/30/2007

US 01/51

PCT/US2007/017409

08/04/2007

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EBS11841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Pro Leu Gly Asp Gly Leu Phe Ala Ser Trp Thr His Glu Lys Asn Trp
85 90 95

Lys Lys Ala His Asn Ile Leu Leu Pro Ser Phe Ser Gln Gln Ala Met
100 105 110

Lys Gly Tyr His Ala Met Met Val Asp Ile Ala Val Gln Leu Val Gln
115 120 125

Lys Trp Glu Arg Leu Asn Ala Asp Glu His Ile Glu Val Ser Glu Asp
130 135 140

Met Thr Arg Leu Thr Leu Asp Thr Ile Gly Leu Cys Gly Phe Asn Tyr
145 150 155 160

Arg Phe Asn Ser Phe Tyr Arg Asp Gln Pro His Pro Phe Ile Ile Ser
165 170 175

Met Val Arg Thr Leu Asp Glu Val Met Asn Lys Leu Gln Arg Ala Asn
180 185 190

Pro Asp Asp Pro Val Tyr Asp Glu Asn Lys Arg Gln Cys Gln Glu Asp
195 200 205

Ile Lys Val Met Asn Asp Leu Val Asp Lys Ile Ile Ala Asp Arg Lys
210 215 220

Ala Arg Gly Glu Gln Ser Asp Asp Leu Leu Thr Gln Met Leu Asn Gly
225 230 235 240

Lys Asp Pro Glu Thr Gly Glu Pro Leu Asp Asp Gly Asn Ile Ser Tyr
245 250 255

Gln Ile Ile Thr Phe Leu Ile Ala Gly His Glu Thr Thr Ser Gly Leu
260 265 270

Leu Ser Phe Ala Leu Tyr Phe Leu Val Lys Asn Pro His Val Leu Gln
275 280 285

Lys Val Ala Glu Glu Ala Ala Arg Val Leu Val Asp Pro Val Pro Ser
290 295 300

Tyr Lys Gln Val Lys Gln Leu Lys Tyr Val Gly Met Val Leu Asn Glu
305 310 315 320

Ala Leu Arg Leu Trp Pro Thr Ala Pro Ala Phe Ser Leu Tyr Ala Lys
325 330 335

Page 69

Printed: 10/30/2007

SEQUENCE

PCT/US2007/017409

409

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Glu Asp Thr Val Leu Gly Gly Glu Tyr Pro Leu Glu Lys Gly Asp Glu
340 345 350

Val Met Val Leu Ile Pro Gln Leu His Arg Asp Lys Thr Ile Trp Gly
355 360 365

Asp Asp Val Glu Glu Phe Arg Pro Glu Arg Phe Glu Asn Pro Ser Ala
370 375 380

Ile Pro Gln His Ala Phe Lys Pro Phe Gly Asn Gly Gln Arg Ala Cys
385 390 395 400

Ile Gly Gln Gln Phe Ala Leu His Glu Ala Thr Leu Val Leu Gly Met
405 410 415

Met Leu Lys His Phe Asp Phe Glu Asp His Thr Asn Tyr Glu Leu Asp
420 425 430

Ile Lys Glu Thr Leu Thr Leu Lys Pro Glu Gly Phe Val Val Lys Ala
435 440 445

Lys Ser Lys Lys Ile Pro Leu Gly Gly Ile Pro Ser Pro Ser Thr Glu
450 455 460

Gln Ser Ala Lys Lys Val Arg Lys Lys Ala Glu Asn Ala His Asn Thr
465 470 475 480

Pro Leu Leu Val Leu Tyr Gly Ser Asn Met Gly Thr Ala Glu Gly Thr
485 490 495

Ala Arg Asp Leu Ala Asp Ile Ala Met Ser Lys Gly Phe Ala Pro Gln
500 505 510

Val Ala Thr Leu Asp Ser His Ala Gly Asn Leu Pro Arg Glu Gly Ala
515 520 525

Val Leu Ile Val Thr Ala Ser Tyr Asn Gly His Pro Asp Asn Ala
530 535 540

Lys Gln Phe Val Asp Trp Leu Asp Gln Ala Ser Ala Asp Glu Val Lys
545 550 555 560

Gly Val Arg Tyr Ser Val Phe Gly Cys Gly Asp Lys Asn Trp Ala Thr
565 570 575

Thr Tyr Gln Lys Val Pro Ala Phe Ile Asp Glu Thr Leu Ala Ala Lys
Page 70

08/04/2007

Printed: 10/30/2007

Sheet 151

PCT/US2007/017409

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

580

585

590

Gly Ala Glu Asn Ile Ala Asp Arg Gly Glu Ala Asp Ala Ser Asp Asp
595 600 605

Phe Glu Gly Thr Tyr Glu Glu Trp Arg Glu His Met Trp Ser Asp Val
610 615 620

Ala Ala Tyr Phe Asn Leu Asp Ile Glu Asn Ser Glu Asp Asn Lys Ser
625 630 635 640

Thr Leu Ser Leu Gln Phe Val Asp Ser Ala Ala Asp Met Pro Leu Ala
645 650 655

Lys Met His Gly Ala Phe Ser Thr Asn Val Val Ala Ser Lys Glu Leu
660 665 670

Gln Gln Pro Gly Ser Ala Arg Ser Thr Arg His Leu Glu Ile Glu Leu
675 680 685

Pro Lys Glu Ala Ser Tyr Gln Glu Gly Asp His Leu Gly Val Ile Pro
690 695 700

Arg Asn Tyr Glu Gly Ile Val Asn Arg Val Thr Ala Arg Phe Gly Leu
705 710 715 720

Asp Ala Ser Gln Gln Ile Arg Leu Glu Ala Glu Glu Glu Lys Leu Ala
725 730 735

His Leu Pro Leu Ala Lys Thr Val Ser Val Glu Glu Leu Leu Gln Tyr
740 745 750

Val Glu Leu Gln Asp Pro Val Thr Arg Thr Gln Leu Arg Ala Met Ala
755 760 765

Ala Lys Thr Val Cys Pro Pro His Lys Val Glu Leu Glu Ala Leu Leu
770 775 780

Glu Lys Gln Ala Tyr Lys Glu Gln Val Leu Ala Lys Arg Leu Thr Met
785 790 795 800

Leu Glu Leu Leu Glu Lys Tyr Pro Ala Cys Glu Met Lys Phe Ser Glu
805 810 815

Phe Ile Ala Leu Leu Pro Ser Ile Arg Pro Arg Tyr Tyr Ser Ile Ser
820 825 830

08/04/2007

Printed: 10/30/2007

8:00:15

PCT/US2007/017409

807/12/409

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Ser Ser Pro Arg Val Asp Glu Lys Gln Ala Ser Ile Thr Val Ser Val
835 840 845

Val Ser Gly Glu Ala Trp Ser Gly Tyr Gly Glu Tyr Lys Gly Ile Ala
850 855 860

Ser Asn Tyr Leu Ala Glu Leu Gln Glu Gly Asp Thr Ile Thr Cys Phe
865 870 875 880

Ile Ser Thr Pro Gln Ser Glu Phe Thr Leu Pro Lys Asp Pro Glu Thr
885 890 895

Pro Leu Ile Met Val Gly Pro Gly Thr Gly Val Ala Pro Phe Arg Gly
900 905 910

Phe Val Gln Ala Arg Lys Gln Leu Lys Glu Gln Gly Gln Ser Leu Gly
915 920 925

Glu Ala His Leu Tyr Phe Gly Cys Arg Ser Pro His Glu Asp Tyr Leu
930 935 940

Tyr Gln Glu Glu Leu Glu Asn Ala Gln Ser Glu Gly Ile Ile Thr Leu
945 950 955 960

His Thr Ala Phe Ser Arg Met Pro Asn Gln Pro Lys Thr Tyr Val Gln
965 970 975

His Val Met Glu Gln Asp Gly Lys Lys Leu Ile Glu Leu Leu Asp Gln
980 985 990

Gly Ala His Phe Tyr Ile Cys Gly Asp Gly Ser Gln Met Ala Pro Ala
995 1000 1005

Val Glu Ala Thr Leu Met Lys Ser Tyr Ala Asp Val His Gln Val
1010 1015 1020

Ser Glu Ala Asp Ala Arg Leu Trp Leu Gln Gln Leu Glu Glu Lys
1025 1030 1035

Gly Arg Tyr Ala Lys Asp Val Trp Ala Gly
1040 1045

<210> 25
<211> 1048
<212> PRT
<213> Artificial sequence

<220>
<223> Cytochrome P450 variant CYP102A1var3-3
Page 72

08/04/2007

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

<400> 25

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

P008-CIT_ST25.txt

Lys Asp Pro Glu Thr Gly Glu Pro Leu Asp Gly Asn Ile Ser Tyr
 245 250 255

Gln Ile Ile Thr Phe Leu Ile Ala Gly His Glu Thr Thr Ser Gly Leu
 260 265 270

Leu Ser Phe Ala Leu Tyr Phe Leu Val Lys Asn Pro His Val Leu Gln
 275 280 285

Lys Val Ala Glu Glu Ala Ala Arg Val Leu Val Asp Pro Val Pro Ser
 290 295 300

Tyr Lys Gln Val Lys Gln Leu Lys Tyr Val Gly Met Val Leu Asn Glu
 305 310 315 320

Ala Leu Arg Leu Trp Pro Thr Ala Pro Ala Phe Ser Leu Tyr Ala Lys
 325 330 335

Glu Asp Thr Val Leu Gly Gly Glu Tyr Pro Leu Glu Lys Gly Asp Glu
 340 345 350

Val Met Val Leu Ile Pro Gln Leu His Arg Asp Lys Thr Ile Trp Gly
 355 360 365

Asp Asp Val Glu Glu Phe Arg Pro Glu Arg Phe Glu Asn Pro Ser Ala
 370 375 380

Ile Pro Gln His Ala Phe Lys Pro Phe Gly Asn Gly Gln Arg Ala Cys
 385 390 395 400

Ile Gly Gln Gln Phe Ala Leu His Glu Ala Thr Leu Val Leu Gly Met
 405 410 415

Met Leu Lys His Phe Asp Phe Glu Asp His Thr Asn Tyr Glu Leu Asp
 420 425 430

Ile Lys Glu Thr Leu Thr Leu Lys Pro Glu Gly Phe Val Val Lys Ala
 435 440 445

Lys Ser Lys Lys Ile Pro Leu Gly Gly Ile Pro Ser Pro Ser Thr Glu
 450 455 460

Gln Ser Ala Lys Lys Val Arg Lys Lys Ala Glu Asn Ala His Asn Thr
 465 470 475 480

Pro Leu Leu Val Leu Tyr Gly Ser Asn Met Gly Thr Ala Glu Gly Thr
 485 490 495

Title: "Methods and Systems for Selective..."

Inventors: Rudi Pasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Ala Arg Asp Leu Ala Asp Ile Ala Met Ser Lys Gly Phe Ala Pro Gln
500 505 510

Val Ala Thr Leu Asp Ser His Ala Gly Asn Leu Pro Arg Glu Gly Ala
515 520 525

Val Leu Ile Val Thr Ala Ser Tyr Asn Gly His Pro Pro Asp Asn Ala
530 535 540

Lys Gln Phe Val Asp Trp Leu Asp Gln Ala Ser Ala Asp Glu Val Lys
545 550 555 560

Gly Val Arg Tyr Ser Val Phe Gly Cys Gly Asp Lys Asn Trp Ala Thr
565 570 575

Thr Tyr Gln Lys Val Pro Ala Phe Ile Asp Glu Thr Leu Ala Ala Lys
580 585 590

Gly Ala Glu Asn Ile Ala Asp Arg Gly Glu Ala Asp Ala Ser Asp Asp
595 600 605

Phe Glu Gly Thr Tyr Glu Glu Trp Arg Glu His Met Trp Ser Asp Val
610 615 620

Ala Ala Tyr Phe Asn Leu Asp Ile Glu Asn Ser Glu Asp Asn Lys Ser
625 630 635 640

Thr Leu Ser Leu Gln Phe Val Asp Ser Ala Ala Asp Met Pro Leu Ala
645 650 655

Lys Met His Gly Ala Phe Ser Thr Asn Val Val Ala Ser Lys Glu Leu
660 665 670

Gln Gln Pro Gly Ser Ala Arg Ser Thr Arg His Leu Glu Ile Glu Leu
675 680 685

Pro Lys Glu Ala Ser Tyr Gln Glu Gly Asp His Leu Gly Val Ile Pro
690 695 700

Arg Asn Tyr Glu Gly Ile Val Asn Arg Val Thr Ala Arg Phe Gly Leu
705 710 715 720

Asp Ala Ser Gln Gln Ile Arg Leu Glu Ala Glu Glu Glu Lys Leu Ala
725 730 735

His Leu Pro Leu Ala Lys Thr Val Ser Val Glu Glu Leu Leu Gln Tyr
740 745 750

Printed: 10/30/2007

Sheet: 57

PCT/US2007/017409

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Val Glu Leu Gln Asp Pro Val Thr Arg Thr Gln Leu Arg Ala Met Ala
755 760 765

Ala Lys Thr Val Cys Pro Pro His Lys Val Glu Leu Glu Ala Leu Leu
770 775 780

Glu Lys Gln Ala Tyr Lys Glu Gln Val Leu Ala Lys Arg Leu Thr Met
785 790 795 800

Leu Glu Leu Leu Glu Lys Tyr Pro Ala Cys Glu Met Lys Phe Ser Glu
805 810 815

Phe Ile Ala Leu Leu Pro Ser Ile Arg Pro Arg Tyr Tyr Ser Ile Ser
820 825 830

Ser Ser Pro Arg Val Asp Glu Lys Gln Ala Ser Ile Thr Val Ser Val
835 840 845

Val Ser Gly Glu Ala Trp Ser Gly Tyr Gly Glu Tyr Lys Gly Ile Ala
850 855 860

Ser Asn Tyr Leu Ala Glu Leu Gln Glu Gly Asp Thr Ile Thr Cys Phe
865 870 875 880

Ile Ser Thr Pro Gln Ser Glu Phe Thr Leu Pro Lys Asp Pro Glu Thr
885 890 895

Pro Leu Ile Met Val Gly Pro Gly Thr Gly Val Ala Pro Phe Arg Gly
900 905 910

Phe Val Gln Ala Arg Lys Gln Leu Lys Glu Gln Gly Gln Ser Leu Gly
915 920 925

Glu Ala His Leu Tyr Phe Gly Cys Arg Ser Pro His Glu Asp Tyr Leu
930 935 940

Tyr Gln Glu Glu Leu Glu Asn Ala Gln Ser Glu Gly Ile Ile Thr Leu
945 950 955 960

His Thr Ala Phe Ser Arg Met Pro Asn Gln Pro Lys Thr Tyr Val Gln
965 970 975

His Val Met Glu Gln Asp Gly Lys Lys Leu Ile Glu Leu Leu Asp Gln
980 985 990

Gly Ala His Phe Tyr Ile Cys Gly Asp Gly Ser Gln Met Ala Pro Ala
Page 76

08/04/2007

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

995

1000

P008-CIT_ST25.txt

1005

Val Glu Ala Thr Leu Met Lys Ser Tyr Ala Asp Val His Gln Val
1010 1015 1020

Ser Glu Ala Asp Ala Arg Leu Trp Leu Gln Gln Leu Glu Glu Lys
1025 1030 1035

Gly Arg Tyr Ala Lys Asp Val Trp Ala Gly
1040 1045

<210> 26
<211> 1048
<212> PRT
<213> Artificial sequence

<220>
<223> Cytochrome P450 variant CYP102A1var3-4

<400> 26

Thr Ile Lys Glu Met Pro Gln Pro Lys Thr Phe Gly Glu Leu Lys Asn
1 5 10 15

Leu Pro Leu Leu Asn Thr Asp Lys Pro Val Gln Ala Leu Met Lys Ile
20 25 30

Ala Asp Glu Leu Gly Glu Ile Phe Lys Phe Glu Ala Pro Gly Arg Val
35 40 45

Thr Arg Tyr Leu Ser Ser Gln Arg Leu Ile Lys Glu Ala Cys Asp Glu
50 55 60

Ser Arg Phe Asp Lys Asn Leu Ser Gln Ala Leu Lys Ala Val Arg Asp
65 70 75 80

Trp Ile Gly Asp Gly Leu Ala Thr Ser Trp Thr His Glu Lys Asn Trp
85 90 95

Lys Lys Ala His Asn Ile Leu Leu Pro Ser Phe Ser Gln Gln Ala Met
100 105 110

Lys Gly Tyr His Ala Met Met Val Asp Ile Ala Val Gln Leu Val Gln
115 120 125

Lys Trp Glu Arg Leu Asn Ala Asp Glu His Ile Glu Val Ser Glu Asp
130 135 140

Met Thr Arg Leu Thr Leu Asp Thr Ile Gly Leu Cys Gly Phe Asn Tyr
145 150 155 160

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Arg Phe Asn Ser Phe Tyr Arg Asp Gln Pro His Pro Phe Ile Ile Ser
 165 170 175

Met Val Arg Thr Leu Asp Glu Val Met Asn Lys Leu Gln Arg Ala Asn
 180 185 190

Pro Asp Asp Pro Val Tyr Asp Glu Asn Lys Arg Gln Cys Gln Glu Asp
 195 200 205

Ile Lys Val Met Asn Asp Leu Val Asp Lys Ile Ile Ala Asp Arg Lys
 210 215 220

Ala Arg Gly Glu Gln Ser Asp Asp Leu Leu Thr Gln Met Leu Asn Gly
 225 230 235 240

Lys Asp Pro Glu Thr Gly Glu Pro Leu Asp Asp Gly Asn Ile Ser Tyr
 245 250 255

Gln Ile Ile Thr Phe Leu Ile Ala Gly His Glu Thr Thr Ser Gly Leu
 260 265 270

Leu Ser Phe Ala Leu Tyr Phe Leu Val Lys Asn Pro His Val Leu Gln
 275 280 285

Lys Val Ala Glu Glu Ala Ala Arg Val Leu Val Asp Pro Val Pro Ser
 290 295 300

Tyr Lys Gln Val Lys Gln Leu Lys Tyr Val Gly Met Val Leu Asn Glu
 305 310 315 320

Ala Leu Arg Leu Trp Pro Thr Ala Pro Ala Phe Ser Leu Tyr Ala Lys
 325 330 335

Glu Asp Thr Val Leu Gly Gly Glu Tyr Pro Leu Glu Lys Gly Asp Glu
 340 345 350

Val Met Val Leu Ile Pro Gln Leu His Arg Asp Lys Thr Ile Trp Gly
 355 360 365

Asp Asp Val Glu Glu Phe Arg Pro Glu Arg Phe Glu Asn Pro Ser Ala
 370 375 380

Ile Pro Gln His Ala Phe Lys Pro Phe Gly Asn Gly Gln Arg Ala Cys
 385 390 395 400

Ile Gly Gln Gln Phe Ala Leu His Glu Ala Thr Leu Val Leu Gly Met
 Page 78

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

405

410

415

Met Leu Lys His Phe Asp Phe Glu Asp His Thr Asn Tyr Glu Leu Asp
420 425 430

Ile Lys Glu Thr Leu Thr Leu Lys Pro Glu Gly Phe Val Val Lys Ala
435 440 445

Lys Ser Lys Lys Ile Pro Leu Gly Gly Ile Pro Ser Pro Ser Thr Glu
450 455 460

Gln Ser Ala Lys Lys Val Arg Lys Lys Ala Glu Asn Ala His Asn Thr
465 470 475 480

Pro Leu Leu Val Leu Tyr Gly Ser Asn Met Gly Thr Ala Glu Gly Thr
485 490 495

Ala Arg Asp Leu Ala Asp Ile Ala Met Ser Lys Gly Phe Ala Pro Gln
500 505 510

Val Ala Thr Leu Asp Ser His Ala Gly Asn Leu Pro Arg Glu Gly Ala
515 520 525

Val Leu Ile Val Thr Ala Ser Tyr Asn Gly His Pro Pro Asp Asn Ala
530 535 540

Lys Gln Phe Val Asp Trp Leu Asp Gln Ala Ser Ala Asp Glu Val Lys
545 550 555 560

Gly Val Arg Tyr Ser Val Phe Gly Cys Gly Asp Lys Asn Trp Ala Thr
565 570 575

Thr Tyr Gln Lys Val Pro Ala Phe Ile Asp Glu Thr Leu Ala Ala Lys
580 585 590

Gly Ala Glu Asn Ile Ala Asp Arg Gly Glu Ala Asp Ala Ser Asp Asp
595 600 605

Phe Glu Gly Thr Tyr Glu Glu Trp Arg Glu His Met Trp Ser Asp Val
610 615 620

Ala Ala Tyr Phe Asn Leu Asp Ile Glu Asn Ser Glu Asp Asn Lys Ser
625 630 635 640

Thr Leu Ser Leu Gln Phe Val Asp Ser Ala Ala Asp Met Pro Leu Ala
645 650 655

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Lys Met His Gly Ala Phe Ser Thr Asn Val Val Ala Ser Lys⁶⁶⁰ Glu Leu⁶⁶⁵

Gln Gln Pro Gly Ser Ala Arg Ser Thr Arg His Leu Glu Ile Glu Leu⁶⁷⁵
680

Pro Lys Glu Ala Ser Tyr Gln Glu Gly Asp His Leu Gly Val Ile Pro⁶⁹⁰
695 700

Arg Asn Tyr Glu Gly Ile Val Asn Arg Val Thr Ala Arg Phe Gly Leu⁷⁰⁵
710 715 720

Asp Ala Ser Gln Gln Ile Arg Leu Glu Ala Glu Glu Glu Lys Leu Ala⁷²⁵
730 735

His Leu Pro Leu Ala Lys Thr Val Ser Val Glu Glu Leu Leu Gln Tyr⁷⁴⁰
745 750

Val Glu Leu Gln Asp Pro Val Thr Arg Thr Gln Leu Arg Ala Met Ala⁷⁵⁵
760 765

Ala Lys Thr Val Cys Pro Pro His Lys Val Glu Leu Glu Ala Leu Leu⁷⁷⁰
775 780

Glu Lys Gln Ala Tyr Lys Glu Gln Val Leu Ala Lys Arg Leu Thr Met⁷⁸⁵
790 795 800

Leu Glu Leu Leu Glu Lys Tyr Pro Ala Cys Glu Met Lys Phe Ser Glu⁸⁰⁵
810 815

Phe Ile Ala Leu Leu Pro Ser Ile Arg Pro Arg Tyr Tyr Ser Ile Ser⁸²⁰
825 830

Ser Ser Pro Arg Val Asp Glu Lys Gln Ala Ser Ile Thr Val Ser Val⁸³⁵
840 845

Val Ser Gly Glu Ala Trp Ser Gly Tyr Gly Glu Tyr Lys Gly Ile Ala⁸⁵⁰
855 860

Ser Asn Tyr Leu Ala Glu Leu Gln Glu Gly Asp Thr Ile Thr Cys Phe⁸⁶⁵
870 875 880

Ile Ser Thr Pro Gln Ser Glu Phe Thr Leu Pro Lys Asp Pro Glu Thr⁸⁸⁵
890 895

Pro Leu Ile Met Val Gly Pro Gly Thr Gly Val Ala Pro Phe Arg Gly⁹⁰⁰
905 910

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511641342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Phe Val Gln Ala Arg Lys Gln Leu Lys Glu Gln Gly Gln Ser Leu Gly
915 920 925

Glu Ala His Leu Tyr Phe Gly Cys Arg Ser Pro His Glu Asp Tyr Leu
930 935 940

Tyr Gln Glu Glu Leu Glu Asn Ala Gln Ser Glu Gly Ile Ile Thr Leu
945 950 955 960

His Thr Ala Phe Ser Arg Met Pro Asn Gln Pro Lys Thr Tyr Val Gln
965 970 975

His Val Met Glu Gln Asp Gly Lys Lys Leu Ile Glu Leu Leu Asp Gln
980 985 990

Gly Ala His Phe Tyr Ile Cys Gly Asp Gly Ser Gln Met Ala Pro Ala
995 1000 1005

Val Glu Ala Thr Leu Met Lys Ser Tyr Ala Asp Val His Gln Val
1010 1015 1020

Ser Glu Ala Asp Ala Arg Leu Trp Leu Gln Gln Leu Glu Glu Lys
1025 1030 1035

Gly Arg Tyr Ala Lys Asp Val Trp Ala Gly
1040 1045

<210> 27
<211> 1048
<212> PRT
<213> Artificial sequence

<220>
<223> Cytochrome P450 variant CYP102A1var3-5
<400> 27

Thr Ile Lys Glu Met Pro Gln Pro Lys Thr Phe Gly Glu Leu Lys Asn
1 5 10 15

Leu Pro Leu Leu Asn Thr Asp Lys Pro Val Gln Ala Leu Met Lys Ile
20 25 30

Ala Asp Glu Leu Gly Glu Ile Phe Lys Phe Glu Ala Pro Gly Arg Val
35 40 45

Thr Arg Tyr Leu Ser Ser Gln Arg Leu Ile Lys Glu Ala Cys Asp Glu
50 55 60

P008-CIT_ST25.txt

Ser Arg Phe Asp Lys Asn Leu Ser Gln Ala Leu Lys Ala Val Arg Asp
 65 70 75 80

Phe Gly Gly Asp Gly Leu Val Thr Ser Trp Thr His Glu Lys Asn Trp
 85 90 95

Lys Lys Ala His Asn Ile Leu Leu Pro Ser Phe Ser Gln Gln Ala Met
 100 105 110

Lys Gly Tyr His Ala Met Met Val Asp Ile Ala Val Gln Leu Val Gln
 115 120 125

Lys Trp Glu Arg Leu Asn Ala Asp Glu His Ile Glu Val Ser Glu Asp
 130 135 140

Met Thr Arg Leu Thr Leu Asp Thr Ile Gly Leu Cys Gly Phe Asn Tyr
 145 150 155 160

Arg Phe Asn Ser Phe Tyr Arg Asp Gln Pro His Pro Phe Ile Ile Ser
 165 170 175

Met Val Arg Ala Leu Asp Glu Val Met Asn Lys Leu Gln Arg Ala Asn
 180 185 190

Pro Asp Asp Pro Ala Tyr Asp Glu Asn Lys Arg Gln Cys Gln Glu Asp
 195 200 205

Ile Lys Val Met Asn Asp Leu Val Asp Lys Ile Ile Ala Asp Arg Lys
 210 215 220

Ala Arg Gly Glu Gln Ser Asp Asp Leu Leu Thr Gln Met Leu Asn Gly
 225 230 235 240

Lys Asp Pro Glu Thr Gly Glu Pro Leu Asp Asp Gly Asn Ile Ser Tyr
 245 250 255

Gln Ile Ile Thr Phe Leu Ile Ala Gly His Glu Thr Thr Ser Gly Leu
 260 265 270

Leu Ser Phe Ala Leu Tyr Phe Leu Val Lys Asn Pro His Val Leu Gln
 275 280 285

Lys Val Ala Glu Glu Ala Ala Arg Val Leu Val Asp Pro Val Pro Ser
 290 295 300

Tyr Lys Gln Val Lys Gln Leu Lys Tyr Val Gly Met Val Leu Asn Glu
 305 310 315 320

Title: "Methods and systems for selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Ala Leu Arg Leu Trp Pro Thr Val Pro Ala Phe Ser Leu Tyr Ala Lys
325 330 335

Glu Asp Thr Val Leu Gly Gly Glu Tyr Pro Leu Glu Lys Gly Asp Glu
340 345 350

Val Met Val Leu Ile Pro Gln Leu His Arg Asp Lys Thr Ile Trp Gly
355 360 365

Asp Asp Val Glu Glu Phe Arg Pro Glu Arg Phe Glu Asn Pro Ser Ala
370 375 380

Ile Pro Gln His Ala Phe Lys Pro Phe Gly Asn Gly Gln Arg Ala Cys
385 390 395 400

Ile Gly Gln Gln Phe Ala Leu His Glu Ala Thr Leu Val Leu Gly Met
405 410 415

Met Leu Lys His Phe Asp Phe Glu Asp His Thr Asn Tyr Glu Leu Asp
420 425 430

Ile Lys Glu Thr Leu Thr Leu Lys Pro Glu Gly Phe Val Val Lys Ala
435 440 445

Lys Ser Lys Lys Ile Pro Leu Gly Gly Ile Pro Ser Pro Ser Thr Glu
450 455 460

Gln Ser Ala Lys Lys Val Arg Lys Lys Ala Glu Asn Ala His Asn Thr
465 470 475 480

Pro Leu Leu Val Leu Tyr Gly Ser Asn Met Gly Thr Ala Glu Gly Thr
485 490 495

Ala Arg Asp Leu Ala Asp Ile Ala Met Ser Lys Gly Phe Ala Pro Gln
500 505 510

Val Ala Thr Leu Asp Ser His Ala Gly Asn Leu Pro Arg Glu Gly Ala
515 520 525

Val Leu Ile Val Thr Ala Ser Tyr Asn Gly His Pro Pro Asp Asn Ala
530 535 540

Lys Gln Phe Val Asp Trp Leu Asp Gln Ala Ser Ala Asp Glu Val Lys
545 550 555 560

Gly Val Arg Tyr Ser Val Phe Gly Cys Gly Asp Lys Asn Trp Ala Thr
565 570 575

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Thr Tyr Gln Lys Val Pro Ala Phe Ile Asp Glu Thr Leu Ala Ala Lys
580 585 590

Gly Ala Glu Asn Ile Ala Asp Arg Gly Glu Ala Asp Ala Ser Asp Asp
595 600 605

Phe Glu Gly Thr Tyr Glu Glu Trp Arg Glu His Met Trp Ser Asp Val
610 615 620

Ala Ala Tyr Phe Asn Leu Asp Ile Glu Asn Ser Glu Asp Asn Lys Ser
625 630 635 640

Thr Leu Ser Leu Gln Phe Val Asp Ser Ala Ala Asp Met Pro Leu Ala
645 650 655

Lys Met His Gly Ala Phe Ser Thr Asn Val Val Ala Ser Lys Glu Leu
660 665 670

Gln Gln Pro Gly Ser Ala Arg Ser Thr Arg His Leu Glu Ile Glu Leu
675 680 685

Pro Lys Glu Ala Ser Tyr Gln Glu Gly Asp His Leu Gly Val Ile Pro
690 695 700

Arg Asn Tyr Glu Gly Ile Val Asn Arg Val Thr Ala Arg Phe Gly Leu
705 710 715 720

Asp Ala Ser Gln Gln Ile Arg Leu Glu Ala Glu Glu Glu Lys Leu Ala
725 730 735

His Leu Pro Leu Ala Lys Thr Val Ser Val Glu Glu Leu Leu Gln Tyr
740 745 750

Val Glu Leu Gln Asp Pro Val Thr Arg Thr Gln Leu Arg Ala Met Ala
755 760 765

Ala Lys Thr Val Cys Pro Pro His Lys Val Glu Leu Glu Ala Leu Leu
770 775 780

Glu Lys Gln Ala Tyr Lys Glu Gln Val Leu Ala Lys Arg Leu Thr Met
785 790 795 800

Leu Glu Leu Leu Glu Lys Tyr Pro Ala Cys Glu Met Lys Phe Ser Glu
805 810 815

Phe Ile Ala Leu Leu Pro Ser Ile Arg Pro Arg Tyr Tyr Ser Ile Ser
Page 84

Printed: 10/30/2007

Sheet 1

PCT/US2007/017409

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

820.

825

830

Ser Ser Pro Arg Val Asp Glu Lys Gln Ala Ser Ile Thr Val Ser Val
835 840 845

Val Ser Gly Glu Ala Trp Ser Gly Tyr Gly Glu Tyr Lys Gly Ile Ala
850 855 860

Ser Asn Tyr Leu Ala Glu Leu Gln Glu Gly Asp Thr Ile Thr Cys Phe
865 870 875 880

Ile Ser Thr Pro Gln Ser Glu Phe Thr Leu Pro Lys Asp Pro Glu Thr
885 890 895

Pro Leu Ile Met Val Gly Pro Gly Thr Gly Val Ala Pro Phe Arg Gly
900 905 910

Phe Val Gln Ala Arg Lys Gln Leu Lys Glu Gln Gly Gln Ser Leu Gly
915 920 925

Glu Ala His Leu Tyr Phe Gly Cys Arg Ser Pro His Glu Asp Tyr Leu
930 935 940

Tyr Gln Glu Glu Leu Glu Asn Ala Gln Ser Glu Gly Ile Ile Thr Leu
945 950 955 960

His Thr Ala Phe Ser Arg Met Pro Asn Gln Pro Lys Thr Tyr Val Gln
965 970 975

His Val Met Glu Gln Asp Gly Lys Lys Leu Ile Glu Leu Leu Asp Gln
980 985 990

Gly Ala His Phe Tyr Ile Cys Gly Asp Gly Ser Gln Met Ala Pro Ala
995 1000 1005

Val Glu Ala Thr Leu Met Lys Ser Tyr Ala Asp Val His Gln Val
1010 1015 1020

Ser Glu Ala Asp Ala Arg Leu Trp Leu Gln Gln Leu Glu Glu Lys
1025 1030 1035

Gly Arg Tyr Ala Lys Asp Val Trp Ala Gly
1040 1045

<210> 28

<211> 1048

<212> PRT

<213> Artificial sequence

P008-CIT_ST25.txt

<220>

<223> Cytochrome P450 variant CYP102A1var3-8

<400> 28

Thr Ile Lys Glu Met Pro Gln Pro Lys Thr Phe Gly Glu Leu Lys Asn
1 5 10 15

Leu Pro Leu Leu Asn Thr Asp Lys Pro Val Gln Ala Leu Met Lys Ile
20 25 30

Ala Asp Glu Leu Gly Glu Ile Phe Lys Phe Glu Ala Pro Gly Cys Val
35 40 45

Thr Arg Tyr Leu Ser Ser Gln Arg Leu Ile Lys Glu Ala Cys Asp Glu
50 55 60

Ser Arg Phe Asp Lys Asn Leu Ser Gln Ala Leu Lys Ala Val Arg Asp
65 70 75 80

Phe Ala Gly Asp Gly Leu Ile Thr Ser Trp Thr His Glu Ile Asn Trp
85 90 95

Lys Lys Ala His Asn Ile Leu Leu Pro Ser Phe Ser Gln Gln Ala Met
100 105 110

Lys Gly Tyr His Ala Met Met Val Asp Ile Ala Val Gln Leu Val Gln
115 120 125

Lys Trp Glu Arg Leu Asn Ala Asp Glu His Ile Glu Val Ser Glu Asp
130 135 140

Met Thr Arg Leu Thr Leu Asp Thr Ile Gly Leu Cys Gly Phe Asn Tyr
145 150 155 160

Arg Phe Asn Ser Phe Tyr Arg Asp Gln Pro His Pro Phe Ile Ile Ser
165 170 175

Met Val Arg Ala Leu Asp Glu Val Met Asn Lys Leu Gln Arg Ala Asn
180 185 190

Pro Asp Asp Pro Ala Tyr Asp Glu Asn Lys Arg Gln Cys Gln Glu Asp
195 200 205

Ile Lys Val Met Asn Asp Leu Val Asp Lys Ile Ile Ala Asp Arg Lys
210 215 220

Ala Arg Gly Glu Gln Ser Asp Asp Leu Leu Thr Gln Met Leu Asn Gly
Page 86

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

225

230

235

240

Lys Asp Pro Glu Thr Gly Glu Pro Leu Asp Asp Gly Asn Ile Ser Tyr
245 250 255

Gln Ile Ile Thr Phe Leu Ile Ala Gly His Glu Thr Thr Ser Gly Leu
260 265 270

Leu Ser Phe Ala Leu Tyr Phe Leu Val Lys Asn Pro His Val Leu Gln
275 280 285

Lys Val Ala Glu Glu Ala Ala Arg Val Leu Val Asp Pro Val Pro Ser
290 295 300

Tyr Lys Gln Val Lys Gln Leu Lys Tyr Val Gly Met Val Leu Asn Glu
305 310 315 320

Ala Leu Arg Leu Trp Pro Thr Ala Pro Ala Phe Ser Leu Tyr Ala Lys
325 330 335

Glu Asp Thr Val Leu Gly Gly Glu Tyr Pro Leu Glu Lys Gly Asp Glu
340 345 350

Val Met Val Leu Ile Pro Gln Leu His Arg Asp Lys Thr Ile Trp Gly
355 360 365

Asp Asp Val Glu Glu Phe Arg Pro Glu Arg Phe Glu Asn Pro Ser Ala
370 375 380

Ile Pro Gln His Ala Phe Lys Pro Phe Gly Asn Gly Gln Arg Ala Cys
385 390 395 400

Ile Gly Gln Gln Phe Ala Leu His Glu Ala Thr Leu Val Leu Gly Met
405 410 415

Met Leu Lys His Phe Asp Phe Glu Asp His Thr Asn Tyr Glu Leu Asp
420 425 430

Ile Lys Glu Thr Leu Thr Leu Lys Pro Glu Gly Phe Val Val Lys Ala
435 440 445

Lys Ser Lys Lys Ile Pro Leu Gly Gly Ile Pro Ser Pro Ser Thr Glu
450 455 460

Gln Ser Ala Lys Lys Val Arg Lys Lys Ala Glu Asn Ala His Asn Thr
465 470 475 480

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Pro Leu Leu Val Leu Tyr Gly Ser Asn Met Gly Thr Ala Glu Gly Thr
 485 490 495

Ala Arg Asp Leu Ala Asp Ile Ala Met Ser Lys Gly Phe Ala Pro Gln
 500 505 510

Val Ala Thr Leu Asp Ser His Ala Gly Asn Leu Pro Arg Glu Gly Ala
 515 520 525

Val Leu Ile Val Thr Ala Ser Tyr Asn Gly His Pro Pro Asp Asn Ala
 530 535 540

Lys Gln Phe Val Asp Trp Leu Asp Gln Ala Ser Ala Asp Glu Val Lys
 545 550 555 560

Gly Val Arg Tyr Ser Val Phe Gly Cys Gly Asp Lys Asn Trp Ala Thr
 565 570 575

Thr Tyr Gln Lys Val Pro Ala Phe Ile Asp Glu Thr Leu Ala Ala Lys
 580 585 590

Gly Ala Glu Asn Ile Ala Asp Arg Gly Glu Ala Asp Ala Ser Asp Asp
 595 600 605

Phe Glu Gly Thr Tyr Glu Glu Trp Arg Glu His Met Trp Ser Asp Val
 610 615 620

Ala Ala Tyr Phe Asn Leu Asp Ile Glu Asn Ser Glu Asp Asn Lys Ser
 625 630 635 640

Thr Leu Ser Leu Gln Phe Val Asp Ser Ala Ala Asp Met Pro Leu Ala
 645 650 655

Lys Met His Gly Ala Phe Ser Thr Asn Val Val Ala Ser Lys Glu Leu
 660 665 670

Gln Gln Pro Gly Ser Ala Arg Ser Thr Arg His Leu Glu Ile Glu Leu
 675 680 685

Pro Lys Glu Ala Ser Tyr Gln Glu Gly Asp His Leu Gly Val Ile Pro
 690 695 700

Arg Asn Tyr Glu Gly Ile Val Asn Arg Val Thr Ala Arg Phe Gly Leu
 705 710 715 720

Asp Ala Ser Gln Gln Ile Arg Leu Glu Ala Glu Glu Glu Lys Leu Ala
 725 730 735

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

His Leu Pro Leu Ala Lys Thr Val Ser Val Glu Glu Leu Leu Gln Tyr
740 745 750

Val Glu Leu Gln Asp Pro Val Thr Arg Thr Gln Leu Arg Ala Met Ala
755 760 765

Ala Lys Thr Val Cys Pro Pro His Lys Val Glu Leu Glu Ala Leu Leu
770 775 780

Glu Lys Gln Ala Tyr Lys Glu Gln Val Leu Ala Lys Arg Leu Thr Met
785 790 795 800

Leu Glu Leu Leu Glu Lys Tyr Pro Ala Cys Glu Met Lys Phe Ser Glu
805 810 815

Phe Ile Ala Leu Leu Pro Ser Ile Arg Pro Arg Tyr Tyr Ser Ile Ser
820 825 830

Ser Ser Pro Arg Val Asp Glu Lys Gln Ala Ser Ile Thr Val Ser Val
835 840 845

Val Ser Gly Glu Ala Trp Ser Gly Tyr Gly Glu Tyr Lys Gly Ile Ala
850 855 860

Ser Asn Tyr Leu Ala Glu Leu Gln Glu Gly Asp Thr Ile Thr Cys Phe
865 870 875 880

Ile Ser Thr Pro Gln Ser Glu Phe Thr Leu Pro Lys Asp Pro Glu Thr
885 890 895

Pro Leu Ile Met Val Gly Pro Gly Thr Gly Val Ala Pro Phe Arg Gly
900 905 910

Phe Val Gln Ala Arg Lys Gln Leu Lys Glu Gln Gly Gln Ser Leu Gly
915 920 925

Glu Ala His Leu Tyr Phe Gly Cys Arg Ser Pro His Glu Asp Tyr Leu
930 935 940

Tyr Gln Glu Glu Leu Glu Asn Ala Gln Ser Glu Gly Ile Ile Thr Leu
945 950 955 960

His Thr Ala Phe Ser Arg Met Pro Asn Gln Pro Lys Thr Tyr Val Gln
965 970 975

His Val Met Glu Gln Asp Gly Lys Lys Leu Ile Glu Leu Leu Asp Gln
980 985 990

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Gly Ala His Phe Tyr Ile Cys Gly Asp Gly Ser Gln Met Ala Pro Ala
995 1000 1005

Val Glu Ala Thr Leu Met Lys Ser Tyr Ala Asp Val His Gln Val
1010 1015 1020

Ser Glu Ala Asp Ala Arg Leu Trp Leu Gln Gln Leu Glu Glu Lys
1025 1030 1035

Gly Arg Tyr Ala Lys Asp Val Trp Ala Gly
1040 1045

<210> 29
<211> 1048
<212> PRT
<213> Artificial sequence

<220>
<223> Cytochrome P450 variant CYP102A1var3-7

<400> 29

Thr Ile Lys Glu Met Pro Gln Pro Lys Thr Phe Gly Glu Leu Lys Asn
1 5 10 15

Leu Pro Leu Leu Asn Thr Asp Lys Pro Val Gln Ala Leu Met Lys Ile
20 25 30

Ala Asp Glu Leu Gly Glu Ile Phe Lys Phe Glu Ala Pro Gly Cys Val
35 40 45

Thr Arg Tyr Leu Ser Ser Gln Arg Leu Ile Lys Glu Ala Cys Asp Glu
50 55 60

Ser Arg Phe Asp Lys Asn Leu Ser Gln Ala Leu Lys Ala Val Arg Asp
65 70 75 80

Phe Ala Gly Asp Gly Leu Ala Thr Ser Trp Thr His Glu Ile Asn Trp
85 90 95

Lys Lys Ala His Asn Ile Leu Leu Pro Ser Phe Ser Gln Gln Ala Met
100 105 110

Lys Gly Tyr His Ala Met Met Val Asp Ile Ala Val Gln Leu Val Gln
115 120 125

Lys Trp Glu Arg Leu Asn Ala Asp Glu His Ile Glu Val Ser Glu Asp
130 135 140

P008-CIT_ST25.txt

Met Thr Arg Leu Thr Leu Asp Thr Ile Gly Leu Cys Gly Phe Asn Tyr
145 150 155 160

Arg Phe Asn Ser Phe Tyr Arg Asp Gln Pro His Pro Phe Ile Ile Ser
165 170 175

Met Val Arg Ala Leu Asp Glu Val Met Asn Lys Leu Gln Arg Ala Asn
180 185 190

Pro Asp Asp Pro Ala Tyr Asp Glu Asn Lys Arg Gln Cys Gln Glu Asp
195 200 205

Ile Lys Val Met Asn Asp Leu Val Asp Lys Ile Ile Ala Asp Arg Lys
210 215 220

Ala Arg Gly Glu Gln Ser Asp Asp Leu Leu Thr Gln Met Leu Asn Gly
225 230 235 240

Lys Asp Pro Glu Thr Gly Glu Pro Leu Asp Asp Gly Asn Ile Ser Tyr
245 250 255

Gln Ile Ile Thr Phe Leu Ile Ala Gly His Glu Thr Thr Ser Gly Leu
260 265 270

Leu Ser Phe Ala Leu Tyr Phe Leu Val Lys Asn Pro His Val Leu Gln
275 280 285

Lys Val Ala Glu Glu Ala Ala Arg Val Leu Val Asp Pro Val Pro Ser
290 295 300

Tyr Lys Gln Val Lys Gln Leu Lys Tyr Val Gly Met Val Leu Asn Glu
305 310 315 320

Ala Leu Arg Leu Trp Pro Thr Ala Pro Ala Phe Ser Leu Tyr Ala Lys
325 330 335

Glu Asp Thr Val Leu Gly Gly Glu Tyr Pro Leu Glu Lys Gly Asp Glu
340 345 350

Val Met Val Leu Ile Pro Gln Leu His Arg Asp Lys Thr Ile Trp Gly
355 360 365

Asp Asp Val Glu Glu Phe Arg Pro Glu Arg Phe Glu Asn Pro Ser Ala
370 375 380

Ile Pro Gln His Ala Phe Lys Pro Phe Gly Asn Gly Gln Arg Ala Cys
385 390 395 400

Printed: 10/30/2007

8500151

PCT/US2007/017409

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Ile Gly Gln Gln Phe Ala Leu His Glu Ala Thr Leu Val Leu Gly Met
405 410 415

Met Leu Lys His Phe Asp Phe Glu Asp His Thr Asn Tyr Glu Leu Asp
420 425 430

Ile Lys Glu Thr Leu Thr Leu Lys Pro Glu Gly Phe Val Val Lys Ala
435 440 445

Lys Ser Lys Lys Ile Pro Leu Gly Gly Ile Pro Ser Pro Ser Thr Glu
450 455 460

Gln Ser Ala Lys Lys Val Arg Lys Lys Ala Glu Asn Ala His Asn Thr
465 470 475 480

Pro Leu Leu Val Leu Tyr Gly Ser Asn Met Gly Thr Ala Glu Gly Thr
485 490 495

Ala Arg Asp Leu Ala Asp Ile Ala Met Ser Lys Gly Phe Ala Pro Gln
500 505 510

Val Ala Thr Leu Asp Ser His Ala Gly Asn Leu Pro Arg Glu Gly Ala
515 520 525

Val Leu Ile Val Thr Ala Ser Tyr Asn Gly His Pro Pro Asp Asn Ala
530 535 540

Lys Gln Phe Val Asp Trp Leu Asp Gln Ala Ser Ala Asp Glu Val Lys
545 550 555 560

Gly Val Arg Tyr Ser Val Phe Gly Cys Gly Asp Lys Asn Trp Ala Thr
565 570 575

Thr Tyr Gln Lys Val Pro Ala Phe Ile Asp Glu Thr Leu Ala Ala Lys
580 585 590

Gly Ala Glu Asn Ile Ala Asp Arg Gly Glu Ala Asp Ala Ser Asp Asp
595 600 605

Phe Glu Gly Thr Tyr Glu Glu Trp Arg Glu His Met Trp Ser Asp Val
610 615 620

Ala Ala Tyr Phe Asn Leu Asp Ile Glu Asn Ser Glu Asp Asn Lys Ser
625 630 635 640

Thr Leu Ser Leu Gln Phe Val Asp Ser Ala Ala Asp Met Pro Leu Ala
Page 92

08/04/2007

Printed: 10/30/2007

Sheet 1

PCT/US2007/017409

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

645

650

655

Lys Met His Gly Ala Phe Ser Thr Asn Val Val Ala Ser Lys Glu Leu
660 665 670

Gln Gln Pro Gly Ser Ala Arg Ser Thr Arg His Leu Glu Ile Glu Leu
675 680 685

Pro Lys Glu Ala Ser Tyr Gln Glu Gly Asp His Leu Gly Val Ile Pro
690 695 700

Arg Asn Tyr Glu Gly Ile Val Asn Arg Val Thr Ala Arg Phe Gly Leu
705 710 715 720

Asp Ala Ser Gln Gln Ile Arg Leu Glu Ala Glu Glu Glu Lys Leu Ala
725 730 735

His Leu Pro Leu Ala Lys Thr Val Ser Val Glu Glu Leu Leu Gln Tyr
740 745 750

Val Glu Leu Gln Asp Pro Val Thr Arg Thr Gln Leu Arg Ala Met Ala
755 760 765

Ala Lys Thr Val Cys Pro Pro His Lys Val Glu Leu Glu Ala Leu Leu
770 775 780

Glu Lys Gln Ala Tyr Lys Glu Gln Val Leu Ala Lys Arg Leu Thr Met
785 790 795 800

Leu Glu Leu Leu Glu Lys Tyr Pro Ala Cys Glu Met Lys Phe Ser Glu
805 810 815

Phe Ile Ala Leu Leu Pro Ser Ile Arg Pro Arg Tyr Tyr Ser Ile Ser
820 825 830

Ser Ser Pro Arg Val Asp Glu Lys Gln Ala Ser Ile Thr Val Ser Val
835 840 845

Val Ser Gly Glu Ala Trp Ser Gly Tyr Gly Glu Tyr Lys Gly Ile Ala
850 855 860

Ser Asn Tyr Leu Ala Glu Leu Gln Glu Gly Asp Thr Ile Thr Cys Phe
865 870 875 880

Ile Ser Thr Pro Gln Ser Glu Phe Thr Leu Pro Lys Asp Pro Glu Thr
885 890 895

08/04/2007

Title: "Methods and Systems for Selective..."

Inventors: Rudi Pasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Pro Leu Ile Met Val Gly Pro Gly Thr Gly Val Ala Pro Phe Arg Gly
900 905 910

Phe Val Gln Ala Arg Lys Gln Leu Lys Glu Gln Gly Gln Ser Leu Gly
915 920 925

Glu Ala His Leu Tyr Phe Gly Cys Arg Ser Pro His Glu Asp Tyr Leu
930 935 940

Tyr Gln Glu Glu Leu Glu Asn Ala Gln Ser Glu Gly Ile Ile Thr Leu
945 950 955 960

His Thr Ala Phe Ser Arg Met Pro Asn Gln Pro Lys Thr Tyr Val Gln
965 970 975

His Val Met Glu Gln Asp Gly Lys Lys Leu Ile Glu Leu Asp Gln
980 985 990

Gly Ala His Phe Tyr Ile Cys Gly Asp Gly Ser Gln Met Ala Pro Ala
995 1000 1005

Val Glu Ala Thr Leu Met Lys Ser Tyr Ala Asp Val His Gln Val
1010 1015 1020

Ser Glu Ala Asp Ala Arg Leu Trp Leu Gln Gln Leu Glu Glu Lys
1025 1030 1035

Gly Arg Tyr Ala Lys Asp Val Trp Ala Gly
1040 1045

- <210> 30
- <211> 1048
- <212> PRT
- <213> Artificial sequence

- <220>
- <223> Cytochrome P450 variant CYP102A1var3-8

<400> 30

Thr Ile Lys Glu Met Pro Gln Pro Lys Thr Phe Gly Glu Leu Lys Asn
1 5 10 15

Leu Pro Leu Leu Asn Thr Asp Lys Pro Val Gln Ala Leu Met Lys Ile
20 25 30

Ala Asp Glu Leu Gly Glu Ile Phe Lys Phe Glu Ala Pro Gly Cys Val
35 40 45

Thr Arg Tyr Leu Ser Ser Gln Arg Leu Ile Lys Glu Ala Cys Asp Glu
Page 94

P008-CIT_ST25.txt

50

55

60

Ser Arg Phe Asp Lys Asn Leu Ser Gln Ala Leu Lys Ala Val Arg Asp
 65 70 75 80

Phe Leu Gly Asp Gly Leu Phe Thr Ser Trp Thr His Glu Ile Asn Trp
 85 90 95

Lys Lys Ala His Asn Ile Leu Leu Pro Ser Phe Ser Gln Gln Ala Met
 100 105 110

Lys Gly Tyr His Ala Met Met Val Asp Ile Ala Val Gln Leu Val Gln
 115 120 125

Lys Trp Glu Arg Leu Asn Ala Asp Glu His Ile Glu Val Ser Glu Asp
 130 135 140

Met Thr Arg Leu Thr Leu Asp Thr Ile Gly Leu Cys Gly Phe Asn Tyr
 145 150 155 160

Arg Phe Asn Ser Phe Tyr Arg Asp Gln Pro His Pro Phe Ile Ile Ser
 165 170 175

Met Val Arg Ala Leu Asp Glu Val Met Asn Lys Leu Gln Arg Ala Asn
 180 185 190

Pro Asp Asp Pro Ala Tyr Asp Glu Asn Lys Arg Gln Cys Gln Glu Asp
 195 200 205

Ile Lys Val Met Asn Asp Leu Val Asp Lys Ile Ile Ala Asp Arg Lys
 210 215 220

Ala Arg Gly Glu Gln Ser Asp Asp Leu Leu Thr Gln Met Leu Asn Gly
 225 230 235 240

Lys Asp Pro Glu Thr Gly Glu Pro Leu Asp Asp Gly Asn Ile Ser Tyr
 245 250 255

Gln Ile Ile Thr Phe Leu Ile Ala Gly His Glu Thr Thr Ser Gly Leu
 260 265 270

Leu Ser Phe Ala Leu Tyr Phe Leu Val Lys Asn Pro His Val Leu Gln
 275 280 285

Lys Val Ala Glu Glu Ala Ala Arg Val Leu Val Asp Pro Val Pro Ser
 290 295 300

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Tyr Lys Gln Val Lys Gln Leu Lys Tyr Val Gly Met Val Leu Asn Glu
305 310 315 320

Ala Leu Arg Leu Trp Pro Thr Ala Pro Ala Phe Ser Leu Tyr Ala Lys
325 330 335

Glu Asp Thr Val Leu Gly Gly Glu Tyr Pro Leu Glu Lys Gly Asp Glu
340 345 350

Val Met Val Leu Ile Pro Gln Leu His Arg Asp Lys Thr Ile Trp Gly
355 360 365

Asp Asp Val Glu Glu Phe Arg Pro Glu Arg Phe Glu Asn Pro Ser Ala
370 375 380

Ile Pro Gln His Ala Phe Lys Pro Phe Gly Asn Gly Gln Arg Ala Cys
385 390 395 400

Ile Gly Gln Gln Phe Ala Leu His Glu Ala Thr Leu Val Leu Gly Met
405 410 415

Met Leu Lys His Phe Asp Phe Glu Asp His Thr Asn Tyr Glu Leu Asp
420 425 430

Ile Lys Glu Thr Leu Thr Leu Lys Pro Glu Gly Phe Val Val Lys Ala
435 440 445

Lys Ser Lys Lys Ile Pro Leu Gly Gly Ile Pro Ser Pro Ser Thr Glu
450 455 460

Gln Ser Ala Lys Lys Val Arg Lys Lys Ala Glu Asn Ala His Asn Thr
465 470 475 480

Pro Leu Leu Val Leu Tyr Gly Ser Asn Met Gly Thr Ala Glu Gly Thr
485 490 495

Ala Arg Asp Leu Ala Asp Ile Ala Met Ser Lys Gly Phe Ala Pro Gln
500 505 510

Val Ala Thr Leu Asp Ser His Ala Gly Asn Leu Pro Arg Glu Gly Ala
515 520 525

Val Leu Ile Val Thr Ala Ser Tyr Asn Gly His Pro Pro Asp Asn Ala
530 535 540

Lys Gln Phe Val Asp Trp Leu Asp Gln Ala Ser Ala Asp Glu Val Lys
545 550 555 560

Printed: 10/30/2007

SECRET

PCT/US2007/017409

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Gly Val Arg Tyr Ser Val Phe Gly Cys Gly Asp Lys Asn Trp Ala Thr
565 570 575

Thr Tyr Gln Lys Val Pro Ala Phe Ile Asp Glu Thr Leu Ala Ala Lys
580 585 590

Gly Ala Glu Asn Ile Ala Asp Arg Gly Glu Ala Asp Ala Ser Asp Asp
595 600 605

Phe Glu Gly Thr Tyr Glu Glu Trp Arg Glu His Met Trp Ser Asp Val
610 615 620

Ala Ala Tyr Phe Asn Leu Asp Ile Glu Asn Ser Glu Asp Asn Lys Ser
625 630 635 640

Thr Leu Ser Leu Gln Phe Val Asp Ser Ala Ala Asp Met Pro Leu Ala
645 650 655

Lys Met His Gly Ala Phe Ser Thr Asn Val Val Ala Ser Lys Glu Leu
660 665 670

Gln Gln Pro Gly Ser Ala Arg Ser Thr Arg His Leu Glu Ile Glu Leu
675 680 685

Pro Lys Glu Ala Ser Tyr Gln Glu Gly Asp His Leu Gly Val Ile Pro
690 695 700

Arg Asn Tyr Glu Gly Ile Val Asn Arg Val Thr Ala Arg Phe Gly Leu
705 710 715 720

Asp Ala Ser Gln Gln Ile Arg Leu Glu Ala Glu Glu Glu Lys Leu Ala
725 730 735

His Leu Pro Leu Ala Lys Thr Val Ser Val Glu Glu Leu Leu Gln Tyr
740 745 750

Val Glu Leu Gln Asp Pro Val Thr Arg Thr Gln Leu Arg Ala Met Ala
755 760 765

Ala Lys Thr Val Cys Pro Pro His Lys Val Glu Leu Glu Ala Leu Leu
770 775 780

Glu Lys Gln Ala Tyr Lys Glu Gln Val Leu Ala Lys Arg Leu Thr Met
785 790 795 800

Leu Glu Leu Leu Glu Lys Tyr Pro Ala Cys Glu Met Lys Phe Ser Glu
805 810 815

08/04/2007

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Phe Ile Ala Leu Leu Pro Ser Ile Arg Pro Arg Tyr Tyr Ser Ile Ser
 820 825 830

Ser Ser Pro Arg Val Asp Glu Lys Gln Ala Ser Ile Thr Val Ser Val
 835 840 845

Val Ser Gly Glu Ala Trp Ser Gly Tyr Gly Glu Tyr Lys Gly Ile Ala
 850 855 860

Ser Asn Tyr Leu Ala Glu Leu Gln Glu Gly Asp Thr Ile Thr Cys Phe
 865 870 875 880

Ile Ser Thr Pro Gln Ser Glu Phe Thr Leu Pro Lys Asp Pro Glu Thr
 885 890 895

Pro Leu Ile Met Val Gly Pro Gly Thr Gly Val Ala Pro Phe Arg Gly
 900 905 910

Phe Val Gln Ala Arg Lys Gln Leu Lys Glu Gln Gly Gln Ser Leu Gly
 915 920 925

Glu Ala His Leu Tyr Phe Gly Cys Arg Ser Pro His Glu Asp Tyr Leu
 930 935 940

Tyr Gln Glu Glu Leu Glu Asn Ala Gln Ser Glu Gly Ile Ile Thr Leu
 945 950 955 960

His Thr Ala Phe Ser Arg Met Pro Asn Gln Pro Lys Thr Tyr Val Gln
 965 970 975

His Val Met Glu Gln Asp Gly Lys Lys Leu Ile Glu Leu Leu Asp Gln
 980 985 990

Gly Ala His Phe Tyr Ile Cys Gly Asp Gly Ser Gln Met Ala Pro Ala
 995 1000 1005

Val Glu Ala Thr Leu Met Lys Ser Tyr Ala Asp Val His Gln Val
 1010 1015 1020

Ser Glu Ala Asp Ala Arg Leu Trp Leu Gln Gln Leu Glu Glu Lys
 1025 1030 1035

Gly Arg Tyr Ala Lys Asp Val Trp Ala Gly
 1040 1045

P008-CIT_ST25.txt

<211> 1048
<212> PRT
<213> Artificial sequence

<220>
<223> Cytochrome P450 variant CYP102A1var3-9

<400> 31

Thr Ile Lys Glu Met Pro Gln Pro Lys Thr Phe Gly Glu Leu Lys Asn
1 5 10 15

Leu Pro Leu Leu Asn Thr Asp Lys Pro Val Gln Ala Leu Met Lys Ile
20 25 30

Ala Asp Glu Leu Gly Glu Ile Phe Lys Phe Glu Ala Pro Gly Cys Val
35 40 45

Thr Arg Tyr Leu Ser Ser Gln Arg Leu Ile Lys Glu Ala Cys Asp Glu
50 55 60

Ser Arg Phe Asp Lys Asn Leu Ser Gln Ala Leu Lys Thr Val Arg Asp
65 70 75 80

Phe Gly Gly Asp Gly Leu Val Thr Ser Trp Thr His Glu Ile Asn Trp
85 90 95

Lys Lys Ala His Asn Ile Leu Leu Pro Ser Phe Ser Gln Gln Ala Met
100 105 110

Lys Gly Tyr His Ala Met Met Val Asp Ile Ala Val Gln Leu Val Gln
115 120 125

Lys Trp Glu Arg Leu Asn Ala Asp Glu His Ile Glu Val Ser Glu Asp
130 135 140

Met Thr Arg Leu Thr Leu Asp Thr Ile Gly Leu Cys Gly Phe Asn Tyr
145 150 155 160

Arg Phe Asn Ser Phe Tyr Arg Asp Gln Pro His Pro Phe Ile Ile Ser
165 170 175

Met Val Arg Ala Leu Asp Glu Val Met Asn Lys Leu Gln Arg Ala Asn
180 185 190

Pro Asp Asp Pro Ala Tyr Asp Glu Asn Lys Arg Gln Cys Gln Glu Asp
195 200 205

Ile Lys Val Met Asn Asp Leu Val Asp Lys Ile Ile Ala Asp Arg Lys
210 215 220

P008-CIT_ST25.txt

Ala Arg Gly Glu Gln Ser Asp Asp Leu Leu Thr Gln Met Leu Asn Gly
225 230 235 240

Lys Asp Pro Glu Thr Gly Glu Pro Leu Asp Asp Gly Asn Ile Ser Tyr
245 250 255

Gln Ile Ile Thr Phe Leu Ile Ala Gly His Glu Thr Thr Ser Gly Leu
260 265 270

Leu Ser Phe Ala Leu Tyr Phe Leu Val Lys Asn Pro His Val Leu Gln
275 280 285

Lys Val Ala Glu Glu Ala Ala Arg Val Leu Val Asp Pro Val Pro Ser
290 295 300

Tyr Lys Gln Val Lys Gln Leu Lys Tyr Val Gly Met Val Leu Asn Gly
305 310 315 320

Ala Leu Arg Leu Trp Pro Thr Leu Pro Ala Phe Ser Leu Tyr Ala Lys
325 330 335

Glu Asp Thr Val Leu Gly Gly Glu Tyr Pro Leu Glu Lys Gly Asp Glu
340 345 350

Val Met Val Leu Ile Pro Gln Leu His Arg Asp Lys Thr Ile Trp Gly
355 360 365

Asp Asp Val Glu Glu Phe Arg Pro Glu Arg Phe Glu Asn Pro Ser Ala
370 375 380

Ile Pro Gln His Ala Phe Lys Pro Phe Gly Asn Gly Gln Arg Ala Cys
385 390 395 400

Ile Gly Gln Gln Phe Ala Leu His Glu Ala Thr Leu Val Leu Gly Met
405 410 415

Met Leu Lys His Phe Asp Phe Glu Asp His Thr Asn Tyr Glu Leu Asp
420 425 430

Ile Lys Glu Thr Leu Thr Leu Lys Pro Glu Gly Phe Val Val Lys Ala
435 440 445

Lys Ser Lys Lys Ile Pro Leu Gly Gly Ile Pro Ser Pro Ser Thr Glu
450 455 460

Gln Ser Ala Lys Lys Val Arg Lys Lys Ala Glu Asn Ala His Asn Thr
Page 100

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

465

470

475

480

Pro Leu Leu Val Leu Tyr Gly Ser Asn Met Gly Thr Ala Glu Gly Thr
 485 490 495

Ala Arg Asp Leu Ala Asp Ile Ala Met Ser Lys Gly Phe Ala Pro Gln
 500 505 510

Val Ala Thr Leu Asp Ser His Ala Gly Asn Leu Pro Arg Glu Gly Ala
 515 520 525

Val Leu Ile Val Thr Ala Ser Tyr Asn Gly His Pro Pro Asp Asn Ala
 530 535 540

Lys Gln Phe Val Asp Trp Leu Asp Gln Ala Ser Ala Asp Glu Val Lys
 545 550 555 560

Gly Val Arg Tyr Ser Val Phe Gly Cys Gly Asp Lys Asn Trp Ala Thr
 565 570 575

Thr Tyr Gln Lys Val Pro Ala Phe Ile Asp Glu Thr Leu Ala Ala Lys
 580 585 590

Gly Ala Glu Asn Ile Ala Asp Arg Gly Glu Ala Asp Ala Ser Asp Asp
 595 600 605

Phe Glu Gly Thr Tyr Glu Glu Trp Arg Glu His Met Trp Ser Asp Val
 610 615 620

Ala Ala Tyr Phe Asn Leu Asp Ile Glu Asn Ser Glu Asp Asn Lys Ser
 625 630 635 640

Thr Leu Ser Leu Gln Phe Val Asp Ser Ala Ala Asp Met Pro Leu Ala
 645 650 655

Lys Met His Gly Ala Phe Ser Thr Asn Val Val Ala Ser Lys Glu Leu
 660 665 670

Gln Gln Pro Gly Ser Ala Arg Ser Thr Arg His Leu Glu Ile Glu Leu
 675 680 685

Pro Lys Glu Ala Ser Tyr Gln Glu Gly Asp His Leu Gly Val Ile Pro
 690 695 700

Arg Asn Tyr Glu Gly Ile Val Asn Arg Val Thr Ala Arg Phe Gly Leu
 705 710 715 720

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Asp Ala Ser Gln Gln Ile Arg Leu Glu Ala Glu Glu Glu Lys Leu Ala
725 730 735His Leu Pro Leu Ala Lys Thr Val Ser Val Glu Glu Leu Leu Gln Tyr
740 745 750Val Glu Leu Gln Asp Pro Val Thr Arg Thr Gln Leu Arg Ala Met Ala
755 760 765Ala Lys Thr Val Cys Pro Pro His Lys Val Glu Leu Glu Ala Leu Leu
770 775 780Glu Lys Gln Ala Tyr Lys Glu Gln Val Leu Ala Lys Arg Leu Thr Met
785 790 795 800Leu Glu Leu Leu Glu Lys Tyr Pro Ala Cys Glu Met Lys Phe Ser Glu
805 810 815Phe Ile Ala Leu Leu Pro Ser Ile Arg Pro Arg Tyr Tyr Ser Ile Ser
820 825 830Ser Ser Pro Arg Val Asp Glu Lys Gln Ala Ser Ile Thr Val Ser Val
835 840 845Val Ser Gly Glu Ala Trp Ser Gly Tyr Gly Glu Tyr Lys Gly Ile Ala
850 855 860Ser Asn Tyr Leu Ala Glu Leu Gln Glu Gly Asp Thr Ile Thr Cys Phe
865 870 875 880Ile Ser Thr Pro Gln Ser Glu Phe Thr Leu Pro Lys Asp Pro Glu Thr
885 890 895Pro Leu Ile Met Val Gly Pro Gly Thr Gly Val Ala Pro Phe Arg Gly
900 905 910Phe Val Gln Ala Arg Lys Gln Leu Lys Glu Gln Gly Gln Ser Leu Gly
915 920 925Glu Ala His Leu Tyr Phe Gly Cys Arg Ser Pro His Glu Asp Tyr Leu
930 935 940Tyr Gln Glu Glu Leu Glu Asn Ala Gln Ser Glu Gly Ile Ile Thr Leu
945 950 955 960His Thr Ala Phe Ser Arg Met Pro Asn Gln Pro Lys Thr Tyr Val Gln
965 970 975

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

His Val Met Glu Gln Asp Gly Lys Lys Leu Ile Glu Leu Asp Gln
 980 985 990

Gly Ala His Phe Tyr Ile Cys Gly Asp Gly Ser Gln Met Ala Pro Ala
 995 1000 1005

Val Glu Ala Thr Leu Met Lys Ser Tyr Ala Asp Val His Gln Val
 1010 1015 1020

Ser Glu Ala Asp Ala Arg Leu Trp Leu Gln Gln Leu Glu Glu Lys
 1025 1030 1035

Gly Arg Tyr Ala Lys Asp Val Trp Ala Gly
 1040 1045

<210> 32
 <211> 1048
 <212> PRT
 <213> Artificial sequence

<220>
 <223> Cytochrome P450 variant CYP102A1var3-10

<400> 32

Thr Ile Lys Glu Met Pro Gln Pro Lys Thr Phe Gly Glu Leu Lys Asn
 1 5 10 15

Leu Pro Leu Leu Asn Thr Asp Lys Pro Val Gln Ala Leu Met Lys Ile
 20 25 30

Ala Asp Glu Leu Gly Glu Ile Phe Lys Phe Glu Ala Pro Gly Cys Val
 35 40 45

Thr Arg Tyr Ile Ser Ser Gln Arg Leu Ile Lys Glu Ala Cys Asp Glu
 50 55 60

Ser Arg Phe Asp Lys Asn Leu Ser Gln Ala Leu Lys Ala Phe Arg Asp
 65 70 75 80

Phe Ser Gly Asp Gly Leu Phe Thr Ser Trp Thr His Glu Ile Asn Trp
 85 90 95

Lys Lys Ala His Asn Ile Leu Leu Pro Ser Phe Ser Gln Gln Ala Met
 100 105 110

Lys Gly Tyr His Ala Met Met Val Asp Ile Ala Val Gln Leu Val Gln
 115 120 125

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Lys Trp Glu Arg Leu Asn Ala Asp, Glu His Ile Glu Val Ser Glu Asp
 130 135 140

Met Thr Arg Leu Thr Leu Asp Thr Ile Gly Leu Cys Gly Phe Asn Tyr
 145 150 155 160

Arg Phe Asn Ser Phe Tyr Arg Asp Gln Pro His Pro Phe Ile Ile Ser
 165 170 175

Met Val Arg Ala Leu Asp Glu Val Met Asn Lys Leu Gln Arg Ala Asn
 180 185 190

Pro Asp Asp, Pro Ala Tyr Asp Glu Asn Lys Arg Gln Cys Gln Glu Asp
 195 200 205

Ile Lys Val Met Asn Asp Leu Val Asp Lys Ile Ile Ala Asp Arg Lys
 210 215 220

Ala Arg Gly Glu Gln Ser Asp Asp Leu Leu Thr Gln Met Leu Asn Gly
 225 230 235 240

Lys Asp Pro Glu Thr Gly Glu Pro Leu Asp Asp Gly Asn Ile Ser Tyr
 245 250 255

Gln Ile Ile, Thr Phe Leu Ile Ala Gly His Glu Thr Thr Ser Gly Leu
 260 265 270

Leu Ser Phe Ala Leu Tyr Phe Leu Val Lys Asn Pro His Val Leu Gln
 275 280 285

Lys Val Ala Glu Glu Ala Ala Arg Val Leu Val Asp Pro Val Pro Ser
 290 295 300

Tyr Lys Gln Val Lys Gln Leu Lys Tyr Val Gly Met Val Leu Asn Glu
 305 310 315 320

Ala Leu Arg Leu Trp Pro Thr Phe Pro Ala Phe Ser Leu Tyr Ala Lys
 325 330 335

Glu Asp Thr Val Leu Gly Gly Glu Tyr Pro Leu Glu Lys Gly Asp Glu
 340 345 350

Val Met Val Leu Ile Pro Gln Leu His Arg Asp Lys Thr Val Trp Gly
 355 360 365

Asp Asp Val Glu Glu Phe Arg Pro Glu Arg Phe Glu Asn Pro Ser Ala
 370 375 380

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Ile Pro Gln His Ala Phe Lys Pro Phe Gly Asn Gly Gln Arg Ala Cys
 385 390 395 400

Ile Gly Gln Gln Phe Ala Leu His Glu Ala Thr Leu Val Leu Gly Met
 405 410 415

Met Leu Lys His Phe Asp Phe Glu Asp His Thr Asn Tyr Glu Leu Asp
 420 425 430

Ile Lys Glu Thr Leu Thr Leu Lys Pro Glu Gly Phe Val Val Lys Ala
 435 440 445

Lys Ser Lys Lys Ile Pro Leu Gly Gly Ile Pro Ser Pro Ser Thr Gly
 450 455 460

Gln Ser Ala Lys Lys Val Arg Lys Lys Ala Glu Asn Ala His Asn Thr
 465 470 475 480

Pro Leu Leu Val Leu Tyr Gly Ser Asn Met Gly Thr Ala Glu Gly Thr
 485 490 495

Ala Arg Asp Leu Ala Asp Ile Ala Met Ser Lys Gly Phe Ala Pro Gln
 500 505 510

Val Ala Thr Leu Asp Ser His Ala Gly Asn Leu Pro Arg Glu Gly Ala
 515 520 525

Val Leu Ile Val Thr Ala Ser Tyr Asn Gly His Pro Pro Asp Asn Ala
 530 535 540

Lys Gln Phe Val Asp Trp Leu Asp Gln Ala Ser Ala Asp Glu Val Lys
 545 550 555 560

Gly Val Arg Tyr Ser Val Phe Gly Cys Gly Asp Lys Asn Trp Ala Thr
 565 570 575

Thr Tyr Gln Lys Val Pro Ala Phe Ile Asp Glu Thr Leu Ala Ala Lys
 580 585 590

Gly Ala Glu Asn Ile Ala Asp Arg Gly Glu Ala Asp Ala Ser Asp Asp
 595 600 605

Phe Glu Gly Thr Tyr Glu Glu Trp Arg Glu His Met Trp Ser Asp Val
 610 615 620

Ala Ala Tyr Phe Asn Leu Asp Ile Glu Asn Ser Glu Asp Asn Lys Ser
 625 630 635 640

Page 105

P008-CIT_ST25.txt

Thr Leu Ser Leu Gln Phe Val Asp Ser Ala Ala Asp Met Pro Leu Ala
645 650 655

Lys Met His Gly Ala Phe Ser Thr Asn Val Val Ala Ser Lys Glu Leu
660 665 670

Gln Gln Pro Gly Ser Ala Arg Ser Thr Arg His Leu Glu Ile Glu Leu
675 680 685

Pro Lys Glu Ala Ser Tyr Gln Glu Gly Asp His Leu Gly Val Ile Pro
690 695 700

Arg Asn Tyr Glu Gly Thr Val Asn Arg Val Thr Ala Arg Phe Gly Leu
705 710 715 720

Asp Ala Ser Gln Gln Ile Arg Leu Glu Ala Glu Glu Glu Lys Leu Ala
725 730 735

His Leu Pro Leu Ala Lys Thr Val Ser Val Glu Glu Leu Leu Gln Tyr
740 745 750

Val Glu Leu Gln Asp Pro Val Thr Arg Thr Gln Leu Arg Ala Met Ala
755 760 765

Ala Lys Thr Val Cys Pro Pro His Lys Val Glu Leu Glu Ala Leu Leu
770 775 780

Glu Lys Gln Ala Tyr Lys Glu Gln Val Leu Ala Lys Arg Leu Thr Met
785 790 795 800

Leu Glu Leu Leu Glu Lys Tyr Pro Ala Cys Glu Met Lys Phe Ser Glu
805 810 815

Phe Ile Ala Leu Leu Pro Ser Ile Arg Pro Arg Tyr Tyr Ser Ile Ser
820 825 830

Ser Ser Pro Arg Val Asp Glu Lys Gln Ala Ser Ile Thr Val Ser Val
835 840 845

Val Ser Gly Glu Ala Trp Ser Gly Tyr Gly Glu Tyr Lys Gly Ile Ala
850 855 860

Ser Asn Tyr Leu Ala Glu Leu Gln Glu Gly Asp Thr Ile Thr Cys Phe
865 870 875 880

Ile Ser Thr Pro Gln Ser Glu Phe Thr Leu Pro Lys Asp Pro Glu Thr
Page 106

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

885

P008-CIT_ST25.txt

890

895

Pro Leu Ile Met Val Gly Pro Gly Thr Gly Val Ala Pro Phe Arg Gly
900 905 910

Phe Val Gln Ala Arg Lys Gln Leu Lys Glu Gln Gly Gln Ser Leu Gly
915 920 925

Glu Ala His Leu Tyr Phe Gly Cys Arg Ser Pro His Glu Asp Tyr Leu
930 935 940

Tyr Gln Glu Glu Leu Glu Asn Ala Gln Ser Glu Gly Ile Ile Thr Leu
945 950 955 960

His Thr Ala Phe Ser Arg Met Pro Asn Gln Pro Lys Thr Tyr Val Gln
965 970 975

His Val Met Glu Gln Asp Gly Lys Lys Leu Ile Glu Leu Leu Asp Gln
980 985 990

Gly Ala His Phe Tyr Ile Cys Gly Asp Gly Ser Gln Met Ala Pro Ala
995 1000 1005

Val Glu Ala Thr Leu Met Lys Ser Tyr Ala Asp Val His Gln Val
1010 1015 1020

Ser Glu Ala Asp Ala Arg Leu Trp Leu Gln Gln Leu Glu Glu Lys
1025 1030 1035

Gly Arg Tyr Ala Lys Asp Val Trp Ala Gly
1040 1045

<210> 33
<211> 1048
<212> PRT
<213> Artificial sequence

<220>
<223> Cytochrome P450 variant CYP102A1var3-11

<400> 33

Thr Ile Lys Glu Met Pro Gln Pro Lys Thr Phe Gly Glu Leu Lys Asn
1 5 10 15

Leu Pro Leu Leu Asn Thr Asp Lys Pro Val Gln Ala Leu Met Lys Ile.
20 25 30

Ala Asp Glu Leu Gly Glu Ile Phe Lys Phe Glu Ala Pro Gly Cys Val
35 40 45

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Thr Arg Tyr Ile Ser Ser Gln Arg Leu Ile Lys Glu Ala Cys Asp Glu
50 55 60

Ser Arg Phe Asp Lys Asn Leu Ser Gln Ala Leu Lys Ala Phe Arg Asp
65 70 75 80

Phe Ser Gly Asp Gly Leu Phe Thr Ser Trp Thr His Glu Ile Asn Trp
85 90 95

Lys Lys Ala His Asn Ile Leu Leu Pro Ser Phe Ser Gln Gln Ala Met
100 105 110

Lys Gly Tyr His Ala Met Met Val Asp Ile Ala Val Gln Leu Val Gln
115 120 125

Lys Trp Glu Arg Leu Asn Ala Asp Glu His Ile Glu Val Ser Glu Asp
130 135 140

Met Thr Arg Leu Thr Leu Asp Thr Ile Gly Leu Cys Gly Phe Asn Tyr
145 150 155 160

Arg Phe Asn Ser Phe Tyr Arg Asp Gln Pro His Pro Phe Ile Ile Ser
165 170 175

Met Val Arg Ala Leu Asp Glu Val Met Asn Lys Leu Gln Arg Ala Asn
180 185 190

Pro Asp Asp Pro Ala Tyr Asp Glu Asn Lys Arg Gln Cys Gln Glu Asp
195 200 205

Ile Lys Val Met Asn Asp Leu Val Asp Lys Ile Ile Ala Asp Arg Lys
210 215 220

Ala Arg Gly Glu Gln Ser Asp Asp Leu Leu Thr Gln Met Leu Asn Gly
225 230 235 240

Lys Asp Pro Glu Thr Gly Glu Pro Leu Asp Asp Gly Asn Ile Ser Tyr
245 250 255

Gln Ile Ile Thr Phe Leu Ile Ala Gly His Glu Thr Thr Ser Gly Leu
260 265 270

Leu Ser Phe Ala Leu Tyr Phe Leu Val Lys Asn Pro His Val Leu Gln
275 280 285

Lys Val Ala Glu Glu Ala Ala Arg Val Leu Val Asp Pro Val Pro Ser
Page 108

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

290

295

P008-CIT_ST25.txt
300

Tyr Lys Gln Val Lys Gln Leu Lys Tyr Val Gly Met Val Leu Asn Glu
305 310 315 320

Ala Leu Arg Leu Trp Pro Thr Leu Pro Ala Phe Ser Leu Tyr Ala Lys
325 330 335

Glu Asp Thr Val Leu Gly Gly Glu Tyr Pro Leu Glu Asn Gly Asp Glu
340 345 350

Val Met Val Leu Ile Pro Gln Leu His Arg Asp Lys Thr Val Trp Gly
355 360 365

Asp Asp Val Glu Glu Phe Arg Pro Glu Arg Phe Glu Asn Pro Ser Ala
370 375 380

Ile Pro Gln His Ala Phe Lys Pro Phe Gly Asn Gly Gln Arg Ala Cys
385 390 395 400

Ile Gly Gln Gln Phe Ala Leu His Glu Ala Thr Leu Val Leu Gly Met
405 410 415

Met Leu Lys His Phe Asp Phe Glu Asp His Thr Asn Tyr Glu Leu Asp
420 425 430

Ile Lys Glu Thr Leu Thr Leu Lys Pro Glu Gly Phe Val Val Lys Ala
435 440 445

Lys Ser Lys Lys Ile Pro Leu Gly Gly Ile Pro Ser Pro Ser Thr Gly
450 455 460

Gln Ser Ala Lys Lys Val Arg Lys Lys Ala Glu Asn Ala His Asn Thr
465 470 475 480

Pro Leu Leu Val Leu Tyr Gly Ser Asn Met Gly Thr Ala Glu Gly Thr
485 490 495

Ala Arg Asp Leu Ala Asp Ile Ala Met Ser Lys Gly Phe Ala Pro Gln
500 505 510

Val Ala Thr Leu Asp Ser His Ala Gly Asn Leu Pro Arg Glu Gly Ala
515 520 525

Val Leu Ile Val Thr Ala Ser Tyr Asn Gly His Pro Pro Asp Asn Ala
530 535 540

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Lys Gln Phe Val Asp Trp Leu Asp Gln Ala Ser Ala Asp Glu Val Lys
 545 550 555 560

Gly Val Arg Tyr Ser Val Phe Gly Cys Gly Asp Lys Asn Trp Ala Thr
 565 570 575

Thr Tyr Gln Lys Val Pro Ala Phe Ile Asp Glu Thr Leu Ala Ala Lys
 580 585 590

Gly Ala Glu Asn Ile Ala Asp Arg Gly Glu Ala Asp Ala Ser Asp Asp
 595 600 605

Phe Glu Gly Thr Tyr Glu Glu Trp Arg Glu His Met Trp Ser Asp Val
 610 615 620

Ala Ala Tyr Phe Asn Leu Asp Ile Glu Asn Ser Glu Asp Asn Lys Ser
 625 630 635 640

Thr Leu Ser Leu Gln Phe Val Asp Ser Ala Ala Asp Met Pro Leu Ala
 645 650 655

Lys Met His Gly Ala Phe Ser Thr Asn Val Val Ala Ser Lys Glu Leu
 660 665 670

Gln Gln Pro Gly Ser Ala Arg Ser Thr Arg His Leu Glu Ile Glu Leu
 675 680 685

Pro Lys Glu Ala Ser Tyr Gln Glu Gly Asp His Leu Gly Val Ile Pro
 690 695 700

Arg Asn Tyr Glu Gly Thr Val Asn Arg Val Thr Ala Arg Phe Gly Leu
 705 710 715 720

Asp Ala Ser Gln Gln Ile Arg Leu Glu Ala Glu Glu Glu Lys Leu Ala
 725 730 735

His Leu Pro Leu Ala Lys Thr Val Ser Val Glu Glu Leu Leu Gln Tyr
 740 745 750

Val Glu Leu Gln Asp Pro Val Thr Arg Thr Gln Leu Arg Ala Met Ala
 755 760 765

Ala Lys Thr Val Cys Pro Pro His Lys Val Glu Leu Glu Ala Leu Leu
 770 775 780

Glu Lys Gln Ala Tyr Lys Glu Gln Val Leu Ala Lys Arg Leu Thr Met
 785 790 795 800

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Leu Glu Leu Leu Glu Lys Tyr Pro Ala Cys Glu Met Lys Phe Ser Glu
805 810 815

Phe Ile Ala Leu Leu Pro Ser Ile Arg Pro Arg Tyr Tyr Ser Ile Ser
820 825 830

Ser Ser Pro Arg Val Asp Glu Lys Gln Ala Ser Ile Thr Val Ser Val
835 840 845

Val Ser Gly Glu Ala Trp Ser Gly Tyr Gly Glu Tyr Lys Gly Ile Ala
850 855 860

Ser Asn Tyr Leu Ala Glu Leu Gln Glu Gly Asp Thr Ile Thr Cys Phe
865 870 875 880

Ile Ser Thr Pro Gln Ser Glu Phe Thr Leu Pro Lys Asp Pro Glu Thr
885 890 895

Pro Leu Ile Met Val Gly Pro Gly Thr Gly Val Ala Pro Phe Arg Gly
900 905 910

Phe Val Gln Ala Arg Lys Gln Leu Lys Glu Gln Gly Gln Ser Leu Gly
915 920 925

Glu Ala His Leu Tyr Phe Gly Cys Arg Ser Pro His Glu Asp Tyr Leu
930 935 940

Tyr Gln Glu Glu Leu Glu Asn Ala Gln Ser Glu Gly Ile Ile Thr Leu
945 950 955 960

His Thr Ala Phe Ser Arg Met Pro Asn Gln Pro Lys Thr Tyr Val Gln
965 970 975

His Val Met Glu Gln Asp Gly Lys Lys Leu Ile Glu Leu Leu Asp Gln
980 985 990

Gly Ala His Phe Tyr Ile Cys Gly Asp Gly Ser Gln Met Ala Pro Ala
995 1000 1005

Val Glu Ala Thr Leu Met Lys Ser Tyr Ala Asp Val His Gln Val
1010 1015 1020

Ser Glu Ala Asp Ala Arg Leu Trp Leu Gln Gln Leu Glu Glu Lys
1025 1030 1035

Gly Arg Tyr Ala Lys Asp Val Trp Ala Gly
1040 1045

<210> 34
<211> 1048
<212> PRT
<213> Artificial sequence

<220>
<223> Cytochrome P450 variant CYP102A1var3-12

<400> 34

Thr Ile Lys Glu Met Pro Gln Pro Lys Thr Phe Gly Glu Leu Lys Asn
1 5 10 15

Leu Pro Leu Leu Asn Thr Asp Lys Pro Val Gln Ala Leu Met Lys Ile
20 25 30

Ala Asp Glu Leu Gly Glu Ile Phe Lys Phe Glu Ala Pro Gly Cys Val
35 40 45

Thr Arg Tyr Ile Ser Ser Gln Arg Leu Ile Lys Glu Ala Cys Asp Glu
50 55 60

Ser Arg Phe Asp Lys Asn Leu Ser Gln Ala Leu Lys Ala Phe Arg Asp
65 70 75 80

Phe Ser Gly Asp Gly Leu Phe Thr Ser Trp Thr His Glu Ile Asn Trp
85 90 95

Lys Lys Ala His Asn Ile Leu Leu Pro Ser Phe Ser Gln Gln Ala Met
100 105 110

Lys Gly Tyr His Ala Met Met Val Asp Ile Ala Val Gln Leu Val Gln
115 120 125

Lys Trp Glu Arg Leu Asn Ala Asp Glu His Ile Glu Val Ser Glu Asp
130 135 140

Met Thr Arg Leu Thr Leu Asp Thr Ile Gly Leu Cys Gly Phe Asn Tyr
145 150 155 160

Arg Phe Asn Ser Phe Tyr Arg Asp Gln Pro His Pro Phe Ile Ile Ser
165 170 175

Met Val Arg Ala Leu Asp Glu Val Met Asn Lys Pro Gln Arg Ala Asn
180 185 190

Pro Asp Asp Pro Ala Tyr Asp Glu Asn Lys Arg Gln Cys Gln Glu Asp
195 200 205

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Ile Lys Val Met Asn Asp Leu Val Asp Lys Ile Ile Ala Asp Arg Lys.
210 215 220

Ala Arg Gly Glu Gln Ser Asp Asp Leu Leu Thr Gln Met Leu Asn Gly
225 230 235 240

Lys Asp Pro Glu Thr Gly Glu Pro Leu Asp Asp Gly Asn Ile Ser Tyr
245 250 255

Gln Ile Ile Thr Phe Leu Ile Ala Gly His Glu Thr Thr Ser Gly Leu
260 265 270

Leu Ser Phe Ala Leu Tyr Phe Leu Val Lys Asn Pro His Val Leu Gln
275 280 285

Lys Val Ala Glu Glu Ala Ala Arg Val Leu Val Asp Pro Val Pro Ser
290 295 300

Tyr Lys Gln Val Lys Gln Leu Lys Tyr Val Gly Met Val Leu Asn Glu
305 310 315 320

Ala Leu Arg Leu Trp Pro Thr Phe Pro Ala Phe Ser Leu Tyr Ala Lys
325 330 335

Glu Asp Thr Val Leu Gly Gly Glu Tyr Pro Leu Glu Lys Gly Asp Glu
340 345 350

Val Met Val Leu Ile Pro Gln Leu His Arg Asp Lys Thr Val Trp Gly
355 360 365

Asp Asp Val Glu Glu Phe Arg Pro Glu Arg Phe Glu Asn Pro Ser Ala
370 375 380

Ile Pro Gln His Ala Phe Lys Pro Phe Gly Asn Gly Gln Arg Ala Cys
385 390 395 400

Ile Gly Gln Gln Phe Ala Leu His Glu Ala Thr Leu Val Leu Gly Met
405 410 415

Met Leu Lys His Phe Asp Phe Glu Asp His Thr Asn Tyr Glu Leu Asp
420 425 430

Ile Lys Glu Thr Leu Thr Leu Lys Pro Glu Gly Phe Val Val Lys Ala
435 440 445

Lys Ser Lys Lys Ile Pro Leu Gly Gly Ile Pro Ser Pro Ser Thr Gly
450 455 460

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Gln Ser Ala Lys Lys Val Arg Lys Lys Ala Glu Asn Ala His Asn Thr
 465 470 475 480

Pro Leu Leu Val Leu Tyr Gly Ser Asn Met Gly Thr Ala Glu Gly Thr
 485 490 495

Ala Arg Asp Leu Ala Asp Ile Ala Met Ser Lys Gly Phe Ala Pro Gln
 500 505 510

Val Ala Thr Leu Asp Ser His Ala Gly Asn Leu Pro Arg Glu Gly Ala
 515 520 525

Val Leu Ile Val Thr Ala Ser Tyr Asn Gly His Pro Pro Asp Asn Ala
 530 535 540

Lys Gln Phe Val Asp Trp Leu Asp Gln Ala Ser Ala Asp Glu Val Lys
 545 550 555 560

Gly Val Arg Tyr Ser Val Phe Gly Cys Gly Asp Lys Asn Trp Ala Thr
 565 570 575

Thr Tyr Gln Lys Val Pro Ala Phe Ile Asp Glu Thr Leu Ala Ala Lys
 580 585 590

Gly Ala Glu Asn Ile Ala Asp Arg Gly Glu Ala Asp Ala Ser Asp Asp
 595 600 605

Phe Glu Gly Thr Tyr Glu Glu Trp Arg Glu His Met Trp Ser Asp Val
 610 615 620

Ala Ala Tyr Phe Asn Leu Asp Ile Glu Asn Ser Glu Asp Asn Lys Ser
 625 630 635 640

Thr Leu Ser Leu Gln Phe Val Asp Ser Ala Ala Asp Met Pro Leu Ala
 645 650 655

Lys Met His Gly Ala Phe Ser Thr Asn Val Val Ala Ser Lys Glu Leu
 660 665 670

Gln Gln Pro Gly Ser Ala Arg Ser Thr Arg His Leu Glu Ile Glu Leu
 675 680 685

Pro Lys Glu Ala Ser Tyr Gln Glu Gly Asp His Leu Gly Val Ile Pro
 690 695 700

Arg Asn Tyr Glu Gly Thr Val Asn Arg Val Thr Ala Arg Phe Gly Leu

P008-CIT_ST25.txt

705

710

715

720

Asp Ala Ser Gln Gln Ile Arg Leu Glu Ala Glu Glu Glu Lys Leu Ala
725 730 735

His Leu Pro Leu Ala Lys Thr Val Ser Val Glu Glu Leu Leu Gln Tyr
740 745 750

Val Glu Leu Gln Asp Pro Val Thr Arg Thr Gln Leu Arg Ala Met Ala
755 760 765

Ala Lys Thr Val Cys Pro Pro His Lys Val Glu Leu Glu Ala Leu Leu
770 775 780

Glu Lys Gln Ala Tyr Lys Glu Gln Val Leu Ala Lys Arg Leu Thr Met
785 790 795 800

Leu Glu Leu Leu Glu Lys Tyr Pro Ala Cys Glu Met Lys Phe Ser Glu
805 810 815

Phe Ile Ala Leu Leu Pro Ser Ile Arg Pro Arg Tyr Tyr Ser Ile Ser
820 825 830

Ser Ser Pro Arg Val Asp Glu Lys Gln Ala Ser Ile Thr Val Ser Val
835 840 845

Val Ser Gly Glu Ala Trp Ser Gly Tyr Gly Glu Tyr Lys Gly Ile Ala
850 855 860

Ser Asn Tyr Leu Ala Glu Leu Gln Glu Gly Asp Thr Ile Thr Cys Phe
865 870 875 880

Ile Ser Thr Pro Gln Ser Glu Phe Thr Leu Pro Lys Asp Pro Glu Thr
885 890 895

Pro Leu Ile Met Val Gly Pro Gly Thr Gly Val Ala Pro Phe Arg Gly
900 905 910

Phe Val Gln Ala Arg Lys Gln Leu Lys Glu Gln Gly Gln Ser Leu Gly
915 920 925

Glu Ala His Leu Tyr Phe Gly Cys Arg Ser Pro His Glu Asp Tyr Leu
930 935 940

Tyr Gln Glu Glu Leu Glu Asn Ala Gln Ser Glu Gly Ile Ile Thr Leu
945 950 955 960

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

His Thr Ala Phe Ser Arg Met Pro Asn Gln Pro Lys Thr Tyr Val Gln
 965 970 975

His Val Met Glu Gln Asp Gly Lys Lys Leu Ile Glu Leu Leu Asp Gln
 980 985 990

Gly Ala His Phe Tyr Ile Cys Gly Asp Gly Ser Gln Met Ala Pro Ala
 995 1000 1005

Val Glu Ala Thr Leu Met Lys Ser Tyr Ala Asp Val His Gln Val
 1010 1015 1020

Ser Glu Ala Asp Ala Arg Leu Trp Leu Gln Gln Leu Glu Glu Lys
 1025 1030 1035

Gly Arg Tyr Ala Lys Asp Val Trp Ala Gly
 1040 1045

<210> 35

<211> 1048

<212> PRT

<213> Artificial sequence

<220>

<223> Cytochrome P450 variant CYP102A1var3-13

<400> 35

Thr Ile Lys Glu Met Pro Gln Pro Lys Thr Phe Gly Glu Leu Lys Asn
 1 5 10 15

Leu Pro Leu Leu Asn Thr Asp Lys Pro Val Gln Ala Leu Met Lys Ile
 20 25 30

Ala Asp Glu Leu Gly Glu Ile Phe Lys Phe Glu Ala Pro Gly Cys Val
 35 40 45

Thr Arg Tyr Leu Ser Ser Gln Arg Leu Ile Lys Glu Ala Cys Asp Glu
 50 55 60

Ser Arg Phe Asp Lys Asn Leu Ser Gln Ala Leu Lys Thr Val Arg Asp
 65 70 75 80

Phe Gly Gly Asp Gly Leu Phe Thr Ser Trp Thr His Glu Ile Asn Trp
 85 90 95

Lys Lys Ala His Asn Ile Leu Leu Pro Ser Phe Ser Gln Gln Ala Met
 100 105 110

Lys Gly Tyr His Ala Met Met Val Asp Ile Ala Val Gln Leu Val Gln
 Page 116

P008-CIT_ST25.txt

115

120

125

Lys Trp Glu Arg Leu Asn Ala Asp Glu His Ile Glu Val Ser Glu Asp
 130 135 140

Met Thr Arg Leu Thr Leu Asp Thr Ile Gly Leu Cys Gly Phe Asn Tyr
 145 150 155 160

Arg Phe Asn Ser Phe Tyr Arg Asp Gln Pro His Pro Phe Ile Ile Ser
 165 170 175

Met Val Arg Ala Leu Asp Glu Val Met Asn Lys Leu Gln Arg Ala Asn
 180 185 190

Pro Asp Asp Pro Ala Tyr Asp Glu Asn Lys Arg Gln Cys Gln Glu Asp
 195 200 205

Ile Lys Val Met Asn Asp Leu Val Asp Lys Ile Ile Ala Asp Arg Lys
 210 215 220

Ala Arg Gly Glu Gln Ser Asp Asp Leu Leu Thr Gln Met Leu Asn Gly
 225 230 235 240

Lys Asp Pro Glu Thr Gly Glu Pro Leu Asp Asp Gly Asn Ile Ser Tyr
 245 250 255

Gln Ile Ile Thr Phe Leu Ile Ala Gly His Glu Thr Thr Ser Gly Leu
 260 265 270

Leu Ser Phe Ala Leu Tyr Phe Leu Val Lys Asn Pro His Val Leu Gln
 275 280 285

Lys Val Ala Glu Glu Ala Ala Arg Val Leu Val Asp Pro Val Pro Ser
 290 295 300

Tyr Lys Gln Val Lys Gln Leu Lys Tyr Val Gly Met Val Leu Asn Glu
 305 310 315 320

Ala Leu Arg Leu Trp Pro Thr Leu Pro Ala Phe Ser Leu Tyr Ala Lys
 325 330 335

Glu Asp Thr Val Leu Gly Gly Glu Tyr Pro Leu Glu Lys Gly Asp Glu
 340 345 350

Val Met Val Leu Ile Pro Gln Leu His Arg Asp Lys Thr Ile Trp Gly
 355 360 365

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Asp Asp Val Glu Glu Phe Arg Pro Glu Arg Phe Glu Asn Pro Ser Ala
 370 375 380

Ile Pro Gln His Ala Phe Lys Pro Phe Gly Asn Gly Gln Arg Ala Cys
 385 390 395 400

Ile Gly Gln Gln Phe Ala Leu His Glu Ala Thr Leu Val Leu Gly Met
 405 410 415

Met Leu Lys His Phe Asp Phe Glu Asp His Thr Asn Tyr Glu Leu Asp
 420 425 430

Ile Lys Glu Thr Leu Thr Leu Lys Pro Glu Gly Phe Val Val Lys Ala
 435 440 445

Lys Ser Lys Lys Ile Pro Leu Gly Gly Ile Pro Ser Thr Glu
 450 455 460

Gln Ser Ala Lys Lys Val Arg Lys Lys Ala Glu Asn Ala His Asn Thr
 465 470 475 480

Pro Leu Leu Val Leu Tyr Gly Ser Asn Met Gly Thr Ala Glu Gly Thr
 485 490 495

Ala Arg Asp Leu Ala Asp Ile Ala Met Ser Lys Gly Phe Ala Pro Gln
 500 505 510

Val Ala Thr Leu Asp Ser His Ala Gly Asn Leu Pro Arg Glu Gly Ala
 515 520 525

Val Leu Ile Val Thr Ala Ser Tyr Asn Gly His Pro Asp Asn Ala
 530 535 540

Lys Gln Phe Val Asp Trp Leu Asp Gln Ala Ser Ala Asp Glu Val Lys
 545 550 555 560

Gly Val Arg Tyr Ser Val Phe Gly Cys Gly Asp Lys Asn Trp Ala Thr
 565 570 575

Thr Tyr Gln Lys Val Pro Ala Phe Ile Asp Glu Thr Leu Ala Ala Lys
 580 585 590

Gly Ala Glu Asn Ile Ala Asp Arg Gly Glu Ala Asp Ala Ser Asp Asp
 595 600 605

Phe Glu Gly Thr Tyr Glu Glu Trp Arg Glu His Met Trp Ser Asp Val
 610 615 620

Printed: 10/30/2007

SPOLIST

PCT/US2007/017409

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EBS11841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Ala Ala Tyr Phe Asn Leu Asp Ile Glu Asn Ser Glu Asp Asn Lys Ser
625 630 635 640

Thr Leu Ser Leu Gln Phe Val Asp Ser Ala Ala Asp Met Pro Leu Ala
645 650 655

Lys Met His Gly Ala Phe Ser Thr Asn Val Val Ala Ser Lys Glu Leu
660 665 670

Gln Gln Pro Gly Ser Ala Arg Ser Thr Arg His Leu Glu Ile Glu Leu
675 680 685

Pro Lys Glu Ala Ser Tyr Gln Glu Gly Asp His Leu Gly Val Ile Pro
690 695 700

Arg Asn Tyr Glu Gly Ile Val Asn Arg Val Thr Ala Arg Phe Gly Leu
705 710 715 720

Asp Ala Ser Gln Gln Ile Arg Leu Glu Ala Glu Glu Glu Lys Leu Ala
725 730 735

His Leu Pro Leu Ala Lys Thr Val Ser Val Glu Glu Leu Leu Gln Tyr
740 745 750

Val Glu Leu Gln Asp Pro Val Thr Arg Thr Gln Leu Arg Ala Met Ala
755 760 765

Ala Lys Thr Val Cys Pro Pro His Lys Val Glu Leu Glu Ala Leu Leu
770 775 780

Glu Lys Gln Ala Tyr Lys Glu Gln Val Leu Ala Lys Arg Leu Thr Met
785 790 795 800

Leu Glu Leu Leu Glu Lys Tyr Pro Ala Cys Glu Met Lys Phe Ser Glu
805 810 815

Phe Ile Ala Leu Leu Pro Ser Ile Arg Pro Arg Tyr Tyr Ser Ile Ser
820 825 830

Ser Ser Pro Arg Val Asp Glu Lys Gln Ala Ser Ile Thr Val Ser Val
835 840 845

Val Ser Gly Glu Ala Trp Ser Gly Tyr Gly Glu Tyr Lys Gly Ile Ala
850 855 860

Ser Asn Tyr Leu Ala Glu Leu Gln Glu Gly Asp Thr Ile Thr Cys Phe
865 870 875 880

Page 119

P008-CIT_ST25.txt

Ile Ser Thr Pro Gln Ser Glu Phe Thr Leu Pro Lys Asp Pro Glu Thr
885 890 895

Pro Leu Ile Met Val Gly Pro Gly Thr Gly Val Ala Pro Phe Arg Gly
900 905 910

Phe Val Gln Ala Arg Lys Gln Leu Lys Glu Gln Gly Gln Ser Leu Gly
915 920 925

Glu Ala His Leu Tyr Phe Gly Cys Arg Ser Pro His Glu Asp Tyr Leu
930 935 940

Tyr Gln Glu Glu Leu Glu Asn Ala Gln Ser Glu Gly Ile Ile Thr Leu
945 950 955 960

His Thr Ala Phe Ser Arg Met Pro Asn Gln Pro Lys Thr Tyr Val Gln
965 970 975

His Val Met Glu Gln Asp Gly Lys Lys Leu Ile Glu Leu Leu Asp Gln
980 985 990

Gly Ala His Phe Tyr Ile Cys Gly Asp Gly Ser Gln Met Ala Pro Ala
995 1000 1005

Val Glu Ala Thr Leu Met Lys Ser Tyr Ala Asp Val His Gln Val
1010 1015 1020

Ser Glu Ala Asp Ala Arg Leu Trp Leu Gln Gln Leu Glu Glu Lys
1025 1030 1035

Gly Arg Tyr Ala Lys Asp Val Trp Ala Gly
1040 1045

<210> 36

<211> 1048

<212> -PRT

<213> Artificial sequence

<220>

<223> Cytochrome P450 variant CYP102A1var3-14

<400> 36

Thr Ile Lys Glu Met Pro Gln Pro Lys Thr Phe Gly Glu Leu Lys Asn
1 5 10 15

Leu Pro Leu Leu Asn Thr Asp Lys Pro Val Gln Ala Leu Met Lys Ile
20 25 30

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Ala Asp Glu Leu Gly Glu Ile Phe Lys Phe Glu Ala Pro Gly Arg Val
 35 40 45

Thr Arg Tyr Leu Ser Ser Gln Arg Leu Ile Lys Glu Ala Cys Asp Glu
 50 55 60

Ser Arg Phe Asp Lys Asn Leu Ser Gln Ala Leu Lys Ala Val Arg Asp
 65 70 75 80

Arg Val Gly Asp Gly Leu Ala Thr Ser Trp Thr His Glu Lys Asn Trp
 85 90 95

Lys Lys Ala His Asn Ile Leu Leu Pro Ser Phe Ser Gln Gln Ala Met
 100 105 110

Lys Gly Tyr His Ala Met Met Val Asp Ile Ala Val Gln Leu Val Gln
 115 120 125

Lys Trp Glu Arg Leu Asn Ala Asp Glu His Ile Glu Val Ser Glu Asp
 130 135 140

Met Thr Arg Leu Thr Leu Asp Thr Ile Gly Leu Cys Gly Phe Asn Tyr
 145 150 155 160

Arg Phe Asn Ser Phe Tyr Arg Asp Gln Pro His Pro Phe Ile Ile Ser
 165 170 175

Met Val Arg Thr Leu Asp Glu Val Met Asn Lys Leu Gln Arg Ala Asn
 180 185 190

Pro Asp Asp Pro Val Tyr Asp Glu Asn Lys Arg Gln Cys Gln Glu Asp
 195 200 205

Ile Lys Val Met Asn Asp Leu Val Asp Lys Ile Ile Ala Asp Arg Lys
 210 215 220

Ala Arg Gly Glu Gln Ser Asp Asp Leu Leu Thr Gln Met Leu Asn Gly
 225 230 235 240

Lys Asp Pro Glu Thr Gly Glu Pro Leu Asp Asp Gly Asn Ile Ser Tyr
 245 250 255

Gln Ile Ile Thr Phe Leu Ile Ala Gly His Glu Thr Thr Ser Gly Leu
 260 265 270

Leu Ser Phe Ala Leu Tyr Phe Leu Val Lys Asn Pro His Val Leu Gln
 275 280 285

Page 121

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Lys Val Ala Glu Glu Ala Ala Arg Val Leu Val Asp Pro Val Pro Ser
290 295 300

Tyr Lys Gln Val Lys Gln Leu Lys Tyr Val Gly Met Val Leu Asn Glu
305 310 315 320

Ala Leu Arg Leu Trp Pro Thr Ala Pro Ala Phe Ser Leu Tyr Ala Lys
325 330 335

Glu Asp Thr Val Leu Gly Gly Glu Tyr Pro Leu Glu Lys Gly Asp Glu
340 345 350

Val Met Val Leu Ile Pro Gln Leu His Arg Asp Lys Thr Ile Trp Gly
355 360 365

Asp Asp Val Glu Glu Phe Arg Pro Glu Arg Phe Glu Asn Pro Ser Ala
370 375 380

Ile Pro Gln His Ala Phe Lys Pro Phe Gly Asn Gly Gln Arg Ala Cys
385 390 395 400

Ile Gly Gln Gln Phe Ala Leu His Glu Ala Thr Leu Val Leu Gly Met
405 410 415

Met Leu Lys His Phe Asp Phe Glu Asp His Thr Asn Tyr Glu Leu Asp
420 425 430

Ile Lys Glu Thr Leu Thr Leu Lys Pro Glu Gly Phe Val Val Lys Ala
435 440 445

Lys Ser Lys Lys Ile Pro Leu Gly Gly Ile Pro Ser Pro Ser Thr Glu
450 455 460

Gln Ser Ala Lys Lys Val Arg Lys Lys Ala Glu Asn Ala His Asn Thr
465 470 475 480

Pro Leu Leu Val Leu Tyr Gly Ser Asn Met Gly Thr Ala Glu Gly Thr
485 490 495

Ala Arg Asp Leu Ala Asp Ile Ala Met Ser Lys Gly Phe Ala Pro Gln
500 505 510

Val Ala Thr Leu Asp Ser His Ala Gly Asn Leu Pro Arg Glu Gly Ala
515 520 525

Val Leu Ile Val Thr Ala Ser Tyr Asn Gly His Pro Pro Asp Asn Ala
Page 122

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

530

535

540

Lys Gln Phe Val Asp Trp Leu Asp Gln Ala Ser Ala Asp Glu Val Lys
 545 550 555 560

Gly Val Arg Tyr Ser Val Phe Gly Cys Gly Asp Lys Asn Trp Ala Thr
 565 570 575

Thr Tyr Gln Lys Val Pro Ala Phe Ile Asp Glu Thr Leu Ala Ala Lys
 580 585 590

Gly Ala Glu Asn Ile Ala Asp Arg Gly Glu Ala Asp Ala Ser Asp Asp
 595 600 605

Phe Glu Gly Thr Tyr Glu Glu Trp Arg Glu His Met Trp Ser Asp Val
 610 615 620

Ala Ala Tyr Phe Asn Leu Asp Ile Glu Asn Ser Glu Asp Asn Lys Ser
 625 630 635 640

Thr Leu Ser Leu Gln Phe Val Asp Ser Ala Ala Asp Met Pro Leu Ala
 645 650 655

Lys Met His Gly Ala Phe Ser Thr Asn Val Val Ala Ser Lys Glu Leu
 660 665 670

Gln Gln Pro Gly Ser Ala Arg Ser Thr Arg His Leu Glu Ile Glu Leu
 675 680 685

Pro Lys Glu Ala Ser Tyr Gln Glu Gly Asp His Leu Gly Val Ile Pro
 690 695 700

Arg Asn Tyr Glu Gly Ile Val Asn Arg Val Thr Ala Arg Phe Gly Leu
 705 710 715 720

Asp Ala Ser Gln Gln Ile Arg Leu Glu Ala Glu Glu Glu Lys Leu Ala
 725 730 735

His Leu Pro Leu Ala Lys Thr Val Ser Val Glu Glu Leu Leu Gln Tyr
 740 745 750

Val Glu Leu Gln Asp Pro Val Thr Arg Thr Gln Leu Arg Ala Met Ala
 755 760 765

Ala Lys Thr Val Cys Pro Pro His Lys Val Glu Leu Glu Ala Leu Leu
 770 775 780

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Glu Lys Gln Ala Tyr Lys Glu Gln Val Leu Ala Lys Arg Leu Thr Met
 785 790 795 800

Leu Glu Leu Leu Glu Lys Tyr Pro Ala Cys Glu Met Lys Phe Ser Glu
 805 810 815

Phe Ile Ala Leu Leu Pro Ser Ile Arg Pro Arg Tyr Tyr Ser Ile Ser
 820 825 830

Ser Ser Pro Arg Val Asp Glu Lys Gln Ala Ser Ile Thr Val Ser Val
 835 840 845

Val Ser Gly Glu Ala Trp Ser Gly Tyr Gly Glu Tyr Lys Gly Ile Ala
 850 855 860

Ser Asn Tyr Leu Ala Glu Leu Gln Glu Gly Asp Thr Ile Thr Cys Phe
 865 870 875 880

Ile Ser Thr Pro Gln Ser Glu Phe Thr Leu Pro Lys Asp Pro Glu Thr
 885 890 895

Pro Leu Ile Met Val Gly Pro Gly Thr Gly Val Ala Pro Phe Arg Gly
 900 905 910

Phe Val Gln Ala Arg Lys Gln Leu Lys Glu Gln Gly Gln Ser Leu Gly
 915 920 925

Glu Ala His Leu Tyr Phe Gly Cys Arg Ser Pro His Glu Asp Tyr Leu
 930 935 940

Tyr Gln Glu Glu Leu Glu Asn Ala Gln Ser Glu Gly Ile Ile Thr Leu
 945 950 955 960

His Thr Ala Phe Ser Arg Met Pro Asn Gln Pro Lys Thr Tyr Val Gln
 965 970 975

His Val Met Glu Gln Asp Gly Lys Lys Leu Ile Glu Leu Leu Asp Gln
 980 985 990

Gly Ala His Phe Tyr Ile Cys Gly Asp Gly Ser Gln Met Ala Pro Ala
 995 1000 1005

Val Glu Ala Thr Leu Met Lys Ser Tyr Ala Asp Val His Gln Val
 1010 1015 1020

Ser Glu Ala Asp Ala Arg Leu Trp Leu Gln Gln Leu Glu Glu Lys
 1025 1030 1035

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: BB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Gly Arg Tyr Ala Lys Asp Val Trp Ala Gly
1040 1045<210> 37
<211> 1048
<212> PRT
<213> Artificial sequence<220>
<223> Cytochrome P450 variant CYP102A1var3-15

<400> 37

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

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Pro Asp Asp Pro Val Tyr Asp Glu Asn Lys Arg Gln Cys Gln Glu Asp
195 200 205

Ile Lys Val Met Asn Asp Leu Val Asp Lys Ile Ile Ala Asp Arg Lys
210 215 220

Ala Arg Gly Glu Gln Ser Asp Asp Leu Leu Thr Gln Met Leu Asn Gly
225 230 235 240

Lys Asp Pro Glu Thr Gly Glu Pro Leu Asp Asp Gly Asn Ile Ser Tyr
245 250 255

Gln Ile Ile Thr Phe Leu Ile Ala Gly His Glu Thr Thr Ser Gly Leu
260 265 270

Leu Ser Phe Ala Leu Tyr Phe Leu Val Lys Asn Pro His Val Leu Gln
275 280 285

Lys Val Ala Glu Glu Ala Ala Arg Val Leu Val Asp Pro Val Pro Ser
290 295 300

Tyr Lys Gln Val Lys Gln Leu Lys Tyr Val Gly Met Val Leu Asn Glu
305 310 315 320

Ala Leu Arg Leu Trp Pro Thr Ala Pro Ala Phe Ser Leu Tyr Ala Lys
325 330 335

Glu Asp Thr Val Leu Gly Gly Glu Tyr Pro Leu Glu Lys Gly Asp Glu
340 345 350

Val Met Val Leu Ile Pro Gln Leu His Arg Asp Lys Thr Ile Trp Gly
355 360 365

Asp Asp Val Glu Glu Phe Arg Pro Glu Arg Phe Glu Asn Pro Ser Ala
370 375 380

Ile Pro Gln His Ala Phe Lys Pro Phe Gly Asn Gly Gln Arg Ala Cys
385 390 395 400

Ile Gly Gln Gln Phe Ala Leu His Glu Ala Thr Leu Val Leu Gly Met
405 410 415

Met Leu Lys His Phe Asp Phe Glu Asp His Thr Asn Tyr Glu Leu Asp
420 425 430

Ile Lys Glu Thr Leu Thr Leu Lys Pro Glu Gly Phe Val Lys Ala
435 440 445

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Lys Ser Lys Lys Ile Pro Leu Gly Gly Ile Pro Ser Pro Ser Thr Glu
450 455 460

Gln Ser Ala Lys Lys Val Arg Lys Lys Ala Glu Asn Ala His Asn Thr
465 470 475 480

Pro Leu Leu Val Leu Tyr Gly Ser Asn Met Gly Thr Ala Glu Gly Thr
485 490 495

Ala Arg Asp Leu Ala Asp Ile Ala Met Ser Lys Gly Phe Ala Pro Gln
500 505 510

Val Ala Thr Leu Asp Ser His Ala Gly Asn Leu Pro Arg Glu Gly Ala
515 520 525

Val Leu Ile Val Thr Ala Ser Tyr Asn Gly His Pro Pro Asp Asn Ala
530 535 540

Lys Gln Phe Val Asp Trp Leu Asp Gln Ala Ser Ala Asp Glu Val Lys
545 550 555 560

Gly Val Arg Tyr Ser Val Phe Gly Cys Gly Asp Lys Asn Trp Ala Thr
565 570 575

Thr Tyr Gln Lys Val Pro Ala Phe Ile Asp Glu Thr Leu Ala Ala Lys
580 585 590

Gly Ala Glu Asn Ile Ala Asp Arg Gly Glu Ala Asp Ala Ser Asp Asp
595 600 605

Phe Glu Gly Thr Tyr Glu Glu Trp Arg Glu His Met Trp Ser Asp Val
610 615 620

Ala Ala Tyr Phe Asn Leu Asp Ile Glu Asn Ser Glu Asp Asn Lys Ser
625 630 635 640

Thr Leu Ser Leu Gln Phe Val Asp Ser Ala Ala Asp Met Pro Leu Ala
645 650 655

Lys Met His Gly Ala Phe Ser Thr Asn Val Val Ala Ser Lys Glu Leu
660 665 670

Gln Gln Pro Gly Ser Ala Arg Ser Thr Arg His Leu Glu Ile Glu Leu
675 680 685

Pro Lys Glu Ala Ser Tyr Gln Glu Gly Asp His Leu Gly Val Ile Pro
690 695 700

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Arg Asn Tyr Glu Gly Ile Val Asn Arg Val Thr Ala Arg Phe Gly Leu
705 710 715 720

Asp Ala Ser Gln Gln Ile Arg Leu Glu Ala Glu Glu Glu Lys Leu Ala
725 730 735

His Leu Pro Leu Ala Lys Thr Val Ser Val Glu Glu Leu Leu Gln Tyr
740 745 750

Val Glu Leu Gln Asp Pro Val Thr Arg Thr Gln Leu Arg Ala Met Ala
755 760 765

Ala Lys Thr Val Cys Pro Pro His Lys Val Glu Leu Glu Ala Leu Leu
770 775 780

Glu Lys Gln Ala Tyr Lys Glu Gln Val Leu Ala Lys Arg Leu Thr Met
785 790 795 800

Leu Glu Leu Leu Glu Lys Tyr Pro Ala Cys Glu Met Lys Phe Ser Glu
805 810 815

Phe Ile Ala Leu Leu Pro Ser Ile Arg Pro Arg Tyr Tyr Ser Ile Ser
820 825 830

Ser Ser Pro Arg Val Asp Glu Lys Gln Ala Ser Ile Thr Val Ser Val
835 840 845

Val Ser Gly Glu Ala Trp Ser Gly Tyr Gly Glu Tyr Lys Gly Ile Ala
850 855 860

Ser Asn Tyr Leu Ala Glu Leu Gln Glu Gly Asp Thr Ile Thr Cys Phe
865 870 875 880

Ile Ser Thr Pro Gln Ser Glu Phe Thr Leu Pro Lys Asp Pro Glu Thr
885 890 895

Pro Leu Ile Met Val Gly Pro Gly Thr Gly Val Ala Pro Phe Arg Gly
900 905 910

Phe Val Gln Ala Arg Lys Gln Leu Lys Glu Gln Gly Gln Ser Leu Gly
915 920 925

Glu Ala His Leu Tyr Phe Gly Cys Arg Ser Pro His Glu Asp Tyr Leu
930 935 940

Tyr Gln Glu Glu Leu Glu Asn Ala Gln Ser Glu Gly Ile Ile Thr Leu
Page 128

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

945

950

955

960

His Thr Ala Phe Ser Arg Met Pro Asn Gln Pro Lys Thr Tyr Val Gln
965 970 975

His Val Met Glu Gln Asp Gly Lys Lys Leu Ile Glu Leu Leu Asp Gln
980 985 990

Gly Ala His Phe Tyr Ile Cys Gly Asp Gly Ser Gln Met Ala Pro Ala
995 1000 1005

Val Glu Ala Thr Leu Met Lys Ser Tyr Ala Asp Val His Gln Val
1010 1015 1020

Ser Glu Ala Asp Ala Arg Leu Trp Leu Gln Gln Leu Glu Glu Lys
1025 1030 1035

Gly Arg Tyr Ala Lys Asp Val Trp Ala Gly
1040 1045

<210> 38
<211> 1048
<212> PRT
<213> Artificial sequence

<220>
<223> Cytochrome P450 variant CYP102A1var3-16

<400> 38

Thr Ile Lys Glu Met Pro Gln Pro Lys Thr Phe Gly Glu Leu Lys Asn
1 5 10 15

Leu Pro Leu Leu Asn Thr Asp Lys Pro Val Gln Ala Leu Met Lys Ile
20 25 30

Ala Asp Glu Leu Gly Glu Ile Phe Lys Phe Glu Ala Pro Gly Cys Val
35 40 45

Thr Arg Tyr Leu Ser Ser Gln Arg Leu Ile Lys Glu Ala Cys Asp Glu
50 55 60

Ser Arg Phe Asp Lys Asn Leu Ser Gln Ala Leu Lys Ala Phe Arg Asp
65 70 75 80

Phe Ser Gly Asp Gly Leu Phe Thr Ser Trp Thr His Glu Ile Asn Trp
85 90 95

Lys Lys Ala His Asn Ile Leu Leu Pro Ser Phe Ser Gln Gln Ala Met
100 105 110

P008-CIT_ST25.txt

Lys Gly Tyr His Ala Met Met Val Asp Ile Ala Val Gln Leu Val Gln
115 120 125

Lys Trp Glu Arg Leu Asn Ala Asp Glu His Ile Glu Val Ser Glu Asp
130 135 140

Met Thr Arg Leu Thr Leu Asp Thr Ile Gly Leu Cys Gly Phe Asn Tyr
145 150 155 160

Arg Phe Asn Ser Phe Tyr Arg Asp Gln Pro His Pro Phe Ile Ile Ser
165 170 175

Met Val Arg Ala Leu Asp Glu Val Met Asn Lys Leu Gln Arg Ala Asn
180 185 190

Pro Asp Asp Pro Ala Tyr Asp Glu Asn Lys Arg Gln Cys Gln Glu Asp
195 200 205

Ile Lys Val Met Asn Asp Leu Val Asp Lys Ile Ile Ala Asp Arg Lys
210 215 220

Ala Arg Gly Glu Gln Ser Asp Asp Leu Leu Thr Gln Met Leu Asn Gly
225 230 235 240

Lys Asp Pro Glu Thr Gly Glu Pro Leu Asp Asp Gly Asn Ile Ser Tyr
245 250 255

Gln Ile Ile Thr Phe Leu Ile Ala Gly His Glu Thr Thr Ser Gly Leu
260 265 270

Leu Ser Phe Ala Leu Tyr Phe Leu Val Lys Asn Pro His Val Leu Gln
275 280 285

Lys Val Ala Glu Glu Ala Ala Arg Val Leu Val Asp Pro Val Pro Ser
290 295 300

Tyr Lys Gln Val Lys Gln Leu Lys Tyr Val Gly Met Val Leu Asn Glu
305 310 315 320

Ala Leu Arg Leu Trp Pro Thr Phe Pro Ala Phe Ser Leu Tyr Ala Lys
325 330 335

Glu Asp Thr Val Leu Gly Gly Glu Tyr Pro Leu Glu Lys Gly Asp Glu
340 345 350

Val Met Val Leu Ile Pro Gln Leu His Arg Asp Lys Thr Ile Trp Gly
Page 130

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No.: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

365

355

360

Asp Asp Val Glu Glu Phe Arg Pro Glu Arg Phe Glu Asn Pro Ser Ala
 370 375 380

Ile Pro Gln His Ala Phe Lys Pro Phe Gly Asn Gly Gln Arg Ala Cys
 385 390 395 400

Ile Gly Gln Gln Phe Ala Leu His Glu Ala Thr Leu Val Leu Gly Met
 405 410 415

Met Leu Lys His Phe Asp Phe Glu Asp His Thr Asn Tyr Glu Leu Asp
 420 425 430

Ile Lys Glu Thr Leu Thr Leu Lys Pro Glu Gly Phe Val Val Lys Ala
 435 440 445

Lys Ser Lys Lys Ile Pro Leu Gly Gly Ile Pro Ser Pro Ser Thr Gly
 450 455 460

Gln Ser Ala Lys Lys Val Arg Lys Lys Ala Glu Asn Ala His Asn Thr
 465 470 475 480

Pro Leu Leu Val Leu Tyr Gly Ser Asn Met Gly Thr Ala Glu Gly Thr
 485 490 495

Ala Arg Asp Leu Ala Asp Ile Ala Met Ser Lys Gly Phe Ala Pro Gln
 500 505 510

Val Ala Thr Leu Asp Ser His Ala Gly Asn Leu Pro Arg Glu Gly Ala
 515 520 525

Val Leu Ile Val Thr Ala Ser Tyr Asn Gly His Pro Pro Asp Asn Ala
 530 535 540

Lys Gln Phe Val Asp Trp Leu Asp Gln Ala Ser Ala Asp Glu Val Lys
 545 550 555 560

Gly Val Arg Tyr Ser Val Phe Gly Cys Gly Asp Lys Asn Trp Ala Thr
 565 570 575

Thr Tyr Gln Lys Val Pro Ala Phe Ile Asp Glu Thr Leu Ala Ala Lys
 580 585 590

Gly Ala Glu Asn Ile Ala Asp Arg Gly Glu Ala Asp Ala Ser Asp Asp
 595 600 605

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Phe Glu Gly Thr Tyr Glu Glu Trp Arg Glu His Met Trp Ser Asp Val
 610 615 620

Ala Ala Tyr Phe Asn Leu Asp Ile Glu Asn Ser Glu Asp Asn Lys Ser
 625 630 635 640

Thr Leu Ser Leu Gln Phe Val Asp Ser Ala Ala Asp Met Pro Leu Ala
 645 650 655

Lys Met His Gly Ala Phe Ser Thr Asn Val Val Ala Ser Lys Glu Leu
 660 665 670

Gln Gln Pro Gly Ser Ala Arg Ser Thr Arg His Leu Glu Ile Glu Leu
 675 680 685

Pro Lys Glu Ala Ser Tyr Gln Glu Gly Asp His Leu Gly Val Ile Pro
 690 695 700

Arg Asn Tyr Glu Gly Thr Val Asn Arg Val Thr Ala Arg Phe Gly Leu
 705 710 715 720

Asp Ala Ser Gln Gln Ile Arg Leu Glu Ala Glu Glu Glu Lys Leu Ala
 725 730 735

His Leu Pro Leu Ala Lys Thr Val Ser Val Glu Glu Leu Leu Gln Tyr
 740 745 750

Val Glu Leu Gln Asp Pro Val Thr Arg Thr Gln Leu Arg Ala Met Ala
 755 760 765

Ala Lys Thr Val Cys Pro Pro His Lys Val Glu Leu Glu Ala Leu Leu
 770 775 780

Glu Lys Gln Ala Tyr Lys Glu Gln Val Leu Ala Lys Arg Leu Thr Met
 785 790 795 800

Leu Glu Leu Leu Glu Lys Tyr Pro Ala Cys Glu Met Lys Phe Ser Glu
 805 810 815

Phe Ile Ala Leu Leu Pro Ser Ile Arg Pro Arg Tyr Tyr Ser Ile Ser
 820 825 830

Ser Ser Pro Arg Val Asp Glu Lys Gln Ala Ser Ile Thr Val Ser Val
 835 840 845

Val Ser Gly Glu Ala Trp Ser Gly Tyr Gly Glu Tyr Lys Gly Ile Ala
 850 855 860

P008-CIT_ST25.txt

Ser Asn Tyr Leu Ala Glu Leu Gln Glu Gly Asp Thr Ile Thr Cys Phe
865 870 875 880

Ile Ser Thr Pro Gln Ser Glu Phe Thr Leu Pro Lys Asp Pro Glu Thr
885 890 895

Pro Leu Ile Met Val Gly Pro Gly Thr Gly Val Ala Pro Phe Arg Gly
900 905 910

Phe Val Gln Ala Arg Lys Gln Leu Lys Glu Gln Gly Gln Ser Leu Gly
915 920 925

Glu Ala His Leu Tyr Phe Gly Cys Arg Ser Pro His Glu Asp Tyr Leu
930 935 940

Tyr Gln Glu Glu Leu Glu Asn Ala Gln Ser Glu Gly Ile Ile Thr Leu
945 950 955 960

His Thr Ala Phe Ser Arg Met Pro Asn Gln Pro Lys Thr Tyr Val Gln
965 970 975

His Val Met Glu Gln Asp Gly Lys Lys Leu Ile Glu Leu Leu Asp Gln
980 985 990

Gly Ala His Phe Tyr Ile Cys Gly Asp Gly Ser Gln Met Ala Pro Ala
995 1000 1005

Val Glu Ala Thr Leu Met Lys Ser Tyr Ala Asp Val His Gln Val
1010 1015 1020

Ser Glu Ala Asp Ala Arg Leu Trp Leu Gln Gln Leu Glu Glu Lys
1025 1030 1035

Gly Arg Tyr Ala Lys Asp Val Trp Ala Gly
1040 1045

- <210> 39
- <211> 1048
- <212> PRT
- <213> Artificial sequence
- <220>
- <223> Cytochrome P450 variant CYP102A1var3-17
- <400> 39

Thr Ile Lys Glu Met Pro Gln Pro Lys Thr Phe Gly Glu Leu Lys Asn
1 5 10 15

P008-CIT_ST25.txt

Leu Pro Leu Leu Asn Thr Asp Lys Pro Val Gln Ala Leu Met Lys Ile
20 25 30

Ala Asp Glu Leu Gly Glu Ile Phe Lys Phe Glu Ala Pro Gly Arg Val
35 40 45

Thr Arg Tyr Leu Ser Ser Gln Arg Leu Ile Lys Glu Ala Cys Asp Glu
50 55 60

Ser Arg Phe Asp Lys Asn Leu Ser Gln Ala Leu Lys Ala Val Arg Asp
65 70 75 80

Val Thr Gly Asp Gly Leu Ala Thr Ser Trp Thr His Glu Lys Asn Trp
85 90 95

Lys Lys Ala His Asn Ile Leu Leu Pro Ser Phe Ser Gln Gln Ala Met
100 105 110

Lys Gly Tyr His Ala Met Met Val Asp Ile Ala Val Gln Leu Val Gln
115 120 125

Lys Trp Glu Arg Leu Asn Ala Asp Glu His Ile Glu Val Ser Glu Asp
130 135 140

Met Thr Arg Leu Thr Leu Asp Thr Ile Gly Leu Cys Gly Phe Asn Tyr
145 150 155 160

Arg Phe Asn Ser Phe Tyr Arg Asp Gln Pro His Pro Phe Ile Ile Ser
165 170 175

Met Val Arg Thr Leu Asp Glu Val Met Asn Lys Leu Gln Arg Ala Asn
180 185 190

Pro Asp Asp Pro Val Tyr Asp Glu Asn Lys Arg Gln Cys Gln Glu Asp
195 200 205

Ile Lys Val Met Asn Asp Leu Val Asp Lys Ile Ile Ala Asp Arg Lys
210 215 220

Ala Arg Gly Glu Gln Ser Asp Asp Leu Leu Thr Gln Met Leu Asn Gly
225 230 235 240

Lys Asp Pro Glu Thr Gly Glu Pro Leu Asp Asp Gly Asn Ile Ser Tyr
245 250 255

Gln Ile Ile Thr Phe Leu Ile Ala Gly His Glu Thr Thr Ser Gly Leu
260 265 270

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Leu Ser Phe Ala Leu Tyr Phe Leu Val Lys Asn Pro His Val Leu Gln
275 280 285

Lys Val Ala Glu Glu Ala Ala Arg Val Leu Val Asp Pro Val Pro Ser
290 295 300

Tyr Lys Gln Val Lys Gln Leu Lys Tyr Val Gly Met Val Leu Asn Glu
305 310 315 320

Ala Leu Arg Leu Trp Pro Thr Ala Pro Ala Phe Ser Leu Tyr Ala Lys
325 330 335

Glu Asp Thr Val Leu Gly Gly Glu Tyr Pro Leu Glu Lys Gly Asp Glu
340 345 350

Val Met Val Leu Ile Pro Gln Leu His Arg Asp Lys Thr Ile Trp Gly
355 360 365

Asp Asp Val Glu Glu Phe Arg Pro Glu Arg Phe Glu Asn Pro Ser Ala
370 375 380

Ile Pro Gln His Ala Phe Lys Pro Phe Gly Asn Gly Gln Arg Ala Cys
385 390 395 400

Ile Gly Gln Gln Phe Ala Leu His Glu Ala Thr Leu Val Leu Gly Met
405 410 415

Met Leu Lys His Phe Asp Phe Glu Asp His Thr Asn Tyr Glu Leu Asp
420 425 430

Ile Lys Glu Thr Leu Thr Leu Lys Pro Glu Gly Phe Val Val Lys Ala
435 440 445

Lys Ser Lys Lys Ile Pro Leu Gly Gly Ile Pro Ser Pro Ser Thr Glu
450 455 460

Gln Ser Ala Lys Lys Val Arg Lys Lys Ala Glu Asn Ala His Asn Thr
465 470 475 480

Pro Leu Leu Val Leu Tyr Gly Ser Asn Met Gly Thr Ala Glu Gly Thr
485 490 495

Ala Arg Asp Leu Ala Asp Ile Ala Met Ser Lys Gly Phe Ala Pro Gln
500 505 510

Val Ala Thr Leu Asp Ser His Ala Gly Asn Leu Pro Arg Glu Gly Ala
515 520 525

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Val Leu Ile Val Thr Ala Ser Tyr Asn Gly His Pro Pro Asp Asn Ala
530 535 540

Lys Gln Phe Val Asp Trp Leu Asp Gln Ala Ser Ala Asp Glu Val Lys
545 550 555 560

Gly Val Arg Tyr Ser Val Phe Gly Cys Gly Asp Lys Asn Trp Ala Thr
565 570 575

Thr Tyr Gln Lys Val Pro Ala Phe Ile Asp Glu Thr Leu Ala Ala Lys
580 585 590

Gly Ala Glu Asn Ile Ala Asp Arg Gly Glu Ala Asp Ala Ser Asp Asp
595 600 605

Phe Glu Gly Thr Tyr Glu Glu Trp Arg Glu His Met Trp Ser Asp Val
610 615 620

Ala Ala Tyr Phe Asn Leu Asp Ile Glu Asn Ser Glu Asp Asn Lys Ser
625 630 635 640

Thr Leu Ser Leu Gln Phe Val Asp Ser Ala Ala Asp Met Pro Leu Ala
645 650 655

Lys Met His Gly Ala Phe Ser Thr Asn Val Val Ala Ser Lys Glu Leu
660 665 670

Gln Gln Pro Gly Ser Ala Arg Ser Thr Arg His Leu Glu Ile Glu Leu
675 680 685

Pro Lys Glu Ala Ser Tyr Gln Glu Gly Asp His Leu Gly Val Ile Pro
690 695 700

Arg Asn Tyr Glu Gly Ile Val Asn Arg Val Thr Ala Arg Phe Gly Leu
705 710 715 720

Asp Ala Ser Gln Gln Ile Arg Leu Glu Ala Glu Glu Glu Lys Leu Ala
725 730 735

His Leu Pro Leu Ala Lys Thr Val Ser Val Glu Glu Leu Leu Gln Tyr
740 745 750

Val Glu Leu Gln Asp Pro Val Thr Arg Thr Gln Leu Arg Ala Met Ala
755 760 765

Ala Lys Thr Val Cys Pro Pro His Lys Val Glu Leu Glu Ala Leu Leu
Page 136

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

770

775

P008-CIT_ST25.txt
780

Glu Lys Gln Ala Tyr Lys Glu Gln Val Leu Ala Lys Arg Leu Thr Met
785 790 795 800

Leu Glu Leu Leu Glu Lys Tyr Pro Ala Cys Glu Met Lys Phe Ser Glu
805 810 815

Phe Ile Ala Leu Leu Pro Ser Ile Arg Pro Arg Tyr Tyr Ser Ile Ser
820 825 830

Ser Ser Pro Arg Val Asp Glu Lys Gln Ala Ser Ile Thr Val Ser Val
835 840 845

Val Ser Gly Glu Ala Trp Ser Gly Tyr Gly Glu Tyr Lys Gly Ile Ala
850 855 860

Ser Asn Tyr Leu Ala Glu Leu Gln Glu Gly Asp Thr Ile Thr Cys Phe
865 870 875 880

Ile Ser Thr Pro Gln Ser Glu Phe Thr Leu Pro Lys Asp Pro Glu Thr
885 890 895

Pro Leu Ile Met Val Gly Pro Gly Thr Gly Val Ala Pro Phe Arg Gly
900 905 910

Phe Val Gln Ala Arg Lys Gln Leu Lys Glu Gln Gly Gln Ser Leu Gly
915 920 925

Glu Ala His Leu Tyr Phe Gly Cys Arg Ser Pro His Glu Asp Tyr Leu
930 935 940

Tyr Gln Glu Glu Leu Glu Asn Ala Gln Ser Glu Gly Ile Ile Thr Leu
945 950 955 960

His Thr Ala Phe Ser Arg Met Pro Asn Gln Pro Lys Thr Tyr Val Gln
965 970 975

His Val Met Glu Gln Asp Gly Lys Lys Leu Ile Glu Leu Leu Asp Gln
980 985 990

Gly Ala His Phe Tyr Ile Cys Gly Asp Gly Ser Gln Met Ala Pro Ala
995 1000 1005

Val Glu Ala Thr Leu Met Lys Ser Tyr Ala Asp Val His Gln Val
1010 1015 1020

Printed: 10/30/2007

SECRET

PCT/US2007/017409

Title: "Methods and systems for selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt
Ser Glu Ala Asp Ala Arg Leu Trp Leu Gln Gln Leu Glu Glu Lys
1025 1030 1035

Gly Arg Tyr Ala Lys Asp Val Trp Ala Gly
1040 1045

<210> 40
<211> 1048
<212> PRT
<213> Artificial sequence

<220>
<223> Cytochrome P450 variant CYP102A1var3-18
<400> 40

Thr Ile Lys Glu Met Pro Gln Pro Lys Thr Phe Gly Glu Leu Lys Asn
1 5 10 15

Leu Pro Leu Leu Asn Thr Asp Lys Pro Val Gln Ala Leu Met Lys Ile
20 25 30

Ala Asp Glu Leu Gly Glu Ile Phe Lys Phe Glu Ala Pro Gly Cys Val
35 40 45

Thr Arg Tyr Ile Ser Ser Gln Arg Leu Ile Lys Glu Ala Cys Asp Glu
50 55 60

Ser Arg Phe Asp Lys Asn Leu Ser Gln Ala Leu Lys Ala Phe Arg Asp
65 70 75 80

Phe Ser Gly Asp Gly Leu Phe Thr Ser Trp Thr His Glu Ile Asn Trp
85 90 95

Lys Lys Ala His Asn Ile Leu Leu Pro Ser Phe Ser Gln Gln Ala Met
100 105 110

Lys Gly Tyr His Ala Met Met Val Asp Ile Ala Val Gln Leu Val Gln
115 120 125

Lys Trp Glu Arg Leu Asn Ala Asp Glu His Ile Glu Val Ser Glu Asp
130 135 140

Met Thr Arg Leu Thr Leu Asp Thr Ile Gly Leu Cys Gly Phe Asn Tyr
145 150 155 160

Arg Phe Asn Ser Phe Tyr Arg Asp Gln Pro His Pro Phe Ile Ile Ser
165 170 175

Met Val Arg Ala Leu Asp Glu Val Met Asn Lys Pro Gln Arg Ala Asn
Page 138

08/04/2007

Printed: 10/30/2007

Sheet 1

PCT/US2007/017409

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT.

180

P008-CIT_ST25.txt
185

190

Pro Asp Asp Pro Ala Tyr Asp Glu Asn Lys Arg Gln Cys Gln Glu Asp
195 200 205

Ile Lys Val Met Asn Asp Leu Val Asp Lys Ile Ile Ala Asp Arg Lys
210 215 220

Ala Arg Gly Glu Gln Ser Asp Asp Leu Leu Thr Gln Met Leu Asn Gly
225 230 235 240

Lys Asp Pro Glu Thr Gly Glu Pro Leu Asp Asp Gly Asn Ile Ser Tyr
245 250 255

Gln Ile Ile Thr Phe Leu Ile Ala Gly His Glu Thr Thr Ser Gly Leu
260 265 270

Leu Ser Phe Ala Leu Tyr Phe Leu Val Lys Asn Pro His Val Leu Gln
275 280 285

Lys Val Ala Glu Glu Ala Ala Arg Val Leu Val Asp Pro Val Pro Ser
290 295 300

Tyr Lys Gln Val Lys Gln Leu Lys Tyr Val Gly Met Val Leu Asn Glu
305 310 315 320

Ala Leu Arg Leu Trp Pro Thr Phe Pro Ala Phe Ser Leu Tyr Ala Lys
325 330 335

Glu Asp Thr Val Leu Gly Gly Glu Tyr Pro Leu Glu Lys Gly Asp Glu
340 345 350

Val Met Val Leu Ile Pro Gln Leu His Arg Asp Lys Thr Val Trp Gly
355 360 365

Asp Asp Val Glu Glu Phe Arg Pro Glu Arg Phe Glu Asn Pro Ser Ala
370 375 380

Ile Pro Gln His Ala Phe Lys Pro Phe Gly Asn Gly Gln Arg Ala Cys
385 390 395 400

Ile Gly Gln Gln Phe Ala Leu His Glu Ala Thr Leu Val Leu Gly Met
405 410 415

Met Leu Lys His Phe Asp Phe Glu Asp His Thr Asn Tyr Glu Leu Asp
420 425 430

08/04/2007

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT-ST25.LXI

Ile Lys Glu Thr Leu Thr Leu Lys Pro Glu Gly Phe Val Val Lys Ala
 435 440 445

Lys Ser Lys Lys Ile Pro Leu Gly Gly Ile Pro Ser Pro Ser Thr Gly
 450 455 460

Gln Ser Ala Lys Lys Val Arg Lys Lys Ala Glu Asn Ala His Asn Thr
 465 470 475 480

Pro Leu Leu Val Leu Tyr Gly Ser Asn Met Gly Thr Ala Glu Gly Thr
 485 490 495

Ala Arg Asp Leu Ala Asp Ile Ala Met Ser Lys Gly Phe Ala Pro Gln
 500 505 510

Val Ala Thr Leu Asp Ser His Ala Gly Asn Leu Pro Arg Glu Gly Ala
 515 520 525

Val Leu Ile Val Thr Ala Ser Tyr Asn Gly His Pro Pro Asp Asn Ala
 530 535 540

Lys Gln Phe Val Asp Trp Leu Asp Gln Ala Ser Ala Asp Glu Val Lys
 545 550 555 560

Gly Val Arg Tyr Ser Val Phe Gly Cys Gly Asp Lys Asn Trp Ala Thr
 565 570 575

Thr Tyr Gln Lys Val Pro Ala Phe Ile Asp Glu Thr Leu Ala Ala Lys
 580 585 590

Gly Ala Glu Asn Ile Ala Asp Arg Gly Glu Ala Asp Ala Ser Asp Asp
 595 600 605

Phe Glu Gly Thr Tyr Glu Glu Trp Arg Glu His Met Trp Ser Asp Val
 610 615 620

Ala Ala Tyr Phe Asn Leu Asp Ile Glu Asn Ser Glu Asp Asn Lys Ser
 625 630 635 640

Thr Leu Ser Leu Gln Phe Val Asp Ser Ala Ala Asp Met Pro Leu Ala
 645 650 655

Lys Met His Gly Ala Phe Ser Thr Asn Val Val Ala Ser Lys Glu Leu
 660 665 670

Gln Gln Pro Gly Ser Ala Arg Ser Thr Arg His Leu Glu Ile Glu Leu
 675 680 685

P008-CIT_ST25.txt

Pro Lys Glu Ala Ser Tyr Gln Glu Gly Asp His Leu Gly Val Ile Pro
690 695 700

Arg Asn Tyr Glu Gly Thr Val Asn Arg Val Thr Ala Arg Phe Gly Leu
705 710 715 720

Asp Ala Ser Gln Gln Ile Arg Leu Glu Ala Glu Glu Glu Lys Leu Ala
725 730 735

His Leu Pro Leu Ala Lys Thr Val Ser Val Glu Glu Leu Leu Gln Tyr
740 745 750

Val Glu Leu Gln Asp Pro Val Thr Arg Thr Gln Leu Arg Ala Met Ala
755 760 765

Ala Lys Thr Val Cys Pro Pro His Lys Val Glu Leu Glu Ala Leu Leu
770 775 780

Glu Lys Gln Ala Tyr Lys Glu Gln Val Leu Ala Lys Arg Leu Thr Met
785 790 795 800

Leu Glu Leu Leu Glu Lys Tyr Pro Ala Cys Glu Met Lys Phe Ser Glu
805 810 815

Phe Ile Ala Leu Leu Pro Ser Ile Arg Pro Arg Tyr Tyr Ser Ile Ser
820 825 830

Ser Ser Pro Arg Val Asp Glu Lys Gln Ala Ser Ile Thr Val Ser Val
835 840 845

Val Ser Gly Glu Ala Trp Ser Gly Tyr Gly Glu Tyr Lys Gly Ile Ala
850 855 860

Ser Asn Tyr Leu Ala Glu Leu Gln Glu Gly Asp Thr Ile Thr Cys Phe
865 870 875 880

Ile Ser Thr Pro Gln Ser Glu Phe Thr Leu Pro Lys Asp Pro Glu Thr
885 890 895

Pro Leu Ile Met Val Gly Pro Gly Thr Gly Val Ala Pro Phe Arg Gly
900 905 910

Phe Val Gln Ala Arg Lys Gln Leu Lys Glu Gln Gly Gln Ser Leu Gly
915 920 925

Glu Ala His Leu Tyr Phe Gly Cys Arg Ser Pro His Glu Asp Tyr Leu
930 935 940

P008-CIT_ST25.txt

Tyr Gln Glu Glu Leu Glu Asn Ala Gln Ser Glu Gly Ile Ile Thr Leu
945 950 955 960

His Thr Ala Phe Ser Arg Met Pro Asn Gln Pro Lys Thr Tyr Val Gln
965 970 975

His Val Met Glu Gln Asp Gly Lys Lys Leu Ile Glu Leu Leu Asp Gln
980 985 990

Gly Ala His Phe Tyr Ile Cys Gly Asp Gly Ser Gln Met Ala Pro Ala
995 1000 1005

Val Glu Ala Thr Leu Met Lys Ser Tyr Ala Asp Val His Gln Val
1010 1015 1020

Ser Glu Ala Asp Ala Arg Leu Trp Leu Gln Gln Leu Glu Glu Lys
1025 1030 1035

Gly Arg Tyr Ala Lys Asp Val Trp Ala Gly
1040 1045

<210> 41
<211> 1048
<212> PRT
<213> Artificial sequence

<220>
<223> Cytochrome P450 variant CYP102A1var3-19

<400> 41

Thr Ile Lys Glu Met Pro Gln Pro Lys Thr Phe Gly Glu Leu Lys Asn
1 5 10 15

Leu Pro Leu Leu Asn Thr Asp Lys Pro Val Gln Ala Leu Met Lys Ile
20 25 30

Ala Asp Glu Leu Gly Glu Ile Phe Lys Phe Glu Ala Pro Gly Cys Val
35 40 45

Thr Arg Tyr Ile Ser Ser Gln Arg Leu Ile Lys Glu Ala Cys Asp Glu
50 55 60

Ser Arg Phe Asp Lys Asn Leu Ser Gln Ser Leu Lys Ala Phe Arg Asp
65 70 75 80

Phe Ser Gly Asp Gly Leu Phe Thr Ser Trp Thr His Glu Ile Asn Trp
85 90 95

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Lys Lys Ala His Asn Ile Leu Leu Pro Ser Phe Ser Gln Gln Ala Met
100 105 110

Lys Gly Tyr His Ala Met Met Val Asp Ile Ala Val Gln Leu Val Gln
115 120 125

Lys Trp Glu Arg Leu Asn Ala Asp Glu His Ile Glu Val Ser Glu Asp
130 135 140

Met Thr Arg Leu Thr Leu Asp Thr Ile Gly Leu Cys Gly Phe Asn Tyr
145 150 155 160

Arg Phe Asn Ser Phe Tyr Arg Asp Gln Pro His Pro Phe Ile Ile Ser
165 170 175

Met Val Arg Ala Leu Asp Glu Ala Met Asn Lys Pro Gln Arg Ala Asn
180 185 190

Pro Asp Asp Pro Ala Tyr Asp Glu Asn Lys Arg Gln Cys Gln Glu Asp
195 200 205

Ile Lys Val Met Asn Asp Leu Val Asp Lys Ile Ile Ala Asp Arg Lys
210 215 220

Ala Arg Gly Glu Gln Ser Asp Asp Leu Leu Thr Gln Met Leu Asn Gly
225 230 235 240

Lys Asp Pro Glu Thr Gly Glu Pro Leu Asp Asp Gly Asn Ile Ser Tyr
245 250 255

Gln Ile Ile Thr Phe Leu Ile Ala Gly His Glu Thr Thr Ser Gly Leu
260 265 270

Leu Ser Phe Ala Leu Tyr Phe Leu Val Lys Asn Pro His Val Leu Gln
275 280 285

Lys Val Ala Glu Glu Ala Ala Arg Val Leu Val Asp Pro Val Pro Ser
290 295 300

Tyr Lys Gln Val Lys Gln Leu Lys Tyr Val Gly Met Val Leu Asn Glu
305 310 315 320

Ala Leu Arg Leu Trp Pro Thr Phe Pro Ala Phe Ser Leu Tyr Ala Lys
325 330 335

Glu Asp Thr Val Leu Gly Gly Glu Tyr Pro Leu Glu Lys Gly Asp Glu
340 345 350

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT
P008-CIT_ST25.txt

Val Met Val Leu Ile Pro Gln Leu His Arg Asp Lys Thr Val Trp Gly
355 360 365

Asp Asp Val Glu Glu Phe Arg Pro Glu Arg Phe Glu Asn Pro Ser Ala
370 375 380

Ile Pro Gln His Ala Phe Lys Pro Phe Gly Asn Gly Gln Arg Ala Cys
385 390 395 400

Ile Gly Gln Gln Phe Ala Leu His Glu Ala Thr Leu Val Leu Gly Met
405 410 415

Met Leu Lys His Phe Asp Phe Glu Asp His Thr Asn Tyr Glu Leu Asp
420 425 430

Ile Lys Glu Thr Leu Thr Leu Lys Pro Glu Gly Phe Val Val Lys Ala
435 440 445

Lys Ser Lys Lys Ile Pro Leu Gly Gly Ile Pro Ser Pro Ser Thr Gly
450 455 460

Gln Ser Ala Lys Lys Val Arg Lys Lys Ala Glu Asn Ala His Asn Thr
465 470 475 480

Pro Leu Leu Val Leu Tyr Gly Ser Asn Met Gly Thr Ala Glu Gly Thr
485 490 495

Ala Arg Asp Leu Ala Asp Ile Ala Met Ser Lys Gly Phe Ala Pro Gln
500 505 510

Val Ala Thr Leu Asp Ser His Ala Gly Asn Leu Pro Arg Glu Gly Ala
515 520 525

Val Leu Ile Val Thr Ala Ser Tyr Asn Gly His Pro Pro Asp Asn Ala
530 535 540

Lys Gln Phe Val Asp Trp Leu Asp Gln Ala Ser Ala Asp Glu Val Lys
545 550 555 560

Gly Val Arg Tyr Ser Val Phe Gly Cys Gly Asp Lys Asn Trp Ala Thr
565 570 575

Thr Tyr Gln Lys Val Pro Ala Phe Ile Asp Glu Thr Leu Ala Ala Lys
580 585 590

Gly Ala Glu Asn Ile Ala Asp Arg Gly Glu Ala Asp Ala Ser Asp Asp

595

600

P008-CIT_ST25.txt
605

Phe Glu Gly Thr Tyr Glu Glu Trp Arg Glu His Met Trp Ser Asp Val
610 615 620

Ala Ala Tyr Phe Asn Leu Asp Ile Glu Asn Ser Glu Asp Asn Lys Ser
625 630 635 640

Thr Leu Ser Leu Gln Phe Val Asp Ser Ala Ala Asp Met Pro Leu Ala
645 650 655

Lys Met His Gly Ala Phe Ser Thr Asn Val Val Ala Ser Lys Glu Leu
660 665 670

Gln Gln Pro Gly Ser Ala Arg Ser Thr Arg His Leu Glu Ile Glu Leu
675 680 685

Pro Lys Glu Ala Ser Tyr Gln Glu Gly Asp His Leu Gly Val Ile Pro
690 695 700

Arg Asn Tyr Glu Gly Thr Val Asn Arg Val Thr Ala Arg Phe Gly Leu
705 710 715 720

Asp Ala Ser Gln Gln Ile Arg Leu Glu Ala Glu Glu Glu Lys Leu Ala
725 730 735

His Leu Pro Leu Ala Lys Thr Val Ser Val Glu Glu Leu Leu Gln Tyr
740 745 750

Val Glu Leu Gln Asp Pro Val Thr Arg Thr Gln Leu Arg Ala Met Ala
755 760 765

Ala Lys Thr Val Cys Pro Pro His Lys Val Glu Leu Glu Ala Leu Leu
770 775 780

Glu Lys Gln Ala Tyr Lys Glu Gln Val Leu Ala Lys Arg Leu Thr Met
785 790 795 800

Leu Glu Leu Leu Glu Lys Tyr Pro Ala Cys Glu Met Lys Phe Ser Glu
805 810 815

Phe Ile Ala Leu Leu Pro Ser Ile Arg Pro Arg Tyr Tyr Ser Ile Ser
820 825 830

Ser Ser Pro Arg Val Asp Glu Lys Gln Ala Ser Ile Thr Val Ser Val
835 840 845

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Val Ser Gly Glu Ala Trp Ser Gly Tyr Gly Glu Tyr Lys Gly Ile Ala
 850 855 860

Ser Asn Tyr Leu Ala Glu Leu Gln Glu Gly Asp Thr Ile Thr Cys Phe
 865 870 875 880

Ile Ser Thr Pro Gln Ser Glu Phe Thr Leu Pro Lys Asp Pro Glu Thr
 885 890 895

Pro Leu Ile Met Val Gly Pro Gly Thr Gly Val Ala Pro Phe Arg Gly
 900 905 910

Phe Val Gln Ala Arg Lys Gln Leu Lys Glu Gln Gly Gln Ser Leu Gly
 915 920 925

Glu Ala His Leu Tyr Phe Gly Cys Arg Ser Pro His Glu Asp Tyr Leu
 930 935 940

Tyr Gln Glu Glu Leu Glu Asn Ala Gln Ser Glu Gly Ile Ile Thr Leu
 945 950 955 960

His Thr Ala Phe Ser Arg Met Pro Asn Gln Pro Lys Thr Tyr Val Gln
 965 970 975

His Val Met Glu Gln Asp Gly Lys Lys Leu Ile Glu Leu Leu Asp Gln
 980 985 990

Gly Ala His Phe Tyr Ile Cys Gly Asp Gly Ser Gln Met Ala Pro Ala
 995 1000 1005

Val Glu Ala Thr Leu Met Lys Ser Tyr Ala Asp Val His Gln Val
 1010 1015 1020

Ser Glu Ala Asp Ala Arg Leu Trp Leu Gln Gln Leu Glu Glu Lys
 1025 1030 1035

Gly Arg Tyr Ala Lys Asp Val Trp Ala Gly
 1040 1045

<210> 42
 <211> 1048
 <212> PRT
 <213> Artificial sequence

<220>
 <223> Cytochrome P450 variant CYP102A1var3-20

<400> 42

Thr Ile Lys Glu Met Pro Gln Pro Lys Thr Phe Gly Glu Leu Lys Asn

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

1

5

10

15

Leu Pro Leu Leu Asn Thr Asp Lys Pro Val Gln Ala Leu Met Lys Ile
20 25 30

Ala Asp Glu Leu Gly Glu Ile Phe Lys Phe Glu Ala Pro Gly Cys Val
35 40 45

Thr Arg Tyr Leu Ser Ser Gln Arg Leu Ile Lys Glu Ala Cys Asp Glu
50 55 60

Ser Arg Phe Asp Lys Asn Leu Ser Gln Ala Leu Lys Ala Val Arg Asp
65 70 75 80

Phe Val Gly Asp Gly Leu Phe Thr Ser Trp Thr His Glu Ile Asn Trp
85 90 95

Lys Lys Ala His Asn Ile Leu Leu Pro Ser Phe Ser Gln Gln Ala Met
100 105 110

Lys Gly Tyr His Ala Met Met Val Asp Ile Ala Val Gln Leu Val Gln
115 120 125

Lys Trp Glu Arg Leu Asn Ala Asp Glu His Ile Glu Val Ser Glu Asp
130 135 140

Met Thr Arg Leu Thr Leu Asp Thr Ile Gly Leu Cys Gly Phe Asn Tyr
145 150 155 160

Arg Phe Asn Ser Phe Tyr Arg Asp Gln Pro His Pro Phe Ile Ile Ser
165 170 175

Met Val Arg Ala Leu Asp Glu Val Met Asn Lys Leu Gln Arg Ala Asn
180 185 190

Pro Asp Asp Pro Ala Tyr Asp Glu Asn Lys Arg Gln Cys Gln Glu Asp
195 200 205

Ile Lys Val Met Asn Asp Leu Val Asp Lys Ile Ile Ala Asp Arg Lys
210 215 220

Ala Arg Gly Glu Gln Ser Asp Asp Leu Leu Thr Gln Met Leu Asn Gly
225 230 235 240

Lys Asp Pro Glu Thr Gly Glu Pro Leu Asp Asp Gly Asn Ile Ser Tyr
245 250 255

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Gln Ile Ile Thr Phe Leu Ile Ala Gly His Glu Thr Thr Ser Gly Leu
 260 265 270

Leu Ser Phe Ala Leu Tyr Phe Leu Val Lys Asn Pro His Val Leu Gln
 275 280 285

Lys Val Ala Glu Glu Ala Ala Arg Val Leu Val Asp Pro Val Pro Ser
 290 295 300

Tyr Lys Gln Val Lys Gln Leu Lys Tyr Val Gly Met Val Leu Asn Glu
 305 310 315 320

Ala Leu Arg Leu Trp Pro Thr Val Pro Ala Phe Ser Leu Tyr Ala Lys
 325 330 335

Glu Asp Thr Val Leu Gly Gly Glu Tyr Pro Leu Glu Lys Gly Asp Glu
 340 345 350

Val Met Val Leu Ile Pro Gln Leu His Arg Asp Lys Thr Ile Trp Gly
 355 360 365

Asp Asp Val Glu Glu Phe Arg Pro Glu Arg Phe Glu Asn Pro Ser Ala
 370 375 380

Ile Pro Gln His Ala Phe Lys Pro Phe Gly Asn Gly Gln Arg Ala Cys
 385 390 395 400

Ile Gly Gln Gln Phe Ala Leu His Glu Ala Thr Leu Val Leu Gly Met
 405 410 415

Met Leu Lys His Phe Asp Phe Glu Asp His Thr Asn Tyr Glu Leu Asp
 420 425 430

Ile Lys Glu Thr Leu Thr Leu Lys Pro Glu Gly Phe Val Val Lys Ala
 435 440 445

Lys Ser Lys Lys Ile Pro Leu Gly Gly Ile Pro Ser Pro Ser Thr Glu
 450 455 460

Gln Ser Ala Lys Lys Val Arg Lys Lys Ala Glu Asn Ala His Asn Thr
 465 470 475 480

Pro Leu Leu Val Leu Tyr Gly Ser Asn Met Gly Thr Ala Glu Gly Thr
 485 490 495

Ala Arg Asp Leu Ala Asp Ile Ala Met Ser Lys Gly Phe Ala Pro Gln
 500 505 510

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Val Ala Thr Leu Asp Ser His Ala Gly Asn Leu Pro Arg Glu Gly Ala
 515 520 525

Val Leu Ile Val Thr Ala Ser Tyr Asn Gly His Pro Pro Asp Asn Ala
 530 535 540

Lys Gln Phe Val Asp Trp Leu Asp Gln Ala Ser Ala Asp Glu Val Lys
 545 550 555 560

Gly Val Arg Tyr Ser Val Phe Gly Cys Gly Asp Lys Asn Trp Ala Thr
 565 570 575

Thr Tyr Gln Lys Val Pro Ala Phe Ile Asp Glu Thr Leu Ala Ala Lys
 580 585 590

Gly Ala Glu Asn Ile Ala Asp Arg Gly Glu Ala Asp Ala Ser Asp Asp
 595 600 605

Phe Glu Gly Thr Tyr Glu Glu Trp Arg Glu His Met Trp Ser Asp Val
 610 615 620

Ala Ala Tyr Phe Asn Leu Asp Ile Glu Asn Ser Glu Asp Asn Lys Ser
 625 630 635 640

Thr Leu Ser Leu Gln Phe Val Asp Ser Ala Ala Asp Met Pro Leu Ala
 645 650 655

Lys Met His Gly Ala Phe Ser Thr Asn Val Val Ala Ser Lys Glu Leu
 660 665 670

Gln Gln Pro Gly Ser Ala Arg Ser Thr Arg His Leu Glu Ile Glu Leu
 675 680 685

Pro Lys Glu Ala Ser Tyr Gln Glu Gly Asp His Leu Gly Val Ile Pro
 690 695 700

Arg Asn Tyr Glu Gly Ile Val Asn Arg Val Thr Ala Arg Phe Gly Leu
 705 710 715 720

Asp Ala Ser Gln Gln Ile Arg Leu Glu Ala Glu Glu Glu Lys Leu Ala
 725 730 735

His Leu Pro Leu Ala Lys Thr Val Ser Val Glu Glu Leu Leu Gln Tyr
 740 745 750

Val Glu Leu Gln Asp Pro Val Thr Arg Thr Gln Leu Arg Ala Met Ala
 755 760 765

Inventors: Rudi Fasan et al.

Express Mailing Label No: EBS11841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Ala Lys Thr Val Cys Pro Pro His Lys Val Glu Leu Glu Ala Leu Leu
 770 775 780

Glu Lys Gln Ala Tyr Lys Glu Gln Val Leu Ala Lys Arg Leu Thr Met
 785 790 795 800

Leu Glu Leu Leu Glu Lys Tyr Pro Ala Cys Glu Met Lys Phe Ser Glu
 805 810 815

Phe Ile Ala Leu Leu Pro Ser Ile Arg Pro Arg Tyr Tyr Ser Ile Ser
 820 825 830

Ser Ser Pro Arg Val Asp Glu Lys Gln Ala Ser Ile Thr Val Ser Val
 835 840 845

Val Ser Gly Glu Ala Trp Ser Gly Tyr Gly Glu Tyr Lys Gly Ile Ala
 850 855 860

Ser Asn Tyr Leu Ala Glu Leu Gln Glu Gly Asp Thr Ile Thr Cys Phe
 865 870 875 880

Ile Ser Thr Pro Gln Ser Glu Phe Thr Leu Pro Lys Asp Pro Glu Thr
 885 890 895

Pro Leu Ile Met Val Gly Pro Gly Thr Gly Val Ala Pro Phe Arg Gly
 900 905 910

Phe Val Gln Ala Arg Lys Gln Leu Lys Glu Gln Gly Gln Ser Leu Gly
 915 920 925

Glu Ala His Leu Tyr Phe Gly Cys Arg Ser Pro His Glu Asp Tyr Leu
 930 935 940

Tyr Gln Glu Glu Leu Glu Asn Ala Gln Ser Glu Gly Ile Ile Thr Leu
 945 950 955 960

His Thr Ala Phe Ser Arg Met Pro Asn Gln Pro Lys Thr Tyr Val Gln
 965 970 975

His Val Met Glu Gln Asp Gly Lys Lys Leu Ile Glu Leu Leu Asp Gln
 980 985 990

Gly Ala His Phe Tyr Ile Cys Gly Asp Gly Ser Gln Met Ala Pro Ala
 995 1000 1005

Val Glu Ala Thr Leu Met Lys Ser Tyr Ala Asp Val His Gln Val
 Page 150

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT.

P008-CIT_ST25.txt

1010

1015

1020

Ser Glu Ala Asp Ala Arg Leu Trp Leu Gln Gln Leu Glu Glu Lys
 1025 1030 1035

Gly Arg Tyr Ala Lys Asp Val Trp Ala Gly
 1040 1045

<210> 43
 <211> 1048
 <212> PRT
 <213> Artificial sequence

<220>
 <223> Cytochrome P450 variant CYP102A1var3-21

<400> 43

Thr Ile Lys Glu Met Pro Gln Pro Lys Thr Phe Gly Glu Leu Lys Asn
 1 5 10 15

Leu Pro Leu Leu Asn Thr Asp Lys Pro Val Gln Ala Leu Met Lys Ile
 20 25 30

Ala Asp Glu Leu Gly Glu Ile Phe Lys Phe Glu Ala Pro Gly Cys Val
 35 40 45

Thr Arg Tyr Leu Ser Ser Gln Arg Leu Ile Lys Glu Ala Cys Asp Glu
 50 55 60

Ser Arg Phe Asp Lys Asn Leu Ser Gln Ala Leu Lys Ala Val Arg Asp
 65 70 75 80

Phe Ala Gly Asp Gly Leu Val Thr Ser Trp Thr His Glu Ile Asn Trp
 85 90 95

Lys Lys Ala His Asn Ile Leu Leu Pro Ser Phe Ser Gln Gln Ala Met
 100 105 110

Lys Gly Tyr His Ala Met Met Val Asp Ile Ala Val Gln Leu Val Gln
 115 120 125

Lys Trp Glu Arg Leu Asn Ala Asp Glu His Ile Glu Val Ser Glu Asp
 130 135 140

Met Thr Arg Leu Thr Leu Asp Thr Ile Gly Leu Cys Gly Phe Asn Tyr
 145 150 155 160

Arg Phe Asn Ser Phe Tyr Arg Asp Gln Pro His Pro Phe Ile Ile Ser
 165 170 175

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Met Val Arg Ala Leu Asp Glu Val Met Asn Lys Leu Gln Arg Ala Asn
180 185 190

Pro Asp Asp Pro Ala Tyr Asp Glu Asn Lys Arg Gln Cys Gln Glu Asp
195 200 205

Ile Lys Val Met Asn Asp Leu Val Asp Lys Ile Ile Ala Asp Arg Lys
210 215 220

Ala Arg Gly Glu Gln Ser Asp Asp Leu Leu Thr Gln Met Leu Asn Gly
225 230 235 240

Lys Asp Pro Glu Thr Gly Glu Pro Leu Asp Asp Gly Asn Ile Ser Tyr
245 250 255

Gln Ile Ile Thr Phe Leu Ala Ala Gly His Glu Thr Thr Ser Gly Leu
260 265 270

Leu Ser Phe Ala Leu Tyr Phe Leu Val Lys Asn Pro His Val Leu Gln
275 280 285

Lys Val Ala Glu Glu Ala Ala Arg Val Leu Val Asp Pro Val Pro Ser
290 295 300

Tyr Lys Gln Val Lys Gln Leu Lys Tyr Val Gly Met Val Leu Asn Glu
305 310 315 320

Ala Leu Arg Leu Trp Pro Thr Ala Pro Ala Phe Ser Leu Tyr Ala Lys
325 330 335

Glu Asp Thr Val Leu Gly Gly Glu Tyr Pro Leu Glu Lys Gly Asp Glu
340 345 350

Val Met Val Leu Ile Pro Gln Leu His Arg Asp Lys Thr Ile Trp Gly
355 360 365

Asp Asp Val Glu Glu Phe Arg Pro Glu Arg Phe Glu Asn Pro Ser Ala
370 375 380

Ile Pro Gln His Ala Phe Lys Pro Phe Gly Asn Gly Gln Arg Ala Cys
385 390 395 400

Ile Gly Gln Gln Phe Ala Leu His Glu Ala Thr Leu Val Leu Gly Met
405 410 415

Met Leu Lys His Phe Asp Phe Glu Asp His Thr Asn Tyr Glu Leu Asp
Page 152

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

420

425

430

Ile Lys Glu Thr Leu Thr Leu Lys Pro Glu Gly Phe Val Val Lys Ala
 435 440 445

Lys Ser Lys Lys Ile Pro Leu Gly Gly Ile Pro Ser Pro Ser Thr Glu
 450 455 460

Gln Ser Ala Lys Lys Val Arg Lys Lys Ala Glu Asn Ala His Asn Thr
 465 470 475 480

Pro Leu Leu Val Leu Tyr Gly Ser Asn Met Gly Thr Ala Glu Gly Thr
 485 490 495

Ala Arg Asp Leu Ala Asp Ile Ala Met Ser Lys Gly Phe Ala Pro Gln
 500 505 510

Val Ala Thr Leu Asp Ser His Ala Gly Asn Leu Pro Arg Glu Gly Ala
 515 520 525

Val Leu Ile Val Thr Ala Ser Tyr Asn Gly His Pro Pro Asp Asn Ala
 530 535 540

Lys Gln Phe Val Asp Trp Leu Asp Gln Ala Ser Ala Asp Glu Val Lys
 545 550 555 560

Gly Val Arg Tyr Ser Val Phe Gly Cys Gly Asp Lys Asn Trp Ala Thr
 565 570 575

Thr Tyr Gln Lys Val Pro Ala Phe Ile Asp Glu Thr Leu Ala Ala Lys
 580 585 590

Gly Ala Glu Asn Ile Ala Asp Arg Gly Glu Ala Asp Ala Ser Asp Asp
 595 600 605

Phe Glu Gly Thr Tyr Glu Glu Trp Arg Glu His Met Trp Ser Asp Val
 610 615 620

Ala Ala Tyr Phe Asn Leu Asp Ile Glu Asn Ser Glu Asp Asn Lys Ser
 625 630 635 640

Thr Leu Ser Leu Gln Phe Val Asp Ser Ala Ala Asp Met Pro Leu Ala
 645 650 655

Lys Met His Gly Ala Phe Ser Thr Asn Val Val Ala Ser Lys Glu Leu
 660 665 670

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al:

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Gln Gln Pro Gly Ser Ala Arg Ser Thr Arg His Leu Glu Ile Glu Leu
675 680 685

Pro Lys Glu Ala Ser Tyr Gln Glu Gly Asp His Leu Gly Val Ile Pro
690 695 700

Arg Asn Tyr Glu Gly Ile Val Asn Arg Val Thr Ala Arg Phe Gly Leu
705 710 715 720

Asp Ala Ser Gln Gln Ile Arg Leu Glu Ala Glu Glu Glu Lys Leu Ala
725 730 735

His Leu Pro Leu Ala Lys Thr Val Ser Val Glu Glu Leu Leu Gln Tyr
740 745 750

Val Glu Leu Gln Asp Pro Val Thr Arg Thr Gln Leu Arg Ala Met Ala
755 760 765

Ala Lys Thr Val Cys Pro Pro His Lys Val Glu Leu Glu Ala Leu Leu
770 775 780

Glu Lys Gln Ala Tyr Lys Glu Gln Val Leu Ala Lys Arg Leu Thr Met
785 790 795 800

Leu Glu Leu Leu Glu Lys Tyr Pro Ala Cys Glu Met Lys Phe Ser Glu
805 810 815

Phe Ile Ala Leu Leu Pro Ser Ile Arg Pro Arg Tyr Tyr Ser Ile Ser
820 825 830

Ser Ser Pro Arg Val Asp Glu Lys Gln Ala Ser Ile Thr Val Ser Val
835 840 845

Val Ser Gly Glu Ala Trp Ser Gly Tyr Gly Glu Tyr Lys Gly Ile Ala
850 855 860

Ser Asn Tyr Leu Ala Glu Leu Gln Glu Gly Asp Thr Ile Thr Cys Phe
865 870 875 880

Ile Ser Thr Pro Gln Ser Glu Phe Thr Leu Pro Lys Asp Pro Glu Thr
885 890 895

Pro Leu Ile Met Val Gly Pro Gly Thr Gly Val Ala Pro Phe Arg Gly
900 905 910

Phe Val Gln Ala Arg Lys Gln Leu Lys Glu Gln Gly Gln Ser Leu Gly
915 920 925

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Glu Ala His Leu Tyr Phe Gly Cys Arg Ser Pro His Glu Asp Tyr Leu
930 935 940

Tyr Gln Glu Glu Leu Glu Asn Ala Gln Ser Glu Gly Ile Ile Thr Leu
945 950 955 960

His Thr Ala Phe Ser Arg Met Pro Asn Gln Pro Lys Thr Tyr Val Gln
965 970 975

His Val Met Glu Gln Asp Gly Lys Lys Leu Ile Glu Leu Leu Asp Gln
980 985 990

Gly Ala His Phe Tyr Ile Cys Gly Asp Gly Ser Gln Met Ala Pro Ala
995 1000 1005

Val Glu Ala Thr Leu Met Lys Ser Tyr Ala Asp Val His Gln Val
1010 1015 1020

Ser Glu Ala Asp Ala Arg Leu Trp Leu Gln Gln Leu Glu Glu Lys
1025 1030 1035

Gly Arg Tyr Ala Lys Asp Val Trp Ala Gly
1040 1045

<210> 44

<211> 1048

<212> PRT

<213> Artificial sequence

<220>

<223> Cytochrome P450 variant CYP102A1var3-22

<400> 44

Thr Ile Lys Glu Met Pro Gln Pro Lys Thr Phe Gly Glu Leu Lys Asn
1 5 10 15

Leu Pro Leu Leu Asn Thr Asp Lys Pro Val Gln Ala Leu Met Lys Ile
20 25 30

Ala Asp Glu Leu Gly Glu Ile Phe Lys Phe Glu Ala Pro Gly Cys Val
35 40 45

Thr Arg Tyr Leu Ser Ser Gln Arg Leu Ile Lys Glu Ala Cys Asp Glu
50 55 60

Ser Arg Phe Asp Lys Asn Leu Ser Gln Ala Leu Lys Ala Val Arg Asp
65 70 75 80

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasàn et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Phe Phe Gly Asp Gly Leu Phe Thr Ser Trp Thr His Glu Ile Asn Trp
85 90 95

Lys Lys Ala His Asn Ile Leu Leu Pro Ser Phe Ser Gln Gln Ala Met
100 105 110

Lys Gly Tyr His Ala Met Met Val Asp Ile Ala Val Gln Leu Val Gln
115 120 125

Lys Trp Glu Arg Leu Asn Ala Asp Glu His Ile Glu Val Ser Glu Asp
130 135 140

Met Thr Arg Leu Thr Leu Asp Thr Ile Gly Leu Cys Gly Phe Asn Tyr
145 150 155 160

Arg Phe Asn Ser Phe Tyr Arg Asp Gln Pro His Pro Phe Ile Ile Ser
165 170 175

Met Val Arg Ala Leu Asp Glu Val Met Asn Lys Leu Gln Arg Ala Asn
180 185 190

Pro Asp Asp Pro Ala Tyr Asp Glu Asn Lys Arg Gln Cys Gln Glu Asp
195 200 205

Ile Lys Val Met Asn Asp Leu Val Asp Lys Ile Ile Ala Asp Arg Lys
210 215 220

Ala Arg Gly Glu Gln Ser Asp Asp Leu Leu Thr Gln Met Leu Asn Gly
225 230 235 240

Lys Asp Pro Glu Thr Gly Glu Pro Leu Asp Asp Gly Asn Ile Ser Tyr
245 250 255

Gln Ile Ile Thr Phe Leu Ala Ala Gly His Glu Thr Thr Ser Gly Leu
260 265 270

Leu Ser Phe Ala Leu Tyr Phe Leu Val Lys Asn Pro His Val Leu Gln
275 280 285

Lys Val Ala Glu Glu Ala Ala Arg Val Leu Val Asp Pro Val Pro Ser
290 295 300

Tyr Lys Gln Val Lys Gln Leu Lys Tyr Val Gly Met Val Leu Asn Glu
305 310 315 320

Ala Leu Arg Leu Trp Pro Thr Val Pro Ala Phe Ser Leu Tyr Ala Lys
325 330 335

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Glu Asp Thr Val Leu Gly Gly Glu Tyr Pro Leu Glu Lys Gly Asp Glu
 340 345 350

Val Met Val Leu Ile Pro Gln Leu His Arg Asp Lys Thr Ile Trp Gly
 355 360 365

Asp Asp Val Glu Glu Phe Arg Pro Glu Arg Phe Glu Asn Pro Ser Ala
 370 375 380

Ile Pro Gln His Ala Phe Lys Pro Phe Gly Asn Gly Gln Arg Ala Cys
 385 390 395 400

Ile Gly Gln Gln Phe Ala Leu His Glu Ala Thr Leu Val Leu Gly Met
 405 410 415

Met Leu Lys His Phe Asp Phe Glu Asp His Thr Asn Tyr Glu Leu Asp
 420 425 430

Ile Lys Glu Thr Leu Thr Leu Lys Pro Glu Gly Phe Val Val Lys Ala
 435 440 445

Lys Ser Lys Lys Ile Pro Leu Gly Gly Ile Pro Ser Pro Ser Thr Glu
 450 455 460

Gln Ser Ala Lys Lys Val Arg Lys Lys Ala Glu Asn Ala His Asn Thr
 465 470 475 480

Pro Leu Leu Val Leu Tyr Gly Ser Asn Met Gly Thr Ala Glu Gly Thr
 485 490 495

Ala Arg Asp Leu Ala Asp Ile Ala Met Ser Lys Gly Phe Ala Pro Gln
 500 505 510

Val Ala Thr Leu Asp Ser His Ala Gly Asn Leu Pro Arg Glu Gly Ala
 515 520 525

Val Leu Ile Val Thr Ala Ser Tyr Asn Gly His Pro Pro Asp Asn Ala
 530 535 540

Lys Gln Phe Val Asp Trp Leu Asp Gln Ala Ser Ala Asp Glu Val Lys
 545 550 555 560

Gly Val Arg Tyr Ser Val Phe Gly Cys Gly Asp Lys Asn Trp Ala Thr
 565 570 575

Thr Tyr Gln Lys Val Pro Ala Phe Ile Asp Glu Thr Leu Ala Ala Lys
 580 585 590

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Gly Ala Glu Asn Ile Ala Asp Arg Gly Glu Ala Asp Ala Ser Asp Asp
595 600 605

Phe Glu Gly Thr Tyr Glu Glu Trp Arg Glu His Met Trp Ser Asp Val
610 615 620

Ala Ala Tyr Phe Asn Leu Asp Ile Glu Asn Ser Glu Asp Asn Lys Ser
625 630 635 640

Thr Leu Ser Leu Gln Phe Val Asp Ser Ala Ala Asp Met Pro Leu Ala
645 650 655

Lys Met His Gly Ala Phe Ser Thr Asn Val Val Ala Ser Lys Glu Leu
660 665 670

Gln Gln Pro Gly Ser Ala Arg Ser Thr Arg His Leu Glu Ile Glu Leu
675 680 685

Pro Lys Glu Ala Ser Tyr Gln Glu Gly Asp His Leu Gly Val Ile Pro
690 695 700

Arg Asn Tyr Glu Gly Ile Val Asn Arg Val Thr Ala Arg Phe Gly Leu
705 710 715 720

Asp Ala Ser Gln Gln Ile Arg Leu Glu Ala Glu Glu Lys Leu Ala
725 730 735

His Leu Pro Leu Ala Lys Thr Val Ser Val Glu Glu Leu Leu Gln Tyr
740 745 750

Val Glu Leu Gln Asp Pro Val Thr Arg Thr Gln Leu Arg Ala Met Ala
755 760 765

Ala Lys Thr Val Cys Pro Pro His Lys Val Glu Leu Glu Ala Leu Leu
770 775 780

Glu Lys Gln Ala Tyr Lys Glu Gln Val Leu Ala Lys Arg Leu Thr Met
785 790 795 800

Leu Glu Leu Leu Glu Lys Tyr Pro Ala Cys Glu Met Lys Phe Ser Glu
805 810 815

Phe Ile Ala Leu Leu Pro Ser Ile Arg Pro Arg Tyr Tyr Ser Ile Ser
820 825 830

Ser Ser Pro Arg Val Asp Glu Lys Gln Ala Ser Ile Thr Val Ser Val
Page 158

Printed: 10/30/2007

SHR0151

PCT/US2007/017409

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

835

840

P008-CIT_ST25.txt

845

Val Ser Gly Glu Ala Trp Ser Gly Tyr Gly Glu Tyr Lys Gly Ile Ala
850 855 860

Ser Asn Tyr Leu Ala Glu Leu Gln Glu Gly Asp Thr Ile Thr Cys Phe
865 870 875 880

Ile Ser Thr Pro Gln Ser Glu Phe Thr Leu Pro Lys Asp Pro Glu Thr
885 890 895

Pro Leu Ile Met Val Gly Pro Gly Thr Gly Val Ala Pro Phe Arg Gly
900 905 910

Phe Val Gln Ala Arg Lys Gln Leu Lys Glu Gln Gly Gln Ser Leu Gly
915 920 925

Glu Ala His Leu Tyr Phe Gly Cys Arg Ser Pro His Glu Asp Tyr Leu
930 935 940

Tyr Gln Glu Glu Leu Glu Asn Ala Gln Ser Glu Gly Ile Ile Thr Leu
945 950 955 960

His Thr Ala Phe Ser Arg Met Pro Asn Gln Pro Lys Thr Tyr Val Gln
965 970 975

His Val Met Glu Gln Asp Gly Lys Lys Leu Ile Glu Leu Leu Asp Gln
980 985 990

Gly Ala His Phe Tyr Ile Cys Gly Asp Gly Ser Gln Met Ala Pro Ala
995 1000 1005

Val Glu Ala Thr Leu Met Lys Ser Tyr Ala Asp Val His Gln Val
1010 1015 1020

Ser Glu Ala Asp Ala Arg Leu Trp Leu Gln Gln Leu Glu Glu Lys
1025 1030 1035

Gly Arg Tyr Ala Lys Asp Val Trp Ala Gly
1040 1045

<210> 45

<211> 1048

<212> PRT

<213> Artificial sequence

<220>

<223> Cytochrome P450 variant CYP102A1var3-23

08/04/2007

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

<400> 45

Thr Ile Lys Glu Met Pro Gln Pro Lys Thr Phe Gly Glu Leu Lys Asn
1 5 10 15

Leu Pro Leu Leu Asn Thr Asp Lys Pro Val Gln Ala Leu Met Lys Ile
20 25 30

Ala Asp Glu Leu Gly Glu Ile Phe Lys Phe Glu Ala Pro Gly Cys Val
35 40 45

Thr Arg Tyr Leu Ser Ser Gln Arg Leu Ile Lys Glu Ala Cys Asp Glu
50 55 60

Ser Arg Phe Asp Lys Asn Leu Ser Gln Ala Leu Lys Ala Val Arg Asp
65 70 75 80

Phe Ala Gly Asp Gly Leu Phe Thr Ser Trp Thr His Glu Ile Asn Trp
85 90 95

Lys Lys Ala His Asn Ile Leu Leu Pro Ser Phe Ser Gln Gln Ala Met
100 105 110

Lys Gly Tyr His Ala Met Met Val Asp Ile Ala Val Gln Leu Val Gln
115 120 125

Lys Trp Glu Arg Leu Asn Ala Asp Glu His Ile Glu Val Ser Glu Asp
130 135 140

Met Thr Arg Leu Thr Leu Asp Thr Ile Gly Leu Cys Gly Phe Asn Tyr
145 150 155 160

Arg Phe Asn Ser Phe Tyr Arg Asp Gln Pro His Pro Phe Ile Ile Ser
165 170 175

Met Val Arg Ala Leu Asp Glu Val Met Asn Lys Leu Gln Arg Ala Asn
180 185 190

Pro Asp Asp Pro Ala Tyr Asp Glu Asn Lys Arg Gln Cys Gln Glu Asp
195 200 205

Ile Lys Val Met Asn Asp Leu Val Asp Lys Ile Ile Ala Asp Arg Lys
210 215 220

Ala Arg Gly Glu Gln Ser Asp Asp Leu Leu Thr Gln Met Leu Asn Gly
225 230 235 240

Lys Asp Pro Glu Thr Gly Glu Pro Leu Asp Asp Gly Asn Ile Ser Tyr
Page 160

Printed 10/30/2007

GENE

PCT/US2007/017409

Title: "Methods and Systems for Selective"

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

245

250

255

Gln Ile Ile Thr Phe Leu Ile Ala Gly His Glu Thr Thr Ser Gly Leu
260 265 270

Leu Ser Phe Ala Leu Tyr Phe Leu Val Lys Asn Pro His Val Leu Gln
275 280 285

Lys Val Ala Glu Glu Ala Ala Arg Val Leu Val Asp Pro Val Pro Ser
290 295 300

Tyr Lys Gln Val Lys Gln Leu Lys Tyr Val Gly Met Val Leu Asn Glu
305 310 315 320

Ala Leu Arg Leu Trp Pro Thr Val Pro Ala Phe Ser Leu Tyr Ala Lys
325 330 335

Glu Asp Thr Val Leu Gly Gly Glu Tyr Pro Leu Glu Lys Gly Asp Glu
340 345 350

Val Met Val Leu Ile Pro Gln Leu His Arg Asp Lys Thr Ile Trp Gly
355 360 365

Asp Asp Val Glu Glu Phe Arg Pro Glu Arg Phe Glu Asn Pro Ser Ala
370 375 380

Ile Pro Gln His Ala Phe Lys Pro Phe Gly Asn Gly Gln Arg Ala Cys
385 390 395 400

Ile Gly Gln Gln Phe Ala Leu His Glu Ala Thr Leu Val Leu Gly Met
405 410 415

Met Leu Lys His Phe Asp Phe Glu Asp His Thr Asn Tyr Glu Leu Asp
420 425 430

Ile Lys Glu Thr Leu Thr Leu Lys Pro Glu Gly Phe Val Val Lys Ala
435 440 445

Lys Ser Lys Lys Ile Pro Leu Gly Gly Ile Pro Ser Pro Ser Thr Glu
450 455 460

Gln Ser Ala Lys Lys Val Arg Lys Lys Ala Glu Asn Ala His Asn Thr
465 470 475 480

Pro Leu Leu Val Leu Tyr Gly Ser Asn Met Gly Thr Ala Glu Gly Thr
485 490 495

Title: "Methods and systems for selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Ala Arg Asp Leu Ala Asp Ile Ala Met Ser Lys Gly Phe Ala Pro Gln
 500 505 510

Val Ala Thr Leu Asp Ser His Ala Gly Asn Leu Pro Arg Glu Gly Ala
 515 520 525

Val Leu Ile Val Thr Ala Ser Tyr Asn Gly His Pro Pro Asp Asn Ala
 530 535 540

Lys Gln Phe Val Asp Trp Leu Asp Gln Ala Ser Ala Asp Glu Val Lys
 545 550 555 560

Gly Val Arg Tyr Ser Val Phe Gly Cys Gly Asp Lys Asn Trp Ala Thr
 565 570 575

Thr Tyr Gln Lys Val Pro Ala Phe Ile Asp Glu Thr Leu Ala Ala Lys
 580 585 590

Gly Ala Glu Asn Ile Ala Asp Arg Gly Glu Ala Asp Ala Ser Asp Asp
 595 600 605

Phe Glu Gly Thr Tyr Glu Glu Trp Arg Glu His Met Trp Ser Asp Val
 610 615 620

Ala Ala Tyr Phe Asn Leu Asp Ile Glu Asn Ser Glu Asp Asn Lys Ser
 625 630 635 640

Thr Leu Ser Leu Gln Phe Val Asp Ser Ala Ala Asp Met Pro Leu Ala
 645 650 655

Lys Met His Gly Ala Phe Ser Thr Asn Val Val Ala Ser Lys Glu Leu
 660 665 670

Gln Gln Pro Gly Ser Ala Arg Ser Thr Arg His Leu Glu Ile Glu Leu
 675 680 685

Pro Lys Glu Ala Ser Tyr Gln Glu Gly Asp His Leu Gly Val Ile Pro
 690 695 700

Arg Asn Tyr Glu Gly Ile Val Asn Arg Val Thr Ala Arg Phe Gly Leu
 705 710 715 720

Asp Ala Ser Gln Gln Ile Arg Leu Glu Ala Glu Glu Glu Lys Leu Ala
 725 730 735

His Leu Pro Leu Ala Lys Thr Val Ser Val Glu Glu Leu Leu Gln Tyr
 740 745 750

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Val Glu Leu Gln Asp Pro Val Thr Arg Thr Gln Leu Arg Ala Met Ala
755 760 765

Ala Lys Thr Val Cys Pro Pro His Lys Val Glu Leu Glu Ala Leu Leu
770 775 780

Glu Lys Gln Ala Tyr Lys Glu Gln Val Leu Ala Lys Arg Leu Thr Met
785 790 795 800

Leu Glu Leu Leu Glu Lys Tyr Pro Ala Cys Glu Met Lys Phe Ser Glu
805 810 815

Phe Ile Ala Leu Leu Pro Ser Ile Arg Pro Arg Tyr Tyr Ser Ile Ser
820 825 830

Ser Ser Pro Arg Val Asp Glu Lys Gln Ala Ser Ile Thr Val Ser Val
835 840 845

Val Ser Gly Glu Ala Trp Ser Gly Tyr Gly Glu Tyr Lys Gly Ile Ala
850 855 860

Ser Asn Tyr Leu Ala Glu Leu Gln Glu Gly Asp Thr Ile Thr Cys Phe
865 870 875 880

Ile Ser Thr Pro Gln Ser Glu Phe Thr Leu Pro Lys Asp Pro Glu Thr
885 890 895

Pro Leu Ile Met Val Gly Pro Gly Thr Gly Val Ala Pro Phe Arg Gly
900 905 910

Phe Val Gln Ala Arg Lys Gln Leu Lys Glu Gln Gly Gln Ser Leu Gly
915 920 925

Glu Ala His Leu Tyr Phe Gly Cys Arg Ser Pro His Glu Asp Tyr Leu
930 935 940

Tyr Gln Glu Glu Leu Glu Asn Ala Gln Ser Glu Gly Ile Ile Thr Leu
945 950 955 960

His Thr Ala Phe Ser Arg Met Pro Asn Gln Pro Lys Thr Tyr Val Gln
965 970 975

His Val Met Glu Gln Asp Gly Lys Lys Leu Ile Glu Leu Leu Asp Gln
980 985 990

Gly Ala His Phe Tyr Ile Cys Gly Asp Gly Ser Gln Met Ala Pro Ala
995 1000 1005

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Val Glu Ala Thr Leu Met Lys Ser Tyr Ala Asp Val His Gln Val
 1010 1015 1020

Ser Glu Ala Asp Ala Arg Leu Trp Leu Gln Gln Leu Glu Glu Lys
 1025 1030 1035

Gly Arg Tyr Ala Lys Asp Val Trp Ala Gly
 1040 1045

<210> 46
 <211> 1048
 <212> PRT
 <213> Artificial sequence

<220>
 <223> Cytochrome P450 variant CYP102A1var4

<400> 46

Thr Ile Lys Glu Met Pro Gln Pro Lys Thr Phe Gly Glu Leu Lys Asn
 1 5 10 15

Leu Pro Leu Leu Asn Thr Asp Lys Pro Val Gln Ala Leu Met Lys Ile
 20 25 30

Ala Asp Glu Leu Gly Glu Ile Phe Lys Phe Glu Ala Pro Gly Arg Val
 35 40 45

Thr Arg Tyr Leu Ser Ser Gln Arg Leu Ile Lys Glu Ala Cys Asp Glu
 50 55 60

Ser Arg Phe Asp Lys Asn Leu Ser Gln Ala Leu Lys Phe Val Arg Asp
 65 70 75 80

Phe Ala Gly Asp Gly Leu Ala Thr Ser Trp Thr His Glu Lys Asn Trp
 85 90 95

Lys Lys Ala His Asn Ile Leu Leu Pro Ser Phe Ser Gln Gln Ala Met
 100 105 110

Lys Gly Tyr His Ala Met Met Val Asp Ile Ala Val Gln Leu Val Gln
 115 120 125

Lys Trp Glu Arg Leu Asn Ala Asp Glu His Ile Glu Val Pro Glu Asp
 130 135 140

Met Thr Arg Leu Thr Leu Asp Thr Ile Gly Leu Cys Gly Phe Asn Tyr
 145 150 155 160

Printed: 10/30/2007

Sheet 151

PCT/US2007/017409

Title: "Methods and systems for selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Arg Phe Asn Ser Phe Tyr Arg Asp Gln Pro His Pro Phe Ile Thr Ser
165 170 175

Met Val Arg Ala Leu Asp Glu Ala Met Asn Lys Leu Gln Arg Ala Asn
180 185 190

Pro Asp Asp Pro Ala Tyr Asp Glu Asn Lys Arg Gln Phe Gln Glu Asp
195 200 205

Ile Lys Val Met Asn Asp Leu Val Asp Lys Ile Ile Ala Asp Arg Lys
210 215 220

Ala Ser Gly Glu Gln Ser Asp Asp Leu Leu Thr His Met Leu Asn Gly
225 230 235 240

Lys Asp Pro Glu Thr Gly Glu Pro Leu Asp Asp Glu Asn Ile Arg Tyr
245 250 255

Gln Ile Ile Thr Phe Leu Ile Ala Gly His Glu Thr Thr Ser Gly Leu
260 265 270

Leu Ser Phe Ala Leu Tyr Phe Leu Val Lys Asn Pro His Val Leu Gln
275 280 285

Lys Ala Ala Glu Glu Ala Ala Arg Val Leu Val Asp Pro Val Pro Ser
290 295 300

Tyr Lys Gln Val Lys Gln Leu Lys Tyr Val Gly Met Val Leu Asn Glu
305 310 315 320

Ala Leu Arg Leu Trp Pro Thr Ala Pro Ala Phe Ser Leu Tyr Ala Lys
325 330 335

Glu Asp Thr Val Leu Gly Gly Glu Tyr Pro Leu Glu Lys Gly Asp Glu
340 345 350

Leu Met Val Leu Ile Pro Gln Leu His Arg Asp Lys Thr Ile Trp Gly
355 360 365

Asp Asp Val Glu Glu Phe Arg Pro Glu Arg Phe Glu Asn Pro Ser Ala
370 375 380

Ile Pro Gln His Ala Phe Lys Pro Phe Gly Asn Gly Gln Arg Ala Cys
385 390 395 400

Ile Gly Gln Gln Phe Ala Leu His Glu Ala Thr Leu Val Leu Gly Met
405 410 415

Page 165

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Met Leu Lys His Phe Asp Phe Glu Asp His Thr Asn Tyr Glu Leu Asp
 420 425 430

Ile Lys Glu Thr Leu Thr Leu Lys Pro Glu Gly Phe Val Val Lys Ala
 435 440 445

Lys Ser Lys Lys Ile Pro Leu Gly Gly Ile Pro Ser Pro Ser Thr Glu
 450 455 460

Gln Ser Ala Lys Lys Val Arg Lys Lys Ala Glu Asn Ala His Asn Thr
 465 470 475 480

Pro Leu Leu Val Leu Tyr Gly Ser Asn Met Gly Thr Ala Glu Gly Thr
 485 490 495

Ala Arg Asp Leu Ala Asp Ile Ala Met Ser Lys Gly Phe Ala Pro Gln
 500 505 510

Val Ala Thr Leu Asp Ser His Ala Gly Asn Leu Pro Arg Glu Gly Ala
 515 520 525

Val Leu Ile Val Thr Ala Ser Tyr Asn Gly His Pro Pro Asp Asn Ala
 530 535 540

Lys Gln Phe Val Asp Trp Leu Asp Gln Ala Ser Ala Asp Glu Val Lys
 545 550 555 560

Gly Val Arg Tyr Ser Val Phe Gly Cys Gly Asp Lys Asn Trp Ala Thr
 565 570 575

Thr Tyr Gln Lys Val Pro Ala Phe Ile Asp Glu Thr Leu Ala Ala Lys
 580 585 590

Gly Ala Glu Asn Ile Ala Asp Arg Gly Glu Ala Asp Ala Ser Asp Asp
 595 600 605

Phe Glu Gly Thr Tyr Glu Glu Trp Arg Glu His Met Trp Ser Asp Val
 610 615 620

Ala Ala Tyr Phe Asn Leu Asp Ile Glu Asn Ser Glu Asp Asn Lys Ser
 625 630 635 640

Thr Leu Ser Leu Gln Phe Val Asp Ser Ala Ala Asp Met Pro Leu Ala
 645 650 655

Lys Met His Gly Ala Phe Ser Thr Asn Val Val Ala Ser Lys Glu Leu
 Page 166

Printed: 10/30/2007

SP0015

PCT/US2007/017409

100

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt
665 670

660

Gln Gln Pro Gly Ser Ala Arg Ser Thr Arg His Leu Glu Ile Glu Leu
675 680 685

Pro Lys Glu Ala Ser Tyr Gln Glu Gly Asp His Leu Gly Val Ile Pro
690 695 700

Arg Asn Tyr Glu Gly Ile Val Asn Arg Val Thr Ala Arg Phe Gly Leu
705 710 715 720

Asp Ala Ser Gln Gln Ile Arg Leu Glu Ala Glu Glu Glu Lys Leu Ala
725 730 735

His Leu Pro Leu Ala Lys Thr Val Ser Val Glu Glu Leu Leu Gln Tyr
740 745 750

Val Glu Leu Gln Asp Pro Val Thr Arg Thr Gln Leu Arg Ala Met Ala
755 760 765

Ala Lys Thr Val Cys Pro Pro His Lys Val Glu Leu Glu Ala Leu Leu
770 775 780

Glu Lys Gln Ala Tyr Lys Glu Gln Val Leu Ala Lys Arg Leu Thr Met
785 790 795 800

Leu Glu Leu Leu Glu Lys Tyr Pro Ala Cys Glu Met Lys Phe Ser Glu
805 810 815

Phe Ile Ala Leu Leu Pro Ser Ile Arg Pro Arg Tyr Tyr Ser Ile Ser
820 825 830

Ser Ser Pro Arg Val Asp Glu Lys Gln Ala Ser Ile Thr Val Ser Val
835 840 845

Val Ser Gly Glu Ala Trp Ser Gly Tyr Gly Glu Tyr Lys Gly Ile Ala
850 855 860

Ser Asn Tyr Leu Ala Glu Leu Gln Glu Gly Asp Thr Ile Thr Cys Phe
865 870 875 880

Ile Ser Thr Pro Gln Ser Glu Phe Thr Leu Pro Lys Asp Pro Glu Thr
885 890 895

Pro Leu Ile Met Val Gly Pro Gly Thr Gly Val Ala Pro Phe Arg Gly
900 905 910

08/04/2007

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Phe Val Gln Ala Arg Lys Gln Leu Lys Glu Gln Gly Gln Ser Leu Gly
915 920 925

Glu Ala His Leu Tyr Phe Gly Cys Arg Ser Pro His Glu Asp Tyr Leu
930 935 940

Tyr Gln Glu Glu Leu Glu Asn Ala Gln Ser Glu Gly Ile Ile Thr Leu
945 950 955 960

His Thr Ala Phe Ser Arg Met Pro Asn Gln Pro Lys Thr Tyr Val Gln
965 970 975

His Val Met Glu Gln Asp Gly Lys Lys Leu Ile Glu Leu Leu Asp Gln
980 985 990

Gly Ala His Phe Tyr Ile Cys Gly Asp Gly Ser Gln Met Ala Pro Ala
995 1000 1005

Val Glu Ala Thr Leu Met Lys Ser Tyr Ala Asp Val His Gln Val
1010 1015 1020

Ser Glu Ala Asp Ala Arg Leu Trp Leu Gln Gln Leu Glu Glu Lys
1025 1030 1035

Gly Arg Tyr Ala Lys Asp Val Trp Ala Gly
1040 1045

<210> 47
<211> 1048
<212> PRT
<213> Artificial sequence

<220>
<223> Cytochrome P450 variant CYP102A1var5

<400> 47

Thr Ile Lys Glu Met Pro Gln Pro Lys Thr Phe Gly Glu Leu Lys Asn
1 5 10 15

Leu Pro Leu Leu Asn Thr Asp Lys Pro Val Gln Ala Leu Met Lys Ile
20 25 30

Ala Asp Glu Leu Gly Glu Ile Phe Lys Phe Glu Ala Pro Gly Arg Val
35 40 45

Thr Arg Tyr Leu Ser Ser Gln Arg Leu Ile Lys Glu Ala Cys Asp Glu
50 55 60

Ser Arg Phe Asp Lys Asn Leu Ser Gln Ala Leu Lys Phe Val Arg Asp
Page 168

P008-CIT_ST25.txt

65

70

75

80

Phe Ala Gly Asp Gly₈₅ Leu Val Thr Ser Trp Thr His Glu Lys Asn Trp₉₅

Lys Lys Ala His Asn Ile Leu Leu Pro Ser Phe Ser Gln Gln Ala Met₁₀₀
105 110

Lys Gly Tyr His Ala Met Met Val Asp Ile Ala Val Gln Leu Val Gln₁₁₅
120 125

Lys Trp Glu Arg Leu Asn Ala Asp Glu His Ile Glu Val Pro Glu Asp₁₃₀
135 140

Met Thr Arg Leu Thr Leu Asp Thr Ile Gly Leu Cys Gly Phe Asn Tyr₁₄₅
150 155 160

Arg Phe Asn Ser Phe Tyr Arg Asp Gln Pro His Pro Phe Ile Thr Ser₁₆₅
170 175

Met Val Arg Ala Leu Asp Glu Ala Met Asn Lys Leu Gln Arg Ala Asn₁₈₀
185 190

Pro Asp Asp Pro Ala Tyr Asp Glu Asn Lys Arg Gln Phe Gln Glu Asp₁₉₅
200 205

Ile Lys Val Met Asn Asp Leu Val Asp Lys Ile Ile Ala Asp Arg Lys₂₁₀
215 220

Ala Ser Gly Glu Gln Ser Asp Asp Leu Leu Thr His Met Leu Asn Gly₂₂₅
230 235 240

Lys Asp Pro Glu Thr Gly Glu Pro Leu Asp Asp Glu Asn Ile Arg Tyr₂₄₅
250 255

Gln Ile Ile Thr Phe Leu Ile Ala Gly His Glu Thr Thr Ser Gly Leu₂₆₀
265 270

Leu Ser Phe Ala Leu Tyr Phe Leu Val Lys Asn Pro His Val Leu Gln₂₇₅
280 285

Lys Ala Ala Glu Glu Ala Ala Arg Val Leu Val Asp Pro Val Pro Ser₂₉₀
295 300

Tyr Lys Gln Val Lys Gln Leu Lys Tyr Val Gly Met Val Leu Asn Glu₃₀₅
310 315 320

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Ala Leu Arg Leu Trp Pro Thr Ala Pro Ala Phe Ser Leu Tyr Ala Lys
325 330 335

Glu Asp Thr Val Leu Gly Gly Glu Tyr Pro Leu Glu Lys Gly Asp Glu
340 345 350

Leu Met Val Leu Ile Pro Gln Leu His Arg Asp Lys Thr Ile Trp Gly
355 360 365

Asp Asp Val Glu Glu Phe Arg Pro Glu Arg Phe Glu Asn Pro Ser Ala
370 375 380

Ile Pro Gln His Ala Phe Lys Pro Phe Gly Asn Gly Gln Arg Ala Cys
385 390 395 400

Ile Gly Gln Gln Phe Ala Leu His Glu Ala Thr Leu Val Leu Gly Met
405 410 415

Met Leu Lys His Phe Asp Phe Glu Asp His Thr Asn Tyr Glu Leu Asp
420 425 430

Ile Lys Glu Thr Leu Thr Leu Lys Pro Glu Gly Phe Val Val Lys Ala
435 440 445

Lys Ser Lys Lys Ile Pro Leu Gly Gly Ile Pro Ser Pro Ser Thr Glu
450 455 460

Gln Ser Ala Lys Lys Val Arg Lys Lys Ala Glu Asn Ala His Asn Thr
465 470 475 480

Pro Leu Leu Val Leu Tyr Gly Ser Asn Met Gly Thr Ala Glu Gly Thr
485 490 495

Ala Arg Asp Leu Ala Asp Ile Ala Met Ser Lys Gly Phe Ala Pro Gln
500 505 510

Val Ala Thr Leu Asp Ser His Ala Gly Asn Leu Pro Arg Glu Gly Ala
515 520 525

Val Leu Ile Val Thr Ala Ser Tyr Asn Gly His Pro Pro Asp Asn Ala
530 535 540

Lys Gln Phe Val Asp Trp Leu Asp Gln Ala Ser Ala Asp Glu Val Lys
545 550 555 560

Gly Val Arg Tyr Ser Val Phe Gly Cys Gly Asp Lys Asn Trp Ala Thr
565 570 575

Printed: 10/30/2007

18-01-157

PCT/US2007/017409

15059/2009

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Thr Tyr Gln Lys Val Pro Ala Phe Ile Asp Glu Thr Leu Ala Ala Lys
580 585 590

Gly Ala Glu Asn Ile Ala Asp Arg Gly Glu Ala Asp Ala Ser Asp Asp
595 600 605

Phe Glu Gly Thr Tyr Glu Glu Trp Arg Glu His Met Trp Ser Asp Val
610 615 620

Ala Ala Tyr Phe Asn Leu Asp Ile Glu Asn Ser Glu Asp Asn Lys Ser
625 630 635 640

Thr Leu Ser Leu Gln Phe Val Asp Ser Ala Ala Asp Met Pro Leu Ala
645 650 655

Lys Met His Gly Ala Phe Ser Thr Asn Val Val Ala Ser Lys Glu Leu
660 665 670

Gln Gln Pro Gly Ser Ala Arg Ser Thr Arg His Leu Glu Ile Glu Leu
675 680 685

Pro Lys Glu Ala Ser Tyr Gln Glu Gly Asp His Leu Gly Val Ile Pro
690 695 700

Arg Asn Tyr Glu Gly Ile Val Asn Arg Val Thr Ala Arg Phe Gly Leu
705 710 715 720

Asp Ala Ser Gln Gln Ile Arg Leu Glu Ala Glu Glu Glu Lys Leu Ala
725 730 735

His Leu Pro Leu Ala Lys Thr Val Ser Val Glu Glu Leu Leu Gln Tyr
740 745 750

Val Glu Leu Gln Asp Pro Val Thr Arg Thr Gln Leu Arg Ala Met Ala
755 760 765

Ala Lys Thr Val Cys Pro Pro His Lys Val Glu Leu Glu Ala Leu Leu
770 775 780

Glu Lys Gln Ala Tyr Lys Glu Gln Val Leu Ala Lys Arg Leu Thr Met
785 790 795 800

Leu Glu Leu Leu Glu Lys Tyr Pro Ala Cys Glu Met Lys Phe Ser Glu
805 810 815

Phe Ile Ala Leu Leu Pro Ser Ile Arg Pro Arg Tyr Tyr Ser Ile Ser
820 825 830

Ser Ser Pro Arg Val Asp Glu Lys Gln Ala Ser Ile Thr Val Ser Val
835 840 845

Val Ser Gly Glu Ala Trp Ser Gly Tyr Gly Glu Tyr Lys Gly Ile Ala
850 855 860

Ser Asn Tyr Leu Ala Glu Leu Gln Glu Gly Asp Thr Ile Thr Cys Phe
865 870 875 880

Ile Ser Thr Pro Gln Ser Glu Phe Thr Leu Pro Lys Asp Pro Glu Thr
885 890 895

Pro Leu Ile Met Val Gly Pro Gly Thr Gly Val Ala Pro Phe Arg Gly
900 905 910

Phe Val Gln Ala Arg Lys Gln Leu Lys Glu Gln Gly Gln Ser Leu Gly
915 920 925

Glu Ala His Leu Tyr Phe Gly Cys Arg Ser Pro His Glu Asp Tyr Leu
930 935 940

Tyr Gln Glu Glu Leu Glu Asn Ala Gln Ser Glu Gly Ile Ile Thr Leu
945 950 955 960

His Thr Ala Phe Ser Arg Met Pro Asn Gln Pro Lys Thr Tyr Val Gln
965 970 975

His Val Met Glu Gln Asp Gly Lys Lys Leu Ile Glu Leu Leu Asp Gln
980 985 990

Gly Ala His Phe Tyr Ile Cys Gly Asp Gly Ser Gln Met Ala Pro Ala
995 1000 1005

Val Glu Ala Thr Leu Met Lys Ser Tyr Ala Asp Val His Gln Val
1010 1015 1020

Ser Glu Ala Asp Ala Arg Leu Trp Leu Gln Gln Leu Glu Glu Lys
1025 1030 1035

Gly Arg Tyr Ala Lys Asp Val Trp Ala Gly
1040 1045

<210> 48
<211> 1048
<212> PRT
<213> Artificial sequence

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

<220>

<223> Cytochrome P450 variant CYP102A1var6

<400> 48

Thr Ile Lys Glu Met Pro Gln Pro Lys Thr Phe Gly Glu Leu Lys Asn
1 5 10 15

Leu Pro Leu Leu Asn Thr Asp Lys Pro Val Gln Ala Leu Met Lys Ile
20 25 30

Ala Asp Glu Leu Gly Glu Ile Phe Lys Phe Glu Ala Pro Gly Arg Val
35 40 45

Thr Arg Tyr Leu Ser Ser Gln Arg Leu Ile Lys Glu Ala Cys Asp Glu
50 55 60

Ser Arg Phe Asp Lys Asn Leu Ser Gln Ala Leu Lys Phe Val Arg Asp
65 70 75 80

Phe Ala Gly Asp Gly Leu Val Thr Ser Trp Thr His Glu Lys Asn Trp
85 90 95

Lys Lys Ala His Asn Ile Leu Leu Pro Ser Phe Ser Gln Gln Ala Met
100 105 110

Lys Gly Tyr His Ala Met Met Val Asp Ile Ala Val Gln Leu Val Gln
115 120 125

Lys Trp Glu Arg Leu Asn Ala Asp Glu His Ile Glu Val Pro Glu Asp
130 135 140

Met Thr Arg Leu Thr Leu Asp Thr Ile Gly Leu Cys Gly Phe Asn Tyr
145 150 155 160

Arg Phe Asn Ser Phe Tyr Arg Asp Gln Pro His Pro Phe Ile Thr Ser
165 170 175

Met Val Arg Ala Leu Asp Glu Ala Met Asn Lys Gln Gln Arg Ala Asn
180 185 190

Pro Asp Asp Pro Ala Tyr Asp Glu Asn Lys Arg Gln Phe Gln Glu Asp
195 200 205

Ile Lys Val Met Asn Asp Leu Val Asp Lys Ile Ile Ala Asp Arg Lys
210 215 220

Ala Ser Gly Glu Gln Ser Asp Asp Leu Leu Thr His Met Leu Asn Gly
225 230 235 240

Page 173

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Lys Asp Pro Glu Thr Gly Glu Pro Leu Asp Asp Glu Asn Ile Arg Tyr
245 250 255

Gln Ile Ile Thr Phe Leu Ile Ala Gly His Glu Thr Thr Ser Gly Leu
260 265 270

Leu Ser Phe Ala Leu Tyr Phe Leu Val Lys Asn Pro His Val Leu Gln
275 280 285

Lys Ala Ala Glu Glu Ala Ala Arg Val Leu Val Asp Pro Val Pro Ser
290 295 300

Tyr Lys Gln Val Lys Gln Leu Lys Tyr Val Gly Met Val Leu Asn Glu
305 310 315 320

Ala Leu Arg Leu Trp Pro Thr Ala Pro Ala Phe Ser Leu Tyr Ala Lys
325 330 335

Glu Asp Thr Val Leu Gly Gly Glu Tyr Pro Leu Glu Lys Gly Asp Glu
340 345 350

Leu Met Val Leu Ile Pro Gln Leu His Arg Asp Lys Thr Ile Trp Gly
355 360 365

Asp Asp Val Glu Glu Phe Arg Pro Glu Arg Phe Glu Asn Pro Ser Ala
370 375 380

Ile Pro Gln His Ala Phe Lys Pro Phe Gly Asn Gly Gln Arg Ala Cys
385 390 395 400

Ile Gly Gln Gln Phe Ala Leu His Glu Ala Thr Leu Val Leu Gly Met
405 410 415

Met Leu Lys His Phe Asp Phe Glu Asp His Thr Asn Tyr Glu Leu Asp
420 425 430

Ile Lys Glu Thr Leu Thr Leu Lys Pro Glu Gly Phe Val Val Lys Ala
435 440 445

Lys Ser Lys Lys Ile Pro Leu Gly Gly Ile Pro Ser Pro Ser Thr Glu
450 455 460

Gln Ser Ala Lys Lys Val Arg Lys Lys Ala Glu Asn Ala His Asn Thr
465 470 475 480

Pro Leu Leu Val Leu Tyr Gly Ser Asn Met Gly Thr Ala Glu Gly Thr
Page 174

Inventors: Rudi Fasan et al.
Express Mailing Label No: EB511841342US
Attorney Docket: P008-CIT

485 P008-CIT_ST25.txt 490 495

Ala Arg Asp Leu Ala Asp Ile Ala Met Ser Lys Gly Phe Ala Pro Gln
500 505 510

Val Ala Thr Leu Asp Ser His Ala Gly Asn Leu Pro Arg Glu Gly Ala
515 520 525

Val Leu Ile Val Thr Ala Ser Tyr Asn Gly His Pro Pro Asp Asn Ala
530 535 540

Lys Gln Phe Val Asp Trp Leu Asp Gln Ala Ser Ala Asp Glu Val Lys
545 550 555 560

Gly Val Arg Tyr Ser Val Phe Gly Cys Gly Asp Lys Asn Trp Ala Thr
565 570 575

Thr Tyr Gln Lys Val Pro Ala Phe Ile Asp Glu Thr Leu Ala Ala Lys
580 585 590

Gly Ala Glu Asn Ile Ala Asp Arg Gly Glu Ala Asp Ala Ser Asp Asp
595 600 605

Phe Glu Gly Thr Tyr Glu Glu Trp Arg Glu His Met Trp Ser Asp Val
610 615 620

Ala Ala Tyr Phe Asn Leu Asp Ile Glu Asn Ser Glu Asp Asn Lys Ser
625 630 635 640

Thr Leu Ser Leu Gln Phe Val Asp Ser Ala Ala Asp Met Pro Leu Ala
645 650 655

Lys Met His Gly Ala Phe Ser Thr Asn Val Val Ala Ser Lys Glu Leu
660 665 670

Gln Gln Pro Gly Ser Ala Arg Ser Thr Arg His Leu Glu Ile Glu Leu
675 680 685

Pro Lys Glu Ala Ser Tyr Gln Glu Gly Asp His Leu Gly Val Ile Pro
690 695 700

Arg Asn Tyr Glu Gly Ile Val Asn Arg Val Thr Ala Arg Phe Gly Leu
705 710 715 720

Asp Ala Ser Gln Gln Ile Arg Leu Glu Ala Glu Glu Glu Lys Leu Ala
725 730 735

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

His Leu Pro Leu Ala Lys Thr Val Ser Val Glu Glu Leu Leu Gln Tyr
 740 745 750

Val Glu Leu Gln Asp Pro Val Thr Arg Thr Gln Leu Arg Ala Met Ala
 755 760 765

Ala Lys Thr Val Cys Pro Pro His Lys Val Glu Leu Glu Ala Leu Leu
 770 775 780

Glu Lys Gln Ala Tyr Lys Glu Gln Val Leu Ala Lys Arg Leu Thr Met
 785 790 795 800

Leu Glu Leu Leu Glu Lys Tyr Pro Ala Cys Glu Met Lys Phe Ser Glu
 805 810 815

Phe Ile Ala Leu Leu Pro Ser Ile Arg Pro Arg Tyr Tyr Ser Ile Ser
 820 825 830

Ser Ser Pro Arg Val Asp Glu Lys Gln Ala Ser Ile Thr Val Ser Val
 835 840 845

Val Ser Gly Glu Ala Trp Ser Gly Tyr Gly Glu Tyr Lys Gly Ile Ala
 850 855 860

Ser Asn Tyr Leu Ala Glu Leu Gln Glu Gly Asp Thr Ile Thr Cys Phe
 865 870 875 880

Ile Ser Thr Pro Gln Ser Glu Phe Thr Leu Pro Lys Asp Pro Glu Thr
 885 890 895

Pro Leu Ile Met Val Gly Pro Gly Thr Gly Val Ala Pro Phe Arg Gly
 900 905 910

Phe Val Gln Ala Arg Lys Gln Leu Lys Glu Gln Gly Gln Ser Leu Gly
 915 920 925

Glu Ala His Leu Tyr Phe Gly Cys Arg Ser Pro His Glu Asp Tyr Leu
 930 935 940

Tyr Gln Glu Glu Leu Glu Asn Ala Gln Ser Glu Gly Ile Ile Thr Leu
 945 950 955 960

His Thr Ala Phe Ser Arg Met Pro Asn Gln Pro Lys Thr Tyr Val Gln
 965 970 975

His Val Met Glu Gln Asp Gly Lys Lys Leu Ile Glu Leu Leu Asp Gln
 980 985 990

P008-CIT_ST25.txt

Gly Ala His Phe Tyr Ile Cys Gly Asp Gly Ser Gln Met Ala Pro Ala
 995 1000 1005

Val Glu Ala Thr Leu Met Lys Ser Tyr Ala Asp Val His Gln Val
 1010 1015 1020

Ser Glu Ala Asp Ala Arg Leu Trp Leu Gln Gln Leu Glu Glu Lys
 1025 1030 1035

Gly Arg Tyr Ala Lys Asp Val Trp Ala Gly
 1040 1045

<210> 49
 <211> 1048
 <212> PRT
 <213> Artificial sequence

<220>
 <223> Cytochrome P450 variant CYP102A1var7

<400> 49

Thr Ile Lys Glu Met Pro Gln Pro Lys Thr Phe Gly Glu Leu Lys Asn
 1 5 10 15

Leu Pro Leu Leu Asn Thr Asp Lys Pro Val Gln Ala Leu Met Lys Ile
 20 25 30

Ala Asp Glu Leu Gly Glu Ile Phe Lys Phe Glu Ala Pro Gly Arg Val
 35 40 45

Thr Arg Tyr Leu Ser Ser Gln Arg Leu Ile Lys Glu Ala Cys Asp Glu
 50 55 60

Ser Arg Phe Asp Lys Asn Leu Ser Gln Gly Leu Lys Phe Val Arg Asp
 65 70 75 80

Phe Ala Gly Asp Gly Leu Val Thr Ser Trp Thr His Glu Lys Asn Trp
 85 90 95

Lys Lys Ala His Asn Ile Leu Leu Pro Ser Phe Ser Gln Gln Ala Met
 100 105 110

Lys Gly Tyr His Ala Met Met Val Asp Ile Ala Val Gln Leu Val Gln
 115 120 125

Lys Trp Glu Arg Leu Asn Ala Asp Glu His Ile Glu Val Pro Glu Asp
 130 135 140

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT.

P008-CIT-ST25.txt

Met Thr Arg Leu Thr Leu Asp Thr Ile Gly Leu Cys Gly Phe Asn Tyr
 145 150 155 160

Arg Phe Asn Ser Phe Tyr Arg Asp Gln Pro His Pro Phe Ile Thr Ser
 165 170 175

Met Val Arg Ala Leu Asp Glu Ala Met Asn Lys Gln Gln Arg Ala Asn
 180 185 190

Pro Asp Asp Pro Ala Tyr Asp Glu Asn Lys Arg Gln Phe Gln Glu Asp
 195 200 205

Ile Lys Val Met Asn Asp Leu Val Asp Lys Ile Ile Ala Asp Arg Lys
 210 215 220

Ala Ser Gly Glu Gln Ser Asp Asp Leu Leu Thr His Met Leu Asn Gly
 225 230 235 240

Lys Asp Pro Glu Thr Gly Glu Pro Leu Asp Asp Glu Asn Ile Arg Tyr
 245 250 255

Gln Ile Ile Thr Phe Leu Ile Ala Gly His Glu Thr Thr Ser Gly Leu
 260 265 270

Leu Ser Phe Ala Leu Tyr Phe Leu Val Lys Asn Pro His Val Leu Gln
 275 280 285

Lys Ala Ala Glu Glu Ala Ala Arg Val Leu Val Asp Pro Val Pro Ser
 290 295 300

Tyr Lys Gln Val Lys Gln Leu Lys Tyr Val Gly Met Val Leu Asn Glu
 305 310 315 320

Ala Leu Arg Leu Trp Pro Thr Ala Pro Ala Phe Ser Leu Tyr Ala Lys
 325 330 335

Glu Asp Thr Val Leu Gly Gly Glu Tyr Pro Leu Glu Lys Gly Asp Glu
 340 345 350

Leu Met Val Leu Ile Pro Gln Leu His Arg Asp Lys Thr Ile Trp Gly
 355 360 365

Asp Asp Val Glu Glu Phe Arg Pro Glu Arg Phe Glu Asn Pro Ser Ala
 370 375 380

Ile Pro Gln His Ala Phe Lys Pro Phe Gly Asn Gly Gln Arg Ala Cys
 385 390 395 400

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Ile Gly Gln Gln Phe Ala Leu His Glu Ala Thr Leu Val Leu Gly Met
405 410 415

Met Leu Lys His Phe Asp Phe Glu Asp His Thr Asn Tyr Glu Leu Asp
420 425 430

Ile Lys Glu Thr Leu Thr Leu Lys Pro Glu Gly Phe Val Val Lys Ala
435 440 445

Lys Ser Lys Lys Ile Pro Leu Gly Gly Ile Pro Ser Pro Ser Thr Glu
450 455 460

Gln Ser Ala Lys Lys Val Arg Lys Lys Ala Glu Asn Ala His Asn Thr
465 470 475 480

Pro Leu Leu Val Leu Tyr Gly Ser Asn Met Gly Thr Ala Glu Gly Thr
485 490 495

Ala Arg Asp Leu Ala Asp Ile Ala Met Ser Lys Gly Phe Ala Pro Gln
500 505 510

Val Ala Thr Leu Asp Ser His Ala Gly Asn Leu Pro Arg Glu Gly Ala
515 520 525

Val Leu Ile Val Thr Ala Ser Tyr Asn Gly His Pro Pro Asp Asn Ala
530 535 540

Lys Gln Phe Val Asp Trp Leu Asp Gln Ala Ser Ala Asp Glu Val Lys
545 550 555 560

Gly Val Arg Tyr Ser Val Phe Gly Cys Gly Asp Lys Asn Trp Ala Thr
565 570 575

Thr Tyr Gln Lys Val Pro Ala Phe Ile Asp Glu Thr Leu Ala Ala Lys
580 585 590

Gly Ala Glu Asn Ile Ala Asp Arg Gly Glu Ala Asp Ala Ser Asp Asp
595 600 605

Phe Glu Gly Thr Tyr Glu Glu Trp Arg Glu His Met Trp Ser Asp Val
610 615 620

Ala Ala Tyr Phe Asn Leu Asp Ile Glu Asn Ser Glu Asp Asn Lys Ser
625 630 635 640

Thr Leu Ser Leu Gln Phe Val Asp Ser Ala Ala Asp Met Pro Leu Ala
645 650 655

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Lys Met His Gly Ala Phe Ser Thr Asn Val Val Ala Ser Lys Glu Leu
660 665 670

Gln Gln Pro Gly Ser Ala Arg Ser Thr Arg His Leu Glu Ile Glu Leu
675 680 685

Pro Lys Glu Ala Ser Tyr Gln Glu Gly Asp His Leu Gly Val Ile Pro
690 695 700

Arg Asn Tyr Glu Gly Ile Val Asn Arg Val Thr Ala Arg Phe Gly Leu
705 710 715 720

Asp Ala Ser Gln Gln Ile Arg Leu Glu Ala Glu Glu Glu Lys Leu Ala
725 730 735

His Leu Pro Leu Ala Lys Thr Val Ser Val Glu Glu Leu Leu Gln Tyr
740 745 750

Val Glu Leu Gln Asp Pro Val Thr Arg Thr Gln Leu Arg Ala Met Ala
755 760 765

Ala Lys Thr Val Cys Pro Pro His Lys Val Glu Leu Glu Ala Leu Leu
770 775 780

Glu Lys Gln Ala Tyr Lys Glu Gln Val Leu Ala Lys Arg Leu Thr Met
785 790 795 800

Leu Glu Leu Leu Glu Lys Tyr Pro Ala Cys Glu Met Lys Phe Ser Glu
805 810 815

Phe Ile Ala Leu Leu Pro Ser Ile Arg Pro Arg Tyr Tyr Ser Ile Ser
820 825 830

Ser Ser Pro Arg Val Asp Glu Lys Gln Ala Ser Ile Thr Val Ser Val
835 840 845

Val Ser Gly Glu Ala Trp Ser Gly Tyr Gly Glu Tyr Lys Gly Ile Ala
850 855 860

Ser Asn Tyr Leu Ala Glu Leu Gln Glu Gly Asp Thr Ile Thr Cys Phe
865 870 875 880

Ile Ser Thr Pro Gln Ser Glu Phe Thr Leu Pro Lys Asp Pro Glu Thr
885 890 895

Pro Leu Ile Met Val Gly Pro Gly Thr Gly Val Ala Pro Phe Arg Gly

Title: "Methods and Systems for selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

900

P008-CIT_ST25.txt
905

910

Phe Val Gln Ala Arg Lys Gln Leu Lys Glu Gln Gly Gln Ser Leu Gly
 915 920 925

Glu Ala His Leu Tyr Phe Gly Cys Arg Ser Pro His Glu Asp Tyr Leu
 930 935 940

Tyr Gln Glu Glu Leu Glu Asn Ala Gln Ser Glu Gly Ile Ile Thr Leu
 945 950 955 960

His Thr Ala Phe Ser Arg Met Pro Asn Gln Pro Lys Thr Tyr Val Gln
 965 970 975

His Val Met Glu Gln Asp Gly Lys Lys Leu Ile Glu Leu Leu Asp Gln
 980 985 990

Gly Ala His Phe Tyr Ile Cys Gly Asp Gly Ser Gln Met Ala Pro Ala
 995 1000 1005

Val Glu Ala Thr Leu Met Lys Ser Tyr Ala Asp Val His Gln Val
 1010 1015 1020

Ser Glu Ala Asp Ala Arg Leu Trp Leu Gln Gln Leu Glu Glu Lys
 1025 1030 1035

Gly Arg Tyr Ala Lys Asp Val Trp Ala Gly
 1040 1045

<210> 50
 <211> 1048
 <212> PRT
 <213> Artificial sequence

<220>
 <223> Cytochrome P450 variant CYP102A1var8

<400> 50

Thr Ile Lys Glu Met Pro Gln Pro Lys Thr Phe Gly Glu Leu Lys Asn
 1 5 10 15

Leu Pro Leu Leu Asn Thr Asp Lys Pro Val Gln Ala Leu Met Lys Ile
 20 25 30

Ala Asp Glu Leu Gly Glu Ile Phe Lys Phe Glu Ala Pro Gly Leu Val
 35 40 45

Thr Arg Tyr Leu Ser Ser Gln Arg Leu Ile Lys Glu Ala Cys Asp Glu
 50 55 60

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Pocket: P008-CIT

P008-CIT_ST25.txt

Ser Arg Phe Asp Lys Asn Leu Ser Gln Ala Leu Lys Phe Val Arg Asp
65 70 75 80

Phè Ala Gly Asp Gly Leu Val Thr Ser Trp Thr His Glu Lys Asn Trp
85 90 95

Lys Lys Ala His Asn Ile Leu Leu Pro Ser Phe Ser Gln Gln Ala Met
100 105 110

Lys Gly Tyr His Ala Met Met Val Asp Ile Ala Val Gln Leu Val Gln
115 120 125

Lys Trp Glu Arg Leu Asn Ala Asp Glu His Ile Glu Val Pro Glu Asp
130 135 140

Met Thr Arg Leu Thr Leu Asp Thr Ile Gly Leu Cys Gly Phe Asn Tyr
145 150 155 160

Arg Phe Asn Ser Phe Tyr Arg Asp Gln Pro His Pro Phe Ile Thr Ser
165 170 175

Met Val Arg Ala Leu Asp Glu Ala Met Asn Lys Gln Gln Arg Ala Asn
180 185 190

Pro Asp Asp Pro Ala Tyr Asp Glu Asn Lys Arg Gln Phe Gln Glu Asp
195 200 205

Ile Lys Val Met Asn Asp Leu Val Asp Lys Ile Ile Ala Asp Arg Lys
210 215 220

Ala Ser Gly Glu Gln Ser Asp Asp Leu Leu Thr His Met Leu Asn Gly
225 230 235 240

Lys Asp Pro Glu Thr Gly Glu Pro Leu Asp Asp Glu Asn Ile Arg Tyr
245 250 255

Gln Ile Ile Thr Phe Leu Ile Ala Gly His Glu Thr Thr Ser Gly Leu
260 265 270

Leu Ser Phe Ala Leu Tyr Phe Leu Val Lys Asn Pro His Val Leu Gln
275 280 285

Lys Ala Ala Glu Glu Ala Ala Arg Val Leu Val Asp Pro Val Pro Ser
290 295 300

Tyr Lys Gln Val Lys Gln Leu Lys Tyr Val Gly Met Val Leu Asn Glu
Page 182

Printed: 10/30/2007

SEQUENCE

PCT/US2007/017409

1030217409

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

305

310

315

320

Ala Leu Arg Leu Trp Pro Thr Ala Pro Ala Phe Ser Leu Tyr Ala Lys
325 330

Glu Asp Thr Val Leu Gly Gly Glu Tyr Pro Leu Glu Lys Gly Asp Glu
340 345 350

Leu Met Val Leu Ile Pro Gln Leu His Arg Asp Lys Thr Ile Trp Gly
355 360 365

Asp Asp Val Glu Glu Phe Arg Pro Glu Arg Phe Glu Asn Pro Ser Ala
370 375 380

Ile Pro Gln His Ala Phe Lys Pro Phe Gly Asn Gly Gln Arg Ala Cys
385 390 395 400

Ile Gly Gln Gln Phe Ala Leu His Glu Ala Thr Leu Val Leu Gly Met
405 410 415

Met Leu Lys His Phe Asp Phe Glu Asp His Thr Asn Tyr Glu Leu Asp
420 425 430

Ile Lys Glu Thr Leu Thr Leu Lys Pro Glu Gly Phe Val Val Lys Ala
435 440 445

Lys Ser Lys Lys Ile Pro Leu Gly Gly Ile Pro Ser Pro Ser Thr Glu
450 455 460

Gln Ser Ala Lys Lys Val Arg Lys Lys Ala Glu Asn Ala His Asn Thr
465 470 475 480

Pro Leu Leu Val Leu Tyr Gly Ser Asn Met Gly Thr Ala Glu Gly Thr
485 490 495

Ala Arg Asp Leu Ala Asp Ile Ala Met Ser Lys Gly Phe Ala Pro Gln
500 505 510

Val Ala Thr Leu Asp Ser His Ala Gly Asn Leu Pro Arg Glu Gly Ala
515 520 525

Val Leu Ile Val Thr Ala Ser Tyr Asn Gly His Pro Pro Asp Asn Ala
530 535 540

Lys Gln Phe Val Asp Trp Leu Asp Gln Ala Ser Ala Asp Glu Val Lys
545 550 555 560

08/04/2007

P008-CIT_ST25.txt

Gly Val Arg Tyr Ser Val Phe Gly Cys Gly Asp Lys Asn Trp Ala Thr
565 570 575

Thr Tyr Gln Lys Val Pro Ala Phe Ile Asp Glu Thr Leu Ala Ala Lys
580 585 590

Gly Ala Glu Asn Ile Ala Asp Arg Gly Glu Ala Asp Ala Ser Asp Asp
595 600 605

Phe Glu Gly Thr Tyr Glu Glu Trp Arg Glu His Met Trp Ser Asp Val
610 615 620

Ala Ala Tyr Phe Asn Leu Asp Ile Glu Asn Ser Glu Asp Asn Lys Ser
625 630 635 640

Thr Leu Ser Leu Gln Phe Val Asp Ser Ala Ala Asp Met Pro Leu Ala
645 650 655

Lys Met His Gly Ala Phe Ser Thr Asn Val Val Ala Ser Lys Glu Leu
660 665 670

Gln Gln Pro Gly Ser Ala Arg Ser Thr Arg His Leu Glu Ile Glu Leu
675 680 685

Pro Lys Glu Ala Ser Tyr Gln Glu Gly Asp His Leu Gly Val Ile Pro
690 695 700

Arg Asn Tyr Glu Gly Ile Val Asn Arg Val Thr Ala Arg Phe Gly Leu
705 710 715 720

Asp Ala Ser Gln Gln Ile Arg Leu Glu Ala Glu Glu Glu Lys Leu Ala
725 730 735

His Leu Pro Leu Ala Lys Thr Val Ser Val Glu Glu Leu Leu Gln Tyr
740 745 750

Val Glu Leu Gln Asp Pro Val Thr Arg Thr Gln Leu Arg Ala Met Ala
755 760 765

Ala Lys Thr Val Cys Pro Pro His Lys Val Glu Leu Glu Ala Leu Leu
770 775 780

Glu Lys Gln Ala Tyr Lys Glu Gln Val Leu Ala Lys Arg Leu Thr Met
785 790 795 800

Leu Glu Leu Leu Glu Lys Tyr Pro Ala Cys Glu Met Lys Phe Ser Glu
805 810 815

Printed: 10/30/2007

8:40:15

PCT/US2007/017409

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Phe Ile Ala Leu Leu Pro Ser Ile Arg Pro Arg Tyr Tyr Ser Ile Ser
820 825 830

Ser Ser Pro Arg Val Asp Glu Lys Gln Ala Ser Ile Thr Val Ser Val
835 840 845

Val Ser Gly Glu Ala Trp Ser Gly Tyr Gly Glu Tyr Lys Gly Ile Ala
850 855 860

Ser Asn Tyr Leu Ala Glu Leu Gln Glu Gly Asp Thr Ile Thr Cys Phe
865 870 875 880

Ile Ser Thr Pro Gln Ser Glu Phe Thr Leu Pro Lys Asp Pro Glu Thr
885 890 895

Pro Leu Ile Met Val Gly Pro Gly Thr Gly Val Ala Pro Phe Arg Gly
900 905 910

Phe Val Gln Ala Arg Lys Gln Leu Lys Glu Gln Gly Gln Ser Leu Gly
915 920 925

Glu Ala His Leu Tyr Phe Gly Cys Arg Ser Pro His Glu Asp Tyr Leu
930 935 940

Tyr Gln Glu Glu Leu Glu Asn Ala Gln Ser Glu Gly Ile Ile Thr Leu
945 950 955 960

His Thr Ala Phe Ser Arg Met Pro Asn Gln Pro Lys Thr Tyr Val Gln
965 970 975

His Val Met Glu Gln Asp Gly Lys Lys Leu Ile Glu Leu Leu Asp Gln
980 985 990

Gly Ala His Phe Tyr Ile Cys Gly Asp Gly Ser Gln Met Ala Pro Ala
995 1000 1005

Val Glu Ala Thr Leu Met Lys Ser Tyr Ala Asp Val His Gln Val
1010 1015 1020

Ser Glu Ala Asp Ala Arg Leu Trp Leu Gln Gln Leu Glu Glu Lys
1025 1030 1035

Gly Arg Tyr Ala Lys Asp Val Trp Ala Gly
1040 1045

<210> 51
<211> 1048

08/04/2007

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

<212> PRT
 <213> Artificial sequence

<220>
 <223> Cytochrome P450 variant CYP102A1var9

<400> 51

Thr Ile Lys Glu Met Pro Gln Pro Lys Thr Phe Gly Glu Leu Lys Asn
 1 5 10 15

Leu Pro Leu Leu Asn Thr Asp Lys Pro Val Gln Ala Leu Met Lys Ile
 20 25 30

Ala Asp Glu Leu Gly Glu Ile Phe Lys Phe Glu Ala Pro Gly Arg Val
 35 40 45

Thr Arg Tyr Leu Ser Ser Gln Arg Leu Ile Lys Glu Ala Cys Asp Glu
 50 55 60

Ser Arg Phe Asp Lys Asn Leu Ser Gln Ala Leu Lys Phe Val Arg Asp
 65 70 75 80

Phe Ala Gly Asp Gly Leu Ala Thr Ser Trp Thr His Glu Lys Asn Trp
 85 90 95

Lys Lys Ala His Asn Ile Leu Leu Pro Ser Phe Ser Gln Gln Ala Met
 100 105 110

Lys Gly Tyr His Ala Met Met Val Asp Ile Ala Val Gln Leu Val Gln
 115 120 125

Lys Trp Glu Arg Leu Asn Ala Asp Glu His Ile Glu Val Pro Glu Asp
 130 135 140

Met Thr Arg Leu Thr Leu Asp Thr Ile Gly Leu Cys Gly Phe Asn Tyr
 145 150 155 160

Arg Phe Asn Ser Phe Tyr Arg Asp Gln Pro His Pro Phe Ile Thr Ser
 165 170 175

Met Val Arg Ala Leu Asp Glu Ala Met Asn Lys Leu Gln Arg Ala Asn
 180 185 190

Pro Asp Asp Pro Ala Tyr Asp Glu Asn Lys Arg Gln Phe Gln Glu Asp
 195 200 205

Ile Lys Val Met Asn Asp Leu Val Asp Lys Ile Ile Ala Asp Arg Lys
 210 215 220

Printed: 10/30/2007

PCT/US2007/017409

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511641342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Ala Ser Gly Glu Gln Ser Asp Asp Leu Leu Ala His Met Leu Asn Gly
225 230 235 240

Lys Asp Pro Glu Thr Gly Glu Pro Leu Asp Asp Glu Asn Ile Arg Tyr
245 250 255

Gln Ile Ile Thr Phe Leu Ile Ala Gly His Glu Thr Thr Ser Gly Leu
260 265 270

Leu Ser Phe Ala Leu Tyr Phe Leu Val Lys Asn Pro His Val Leu Gln
275 280 285

Lys Ala Ala Glu Glu Ala Ala Arg Val Leu Val Asp Pro Val Pro Ser
290 295 300

Tyr Lys Gln Val Lys Gln Leu Lys Tyr Val Gly Met Val Leu Asn Glu
305 310 315 320

Ala Leu Arg Leu Trp Pro Thr Ala Pro Ala Phe Ser Leu Tyr Ala Lys
325 330 335

Glu Asp Thr Val Leu Gly Gly Glu Tyr Pro Leu Glu Lys Gly Asp Glu
340 345 350

Leu Met Val Leu Ile Pro Gln Leu His Arg Asp Lys Thr Ile Trp Gly
355 360 365

Asp Asp Val Glu Glu Phe Arg Pro Glu Arg Phe Glu Asn Pro Ser Ala
370 375 380

Ile Pro Gln His Ala Phe Lys Pro Phe Gly Asn Gly Gln Arg Ala Cys
385 390 395 400

Ile Gly Gln Gln Phe Ala Leu His Glu Ala Thr Leu Val Leu Gly Met
405 410 415

Met Leu Lys His Phe Asp Phe Glu Asp His Thr Asn Tyr Glu Leu Asp
420 425 430

Ile Lys Glu Thr Leu Thr Leu Lys Pro Glu Gly Phe Val Val Lys Ala
435 440 445

Lys Ser Lys Lys Ile Pro Leu Gly Gly Ile Pro Ser Pro Ser Thr Glu
450 455 460

Gln Ser Ala Lys Lys Val Ala Lys Lys Ala Glu Asn Ala His Asn Thr
465 470 475 480

Page 187

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Pro Leu Leu Val Leu Tyr Gly Ser Asn Met Gly Thr Ala Lys Gly Thr
 485 490 495

Ala Arg Asp Leu Ala Asp Ile Ala Met Ser Lys Gly Phe Ala Pro Gln
 500 505 510

Val Ala Thr Leu Asp Ser His Ala Gly Asn Leu Pro Arg Glu Gly Ala
 515 520 525

Val Leu Ile Val Thr Ala Ser Tyr Asn Gly His Pro Pro Asp Asn Ala
 530 535 540

Lys Gln Phe Val Asp Trp Leu Asp Gln Ala Ser Ala Asp Glu Val Lys
 545 550 555 560

Gly Val Arg Tyr Ser Val Phe Gly Cys Gly Asp Lys Asn Trp Ala Thr
 565 570 575

Thr Tyr Gln Lys Val Pro Ala Phe Ile Asp Glu Thr Leu Ala Ala Lys
 580 585 590

Gly Ala Glu Asn Ile Ala Asp Arg Gly Glu Ala Asp Ala Ser Asp Asp
 595 600 605

Phe Glu Gly Thr Tyr Glu Glu Trp Arg Glu His Met Trp Ser Asp Val
 610 615 620

Ala Ala Tyr Phe Asn Leu Asp Ile Glu Asn Ser Glu Asp Asn Lys Ser
 625 630 635 640

Thr Leu Ser Leu Gln Phe Val Asp Ser Ala Ala Asp Met Pro Leu Ala
 645 650 655

Lys Met His Gly Ala Phe Ser Thr Asn Val Val Ala Ser Lys Glu Leu
 660 665 670

Gln Gln Pro Gly Ser Ala Arg Ser Thr Arg His Leu Glu Ile Glu Leu
 675 680 685

Pro Lys Glu Ala Ser Tyr Gln Glu Gly Asp His Leu Gly Val Ile Pro
 690 695 700

Arg Asn Tyr Glu Gly Ile Val Asn Arg Val Thr Ala Arg Phe Gly Leu
 705 710 715 720

Asp Ala Ser Gln Gln Ile Arg Leu Glu Ala Glu Glu Glu Lys Leu Ala

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

725

730

735

His Leu Pro Leu Ala Lys Thr Val Ser Val Glu Glu Leu Leu Gln Tyr
 740 745 750

Val Glu Leu Gln Asp Pro Val Thr Arg Thr Gln Leu Arg Ala Met Ala
 755 760 765

Ala Lys Thr Val Cys Pro Pro His Lys Val Glu Leu Glu Ala Leu Leu
 770 775 780

Glu Lys Gln Ala Tyr Lys Glu Gln Val Leu Ala Lys Arg Leu Thr Met
 785 790 795 800

Leu Glu Leu Leu Glu Lys Tyr Pro Ala Cys Glu Met Lys Phe Ser Glu
 805 810 815

Phe Ile Ala Leu Leu Pro Ser Ile Arg Pro Arg Tyr Tyr Ser Ile Ser
 820 825 830

Ser Ser Pro Arg Val Asp Glu Lys Gln Ala Ser Ile Thr Val Ser Val
 835 840 845

Val Ser Gly Glu Ala Trp Ser Gly Tyr Gly Glu Tyr Lys Gly Ile Ala
 850 855 860

Ser Asn Tyr Leu Ala Glu Leu Gln Glu Gly Asp Thr Ile Thr Cys Phe
 865 870 875 880

Ile Ser Thr Pro Gln Ser Glu Phe Thr Leu Pro Lys Asp Pro Glu Thr
 885 890 895

Pro Leu Ile Met Val Gly Pro Gly Thr Gly Val Ala Pro Phe Arg Gly
 900 905 910

Phe Val Gln Ala Arg Lys Gln Leu Lys Glu Gln Gly Gln Ser Leu Gly
 915 920 925

Glu Ala His Leu Tyr Phe Gly Cys Arg Ser Pro His Glu Asp Tyr Leu
 930 935 940

Tyr Gln Glu Glu Leu Glu Asn Ala Gln Ser Glu Gly Ile Ile Thr Leu
 945 950 955 960

His Thr Ala Phe Ser Arg Met Pro Asn Gln Pro Lys Thr Tyr Val Gln
 965 970 975

P008-CIT_ST25.txt

His Val Met Glu Gln Asp Gly Lys Lys Leu Ile Glu Leu Leu Asp Gln
980 985 990

Gly Ala His Phe Tyr Ile Cys Gly Asp Gly Ser Gln Met Ala Pro Ala
995 1000 1005

Val Glu Ala Thr Leu Met Lys Ser Tyr Ala Asp Val His Gln Val
1010 1015 1020

Glu Glu Ala Asp Ala Arg Leu Trp Leu Gln Gln Leu Glu Glu Lys
1025 1030 1035

Gly Arg Tyr Ala Lys Asp Val Trp Ala Gly
1040 1045

<210> 52
<211> 1048
<212> PRT
<213> Artificial sequence

<220>
<223> Cytochrome P450 variant CYP102A1var9-1

<400> 52

Thr Ile Lys Glu Met Pro Gln Pro Lys Thr Phe Gly Glu Leu Lys Asn
1 5 10 15

Leu Pro Leu Leu Asn Thr Asp Lys Pro Val Gln Ala Leu Met Lys Ile
20 25 30

Ala Asp Glu Leu Gly Glu Ile Phe Lys Phe Glu Ala Pro Gly Arg Val
35 40 45

Thr Arg Tyr Leu Ser Ser Gln Arg Leu Ile Lys Glu Ala Cys Asp Glu
50 55 60

Ser Arg Phe Asp Lys Asn Leu Ser Gln Ala Leu Lys Phe Val Arg Asp
65 70 75 80

Phe Ala Gly Asp Gly Leu Ala Thr Ser Trp Thr His Glu Lys Asn Trp
85 90 95

Lys Lys Ala His Asn Ile Leu Leu Pro Ser Phe Ser Gln Gln Ala Met
100 105 110

Lys Gly Tyr His Ala Met Met Val Asp Ile Ala Val Gln Leu Val Gln
115 120 125

Lys Trp Glu Arg Leu Asn Ala Asp Glu His Ile Glu Val Pro Glu Asp
Page 190

Printed: 10/30/2007

167015

PCT/US2007/017409

1507/17409

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.TXT

140

130

135

Met Thr Arg Leu Thr Leu Asp Thr Ile Gly Leu Cys Gly Phe Asn Tyr
145 150 155 160

Arg Phe Asn Ser Phe Tyr Arg Asp Gln Pro His Pro Phe Ile Thr Ser
165 170 175

Met Val Arg Ala Leu Asp Glu Lys Met Asn Lys Leu Gln Arg Ala Asn
180 185 190

Pro Asp Asp Pro Ala Tyr Asp Glu Asn Lys Arg Gln Phe Gln Glu Asp
195 200 205

Ile Lys Val Met Asn Asp Leu Val Asp Lys Ile Ile Ala Asp Arg Lys
210 215 220

Ala Ser Gly Glu Gln Ser Asp Asp Leu Leu Ala His Met Leu Asn Gly
225 230 235 240

Lys Asp Pro Glu Thr Gly Glu Pro Leu Asp Asp Glu Asn Ile Arg Tyr
245 250 255

Gln Ile Ile Thr Phe Leu Ile Ala Gly His Glu Thr Thr Ser Gly Leu
260 265 270

Leu Ser Phe Ala Leu Tyr Phe Leu Val Lys Asn Pro His Val Leu Gln
275 280 285

Lys Ala Ala Glu Glu Ala Ala Arg Val Leu Val Asp Pro Val Pro Ser
290 295 300

Tyr Lys Gln Val Lys Gln Leu Lys Tyr Val Gly Met Val Leu Asn Glu
305 310 315 320

Ala Leu Arg Leu Trp Pro Thr Ala Pro Ala Phe Ser Leu Tyr Ala Lys
325 330 335

Glu Asp Thr Val Leu Gly Gly Glu Tyr Pro Leu Glu Lys Gly Asp Glu
340 345 350

Leu Met Val Leu Ile Pro Gln Leu His Arg Asp Lys Thr Ile Trp Gly
355 360 365

Asp Asp Val Glu Glu Phe Arg Pro Glu Arg Phe Glu Asn Pro Ser Ala
370 375 380

08/04/2007

Patented 10/30/2007

SECRET

PCT/US2007/017409

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Ile Pro Gln His Ala Phe Lys Pro Phe Gly Asn Gly Gln Arg Ala Cys
385 390 395 400

Ile Gly Gln Gln Phe Ala Leu His Glu Ala Thr Leu Val Leu Gly Met
405 410 415

Met Leu Lys His Phe Asp Phe Glu Asp His Thr Asn Tyr Glu Leu Asp
420 425 430

Ile Lys Glu Thr Leu Thr Leu Lys Pro Glu Gly Phe Val Val Lys Ala
435 440 445

Lys Ser Lys Lys Ile Pro Leu Gly Gly Ile Pro Ser Pro Ser Thr Glu
450 455 460

Gln Ser Ala Lys Lys Val Ala Lys Lys Ala Glu Asn Ala His Asn Thr
465 470 475 480

Pro Leu Leu Val Leu Tyr Gly Ser Asn Met Gly Thr Ala Lys Gly Thr
485 490 495

Ala Arg Asp Leu Ala Asp Ile Ala Met Ser Lys Gly Phe Ala Pro Gln
500 505 510

Val Ala Thr Leu Asp Ser His Ala Gly Asn Leu Pro Arg Glu Gly Ala
515 520 525

Val Leu Ile Val Thr Ala Ser Tyr Asn Gly His Pro Pro Asp Asn Ala
530 535 540

Lys Gln Phe Val Asp Trp Leu Asp Gln Ala Ser Ala Asp Glu Val Lys
545 550 555 560

Gly Val Arg Tyr Ser Val Phe Gly Cys Gly Asp Lys Asn Trp Ala Thr
565 570 575

Thr Tyr Gln Lys Val Pro Ala Phe Ile Asp Glu Thr Leu Ala Ala Lys
580 585 590

Gly Ala Glu Asn Ile Ala Asp Arg Gly Glu Ala Asp Ala Ser Asp Asp
595 600 605

Phe Glu Gly Thr Tyr Glu Glu Trp Arg Glu His Met Trp Ser Asp Val
610 615 620

Ala Ala Tyr Phe Asn Leu Asp Ile Glu Asn Ser Glu Asp Asn Lys Ser
625 630 635 640

08/04/2007

Printed: 10/30/2007

Seq: 15

PCT/US2007/017409

050717409

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Thr Leu Ser Leu Gln Phe Val Asp Ser Ala Ala Asp Met Pro Leu Ala
645 650 655

Lys Met His Gly Ala Phe Ser Thr Asn Val Val Ala Ser Lys Glu Leu
660 665 670

Gln Gln Pro Gly Ser Ala Arg Ser Thr Arg His Leu Glu Ile Glu Leu
675 680 685

Pro Lys Glu Ala Ser Tyr Gln Glu Gly Asp His Leu Gly Val Ile Pro
690 695 700

Arg Asn Tyr Glu Gly Ile Val Asn Arg Val Thr Ala Arg Phe Gly Leu
705 710 715 720

Asp Ala Ser Gln Gln Ile Arg Leu Glu Ala Glu Glu Glu Lys Leu Ala
725 730 735

His Leu Pro Leu Ala Lys Thr Val Ser Val Glu Glu Leu Leu Gln Tyr
740 745 750

Val Glu Leu Gln Asp Pro Val Thr Arg Thr Gln Leu Arg Ala Met Ala
755 760 765

Ala Lys Thr Val Cys Pro Pro His Lys Val Glu Leu Glu Ala Leu Leu
770 775 780

Glu Lys Gln Ala Tyr Lys Glu Gln Val Leu Ala Lys Arg Leu Thr Met
785 790 795 800

Leu Glu Leu Leu Glu Lys Tyr Pro Ala Cys Glu Met Lys Phe Ser Glu
805 810 815

Phe Ile Ala Leu Leu Pro Ser Ile Arg Pro Arg Tyr Tyr Ser Ile Ser
820 825 830

Ser Ser Pro Arg Val Asp Glu Lys Gln Ala Ser Ile Thr Val Ser Val
835 840 845

Val Ser Gly Glu Ala Trp Ser Gly Tyr Gly Glu Tyr Lys Gly Ile Ala
850 855 860

Ser Asn Tyr Leu Ala Glu Leu Gln Glu Gly Asp Thr Ile Thr Cys Phe
865 870 875 880

Ile Ser Thr Pro Gln Ser Glu Phe Thr Leu Pro Lys Asp Pro Glu Thr
885 890 895

Page 193

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Pro Leu Ile Met Val Gly Pro Gly Thr Gly Val Ala Pro Phe Arg Gly
 900 905 910

Phe Val Gln Ala Arg Lys Gln Leu Lys Glu Gln Gly Gln Ser Leu Gly
 915 920 925

Glu Ala His Leu Tyr Phe Gly Cys Arg Ser Pro His Glu Asp Tyr Leu
 930 935 940

Tyr Gln Glu Glu Leu Glu Asn Ala Gln Ser Glu Gly Ile Ile Thr Leu
 945 950 955 960

His Thr Ala Phe Ser Arg Met Pro Asn Gln Pro Lys Thr Tyr Val Gln
 965 970 975

His Val Met Glu Gln Asp Gly Lys Lys Leu Ile Glu Leu Leu Asp Gln
 980 985 990

Gly Ala His Phe Tyr Ile Cys Gly Asp Gly Ser Gln Met Ala Pro Ala
 995 1000 1005

Val Glu Ala Thr Leu Met Lys Ser Tyr Ala Asp Val His Gln Val
 1010 1015 1020

Glu Glu Ala Asp Ala Arg Leu Trp Leu Gln Gln Leu Glu Glu Lys
 1025 1030 1035

Gly Arg Tyr Ala Lys Asp Val Trp Ala Gly
 1040 1045

<210> 53

<211> 417

<212> PRT

<213> Bacillus Subtilis

<400> 53

Met Asn Glu Gln Ile Pro His Asp Lys Ser Leu Asp Asn Ser Leu Thr
 1 5 10 15

Leu Leu Lys Glu Gly Tyr Leu Phe Ile Lys Asn Arg Thr Glu Arg Tyr
 20 25 30

Asn Ser Asp Leu Phe Gln Ala Arg Leu Leu Gly Lys Asn Phe Ile Cys
 35 40 45

Met Thr Gly Ala Glu Ala Ala Lys Val Phe Tyr Asp Thr Asp Arg Phe
 50 55 60

Title: "Methods and Systems for Selective..."

Inventors: Rudi Pasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Gln Arg Gln Asn Ala Leu Pro Lys Arg Val Gln Lys Ser Leu Phe Gly
65 70 75 80

Val Asn Ala Ile Gln Gly Met Asp Gly Ser Ala His Ile His Arg Lys
85 90 95

Met Leu Phe Leu Ser Leu Met Thr Pro Pro His Gln Lys Arg Leu Ala
100 105 110

Glu Leu Met Thr Glu Glu Trp Lys Ala Ala Val Thr Arg Trp Glu Lys
115 120 125

Ala Asp Glu Val Val Leu Phe Glu Glu Ala Lys Glu Ile Leu Cys Arg
130 135 140

Val Ala Cys Tyr Trp Ala Gly Val Pro Leu Lys Glu Thr Glu Val Lys
145 150 155 160

Glu Arg Ala Asp Asp Phe Ile Asp Met Val Asp Ala Phe Gly Ala Val
165 170 175

Gly Pro Arg His Trp Lys Gly Arg Arg Ala Arg Pro Arg Ala Glu Glu
180 185 190

Trp Ile Glu Val Met Ile Glu Asp Ala Arg Ala Gly Leu Lys Thr
195 200 205

Thr Ser Gly Thr Ala Leu His Glu Met Ala Phe His Thr Gln Glu Asp
210 215 220

Gly Ser Gln Leu Asp Ser Arg Met Ala Ala Ile Glu Leu Ile Asn Val
225 230 235 240

Leu Arg Pro Ile Val Ala Ile Ser Tyr Phe Leu Val Phe Ser Ala Leu
245 250 255

Ala Leu His Glu His Pro Lys Tyr Lys Glu Trp Leu Arg Ser Gly Asn
260 265 270

Ser Arg Glu Arg Glu Met Phe Val Gln Glu Val Arg Arg Tyr Tyr Pro
275 280 285

Phe Gly Pro Phe Leu Gly Ala Leu Val Lys Lys Asp Phe Val Trp Asn
290 295 300

Asn Cys Glu Phe Lys Lys Gly Thr Ser Val Leu Leu Asp Leu Tyr Gly
Page 195

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

305

310

315

320

Thr Asn His Asp Pro Arg Leu Trp Asp His Pro Asp Glu Phe Arg Pro
325 330 335

Glu Arg Phe Ala Glu Arg Glu Glu Asn Leu Phe Asp Met Ile Pro Gln
340 345 350

Gly Gly Gly His Ala Glu Lys Gly His Arg Cys Pro Gly Glu Gly Ile
355 360 365

Thr Ile Glu Val Met Lys Ala Ser Leu Asp Phe Leu Val His Gln Ile
370 375 380

Glu Tyr Asp Val Pro Glu Gln Ser Leu His Tyr Ser Leu Ala Arg Met
385 390 395 400

Pro Ser Leu Pro Glu Ser Gly Phe Val Met Ser Gly Ile Arg Arg Lys
405 410 415

Ser

<210> 54
<211> 420
<212> PRT
<213> Mycobacterium sp

<220>
<221> MISC_FEATURE
<222> (1)..(420)
<223> Cytochrome P450 enzyme CYP153A6

<400> 54

Met Thr Glu Met Thr Val Ala Ala Ser Asp Ala Thr Asn Ala Ala Tyr
1 5 10 15

Gly Met Ala Leu Glu Asp Ile Asp Val Ser Asn Pro Val Leu Phe Arg
20 25 30

Asp Asn Thr Trp His Pro Tyr Phe Lys Arg Leu Arg Glu Glu Asp Pro
35 40 45

Val His Tyr Cys Lys Ser Ser Met Phe Gly Pro Tyr Trp Ser Val Thr
50 55 60

Lys Tyr Arg Asp Ile Met Ala Val Glu Thr Asn Pro Lys Val Phe Ser
65 70 75 80

Printed: 10/30/2007

SECRET

PCT/US2007/017409

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Ser Glu Ala Lys Ser Gly Gly Ile Thr Ile Met Asp Asp Asn Ala Ala
85 90 95

Ala Ser Leu Pro Met Phe Ile Ala Met Asp Pro Pro Lys His Asp Val
100 105 110

Gln Arg Lys Thr Val Ser Pro Ile Val Ala Pro Glu Asn Leu Ala Thr
115 120 125

Met Glu Ser Val Ile Arg Gln Arg Thr Ala Asp Leu Leu Asp Gly Leu
130 135 140

Pro Ile Asn Glu Glu Phe Asp Trp Val His Arg Val Ser Ile Glu Leu
145 150 155 160

Thr Thr Lys Met Leu Ala Thr Leu Phe Asp Phe Pro Trp Asp Asp Arg
165 170 175

Ala Lys Leu Thr Arg Trp Ser Asp Val Thr Thr Ala Leu Pro Gly Gly
180 185 190

Gly Ile Ile Asp Ser Glu Glu Gln Arg Met Ala Glu Leu Met Glu Cys
195 200 205

Ala Thr Tyr Phe Thr Glu Leu Trp Asn Gln Arg Val Asn Ala Glu Pro
210 215 220

Lys Asn Asp Leu Ile Ser Met Met Ala His Ser Glu Ser Thr Arg His
225 230 235 240

Met Ala Pro Glu Glu Tyr Leu Gly Asn Ile Val Leu Leu Ile Val Gly
245 250 255

Gly Asn Asp Thr Thr Arg Asn Ser Met Thr Gly Gly Val Leu Ala Leu
260 265 270

Asn Glu Phe Pro Asp Glu Tyr Arg Lys Leu Ser Ala Asn Pro Ala Leu
275 280 285

Ile Ser Ser Met Val Ser Glu Ile Ile Arg Trp Gln Thr Pro Leu Ser
290 295 300

His Met Arg Arg Thr Ala Leu Glu Asp Ile Glu Phe Gly Gly Lys His
305 310 315 320

Ile Arg Gln Gly Asp Lys Val Val Met Trp Tyr Val Ser Gly Asn Arg
325 330 335

Page 197

03/04/2007

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Asp Pro Glu Ala Ile Asp Asn Pro Asp Thr Phe Ile Ile Asp Arg Ala
340 345 350

Lys Pro Arg Gln His Leu Ser Phe Gly Phe Gly Ile His Arg Cys Val
355 360 365

Gly Asn Arg Leu Ala Glu Leu Gln Leu Asn Ile Leu Trp Glu Glu Ile
370 375 380

Leu Lys Arg Trp Pro Asp Pro Leu Gln Ile Gln Val Leu Gln Glu Pro
385 390 395 400

Thr Arg Val Leu Ser Pro Phe Val Lys Gly Tyr Glu Ser Leu Pro Val
405 410 415

Arg Ile Asn Ala
420

<210> 55
<211> 416
<212> PRT
<213> Sphingopyxis macroglutabida

<220>
<221> MISC_FEATURE
<222> (1) (416)
<223> Cytochrome P450 enzyme CYP153A7

<400> 55

Met Glu His Thr Gly Gln Ser Ala Ala Ala Thr Met Pro Leu Asp Ser
1 5 10 15

Ile Asp Val Ser Ile Pro Glu Leu Phe Tyr Asn Asp Ser Val Gly Glu
20 25 30

Tyr Phe Lys Arg Leu Arg Lys Asp Asp Pro Val His Tyr Cys Ala Asp
35 40 45

Ser Ala Phe Gly Pro Tyr Trp Ser Ile Thr Lys Tyr Asn Asp Ile Met
50 55 60

His Val Asp Thr Asn His Asp Ile Phe Ser Ser Asp Ala Gly Tyr Gly
65 70 75 80

Gly Ile Ile Ile Asp Asp Gly Ile Gln Lys Gly Gly Asp Gly Gly Leu
85 90 95

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Asp Leu Pro Asn Phe Ile Ala Met Asp Arg Pro Arg His Asp Glu Gln
 100 105 110

Arg Lys Ala Val Ser Pro Ile Val Ala Pro Ala Asn Leu Ala Ala Leu
 115 120 125

Glu Gly Thr Ile Arg Glu Arg Val Ser Lys Thr Leu Asp Gly Leu Pro
 130 135 140

Val Gly Glu Glu Phe Asp Trp Val Asp Arg Val Ser Ile Glu Ile Thr
 145 150 155 160

Thr Gln Met Leu Ala Thr Leu Phe Asp Phe Pro Phe Glu Glu Arg Arg
 165 170 175

Lys Leu Thr Arg Trp Ser Asp Val Thr Thr Ala Ala Pro Gly Gly Gly
 180 185 190

Val Val Glu Ser Trp Asp Gln Arg Lys Thr Glu Leu Leu Glu Cys Ala
 195 200 205

Ala Tyr Phe Gln Val Leu Trp Asn Glu Arg Val Asn Lys Asp Pro Gly
 210 215 220

Asn Asp Leu Ile Ser Met Leu Ala His Ser Pro Ala Thr Arg Asn Met
 225 230 235 240

Thr Pro Glu Glu Tyr Leu Gly Asn Val Leu Leu Leu Ile Val Gly Gly
 245 250 255

Asn Asp Thr Thr Arg Asn Ser Met Thr Gly Gly Val Leu Ala Leu His
 260 265 270

Lys Asn Pro Asp Gln Phe Ala Lys Leu Lys Ala Asn Pro Ala Leu Val
 275 280 285

Glu Thr Met Val Pro Glu Ile Ile Arg Trp Gln Thr Pro Leu Ala His
 290 295 300

Met Arg Arg Thr Ala Ile Ala Asp Ser Glu Leu Gly Gly Lys Thr Ile
 305 310 315 320

Arg Lys Gly Asp Lys Val Val Met Trp Tyr Tyr Ser Gly Asn Arg Asp
 325 330 335

Asp Glu Val Ile Asp Arg Pro Glu Glu Phe Ile Ile Asp Arg Pro Arg
 340 345 350

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Pro Arg Gln His Leu Ser Phe Gly Phe Gly Ile His Arg Cys Val Gly
355 360 365

Asn Arg Leu Ala Glu Met Gln Leu Arg Ile Leu Trp Glu Glu Ile Leu
370 375 380

Thr Arg Phe Ser Arg Ile Glu Val Met Ala Glu Pro Glu Arg Val Arg
385 390 395 400

Ser Asn Phe Val Arg Gly Tyr Ala Lys Met Met Val Arg Val His Ala
405 410 415

<210> 56
<211> 419
<212> PRT
<213> Sphingopyxis macroglutabida

<220>
<221> MISC_FEATURE
<222> (1)..(419)
<223> Cytochrome P450 enzyme CYP153A8

<400> 56

Met Asp Thr Asp Met Val Glu Pro Asn Ile Arg Glu Lys Val Ala Phe
1 5 10 15

Ile Pro Ile Asp Glu Ile Asp Val Ala Arg Pro Ser Leu Phe Gln Lys
20 25 30

Asp Thr Val Gly Leu Phe Phe Glu Arg Leu Arg Arg Glu Glu Pro Val
35 40 45

His Tyr Cys Arg Glu Ser Tyr Val Gly Pro Tyr Trp Ser Ile Thr Lys
50 55 60

Phe Asp Asp Ile Met Ala Val Asp Thr Asn His Lys Val Phe Ser Ser
65 70 75 80

Glu Ala Lys Leu Gly Gly Ile Ala Ile Glu Asp Met His Ser Ala Lys
85 90 95

Ser Ala Leu Glu Leu Glu Met Phe Ile Ala Met Asp Pro Pro Lys His
100 105 110

Asn Gln Gln Arg Lys Ala Val Thr Gly Ala Val Ala Pro Ser Asn Leu
115 120 125

Leu Leu Leu Glu Pro Thr Ile Arg Glu Arg Ala Cys Gln Ile Leu Asp
Page 200

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

140

130

135

Asp Leu Pro Val Gly Glu Asp Ile Asp Trp Val Asp Lys Val Ala Val
 145 150 155 160

Glu Leu Thr Thr Met Thr Leu Ala Thr Leu Phe Asp Phe Pro Trp Glu
 165 170 175

Glu Arg Arg Lys Thr Arg Trp Ser Asp Val Thr Thr Ala Ala Pro Glu
 180 185 190

Thr Gly Ile Val Ala Ser Tyr Glu Ala Arg Arg Ala Glu Leu Ile Glu
 195 200 205

Cys Ala Met Tyr Phe Lys Gly Leu Trp Glu Gln Arg Ile Asn Ala Glu
 210 215 220

Pro Lys Asn Asp Leu Ile Ser Met Met Ala His Ser Pro Ala Thr Arg
 225 230 235 240

Asp Met Pro Phe Leu Glu Phe Leu Gly Asn Leu Leu Leu Ile Val
 245 250 255

Gly Gly Asn Asp Thr Thr Arg Asn Ser Ile Ser Gly Gly Val Leu Ala
 260 265 270

Leu Asn Gln Asn Pro Asp Ala Tyr Leu Lys Leu Asn Asn Asp Pro Gly
 275 280 285

Leu Ile Thr Ser Met Val Pro Glu Ile Ile Arg Trp Gln Thr Pro Leu
 290 295 300

Thr His Met Arg Arg Thr Ala Leu Gln Asp Trp Glu Ile Gly Gly Lys
 305 310 315 320

Lys Ile Arg Lys Gly Asp Lys Val Val Met Trp Tyr Leu Ser Gly Asn
 325 330 335

Arg Asp Glu Thr Val Ile Asp Arg Ala Asp Glu Phe Ile Ile Asp Arg
 340 345 350

Lys Asn Pro Arg His His Leu Ser Phe Gly Tyr Gly Ile His Arg Cys
 355 360 365

Met Gly Asn Arg Leu Ala Glu Leu Gln Leu Arg Ile Ile Trp Glu Glu
 370 375 380

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Ile His Lys Arg Phe Ala Lys Ile Glu Val Thr Gly Glu Pro Glu Arg
385 390 395 400

Leu Phe Ser Asn Leu Val Arg Gly Ile Thr Lys Leu Pro Val Arg Leu
405 410 415

His' Ala Arg

<210> 57
<211> 425
<212> PRT
<213> Sphingopyxis macroglabida

<220>
<221> MISC_FEATURE
<222> (1)..(425)
<223> Cytochrome P450 enzyme CYP153A11

<400> 57

Met Ala Thr Arg Ser Met Gln Ser Gly Pro Asp Arg Glu Glu Pro Asp
1 5 10 15

Arg Pro Ile Ala Glu Ile Pro Leu Ala Glu Ile Asp Val Ser Arg Pro
20 25 30

Ser Leu Phe Gln Ser Asp Lys Val Gly Ala Phe Phe Glu Arg Leu Arg
35 40 45

Arg Glu Asp Pro Val His Tyr Cys Ser Glu Ser Ala Phe Gly Pro Tyr
50 55 60

Trp Ser Ile Thr Arg Tyr Asn Asp Ile Met Ala Val Asp Thr Asn His
65 70 75 80

Lys Leu Phe Ser Ser Glu Ala Lys Leu Gly Gly Ile Ala Ile Gln Asp
85 90 95

Met His Asn Asp Ala Thr Asn Leu Glu Leu Met Phe Ile Ala Met
100 105 110

Asp Gln Pro Lys His Asp Ala Gln Arg Lys Ala Val Thr Pro Ala Val
115 120 125

Ala Pro Ser Asn Leu Leu Leu Leu Glu Pro Val Ile Arg Glu Arg Ala
130 135 140

Gly Ala Ile Leu Asp Ser Leu Pro Val Gly Glu Glu Ile Asp Trp Val
145 150 155 160

Printed: 10/30/2007

SP001ST

PCT/US2007/017499

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Lys Ser Val Ser Val Glu Leu Thr Thr Met Thr Leu Ala Thr Leu Phe
165 170 175

Asp Phe Pro Trp Asp Glu Arg Ala Lys Leu Thr Arg Trp Ser Asp Val
180 185 190

Thr Thr Ala Ile Pro Gly Ser Gly Ile Val Glu Ser Asn Glu Gln Arg
195 200 205

Arg Gln Glu Leu Ile Glu Cys Ala Met Tyr Phe Lys Gly Leu Trp Asp
210 215 220

Gln Arg Ile Asp Arg Ser Glu Gly Ser Asp Leu Ile Thr Met Met Ala
225 230 235 240

Asn Ser Pro Ala Thr Arg Glu Met Pro Phe Leu Glu Phe Leu Gly Asn
245 250 255

Leu Leu Leu Leu Ile Val Gly Gly Asn Asp Thr Thr Arg Asn Ser Ile
260 265 270

Ser Gly Gly Val Ile Ala Leu Asn Gln Asn Pro Asp Gln Tyr Glu Lys
275 280 285

Leu Arg Gln His Pro Ser Leu Ile Gly Ser Met Val Pro Glu Ile Ile
290 295 300

Arg Trp Gln Thr Pro Leu Thr His Met Arg Arg Thr Ala Leu Ala Asp
305 310 315 320

Ser Glu Ile Gly Gly Lys Arg Ile Ala Lys Gly Asp Lys Val Val Met
325 330 335

Trp Tyr Leu Ser Gly Asn Arg Asp Glu Thr Val Ile Glu Arg Pro Glu
340 345 350

Glu Phe Ile Ile Asp Arg Lys Asn Pro Arg Gln His Leu Ser Phe Gly
355 360 365

Tyr Gly Ile His Arg Cys Met Gly Asn Arg Leu Ala Glu Leu Gln Leu
370 375 380

Arg Ile Ile Trp Glu Glu Ile His Lys Arg Phe Arg Leu Val Glu Met
385 390 395 400

Val Gly Glu Pro Glu Arg Leu Leu Ser Asn Leu Val Arg Gly Ile Thr

08/04/2007

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

405

410

415

Arg Leu Pro Val Lys Leu His Ala His
420 425

<210> 58
<211> 429
<212> PRT
<213> Sphingopyxis macrogoltabida

<220>
<221> MISC_FEATURE
<222> (1)...(429)
<223> Cytochrome P450 enzyme CYP153D2

<400> 58

Met Ala Thr Val Ile Arg Glu Thr Pro Ala Asp Leu His Pro Leu Asp
1 5 10 15

Leu Ser Arg Ala Asp Leu Trp Arg Glu Asp Gln Trp Gln Glu Pro Met
20 25 30

Arg Gln Leu Arg Ala Glu Ser Pro Ile Tyr Tyr Cys Glu Asp Ser Lys
35 40 45

Phe Gly Pro Tyr Trp Ser Val Thr Thr Tyr Lys Pro Ile Gln His Ile
50 55 60

Glu Ala Leu Pro Lys Ile Phe Ser Ser Ser Trp Glu Tyr Gly Gly Ile
65 70 75 80

Thr Val Ala Gly Asp Gly Ile Glu His Leu Lys Glu Gly Glu Ile Pro
85 90 95

Met Pro Met Phe Ile Ala Met Asp Pro Pro Gln His Thr Ala Gln Arg
100 105 110

Arg Thr Val Ala Pro Ala Phe Gly Pro Ser Glu Ile Glu Arg Met Arg
115 120 125

Ala Asp Thr Gln Ala Arg Thr Ala Ala Leu Ile Asp Thr Leu Pro Val
130 135 140

Gly Glu Ala Phe Asp Trp Val Glu Arg Leu Ser Ile Glu Leu Thr Thr
145 150 155 160

Asp Met Leu Ala Ile Leu Phe Asp Phe Pro Trp Glu Asn Arg His Asn
165 170 175

Printed: 10/30/2007

SPRINT

PCT/US2007/017409

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Leu Thr Arg Trp Ser Asp Ala Leu Gly Asp Ile Glu Ser Phe Asn Thr
180 185 190

Leu Glu Glu Arg Gln Gln Arg Leu Ala Thr Ala Phe Glu Met Gly Ala
195 200 205

Ala Phe Lys Glu Leu Trp Asp His Lys Ala Lys Asn Pro Gly Lys His
210 215 220

Asp Leu Ile Ser Ile Met Leu Gln Ser Asp Ala Met Asn His Met Ser
225 230 235 240

His Glu Glu Phe Met Gly Asn Leu Ile Leu Leu Ile Val Gly Gly Asn
245 250 255

Asp Thr Thr Arg Asn Ser Met Ser Ala Tyr Ala Tyr Gly Leu His Cys
260 265 270

Phe Pro Glu Glu Arg Ala Lys Leu Glu Ala Asn His Asp Pro Asp Leu
275 280 285

Ala Val Asn Ala Met His Glu Ile Ile Arg Trp Gln Thr Pro Leu Ala
290 295 300

His Met Arg Arg Thr Ala Leu Glu Asp Thr Glu Leu Phe Gly His Gln
305 310 315 320

Ile Arg Ala Arg Asp Lys Ile Ala Leu Trp Tyr Ala Ser Ala Asn Arg
325 330 335

Asp Glu Ser Ile Phe Pro Asp Gly Asp Arg Ile Ile Val Asp Arg Glu
340 345 350

Asn Ala Arg Arg His Leu Ala Phe Gly Tyr Gly Ile His Arg Cys Val
355 360 365

Gly Ala Arg Val Ala Glu Leu Gln Leu Thr Thr Leu Ile Ser Glu Met
370 375 380

Gln Lys Arg Arg Leu Arg Val Asn Val Leu Ala Glu Pro Glu Arg Val
385 390 395 400

Asn Ala Ser Phe Val His Val Ser Pro His Ala Gly Arg Thr Arg Ala
405 410 415

Leu Leu Thr Ala Val Thr Ala Gly Pro Ile Ser Ala Arg
420 425

Page 205

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan'et al.

Express/Mailing Label No: EB511841342US

Attorney Docket: P008-CIT.

P008-CIT_ST25.txt

<210> 59
 <211> 416
 <212> PRT
 <213> Sphingopyxis macroglutabida

<220>
 <221> MISC_FEATURE
 <222> (1) (416)
 <223> Cytochrome P450 enzyme CYP153D3

<400> 59

Met Ala Ser Thr Ala Thr Leu Val Arg Thr Ala Ser Pro Ile Ala Pro
 1 5 10 15

Ile Asp Val Ser Leu Pro Glu Leu Tyr Ala Glu Asp Arg Trp Gln Glu
 20 25 30

Pro Phe Arg Thr Leu Arg Ala Gln Ala Pro Ile Gln Tyr Val Pro Asp
 35 40 45

Ser Lys Phe Gly Pro Tyr Trp Ser Val Thr Thr Tyr Lys Pro Ile Val
 50 55 60

Tyr Ile Glu Ala Leu Pro Lys Leu Phe Ser Ser Ser Trp Gln Tyr Gly
 65 70 75 80

Gly Ile Ser Ile Ala Phe Asp Ser Asp Lys Leu Leu Glu His Glu Val
 85 90 95

Arg Gln Pro Met Phe Ile Ala Met Asp Pro Pro Gln His Thr Ala Gln
 100 105 110

Arg Arg Thr Val Ala Xaa Ser Phe Gly Pro Ser Glu Val Ala Ala Met
 115 120 125

Lys Ala Glu Val Gln Leu Arg Thr Gly Ala Leu Asp Ser Leu Pro
 130 135 140

Val Gly Asp Pro Phe Asp Trp Val Gln Lys Val Ser Ile Glu Leu Thr
 145 150 155 160

Thr Gly Met Leu Ala Arg Leu Phe Asp Phe Pro Trp Glu Glu Arg His
 165 170 175

Asn Leu Thr His Trp Ser Asp Ile Gly Gly Asp Val Glu Leu Ile Arg
 180 185 190

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Ser Pro Glu Gly Leu Val Glu Arg Asn Thr Lys Leu Leu Gln Met Gly
 195 200 205

Met Ala Phe Ala Ala Leu Trp Gln Glu Lys Ala Gln Asn Pro Gly Lys
 210 215 220

Asp Leu Ile Ser Val Met Leu Lys Ser Asp Ala Met Asn His Met Ser
 225 230 235 240

Asn Glu Glu Phe Ile Gly Asn Leu Val Leu Leu Ile Val Gly Gly Asn
 245 250 255

Asp Thr Thr Arg Asn Ser Met Ser Ser Tyr Ala Tyr Gly Leu Ala Gln
 260 265 270

Phe Pro Glu Glu Arg Ala Lys Leu Glu Ala Asn Pro Ala Leu Ile Pro
 275 280 285

Asn Ala Val Gln Glu Leu Ile Arg Trp Gln Thr Pro Leu Ala His Met
 290 295 300

Arg Arg Thr Val Glu Glu Asp Thr Glu Ile Xaa Gly Gln Xaa Xaa Lys
 305 310 315 320

Lys Gly Asp Lys Val Val Leu Trp Tyr Leu Ser Ala Asn Arg Asp Gly
 325 330 335

Thr Val Phe Lys Asp Ala Asp Arg Ile Ile Val Gly Arg Glu Asn Ala
 340 345 350

Arg Arg His Leu Ser Phe Gly Tyr Gly Ile His Arg Cys Val Gly Ala
 355 360 365

Arg Val Ala Glu Leu Gln Leu Val Thr Leu Leu Glu Glu Met Ala Lys
 370 375 380

Arg Arg Leu Arg Ala Asn Val Leu Ala Glu Pro Val Arg Val Pro Ala
 385 390 395 400

Cys Phe Val His Gly Tyr Lys Ser Leu Gln Val Glu Leu Ser His Tyr
 405 410 415

<210> 60

<211> 470

<212> PRT

<213> Alcanivorax borkumensis

<220>

Printed: 10/30/2007

5:00:15

PCT/US2007/017409

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

<221> MISC_FEATURE

<222> (1)...(470)

<223> Cytochrome P450 enzyme CYP153A1kBurk

<400> 60

Met Ser Thr Ser Ser Ser Thr Ser Asn Asp Ile Gln Ala Lys Val Ile
1 5 10 15

Asn Ala Thr Ser Lys Val Val Pro Met His Leu Gln Ile Lys Ala Leu
20 25 30

Lys Asn Leu Met Lys Val Lys Arg Lys Thr Ile Gly Thr Ser Arg Pro
35 40 45

Gln Val His Phe Val Glu Thr Asp Leu Pro Asp Val Asn Asp Leu Ala
50 55 60

Ile Glu Asp Ile Asp Thr Ser Asn Pro Phe Leu Tyr Arg Gln Gly Lys
65 70 75 80

Ala Asn Ala Tyr Phe Lys Arg Leu Arg Asp Glu Ala Pro Val His Tyr
85 90 95

Gln Lys Asn Ser Ala Phe Gly Pro Phe Trp Ser Val Thr Arg Tyr Glu
100 105 110

Asp Ile Val Phe Val Asp Lys Ser His Asp Leu Phe Ser Ala Glu Pro
115 120 125

Gln Ile Ile Leu Gly Asp Pro Pro Glu Gly Leu Ser Val Glu Met Phe
130 135 140

Ile Ala Met Asp Pro Pro Lys His Asp Val Gln Arg Arg Ala Val Gln
145 150 155 160

Gly Val Val Ala Pro Lys Asn Leu Lys Glu Met Glu Gly Leu Ile Arg
165 170 175

Lys Arg Thr Gly Asp Val Leu Asp Ser Leu Pro Leu Asp Thr Pro Phe
180 185 190

Asn Trp Val Pro Val Val Ser Lys Glu Leu Thr Gly Arg Met Leu Ala
195 200 205

Ser Leu Leu Asp Phe Pro Tyr Asp Glu Arg Glu Lys Leu Val Gly Trp
210 215 220

Ser Asp Arg Leu Ser Gly Ala Ser Ser Ala Thr Gly Gly Glu Phe Thr
Page 208

08/04/2007

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

225

230

235

240

Asn Glu Asp Val Phe Phe Asp Asp Ala Ala Asp Met Ala Trp Ala Phe
 245 250 255

Ser Lys Leu Trp Arg Asp Lys Glu Ala Arg Gln Lys Ala Gly Glu Glu
 260 265 270

Pro Gly Phe Asp Leu Ile Ser Met Leu Gln Ser Asn Glu Asp Thr Lys
 275 280 285

Asp Leu Ile Asn Arg Pro Leu Glu Phe Ile Gly Asn Leu Ala Leu Leu
 290 295 300

Ile Val Gly Gly Asn Asp Thr Thr Arg Asn Ser Met Ser Gly Gly Val
 305 310 315 320

Leu Ala Leu Asn Gln Phe Pro Glu Gln Phe Glu Lys Leu Lys Ala Asn
 325 330 335

Pro Lys Leu Ile Pro Asn Met Val Ser Glu Ile Ile Arg Trp Gln Thr
 340 345 350

Pro Leu Ala Tyr Met Arg Arg Val Ala Lys Gln Asp Val Glu Leu Asn
 355 360 365

Gly Glu Thr Ile Lys Lys Gly Asp Arg Val Leu Met Trp Tyr Ala Ser
 370 375 380

Gly Asn Gln Asp Glu Arg Lys Phe Glu Asn Pro Glu Gln Phe Ile Ile
 385 390 395 400

Asp Arg Lys Asp Thr Arg Asn His Val Ser Phe Gly Tyr Gly Val His
 405 410 415

Arg Cys Met Gly Asn Arg Leu Ala Glu Leu Gln Leu Arg Ile Leu Trp
 420 425 430

Glu Glu Leu Leu Pro Arg Phe Glu Asn Ile Glu Val Ile Gly Glu Pro
 435 440 445

Glu Arg Val Gln Ser Asn Phe Val Arg Gly Tyr Ser Lys Met Met Val
 450 455 460

Lys Leu Thr Ala Lys Lys
 465 470

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

<210> 61
 <211> 497
 <212> PRT
 <213> Acinetobacter 'sp EB104

<220>
 <221> MISC_FEATURE
 <222> (1)..(497)
 <223> Cytochrome P450 enzyme CYP153EB104

<400> 61

Met Asn Ser Val Ala Glu Ile Phe Glu Lys Ile Thr Gln Thr Val Thr
 1 5 10 15

Ser Thr Ala Ala Asp Val Ala Thr Thr Val Thr Asp Lys Val Lys Ser
 20 25 30

Asn Glu Gln Phe Gln Thr Gly Lys Gln Phe Leu His Gly Gln Val Thr
 35 40 45

Arg Phe Val Pro Leu His Thr Gln Val Arg Gly Ile Gln Trp Met Gln
 50 55 60

Lys Ala Lys Phe Arg Val Phe Asn Val Gln Glu Phe Pro Ala Phe Ile
 65 70 75 80

Glu Gln Pro Ile Pro Glu Val Ala Thr Leu Ala Leu Ala Glu Ile Asp
 85 90 95

Val Ser Asn Pro Phe Leu Tyr Lys Gln Lys Lys Trp Gln Ser Tyr Phe
 100 105 110

Lys Arg Leu Arg Asp Glu Ala Pro Val His Tyr Gln Ala Asn Ser Pro
 115 120 125

Phe Gly Ala Phe Trp Ser Val Thr Arg Tyr Asp Asp Ile Val Tyr Val
 130 135 140

Asp Lys Asn His Glu Ile Phe Ser Ala Glu Pro Val Ile Ala Ile Gly
 145 150 155 160

Asn Thr Pro Pro Gly Leu Asp Ala Glu Met Phe Ile Ala Met Asp Pro
 165 170 175

Pro Lys His Asp Val Gln Arg Gln Ala Val Gln Asp Val Val Ala Pro
 180 185 190

Lys Asn Leu Lys Glu Leu Glu Gly Leu Ile Arg Leu Arg Val Gln Gly
 195 200 205

Printed: 10/30/2007

USP0151

PCT/US2007/017409

10307517409

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Val Leu Asp Gln Leu-Pro Thr Asp Gln Pro Phe Asp Trp Val Gln Asn
210 215 220

Val Ser Ile Glu Leu Thr Ala Arg Met Leu Ala Thr Leu Phe Asp Phe
225 230 235 240

Pro Tyr Glu Lys Arg His Lys Leu Val Glu Trp Ser Asp Leu Met Ala
245 250 255

Gly Thr Ala Glu Ala Thr Gly Gly Thr Val Thr Asn Leu Asp Glu Ile
260 265 270

Phe Asp Ala Ala Val Asp Ala Ala Lys His Phe Ala Glu Leu Trp His
275 280 285

Arg Lys Ala Ala Gln Lys Ser Ala Gly Ala Glu Met Gly Tyr Asp Leu
290 295 300

Ile Ser Leu Met Gln Ser Asn Glu Ala Thr Lys Asp Leu Ile Tyr Arg
305 310 315 320

Pro Met Glu Phe Met Gly Asn Leu Val Leu Leu Ile Val Gly Gly Asn
325 330 335

Asp Thr Thr Arg Asn Ser Met Thr Gly Gly Val Tyr Ala Leu Asn Leu
340 345 350

Phe Pro Asn Glu Phe Val Lys Leu Lys Asn Asn Pro Ser Leu Ile Pro
355 360 365

Asn Met Val Ser Glu Ile Ile Arg Trp Gln Thr Pro Leu Ala Tyr Met
370 375 380

Arg Arg Ile Ala Lys Gln Asp Val Glu Leu Asn Gly Gln Thr Ile Lys
385 390 395 400

Lys Gly Asp Lys Val Val Met Trp Tyr Val Ser Gly Asn Arg Asp Glu
405 410 415

Arg Val Ile Glu Arg Pro Asp Glu Leu Ile Ile Asp Arg Lys Gly Ala
420 425 430

Arg Asn His Leu Ser Phe Gly Phe Gly Val His Arg Cys Met Gly Asn
435 440 445

Arg Leu Ala Glu Met Gln Leu Arg Ile Leu Trp Glu Glu Leu Leu Gln
Page 211

08/04/2007

Printed: 10/30/2007

SEQUENCE

PCT/US2007/017409

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

450

455

460

Arg Phe Glu Asn Ile Glu Val Leu Gly Glu Pro Glu Ile Val Gln Ser
465 470 475 480

Asn Phe Val Arg Gly Tyr Ala Lys Met Met Val Lys Leu Thr Ala Lys
485 490 495

Ala

<210> 62
<211> 497
<212> PRT
<213> Acinetobacter sp OC4

<220>
<221> MISC_FEATURE
<222> (1)..(497)
<223> Cytochrome P450 enzyme CYP1530C4

<400> 62

Met Asn Ser Val Ala Glu Ile Phe Glu Lys Ile Thr Gln Thr Val Thr
1 5 10 15

Ser Thr Ala Ala Asp Val Ala Thr Thr Val Thr Asp Lys Val Lys Ser
20 25 30

Asn Glu Gln Phe Gln Thr Gly Lys Gln Phe Leu His Gly Gln Val Thr
35 40 45

Arg Phe Val Pro Leu His Thr Gln Val Arg Gly Ile Gln Trp Met Gln
50 55 60

Lys Ala Lys Phe Arg Val Phe Asn Val Gln Glu Phe Pro Ala Phe Ile
65 70 75 80

Glu Gln Pro Ile Pro Glu Val Ala Thr Leu Ala Leu Ala Glu Ile Asp
85 90 95

Val Ser Asn Pro Phe Leu Tyr Lys Gln Lys Lys Trp Gln Ser Tyr Phe
100 105 110

Lys Arg Leu Arg Asp Glu Ala Pro Val His Tyr Gln Ala Asn Ser Pro
115 120 125

Phe Gly Ala Phe Trp Ser Val Thr Arg Tyr Asp Asp Ile Val Tyr Val
130 135 140

Page 212

08/04/2007

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Asp Lys Asn His Glu Ile Phe Ser Ala Glu Pro Val Ile Ala Ile Gly
 145 150 155 160

Asn Thr Pro Pro Gly Leu Gly Ala Glu Met Phe Ile Ala Met Asp Pro
 165 170 175

Pro Lys His Asp Val Gln Arg Gln Ala Val Gln Asp Val Val Ala Pro
 180 185 190

Lys Asn Leu Lys Glu Leu Glu Gly Leu Ile Arg Leu Arg Val Gln Glu
 195 200 205

Val Leu Asp Gln Leu Pro Thr Asp Gln Pro Phe Asp Trp Val Gln Asn
 210 215 220

Val Ser Ile Glu Leu Thr Ala Arg Met Leu Ala Thr Leu Phe Asp Phe
 225 230 235 240

Pro Tyr Glu Lys Arg His Lys Leu Val Glu Trp Ser Asp Leu Met Ala
 245 250 255

Gly Thr Ala Glu Ala Thr Gly Gly Thr Val Thr Asn Leu Asp Glu Ile
 260 265 270

Phe Asp Ala Ala Val Asp Ala Ala Lys His Phe Ala Glu Leu Trp His
 275 280 285

Arg Lys Ala Ala Gln Lys Ser Ala Gly Ala Glu Met Gly Tyr Asp Leu
 290 295 300

Ile Ser Leu Met Gln Ser Asn Glu Ala Thr Lys Asp Leu Ile Tyr Arg
 305 310 315 320

Pro Met Glu Phe Met Gly Asn Leu Val Leu Leu Ile Val Gly Gly Asn
 325 330 335

Asp Thr Thr Arg Asn Ser Met Thr Gly Gly Val Tyr Ala Leu Asn Leu
 340 345 350

Phe Pro Asn Glu Phe Val Lys Leu Lys Asn Asn Pro Ser Leu Ile Pro
 355 360 365

Asn Met Val Ser Glu Ile Ile Arg Trp Gln Thr Pro Leu Ala Tyr Met
 370 375 380

Arg Arg Ile Ala Lys Gln Asp Val Glu Leu Asn Gly Gln Thr Ile Lys
 385 390 395 400

Printed: 10/30/2007

ST

PCT/US2007/017409

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Lys Gly Asp Lys Val Val Met Trp Tyr Val Ser Gly Asn Arg Asp Glu
405 410 415

Arg Val Ile Glu Arg Pro Asp Glu Leu Ile Ile Asp Arg Lys Gly Ala
420 425 430

Arg Asn His Leu Ser Phe Gly Phe Gly Val His Arg Cys Met Gly Asn
435 440 445

Arg Leu Ala Glu Met Gln Leu Arg Ile Leu Trp Glu Glu Leu Leu Gln
450 455 460

Arg Phe Glu Asn Ile Glu Val Leu Gly Glu Pro Glu Ile Val Gln Ser
465 470 475 480

Asn Phe Val Arg Gly Tyr Ala Lys Met Met Val Lys Leu Thr Ala Lys
485 490 495

Ala

<210> 63
<211> 1059
<212> PRT
<213> Artificial Sequence

<220>
<223> Cytochrome P450 variant CYP102A2var1

<400> 63

Lys Glu Thr Ser Pro Ile Pro Gln Pro Lys Thr Phe Gly Pro Leu Gly
1 5 10 15

Asn Leu Pro Leu Ile Asp Lys Asp Lys Pro Thr Leu Ser Leu Ile Lys
20 25 30

Leu Ala Glu Glu Gln Gly Pro Ile Phe Gln Ile His Thr Pro Ala Gly
35 40 45

Thr Thr Ile Val Val Ser Gly His Glu Leu Val Lys Glu Val Cys Asp
50 55 60

Glu Glu Arg Phe Asp Lys Ser Ile Glu Gly Ala Leu Glu Lys Val Arg
65 70 75 80

Ala Phe Ser Gly Asp Gly Leu Ala Thr Ser Trp Thr His Glu Pro Asn
85 90 95

Printed: 10/30/2007

8:01:51

PCT/US2007/017409

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Trp Arg Lys Ala His Asn Ile Leu Met Pro Thr Phe Ser Gln Arg Ala
100 105 110

Met Lys Asp Tyr His Glu Lys Met Val Asp Ile Ala Val Gln Leu Ile
115 120 125

Gln Lys Trp Ala Arg Leu Asn Pro Asn Glu Ala Val Asp Val Pro Gly
130 135 140

Asp Met Thr Arg Leu Thr Leu Asp Thr Ile Gly Leu Cys Gly Phe Asn
145 150 155 160

Tyr Arg Phe Asn Ser Tyr Tyr Arg Glu Thr Pro His Pro Phe Ile Asn
165 170 175

Ser Met Val Arg Ala Leu Asp Glu Ala Met His Gln Met Gln Arg Leu
180 185 190

Asp Val Gln Asp Lys Leu Met Val Arg Thr Lys Arg Gln Phe Arg Tyr
195 200 205

Asp Ile Gln Thr Met Phe Ser Leu Val Asp Ser Ile Ile Ala Glu Arg
210 215 220

Arg Ala Asn Gly Asp Gln Asp Glu Lys Asp Leu Leu Ala Arg Met Leu
225 230 235 240

Asn Val Glu Asp Pro Glu Thr Gly Glu Lys Leu Asp Asp Glu Asn Ile
245 250 255

Arg Phe Gln Ile Ile Thr Phe Leu Ile Ala Gly His Glu Thr Thr Ser
260 265 270

Gly Leu Leu Ser Phe Ala Thr Tyr Phe Leu Leu Lys His Pro Asp Lys
275 280 285

Leu Lys Lys Ala Tyr Glu Glu Val Asp Arg Val Leu Thr Asp Ala Ala
290 295 300

Pro Thr Tyr Lys Gln Val Leu Glu Leu Thr Tyr Ile Arg Met Ile Leu
305 310 315 320

Asn Glu Ser Leu Arg Leu Trp Pro Thr Ala Pro Ala Phe Ser Leu Tyr
325 330 335

Pro Lys Glu Asp Thr Val Ile Gly Gly Lys Phe Pro Ile Thr Thr Asn
340 345 350

Page 215

08/04/2007

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Asp Arg Ile Ser Val Leu Ile Pro Gln Leu His Arg Asp Arg Asp Ala
355 360 365

Trp Gly Lys Asp Ala Glu Glu Phe Arg Pro Glu Arg Phe Glu His Gln
370 375 380

Asp Gln Val Pro His His Ala Tyr Lys Pro Phe Gly Asn Gly Gln Arg
385 390 395 400

Ala Cys Ile Gly Met Gln Phe Ala Leu His Glu Ala Thr Leu Val Leu
405 410 415

Gly Met Ile Leu Lys Tyr Phe Thr Leu Ile Asp His Glu Asn Tyr Glu
420 425 430

Leu Asp Ile Lys Gln Thr Leu Thr Leu Lys Pro Gly Asp Phe His Ile
435 440 445

Ser Val Gln Ser Arg His Gln Glu Ala Ile His Ala Asp Val Gln Ala
450 455 460

Ala Glu Lys Ala Ala Pro Asp Glu Gln Lys Glu Lys Thr Glu Ala Lys
465 470 475 480

Gly Ala Ser Val Ile Gly Leu Asn Asn Arg Pro Leu Leu Val Leu Tyr
485 490 495

Gly Ser Asp Thr Gly Thr Ala Glu Gly Val Ala Arg Glu Leu Ala Asp
500 505 510

Thr Ala Ser Leu His Gly Val Arg Thr Lys Thr Ala Pro Leu Asn Asp
515 520 525

Arg Ile Gly Lys Leu Pro Lys Glu Gly Ala Val Val Ile Val Thr Ser
530 535 540

Ser Tyr Asn Gly Lys Pro Pro Ser Asn Ala Gly Gln Phe Val Gln Trp
545 550 555 560

Leu Gln Glu Ile Lys Pro Gly Glu Leu Glu Gly Val His Tyr Ala Val
565 570 575

Phe Gly Cys Gly Asp His Asn Trp Ala Ser Thr Tyr Gln Tyr Val Pro
580 585 590

Arg Phe Ile Asp Glu Gln Leu Ala Glu Lys Gly Ala Thr Arg Phe Ser
Page 216

Printed: 10/30/2007

1810151

PCT/US2007/017409

Title: "Methods and Systems for Selective A."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

595

600

P008-CIT_ST25.txt

605

Ala Arg Gly Glu Gly Asp Val Ser Gly Asp Phe Glu Gly Gln Leu Asp
610 615 620

Glu Trp Lys Lys Ser Met Trp Ala Asp Ala Ile Lys Ala Phe Gly Leu
625 630 635 640

Glu Leu Asn Glu Asn Ala Asp Lys Glu Arg Ser Thr Leu Ser Leu Gln
645 650 655

Phe Val Arg Gly Leu Gly Glu Ser Pro Leu Ala Arg Ser Tyr Glu Ala
660 665 670

Ser His Ala Ser Ile Ala Glu Asn Arg Glu Leu Gln Ser Ala Asp Ser
675 680 685

Asp Arg Ser Thr Arg His Ile Glu Ile Ala Leu Pro Pro Asp Val Glu
690 695 700

Tyr Gln Glu Gly Asp His Leu Gly Val Leu Pro Lys Asn Ser Gln Thr
705 710 715 720

Asn Val Ser Arg Ile Leu His Arg Phe Gly Leu Lys Gly Thr Asp Gln
725 730 735

Val Thr Leu Ser Ala Ser Gly Arg Ser Ala Gly His Leu Pro Leu Gly
740 745 750

Arg Pro Val Ser Leu His Asp Leu Leu Ser Tyr Ser Val Glu Val Gln
755 760 765

Glu Ala Ala Thr Arg Ala Gln Ile Arg Glu Leu Ala Ser Phe Thr Val
770 775 780

Cys Pro Pro His Arg Arg Glu Leu Glu Glu Leu Ser Ala Glu Gly Val
785 790 795 800

Tyr Gln Glu Gln Ile Leu Lys Lys Arg Ile Ser Met Leu Asp Leu Leu
805 810 815

Glu Lys Tyr Glu Ala Cys Asp Met Pro Phe Glu Arg Phe Leu Glu Leu
820 825 830

Leu Arg Pro Leu Lys Pro Arg Tyr Tyr Ser Ile Ser Ser Ser Pro Arg
835 840 845

Title: "Methods and Systems for Selective..."

Inventors: Rudi Pasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT-ST25.txt

Val Asn Pro Arg Gln Ala Ser Ile Thr Val Gly Val Val Arg Gly Pro
850 855 860

Ala Trp Ser Gly Arg Gly Glu Tyr Arg Gly Val Ala Ser Asn Asp Leu
865 870 875 880

Ala Glu Arg Gln Ala Gly Asp Asp Val Val Met Phe Ile Arg Thr Pro
885 890 895

Glu Ser Arg Phe Gln Leu Pro Lys Asp Pro Glu Thr Pro Ile Ile Met
900 905 910

Val Gly Pro Gly Thr Gly Val Ala Pro Phe Arg Gly Phe Leu Gln Ala
915 920 925

Arg Asp Val Leu Lys Arg Glu Gly Lys Thr Leu Gly Glu Ala His Leu
930 935 940

Tyr Phe Gly Cys Arg Asn Asp Arg Asp Phe Ile Tyr Arg Asp Glu Leu
945 950 955 960

Glu Arg Phe Glu Lys Asp Gly Ile Val Thr Val His Thr Ala Phe Ser
965 970 975

Arg Lys Glu Gly Met Pro Lys Thr Tyr Val Gln His Leu Met Ala Asp
980 985 990

Gln Ala Asp Thr Leu Ile Ser Ile Leu Asp Arg Gly Gly Arg Leu Tyr
995 1000 1005

Val Cys Gly Asp Gly Ser Lys Met Ala Pro Asp Val Glu Ala Ala
1010 1015 1020

Leu Gln Lys Ala Tyr Gln Ala Val His Gly Thr Gly Glu Gln Glu
1025 1030 1035

Ala Gln Asn Trp Leu Arg His Leu Gln Asp Thr Gly Met Tyr Ala
1040 1045 1050

Lys Asp Val Trp Ala Gly
1055

<210> 64
<211> 1052
<212> PRT
<213> Artificial Sequence

<220>
<223> Cytochrome P450 variant CYP102A3var1

Printed: 10/30/2007

PCT/US2007/017409

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

<400> 64

Lys Gln Ala Ser Ala Ile Pro Gln Pro Lys Thr Tyr Gly Pro Leu Lys
1 5 10 15

Asn Leu Pro His Leu Glu Lys Glu Gln Leu Ser Gln Ser Leu Trp Arg
20 25 30

Ile Ala Asp Glu Leu Gly Pro Ile Phe Arg Phe Asp Phe Pro Gly Val
35 40 45

Ser Ser Val Phe Val Ser Gly His Asn Leu Val Ala Glu Val Cys Asp
50 55 60

Glu Lys Arg Phe Asp Lys Asn Leu Gly Lys Gly Leu Gln Lys Val Arg
65 70 75 80

Glu Phe Gly Gly Asp Gly Leu Ala Thr Ser Trp Thr His Glu Pro Asn
85 90 95

Trp Gln Lys Ala His Arg Ile Leu Leu Pro Ser Phe Ser Gln Lys Ala
100 105 110

Met Lys Gly Tyr His Ser Met Met Leu Asp Ile Ala Thr Gln Leu Ile
115 120 125

Gln Lys Trp Ser Arg Leu Asn Pro Asn Glu Glu Ile Asp Val Ala Asp
130 135 140

Asp Met Thr Arg Leu Thr Leu Asp Thr Ile Gly Leu Cys Gly Phe Asn
145 150 155 160

Tyr Arg Phe Asn Ser Phe Tyr Arg Asp Ser Gln His Pro Phe Ile Thr
165 170 175

Ser Met Leu Arg Ala Leu Lys Glu Ala Met Asn Gln Ser Lys Arg Leu
180 185 190

Gly Leu Gln Asp Lys Met Met Val Lys Thr Lys Leu Gln Phe Gln Lys
195 200 205

Asp Ile Glu Val Met Asn Ser Leu Val Asp Arg Met Ile Ala Glu Arg
210 215 220

Lys Ala Asn Pro Asp Glu Asn Ile Lys Asp Leu Leu Ser Leu Met Leu
225 230 235 240

Printed: 10/30/2007

SECRET

PCT/US2007/017409

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt.

--Tyr Ala Lys Asp Pro Val Thr Gly Glu Thr Leu Asp Asp Glu Asn Ile
245 250 255

Arg Tyr Gln Ile Ile Thr Phe Leu Ile Ala Gly His Glu Thr Thr Ser
260 265 270

Gly Leu Leu Ser Phe Ala Ile Tyr Cys Leu Leu Thr His Pro Glu Lys
275 280 285

Leu Lys Lys Ala Gln Glu Glu Ala Asp Arg Val Leu Thr Asp Asp Thr
290 295 300

Pro Glu Tyr Lys Gln Ile Gln Gln Leu Lys Tyr Ile Arg Met Val Leu
305 310 315 320

Asn Glu Thr Leu Arg Leu Tyr Pro Thr Ala Pro Ala Phe Ser Leu Tyr
325 330 335

Ala Lys Glu Asp Thr Val Leu Gly Gly Glu Tyr Pro Ile Ser Lys Gly
340 345 350

Gln Pro Val Thr Val Leu Ile Pro Lys Leu His Arg Asp Gln Asn Ala
355 360 365

Trp Gly Pro Asp Ala Glu Asp Phe Arg Pro Glu Arg Phe Glu Asp Pro
370 375 380

Ser Ser Ile Pro His His Ala Tyr Lys Pro Phe Gly Asn Gly Gln Arg
385 390 395 400

Ala Cys Ile Gly Met Gln Phe Ala Leu Gln Glu Ala Thr Met Val Leu
405 410 415

Gly Leu Val Leu Lys His Phe Glu Leu Ile Asn His Thr Gly Tyr Glu
420 425 430

Leu Lys Ile Lys Glu Ala Leu Thr Ile Lys Pro Asp Asp Phe Lys Ile
435 440 445

Thr Val Lys Pro Arg Lys Thr Ala Ala Ile Asn Val Gln Arg Lys Glu
450 455 460

Gln Ala Asp Ile Lys Ala Glu Thr Lys Pro Lys Glu Thr Lys Pro Lys
465 470 475 480

His Gly Thr Pro Leu Leu Val Leu Phe Gly Ser Asn Leu Gly Thr Ala
485 490 495

08/04/2007

Printed: 10/30/2007

SECRET

PCT/US2007/017409

156-7409

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Glu Gly Ile Ala Gly Glu Leu Ala Ala Gln Gly Arg Gln Met Gly Phe
500 505 510

Thr Ala Glu Thr Ala Pro Leu Asp Asp Tyr Ile Gly Lys Leu Pro Glu
515 520 525

Glu Gly Ala Val Val Ile Val Thr Ala Ser Tyr Asn Gly Ala Pro Pro
530 535 540

Asp Asn Ala Ala Gly Phe Val Glu Trp Leu Lys Glu Leu Glu Glu Gly
545 550 555 560

Gln Leu Lys Gly Val Ser Tyr Ala Val Phe Gly Cys Gly Asn Arg Ser
565 570 575

Trp Ala Ser Thr Tyr Gln Arg Ile Pro Arg Leu Ile Asp Asp Met Met
580 585 590

Lys Ala Lys Gly Ala Ser Arg Leu Thr Ala Ile Gly Glu Gly Asp Ala
595 600 605

Ala Asp Asp Phe Glu Ser His Arg Glu Ser Trp Glu Asn Arg Phe Trp
610 615 620

Lys Glu Thr Met Asp Ala Phe Asp Ile Asn Glu Ile Ala Gln Lys Glu
625 630 635 640

Asp Arg Pro Ser Leu Ser Ile Thr Phe Leu Ser Glu Ala Thr Glu Thr
645 650 655

Pro Val Ala Lys Ala Tyr Gly Ala Phe Glu Gly Ile Val Leu Glu Asn
660 665 670

Arg Glu Leu Gln Thr Ala Ala Ser Thr Arg Ser Thr Arg His Ile Glu
675 680 685

Leu Glu Ile Pro Ala Gly Lys Thr Tyr Lys Glu Gly Asp His Ile Gly
690 695 700

Ile Leu Pro Lys Asn Ser Arg Glu Leu Val Gln Arg Val Leu Ser Arg
705 710 715 720

Phe Gly Leu Gln Ser Asn His Val Ile Lys Val Ser Gly Ser Ala His
725 730 735

Met Ala His Leu Pro Met Asp Arg Pro Ile Lys Val Val Asp Leu Leu
740 745 750

08/04/2007

Inventors: Rudi Pasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Ser Ser Tyr Val Glu Leu Gln Glu Pro Ala Ser Arg Leu Gln Leu Arg
 755 760 765

Glu Leu Ala Ser Tyr Thr Val Cys Pro Pro His Gln Lys Glu Leu Glu
 770 775 780

Gln Leu Val Ser Asp Asp Gly Ile Tyr Lys Glu Gln Val Leu Ala Lys
 785 790 795 800

Arg Leu Thr Met Leu Asp Phe Leu Glu Asp Tyr Pro Ala Cys Glu Met
 805 810 815

Pro Phe Glu Arg Phe Leu Ala Leu Leu Pro Ser Leu Lys Pro Arg Tyr
 820 825 830

Tyr Ser Ile Ser Ser Ser Pro Lys Val His Ala Asn Ile Val Ser Met
 835 840 845

Thr Val Gly Val Val Lys Ala Ser Ala Trp Ser Gly Arg Gly Glu Tyr
 850 855 860

Arg Gly Val Ala Ser Asn Tyr Leu Ala Glu Leu Asn Thr Gly Asp Ala
 865 870 875 880

Ala Ala Cys Phe Ile Arg Thr Pro Gln Ser Gly Phe Gln Met Pro Asn
 885 890 895

Asp Pro Glu Thr Pro Met Ile Met Val Gly Pro Gly Thr Gly Ile Ala
 900 905 910

Pro Phe Arg Gly Phe Ile Gln Ala Arg Ser Val Leu Lys Lys Glu Gly
 915 920 925

Ser Thr Leu Gly Glu Ala Leu Leu Tyr Phe Gly Cys Arg Arg Pro Asp
 930 935 940

His Asp Asp Leu Tyr Arg Glu Glu Leu Asp Gln Ala Glu Gln Asp Gly
 945 950 955 960

Leu Val Thr Ile Arg Arg Cys Tyr Ser Arg Val Glu Asn Glu Pro Lys
 965 970 975

Gly Tyr Val Gln His Leu Leu Lys Gln Asp Thr Gln Lys Leu Met Thr
 980 985 990

Leu Ile Glu Lys Gly Ala His Ile Tyr Val Cys Gly Asp Gly Ser Gln
 Page 222

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No.: EB511841342US

Attorney Docket: P008-CIT

995

1000

P008-CIT_ST25.txt

1005

Met Ala Pro Asp Val Glu Arg Thr Leu Arg Leu Ala Tyr Glu Ala
1010 1015 1020

Glu Lys Ala Ala Ser Gln Glu Glu Ser Ala Val Trp Leu Gln Lys
1025 1030 1035

Leu Gln Asp Gln Arg Arg Tyr Val Lys Asp Val Trp Thr Gly
1040 1045 1050

<210> 65
<211> 414
<212> PRT
<213> Artificial Sequence

<220>
<223> Cytochrome P450 variant CYP101A1var1

<400> 65

Thr Thr Glu Thr Ile Gln Ser Asn Ala Asn Leu Ala Pro Leu Pro Pro
1 5 10 15

His Val Pro Glu His Leu Val Phe Asp Phe Asp Met Tyr Asn Pro Ser
20 25 30

Asn Leu Ser Ala Gly Val Gln Glu Ala Trp Ala Val Leu Gln Glu Ser
35 40 45

Asn Val Pro Asp Leu Val Trp Thr Arg Cys Asn Gly Gly His Trp Ile
50 55 60

Ala Thr Arg Gly Gln Leu Ile Arg Glu Ala Tyr Glu Asp Tyr Arg His
65 70 75 80

Phe Ser Ser Glu Cys Pro Phe Ile Pro Arg Glu Ala Gly Glu Ala Ala
85 90 95

Asp Phe Ile Pro Thr Ser Met Asp Pro Pro Glu Gln Arg Gln Phe Arg
100 105 110

Ala Leu Ala Asn Gln Val Val Gly Met Pro Val Val Asp Lys Leu Glu
115 120 125

Asn Arg Ile Gln Glu Leu Ala Cys Ser Leu Ile Glu Ser Leu Arg Pro
130 135 140

Gln Gly Gln Cys Asn Phe Thr Glu Asp Tyr Ala Glu Pro Phe Pro Ile
145 150 155 160

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Arg Ile Phe Met Leu Leu Ala Gly Leu Pro Glu Glu Asp Ile Pro His
 165 170 175

Leu Lys Tyr Leu Thr Asp Gln Met Thr Arg Pro Asp Gly Ser Met Thr
 180 185 190

Phe Ala Glu Ala Lys Glu Ala Leu Tyr Asp Tyr Leu Ile Pro Ile Ile
 195 200 205

Glu Gln Arg Arg Gln Lys Pro Gly Thr Asp Ala Ile Ser Ile Val Ala
 210 215 220

Asn Gly Gln Val Asn Gly Arg Pro Ile Thr Ser Asp Glu Ala Lys Arg
 225 230 235 240

Met Cys Gly Leu Leu Leu Val Gly Gly Leu Asp Thr Val Val Asn Phe
 245 250 255

Leu Ser Phe Ser Met Glu Phe Leu Ala Lys Ser Pro Glu His Arg Gln
 260 265 270

Glu Leu Ile Glu Arg Pro Glu Arg Ile Pro Ala Ala Cys Glu Glu Leu
 275 280 285

Leu Arg Arg Phe Ser Leu Val Ala Asp Gly Arg Ile Leu Thr Ser Asp
 290 295 300

Tyr Glu Phe His Gly Val Gln Leu Lys Lys Gly Asp Gln Ile Leu Leu
 305 310 315 320

Pro Gln Met Leu Ser Gly Leu Asp Glu Arg Glu Asn Ala Cys Pro Met
 325 330 335

His Val Asp Phe Ser Arg Gln Lys Val Ser His Thr Thr Phe Gly His
 340 345 350

Gly Ser His Leu Cys Leu Gly Gln His Leu Ala Arg Arg Glu Ile Ile
 355 360 365

Val Thr Leu Lys Glu Trp Leu Thr Arg Ile Pro Asp Phe Ser Ile Ala
 370 375 380

Pro Gly Ala Gln Ile Gln His Lys Ser Gly Ile Val Ser Gly Val Gln
 385 390 395 400

Ala Leu Pro Leu Val Trp Asp Pro Ala Thr Lys Ala Val
 Page 224

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

405

410

<210> 66
<211> 414
<212> PRT
<213> Artificial Sequence

<220>
<223> Cytochrome P450 variant CYP101A1var2

<400> 66

Thr Thr Glu Thr Ile Gln Ser Asn Ala Asn Leu Ala Pro Leu Pro Pro
1 5 10 15

His Val Pro Glu His Leu Val Phe Asp Phe Asp Met Tyr Asn Pro Ser
20 25 30

Asn Leu Ser Ala Gly Val Gln Glu Ala Trp Ala Val Leu Gln Glu Ser
35 40 45

Asn Val Pro Asp Leu Val Trp Thr Arg Cys Asn Gly Gly His Trp Ile
50 55 60

Ala Thr Arg Gly Gln Leu Ile Arg Glu Ala Tyr Glu Asp Tyr Arg His
65 70 75 80

Phe Ser Ser Glu Cys Pro Phe Ile Pro Arg Glu Ala Gly Glu Ala Phe
85 90 95

Asp Phe Ile Pro Thr Ser Met Asp Pro Pro Glu Gln Arg Gln Phe Arg
100 105 110

Ala Leu Ala Asn Gln Val Val Gly Met Pro Val Val Asp Lys Leu Glu
115 120 125

Asn Arg Ile Gln Glu Leu Ala Cys Ser Leu Ile Glu Ser Leu Arg Pro
130 135 140

Gln Gly Gln Cys Asn Phe Thr Glu Asp Tyr Ala Glu Pro Phe Pro Ile
145 150 155 160

Arg Ile Phe Met Leu Leu Ala Gly Leu Pro Glu Glu Asp Ile Pro His
165 170 175

Leu Lys Tyr Leu Thr Asp Gln Met Thr Arg Pro Asp Gly Ser Met Thr
180 185 190

Phe Ala Glu Ala Lys Glu Ala Leu Tyr Asp Tyr Leu Ile Pro Ile Ile
195 200 205

Page 225

Printed: 10/30/2007

Sheet 1

PCT/US2007/017409

109

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No.: EB5118413420S

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Glu Gln Arg Arg Gln Lys Pro Gly Thr Asp Ala Ile Ser Ile Val Ala
210 215 220

Asn Gly Gln Val Asn Gly Arg Pro Ile Thr Ser Asp Glu Ala Lys Arg
225 230 235 240

Met Cys Gly Leu Leu Leu Val Gly Gly Leu Asp Thr Val Val Asn Phe
245 250 255

Leu Ser Phe Ser Met Glu Phe Leu Ala Lys Ser Pro Glu His Arg Gln
260 265 270

Glu Leu Ile Glu Arg Pro Glu Arg Ile Pro Ala Ala Cys Glu Glu Leu
275 280 285

Leu Arg Arg Phe Ser Leu Val Ala Asp Gly Arg Ile Leu Thr Ser Asp
290 295 300

Tyr Glu Phe His Gly Val Gln Leu Lys Lys Gly Asp Gln Ile Leu Leu
305 310 315 320

Pro Gln Met Leu Ser Gly Leu Asp Glu Arg Glu Asn Ala Cys Pro Met
325 330 335

His Val Asp Phe Ser Arg Gln Lys Val Ser His Thr Thr Phe Gly His
340 345 350

Gly Ser His Leu Cys Leu Gly Gln His Leu Ala Arg Arg Glu Ile Ile
355 360 365

Val Thr Leu Lys Glu Trp Leu Thr Arg Ile Pro Asp Phe Ser Ile Ala
370 375 380

Pro Gly Ala Gln Ile Gln His Lys Ser Gly Ile Val Ser Gly Val Gln
385 390 395 400

Ala Leu Pro Leu Val Trp Asp Pro Ala Thr Thr Lys Ala Val
405 410

<210> 67
<211> 414
<212> PRT
<213> Artificial Sequence

<220>
<223> Cytochrome P450 variant CYP101A1var2-1

<400> 67

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Thr Thr Glu Thr Ile Gln Ser Asn Ala Asn Leu Ala Pro Leu Pro Pro
1 5 10 15

His Val Pro Glu His Leu Val Phe Asp Phe Asp Met Tyr Asn Pro Ser
20 25 30

Asn Leu Ser Ala Gly Val Gln Glu Ala Trp Ala Val Leu Gln Glu Ser
35 40 45

Asn Val Pro Asp Leu Val Trp Thr Arg Cys Asn Gly Gly His Trp Ile
50 55 60

Ala Thr Arg Gly Gln Leu Ile Arg Glu Ala Tyr Glu Asp Tyr Arg His
65 70 75 80

Phe Ser Ser Glu Cys Pro Trp Ile Pro Arg Glu Ala Gly Glu Ala Phe
85 90 95

Asp Phe Ile Pro Thr Ser Met Asp Pro Pro Glu Gln Arg Gln Phe Arg
100 105 110

Ala Leu Ala Asn Gln Val Val Gly Met Pro Val Val Asp Lys Leu Glu
115 120 125

Asn Arg Ile Gln Glu Leu Ala Cys Ser Leu Ile Glu Ser Leu Arg Pro
130 135 140

Gln Gly Gln Cys Asn Phe Thr Glu Asp Tyr Ala Glu Pro Phe Pro Ile
145 150 155 160

Arg Ile Phe Met Leu Leu Ala Gly Leu Pro Glu Glu Asp Ile Pro His
165 170 175

Leu Lys Tyr Leu Thr Asp Gln Met Thr Arg Pro Asp Gly Ser Met Thr
180 185 190

Phe Ala Glu Ala Lys Glu Ala Leu Tyr Asp Tyr Leu Ile Pro Ile Ile
195 200 205

Glu Gln Arg Arg Gln Lys Pro Gly Thr Asp Ala Ile Ser Ile Val Ala
210 215 220

Asn Gly Gln Val Asn Gly Arg Pro Ile Thr Ser Asp Glu Ala Lys Arg
225 230 235 240

Met Cys Gly Leu Leu Leu Val Gly Gly Leu Asp Thr Val Val Asn Phe
245 250 255

Title: "Methods and Systems for Selective..."

Inventors: Rudi Pasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Leu Ser Phe Ser Met Glu Phe Leu Ala Lys Ser Pro Glu His Arg Gln
 260 265 270

Glu Leu Ile Glu Arg Pro Glu Arg Ile Pro Ala Ala Cys Glu Glu Leu
 275 280 285

Leu Arg Arg Phe Ser Leu Val Ala Asp Gly Arg Ile Leu Thr Ser Asp
 290 295 300

Tyr Glu Phe His Gly Val Gln Leu Lys Lys Gly Asp Gln Ile Leu Leu
 305 310 315 320

Pro Gln Met Leu Ser Gly Leu Asp Glu Arg Glu Asn Ala Cys Pro Met
 325 330 335

His Val Asp Phe Ser Arg Gln Lys Val Ser His Thr Thr Phe Gly His
 340 345 350

Gly Ser His Leu Cys Leu Gly Gln His Leu Ala Arg Arg Glu Ile Ile
 355 360 365

Val Thr Leu Lys Glu Trp Leu Thr Arg Ile Pro Asp Phe Ser Ile Ala
 370 375 380

Pro Gly Ala Gln Ile Gln His Lys Ser Gly Ile Val Ser Gly Val Gln
 385 390 395 400

Ala Leu Pro Leu Val Trp Asp Pro Ala Thr Thr Lys Ala Val
 405 410

<210> 68
 <211> 414

<212> PRT

<213> Artificial Sequence

<220>

<223> Cytochrome P450 variant CYP101A1var2-2

<400> 68

Thr Thr Glu Thr Ile Gln Ser Asn Ala Asn Leu Ala Pro Leu Pro Pro
 1 5 10 15

His Val Pro Glu His Leu Val Phe Asp Phe Asp Met Tyr Asn Pro Ser
 20 25 30

Asn Leu Ser Ala Gly Val Gln Glu Ala Trp Ala Val Leu Gln Glu Ser
 35 40 45

Printed: 10/30/2007

SEQUENCE

PCT/US2007/017409

0150409-400

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Asn Val Pro Asp Leu Val Trp Thr Arg Cys Asn Gly His Trp Ile
50 55 60

Ala Thr Arg Gly Gln Leu Ile Arg Glu Ala Tyr Glu Asp Tyr Arg His
65 70 75 80

Phe Ser Ser Glu Cys Pro Phe Ile Pro Arg Glu Ala Gly Glu Ala Phe
85 90 95

Asp Phe Ile Pro Thr Ser Met Asp Pro Pro Glu Gln Arg Gln Phe Arg
100 105 110

Ala Leu Ala Asn Gln Val Val Gly Met Pro Val Val Asp Lys Leu Glu
115 120 125

Asn Arg Ile Gln Glu Leu Ala Cys Ser Leu Ile Glu Ser Leu Arg Pro
130 135 140

Gln Gly Gln Cys Asn Phe Thr Glu Asp Tyr Ala Glu Pro Phe Pro Ile
145 150 155 160

Arg Ile Phe Met Leu Leu Ala Gly Leu Pro Glu Glu Asp Ile Pro His
165 170 175

Leu Lys Tyr Leu Thr Asp Gln Met Thr Arg Pro Asp Gly Ser Met Thr
180 185 190

Phe Ala Glu Ala Lys Glu Ala Leu Tyr Asp Tyr Leu Ile Pro Ile Ile
195 200 205

Glu Gln Arg Arg Gln Lys Pro Gly Thr Asp Ala Ile Ser Ile Val Ala
210 215 220

Asn Gly Gln Val Asn Gly Arg Pro Ile Thr Ser Asp Glu Ala Lys Arg
225 230 235 240

Met Cys Gly Leu Leu Leu Gly Gly Leu Asp Thr Val Val Asn Phe
245 250 255

Leu Ser Phe Ser Met Glu Phe Leu Ala Lys Ser Pro Glu His Arg Gln
260 265 270

Glu Leu Ile Glu Arg Pro Glu Arg Ile Pro Ala Ala Cys Glu Glu Leu
275 280 285

Leu Arg Arg Phe Ser Leu Val Ala Asp Gly Arg Ile Leu Thr Ser Asp
290 295 300

08/04/2007

Printed: 10/30/2007

SP01131

PCT/US2007/017409

US 2007 017409

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Tyr Glu Phe His Gly Val Gln Leu Lys Lys Gly Asp Gln Ile Leu Leu
305 310 315 320

Pro Gln Met Leu Ser Gly Leu Asp Glu Arg Glu Asn Ala Cys Pro Met
325 330 335

His Val Asp Phe Ser Arg Gln Lys Val Ser His Thr Thr Phe Gly His
340 345 350

Gly Ser His Leu Cys Leu Gly Gln His Leu Ala Arg Arg Glu Ile Ile
355 360 365

Val Thr Leu Lys Glu Trp Leu Thr Arg Ile Pro Asp Phe Ser Ile Ala
370 375 380

Pro Gly Ala Gln Ile Gln His Lys Ser Gly Ile Val Ser Gly Val Gln
385 390 395 400

Ala Leu Pro Leu Val Trp Asp Pro Ala Thr Thr Lys Ala Val
405 410

<210> 69
<211> 414
<212> PRT
<213> Artificial Sequence

<220>
<223> Cytochrome P450 variant CYP101A1var2-3

<400> 69

Thr Thr Glu Thr Ile Gln Ser Asn Ala Asn Leu Ala Pro Leu Pro Pro
1 5 10 15

His Val Pro Glu His Leu Val Phe Asp Phe Asp Met Tyr Asn Pro Ser
20 25 30

Asn Leu Ser Ala Gly Val Gln Glu Ala Trp Ala Val Leu Gln Glu Ser
35 40 45

Asn Val Pro Asp Leu Val Trp Thr Arg Cys Asn Gly Gly His Trp Ile
50 55 60

Ala Thr Arg Gly Gln Leu Ile Arg Glu Ala Tyr Glu Asp Tyr Arg His
65 70 75 80

Phe Ser Ser Glu Cys Pro Trp Ile Pro Arg Glu Ala Gly Glu Ala Phe
85 90 95

Printed: 10/30/2007

Page: 11

PCT/US2007/047409

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt.

Asp Phe Ile Pro Thr Ser Met Asp Pro Pro Glu Gln Arg Gln Phe Arg
100 105 110

Ala Leu Ala Asn Gln Val Val Gly Met Pro Val Val Asp Lys Leu Glu
115 120 125

Asn Arg Ile Gln Glu Leu Ala Cys Ser Leu Ile Glu Ser Leu Arg Pro
130 135 140

Gln Gly Gln Cys Asn Phe Thr Glu Asp Tyr Ala Glu Pro Phe Pro Ile
145 150 155 160

Arg Ile Phe Met Leu Leu Ala Gly Leu Pro Glu Glu Asp Ile Pro His
165 170 175

Leu Lys Tyr Leu Thr Asp Gln Met Thr Arg Pro Asp Gly Ser Met Thr
180 185 190

Phe Ala Glu Ala Lys Glu Ala Leu Tyr Asp Tyr Leu Ile Pro Ile Ile
195 200 205

Glu Gln Arg Arg Gln Lys Pro Gly Thr Asp Ala Ile Ser Ile Val Ala
210 215 220

Asn Gly Gln Val Asn Gly Arg Pro Ile Thr Ser Asp Glu Ala Lys Arg
225 230 235 240

Met Cys Gly Leu Leu Leu Leu Gly Gly Leu Asp Thr Val Val Asn Phe
245 250 255

Leu Ser Phe Ser Met Glu Phe Leu Ala Lys Ser Pro Glu His Arg Gln
260 265 270

Glu Leu Ile Glu Arg Pro Glu Arg Ile Pro Ala Ala Cys Glu Glu Leu
275 280 285

Leu Arg Arg Phe Ser Leu Val Ala Asp Gly Arg Ile Leu Thr Ser Asp
290 295 300

Tyr Glu Phe His Gly Val Gln Leu Lys Lys Gly Asp Gln Ile Leu Leu
305 310 315 320

Pro Gln Met Leu Ser Gly Leu Asp Glu Arg Glu Asn Ala Cys Pro Met
325 330 335

His Val Asp Phe Ser Arg Gln Lys Val Ser His Thr Thr Phe Gly His
340 345 350

Page 231

08/04/2007

Title: "Methods and Systems for Selective..."

Inventors: Rudi Fasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Gly Ser His Leu Cys Leu Gly Gln His Leu Ala Arg Arg Glu Ile Ile
 355 360 365

Val Thr Leu Lys Glu Trp Leu Thr Arg Ile Pro Asp Phe Ser Ile Ala
 370 375 380

Pro Gly Ala Gln Ile Gln His Lys Ser Gly Ile Val Ser Gly Val Gln
 385 390 395 400

Ala Leu Pro Leu Val Trp Asp Pro Ala Thr Thr Lys Ala Val
 405 410

<210> 70
 <211> 417
 <212> PRT
 <213> Bacillus Subtilis

<220>
 <221> MISC_FEATURE
 <222> (1)..(417)
 <223> Cytochrome P450 enzyme CYP152A1

<400> 70

Met Asn Glu Gln Ile Pro His Asp Lys Ser Leu Asp Asn Ser Leu Thr
 1 5 10 15

Leu Leu Lys Glu Gly Tyr Leu Phe Ile Lys Asn Arg Thr Glu Arg Tyr
 20 25 30

Asn Ser Asp Leu Phe Gln Ala Arg Leu Leu Gly Lys Asn Phe Ile Cys
 35 40 45

Met Thr Gly Ala Glu Ala Ala Lys Val Phe Tyr Asp Thr Asp Arg Phe
 50 55 60

Gln Arg Gln Asn Ala Leu Pro Lys Arg Val Gln Lys Ser Leu Phe Gly
 65 70 75 80

Val Asn Ala Ile Gln Gly Met Asp Gly Ser Ala His Ile His Arg Lys
 85 90 95

Met Leu Phe Leu Ser Leu Met Thr Pro Pro His Gln Lys Arg Leu Ala
 100 105 110

Glu Leu Met Thr Glu Glu Trp Lys Ala Ala Val Thr Arg Trp Glu Lys
 115 120 125

P008-CIT_ST25.txt

Ala Asp Glu Val Val Leu Phe Glu Glu Ala Lys Glu Ile Leu Cys Arg
130 135 140

Val Ala Cys Tyr Trp Ala Gly Val Pro Leu Lys Glu Thr Glu Val Lys
145 150 155 160

Glu Arg Ala Asp Asp Phe Ile Asp Met Val Asp Ala Phe Gly Ala Val
165 170 175

Gly Pro Arg His Trp Lys Gly Arg Arg Ala Arg Pro Arg Ala Glu Glu
180 185 190

Trp Ile Glu Val Met Ile Glu Asp Ala Arg Ala Gly Leu Leu Lys Thr
195 200 205

Thr Ser Gly Thr Ala Leu His Glu Met Ala Phe His Thr Gln Glu Asp
210 215 220

Gly Ser Gln Leu Asp Ser Arg Met Ala Ala Ile Glu Leu Ile Asn Val
225 230 235 240

Leu Arg Pro Ile Val Ala Ile Ser Tyr Phe Leu Val Phe Ser Ala Leu
245 250 255

Ala Leu His Glu His Pro Lys Tyr Lys Glu Trp Leu Arg Ser Gly Asn
260 265 270

Ser Arg Glu Arg Glu Met Phe Val Gln Glu Val Arg Arg Tyr Tyr Pro
275 280 285

Phe Gly Pro Phe Leu Gly Ala Leu Val Lys Lys Asp Phe Val Trp Asn
290 295 300

Asn Cys Glu Phe Lys Lys Gly Thr Ser Val Leu Leu Asp Leu Tyr Gly
305 310 315 320

Thr Asn His Asp Pro Arg Leu Trp Asp His Pro Asp Glu Phe Arg Pro
325 330 335

Glu Arg Phe Ala Glu Arg Glu Glu Asn Leu Phe Asp Met Ile Pro Gln
340 345 350

Gly Gly Gly His Ala Glu Lys Gly His Arg Cys Pro Gly Glu Gly Ile
355 360 365

Thr Ile Glu Val Met Lys Ala Ser Leu Asp Phe Leu Val His Gln Ile
370 375 380

Printed: 10/30/2007

SEQUENCE

PCT/US2007/017409

000000000000

Title: "Methods and Systems for Selective..."

Inventors: Rudi Pasan et al.

Express Mailing Label No: EB511841342US

Attorney Docket: P008-CIT

P008-CIT_ST25.txt

Glu Tyr Asp Val Pro Glu Gln Ser Leu His Tyr Ser Leu Ala Arg Met
385 390 395 400

Pro Ser Leu Pro Glu Ser Gly Phe Val Met Ser Gly Ile Arg Arg Lys
405 410 415

Ser