(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) **World Intellectual Property Organization**
International Bureau

(43) **International Publication Date**
4 August 2016 (04.08.2016)

WIPO | PCT

(10) **International Publication Number**
WO 2016/120486 A1

(51) **International Patent Classification**:
C12N 9/10 (2006.01) *C12P 19/56* (2006.01) *C12P 15/00* (2006.01) *C12N 1/18* (2006.01)

(21) **International Application Number**:
PCT/EP2016/052007

(22) **International Filing Date**:
29 January 2016 (29.01.2016)

(25) **Filing Language**: English

(26) **Publication Language**: English

(30) **Priority Data**:
62/110,207 30 January 2015 (30.01.2015) US

(71) **Applicant**: **EVOLVA SA** [CH/CH]; Duggingerstrasse 23, 4153 Reinach (CH).

(72) **Inventors**: **OLSSON, Kim**; Finsensvej 46B, 1tv., 2000 Frederiksberg (DK). **SIMON, Ernesto**; Svaetegade 7, 2nd Floor, 1118 Copenhagen (DK). **DALGAARD MIKKELSEN, Michael**; 1 Bregnevej, 3500 Vaerløse (DK). **CARLSEN, Simon**; Duggingerstrasse 23, CH-4153 Reinach (CH). **DOUCHIN, Veronique**; Aurikelvej 2-4th, 2000 Frederiksberg (DK). **LIM, Swee Chuang**; Amalieparken 87, 4-4, 2665 Vallensbaek Strand (DK). **DURING, Louis**; Classensgade 23, 4th, 2100 Copenhagen (DK).

(74) **Agent**: **SMAGGASGALE, Gillian**; 55 Drury Lane, London WC2B 5SQ (GB).

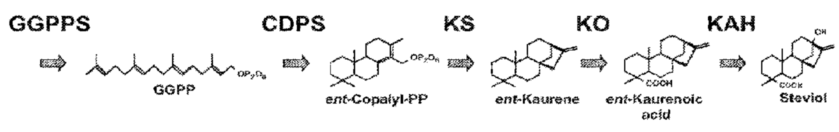
(81) **Designated States** *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) **Designated States** *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Published:
— *with international search report (Art. 21(3))*
— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))*
— *with sequence listing part of description (Rule 5.2(a))*

(54) **Title**: PRODUCTION OF STEVIOL GLYCOSIDES IN RECOMBINANT HOSTS

Figure 1



(57) **Abstract**: The invention relates to recombinant microorganisms and methods for producing steviol glycosides, glycosylated ent-kaurenol, and glycosylated ent-kaurenoic acid.

WO 2016/120486 A1

PRODUCTION OF STEVIOL GLYCOSIDES IN RECOMBINANT HOSTS

BACKGROUND OF THE INVENTION

Field of the Invention

[0001] This disclosure relates to recombinant production of steviol glycosides and steviol glycoside precursors in recombinant hosts. In particular, this disclosure relates to production of steviol glycosides comprising steviol-13-*O*-glucoside (13-SMG), steviol-19-*O*-glucoside (19-SMG), steviol-1,2-bioside, steviol-1,3-bioside, 1,2-stevioside, 1,3-stevioside, rubusoside (Rubu), rebaudioside A (RebA), rebaudioside B (RebB), rebaudioside D (RebD), rebaudioside E (RebE), rebaudioside M (RebM), rebaudioside Q (RebQ), rebaudioside I (RebI), di-glycosylated steviol, tri-glycosylated steviol, tetra-glycosylated steviol, penta-glycosylated steviol, hexa-glycosylated steviol, hepta-glycosylated steviol, glycosylated ent-kaurenol, glycosylated ent-kaurenoic acid, and/or isomers thereof in recombinant hosts.

Description of Related Art

[0002] Sweeteners are well known as ingredients used most commonly in the food, beverage, or confectionary industries. The sweetener can either be incorporated into a final food product during production or for stand-alone use, when appropriately diluted, as a tabletop sweetener or an at-home replacement for sugars in baking. Sweeteners include natural sweeteners such as sucrose, high fructose corn syrup, molasses, maple syrup, and honey and artificial sweeteners such as aspartame, saccharine, and sucralose. Stevia extract is a natural sweetener that can be isolated and extracted from a perennial shrub, *Stevia rebaudiana*. Stevia is commonly grown in South America and Asia for commercial production of stevia extract. Stevia extract, purified to various degrees, is used commercially as a high intensity sweetener in foods and in blends or alone as a tabletop sweetener.

[0003] Chemical structures for several steviol glycosides are shown in Figure 1, including the diterpene steviol and various steviol glycosides. Extracts of the Stevia plant generally comprise steviol glycosides that contribute to the sweet flavor, although the amount of each steviol glycoside often varies, *inter alia*, among different production batches.

[0004] As recovery and purification of steviol glycosides from the Stevia plant have proven to be labor intensive and inefficient, there remains a need for a recombinant production system that can accumulate high yields of desired steviol glycosides, such as RebD and RebM. There also remains a need for improved production of steviol glycosides in recombinant hosts for commercial uses. As well, there remains a need for identifying enzymes selective towards particular substrates to produce one or more specific steviol glycosides. In some aspects, there remains a need to increase the catalytic capability of enzymes with 19-*O* glycosylation activity in order to produce higher yields of steviol glycosides.

SUMMARY OF THE INVENTION

[0005] It is against the above background that the present invention provides certain advantages and advancements over the prior art.

[0006] Although this invention as disclosed herein is not limited to specific advantages or functionalities, the invention provides a recombinant host cell, comprising at least one recombinant gene that is:

(a) a gene encoding a UGT91D2e polypeptide having at least 90% sequence identity to the amino acid sequence set forth in SEQ ID NO:11;

(b) a gene encoding a chimeric polypeptide having at least 70% sequence identity to the amino acid sequence set forth in SEQ ID NO:17 or SEQ ID NO:18;

(c) a gene encoding a UGT85C2 polypeptide having at least 55% sequence identity to the amino acid sequence set forth in SEQ ID NO:7; and/or

(d) a gene encoding a UGT76G1 polypeptide having at least 50% sequence identity to the amino acid sequence set forth in SEQ ID NO:9;

wherein the recombinant host cell is capable of producing a steviol glycoside, glycosylated ent-kaurenol compound, and/or a glycosylated ent-kaurenoic acid compound in a cell culture broth.

[0007] In one aspect of the recombinant host cell disclosed herein, the UGT91D2e polypeptide comprises a UGT91D2e polypeptide having at least one amino acid substitution at residues 93, 99, 114, 144, 148, 152, 195, 196, 199, 211, 213, 221, 286, 384, 426, 438, or 466 of SEQ ID NO:11.

[0008] In one aspect of the recombinant host cell disclosed herein, the UGT85C2 polypeptide comprises a UGT85C2 polypeptide having at least one amino acid substitution at residues 21, 48, 49, 84, 86, 87, 91, 92, 95, 122, 334, or 334 of SEQ ID NO:7.

[0009] In one aspect of the recombinant host cell disclosed herein, the UGT76G1 polypeptide comprises a UGT76G1 polypeptide having at least one amino acid substitution at residues 23, 26, 55, 146, 257, 283, and 337 of SEQ ID NO:9.

[0010] In one aspect of the recombinant host cell disclosed herein, the UGT91D2e polypeptide comprises one or more of the UGT91D2e polypeptide variants comprising: P93V, S99I, S114F, T144K, T144L, T144M, A148K, M152T, L195G, L195C, L195S, L195N, L195V, V196P, K199C, L211H, L211M, L211I, L211C, L211T, L213E, S221I, V286C, V286N, V286S, G384W, G384K, G384Y, E426G, E438H, 3438M or A466V of SEQ ID NO:11.

[0011] In one aspect of the recombinant host cell disclosed herein, the UGT85C2 polypeptide comprises one or more of the UGT85C2 polypeptide variants comprising: Q21L, Q21T, Q21V, F48S, F48H, F48Y, F48R, F48Q, F48W, F48T, I49V, S84G, S84A, S84T, S84C, S84P, S84N, S84V, P86R, P86G, I87H, I87P, I87M, I87Y, L91K, L91R, L91T, L92F, L92I, L92M, I95K, F122S, L334S or L334M of SEQ ID NO:7.

[0012] In one aspect of the recombinant host cell disclosed herein, the UGT76G1 polypeptide comprises one or more of the UGT76G1 polypeptide variants comprising: Q23H, I26W, T146G, H155L, L257G, S253W, T284G, S283N, K337P or T55K of SEQ ID NO:9.

[0013] In one aspect the recombinant host cell disclosed herein further comprises at least one recombinant gene that is:

(a) a gene encoding a geranylgeranyl diphosphate synthase (GGPPS) polypeptide;

(b) a gene encoding an ent-copalyl diphosphate synthase (CDPS) polypeptide;

(c) a gene encoding an ent-kaurene synthase (KS) polypeptide;

(d) a gene encoding an ent-kaurene oxidase (KO) polypeptide;

(e) a gene encoding a cytochrome P450 reductase (CPR) polypeptide; and

(f) a gene encoding an ent-kaurenoic acid hydroxylase (KAH) polypeptide;

(g) a gene encoding a UGT74G1 polypeptide; and/or

(h) a gene encoding an EUGT11 polypeptide;

wherein the recombinant host cell capable of producing a steviol glycoside, glycosylated ent-kaurenol compound, and/or a glycosylated ent-kaurenoic acid compound in a cell culture broth.

[0014] In one aspect of the recombinant host cell disclosed herein,

(a) the GGPPS polypeptide comprises a polypeptide having at least 70% identity to an amino acid sequence set forth in SEQ ID NO:20, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:26, SEQ ID NO:28, SEQ ID NO:30, SEQ ID NO:32, or SEQ ID NO:116;

(b) the CDPS polypeptide comprises a polypeptide having at least 70% identity to an amino acid sequence set forth in SEQ ID NO:34, SEQ ID NO:36, SEQ ID NO:38, SEQ ID NO:40, or SEQ ID NO:42;

(c) the KS polypeptide comprises a polypeptide having at least 70% identity to an amino acid sequence set forth in SEQ ID NO:44, SEQ ID NO:46, SEQ ID NO:48, SEQ ID NO:50, or SEQ ID NO:52;

(d) the KO polypeptide comprises a polypeptide having at least 70% identity to an amino acid sequence set forth in SEQ ID NO:60, SEQ ID NO:62, SEQ ID NO:117, SEQ ID NO:66, SEQ ID NO:68, SEQ ID NO:70, SEQ ID NO:72, SEQ ID NO:74, or SEQ ID NO:76;

(e) the CPR polypeptide comprises a polypeptide having at least 70% identity to an amino acid sequence set forth in SEQ ID NO:78, SEQ ID NO:80, SEQ ID NO:82, SEQ ID NO:84, SEQ ID NO:86, SEQ ID NO:88, SEQ ID NO:90, SEQ ID NO:92;

(f) the KAH polypeptide comprises a polypeptide having at least 70% identity to an amino acid sequence set forth in SEQ ID NO:94, SEQ ID NO:97, SEQ ID NO:100, SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:103, SEQ ID NO:104, SEQ ID NO:106, SEQ ID NO:108, SEQ ID NO:110, SEQ ID NO:112, or SEQ ID NO:114;

(g) the UGT74G1 polypeptide comprises a polypeptide having at least 55% identity to an amino acid sequence set forth in SEQ ID NO:4;

(h) the EUGT11 polypeptide comprises a polypeptide having at least 65% identity to an amino acid sequence set forth in SEQ ID NO:16.

[0015] In one aspect of the recombinant host cell disclosed herein, the cell culture broth comprises:

(a) the steviol glycoside, glycosylated ent-kaurenol compound, and/or the glycosylated ent-kaurenoic acid compound produced by the recombinant host cell,

(b) glucose, fructose and/or sucrose; and/or

(c) supplemental nutrients comprising trace metals, vitamins, salts, yeast nitrogen base (YNB), and/or amino acids.

[0016] In one aspect of the recombinant host cell disclosed herein, the recombinant host comprises a plant cell, a mammalian cell, an insect cell, a fungal cell, an algal cell, or a bacterial cell.

[0017] In one aspect of the recombinant host cell disclosed herein, the bacterial cell comprises *Escherichia* cells, *Lactobacillus* cells, *Lactococcus* cells, *Comebacterium* cells, *Acetobacter* cells, *Acinetobacter* cells, or *Pseudomonas* cells.

[0018] In one aspect of the recombinant host cell disclosed herein, the fungal cell comprises a yeast cell.

[0019] In one aspect of the recombinant host cell disclosed herein, the yeast cell is a cell from S*accharomyces cerevisiae*, *Schizosaccharomyces pombe*, *Yarrowia lipolytica*, *Candida glabrata*, *Ashbya gossypii*, *Cyberlindnera jadinii*, *Pichia pastoris*, *Kluyveromyces lactis*, *Hansenula polymorpha*, *Candida boidinii*, *Arxula adeninivorans*, *Xanthophyllomyces dendrorhous*, or *Candida albicans* species.

[0020] In one aspect of the recombinant host cell disclosed herein, the yeast cell is a *Saccharomycete*.

[0021] In one aspect of the recombinant host cell disclosed herein, the yeast cell is a cell from the *Saccharomyces cerevisiae* species.

[0022] The invention also provides a method of producing a steviol glycoside, glycosylated ent-kaurenol compound, and/or glycosylated ent-kaurenoic acid compound in a cell culture broth, comprising growing the recombinant host cell disclosed herein in a culture medium, under conditions in which one or more of the genes are expressed;

wherein at least one of the genes is a recombinant gene;

wherein the steviol glycoside, glycosylated ent-kaurenol compound, and/or the glycosylated ent-kaurenoic acid compound is produced by the recombinant host cell.

[0023] In one aspect of the methods disclosed herein, one or more of the genes is constitutively expressed and/or expression of one or more of the genes is induced.

[0024] The invention also provides a method for producing a steviol glycoside, glycosylated ent-kaurenol compound, and/or the glycosylated ent-kaurenoic acid compound comprising whole-cell bioconversion of plant-derived components or synthetic steviol or steviol glycosides using one or more of:

(a) a UGT91D2e polypeptide having at least 90% sequence identity to the amino acid sequence set forth in SEQ ID NO:11;

(b) a chimeric polypeptide having at least 70% sequence identity to the amino acid sequence set forth in SEQ ID NO:17 or SEQ ID NO:18;

(c) a UGT85C2 polypeptide having at least 55% sequence identity to the amino acid sequence set forth in SEQ ID NO:7; and/or

(d) a UGT76G1 polypeptide having at least 50% sequence identity to the amino acid sequence set forth in SEQ ID NO:9;

wherein at least one of the polypeptides is a recombinant polypeptide.

[0025] In one aspect of the methods disclosed herein, the whole cell is the recombinant host cell disclosed herein.

[0026] In one aspect of the methods disclosed herein, the recombinant host cell is grown in a fermentor at a temperature for a period of time, wherein the temperature and period of time facilitate the production of the steviol glycoside, glycosylated ent-kaurenol compound, and/or glycosylated ent-kaurenoic acid compound.

[0027] The invention also provides an *in vitro* method for producing a steviol glycoside, glycosylated ent-kaurenol compound, and/or the glycosylated ent-kaurenoic acid compound, comprising adding one or more of:

(a) a UGT91D2e polypeptide having at least 90% sequence identity to the amino acid sequence set forth in SEQ ID NO:11;

(b) a chimeric polypeptide having at least 70% sequence identity to the amino acid sequence set forth in SEQ ID NO:17 or SEQ ID NO:18;

(c) a UGT85C2 polypeptide having at least 55% sequence identity to the amino acid sequence set forth in SEQ ID NO:7; and/or

(d) a UGT76G1 polypeptide having at least 50% sequence identity to the amino acid sequence set forth in SEQ ID NO:9,

and plant-derived components or synthetic steviol or steviol glycosides to a reaction mixture;

wherein at least one of the polypeptides is a recombinant polypeptide; and

(b) synthesizing steviol glycoside, glycosylated ent-kaurenol compound, and/or the glycosylated ent-kaurenoic acid compound in the reaction mixture.

[0028] In one aspect, methods disclosed herein further comprise isolating the steviol glycoside, glycosylated ent-kaurenol compound, and/or the glycosylated ent-kaurenoic acid compound, alone or in combination from the cell culture broth.

[0029] In one aspect of the methods disclosed herein, the isolating step comprises:

(a) providing the cell culture broth comprising the steviol glycoside, glycosylated ent-kaurenol compound, and/or the glycosylated ent-kaurenoic acid compound alone or in combination;

(b) separating a liquid phase of the cell culture broth from a solid phase of the cell culture broth to obtain a supernatant comprising the steviol glycoside, glycosylated ent-kaurenol compound, and/or the glycosylated ent-kaurenoic acid compound alone or in combination;

(c) providing one or more adsorbent resins, comprising providing the adsorbent resins in a packed column; and

(d) contacting the supernatant of step (b) with the one or more adsorbent resins in order to obtain at least a portion of the steviol glycoside, glycosylated ent-kaurenol compound, and/or the glycosylated ent-kaurenoic acid compound alone or in combination thereby isolating the steviol glycoside, glycosylated ent-kaurenol compound, and/or the glycosylated ent-kaurenoic acid compound alone or in combination.

[0030] In one aspect, methods disclosed herein further comprise recovering the the steviol glycoside, glycosylated ent-kaurenol compound, and/or the glycosylated ent-kaurenoic acid compound alone or a composition comprising the steviol glycoside, glycosylated ent-kaurenol compound, and/or the glycosylated ent-kaurenoic acid compound.

[0031] In one aspect of the methods disclosed herein, the recovered composition is enriched for the steviol glycoside, glycosylated ent-kaurenol compound, and/or the glycosylated ent-kaurenoic acid compound relative to a steviol glycoside composition of Stevia plant and has a reduced level of non-steviol glycoside Stevia plant-derived components relative to a plant-derived stevia extract.

[0032] In one aspect of the methods disclosed herein, the cell culture broth comprises:

(a) one or more steviol glycosides, glycosylated ent-kaurenol compounds, and/or glycosylated ent-kaurenoic acid compounds produced by the recombinant host cell disclosed herein,

(b) glucose, fructose, and/or sucrose; and/or

(c) supplemental nutrients comprising trace metals, vitamins, salts, YNB, and/or amino acids.

[0033] In one aspect of the methods disclosed herein, the reaction mixture comprising:

(a) one or more steviol glycosides, glycosylated ent-kaurenol compounds, and/or a glycosylated ent-kaurenoic acid compounds produced in the reaction mixture;

(b) a UGT polypeptide;

(c) UDP-glucose, UDP-rhamnose, UDP-xylose, and/or N-acetyl-glucosamine; and/or

(d) reaction buffer and/or salts.

[0034] In one aspect of the methods disclosed herein, the recombinant host cell comprises a plant cell, a mammalian cell, an insect cell, a fungal cell, an algal cell, or a bacterial cell.

[0035] In one aspect of the methods disclosed herein, the bacterial cell comprises *Escherichia* cells, *Lactobacillus* cells, *Lactococcus* cells, *Comebacterium* cells, *Acetobacter* cells, *Acinetobacter* cells, or *Pseudomonas* cells.

[0036] In one aspect of the methods disclosed herein, the fungal cell comprises a yeast cell.

[0037] In one aspect of the methods disclosed herein, the yeast cell is a cell from S*accharomyces cerevisiae*, *Schizosaccharomyces pombe*, *Yarrowia lipolytica*, *Candida glabrata*, *Ashbya gossypii*, *Cyberlindnera jadinii*, *Pichia pastoris*, *Kluyveromyces lactis*, *Hansenula polymorpha*, *Candida boidinii*, *Arxula adeninivorans*, *Xanthophyllomyces dendrorhous*, or *Candida albicans* species.

[0038] In one aspect of the methods disclosed herein, the yeast cell is a *Saccharomycete*.

[0039] In one aspect of the methods disclosed herein, the yeast cell is a cell from the *Saccharomyces cerevisiae* species.

[0040] In one aspect of the recombinant hosts and methods disclosed herein,

(a) the steviol glycoside comprises 13-SMG, 19-SMG, Steviol-1,2-bioside, Steviol-1,3-bioside, 1,2-stevioside, 1,3-stevioside, rubusoside, RebA, RebB, RebD, RebE, RebM, di-glycosylated tri-glycosylated steviol, tetra-glycosylated steviol, penta-glycosylated steviol, hexa-glycosylated steviol, hepta-glycosylated steviol, and/or isomers thereof;

(b) the glycosylated ent-kaurenol compound comprises di-glycosylated ent-kaurenol, tri-glycosylated ent-kaurenol, and/or isomers thereof; and/or

(c) the glycosylated ent-kaurenoic acid compound comprises di-glycosylated ent-kaurenoic acid, tri-glycosylated ent-kaurenoic acid, and/or isomers thereof.

[0041] In one aspect of the recombinant hosts and methods disclosed herein,

(a) the di-glycosylated steviol comprises compound 2.23 of Table 1;

(b) the tri-glycosylated steviol comprises compound 3.1 and/or compound 3.34 of Table 1;

(c) the tetra-glycosylated steviol comprises compound 4.26 and/or compound 4.33 of Table 1;

(d) the penta-glycosylated steviol comprises compound 5.22, compound 5.24, and/or compound 5.25 of Table 1;

(e) the hexa-glycosylated steviol comprises compound 6.1 and/or compound 6.23 of Table 1;

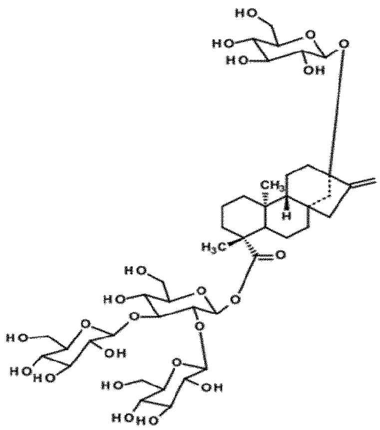
(f) the hepta-glycosylated steviol comprises compound 7.2, compound 7.5, and/or compound 7.13 of Table 1;

(g) the glycosylated ent-kaurenoic acid compound comprises compound KA3.1, compound KA3.2, and/or compound KA2.7 of Table 1; and/or

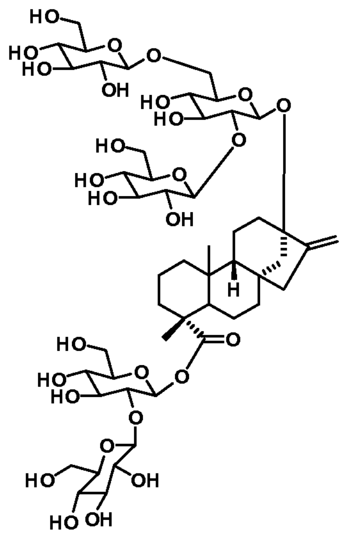
(h) the glycosylated ent-kaurenol compound comprises compound KL2.8 and/or compound KL3.1 co-eluted with compound KL3.6 of Table 1.

[0042] In one aspect of the recombinant hosts and methods disclosed herein,

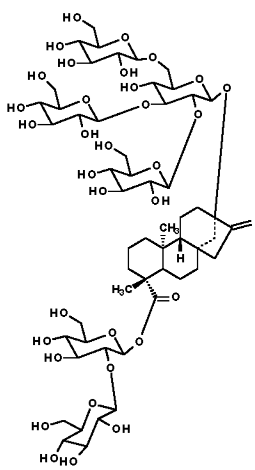
(a) compound 4.26 has the structure:



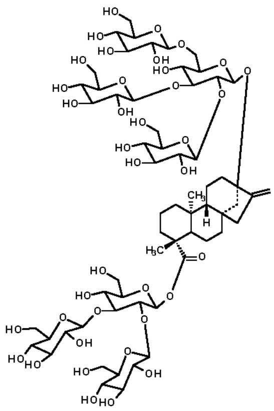
(b) compound 5.22 has the structure:



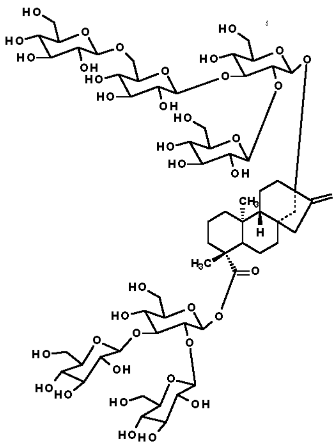
(c) compound 6.1 has the structure:



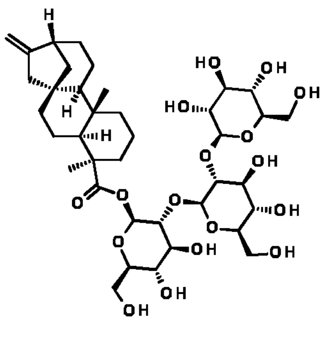
(d) compound 7.2 has the structure:



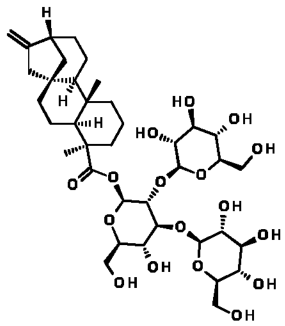
(e) compound 7.5 has the structure:



(f) compound KA3.1 has the structure:

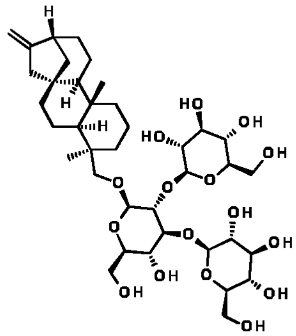


(g) compound KA3.2 has the structure:



; and

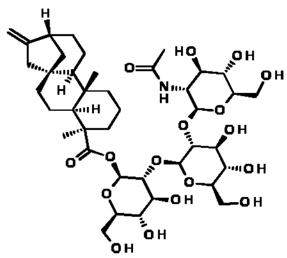
(h) compound KL3.1 has the structure:



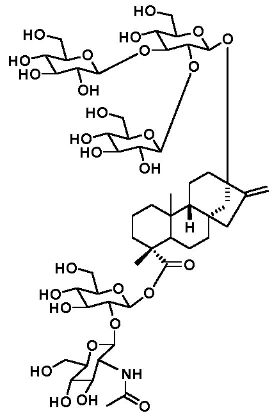
.

[0043] In one aspect of the recombinant hosts and methods disclosed herein,

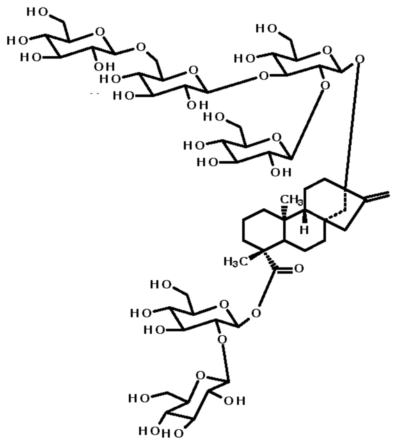
(a) the tri-glycosylated ent-kaurenoic acid comprises a compound having the structure:



(b) the penta-glycosylated steviol comprises a compound having the structure:

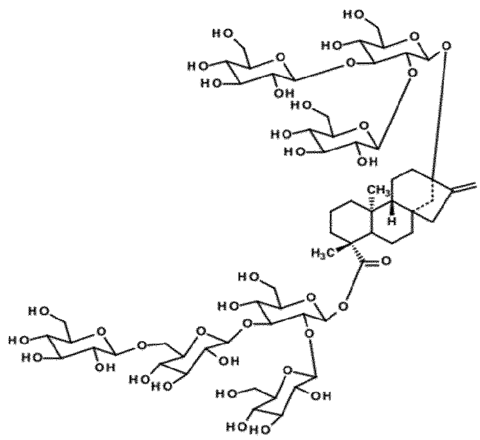


(c) the hexa-glycosylated steviol comprises a compound having the structure:



; and

(d) the hepta-glycosylated steviol comprises a compound having the structure:



.

[0044] The invention also provides a steviol glycoside composition produced by the recombinant host cell disclosed herein or the method disclosed herein, wherein the composition has a steviol glycoside composition enriched for RebD, RebM, or isomers thereof relative to a steviol glycoside composition of Stevia plant and has a reduced level of non-steviol glycoside Stevia plant-derived components relative to a plant-derived stevia extract.

[0045] The invention also provides a cell culture broth comprising:

(a) the recombinant host cell disclosed herein; and

(b) one or more steviol glycosides, glycosylated ent-kaurenol compounds, and/or glycosylated ent-kaurenoic acid compounds produced by the recombinant host cell;

wherein one or more steviol glycosides is present at a concentration of at least 1 mg/liter of the culture broth.

[0046] The invention also provides a cell culture broth comprising:

(a) one or more steviol glycosides, glycosylated ent-kaurenol compounds, and/or glycosylated ent-kaurenoic acid compounds produced by the recombinant host cell disclosed herein,

(b) glucose, fructose, sucrose, xylose, ethanol, and/or glycerol; and/or

(c) supplemental nutrients comprising trace metals, vitamins, salts, YNB, and/or amino acids.

[0047] The invention also provides a cell lysate comprising:

(a) one or more steviol glycosides, glycosylated ent-kaurenol compounds, and/or glycosylated ent-kaurenoic acid compounds produced by the recombinant host cell disclosed herein,

(b) glucose, fructose, sucrose, xylose, ethanol, glycerol, uridine diphosphate (UDP)-glucose, UDP-rhamnose, UDP-xylose, and/or N-acetyl-glucosamine; and/or

(c) supplemental nutrients comprising trace metals, vitamins, salts, YNB, and/or amino acids.

[0048] The invention also provides a reaction mixture comprising:

(a) one or more steviol glycosides, glycosylated ent-kaurenol compounds, and/or a glycosylated ent-kaurenoic acid compounds produced in the reaction mixture;

(b) a UGT polypeptide;

(c) glucose, fructose, sucrose, xylose, ethanol, glycerol, uridine diphosphate (UDP)-glucose, UDP-rhamnose, UDP-xylose, and/or N-acetyl-glucosamine; and/or

(d) reaction buffer and/or salts.

[0049] These and other features and advantages of the present invention will be more fully understood from the following detailed description taken together with the accompanying claims. It is noted that the scope of the claims is defined by the recitations therein and not by the specific discussion of features and advantages set forth in the present description.

BRIEF DESCRIPTION OF THE DRAWINGS

[0050] The following detailed description of the embodiments of the present invention can be best understood when read in conjunction with the following drawings, where like structure is indicated with like reference numerals and in which:

[0051] Figure 1 shows a schematic of the engineered biosynthetic pathway for producing steviol in yeast from geranylgeranyl diphosphate using geranylgeranyl diphosphate synthase (GGPPS), ent-copalyl diphosphate synthase (CDPS), ent-kaurene synthase (KS), ent-kaurene oxidase (KO), and ent-kaurenoic acid hydroxylase (KAH) polypeptides.

[0052] Figure 2 shows representative steviol glycoside glycosylation reactions catalyzed by suitable uridine 5'-diphospho (UDP) glycosyl transferases (UGT) enzymes and chemical structures for several steviol glycoside compounds.

[0053] Figure 3 shows the steviol synthetic intermediate, ent-kaurenol, and its bioconversion product, ent-kaurenoic acid, for the steviol pathway step catalyzed by a KO, along with potential glycosylation by-products (mono-, di-, and/or tri-glycosylated ent-kaurenol and mono-, di-, or tri-glycosylated ent-kaurenoic acid).

[0054] Figure 4A shows accumulation of ent-kaurenoic acid+2Glc (#7), ent-kaurenoic acid+3Glc (isomer 1), and ent-kaurenoic acid+3Glc (isomer 2) by a steviol glycoside-producing *S. cerevisiae* strain deleted of UGT85C2 (SEQ ID NO:7). Figure 4B shows accumulation of 19-SMG by a steviol glycoside-producing *S. cerevisiae* strain deleted of UGT85C2 (SEQ ID NO:7). Figure 4C shows accumulation of steviol, steviol+2Glc (#23), and steviol+3Glc (#34) by a steviol glycoside-producing *S. cerevisiae* strain deleted of UGT85C2 (SEQ ID NO:7). *See* Example 6.

[0055] Figure 5 shows conversion of steviol to rubusoside by bacterial lysates comprising UGT85C2 variants. Bacterial lysates were incubated with steviol for 24 h. *See* Example 7.

[0056] Figure 6A shows production of RebM, RebD, RebA, RebB, 13-SMG, and rubusoside in a steviol glycoside-producing strain expressing UGT76G1 H155L (gray bars), compared to the control steviol glycoside-producing strain expressing wild-type UGT76G1 (black bars). Figure 6B shows production of 1,2-bioside, rubusoside (Rubu), RebG, and RebE in a steviol glycoside-producing strain expressing UGT76G1 H155L (gray bars), compared to a control strain expressing wild-type UGT76G1 (black bars). Figure 6C shows production of quantifiable steviol glycosides (13-SMG + 1,2-bioside + Rubu + RebG + RebB + RebA + RebE + RebD + RebM) and RebD plus RebM titers in a steviol glycoside-producing strain expressing UGT76G1 H155L (gray bars), compared to a control strain expressing wild-type UGT76G1 (black bars). Figure 6D shows production of a tri-glycosylated steviol molecule (steviol+3Glc (#1)), a tetra-glycosylated steviol molecule (steviol+4Glc (#26)), three penta-glycosylated steviol molecules (steviol+5Glc (#22), steviol+5Glc (#24), and steviol+5Glc (#25)), two hexa-glycosylated steviol molecules (steviol+6Glc (isomer 1) and steviol+6Glc (#23)), and two hepta-glycosylated steviol molecules (steviol+7Glc (isomer 2) and steviol+7Glc (#13)) in a steviol glycoside-producing strain expressing UGT76G1 H155L (gray bars), compared to a control strain expressing wild-type UGT76G1 (black bars). *See* Example 9.

[0057] Figure 7A shows NMR-elucidated structures of tri-glycosylated ent-kaurenoic acid (Ent-Kaurenoic Acid+3Glc (isomers 1 and 2)), ent-kaurenoic acid+2Glc+1GlcNAc, and tri-glycosylated ent-kaurenol (ent-kaurenol+3Glc (isomer 1)). Figure 7B shows NMR-elucidated structures of steviol+6Glc (isomer 1) and steviol+7Glc (isomer 2). Figure 7C shows NMR-elucidated structures of steviol+6Glc (isomer 4) and steviol+7Glc (isomer 5). Figure 7D shows NMR-elucidated structures of steviol+4Glc+1GlcNAc (#11) and steviol+4Glc (#26). Figure 7E shows NMR-elucidated structures of steviol+5Glc (#22) and steviol+7Glc (#14). *See* Examples 6, 8, and 9.

[0058] Figures 8A, 8B, and 8C show a ^{1}H NMR spectrum and ^{1}H and ^{13}C NMR chemical shifts (in ppm) for ent-kaurenoic acid+3Glc (isomer 1). Figures 8D, 8E, and 8F show a ^{1}H NMR spectrum and ^{1}H and ^{13}C NMR chemical shifts (in ppm) for ent-kaurenoic acid+3Glc (isomer 2). Figures 8G, 8H, and 8I show a ^{1}H NMR spectrum and ^{1}H and ^{13}C NMR chemical shifts (in ppm) for ent-kaurenoic acid+2Glc+1GlcNAc. Figures 8J, 8K, and 8L show a ^{1}H NMR spectrum and ^{1}H and ^{13}C NMR chemical shifts (in ppm) for ent-kaurenol+3Glc (isomer 1). Figures 8M, 8N, 8O, and 8P show a ^{1}H NMR spectrum and ^{1}H and ^{13}C NMR chemical shifts (in ppm) for steviol+6Glc (isomer 1). Figures 8Q, 8R, 8S, and 8T show a ^{1}H NMR spectrum and ^{1}H and ^{13}C NMR chemical shifts (in ppm) for steviol+7Glc (isomer 2). Figures 8U, 8V, 8W, and 8X show a ^{1}H NMR spectrum and ^{1}H and ^{13}C NMR chemical shifts (in ppm) for steviol+6Glc (isomer 4). Figures 8Y, 8Z, 8AA, and 8AB show a ^{1}H NMR spectrum and ^{1}H and ^{13}C NMR chemical shifts (in ppm) for steviol+7Glc (isomer 5). Figures 8AC, 8AD, 8AE, and 8AF show a ^{1}H NMR spectrum and ^{1}H and ^{13}C NMR chemical shifts (in ppm) for steviol+4Glc+1GlcNAc (#11). Figures 8AG, 8AH, 8AI, and 8AJ show a ^{1}H NMR spectrum and ^{1}H and ^{13}C NMR chemical shifts (in ppm) for steviol+4Glc (#26). Figures 8AK, 8AL, 8AM, and 8AN show a ^{1}H NMR spectrum and ^{1}H and ^{13}C NMR chemical shifts (in ppm) for steviol+5Glc (#22). Figures 8AO, 8AP, 8AQ, and 8AR show a ^{1}H NMR spectrum and ^{1}H and ^{13}C NMR chemical shifts (in ppm) for steviol+7Glc (#14). *See* Examples 6, 8, and 9.

[0059] Figure 9A shows accumulation of ent-kaurenoic acid+2Glc (#7), ent-kaurenoic acid+3Glc (isomer 1), and ent-kaurenoic acid+3Glc (isomer 2) in *S. cerevisiae* expressing UGT76G1 variants. Figure 9B shows accumulation of ent-kaurenol+2Glc (#8) and ent-kaurenol+3Glc (isomer 1) co-eluted with ent-kaurenol+3Glc (#6) in *S. cerevisiae* expressing UGT76G1 variants. *See* Example 8.

[0060] Figure 10A shows accumulation of 1,2-stevioside, RebG, steviol+3Glc (#1), steviol+4Glc (#26), steviol+5Glc (#22), steviol+5Glc (#24), steviol+5Glc (#25), steviol+6Glc (isomer 1), and steviol+6Glc (#23) in *S. cerevisiae* expressing RebD-producing UGT76G1 variants. Figure 10B shows accumulation of 1,2-stevioside, RebG, steviol+3Glc (#1), steviol+4Glc (#26), steviol+5Glc (#22), steviol+5Glc (#24), steviol+5Glc (#25), steviol+6Glc (isomer 1), and steviol+6Glc (#23) in *S. cerevisiae* expressing RebM-producing UGT76G1 variants. Figure 10C shows accumulation of 13-SMG, 1,2-bioside, rubusoside, RebA, RebB, RebD, RebE, and RebM in *S. cerevisiae* expressing UGT76G1 variants. *See* Example 8.

[0061] Figure 11A shows accumulation of ent-kaurenoic acid+2Glc (#7), ent-kaurenoic acid+3Glc (isomer 1), ent-kaurenoic acid+3Glc (isomer 2), ent-kaurenol+2Glc (#8), and ent-kaurenol+3Glc (isomer 1) co-eluted with ent-kaurenol+3Glc (#6) in an *S. cerevisiae* steviol glycoside production strain (control strain comprised three copies of wild-type UGT76G1 (SEQ ID NO:9); variant strains comprised two copies of wild-type UGT76G1 and one copy of a UGT76G1 variant). Figure 11B shows total levels of glycosylated ent-kaurenoic acid (ent-kaurenoic acid+2Glc (#7) + ent-kaurenoic acid+3Glc (isomer 1) + ent-kaurenoic acid+3Glc (isomer 2)) in an *S. cerevisiae* steviol glycoside production strain expressing UGT76G1 variants. Figure 11C shows total levels of glycosylated ent-kaurenol (ent-kaurenol+3Glc (isomer 1) co-eluted with ent-kaurenol+3Glc (#6) and ent-kaurenol+2Glc (#8) in an *S. cerevisiae* steviol glycoside production strain expressing UGT76G1 variants. Figure 11D shows accumulation of 1,2-bioside, 1,2-stevioside, steviol+3Glc (#1), steviol+4Glc (#26), steviol+5Glc (#22), steviol+5Glc (#24), steviol+5Glc (#25), steviol+6Glc (isomer 1), steviol+6Glc (#23), steviol+7Glc (isomer 2), and steviol+7Glc (isomer 5) in an *S. cerevisiae* steviol glycoside production strain expressing UGT76G1 variants. Figure 11E shows accumulation of 13-SMG, 1,2-bioside, rubusoside, RebG, RebA, RebB, RebD, RebE, and RebM in an *S. cerevisiae* steviol glycoside production strain expressing UGT76G1 variants. *See* Example 8.

[0062] Skilled artisans will appreciate that elements in the Figures are illustrated for simplicity and clarity and have not necessarily been drawn to scale. For example, the dimensions of some of the elements in the Figures can be exaggerated relative to other elements to help improve understanding of the embodiment(s) of the present invention.

DETAILED DESCRIPTION OF THE INVENTION

[0063] Before describing the present invention in detail, a number of terms will be defined. As used herein, the singular forms “a,” “an,” and “the” include plural referents unless the context clearly dictates otherwise. For example, reference to a “nucleic acid” means one or more nucleic acids.

[0064] It is noted that terms like “preferably,” “commonly,” and “typically” are not utilized herein to limit the scope of the claimed invention or to imply that certain features are critical, essential, or even important to the structure or function of the claimed invention. Rather, these terms are merely intended to highlight alternative or additional features that can or cannot be utilized in a particular embodiment of the present invention.

[0065] For the purposes of describing and defining the present invention it is noted that the term “substantially” is utilized herein to represent the inherent degree of uncertainty that can be attributed to any quantitative comparison, value, measurement, or other representation. The term “substantially” is also utilized herein to represent the degree by which a quantitative representation can vary from a stated reference without resulting in a change in the basic function of the subject matter at issue.

[0066] Methods well known to those skilled in the art can be used to construct genetic expression constructs and recombinant cells according to this invention. These methods include *in vitro* recombinant DNA techniques, synthetic techniques, *in vivo* recombination techniques, and polymerase chain reaction (PCR) techniques. *See*, for example, techniques as described in Green & Sambrook, 2012, MOLECULAR CLONING: A LABORATORY MANUAL, Fourth Edition, Cold Spring Harbor Laboratory, New York; Ausubel *et al.*, 1989, CURRENT PROTOCOLS IN MOLECULAR BIOLOGY, Greene Publishing Associates and Wiley Interscience, New York, and PCR Protocols: A Guide to Methods and Applications (Innis *et al.*, 1990, Academic Press, San Diego, CA).

[0067] As used herein, the terms “polynucleotide,” “nucleotide,” “oligonucleotide,” and “nucleic acid” can be used interchangeably to refer to nucleic acid comprising DNA, RNA, derivatives thereof, or combinations thereof, in either single-stranded or double-stranded embodiments depending on context as understood by the skilled worker.

[0068] As used herein, the terms “microorganism,” “microorganism host,” “microorganism host cell,” “recombinant host,” and “recombinant host cell” can be used interchangeably. As used herein, the term “recombinant host” is intended to refer to a host, the genome of which has been augmented by at least one DNA sequence. Such DNA sequences include but are not limited to genes that are not naturally present, DNA sequences that are not normally transcribed into RNA or translated into a protein (“expressed”), and other genes or DNA sequences which one desires to introduce into a host. It will be appreciated that typically the genome of a recombinant host described herein is augmented through stable introduction of one or more recombinant genes. Generally, introduced DNA is not originally resident in the host that is the recipient of the DNA, but it is within the scope of this disclosure to isolate a DNA segment from a given host, and to subsequently introduce one or more additional copies of that DNA into the same host, *e.g.*, to enhance production of the product of a gene or alter the expression pattern of a gene. In some instances, the introduced DNA will modify or even replace an endogenous gene or DNA sequence by, *e.g.*, homologous recombination or site-directed mutagenesis. Suitable recombinant hosts include microorganisms.

[0069] As used herein, the term “recombinant gene” refers to a gene or DNA sequence that is introduced into a recipient host, regardless of whether the same or a similar gene or DNA sequence may already be present in such a host. “Introduced,” or “augmented” in this context, is known in the art to mean introduced or augmented by the hand of man. Thus, a recombinant gene can be a DNA sequence from another species or can be a DNA sequence that originated from or is present in the same species but has been incorporated into a host by recombinant methods to form a recombinant host. It will be appreciated that a recombinant gene that is introduced into a host can be identical to a DNA sequence that is normally present in the host being transformed, and is introduced to provide one or more additional copies of the DNA to thereby permit overexpression or modified expression of the gene product of that DNA. In some aspects, said recombinant genes are encoded by cDNA. In other embodiments, recombinant genes are synthetic and/or codon-optimized for expression in *S. cerevisiae*.

[0070] As used herein, the term “engineered biosynthetic pathway” refers to a biosynthetic pathway that occurs in a recombinant host, as described herein. In some aspects, one or more steps of the biosynthetic pathway do not naturally occur in an unmodified host. In some embodiments, a heterologous version of a gene is introduced into a host that comprises an endogenous version of the gene.

[0071] As used herein, the term “endogenous” gene refers to a gene that originates from and is produced or synthesized within a particular organism, tissue, or cell. In some embodiments, the endogenous gene is a yeast gene. In some embodiments, the gene is endogenous to *S. cerevisiae*, including, but not limited to *S. cerevisiae* strain S288C. In some embodiments, an endogenous yeast gene is overexpressed. As used herein, the term “overexpress” is used to refer to the expression of a gene in an organism at levels higher than the level of gene expression in a wild type organism. *See*, *e.g.*, Prelich, 2012, *Genetics* 190:841-54. In some embodiments, an endogenous yeast gene, for example ADH, is deleted. *See*, *e.g.*, Giaever & Nislow, 2014, *Genetics* 197(2):451-65. As used herein, the terms “deletion,” “deleted,” “knockout,” and “knocked out” can be used interchangabley to refer to an endogenous gene that has been manipulated to no longer be expressed in an organism, including, but not limited to, *S. cerevisiae*.

[0072] As used herein, the terms “heterologous sequence” and “heterologous coding sequence” are used to describe a sequence derived from a species other than the recombinant host. In some embodiments, the recombinant host is an *S. cerevisiae* cell, and a heterologous sequence is derived from an organism other than *S. cerevisiae*. A heterologous coding sequence, for example, can be from a prokaryotic microorganism, a eukaryotic microorganism, a plant, an animal, an insect, or a fungus different than the recombinant host expressing the heterologous sequence. In some embodiments, a coding sequence is a sequence that is native to the host.

[0073] A “selectable marker” can be one of any number of genes that complement host cell auxotrophy, provide antibiotic resistance, or result in a color change. Linearized DNA fragments of the gene replacement vector then are introduced into the cells using methods well known in the art (*see* below). Integration of the linear fragments into the genome and the disruption of the gene can be determined based on the selection marker and can be verified by, for example, PCR or Southern blot analysis. Subsequent to its use in selection, a selectable marker can be removed from the genome of the host cell by, *e.g.*, Cre-LoxP systems (*see*, *e.g.*, Gossen *et al.*, 2002, *Ann. Rev. Genetics* 36:153-173 and U.S. 2006/0014264). Alternatively, a gene replacement vector can be constructed in such a way as to include a portion of the gene to be disrupted, where the portion is devoid of any endogenous gene promoter sequence and encodes none, or an inactive fragment of, the coding sequence of the gene.

[0074] As used herein, the terms “variant” and “mutant” are used to describe a protein sequence that has been modified at one or more amino acids, compared to the wild-type sequence of a particular protein.

[0075] As used herein, the term “inactive fragment” is a fragment of the gene that encodes a protein having, *e.g.*, less than about 10% (*e.g.*, less than about 9%, less than about 8%, less than about 7%, less than about 6%, less than about 5%, less than about 4%, less than about 3%, less than about 2%, less than about 1%, or 0%) of the activity of the protein produced from the full-length coding sequence of the gene. Such a portion of a gene is inserted in a vector in such a way that no known promoter sequence is operably linked to the gene sequence, but that a stop codon and a transcription termination sequence are operably linked to the portion of the gene sequence. This vector can be subsequently linearized in the portion of the gene sequence and transformed into a cell. By way of single homologous recombination, this linearized vector is then integrated in the endogenous counterpart of the gene with inactivation thereof.

[0076] As used herein, the term “steviol glycoside” refers to rebaudioside A (RebA) (CAS # 58543-16-1), rebaudioside B (RebB) (CAS # 58543-17-2), rebaudioside C (RebC) (CAS # 63550-99-2), rebaudioside D (RebD) (CAS # 63279-13-0), rebaudioside E (RebE) (CAS # 63279-14-1), rebaudioside F (RebF) (CAS # 438045-89-7), rebaudioside M (RebM) (CAS # 1220616-44-3), rubusoside (CAS # 63849-39-4), dulcoside A (CAS # 64432-06-0), rebaudioside I (RebI) (MassBank Record: FU000332), rebaudioside Q (RebQ), 1,2-stevioside (CAS # 57817-89-7), 1,3-stevioside (RebG), 1,2-bioside (MassBank Record: FU000299), 1,3-bioside, steviol-13-*O*-glucoside (13-SMG), steviol-19-*O*-glucoside (19-SMG), a di-glycosylated steviol, a tri-glycosylated steviol, a tetra-glycosylated steviol, a penta-glycosylated steviol, a hexa-glycosylated steviol, a hepta-glycosylated steviol, and/or isomers thereof. *See* Figure 2; *see also*, Steviol Glycosides Chemical and Technical Assessment 69th JECFA, 2007, prepared by Harriet Wallin, Food Agric. Org. *See* Figure 2, Figure 7, Figure 8, and Table 1; *see also*, Steviol Glycosides Chemical and Technical Assessment 69th JECFA, 2007, prepared by Harriet Wallin, Food Agric. Org. Glycosylated steviol compounds can comprise one or more glucose, N-acetylglucosamine (GlcNAc), rhamnose, and/or xylose moieties. Non-limiting examples of steviol glycosides that can be produced by methods described herein are shown in Table 1, Figure 7, and Figure 8.

[0077] As used herein, the term “glycosylated ent-kaurenol compound” refers to di-glycosylated ent-kaurenol or tri-glycosylated ent-kaurenol. As used herein, the term “glycosylated ent-kaurenoic acid compound” refers to di-glycosylated ent-kaurenoic acid or tri-glycosylated ent-kaurenoic acid. *See* Figure 7, Figure 8, and Table 1. Glycosylated ent-kaurenol compounds and glycosylated ent-kaurenoic acid compounds can comprise one or more glucose, GlcNAc, rhamnose, and/or xylose moieties. Non-limiting examples of glycosylated ent-kaurenol compounds and glycosylated ent-kaurenoic acid compounds that can be produced by methods described herein are shown in Table 1, Figure 7, and Figure 8.

[0078] As used herein, the terms “steviol glycoside precursor” and “steviol glycoside precursor compound” are used to refer to intermediate compounds in the steviol glycoside biosynthetic pathway. Steviol glycoside precursors include, but are not limited to, geranylgeranyl diphosphate (GGPP), ent-copalyl-diphosphate, ent-kaurene, ent-kaurenol, ent-kaurenal, ent-kaurenoic acid, and steviol. *See* Figure 1. In some embodiments, steviol glycoside precursors are themselves steviol glycoside compounds. For example, 19-SMG, rubusoside, stevioside, and RebE are steviol glycoside precursors of RebM. *See* Figure 2. Steviol glycosides and/or steviol glycoside precursors can be produced *in vivo* (*i.e.*, in a recombinant host), *in vitro* (*i.e.*, enzymatically), or by whole cell bioconversion. As used herein, the terms “produce” and “accumulate” can be used interchangeably to describe synthesis of steviol glycosides and steviol glycoside precursors *in vivo*, *in vitro*, or by whole cell bioconversion.

[0079] As used herein, the term “cell culture broth” can be used to refer to a liquid that can support or has supported growth of a host cell, including, but not limited to, a yeast host cell. The components of a cell culture broth can include, for example, a steviol glycoside, a glycosylated ent-kaurenol compound, and/or a glycosylated ent-kaurenoic acid compound produced by the host cell, glucose, fructose, sucrose, trace metals, vitamins, salts, yeast nitrogen base (YNB), and/or amino acids.

[0080] As used herein, the term “cell lysate” can be used to refer to a fluid comprising the components of a lysed cell, *i.e.*, a cell whose membrane has been disrupted chemically or mechanically. A cell lysate can further comprise a steviol glycoside, a glycosylated ent-kaurenol compound, and/or a glycosylated ent-kaurenoic acid compound produced by the host cell, glucose, fructose, sucrose, xylose, rhamnose, uridine diphosphate (UDP)-glucose, UDP-rhamnose, UDP-xylose, GlcNAc, trace metals, vitamins, salts, YNB, and/or amino acids. In some aspects, a cell lysate is a yeast cell lysate, such as an *S. cerevisiae* cell lysate, or a bacterial cell lysate, such as an *E. coli* cell lysate.

[0081] As used herein, the term “reaction mixture” refers to a solution for conducting an *in vitro* reaction. The components of a reaction mixture can include, but are not limited to, a steviol glycoside, a glycosylated ent-kaurenol compound, a glycosylated ent-kaurenoic acid compound, a polypeptide such as a UGT polypeptide, UDP-glucose, UDP-rhamnose, UDP-xylose, GlcNAC, a buffer, and/or salts.

[0082] Recombinant steviol glycoside-producing *Saccharomyces cerevisiae* (*S. cerevisiae*) strains are described in WO 2011/153378, WO 2013/022989, WO 2014/122227, and WO 2014/122328. Methods of producing steviol glycosides in recombinant hosts, by whole cell bio-conversion, and *in vitro* are also described in WO 2011/153378, WO 2013/022989, WO 2014/122227, and WO 2014/122328.

[0083] In some embodiments, steviol glycosides and/or steviol glycoside precursors are produced *in vivo* through expression of one or more enzymes involved in the steviol glycoside biosynthetic pathway in a recombinant host. For example, a steviol-producing recombinant host expressing one or more of a gene encoding a GGPPS polypeptide, a gene encoding a CDPS polypeptide, a gene encoding a KS polypeptide, a gene encoding a KO polypeptide, a gene encoding a KAH polypeptide, a gene encoding a CPR polypeptide, and a gene encoding a UGT polypeptide can produce a steviol glycoside and/or steviol glycoside precursors *in vivo*. *See, e.g.*, Figures 1 and 2. The skilled worker will appreciate that one or more of these genes can be endogenous to the host provided that at least one (and in some embodiments, all) of these genes is a recombinant gene introduced into the recombinant host.

[0084] A recombinant host described herein can comprise a gene encoding a polypeptide capable of synthesizing geranylgeranyl pyrophosphate (GGPP) from farnesyl diphosphate (FPP) and isopentenyl diphosphate (IPP), a gene encoding a polypeptide capable of synthesizing ent-copalyl dirophosphate from GGPP; a gene encoding a polypeptide capable of synthesizing ent-kaurene from ent-copalyl pyrophosphate, a gene encoding a polypeptide capable of synthesizing ent-kaurenoic acid from ent-kaurene, a gene encoding a polypeptide capable of synthesizing steviol from ent-kaurenoic acid; and/or a gene encoding a polypeptide capable of converting NADPH to NADP+. A GGPPS polypeptide can synthesize GGPP from

FPP and IPP. A CDPS polypeptide can synthesize ent-copalyl dirophosphate from GGPP. A KS polypeptide can synthesize ent-kaurene from ent-copalyl pyrophosphate. A KO polypeptide can synthesize ent-kaurenoic acid from ent-kaurene. A KAH polypeptide can synthesize steviol from ent-kaurenoic acid. A CPR polypeptide can convert NADPH to NADP+.

[0085] In another example, a recombinant host expressing a gene encoding a GGPPS polypeptide, a gene encoding a CDPS polypeptide, a gene encoding a KS polypeptide, a gene encoding a KO polypeptide, a gene encoding a KAH polypeptide, and a gene encoding a CPR polypeptide can produce steviol *in vivo*. *See*, *e.g.*, Figure 1. The skilled worker will appreciate that one or more of these genes can be endogenous to the host provided that at least one (and in some embodiments, all) of these genes is a recombinant gene introduced into the recombinant host.

[0086] In another example, a recombinant host expressing a gene encoding a GGPPS polypeptide, a gene encoding a CDPS polypeptide, a gene encoding a KS polypeptide, a gene encoding a KO polypeptide, a gene encoding a KAH polypeptide, a gene encoding a CPR polypeptide, and one or more of a gene encoding a UGT polypeptide can produce a steviol glycoside *in vivo*. *See*, *e.g.*, Figures 1 and 2. The skilled worker will appreciate that one or more of these genes can be endogenous to the host provided that at least one (and in some embodiments, all) of these genes is a recombinant gene introduced into the recombinant host.

[0087] In some aspects, the GGPPS polypeptide comprises a polypeptide having an amino acid sequence set forth in SEQ ID NO:20 (which can be encoded by the nucleotide sequence set forth in SEQ ID NO:19), SEQ ID NO:22 (which can be encoded by the nucleotide sequence set forth in SEQ ID NO:21), SEQ ID NO:24 (which can be encoded by the nucleotide sequence set forth in SEQ ID NO:23), SEQ ID NO:26 (which can be encoded by the nucleotide sequence set forth in SEQ ID NO:25), SEQ ID NO:28 (which can be encoded by the nucleotide sequence set forth in SEQ ID NO:27), SEQ ID NO:30 (which can be encoded by the nucleotide sequence set forth in SEQ ID NO:29), SEQ ID NO:32 (which can be encoded by the nucleotide sequence set forth in SEQ ID NO:31), or SEQ ID NO:116 (which can be encoded by the nucleotide sequence set forth in SEQ ID NO:115).

[0088] In some aspects, the CDPS polypeptide comprises a polypeptide having an amino acid sequence set forth in SEQ ID NO:34 (which can be encoded by the nucleotide sequence set forth in SEQ ID NO:33), SEQ ID NO:36 (which can be encoded by the nucleotide sequence set forth in SEQ ID NO:35), SEQ ID NO:38 (which can be encoded by the nucleotide sequence set forth in SEQ ID NO:37), SEQ ID NO:40 (which can be encoded by the nucleotide sequence set forth in SEQ ID NO:39), or SEQ ID NO:42 (which can be encoded by the nucleotide sequence set forth in SEQ ID NO:41). In some embodiments, the CDPS polypeptide lacks a chloroplast transit peptide.

[0089] In some aspects, the KS polypeptide comprises a polypeptide having an amino acid sequence set forth in SEQ ID NO:44 (which can be encoded by the nucleotide sequence set forth in SEQ ID NO:43), SEQ ID NO:46 (which can be encoded by the nucleotide sequence set forth in SEQ ID NO:45), SEQ ID NO:48 (which can be encoded by the nucleotide sequence set forth in SEQ ID NO:47), SEQ ID NO:50 (which can be encoded by the nucleotide sequence set forth in SEQ ID NO:49), or SEQ ID NO:52 (which can be encoded by the nucleotide sequence set forth in SEQ ID NO:51).

[0090] In some embodiments, a recombinant host comprises a gene encoding a CDPS-KS polypeptide. In some aspects, the CDPS-KS polypeptide comprises a polypeptide having an amino acid sequence set forth in SEQ ID NO:54 (which can be encoded by the nucleotide sequence set forth in SEQ ID NO:53), SEQ ID NO:56 (which can be encoded by the nucleotide sequence set forth in SEQ ID NO:55), or SEQ ID NO:58 (which can be encoded by the nucleotide sequence set forth in SEQ ID NO:57).

[0091] In some aspects, the KO polypeptide comprises a polypeptide having an amino acid sequence set forth in SEQ ID NO:60 (which can be encoded by the nucleotide sequence set forth in SEQ ID NO:59), SEQ ID NO:62 (which can be encoded by the nucleotide sequence set forth in SEQ ID NO:61), SEQ ID NO:117 (which can be encoded by the nucleotide sequence set forth in SEQ ID NO:63 or SEQ ID NO:64), SEQ ID NO:66 (which can be encoded by the nucleotide sequence set forth in SEQ ID NO:65), SEQ ID NO:68 (which can be encoded by the nucleotide sequence set forth in SEQ ID NO:67), SEQ ID NO:70 (which can be encoded by the nucleotide sequence set forth in SEQ ID NO:69), SEQ ID NO:72 (which can be encoded by the nucleotide sequence set forth in SEQ ID NO:71), SEQ ID NO:74 (which can be encoded by the nucleotide sequence set forth in SEQ ID NO:73), or SEQ ID NO:76 (which can be encoded by the nucleotide sequence set forth in SEQ ID NO:75).

[0092] In some aspects, the CPR polypeptide comprises a polypeptide having an amino acid sequence set forth in SEQ ID NO:78 (which can be encoded by the nucleotide sequence set forth in SEQ ID NO:77), SEQ ID NO:80 (which can be encoded by the nucleotide sequence set forth in SEQ ID NO:79), SEQ ID NO:82 (which can be encoded by the nucleotide sequence set forth in SEQ ID NO:81), SEQ ID NO:84 (which can be encoded by the nucleotide sequence set forth in SEQ ID NO:83), SEQ ID NO:86 (which can be encoded by the nucleotide sequence set forth in SEQ ID NO:85), SEQ ID NO:88 (which can be encoded by the nucleotide sequence set forth in SEQ ID NO:87), SEQ ID NO:90 (which can be encoded by the nucleotide sequence set forth in SEQ ID NO:89), or SEQ ID NO:92 (which can be encoded by the nucleotide sequence set forth in SEQ ID NO:91).

[0093] In some aspects, the KAH polypeptide comprises a polypeptide having an amino acid sequence set forth in SEQ ID NO:94 (which can be encoded by the nucleotide sequence set forth in SEQ ID NO:93), SEQ ID NO:97 (which can be encoded by the nucleotide sequence set forth in SEQ ID NO:95 or SEQ ID NO:96), SEQ ID NO:100 (which can be encoded by the nucleotide sequence set forth in SEQ ID NO:98 or SEQ ID NO:99), SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:103, SEQ ID NO:104, SEQ ID NO:106 (which can be encoded by the nucleotide sequence set forth in SEQ ID NO:105), SEQ ID NO:108 (which can be encoded by the nucleotide sequence set forth in SEQ ID NO:107), SEQ ID NO:110 (which can be encoded by the nucleotide sequence set forth in SEQ ID NO:109), SEQ ID NO:112 (which can be encoded by the nucleotide sequence set forth in SEQ ID NO:111), or SEQ ID NO:114 (which can be encoded by the nucleotide sequence set forth in SEQ ID NO:113).

[0094] In some embodiments, a recombinant host comprises a nucleic acid encoding a UGT85C2 polypeptide (SEQ ID NO:7), a nucleic acid encoding a UGT76G1 polypeptide (SEQ ID NO:9), a nucleic acid encoding a UGT74G1 polypeptide (SEQ ID NO:4), a nucleic acid encoding a UGT91D2 polypeptide, and/or a nucleic acid encoding a EUGT11 polypeptide (SEQ ID NO:16). In some aspects, the UGT91D2 polypeptide can be a UGT91D2e polypeptide (SEQ ID NO:11) or a UGT91D2e-b polypeptide (SEQ ID NO:13). In some aspects, the UGT85C2 polypeptide can be encoded by the nucleotide sequence set forth in SEQ ID NO:5 or SEQ ID NO:6, the UGT76G1 polypeptide can be encoded by the nucleotide sequence set forth in SEQ ID NO:8, the UGT74G1 polypeptide can be encoded by the nucleotide sequence set forth in SEQ ID NO:3, the UGT91D2e polypeptide can be encoded by the nucleotide sequence set forth in SEQ ID NO:10, the UGT91D2e-b polypeptide can be encoded by the nucleotide sequence set forth in SEQ ID NO:12, and the EUGT11 polypeptide can be encoded by the nucleotide sequence set forth in SEQ ID NO:14 or SEQ ID NO:15. The skilled worker will appreciate that expression of these genes may be necessary to produce a particular steviol glycoside but that one or more of these genes can be endogenous to the host provided that at least one (and in some embodiments, all) of these genes is a recombinant gene introduced into the recombinant host. In a particular embodiment, a steviol-producing recombinant microorganism comprises exogenous nucleic acids encoding UGT85C2, UGT76G1, or UGT91D2 polypeptides.

[0095] In another particular embodiment, a steviol-producing recombinant microorganism comprises exogenous nucleic acids encoding UGT85C2, UGT76G1, UGT74G1, and UGT91D2 polypeptides. In yet another particular embodiment, a steviol-producing recombinant microorganism comprises exogenous nucleic acids encoding UGT85C2, UGT76G1, UGT74G1, and EUGT11 polypeptides. In yet another particular embodiment, a steviol-producing recombinant microorganism comprises exogenous nucleic acids encoding UGT85C2, UGT76G1, UGT74G1, UGT91D2 (including *inter alia* UGT91D2e, UGT91D2m, UGT91D2e-b, and functional homologs thereof), and EUGT11 polypeptides. In yet another particular embodiment, a steviol-producing recombinant microorganism comprises exogenous nucleic acids encoding UGT85C2, UGT76G1, UGT74G1, UGT91D2, and/or EUGT11 polypeptides. In yet another particular embodiment, a steviol-producing recombinant microorganism comprises exogenous nucleic acids encoding UGT85C2, UCT76G1, UGT74G1, UGT91D2, and/or EUGT11 polypeptides.

[0096] In some embodiments, a recombinant host comprises: (a) a gene encoding a polypeptide capable of beta 1,2 glucosylation of the C2' of the 19-*O* glucose of a steviol glycoside; (b) a gene encoding a polypeptide capable of beta 1,2 glucosylation of the C2' of the 13-*O*-glucose of a steviol glycoside; (c) a gene encoding a polypeptide capable of beta 1,3 glucosylation of the C3' of the 19-*O*-glucose of a steviol glycoside; (d) a gene encoding a polypeptide capable of beta 1,3 glucosylation of the C3' of the 13-*O*-glucose of a steviol glycoside; (e) a gene encoding a polypeptide capable of beta 1,6 glucosylation of the C6' of the 13-*O*-glucose of a steviol glycoside; (f) a gene encoding a polypeptide capable of beta 1,6 glucosylation of the C6' of the 1,3-glucose of a 13-*O* diglucoside moiety of a steviol glycoside; (g) a gene encoding a polypeptide capable of glucosylation of the 13-OH of steviol or a steviol glycoside; (h) a gene encoding a polypeptide capable of glucosylation of the C-19 carboxyl of steviol or a steviol glycoside; (i) a gene encoding a polypeptide capable of beta 1,2 rhamnosylation of the C2' of the 13-*O*-glucose of a steviol glycoside; (j) a gene encoding a polypeptide capable of beta 1,2 xylosylation of the C2' of the 13-*O*-glucose of a steviol glycoside; (o) a gene encoding a polypeptide capable of beta 1,2 GlcNAc transfer to the C2' of the 19-*O* glucose of a steviol glycoside; (k) a gene encoding a polypeptide capable of beta 1,3 GlcNAc transfer to the C2' of the 19-*O* glucose of a steviol glycoside; (l) a gene encoding a polypeptide capable of beta 1,3 GlcNAc transfer to the C2' of the 13-*O*-glucose of a steviol glycoside; (m) a gene encoding a polypeptide capable of GlcNAc transfer to the C-19 carboxyl of steviol or a steviol glycoside; (n) a gene encoding a polypeptide capable of glucosylation of the C-19 carboxyl of kaurenoic acid or kaurenol; (o) a gene encoding a polypeptide capable of beta 1,2 glucosylation of the C2' of the 19-*O* glucose of a kaurenoic acid glycoside or kaurenol glycoside; (p) a gene encoding a polypeptide capable of a beta 1,2 glucosylation of a beta 1,2 diglucoside of kaurenoic acid; (q) a gene encoding a polypeptide capable of beta 1,2 GlcNAc transfer of a beta 1,2 diglucoside of kaurenoic acid; (r) a gene encoding a polypeptide capable of beta 1,3 glucosylation of the C3' of the 19-*O*-glucose of a kaurenoic acid glycoside or kaurenol glycoside; and/or (s) a gene encoding a polypeptide capable of beta 1,6 glucosylation of the C6' of the 1,3-glucose of a 19-*O* diglucoside moiety of a steviol glycoside.

[0097] In some aspects, EUGT11 (SEQ ID NO:14/SEQ ID NO:15, SEQ ID NO:16), UGT91D2e (SEQ ID NO:10, SEQ ID NO:11), UGT91D2e-b (SEQ ID NO:12, SEQ ID NO:13), a variant thereof, or a chimeric protein thereof catalyzes beta 1,2 glucosylation of the C2' of the 19-*O* glucose of a steviol glycoside. Exemplary UGT91D2e variant sequences are set forth in SEQ ID NOs:1, 2, 118-121, 123, and 191-214. In some aspects, UGT91D2e (SEQ ID NO:10, SEQ ID NO:11), UGT91D2e-b (SEQ ID NO:12, SEQ ID NO:13), a variant thereof, or a chimeric protein thereof catalyzes beta 1,2 glucosylation of the C2' of the 13-*O*-glucose of a steviol glycoside. Exemplary UGT91D2e variant sequences are set forth in SEQ ID NOs:1, 2, 118-121, 123, and 191-214. Exemplary UGT91D2e-EUGT11 chimeric protein sequences are set forth in SEQ ID NO:17 and SEQ ID NO:18. In some aspects, UGT76G1 (SEQ ID NO:8, SEQ ID NO:9), a variant thereof, or a chimeric protein thereof catalyzes beta 1,3 glucosylation of the C3' of the 19-*O*-glucose of a steviol glycoside and/or beta 1,3 glucosylation of the C3' of the 13-*O*-glucose of a steviol glycoside. Exemplary UGT76G1 variant sequences are set forth in SEQ ID NOs:181-190 and 217-220. In some aspects, UGT85C2 (SEQ ID NO:5/SEQ ID NO:6, SEQ ID NO:7), a variant thereof, or a chimeric protein thereof catalyzes glucosylation of the 13-OH of steviol or a steviol glycoside. Exemplary UGT85C2 variant sequences are set forth in SEQ ID NOs:127 and 147-180. In some aspects, UGT74G1 (SEQ ID NO:3, SEQ ID NO:4), a variant thereof, or a chimeric protein thereof catalyzes glucosylation of the C-19 carboxyl of steviol or a steviol glycoside. In some aspects, EUGT11 (SEQ ID NO:14/SEQ ID NO:15, SEQ ID NO:16), UGT91D2e (SEQ ID NO:10, SEQ ID NO:11), UGT74G1 (SEQ ID NO:3, SEQ ID NO:4), and/or UGT76G1 (SEQ ID NO:8, SEQ ID NO:9 can accept uridine diphosphate N-acetylglucosamine (UDP-Glc-NAc) as a substrate. In some aspects, UGT74G1 glycosylates ent-kaurenol and ent-kaurenoic acid; UGT76G1 and UGT91D2e subsequently add additional glucose or GlcNAc moieties by either a 1,3- or 1,2-linkage to form tri-glycosylated compounds. *See* Figures 3, 7 and 8.

[0098] In some embodiments, steviol glycosides and/or steviol glycoside precursors are produced through contact of a steviol glycoside precursor with one or more enzymes involved in the steviol glycoside pathway *in vitro*. For example, contacting steviol with a UGT polypeptide can result in production of a steviol glycoside *in vitro*. In some embodiments, a steviol glycoside precursor is produced through contact of an upstream steviol glycoside precursor with one or more enzymes involved in the steviol glycoside pathway *in vitro*. For example, contacting ent-kaurenoic acid with a KAH enzyme can result in production of steviol *in vitro*.

[0099] In some embodiments, a steviol glycoside or steviol glycoside precursor is produced by whole cell bioconversion. For whole cell bioconversion to occur, a host cell expressing one or more enzymes involved in the steviol glycoside pathway takes up and modifies a steviol glycoside precursor in the cell; following modification *in vivo*, a steviol glycoside remains in the cell and/or is excreted into the culture medium. For example, a host cell expressing a gene encoding a UGT polypeptide can take up steviol and glycosylate steviol in the cell; following glycosylation *in vivo*, a steviol glycoside can be excreted into the culture medium. In some embodiments, the cell is permeabilized to take up a substrate to be modified or to excrete a modified product.

[00100] In some embodiments, steviol, one or more steviol glycoside precursors, and/or one or more steviol glycosides are produced by co-culturing of two or more hosts. In some embodiments, one or more hosts, each expressing one or more enzymes involved in the steviol glycoside pathway, produce steviol, one or more steviol glycoside precursors, and/or one or more steviol glycosides. For example, a host comprising a GGPPS, a CDPS, a KO, a KS, a KAH, and/or a CPR and a host comprising one or more UGTs produce one or more steviol glycosides.

[00101] In some embodiments, polypeptides suitable for producing steviol glycosides, such as 1,2-stevioside and RebD, *in vitro*, in a recombinant host, or by whole cell bioconversion include functional homologs of UGT91D2e (SEQ ID NO:10, SEQ ID NO:11), including UGT91D2e-b (SEQ ID NO:12, SEQ ID NO:13); UGT91D2e V286C (SEQ ID NO:1); UGT91D2e G384W (SEQ ID NO:2); UGT91D2e L211M (SEQ ID NO:118); UGT91D2e L195G (SEQ ID NO:119); UGT91D2e V196P (SEQ ID NO:120); UGT91D2e L211H (SEQ ID NO:121); UGT91D2e L213E (SEQ ID NO:191); UGT91D2e S221Y (SEQ ID NO:192); UGT91D2e E438H (SEQ ID NO:193); UGT91D2e M152T (SEQ ID NO:194); UGT91D2e L211C (SEQ ID NO:195); UGT91D2e L195S (SEQ ID NO:196); UGT91D2e L195V (SEQ ID NO:197); UGT91D2e V286S (SEQ ID NO:198); UGT91D2e S221S (SEQ ID NO:199); UGT91D2e P93V M152G (SEQ ID

NO:200); UGT91D2e S99I (SEQ ID NO:201); UGT91D2e T144K P201P (SEQ ID NO:202); UGT91D2e T144L (SEQ ID NO:203); UGT91D2e T144M (SEQ ID NO:204); UGT91D2e A148K L211I (SEQ ID NO:205); UGT91D2e L195N (SEQ ID NO:206); UGT91D2e K199C (SEQ ID NO:207); UGT91D2e L211M E426G A466V (SEQ ID NO:208); UGT91D2e L211T I303I (SEQ ID NO:209); UGT91D2e V286N (SEQ ID NO:210); UGT91D2e S114F V286S (SEQ ID NO:211); UGT91D2e G384K (SEQ ID NO:212); UGT91D2e G384Y (SEQ ID NO:213); UGT91D2e E438M (SEQ ID NO:214); and UGT91D2e L195C (SEQ ID NO:123). *See* Example 3.

[00102] In some embodiments, a useful UGT91D2 homolog can have one or more amino acid substitutions at residues 195, 196, 211, 286, and 384. *See* Table 2. Non-limiting examples of useful UGT91D2e homologs include polypeptides having substitutions (with respect to SEQ ID NO:11) at residue 93 (*e.g.*, a valine at residue 93); 99 (*e.g.*, an isoleucine at residue 99), 114 (*e.g.*, a phenylalanine at residue 114); 144 (*e.g.*, a lysine, leucine, or methionine at residue 144); 148 (*e.g.*, a lysine at residue 148); 152 (*e.g.*, a threonine at residue 152); 195 (*e.g.*, a glycine, cysteine, serine, arginine, or valine at residue 195); 196 (*e.g.*, a proline at residue 196); 199 (*e.g.*, a cysteine at residue 199); 211 (*e.g.*, a methionine, histidine, threonine, cysteine, or isoleucine at residue 211); 213 (*e.g.*, a glutamic acid at 213); 221 (*e.g.*, an isoleucine at residue 221); 286 (*e.g.*, an alanine, cysteine, asparagine, or serine at residue 286); 384 (*e.g.*, a tryptophan, lysine, or tyrosine at residue 384); 426 (*e.g.*, a glycine at residue 426); 438 (*e.g.*, a histidine or methionine at residue 438); or 466 (*e.g.*, a valine at residue 466). *See* Example 3.

[00103] In some embodiments, UGT91D2e variants comprise silent mutations. For example, in some embodiments, UGT91D2e variants comprise silent mutations at residues not limited to residue 130, residue 201, or residue 221. *See* Example 3.

[00104] In some embodiments, UGT91D2e variants not limited to UGT91D2e V286C (SEQ ID NO:1), UGT91D2e G384W (SEQ ID NO:2), UGT91D2e L195V (SEQ ID NO:197), UGT91D2e V286S (SEQ ID NO:198), UGT91D2e T144K P201P (SEQ ID NO:202), UGT91D2e L211T I130I (SEQ ID NO:184), UGT91D2e S11F V286S (SEQ ID NO:211), and UGT91D2e E438M (SEQ ID NO:214) are selective towards rubusoside, with preferential accumulation of 1,2-stevioside. In some embodiments, UGT91D2e variants not limited to UGTD1D2e P93V M152G (SEQ ID NO:200), UGT91D2e S99I (SEQ ID NO:201), UGT91D2e T144L (SEQ ID NO:203), UGT91D2e A148K L221I (SEQ ID NO:205), and UGT91D2e G384K (SEQ ID NO:212) are selective towards RebA, with preferential accumulation of RebD. In some embodiments, UGT91D2e variants not limited to a UGT91D2e variant with a mutation at residue 211 (*e.g.*, UGT91D2e L211M of SEQ ID NO:118) catalyze conversion of rubusoside to 1,2-stevioside and conversion of RebA to RebD, with preferential accumulation of 1,2-stevioside. *See* Example 3 and Tables 2 and 3.

[00105] In some embodiments, polypeptides suitable for producing steviol glycosides, such as RebA, RebD, rubusoside, and/or 1,2-stevioside in a recombinant host include UGT91D2e-b-EUGT11 chimeric enzymes, such as Chim_3 (SEQ ID NO:17) or Chim_7 (SEQ ID NO:18). *See* Example 4 and Table 5.

[00106] In some embodiments, Chim_7 (SEQ ID NO:18) more efficiently converts rubusoside to 1,2-stevioside, compared to EUGT11 and UGT91D2e. In some embodiments, Chim_7 (SEQ ID NO:18) fully consumes a supplied amount of rubusoside. In some embodiments, Chim_7 (SEQ ID NO:18) demonstrates 1.75-fold higher activity towards RebA than UGT91D2e-b (SEQ ID NO:12, SEQ ID NO:13). In some embodiments, Chim_3 (SEQ ID NO:17) selectively converts rubusoside to 1,2-stevioside. *See* Example 4 and Table 5.

[00107] In some embodiments, UGT91D2e-b-EUGT11 chimeric enzymes such as Chim_2 (SEQ ID NO:122); Chim_4 (SEQ ID NO:124); Chim_5 (SEQ ID NO:125); Chim_6 (SEQ ID NO:126); Chim_7 (SEQ ID NO:18); Chim_8 (SEQ ID NO:128); Chim_9 (SEQ ID NO:129); Chim_10 (SEQ ID NO:130); Chim_11 (SEQ ID NO:131); Chim_12 (SEQ ID NO:132); Chim_13 (SEQ ID NO:133); Chim_14 (SEQ ID NO:134) are used to produce steviol glycosides and/or steviol glycoside precursors.

[00108] In some embodiments, a useful UGT85C2 homolog can have one or more amino acid substitutions at residues 21, 48, 49, 84, 86, 87, 91, 92, 95, 122, 304, and 334. *See* Table 7. Non-limiting examples of useful UGT85C2 homologs include polypeptides having substitutions (with respect to SEQ ID NO:7) at residue 21 (*e.g.*, a lysine, threonine, or valine at residue 21), 48 (*e.g.*, a serine, histidine, tyrosine, arginine, glutamine, or tryptophan at residue 48), 49 (*e.g.*, a valine at residue 49), 84 (*e.g.*, a glycine, alanine, threonine, cysteine, proline, valine, or asparagine at residue 84), 86 (*e.g.*, an arginine or glycine at residue 86); 87 (*e.g.*, an histidine, proline, methionine or tyrosine at residue 87); 91 (*e.g.*, an lysine, arginine, or threonine at residue 91); 92 (*e.g.*, an phenylalanine, isoleucine, methionine, or lysine at residue 92); 122 (*e.g.*, an serine at residue 122); 304 (*e.g.*, a serine at residue 304); and 334 (*e.g.*, an serine or methionine at residue 334). *See* SEQ ID NOs:127 and 147-180, Table 7A for UGT85C2 variants analyzed that preferentially catalyze conversion of 19-SMG over conversion of steviol, Table 7B for UGT85C2 variants that preferentially catalyze conversion of steviol over conversion of 19-SMG, and Table 7C for additional UGT85C2 variants that catalyze conversion of 19-SMG and steviol. Also *see* Example 5.

[00109] In some embodiments, a steviol glycoside-producing *S. cerevisiae* strain comprising a recombinant gene encoding a *Synechococcus sp.* GGPPS polypeptide (SEQ ID NO:19, SEQ ID NO:20), a recombinant gene encoding a truncated *Z. mays* CDPS polypeptide (SEQ ID NO:39, SEQ ID NO:40), a recombinant gene encoding an *A. thaliana* KS polypeptide (SEQ ID NO:51, SEQ ID NO:52), a recombinant gene encoding a recombinant *S. rebaudiana* KO polypeptide (SEQ ID NO:59, SEQ ID NO:60), a recombinant gene encoding an *A. thaliana* ATR2 polypeptide (SEQ ID NO:91, SEQ ID NO:92), a recombinant gene encoding an *O. sativa* EUGT11 polypeptide (SEQ ID NO:14/SEQ ID NO:15, SEQ ID NO:16), a recombinant gene encoding an SrKAHe1 polypeptide (SEQ ID NO:93, SEQ ID NO:94), a recombinant gene encoding an *S. rebaudiana* CPR8 polypeptide (SEQ ID NO:85, SEQ ID NO:86), a recombinant gene encoding an *S. rebaudiana* UGT74G1 polypeptide (SEQ ID NO:3, SEQ ID NO:4), a recombinant gene encoding an *S. rebaudiana* UGT76G1 polypeptide (SEQ ID NO:8, SEQ ID NO:9), a recombinant gene encoding an *S. rebaudiana* UGT91D2e polypeptide (SEQ ID NO:10, SEQ ID NO:11), a recombinant KO gene encoded by the nucleotide sequence set forth in SEQ ID NO:67 (corresponding to the amino acid sequence set forth in SEQ ID NO:117), and a recombinant CPR1 gene encoding (SEQ ID NO:77, SEQ ID NO:78) accumulates ent-kaurenoic acid+2Glc (#7), ent-kaurenoic acid+3Glc (isomer 1), ent-kaurenoic acid+3Glc (isomer 2), 19-SMG, steviol, steviol+2Glc (#23), and steviol+3Glc (#34) but does not accumulate ent-kaurenol glycosides. *See* Example 6 and Figures 4A-4C.

[00110] In some embodiments, the S84V F48S, F48H, F48Y, F48R, F48Q, F48T, F48S, I49V, P86R, P86G, and F122S variants of UGT85C2 are selective towards 19-SMG, compared to steviol (Table 7A). In some embodiments, the S84T, I87M I87P, I87Y, L91K, L91R, L91T, L92M, and I95K variants of UGT85C2 are selective towards steviol, compared to 19-SMG (Table 7B). In some embodiments, expression of UGT85C2 T304S (SEQ ID NO:127) in a steviol glycoside-producing host increases accumulation of steviol glycosides, compared to a steviol glycoside-producing host not expressing UGT85C2 T304S (SEQ ID NO:127). *See* Example 5.

[00111] In some embodiments, cell lysates comprising UGT85C2 or a UGT85C2 variant show a preference for either steviol or 19-SMG for a substrate. In some aspects, using steviol as a substrate, the F48H, F48Y, F48T, I49V, S84A, and L92F UGT85C2 variants exhibit high activity during incubation periods of under 40 min, and the F48H, F48Y, F48T, and I49V UGT85C2 variants exhibit high activity during incubation periods of over 40 min (Table 8A). Using 19-SMG as a substrate, the F48H, F48Y, F48T, I49V, and S84A UGT85C2 variants exhibit high activity during incubation periods of under 40 min, and the F48H, I49V, S84A, S84V, L91K, and L92F UGT85C2 variants, as well as the wild-type UGT85C2, exhibit high activity during incubation periods of over 40 min (Table 8B). In some aspects, the L91K, L91R, and L92F UGT85C2 variants exhibit a high 13-SMG/rubusoside ratio, whereas the F48Y, F48T, P86G UGT85C2 variants exhibit a low 13-SMG/rubusoside ratio. *See* Example 7.

[00112] In some embodiments, a useful UGT76G1 homolog can have one or more amino acid substitutions at residues 23, 26, 55, 146, 257, 283, and 337. *See* Example 4. Non-limiting examples of useful UGT76G1 homologs include polypeptides having substitutions (with respect to SEQ ID NO:9) at residue 21 (*e.g.*, a lysine, threonine or valine at residue 21), residue 23 (*e.g.*, a histidine at residue 23); residue 26 (*e.g.*, a tryptophan at residue 26); residue 55 (*e.g.*, a lysine at residue 55); residue 146 (*e.g.*, a glycine at residue 146); residue 257 (*e.g.*, a glycine at residue 257); residue 283 (*e.g.*, a asparagine at residue 283); and residue 337 (*e.g.*, a proline at residue 337). *See* SEQ ID NOs: 181-190. *See* Table 9 and Examples 8 and 9.

[00113] In some embodiments, expression of UGT76G1 variants that increase accumulation of RebD or RebM in steviol glycoside-producing *S. cerevisiae* strains (*see* WO 2014/122227, which has been incorporated by reference in its entirety) alter accumulation of 13-SMG, 1,2-bioside, rubusoside, RebA, RebB, RebD, RebE, RebM, RebG (1,3-stevioside), steviol+3Glc (#1), steviol+4Glc (#26), steviol+5Glc (#22), steviol+5Glc (#24), steviol+5Glc (#25), steviol+6Glc (isomer 1), and steviol+6Glc (#23), compared to expression of wild-type UGT76G1 (SEQ ID NO:9) in steviol glycoside-producing *S. cerevisiae* strains. *See* Figures 6, 10, 11D, and 11E and Examples 8 and 9.

[00114] In some embodiments, expression of UGT variants that increase RebD levels in *S. cerevisiae* also results in increased accumulation of steviol+5Glc (#22), 1,2-stevioside, steviol+6Glc (isomer 1), and steviol+3Glc (#1) but decreased accumulation of steviol+4Glc (#26), steviol+5Glc (#24), and RebG (1,3-stevioside). In some embodiments, expression of UGT76G1 H155L (SEQ ID NO:184) results in increased accumulation of steviol+5Glc (#25) but decreased accumulation of 1,2-stevioside, steviol+3Glc (#1), steviol+4Glc (#26), steviol+5Glc (#22), steviol+6Glc (isomer 1), and steviol+6Glc (#23). In some embodiments, expression of UGT76G1 S253W (SEQ ID NO:186) results in decreased accumulation of 1,2-stevioside and steviol+6Glc (isomer 1). In some embodiments, expression of UGT76G1 284G results in increased accumulation of 1,2-stevioside and steviol+6Glc (isomer 1) but decreased accumulation of RebG, steviol+4Glc (#26), steviol+5Glc (#25), and steviol+6Glc (#23). *See* Figure 10 and Example 8.

[00115] In some embodiments, expression of UGT76G1 Q23H (SEQ ID NO:181), UGT76G1 I26W (SEQ ID NO:182), UGT76G1 T146G (SEQ ID NO:183), UGT76G1 H155L (SEQ ID NO:184), UGT76G1 L257G (SEQ ID NO:185), and UGT76G1 S283N (SEQ ID NO:188) decrease accumulation of steviol+4Glc (#26). In some embodiments, expression of UGT76G1 Q23H (SEQ ID NO:181), UGT76G1 I26W (SEQ ID NO:182), UGT76G1 T146G (SEQ ID NO:183), UGT76G1 L257G (SEQ ID NO:185), or UGT76G1 S283N (SEQ ID NO:188), all of which increase production of RebD, decrease accumulation of steviol+5Glc (#25), compared to a control strain expressing wild-type UGT76G1. In some embodiments, expression of UGT76G1 H155L (SEQ ID NO:184), which increases RebM production, increases accumulation of steviol+5Glc (#25). *See* Figure 11D and Example 8.

[00116] In some embodiments, expression of UGT76G1 Q23H (SEQ ID NO:181), UGT76G1 I26W (SEQ ID NO:182), UGT76G1 T146G (SEQ ID NO:183), UGT76G1 L257G (SEQ ID NO:185), or UGT76G1 S283N (SEQ ID NO:188) increases accumulation of steviol+6Glc (#23), compared to a control strain expressing wild-type UGT76G1. In some embodiments, expression of UGT76G1 H155L (SEQ ID NO:184) decreases accumulation of steviol+6Glc (#23). In some embodiments, expression of UGT76G1 Q23H (SEQ ID NO:181), UGT76G1 I26W (SEQ ID NO:182), UGT76G1 T146G (SEQ ID NO:183), UGT76G1 L257G (SEQ ID NO:185), or UGT76G1 S283N (SEQ ID NO:188) increases accumulation of steviol+7Glc (isomer 2), compared to a control strain expressing wild-type UGT76G1. In some embodiments, expression of UGT76G1 H155L (SEQ ID NO:184) decreases accumulation of steviol+7Glc (isomer 2). In some embodiments, expression of UGT76G1 Q23H (SEQ ID NO:181), UGT76G1 I26W (SEQ ID NO:182), UGT76G1 T146G (SEQ ID NO:183), UGT76G1 L257G (SEQ ID NO:185), or UGT76G1 S283N (SEQ ID NO:188) increases accumulation of steviol+7Glc (isomer 5). *See* Figure 11D and Example 8.

[00117] In some embodiments, a host expressing a gene encoding a UGT variant or UGT chimeric polypeptide produces an increased level of glycosylated ent-kaurenoic acid and/or ent-kaurenol relative to a host not expressing a gene encoding a UGT variant or UGT chimeric polypeptide. In some embodiments, the UGT variant or UGT chimeric polypeptide comprises a UGT91D2e variant, a gene encoding a UGT91D2e-b-EUGT11 chimeric polypeptide, a gene encoding a UGT85C2 variant, and/or a gene encoding a UGT76G1 variant.

[00118] In some embodiments, a host expressing a gene encoding a UGT variant or UGT chimeric polypeptide produces a decreased level of glycosylated ent-kaurenoic acid and/or ent-kaurenol relative to a host not expressing a gene encoding a UGT variant or UGT chimeric polypeptide. In some embodiments, the UGT variant or UGT chimeric polypeptide comprises a UGT91D2e variant, a gene encoding a UGT91D2e-b-EUGT11 chimeric polypeptide, a gene encoding a UGT85C2 variant, and/or a gene encoding a UGT76G1 variant.

[00119] In some embodiments, levels of ent-kaurenoic acid+2Glc (#7), ent-kaurenoic acid+3Glc (isomer 1), ent-kaurenoic acid+3Glc (isomer 2), ent-kaurenol+2Glc (#8), and ent-kaurenol+3Glc (isomer 1) co-eluted with ent-kaurenol+3Glc (#6) are altered in steviol glycoside-producing *S. cerevisiae* strains expressing wild-type UGT76G1 (SEQ ID NO:9), compared to *S. cerevisiae* strains expressing UGT76G1 Q23H (SEQ ID NO:181), UGT76G1 I26W (SEQ ID NO:182), UGT76G1 T146G (SEQ ID NO:183), UGT76G1 H155L (SEQ ID NO:184), UGT76G1 L257G (SEQ ID NO:185), UGT76G1 S253W (SEQ ID NO:186), UGT76G1 T284G (SEQ ID NO:187), UGT76G1 S283N (SEQ ID NO:188), UGT76G1 K337P (SEQ ID NO:189), or UGT76G1 T55K (SEQ ID NO:190). *See* Figure 9, Figures 11A-11C, and Example 8.

[00120] In some embodiments, *S. cerevisiae* strains expressing UGT76G1 variants that increase RebD levels also increase accumulation of ent-kaurenoic acid+2Glc (#7) and ent-kaurenoic acid+2Glc (isomer 1) but decrease accumulation of ent-kaurenoic acid+3Glc (isomer 2), compared to an *S. cerevisiae* strain expressing wild-type UGT76G1. In some embodiments, UGT76G1 variants that increase RebD levels also increase accumulation of ent-kaurenol+2Glc (#8) but decrease accumulation of ent-kaurenol+3Glc (isomer 1) co-eluted with ent-kaurenol+3Glc (#6). In some embodiments, expression of UGT76G1 H155L (SEQ ID NO:184), a variant that increases levels of RebM, decreases accumulation of ent-kaurenoic acid+2Glc (#7) and ent-kaurenoic acid+3Glc (isomer 1). *See* Figure 9 and Example 8.

[00121] In some embodiments, total levels of glycosylated ent-kaurenoic acid (ent-kaurenoic acid+2Glc (#7) + ent-kaurenoic acid+3Glc (isomer 1) + ent-kaurenoic acid+3Glc (isomer 2)) are increased in steviol glycoside-producing *S. cerevisiae* strains expressing UGT76G1 Q23H (SEQ ID NO:181), UGT76G1 I26W (SEQ ID NO:182), and UGT L257G (SEQ ID NO:185). In some embodiments, total levels of glycosylated ent-kaurenol (ent-kaurenol+3Glc (isomer 1) co-eluted with ent-kaurenol+3Glc (#6) and ent-kaurenol+2Glc (#8) are altered for in steviol glycoside-producing *S. cerevisiae* strains expressing UGT76G1 Q23H (SEQ ID NO:181), UGT76G1 I26W (SEQ ID NO:182), and UGT76G1 T146G (SEQ ID NO:183). *See* Figures 11B and 11C and Example 8.

[00122] In some embodiments, UGT variants not limited to variants of UGT76G1, UGT85C2, and/or UGT91D2e alter ratios of steviol glycosides produced to GlcNAc compounds and isomers thereof produced *in vitro*, *in vivo* in a host, and/or by whole cell bioconversion.

Exemplary GlcNAc structures include ent-kaurenoic acid+2Glc+1GlcNAc and steviol+4Glc+1GlcNAc (#11). *See*, *e.g.*, Figures 7A, 7D, 8G-8I, and 8AC-8AF and Examples 6, 8, and 9.

[00123] In some embodiments, a steviol glycoside or steviol glycoside precursor composition produced *in vivo, in vitro*, or by whole cell bioconversion comprises fewer contaminants or less of any particular contaminant than a stevia extract from, *inter alia*, a stevia plant. Contaminants can include plant-derived compounds that contribute to off-flavors. Potential contaminants include pigments, lipids, proteins, phenolics, saccharides, spathulenol and other sesquiterpenes, labdane diterpenes, monoterpenes, decanoic acid, 8,11,14-eicosatrienoic acid, 2-methyloctadecane, pentacosane, octacosane, tetracosane, octadecanol, stigmasterol, β-sitosterol, α-amyrin, β-amyrin, lupeol, β-amryin acetate, pentacyclic triterpenes, centauredin, quercitin, epi-alpha-cadinol, carophyllenes and derivatives, beta-pinene, beta-sitosterol, and gibberellins.

[00124] As used herein, the terms “detectable amount,” “detectable concentration,” “measurable amount,” and “measurable concentration” refer to a level of steviol glycosides measured in area-under-curve (AUC), μM/OD_{600}, mg/L, μM, or mM. Steviol glycoside production (*i.e.*, total, supernatant, and/or intracellular steviol glycoside levels) can be detected and/or analyzed by techniques generally available to one skilled in the art, for example, but not limited to, liquid chromatography-mass spectrometry (LC-MS), thin layer chromatography (TLC), high-performance liquid chromatography (HPLC), ultraviolet-visible spectroscopy/ spectrophotometry (UV-Vis), mass spectrometry (MS), and nuclear magnetic resonance spectroscopy (NMR).

[00125] As used herein, the term “undetectable concentration” refers to a level of a compound that is too low to be measured and/or analyzed by techniques such as TLC, HPLC, UV-Vis, MS, or NMR. In some embodiments, a compound of an “undetectable concentration” is not present in a steviol glycoside or steviol glycoside precursor composition.

[00126] As used herein, the terms “or” and “and/or” is utilized to describe multiple components in combination or exclusive of one another. For example, “x, y, and/or z” can refer to “x” alone, “y” alone, “z” alone, “x, y, and z,” “(x and y) or z,” “x or (y and z),” or “x or y or z.” In some embodiments, “and/or” is used to refer to the exogenous nucleic acids that a recombinant cell comprises, wherein a recombinant cell comprises one or more exogenous nucleic acids selected from a group. In some embodiments, “and/or” is used to refer to production of steviol glycosides and/or steviol glycoside precursors. In some embodiments, “and/or” is used to refer to production of steviol glycosides, wherein one or more steviol glycosides are produced. In some embodiments, “and/or” is used to refer to production of steviol glycosides, wherein one or more steviol glycosides are produced through one or more of the following steps: culturing a recombinant microorganism, synthesizing one or more steviol glycosides in a recombinant microorganism, and/or isolating one or more steviol glycosides.

Functional Homologs

[00127] Functional homologs of the polypeptides described above are also suitable for use in producing steviol glycosides in a recombinant host. A functional homolog is a polypeptide that has sequence similarity to a reference polypeptide, and that carries out one or more of the biochemical or physiological function(s) of the reference polypeptide. A functional homolog and the reference polypeptide can be a natural occurring polypeptide, and the sequence similarity can be due to convergent or divergent evolutionary events. As such, functional homologs are sometimes designated in the literature as homologs, or orthologs, or paralogs. Variants of a naturally occurring functional homolog, such as polypeptides encoded by mutants of a wild type coding sequence, can themselves be functional homologs. Functional homologs can also be created via site-directed mutagenesis of the coding sequence for a polypeptide, or by combining domains from the coding sequences for different naturally-occurring polypeptides (“domain swapping”). Techniques for modifying genes encoding functional polypeptides described herein are known and include, *inter alia*, directed evolution techniques, site-directed mutagenesis techniques and random mutagenesis techniques, and can be useful to increase specific activity of a polypeptide, alter substrate specificity, alter expression levels, alter subcellular location, or modify polypeptide-polypeptide interactions in a desired manner. Such modified polypeptides are considered functional homologs. The term “functional homolog” is sometimes applied to the nucleic acid that encodes a functionally homologous polypeptide.

[00128] Functional homologs can be identified by analysis of nucleotide and polypeptide sequence alignments. For example, performing a query on a database of nucleotide or polypeptide sequences can identify homologs of steviol glycoside biosynthesis polypeptides. Sequence analysis can involve BLAST, Reciprocal BLAST, or PSI-BLAST analysis of non-redundant databases using a UGT amino acid sequence as the reference sequence. Amino acid sequence is, in some instances, deduced from the nucleotide sequence. Those polypeptides in the database that have greater than 40% sequence identity are candidates for further evaluation for suitability as a steviol glycoside biosynthesis polypeptide. Amino acid sequence similarity allows for conservative amino acid substitutions, such as substitution of one hydrophobic residue for another or substitution of one polar residue for another. If desired, manual inspection of such candidates can be carried out in order to narrow the number of candidates to be further evaluated. Manual inspection can be performed by selecting those candidates that appear to have domains present in steviol glycoside biosynthesis polypeptides, *e.g.*, conserved functional domains. In some embodiments, nucleic acids and polypeptides are identified from transcriptome data based on expression levels rather than by using BLAST analysis.

[00129] Conserved regions can be identified by locating a region within the primary amino acid sequence of a steviol glycoside biosynthesis polypeptide that is a repeated sequence, forms some secondary structure (*e.g.*, helices and beta sheets), establishes positively or negatively charged domains, or represents a protein motif or domain. *See, e.g.*, the Pfam web site describing consensus sequences for a variety of protein motifs and domains on the World Wide Web at sanger.ac.uk/Software/Pfam/ and pfam.janelia.org/. The information included at the Pfam database is described in Sonnhammer *et al.*, *Nucl. Acids Res.*, 26:320-322 (1998); Sonnhammer *et al.*, Proteins, 28:405-420 (1997); and Bateman *et al.*, *Nucl. Acids Res.*, 27:260-262 (1999). Conserved regions also can be determined by aligning sequences of the same or related polypeptides from closely related species. Closely related species preferably are from the same family. In some embodiments, alignment of sequences from two different species is adequate to identify such homologs.

[00130] Typically, polypeptides that exhibit at least about 40% amino acid sequence identity are useful to identify conserved regions. Conserved regions of related polypeptides exhibit at least 45% amino acid sequence identity (*e.g.*, at least 50%, at least 60%, at least 70%, at least 80%, or at least 90% amino acid sequence identity). In some embodiments, a conserved region exhibits at least 92%, 94%, 96%, 98%, or 99% amino acid sequence identity.

[00131] For example, polypeptides suitable for producing steviol in a recombinant host include functional homologs of UGTs.

[00132] Methods to modify the substrate specificity of, for example, a UGT, are known to those skilled in the art, and include without limitation site-directed/rational mutagenesis approaches, random directed evolution approaches and combinations in which random mutagenesis/saturation techniques are performed near the active site of the enzyme. For example see Osmani *et al.*, 2009, *Phytochemistry* 70: 325–347.

[00133] A candidate sequence typically has a length that is from 80% to 200% of the length of the reference sequence, *e.g.*, 82, 85, 87, 89, 90, 93, 95, 97, 99, 100, 105, 110, 115, 120, 130, 140, 150, 160, 170, 180, 190, or 200% of the length of the reference sequence. A functional homolog polypeptide typically has a length that is from 95% to 105% of the length of the reference sequence, *e.g.*, 90, 93, 95, 97, 99, 100, 105, 110, 115, or 120% of the length of the reference sequence, or any range between. A % identity for any candidate nucleic acid or polypeptide relative to a reference nucleic acid or polypeptide can be determined as follows. A reference sequence (*e.g.*, a nucleic acid sequence or an amino acid sequence described herein) is aligned to one or more candidate sequences using the computer program Clustal Omega (version 1.2.1, default parameters), which allows alignments of nucleic acid or polypeptide sequences to be carried out across their entire length (global alignment). Chenna *et al.*, 2003, *Nucleic Acids Res.* 31(13):3497-500.

[00134] Clustal Omega calculates the best match between a reference and one or more candidate sequences, and aligns them so that identities, similarities and differences can be determined. Gaps of one or more residues can be inserted into a reference sequence, a candidate sequence, or both, to maximize sequence alignments. For fast pairwise alignment of nucleic acid sequences, the following default parameters are used: word size: 2; window size: 4; scoring method: %age; number of top diagonals: 4; and gap penalty: 5. For multiple alignment of nucleic acid sequences, the following parameters are used: gap opening penalty: 10.0; gap extension penalty: 5.0; and weight transitions: yes. For fast pairwise alignment of protein sequences, the following parameters are used: word size: 1; window size: 5; scoring method:%age; number of top diagonals: 5; gap penalty: 3. For multiple alignment of protein sequences, the following parameters are used: weight matrix: blosum; gap opening penalty: 10.0; gap extension penalty: 0.05; hydrophilic gaps: on; hydrophilic residues: Gly, Pro, Ser, Asn, Asp, Gln, Glu, Arg, and Lys; residue-specific gap penalties: on. The Clustal Omega output is a sequence alignment that reflects the relationship between sequences. Clustal Omega can be run, for example, at the Baylor College of Medicine Search Launcher site on the World Wide Web (searchlauncher.bcm.tmc.edu/multi-align/multi-align.html) and at the European Bioinformatics Institute site at http://www.ebi.ac.uk/Tools/msa/clustalo/.

[00135] To determine a % identity of a candidate nucleic acid or amino acid sequence to a reference sequence, the sequences are aligned using Clustal Omega, the number of identical matches in the alignment is divided by the length of the reference sequence, and the result is multiplied by 100. It is noted that the% identity value can be rounded to the nearest tenth. For example, 78.11, 78.12, 78.13, and 78.14 are rounded down to 78.1, while 78.15, 78.16, 78.17, 78.18, and 78.19 are rounded up to 78.2.

[00136] It will be appreciated that functional UGT proteins can include additional amino acids that are not involved in the enzymatic activities carried out by the enzymes. In some embodiments, UGT proteins are fusion proteins. The terms “chimera,” “fusion polypeptide,” “fusion protein,” “fusion enzyme,” “fusion construct,” “chimeric protein,” “chimeric polypeptide,” “chimeric construct,” and “chimeric enzyme” can be used interchangeably herein to refer to proteins engineered through the joining of two or more genes that code for different proteins. In some embodiments, a nucleic acid sequence encoding a UGT polypeptide can include a tag sequence that encodes a “tag” designed to facilitate subsequent manipulation (*e.g.*, to facilitate purification or detection), secretion, or localization of the encoded polypeptide. Tag sequences can be inserted in the nucleic acid sequence encoding the polypeptide such that the encoded tag is located at either the carboxyl or amino terminus of the polypeptide. Non-limiting examples of encoded tags include green fluorescent protein (GFP), human influenza hemagglutinin (HA), glutathione S transferase (GST), polyhistidine-tag (HIS tag), and Flag™ tag (Kodak, New Haven, CT). Other examples of tags include a chloroplast transit peptide, a mitochondrial transit peptide, an amyloplast peptide, signal peptide, or a secretion tag.

[00137] In some embodiments, a fusion protein is a protein altered by domain swapping. As used herein, the term “domain swapping” is used to describe the process of replacing a domain of a first protein with a domain of a second protein. In some embodiments, the domain of the first protein and the domain of the second protein are functionally identical or functionally similar. In some embodiments, the structure and/or sequence of the domain of the second protein differs from the structure and/or sequence of the domain of the first protein. In some embodiments, a UGT polypeptide is altered by domain swapping.

Steviol and Steviol Glycoside Biosynthesis Nucleic Acids

[00138] A recombinant gene encoding a polypeptide described herein comprises the coding sequence for that polypeptide, operably linked in sense orientation to one or more regulatory regions suitable for expressing the polypeptide. Because many microorganisms are capable of expressing multiple gene products from a polycistronic mRNA, multiple polypeptides can be expressed under the control of a single regulatory region for those microorganisms, if desired. A coding sequence and a regulatory region are considered to be operably linked when the regulatory region and coding sequence are positioned so that the regulatory region is effective for regulating transcription or translation of the sequence. Typically, the translation initiation site of the translational reading frame of the coding sequence is positioned between one and about fifty nucleotides downstream of the regulatory region for a monocistronic gene.

[00139] In many cases, the coding sequence for a polypeptide described herein is identified in a species other than the recombinant host, *i.e.*, is a heterologous nucleic acid. Thus, if the recombinant host is a microorganism, the coding sequence can be from other prokaryotic or eukaryotic microorganisms, from plants or from animals. In some case, however, the coding sequence is a sequence that is native to the host and is being reintroduced into that organism. A native sequence can often be distinguished from the naturally occurring sequence by the presence of non-natural sequences linked to the exogenous nucleic acid, *e.g.*, non-native regulatory sequences flanking a native sequence in a recombinant nucleic acid construct. In addition, stably transformed exogenous nucleic acids typically are integrated at positions other than the position where the native sequence is found. “Regulatory region” refers to a nucleic acid having nucleotide sequences that influence transcription or translation initiation and rate, and stability and/or mobility of a transcription or translation product. Regulatory regions include, without limitation, promoter sequences, enhancer sequences, response elements, protein recognition sites, inducible elements, protein binding sequences, 5’ and 3’ untranslated regions (UTRs), transcriptional start sites, termination sequences, polyadenylation sequences, introns, and combinations thereof. A regulatory region typically comprises at least a core (basal) promoter. A regulatory region also may include at least one control element, such as an enhancer sequence, an upstream element or an upstream activation region (UAR). A regulatory region is operably linked to a coding sequence by positioning the regulatory region and the coding sequence so that the regulatory region is effective for regulating transcription or translation of the sequence. For example, to operably link a coding sequence and a promoter sequence, the translation initiation site of the translational reading frame of the coding sequence is typically positioned between one and about fifty nucleotides downstream of the promoter. A regulatory region can, however, be positioned as much as about 5,000 nucleotides upstream of the translation initiation site, or about 2,000 nucleotides upstream of the transcription start site.

[00140] The choice of regulatory regions to be included depends upon several factors, including, but not limited to, efficiency, selectability, inducibility, desired expression level, and preferential expression during certain culture stages. It is a routine matter for one of skill in the art to modulate the expression of a coding sequence by appropriately selecting and positioning regulatory regions relative to the coding sequence. It will be understood that more than one regulatory region may be present, *e.g.*, introns, enhancers, upstream activation regions, transcription terminators, and inducible elements.

[00141] One or more genes can be combined in a recombinant nucleic acid construct in “modules” useful for a discrete aspect of steviol and/or steviol glycoside production. Combining a plurality of genes in a module, particularly a polycistronic module, facilitates the use of the module in a variety of species. For example, a steviol biosynthesis gene cluster, or a UGT gene cluster, can be combined in a polycistronic module such that, after insertion of a suitable regulatory region, the module can be introduced into a wide variety of species. As another example, a UGT gene cluster can be combined such that each UGT coding sequence is operably linked to a separate regulatory region, to form a UGT module. Such a module can be used in those species for which monocistronic expression is necessary or desirable. In addition to genes useful for steviol or steviol glycoside production, a recombinant construct typically also contains an origin of replication, and one or more selectable markers for maintenance of the construct in appropriate species.

[00142] It will be appreciated that because of the degeneracy of the genetic code, a number of nucleic acids can encode a particular polypeptide; *i.e.*, for many amino acids, there is more than one nucleotide triplet that serves as the codon for the amino acid. Thus, codons in the coding sequence for a given polypeptide can be modified such that optimal expression in a particular host is obtained, using appropriate codon bias tables for that host (*e.g.*, microorganism). As isolated nucleic acids, these modified sequences can exist as purified molecules and can be incorporated into a vector or a virus for use in constructing modules for recombinant nucleic acid constructs.

[00143] In some cases, it is desirable to inhibit one or more functions of an endogenous polypeptide in order to divert metabolic intermediates towards steviol or steviol glycoside biosynthesis. For example, it may be desirable to downregulate synthesis of sterols in a yeast strain in order to further increase steviol or steviol glycoside production, *e.g.*, by downregulating squalene epoxidase. As another example, it may be desirable to inhibit degradative functions of certain endogenous gene products, *e.g.*, glycohydrolases that remove glucose moieties from secondary metabolites or phosphatases as discussed herein. In such cases, a nucleic acid that overexpresses the polypeptide or gene product may be included in a recombinant construct that is transformed into the strain. Alternatively, mutagenesis can be used to generate mutants in genes for which it is desired to increase or enhance function.

Host Microorganisms

[00144] Recombinant hosts can be used to express polypeptides for the producing steviol glycosides. A number of prokaryotes and eukaryotes are suitable for use in constructing the recombinant microorganisms described herein, *e.g.*, gram-negative bacteria, fungi (*i.e.*, yeast), mammalian, insect, plant, and algae cells. A species and strain selected for use as a steviol glycoside production strain is first analyzed to determine which production genes are endogenous to the strain and which genes are not present. Genes for which an endogenous counterpart is not present in the strain are advantageously assembled in one or more recombinant constructs, which are then transformed into the strain in order to supply the missing function(s).

[00145] Typically, the recombinant microorganism is grown in a fermenter at a temperature(s) for a period of time, wherein the temperature and period of time facilitate the production of a steviol glycoside. The constructed and genetically engineered microorganisms provided by the invention can be cultivated using conventional fermentation processes, including, *inter alia*, chemostat, batch, fed-batch cultivations, semi-continuous fermentations such as draw and fill, continuous perfusion fermentation, and continuous perfusion cell culture. Depending on the particular microorganism used in the method, other recombinant genes such as isopentenyl biosynthesis genes and terpene synthase and cyclase genes may also be present and expressed. Levels of substrates and intermediates, *e.g.*, isopentenyl diphosphate, dimethylallyl diphosphate, GGPP, ent-kaurene and ent-kaurenoic acid, can be determined by extracting samples from culture media for analysis according to published methods.

[00146] Carbon sources of use in the instant method include any molecule that can be metabolized by the recombinant host cell to facilitate growth and/or production of the steviol glycosides. Examples of suitable carbon sources include, but are not limited to, sucrose (*e.g.*, as found in molasses), fructose, xylose, ethanol, glycerol, glucose, cellulose, starch, cellobiose or other glucose-comprising polymer. In embodiments employing yeast as a host, for example, carbons sources such as sucrose, fructose, xylose, ethanol, glycerol, and glucose are suitable. The carbon source can be provided to the host organism throughout the cultivation period or alternatively, the organism can be grown for a period of time in the presence of another energy source, *e.g.*, protein, and then provided with a source of carbon only during the fed-batch phase.

[00147] After the recombinant microorganism has been grown in culture for the period of time, wherein the temperature and period of time facilitate the production of a steviol glycoside, steviol and/or one or more steviol glycosides can then be recovered from the culture using various techniques known in the art. In some embodiments, a permeabilizing agent can be added to aid the feedstock entering into the host and product getting out. For example, a crude lysate of the cultured microorganism can be centrifuged to obtain a supernatant. The resulting supernatant can then be applied to a chromatography column, *e.g.*, a C-18 column, and washed with water to remove hydrophilic compounds, followed by elution of the compound(s) of interest with a solvent such as methanol. The compound(s) can then be further purified by preparative HPLC. *See also*, WO 2009/140394.

[00148] It will be appreciated that the various genes and modules discussed herein can be present in two or more recombinant hosts rather than a single host. When a plurality of recombinant hosts is used, they can be grown in a mixed culture to accumulate steviol and/or steviol glycosides.

[00149] Alternatively, the two or more hosts each can be grown in a separate culture medium and the product of the first culture medium, *e.g.*, steviol, can be introduced into second culture medium to be converted into a subsequent intermediate, or into an end product such as, for example, RebA. The product produced by the second, or final host is then recovered. It will also be appreciated that in some embodiments, a recombinant host is grown using nutrient sources other than a culture medium and utilizing a system other than a fermenter.

[00150] Exemplary prokaryotic and eukaryotic species are described in more detail below. However, it will be appreciated that other species can be suitable. For example, suitable species can be in a genus such as *Agaricus*, *Aspergillus*, *Bacillus*, *Candida*, *Corynebacterium*, *Eremothecium*, *Escherichia*, *Fusarium/Gibberella*, *Kluyveromyces*, *Laetiporus*, *Lentinus*, *Phaffia*, *Phanerochaete*, *Pichia*, *Physcomitrella*, *Rhodoturula*, *Saccharomyces*, *Schizosaccharomyces*, *Sphaceloma*, *Xanthophyllomyces* or *Yarrowia*. Exemplary species from such genera include *Lentinus tigrinus*, *Laetiporus sulphureus*, *Phanerochaete chrysosporium*, *Pichia pastoris*, *Cyberlindnera jadinii*, *Physcomitrella patens*, *Rhodoturula glutinis*, *Rhodoturula mucilaginosa*, *Phaffia rhodozyma*, *Xanthophyllomyces dendrorhous*, *Fusarium fujikuroi/Gibberella fujikuroi*, *Candida utilis*, *Candida glabrata*, *Candida albicans*, and *Yarrowia lipolytica*.

[00151] In some embodiments, a microorganism can be a prokaryote such as *Escherichia* bacteria cells, for example, *Escherichia coli* cells; *Lactobacillus* bacteria cells; *Lactococcus* bacteria cells; *Comebacterium* bacteria cells; *Acetobacter* bacteria cells; *Acinetobacter* bacteria cells; or *Pseudomonas* bacterial cells.

[00152] In some embodiments, a microorganism can be an Ascomycete such as *Gibberella fujikuroi*, *Kluyveromyces lactis*, *Schizosaccharomyces pombe*, *Aspergillus niger*, *Yarrowia lipolytica*, *Ashbya gossypii*, or *S. cerevisiae*.

[00153] In some embodiments, a microorganism can be an algal cell such as *Blakeslea trispora, Dunaliella salina, Haematococcus pluvialis, Chlorella sp., Undaria pinnatifida, Sargassum, Laminaria japonica, Scenedesmus almeriensis* species.

[00154] In some embodiments, a microorganism can be a cyanobacterial cell such as *Blakeslea trispora, Dunaliella salina, Haematococcus pluvialis, Chlorella sp., Undaria pinnatifida, Sargassum, Laminaria japonica, Scenedesmus almeriensis*.

<u>*Saccharomyces spp.*</u>

[00155] S*accharomyces* is a widely used chassis organism in synthetic biology, and can be used as the recombinant microorganism platform. For example, there are libraries of mutants, plasmids, detailed computer models of metabolism and other information available for *S. cerevisiae*, allowing for rational design of various modules to enhance product yield. Methods are known for making recombinant microorganisms.

<u>*Aspergillus spp.*</u>

[00156] *Aspergillus* species such as *A. oryzae*, *A. niger* and *A. sojae* are widely used microorganisms in food production and can also be used as the recombinant microorganism platform. Nucleotide sequences are available for genomes of *A. nidulans*, *A. fumigatus*, *A. oryzae*, *A. clavatus*, *A. flavus*, *A. niger*, and *A. terreus*, allowing rational design and modification of endogenous pathways to enhance flux and increase product yield. Metabolic models have been developed for *Aspergillus*, as well as transcriptomic studies and proteomics studies. *A. niger* is cultured for the industrial production of a number of food ingredients such as citric acid and gluconic acid, and thus species such as *A. niger* are generally suitable for producing steviol glycosides.

<u>*E. coli*</u>

[00157] *E. coli*, another widely used platform organism in synthetic biology, can also be used as the recombinant microorganism platform. Similar to *Saccharomyces*, there are libraries of mutants, plasmids, detailed computer models of metabolism and other information available for

E. coli, allowing for rational design of various modules to enhance product yield. Methods similar to those described above for *Saccharomyces* can be used to make recombinant *E. coli* microorganisms.

Agaricus, Gibberella, and Phanerochaete spp.

[00158] *Agaricus*, *Gibberella*, and *Phanerochaete* spp. can be useful because they are known to produce large amounts of isoprenoids in culture. Thus, the terpene precursors for producing large amounts of steviol glycosides are already produced by endogenous genes. Thus, modules comprising recombinant genes for steviol glycoside biosynthesis polypeptides can be introduced into species from such genera without the necessity of introducing mevalonate or MEP pathway genes.

Arxula adeninivorans (Blastobotrys adeninivorans)

[00159] *Arxula adeninivorans* is dimorphic yeast (it grows as budding yeast like the baker's yeast up to a temperature of 42°C, above this threshold it grows in a filamentous form) with unusual biochemical characteristics. It can grow on a wide range of substrates and can assimilate nitrate. It has successfully been applied to the generation of strains that can produce natural plastics or the development of a biosensor for estrogens in environmental samples.

Yarrowia lipolytica

[00160] *Yarrowia lipolytica* is dimorphic yeast (*see Arxula adeninivorans*) and belongs to the family Hemiascomycetes. The entire genome of *Yarrowia lipolytica* is known. *Yarrowia* species is aerobic and considered to be non-pathogenic. *Yarrowia* is efficient in using hydrophobic substrates (*e.g.* alkanes, fatty acids, oils) and can grow on sugars. It has a high potential for industrial applications and is an oleaginous microorgamism. *Yarrowia lipolyptica* can accumulate lipid content to approximately 40% of its dry cell weight and is a model organism for lipid accumulation and remobilization. *See e.g.,* Nicaud, 2012, *Yeast* 29(10):409-18; Beopoulos *et al.,* 2009, *Biochimie* 91(6):692-6; Bankar *et al.*, 2009, *Appl Microbiol Biotechnol.* 84(5):847-65.

Rhodotorula sp.

[00161] *Rhodotorula* is unicellular, pigmented yeast. The oleaginous red yeast, *Rhodotorula glutinis*, has been shown to produce lipids and carotenoids from crude glycerol (Saenge *et al.*, 2011, *Process Biochemistry* 46(1):210-8). *Rhodotorula toruloides* strains have been shown to be an efficient fed-batch fermentation system for improved biomass and lipid productivity (Li *et al.,* 2007, *Enzyme and Microbial Technology* 41:312-7).

Rhodosporidium toruloides

[00162] *Rhodosporidium toruloides* is oleaginous yeast and useful for engineering lipid-production pathways (*See e.g.* Zhu *et al.*, 2013, *Nature Commun.* 3:1112; Ageitos *et al.*, 2011, *Applied Microbiology and Biotechnology* 90(4):1219-27).

Candida boidinii

[00163] *Candida boidinii* is methylotrophic yeast (it can grow on methanol). Like other methylotrophic species such as *Hansenula polymorpha* and *Pichia pastoris*, it provides an excellent platform for producing heterologous proteins. Yields in a multigram range of a secreted foreign protein have been reported. A computational method, IPRO, recently predicted mutations that experimentally switched the cofactor specificity of *Candida boidinii* xylose reductase from NADPH to NADH. *See*, *e.g.*, Mattanovich *et al.*, 2012, *Methods Mol Biol.* 824:329-58; Khoury *et al.*, 2009, *Protein Sci.* 18(10):2125-38.

Hansenula polymorpha (Pichia angusta)

[00164] *Hansenula polymorpha* is methylotrophic yeast (*see Candida boidinii*). It can furthermore grow on a wide range of other substrates; it is thermo-tolerant and can assimilate nitrate (see also *Kluyveromyces lactis*). It has been applied to producing hepatitis B vaccines, insulin and interferon alpha-2a for the treatment of hepatitis C, furthermore to a range of technical enzymes. *See*, *e.g.*, Xu *et al.*, 2014, *Virol Sin.* 29(6):403-9.

Kluyveromyces lactis

[00165] *Kluyveromyces lactis* is yeast regularly applied to the production of kefir. It can grow on several sugars, most importantly on lactose which is present in milk and whey. It has successfully been applied among others for producing chymosin (an enzyme that is usually present in the stomach of calves) for producing cheese. Production takes place in fermenters on a 40,000 L scale. *See*, *e.g.*, van Ooyen *et al.*, 2006, *FEMS Yeast Res.* 6(3):381-92.

Pichia pastoris

[00166] *Pichia pastoris* is methylotrophic yeast (*see Candida boidinii* and *Hansenula polymorpha*). It provides an efficient platform for producing foreign proteins. Platform elements are available as a kit and it is worldwide used in academia for producing proteins. Strains have been engineered that can produce complex human N-glycan (yeast glycans are similar but not identical to those found in humans). *See*, *e.g.*, Piirainen *et al.*, 2014, *N Biotechnol.* 31(6):532-7.

Physcomitrella spp.

[00167] *Physcomitrella mosses*, when grown in suspension culture, have characteristics similar to yeast or other fungal cultures. This genera can be used for producing plant secondary metabolites, which can be difficult to produce in other types of cells.

Steviol Glycoside Compositions

[00168] Steviol glycosides do not necessarily have equivalent performance in different food systems. It is therefore desirable to have the ability to direct the synthesis to steviol glycoside compositions of choice. Recombinant hosts described herein can produce compositions that are selectively enriched for specific steviol glycosides (*e.g.*, RebD or RebM) and have a consistent taste profile. As used herein, the term “enriched” is used to describe a steviol glycoside composition with an increased proportion of a particular steviol glycoside, compared to a steviol glycoside composition (extract) from a stevia plant. Thus, the recombinant hosts described herein can facilitate the production of compositions that are tailored to meet the sweetening profile desired for a given food product and that have a proportion of each steviol glycoside that is consistent from batch to batch. In some embodiments, hosts described herein do not produce or produce a reduced amount of undesired plant by-products found in Stevia extracts. Thus, steviol glycoside compositions produced by the recombinant hosts described herein are distinguishable from compositions derived from *Stevia* plants.

[00169] It will be appreciated that the amount of an individual steviol glycoside (*e.g.*, RebA, RebB, RebD, or RebM) produced by the recombinant host cell disclosed herein can accumulate in the cell culture broth from about 1 to about 7,000 mg/L, *e.g.*, about 1 to about 10 mg/L, about 3 to about 10 mg/L, about 5 to about 20 mg/L, about 10 to about 50 mg/L, about 10 to about 100 mg/L, about 25 to about 500 mg/L, about 100 to about 1,500 mg/L, or about 200 to about 1,000 mg/L, at least about 1,000 mg/L, at least about 1,200 mg/L, at least about at least 1,400 mg/L, at least about 1,600 mg/L, at least about 1,800 mg/L, at least about 2,800 mg/L, or at least about 7,000 mg/L. In some aspects, the amount of an individual steviol glycoside produced by the recombinant host cell disclosed herein can exceed 7,000 mg/L in the cell culture broth.

[00170] It will be appreciated that the amount of a combination of steviol glycosides (*e.g.*, RebA, RebB, RebD, or RebM) produced by the recombinant host cell disclosed herein can accumulate in the cell culture broth from about 1 mg/L to about 7,000 mg/L, *e.g.*, about 200 to about 1,500, at least about 2,000 mg/L, at least about 3,000 mg/L, at least about 4,000 mg/L, at least about 5,000 mg/L, at least about 6,000 mg/L, or at least about 7,000 mg/L. In some aspects, the amount of a combination of steviol glycosides produced by the recombinant host cell disclosed herein can exceed 7,000 mg/L. In general, longer culture times will lead to greater amounts of product. Thus, the recombinant microorganism can be cultured for from 1 day to 7 days, from 1 day to 5 days, from 3 days to 5 days, about 3 days, about 4 days, or about 5 days.

[00171] It will be appreciated that the various genes and modules discussed herein can be present in two or more recombinant microorganisms rather than a single microorganism. When a plurality of recombinant microorganisms is used, they can be grown in a mixed culture to produce steviol and/or steviol glycosides. For example, a first microorganism can comprise one or more biosynthesis genes for producing a steviol glycoside precursor, while a second microorganism comprises steviol glycoside biosynthesis genes. The product produced by the second, or final microorganism is then recovered. It will also be appreciated that in some embodiments, a recombinant microorganism is grown using nutrient sources other than a culture medium and utilizing a system other than a fermenter.

[00172] Alternatively, the two or more microorganisms each can be grown in a separate culture medium and the product of the first culture medium, *e.g.*, steviol, can be introduced into second culture medium to be converted into a subsequent intermediate, or into an end product such as RebA. The product produced by the second, or final microorganism is then recovered. It will also be appreciated that in some embodiments, a recombinant microorganism is grown using nutrient sources other than a culture medium and utilizing a system other than a fermenter.

[00173] Steviol glycosides and compositions obtained by the methods disclosed herein can be used to make food products, dietary supplements and sweetener compositions. *See*, *e.g.*, WO 2011/153378, WO 2013/022989, WO 2014/122227, and WO 2014/122328.

[00174] For example, substantially pure steviol or steviol glycoside such as RebM or RebD can be included in food products such as ice cream, carbonated beverages, fruit juices, yogurts, baked goods, chewing gums, hard and soft candies, and sauces. Substantially pure steviol or steviol glycoside can also be included in non-food products such as pharmaceutical products, medicinal products, dietary supplements and nutritional supplements. Substantially pure steviol or steviol glycosides may also be included in animal feed products for both the agriculture industry and the companion animal industry. Alternatively, a mixture of steviol and/or steviol glycosides can be made by culturing recombinant microorganisms separately, each producing a specific steviol or steviol glycoside, recovering the steviol or steviol glycoside in substantially pure form from each microorganism and then combining the compounds to obtain a mixture comprising each compound in the desired proportion. The recombinant microorganisms described herein permit more precise and consistent mixtures to be obtained compared to current Stevia products.

[00175] In another alternative, a substantially pure steviol or steviol glycoside can be incorporated into a food product along with other sweeteners, *e.g.* saccharin, dextrose, sucrose, fructose, erythritol, aspartame, sucralose, monatin, or acesulfame potassium. The weight ratio of steviol or steviol glycoside relative to other sweeteners can be varied as desired to achieve a satisfactory taste in the final food product. See, *e.g.*, U.S. 2007/0128311. In some embodiments, the steviol or steviol glycoside may be provided with a flavor (*e.g.*, citrus) as a flavor modulator.

[00176] Compositions produced by a recombinant microorganism described herein can be incorporated into food products. For example, a steviol glycoside composition produced by a recombinant microorganism can be incorporated into a food product in an amount ranging from about 20 mg steviol glycoside/kg food product to about 1800 mg steviol glycoside/kg food product on a dry weight basis, depending on the type of steviol glycoside and food product. For example, a steviol glycoside composition produced by a recombinant microorganism can be incorporated into a dessert, cold confectionary (*e.g.*, ice cream), dairy product (*e.g.*, yogurt), or beverage (*e.g.*, a carbonated beverage) such that the food product has a maximum of 500 mg steviol glycoside/kg food on a dry weight basis. A steviol glycoside composition produced by a recombinant microorganism can be incorporated into a baked good (*e.g.*, a biscuit) such that the food product has a maximum of 300 mg steviol glycoside/kg food on a dry weight basis. A steviol glycoside composition produced by a recombinant microorganism can be incorporated into a sauce (*e.g.*, chocolate syrup) or vegetable product (*e.g.*, pickles) such that the food product has a maximum of 1000 mg steviol glycoside/kg food on a dry weight basis. A steviol glycoside composition produced by a recombinant microorganism can be incorporated into bread such that the food product has a maximum of 160 mg steviol glycoside/kg food on a dry weight basis. A steviol glycoside composition produced by a recombinant microorganism, plant, or plant cell can be incorporated into a hard or soft candy such that the food product has a maximum of 1600 mg steviol glycoside/kg food on a dry weight basis. A steviol glycoside composition produced by a recombinant microorganism, plant, or plant cell can be incorporated into a processed fruit product (*e.g.*, fruit juices, fruit filling, jams, and jellies) such that the food product has a maximum of 1000 mg steviol glycoside/kg food on a dry weight basis. In some embodiments, a steviol glycoside composition produced herein is a component of a pharmaceutical composition. *See*, *e.g.*, Steviol Glycosides Chemical and Technical Assessment 69th JECFA, 2007, prepared by Harriet Wallin, Food Agric. Org.; EFSA Panel on Food Additives and Nutrient Sources added to Food (ANS), “Scientific Opinion on the safety of steviol glycosides for the proposed uses as a food additive,” 2010, *EFSA Journal* 8(4):1537; U.S. Food and Drug Administration GRAS Notice 323; U.S Food and Drug Administration GRAS Notice Notice 329; WO 2011/037959; WO 2010/146463; WO 2011/046423; and WO 2011/056834.

[00177] For example, such a steviol glycoside composition can have from 90-99 weight % RebA and an undetectable amount of stevia plant-derived contaminants, and be incorporated into a food product at from 25-1600 mg/kg, *e.g.*, 100-500 mg/kg, 25-100 mg/kg, 250-1000 mg/kg, 50-500 mg/kg or 500-1000 mg/kg on a dry weight basis.

[00178] Such a steviol glycoside composition can be a RebB-enriched composition having greater than 3 weight % RebB and be incorporated into the food product such that the amount of RebB in the product is from 25-1600 mg/kg, *e.g.*, 100-500 mg/kg, 25-100 mg/kg, 250-1000 mg/kg, 50-500 mg/kg or 500-1000 mg/kg on a dry weight basis. Typically, the RebB-enriched composition has an undetectable amount of stevia plant-derived contaminants.

[00179] Such a steviol glycoside composition can be a RebD-enriched composition having greater than 3 weight % RebD and be incorporated into the food product such that the amount of RebD in the product is from 25-1600 mg/kg, *e.g.*, 100-500 mg/kg, 25-100 mg/kg, 250-1000 mg/kg, 50-500 mg/kg or 500-1000 mg/kg on a dry weight basis. Typically, the RebD-enriched composition has an undetectable amount of stevia plant-derived contaminants.

[00180] Such a steviol glycoside composition can be a RebE-enriched composition having greater than 3 weight % RebE and be incorporated into the food product such that the amount of RebE in the product is from 25-1600 mg/kg, *e.g.*, 100-500 mg/kg, 25-100 mg/kg, 250-1000 mg/kg, 50-500 mg/kg or 500-1000 mg/kg on a dry weight basis. Typically, the RebE-enriched composition has an undetectable amount of stevia plant-derived contaminants.

[00181] Such a steviol glycoside composition can be a RebM-enriched composition having greater than 3 weight % RebM and be incorporated into the food product such that the amount of RebM in the product is from 25-1600 mg/kg, *e.g.*, 100-500 mg/kg, 25-100 mg/kg, 250-1000 mg/kg, 50-500 mg/kg or 500-1000 mg/kg on a dry weight basis. Typically, the RebM-enriched composition has an undetectable amount of stevia plant-derived contaminants.

[00182] In some embodiments, a substantially pure steviol or steviol glycoside is incorporated into a tabletop sweetener or "cup-for-cup" product. Such products typically are diluted to the appropriate sweetness level with one or more bulking agents, *e.g.*, maltodextrins, known to those skilled in the art. Steviol glycoside compositions enriched for RebA, RebB, RebD, RebE, or RebM, can be package in a sachet, for example, at from 10,000 to 30,000 mg steviol glycoside/kg product on a dry weight basis, for tabletop use. In some embodiments, a steviol glycoside produced *in vitro*, *in vivo*, or by whole cell bioconversion

[00183] The invention will be further described in the following examples, which do not limit the scope of the invention described in the claims.

EXAMPLES

[00184] The Examples that follow are illustrative of specific embodiments of the invention, and various uses thereof. They are set forth for explanatory purposes only, and are not to be taken as limiting the invention.

Example 1: LC-MS Analytical Procedures

[00185] LC-MS analyses for Examples 3 and 4 were performed using an Agilent 1200 Series HPLC system (Agilent Technologies) fitted with a Phenomenex® Kinetex C18 column (150 x 2.1 mm, 2.6 µm particles, 100 Å pore size) connected to a TSQ Quantum Access (ThermoFisher Scientific) triple quadropole mass spectrometer with a heated electrospray ion (HESI) source. Elution was carried out using a mobile phase of eluent B (MeCN with 0.1% Formic acid) and eluent A (water with 0.1% Formic acid) by increasing the gradient from 10-40% B from min 0.0 to 1.0, increasing 40-50% B in min 1.0 to 6.5, and increasing 50-100% B from min 6.5 to 7.0.

The flow rate was 0.4 mL/min, and the column temperature was 30°C. 1,2-stevioside and RebD were detected using SIM (Single Ion Monitoring) in positive mode.

[00186] LC-MS analyses for Examples 8 and 9 were performed on Waters ACQUITY UPLC® (Waters Corporation) with a Waters ACQUITY UPLC® BEH C18 column (2.1 x 50 mm, 1.7 µm particles, 130 Å pore size) equipped with a pre-column (2.1 x 5 mm, 1.7 µm particles, 130 Å pore size) coupled to a Waters ACQUITY TQD triple quadropole mass spectrometer with electrospray ionization (ESI) operated in negative ionization mode. Compound separation was achieved using a gradient of the two mobile phases: A (water with 0.1% formic acid) and B (MeCN with 0.1% formic acid) by increasing from 20% to 50 % B between 0.3 to 2.0 min, increasing to 100% B at 2.01 min, holding 100% B for 0.6 min, and re-equilibrating for 0.6 min. The flow rate was 0.6 mL/min, and the column temperature was set at 55°C. Steviol glycosides were monitored using SIM (Single Ion Monitoring) and quantified by comparing against authentic standards. *See* Table 1 for m/z trace and retention time values of steviol glycosides detected.

Table 1: LC-MS Analytical Data for Steviol and Steviol Glycosides

Compound	MS Trace	RT (min)	Figure(s)	Table(s)
steviol+5Glc (#22) [also referred to as compound 5.22]	1127.48	0.85	6D, 7E, 8AK-8AN, 10A, 10B, 11D	9C, 9F, 9I
steviol+6Glc (isomer 1) [also referred to as compound 6.1]	1289.53	0.87	6D, 7B, 8M-8P, 10A, 10B, 11D	9C, 9F, 9I
steviol+7Glc (isomer 2) [also referred to as compound 7.2]	1451.581	0.94	6D, 7B, 8Q-8T, 11D	9C, 9F, 9I
steviol+6Glc (#23) [also referred to as compound 6.23]	1289.53	0.97	6D, 10A, 10B, 11D	9F, 9I
RebE	965.42	1.06	6B, 6C, 10C, 11E	9A, 9D, 9G
RebD	1127.48	1.08	6A, 6C, 10C, 11E	2, 3, 5, 9A, 9D, 9G
RebM	1289.53	1.15	6A, 6C, 10C, 11E	9A, 9D, 9G
steviol+7Glc (isomer 5) [also referred to as compound 7.5]	1451.581	1.09	7C, 8Y-8AB, 11D	9F, 9I
steviol+7Glc (#13)	1451.581	0.94	6D	

Compound	MS Trace	RT (min)	Figure(s)	Table(s)
[also referred to as compound 7.13]				
steviol+4Glc (#26) [also referred to as compound 4.26]	965.42	1.21	6D, 7D, 8AG-8AJ, 10A, 10B, 11D	9C, 9F, 9H
steviol+4Glc (#33) [also referred to as compound 4.33]	965.42	1.49		9C, 9I
steviol+5Glc (#24) [also referred to as compound 5.24]	1127.48	1.18	6D, 10A, 10B, 11D	9F, 9I
steviol+4Glc (#25) [also referred to as compound 5.25]	1127.48	1.40	6D, 10A, 10B, 11D	5, 9C, 9F, 9I
RebA	965.42	1.43	6A, 6C, 10C, 11E	9A, 9D, 9G
RebI	1127.48	1.4		9H
1,2-stevioside	803.37	1.43	10B, 11D	2, 3, 5, 9B, 9E, 9H
steviol+3Glc (#1) [also referred to as compound 3.1]	803.37	1.52	6D, 10A, 10B, 11D	9B, 9E
steviol+2Glc (#23) [also referred to as compound 2.23]	641.32	1.57	4C	
steviol+3Glc (#34) [also referred to as compound 3.34]	803.37		4C	9C, 9E
RebQ	965.42	1.59		
1,3-stevioside (RebG)	803.37	1.60	6B-6D, 10B, 11E	9D, 9G
rubusoside	641.32	1.67	5, 6B, 6C, 10C, 11E	5, 8B, 8C, 9D, 9G
RebB	803.37	1.76	6A, 6C, 10C, 11E	9A, 9D, 9G
1,2-bioside	641.32	1.80	6B-D, 10C, 11D, 11E	9A, 9D, 9G
1,3-bioside	641.32	1.95		9E
13-SMG	479.26	2.04	4B, 6A, 6C, 10C, 11E	8A, 8B, 8C, 9A, 9D, 9G
19-SMG	525.27	1.98	4B	7A, 7B, 7C, 8B, 8C, 9E, 9H

Compound	MS Trace	RT (min)	Figure(s)	Table(s)
ent-kaurenoic acid+3Glc (isomer 1) [also referred to as compound KA3.1]	787.37	2.16	4A, 7A, 8A-8C, 9A, 11A, 11B	9B, 9E, 9H
ent-kaurenoic acid+3Glc (isomer 2) [also referred to as compound KA3.2]	787.37	2.28	4A, 7A, 8D-8F, 9A, 11A, 11B	9B, 9E, 9H
ent-kaurenol+3Glc (isomer 1) co-eluted with ent-kaurenol+3Glc (#6) [also referred to as compounds KL3.1 and KL3.6]	773.4	2.36	4A, 7A, 8J-8L, 9B, 11A, 11C	
ent-kaurenoic acid+2Glc (#7) [also referred to as compound KA2.7]	625.32	2.35	4A, 9A, 11A, 11B	9B, 9D, 9H
ent-kaurenol+2Glc (#8) [also referred to as compound KL2.8]	611.34	2.38	9B, 7B, 11A, 11C	9B, 9E
Steviol	317.21	2.39	4C	7A, 7B, 7C, 8A, 8B, 8C, 9F

[00187] Steviol glycosides, including GlcNAc-derivatives, glycosylated ent-kaurenol, and/or glycosylated ent-kaurenoic acid can be isolated using a method described herein. For example, following fermentation, a culture broth can be centrifuged for 30 min at 7000 rpm at 4°C to remove cells, or cells can be removed by filtration. The cell-free lysate can be obtained, for example, by mechanical disruption or enzymatic disruption of the host cells and additional centrifugation to remove cell debris. Mechanical disruption of the dried broth materials can also be performed, such as by sonication. The dissolved or suspended broth materials can be filtered using a micron or sub-micron prior to further purification, such as by preparative chromatography. The fermentation media or cell-free lysate can optionally be treated to remove low molecular weight compounds such as salt; and can optionally be dried prior to purification and re-dissolved in a mixture of water and solvent. The supernatant or cell-free lysate can be purified as follows: a column can be filled with, for example, HP20 Diaion® resin (Supelco) or other suitable non-polar adsorbent or reverse phase chromatography resin, and an aliquot of supernatant or cell-free lysate can be loaded on to the column and washed with water to remove the hydrophilic components. The steviol glycoside product can be eluted by stepwise incremental increases in the solvent concentration in water or a gradient from, *e. g.*, 0% → 100% methanol). The levels of steviol glycosides, glycosylated ent-kaurenol, and/or glycosylated ent-kaurenoic acid in each fraction, including the flow-through, can then be analyzed by LC-MS. Fractions can then be combined and reduced in volume using a vacuum evaporator. Additional purification steps can be utilized, if desired, such as additional chromatography steps and crystallization.

Example 2: Strain Engineering and Fermentation

[00188] Steviol glycoside-producing *S. cerevisiae* strains were constructed as described in WO 2011/153378, WO 2013/022989, WO 2014/122227, and WO 2014/122328, each of which is incorporated by reference in their entirety. For example, a yeast strain comprising one or more copies of a recombinant gene encoding a *Synechococcus sp*. GGPPS polypeptide (SEQ ID NO:19, SEQ ID NO:20), a recombinant gene encoding a truncated *Z. mays* CDPS polypeptide (SEQ ID NO:39, SEQ ID NO:40), a recombinant gene encoding an *A. thaliana* KS polypeptide (SEQ ID NO:51, SEQ ID NO:52), a recombinant gene encoding a recombinant *S. rebaudiana* KO polypeptide (SEQ ID NO:59, SEQ ID NO:60), a recombinant gene encoding an *A. thaliana* ATR2 polypeptide (SEQ ID NO:91, SEQ ID NO:92), a recombinant gene encoding an *O. sativa* EUGT11 polypeptide (SEQ ID NO:14/SEQ ID NO:15, SEQ ID NO:16), a recombinant gene encoding an SrKAHe1 polypeptide (SEQ ID NO:93, SEQ ID NO:94), a recombinant gene encoding an *S. rebaudiana* CPR8 polypeptide (SEQ ID NO:85, SEQ ID NO:86), a recombinant gene encoding an *S. rebaudiana* UGT85C2 polypeptide (SEQ ID NO:5/SEQ ID NO:6, SEQ ID NO:7) or a UGT85C2 variant (or functional homolog) of SEQ ID NO:7, a recombinant gene encoding an *S. rebaudiana* UGT74G1 polypeptide (SEQ ID NO:3, SEQ ID NO:4) or a UGT74G1 variant (or functional homolog) of SEQ ID NO:4, a recombinant gene encoding an *S. rebaudiana* UGT76G1 polypeptide (SEQ ID NO:8, SEQ ID NO:9) or a UGT76G1 variant (or functional homolog) of SEQ ID NO:9, and a recombinant gene encoding an *S. rebaudiana* UGT91D2e polypeptide (SEQ ID NO:10, SEQ ID NO:11) or a UGT91D2e variant (or functional homolog) of SEQ ID NO:11 such as a UGT91D2e-b (SEQ ID NO:12, SEQ ID NO:13) polypeptide produced steviol glycosides.

Example 3: Modulation of Substrate-Specificity of UGT91D2e

[00189] UGT91D1 (GenBank Accession No. AY345980) is highly expressed in the Stevia plant and thought to be a functional UGT. However, its substrate is not a steviol glycoside. This suggests that UGT91D1 has a different substrate than UGT91D2e, which may be defined by the 22 amino acids with which it differs from UGT91D2e. A UGT91D2e site saturation library (SSL) screen of the 22 amino acids differing from UGT91D1 was prepared using Geneart® (Life Technologies) and degenerate NNK-primers.

[00190] UGT91D2 SSL clones were expressed in *E. coli* XJb (DE3) Autolysis™ cells (Zymo Research). Colonies were grown overnight in 96 deep-well plates at 37°C with 1 mL NZCYM (pH 7.0) comprising 15 g Tryptone, 7.5 g NaCl, 7.5 g yeast extract, 1.5 g casamino acids, 3 g $MgSO_4$ and fortified with 100 mg/L ampicillin and 33 mg/L chloramphenicol. 150 µL overnight cultures were transferred to 24 deep-well plates comprising 3 mL NZCYM with ampicillin, 0.1 mM isopropyl-β-D-1-thiogalactopyranoside (IPTG), 3 mM L-arabinose, and 2% (v/v) ethanol and incubated 20 h at 20°C. Cells were pelleted and lysed in 100 µL lysis buffer (10 mM Tris-HCl pH 8.0, 5 mM $MgCl_2$, 1 mM $CaCl_2$, 3 tablets/100 mL Complete mini protease inhibitor cocktail (Roche)) by a single freeze-thaw cycle and 50 µL DNase mix (1 µL 1.4 mg/mL deoxyribonuclease (Calbiochem), 1.2 µL 500 mM $MgCl_2$, and 47.8 µL of 4x PBS buffer). Plates were shaken at 500 rpm for 5 min at 25°C to allow degradation of genomic DNA. Plates were then spun down at 4000 rpm for 30 min at 4°C. *See* WO 2013/022989, which is incorporated by reference in its entirety.

[00191] Activity of UGT91D2e variants was tested *in vitro* to assess the specificity of the UGT91D2e variants towards the substrates, rubusoside and RebA. 6 µL of the lysates were diluted with 24 µL of reaction mixture (final concentration: 100 mM Tris-HCl (pH 8.0), 5 mM $MgCl_2$, 1 mM KCl, 300 µM uridine diphosphate glucose (UDPG), and 100 µM rubusoside or RebA). The reaction mixture was incubated at 30°C for 24 h, and 1,2-stevioside and RebD production was measured by LC-MS. Results are shown in Table 2.

Table 2. Activity of UGT91D2e-b and UGT91D2e variants on rubusoside and RebA, producing 1,2-stevioside and RebD, respectively.

	1,2-stevioside (µM)	RebD (µM)	1,2-stevioside/RebD
UGT91D2e-b (SEQ ID NO:13)	264.9	2.7	98.1
UGT91D2e V286C (SEQ ID NO:1)	59.3	0.0	N/A (No activity on RebA)
UGT91D2e G384W (SEQ ID NO:2)	205.6	0.0	N/A (No activity on RebA)
UGT91D2e L211M (SEQ ID NO:118)	129.7	3.7	35.1
UGT91D2e L195G (SEQ ID NO:119)	178.4	0.9	198.2
UGT91D2e V196P (SEQ ID NO:120)	162.1	2.4	67.5
UGT91D2e L211H (SEQ ID NO:121)	123.5	5.1	24.2

[00192] As shown in Table 2, rubusoside and RebA were substrates of UGT91D2e-b (SEQ ID NO:13), UGT91D2e L211M (SEQ ID NO:118), UGT91D2e L195G (SEQ ID NO:119), UGT91D2e V196P (SEQ ID NO:120), and UGT91D2e L211H (SEQ ID NO:121), as 1,2-stevioside and RebD were produced upon contact of the enzymes with either rubusoside or RebA. However, the ratio of 1,2-stevioside/RebD produced by UGT91D2e-b (SEQ ID NO:13), UGT91D2e L211M (SEQ ID NO:118), UGT91D2e L195G (SEQ ID NO:119), UGT91D2e V196P (SEQ ID NO:120), and UGT91D2e L211H (SEQ ID NO:121) fluctuated from 24.2 to 198.2, indicating that the enzymes were not equally selective towards either substrate. The UGT91D2e V286C and UGT91D2e G384W variants were selective towards rubusoside; no RebD was produced upon contact of either variant with RebA.

[00193] Additional variants of UGT91D2e were found to demonstrate substrate specificity towards rubusoside or RebA using the above-described assay. *See* Table 3. The variants of SEQ ID NO:200 (P93V M152G), SEQ ID NO:201 (S99I), SEQ ID NO:203 (T144L), SEQ ID NO:205 (A148K L221I), SEQ ID NO:212 (G384K) were selective towards RebA. The UGT91D2e variants of SEQ ID NO:197 (L195V), SEQ ID NO:198 (V286S), SEQ ID NO:202 (T144K P201P (*silent*)), SEQ ID NO:209 (L211T I130I (*silent*)), SEQ ID NO:211 (S114F V286S), SEQ ID NO:214 (E438M) were selective towards rubusoside.

Table 3. Activity of UGT91D2e variants on rubusoside and RebA, producing 1,2-stevioside and RebD, respectively.

Variant	1,2-stevioside (µM)	RebD (µM)	1,2-stevioside/RebD
UGT91D2e L213E (SEQ ID NO:191)	13.6	1.1	12.4
UGT91D2e S221Y (SEQ ID NO:192)	13.1	27.1	0.5
UGT91D2e E438H (SEQ ID NO:193)	5.1	1.4	3.6
UGT91D2e M152T (SEQ ID NO:194)	16.8	1.5	11.2
UGT91D2e L211C (SEQ ID NO:195)	7.3	1.6	15.8
UGT91D2e L195S (SEQ ID NO:196)	16.4	1.4	11.7
UGT91D2e L195V (SEQ ID NO:197)	35.9	0.0	N/A (No activity on RebA)
UGT91D2e V286S	14.2	0.0	N/A (No activity on

Variant	1,2-stevioside (µM)	RebD (µM)	1,2-stevioside/RebD
(SEQ ID NO:198)			RebA)
UGT91D2e S221S (*silent*) (SEQ ID NO:199)	16.2	1.7	9.5
UGT91D2e P93V M152G (SEQ ID NO:200)	0.2	2.5	0.1
UGT91D2e S99I (SEQ ID NO:201)	0.2	2.6	0.1
UGT91D2e T144K P201P (*silent*) (SEQ ID NO:202)	1.6	0.0	N/A (No activity on RebA)
UGT91D2e T144L (SEQ ID NO:203)	0.0	2.6	0.0 (No activity on rubusoside)
UGT91D2e T144M (SEQ ID NO:204)	1.3	1.6	0.8
UGT91D2e A148K L211I (SEQ ID NO:205)	0.2	2.7	0.1
UGT91D2e L195N (SEQ ID NO:206)	5.1	1.0	5.1
UGT91D2e K199C (SEQ ID NO:207)	2.6	1.3	2.0
UGT91D2e L211M E426G A466V (SEQ ID NO:208)	79.1	1.1	71.9
UGT91D2e L211T I303I (*silent*) (SEQ ID NO:209)	2.7	0.0	N/A (No activity on RebA)
UGT91D2e V286N (SEQ ID NO:210)	3.0	0.0	N/A (No activity on RebA)
UGT91D2e S114F V286S (SEQ ID NO:211)	5.9	0.0	N/A (No activity on RebA)
UGT91D2e G384K (SEQ ID NO:212)	0.0	2.2	0.0 (No activity on rubusoside)
UGT91D2e G384Y (SEQ ID NO:213)	2.9	1.9	1.5
UGT91D2e E438M (SEQ ID NO:214)	4.7	0.0	N/A (No activity on RebA)
UGT91D2e L195C (SEQ ID NO:123)	3.2	1.3	2.5

Example 4: Evaluation of UGT91D2e-b-EUGT11 Chimeric Enzymes

[00194] UGT91D2e-b-EUGT11 chimeric enzymes were tested *in vitro* to access activity on the substrates, rubusoside and RebA. UGT91D2e-b-EUGT11 chimeras were created by polymerase chain reaction (PCR)-amplification and overlap extension PCR using the primers in Table 4.

Table 4. Primers Used to Create UGT91D2e-b-EUGT11 Chimeric Enzymes.

Description	Sequence	SEQ ID
Vector (forward)	GGCAAGCCACGTTTGGTG	SEQ ID NO:135
Vector (reverse)	GGAGCTGCATGTGTCAGAGG	SEQ ID NO:136
EUGT11 fragment 1 / UGT91D2e-b fragment 2 (forward)	CGATGTATTTCATCACTGGTTGCC ATCCATCGCGGCT	SEQ ID NO:137
EUGT11 / UGT91D2e-b fragment 2 (reverse)	AGCCGCGATGGATGGCAACCAGT GATGAAATACATCG	SEQ ID NO:138
UGT91D2e-b fragment 1 / EUGT11 fragment 2 (forward)	TTATGATTATACTCACTACTGGGC TGCTGCAGCCGCATTG	SEQ ID NO:139
UGT91D2e-b fragment 1 / EUGT11 fragment 2 (reverse)	AGCCGCGATGGATGGCAACCAGT GATGAAATACATCG	SEQ ID NO:140
EUGT11 fragment 2 / UGT91D2e-b fragment 3 (forward)	CAAACCTATTACTTTCCTTGGTTT ACTGCCACCGGAAATAC	SEQ ID NO:141
EUGT11 fragment 2 / UGT91D2e-b fragment 3 (reverse)	GTATTTCCGGTGGCAGTAAACCA AGGAAAGTAATAGGTTTG	SEQ ID NO:142
UGT91D2e-b fragment 2 / EUGT11 fragment 3 (forward)	CCGGTGGTTCCGGTGGGACTAAT GCCTCCATTACATGA	SEQ ID NO:143
UGT91D2e-b fragment 2 / EUGT11 fragment 3 (reverse)	TCATGTAATGGAGGCATTAGTCCC ACCGGAACCACCGG	SEQ ID NO:144
EUGT11 fragment 3 / UGT91D2e-b fragment 4 (forward)	GAACGCAGGTCTGCAGGTTCCAA GAAATGAGGAAGATGG	SEQ ID NO:145
EUGT11 fragment 3 / UGT91D2e-b fragment 4 (reverse)	CCATCTTCCTCATTTCTTGGAACC TGCAGACCTGCGTTC	SEQ ID NO:146

[00195] UGT91D2e-b-EUGT11 chimeric enzymes were expressed in *E. coli* XJb(DE3) Autolysis™ cells (Zymo Research). Colonies were grown in 50 mL NZCYM (pH 7.0) with ampicillin and chloramphenicol and re-inoculated into 500 mL NZCYM with IPTG, L-arabinose, and ethanol. Cell lysate preparations were done in 15 mL lysis buffer followed by 150 µL DNase and 200 µL 500 mM $MgCl_2$. GST-tag affinity purification of the chimeras was performed by adding 1/3 volume of 4x PBS buffer (560 mM NaCl, 10.8 mM KCl, 40 mM Na_2HPO_4, 7.2 mM KH_2PO_4 (pH 7.3)) to the lysate supernatant, followed by incubation (2 h, 4°C) with Glutathione Sepharose 4B (GE Healthcare) and loading onto Poly-Prep® Chromatography Columns (Bio-Rad). The beads were washed twice with 1X PBS buffer and eluted with 50 mM Tris-HCl (pH 8.0) and 10 mM reduced glutathione. Eluted protein was stabilized by addition of glycerol to a final concentration of 50%. SDS-PAGE was performed using NuPAGE® 4-12 % Bis-Tris 1.0 mm precast gels (Invitrogen), NuPAGE MOPS (Invitrogen) running buffer and SimplyBlue SafeStain (Invitrogen). The amounts of chimeras produced were determined from the relative staining intensity of the gel images using ImageJ software.

[00196] Chimeras were screened by adding 20 µL purified UGT91D2e-b, EUGT11, or UGT91D2e-b-EUGT11 chimeric enzymes (0.02 mg/mL) to a total volume of 80 µL reaction mixture comprising 100 mM Tris-HCl (pH 8.0), 5 mM $MgCl_2$, 1 mM KCl, 300 µM uridine diphosphate glucose (UDPG), and 100 µM rubusoside or RebA. The reactions were incubated at 30°C for 24 h, and levels of RebA, RebD, rubusoside, and 1,2-stevioside were measured by LC-MS. Not all of the chimeras purified were active in the above described assay (*see* Table 5 for enzymes having activity on rubusoside and/or RebA).

Table 5. EUGT11, UGT91D2e-b, and EUGT11-UGT91D2e-b chimeric enzyme activity on RebA and rubusoside.

	RebA (µM)	RebD (µM)	rubusoside (µM)	1,2-stevioside (AUC)
EUGT11 (SEQ ID NO:16)	32.230	101.300	34.899	1188497
UGT91D2e-b (SEQ ID NO:13)	97.314	6.580	41.157	2660570
Chim_3 (SEQ ID NO:17)	109.764	NF	138.911	11435
Chim_7 (SEQ ID NO:18)	88.502	11.510	NF	3693895

*NF=Not Found

[00197] As shown in Table 5, Chim_7 (SEQ ID NO:18) more efficiently converted rubusoside to 1,2-stevioside, compared to EUGT11 and UGT91D2e. Chim_7 (SEQ ID NO:18) fully consumed the supplied amount of rubusoside, unlike EUGT11 or UGT91D2e. When incubating EUGT11 with rubusoside, the C19-position of rubusoside was 1,2-glycosylated, and RebE and 1,2-stevioside were also produced (Table 5). Additionally, Chim_7 (SEQ ID NO:18) demonstrated 1.75-fold higher activity towards RebA than UGT91D2e-b. Chim_3 (SEQ ID NO:17) selectively converted rubusoside to 1,2-stevioside; no RebA was converted to RebD by Chim_3 (SEQ ID NO:17) (Table 5).

Example 5: Evaluation of UGT85C2 Variants

[00198] Three homology models of UGT85C2 were generated with the ORCHESTRA module in Sybyl-X 2.0 (Certara) using a combination of the three PDB templates (Model 1: 2PQ6, 2VCE, 2C1X; Model 2: 2PQ6; Model 3: 2PQ6, 2C1X) and using standard settings and sequences for UGT85H2, UGT72B1, and VvGT1 (*see* PDB2PQ6, PDB2VCE, and PCB2C1X). Model geometry and quality were checked with the molprobity and ProQ webservers (*see* Chen *et al.*, Acta Crystallographica. Section D, Biological Crystallography 66(Pt 1):12-21 (2010), Davis *et al.*, Nucleic Acids Research 35:W375-83 (2007), Wallner & Elofsson, Protein Science : A Publication of the Protein Society 12(5):1073-86 (2003). The fluorinated UDPG sugar donor analog, UDP-2FGlc, from PDB:2VCE was imported into the UDPG binding site of UGT85C2 prior to the acceptors steviol, 13-SMG, 19-SMG, or rubusoside. Steviol and steviol glycosides were prepared using the Sybyl-X small molecule builder and docked into the active site of the enzyme with the Surflex Dock suite using standard GeomX settings. The sites for the site saturation library (SSL) were determined by selecting all the residues within 3 Å of the ligands in the docking analysis that were not 100% conserved in the PDB-templates. *See* Table 6.

Table 6. SSL residues for UGT85C2 Docking Analysis.

	UGT85C2 Model #1	UGT85C2 Model #2	UGT85C2 Model #3	Conserved
Phe18	x	x	x	
Pro19	x	x	x	C
Ala20	x	x	x	
Gln21	x	x	x	

	UGT85C2 Model #1	UGT85C2 Model #2	UGT85C2 Model #3	Conserved
Ser22	x	x	x	
His23	x	x	x	C
Lys25		x	x	
Phe48		x	x	
Ile49			x	
Gln52			x	
Glu82		x		
Ala83		x		
Ser84		x		
Pro86			x	
Ile87			x	
Arg88	x		x	
Leu91	x		x	
Leu92	x			
Ile95	x			
Phe122	x			
Thr143	x	x		
Leu144	x	x	x	
Asp198		x		
Val207		x		
Phe210	x			
Thr211	x			
Asn300	x			
Phe301	x			C
Gly302	x		x	C
Ser303	x		x	
Thr304	x	x	x	
Thr305	x	x	x	
Val306			x	
Leu334			x	
Trp359			x	C
Gln362	x			C
His377	x	x		C
Gly379		x	x	C
Trp380	x	x	x	C
Gly381		x	x	
Ser382	x	x	x	C
Tyr398		x	x	

	UGT85C2 Model #1	UGT85C2 Model #2	UGT85C2 Model #3	Conserved
Trp400	x	x	x	
Asp401	x	x	x	
Gln402	x	x		C

x: Residue within 3 Å of steviol, 19-SMG, and UDPG in the docking analysis

C: Conserved residue

[00199] SSL clones were generated for the 34 non-conserved amino acids in Table 6 predicted to be within 3 Å of the ligands residues. A modified version of the whole plasmid amplification method (Zheng *et al*. Nucleic Acids Research 32(14):e115 (2004)) was used with overlapping NNK-primers and Phusion polymerase. 10 µL PCR reaction was treated with 10 U DpnI (New England Biolabs) at 37°C for 1 h, heat inactivated at 65°C for 20 min, and transformed into *E. coli* DH5α cells. Colonies were selected on Luria Broth (LB) + kanamycin agar plates and grown in 4 mL LB fortified with kanamycin. Plasmids were purified using the GeneJET™ miniprep kit (Thermo Fisher Scientific) and sequenced.

[00200] The sequence-verified site saturation library (SSL) clones were transformed into *E. coli* XJb(DE3) Autolysis™ cells (Zymo Research) and selected on LB + kanamycin agar plates. Single colonies were inoculated into 1 mL NZCYM fortified with 30 mg/L kanamycin and incubated overnight at 37°C and 200 rpm orbital shaking. 50 µL of the overnight culture were transferred into 1 mL of fresh NZCYM fortified with 30 mg/L kanamycin, 3 mM arabinose, and 0.1 mM IPTG and incubated overnight at 20°C and 200 rpm orbital shaking. The cells were spun down at 3220 g / 10 min at 4°C and resuspended in 50 µL GT-buffer (10 mM Tris-HCl (pH 7.5), 5 mM $MgCl_2$, 1 mM $CaCl_2$) comprising complete Mini EDTA free protease inhibitor cocktail (1 tablet / 25 mL GT-buffer; Roche Diagnostics). Pellets were resuspended by orbital shaking at 200 rpm / 5 min at 4°C. Cells were incubated at -80°C for minimum 15 min before initiation of lysing step.

[00201] The cells were lysed by heating the samples to 25°C and adding 25 µL DNAse I mix comprising of 2.39 mL 4x His binding buffer (80 mM Tris-HCl (pH 7.5), 500 mM NaCl, 10 mM Imidazole) with 50 µL 1.4 mg/mL DNAse I bovine pancreas (Calbiochem) and 60 µL $MgCl_2$ (500 mM). The lysates were filtered through a 1.2 µm 96-well filterplate (EMD Millipore) and transferred to another 1.2 µm filterplate comprising 50 µL His-select beads (Sigma-Aldrich) prewashed twice with 1X binding buffer. The lysates and beads were then incubated for 2 h at 4°C with 500 rpm orbital shaking. The plates were spun down at 450 g / 2 min. Total protein concentration in the flow-through was measured using the Bradford assay reagent (Sigma-Aldrich), the samples were washed twice by centrifuging the samples, removing supernatants and adding 50 µL 1X His binding buffer. Elution buffer (20 mM Tris-HCl (pH 7.5), 500 mM NaCl, 250 mM imidazole) was added to the beads and incubated for 5 min at 4 °C at 500 rpm orbital shaking and the proteins eluted into a 96 well PCR plate (FrameStar 96, 4titude). The purifications were evaluated by running samples of the flow-through, washing steps and eluate on NuPAGE® SDS-PAGE gel system with 4-12% Bis-Tris precast gels (Invitrogen).

[00202] Activity of the purified UGT85C2 variants was measured. 2.0 µg/mL UGT85C2 variant was incubated for 20 min at 37°C with reaction buffer (100 mM Tris-HCl (pH 8.0), 1 mM KCl, Calf Intestinal Alkaline Phosphatase (New England Biolabs), 120 µM UDPG, and either 40 µM steviol or 40 µM 19-SMG). In this assay, the glucose on UDPG was transferred to steviol or 19-SMG; the products were UDP and either 13-SMG or rubusoside. The phosphates on UDP were then released by a phosphatase, and the amount of phosphate released was measured at Abs_{600} using the Malachite green protocol (Baykov *et al.*, Analytical Biochemistry 171(2):266-70). Values were normalized by total protein released measured by using Bradford reagent (Sigma-Aldrich).

[00203] Candidates were selected as having activity of one standard deviation or higher than wild-type activity or having less than 50% activity on one substrate while maintaining wild-type activity on the other (*e.g.*, exhibiting substrate-specificity). The Abs_{600} ratios of a steviol sample to a 19-SMG sample for wild-type UGT85C2 (SEQ ID NO:7) averaged 0.94, indicating that the wild-type UGT85C2 catalyzes conversion of steviol and 19-SMG with little or no preference of substrate. Table 7A shows the UGT85C2 variants analyzed that preferentially catalyzed conversion of 19-SMG over conversion of steviol, Table 7B shows the UGT85C2 variants analyzed that preferentially catalyzed conversion of steviol over conversion of 19-SMG, and Table 7C shows the UGT85C2 variants analyzed that catalyzed conversion of 19-SMG and steviol with little preference for either substrate. Particular clones generated by the site saturation library (SSL) screen were selected more than once, corresponding to more than one entry in Tables 7A-C.

Table 7A. UGT85C2 SSL screen candidates that were selective towards 19-SMG as a substrate.

Steviol (Abs600)	19-SMG (Abs600)	Steviol/19-SMG Abs600 Ratio	Sum (Abs600)	Mutation	UGT85C2 Variant SEQ ID
0.105	0.165	0.636	0.27	F48S	SEQ ID NO:150
0.099	0.136	0.728	0.235	F48H	SEQ ID NO:151
0.089	0.142	0.627	0.231	F48Y	SEQ ID NO:152
0.080	0.117	0.684	0.197	F48R	SEQ ID NO:153
0.068	0.126	0.540	0.194	F48Q	SEQ ID NO:154
0.068	0.112	0.607	0.18	F48T	SEQ ID NO:156
0.065	0.114	0.570	0.179	F48S	SEQ ID NO:150
0.094	0.141	0.667	0.235	I49V	SEQ ID NO:157
0.078	0.111	0.703	0.189	I49V	SEQ ID NO:157
0.116	0.238	0.487	0.354	S84V	SEQ ID NO:164
-0.020	0.153	19-SMG	0.133	S84V	SEQ ID NO:164
0.096	0.230	0.417	0.326	P86R	SEQ ID NO:165
0.083	0.196	0.423	0.279	P86R	SEQ ID NO:165
0.065	0.17	0.382	0.235	P86R	SEQ ID NO:165
0.042	0.18	0.233	0.222	P86G	SEQ ID NO:166
-0.003	0.169	19-SMG	0.166	P86R	SEQ ID NO:165

Table 7B. UGT85C2 SSL screen candidates that were selective towards steviol as a substrate.

Steviol (Abs600)	19-SMG (Abs600)	Steviol/19-SMG Ratio	Sum (Abs600)	Mutation	UGT85C2 Variant SEQ ID
0.382	-0.081	Steviol	0.301	S84T	SEQ ID NO:160
0.242	-0.083	Steviol	0.159	S84T	SEQ ID NO:160
0.521	-0.033	Steviol	0.488	I87M	SEQ ID NO:169
0.261	0.190	1.374	0.451	I87Y	SEQ ID NO:170
0.372	0.159	2.340	0.531	L91K	SEQ ID NO:171
0.369	0.134	2.754	0.503	L91K	SEQ ID NO:171
0.228	0.104	2.192	0.332	L91R	SEQ ID NO:172
0.202	0.079	2.557	0.281	L91R	SEQ ID NO:172
0.147	0.041	3.585	0.188	L91T	SEQ ID NO:173
0.606	0.266	2.278	0.872	I95K	SEQ ID NO:177

Table 7C. UGT85C2 SSL screen candidates that were not substrate selective towards steviol or 19-SMG.

Steviol (Abs600)	19-SMG (Abs600)	Steviol/19-SMG Ratio	Sum (Abs600)	Mutation	UGT85C2 Variant SEQ ID
0.229	0.268	0.854	0.497	Q21L	SEQ ID NO:147
0.231	0.261	0.885	0.492	Q21T	SEQ ID NO:148
0.214	0.252	0.849	0.466	Q21V	SEQ ID NO:149
0.083	0.098	0.847	0.181	F48W	SEQ ID NO:155
0.359	0.332	1.081	0.691	S84G	SEQ ID NO:158
0.306	0.331	0.924	0.637	S84A	SEQ ID NO:159
0.296	0.292	1.014	0.588	S84C	SEQ ID NO:161
0.250	0.299	0.836	0.549	S84P	SEQ ID NO:162
0.250	0.256	0.977	0.506	S84A	SEQ ID NO:159
0.219	0.262	0.836	0.481	S84N	SEQ ID NO:163
0.355	0.306	1.160	0.661	I87H	SEQ ID NO:167
0.326	0.274	1.190	0.600	I87P	SEQ ID NO:168
0.308	0.282	1.092	0.590	I87M	SEQ ID NO:169
0.279	0.216	1.292	0.495	I87Y	SEQ ID NO:170
0.474	0.426	1.113	0.900	L92F	SEQ ID NO:174
0.387	0.331	1.169	0.718	L92I	SEQ ID NO:175
0.342	0.260	1.315	0.602	L92M	SEQ ID NO:176
0.39	0.598	0.652	0.988	F122S	SEQ ID NO:178
0.297	0.248	1.198	0.545	L334S	SEQ ID NO:179
0.27	0.233	1.159	0.503	L334M	SEQ ID NO:180

[00204] The purified S84V and P86R variants of UGT85C2 were selective towards 19-SMG; UGT85C2 S84V and UGT85C2 P86R did not demonstrate activity on steviol (Table 7A). The purified F48S, F48H, F48Y, F48R, F48Q, F48T, F48S, I49V, P86R, P86G, and F122S UGT85C2 variants also showed selectivity towards 19-SMG (Table 7A). However, the purified S84T and I87M variants of UGT85C2 were selective towards steviol; UGT85C2 S84T and UGT85C2 I87M did not demonstrate activity on 19-SMG (Table 7B). The purified I87P, I87Y, L91K, L91R, L91T, L92M, and I95K UGT85C2 variants also showed selectivity towards steviol (Table 7B).

Example 6: Characterization of Steviol Glycoside-Producing Yeast Strain Deleted of UGT85C2

[00205] A modified version of the steviol glycoside-producing *S. cerevisiae* strain described in Example 2, a recombinant KO gene encoded by the nucleotide sequence set forth in SEQ ID NO:67 (corresponding to the amino acid sequence set forth in SEQ ID NO:117) and a recombinant CPR1 gene encoding (SEQ ID NO:77, SEQ ID NO:78) was deleted for *S. rebaudiana* UGT85C2 polypeptide (SEQ ID NO:5/SEQ ID NO:6, SEQ ID NO:7). Sixteen independent clones were grown in Synthetic Complete (SC) medium at 30ºC for 5 days with shaking (400 rpm for deep wells) prior to harvest. Culture samples (without cell removal) were heated in the presence of DMSO for detection of total glycoside levels with LC-MS.

[00206] As shown in Figure 4A, culture samples of cells deleted of UGT85C2 did not accumulate ent-kaurenol glycosides (ent-kaurenol+3Glc (isomer 1), ent-kaurenol+3Glc (#6), or ent-kaurenol_2Glc (#8), as compared to the control strain (not deleted for UGT85C2). This result suggests that UGT85C2 is responsible for the 19-*O*-glucosylation of ent-kaurenol. Also as shown in Figure 4A, culture samples of cells deleted of UGT85C2 did accumulate ent-kaurenoic acid glycosides (ent-kaurenoic acid+2Glc (#7), ent-kaurenoic acid+3Glc (isomer 1), and ent-kaurenoic acid+3Glc (isomer 2)). Whereas control samples accumulated 13-SMG, culture samples of cells deleted of UGT85C2 accumulated 19-SMG, steviol, steviol+2Glc (#23), and steviol+3Glc (#34). *See* Figures 4B and 4C. Steviol+2Glc (#23) and steviol+3Glc (#34) likely have two or three glucose moieties, respectively, attached on the 19 position of the steviol backbone.

[00207] Structures of isolated tri-glycosylated ent-kaurenoic acid, elucidated by NMR, are shown in Figure 7A, along with a structure of tri-glycosylated ent-kaurenol. These structures were solved by means of standard homo- and heteronuclear multipulse NMR experiments, $^{1}H,^{1}H$-COSY, $^{1}H,^{1}H$-ROESY, $^{1}H,^{13}C$-HSQC, and $^{1}H,^{13}C$-HMBC. Compounds were dissolved in 60 µL DMSO-d6 and measured at 25°C. Spectra of these compounds were acquired on an 800 MHz Bruker Avance instrument (800 MHz for ^{1}H, 201 MHz for ^{13}C) equipped with a cryogenic probe (5 mm CPTCI 1H-13C/15N/D Z-GRD Z44909/0010). In addition, ^{1}H-NMR spectra were obtained for 3 molecules detected by LC-MS that were concordant with a general ent-kaurenoic acid+2Glc, ent-kaurenol+3Glc (isomer 2), and ent-kaurenol+Glc+GlcNAc structures. *See* Figures 8A-8L for ^{1}H NMR spectra and ^{1}H and ^{13}C NMR chemical shifts for these compounds.

[00208] UGT85C2 variants were subsequently cloned into USER vectors (for integration at ChrXII-1) using a forward primer (SEQ ID NO:215) and a reverse primer (SEQ ID NO:216) and the PGK1 promoter. The UGT85C2 variants were then integrated into the steviol glycoside-producing strain deleted of UGT85C2. Transformants were re-streaked from transformation plates. Pre-cultures were set up from re-streaked plates in 500 µL synthetic complete-URA (SC-URA) media in a 96 deep well plate (DWP) and grown at 30°C and 300 rpm overnight. Cultures were set up by transferring 50 µL of the pre-cultures to a 96 well DWP comprising 500 µL SC-URA media.

[00209] After 1 day of incubation, cultures were set up from pre-cultures (50 µL in 500 µL SC-URA) and grown in Duetz system for 5 days (same conditions as for pre-cultures). The OD_{600} was measured on plate reader in a 1:10 dilution, and samples were harvested by transferring 50 µL sample to 50 µL 100% DMSO. The mixtures were heated to 80°C for 10 min and subsequently spun down (4000 rcf, 4°C, 10 min). 15 µL of each supernatant were mixed with 105 µL 50% DMSO (total dilution of 1:16), and the samples were analyzed by LC-MS.

Example 7: Assessment of UGT85C2 Variant Activity in Cell Lysates

[00210] Purified variant UGT85C2 DNA from Example 6 was individually transformed into XJB autolysis z-competent cells. Pre-cultures of three colonies from each transformation plate were inoculated into 600 µL LB comprising kanamycin (600 mg/L) and incubated overnight at 200 rpm and 37˚C in a 96 well DWP. Protein production and cell wall degradation were induced by transferring 50 µL of the pre-cultures to a new 96 well DWP comprising 1mL/well of NZCYM broth comprising kanamycin (600 mg/L) + 3 mL/L 1M Arabinose and 100 µL/L 1M IPTG. Cultures were incubated at 20˚C, 200 rpm for approximately 20 h before pelleting the cells (4000 rcf, 5 min, 4˚C) and removing the supernatant. To each well, 50 µL GT buffer with protease inhibitor (cOmplete™, Mini, EDTA-free Protease Inhibitor Cocktail Tablets, 11836170001 Roche) was added. Pellets were resuspended by shaking at 200 rpm for 5 min at 4˚C. A 75 µL aliquot of each sample was transferred to a PCR plate and frozen at -80˚C. Pellets were thawed at room temperature, and 25 µL/well DNAse mix (2,39 mL 4x binding buffer + 50 µL DNAse I (1.4 mg/mL) + 60 µL $MgCl_2$ (1 M) per plate) were added when samples were nearly thawed. The plate was incubated at room temperature for 5 min with gentle shaking and subsequently centrifuged at 4000 rcf for 5 min. Each supernatant was transferred to a fresh PCR plate for activity measurements.

[00211] Each supernatant was incubated in an assay reaction mix comprising a final concentration of 100 mM Tris (pH 8.0), 4 mM $MgCl_2$, 1 mM KCl, 300 µM UDP-Glucose, and 100 µM substrate. The substrates were either steviol or 19-SMG. A purified wild-type UGT85C2 enzyme and a UGT85C2 bacterial lysate were used as positive controls. Reactions were incubated at 30°C (on a plate shaker), and the reactions were stopped after 20 min, 40 min, and 19 h by mixing 20 µL sample with 20 µL 100% DMSO. The samples were further diluted by adding 60 µL 50% DMSO and subsequently analyzed by LC-MS. AUC values corresponding to measured 13-SMG, 19-SMG, rubusoside, and steviol levels are shown in Tables 8A-C.

Table 8A. Measured 13-SMG and steviol AUC values in UGT85C2 variant activity assay using steviol as a substrate.

	13-SMG			Steviol		
UGT85C2 Variant	20 min	40 min	19 h	20 min	40 min	19 h
F48S (SEQ ID NO:150)	38195	55395	76045	21355	9955	
F48H (SEQ ID NO:151)	49840	64105	79000	17670	4035	
F48Y (SEQ ID NO:152)	36980	53005	83100	26675	16135	
F48R (SEQ ID NO:153)	37990	55510	71810	25540	11075	
F48Q (SEQ ID NO:154)	33660	46010	72550	30565	16135	
F48W (SEQ ID NO:155)	37580	56220	76490	25280	8615	
F48T (SEQ ID NO:156)	40505	57280	78080	20405	10340	
I49V (SEQ ID NO:157)	48345	60720	75420	17545	4305	
S84G (SEQ ID NO:158)	33960	50770	76070	29500	15870	
S84A (SEQ ID NO:159)	43135	62000	75715	21445	5190	
S84C (SEQ ID NO:161)	25780	39330	71060	34285	22700	
S84V (SEQ ID NO:164)	27045	43200	74505	32100	17715	
P86R (SEQ ID NO:165)	23240	34440	71955	33670	25395	
P86G (SEQ ID NO:166)	28000	43525	74300	27640	14380	
I87H (SEQ ID NO:167)	7290	10465	43495	51340	41690	21865
I87P (SEQ ID NO:168)	32165	48565	76700	29475	13945	
I87Y (SEQ ID NO:170)	36905	47250	71390	31220	14065	
L91K (SEQ ID NO:171)	25810	37830	72435	29455	19015	2770
L91R (SEQ ID NO:172)	27560	40235	75830	34275	22140	2470
L92F (SEQ ID NO:174)	49205	62540	72385	15635	3570	

Table 8B. Measured 13-SMG, 19-SMG, and rubusoside AUC values in UGT85C2 variant activity assay using 19-SMG as a substrate.

	19-SMG	rubusoside

UGT85C2 Variant	20 min	40 min	19 h	20 min	40 min	19 h
F48S (SEQ ID NO:150)	171625	147690	3720	18935	30650	92800
F48H (SEQ ID NO:151)	165365	129495	1830	24415	40520	99660
F48Y (SEQ ID NO:152)	161680	128705	2815	23130	39385	97180
F48R (SEQ ID NO:153)	166035	142095	6120	17335	30075	93750
F48Q (SEQ ID NO:154)	169560	145130	3235	16570	28495	81190
F48W (SEQ ID NO:155)	168175	147640	3920	16040	28030	95530
F48T (SEQ ID NO:156)	166190	134425	2960	22445	37520	96620
I49V (SEQ ID NO:157)	170460	133705	1935	20340	35300	97440
S84G (SEQ ID NO:158)	175515	147045	3165	14645	24745	91945
S84A (SEQ ID NO:159)	163565	131735	1790	19805	31845	90090
S84C (SEQ ID NO:161)	183175	159805	44230	11040	17040	77130
S84V (SEQ ID NO:164)	183415	168240	6600	11975	20075	98555
P86R (SEQ ID NO:165)	186925	154290	12670	12075	20350	85755
P86G (SEQ ID NO:166)	175265	146080	5720	17660	29815	93195
I87H (SEQ ID NO:167)	197170	191250	149025	3045	5300	27610
I87P (SEQ ID NO:168)	167935	143945	8795	16675	28290	96865
I87Y (SEQ ID NO:170)	176815	142820	4750	16635	26615	93205
L91K (SEQ ID NO:171)	188110	182210	177120	5350	8545	20345
L91R (SEQ ID NO:172)	188750	180040	149165	7535	12140	29160
L92F (SEQ ID NO:174)	187295	155170	2695	11335	22340	98920

Table 8C. Measured 13-SMG, 19-SMG, rubusoside, and steviol AUC values in control UGT85C2 assays.

	13-SMG			19-SMG			rubusoside			Steviol		
	20 min	40 min	19 h	20 min	40 min	19 h	20 min	40 min	19 h	20 min	40 min	19 h
Substrate: Steviol WT UGT85C2 (SEQ ID NO:7)	60635	67575	73750						490			
Substrate: 19-SMG WT UGT85C2 (SEQ ID NO:7)				53380	4635	1775	85560	108620	100300			
Substrate: Steviol No UGT85C2										53745	46585	54250
Substrate: 19-SMG No UGT85C2				224605	206230	199490						

[00212] Accumulation of 19-SMG and rubusoside was not observed in UGT85C2 variant activity assays using steviol as a substrate. Using steviol as the substrate, the F48H, F48Y, F48T, I49V, S84A, and L92F UGT85C2 variants demonstrated high activity during incubation periods of under 40 min, and the F48H, F48Y, F48T, and I49V UGT85C2 variants demonstrated high activity during incubation periods of over 40 min (Table 8A). Using 19-SMG as the substrate, the F48H, F48Y, F48T, I49V, and S84A UGT85C2 variants demonstrated high activity during incubation periods of under 40 min, and the F48H, I49V, S84A, S84V, L91K, and L92F UGT85C2 variants, as well as the wild-type UGT85C2, demonstrated high activity during incubation periods of over 40 min (Table 8B). Slow conversion of steviol and 19-SMG was observed for UGT85C2 I87H (Tables 8A and 8B).

[00213] 13-SMG/rubusoside ratios were calculated for the UGT85C2 variants. A high 13-SMG/rubusoside ratio indicates preference of a UGT85C2 variant for steviol, whereas a low 13-SMG/rubusoside ratio indicates preference of a UGT85C2 variant for 19-SMG. The L91K, L91R, and L92F UGT85C2 variants demonstrated a high 13-SMG/rubusoside ratio, whereas the F48Y, F48T, P86G UGT85C2 variants demonstrated a low 13-SMG/rubusoside ratio.

[00214] The UGT85C2 variants were found to convert steviol to rubusoside after 24 h. Rubusoside levels (in AUC) are shown in Figure 5. Mutations in the amino acid 48 and 49 positions produced increased levels of rubusoside, as compared to the control. The variants with mutations in amino acids at position 86, 91 and 92 seem to produce lower levels of rubusoside.

Example 8: Evaluation of UGT76G1 Variants

[00215] UGT76G1 variants were tested in a modified version of a steviol glycoside-producing *S. cerevisiae* strain as described in Example 2 to determine the effects on steviol glycosides, tri-glycosylated ent-kaurenol, and tri-glycosylated ent-kaurenoic acid levels. The background strain was described in Example 9 of WO 2014/122227, wherein both copies of UGT76G1 were deleted by homologous recombination using selective markers. The strain comprised a reintegrated wild-type UGT76G1 (WT control) or variants of UGT76G1 at the chromosome level.

[00216] Expression of UGT76G1 H155L (SEQ ID NO:184) increased the ratio of RebM/RebD produced, as compared to wild-type UGT76G1. Expression of UGT76G1 Q23H (SEQ ID NO:181), UGT76G1 T146G (SEQ ID NO:183), UGT76G1 L257G (SEQ ID NO:185), or UGT76G1 S283N (SEQ ID NO:188) in the strain all resulted in increased accumulation of ent-kaurenoic acid+2Glc (#7), 1,2-bioside, 1,2-stevioside, RebE, RebD, steviol+5Glc (#22), and steviol+6Glc (isomer 1), increased the ratio of RebD/RebM produced, and decreased accumulation of RebB and RebA, as compared to wild-type UGT76G1. *See* Tables 9A-9C. Specifically, expression of UGT76G1 T146G (SEQ ID NO:183), resulted in increased accumulation of ent-kaurenoic acid+3Glc (isomer 1), steviol+3Glc (#1), and Stev3Glc (#34), as compared to wild-type UGT76G1. Expression of UGT76G1 L257G (SEQ ID NO:185) increased the amount of steviol+7Glc (isomer 2), as compared to wild-type UGT76G1. Expression of UGT76G1 S283N (SEQ ID NO:188) increased the amount of steviol+3Glc (#1) and Stev3Glc (#34), as compared to wild-type UGT76G1. *See* Tables 9A-9C.

Table 9A. Accumulation of steviol glycosides (in µM) in a host comprising wild-type UGT76G1 or a UGT76G1 variant.

	13-SMG	1,2-bioside	RebB	RebA	RebE	RebD	RebM
Wild-type (SEQ ID NO:9)	13.5 ± 3.8	N/A	1.5 ± 0.4	4.7 ± 1.9	N/A	5.2 ± 2.5	29.3 ± 15.5
H155L (SEQ ID NO:184)	13.9 ± 2.4	N/A	1.8 ± 0.2	6.5 ± 1.5	N/A	2.1 ± 0.3	38.8 ± 12.6
Q23H (SEQ ID NO:181)	13.4 ± 2.2	1.8 ± 0.4	0.9 ± 0.1	1.3 ± 0.2	4.6 ± 0.6	17.7 ± 6.4	1.9 ± 0.7
T146G (SEQ ID NO:183)	13.9 ± 2.7	2.0 ± 0.4	0.6 ± 0.3	0.7 ± 0.5	7.4 ± 1.9	14.1 ± 3.5	1.1 ± 0.2
L257G (SEQ ID NO:185)	13.6 ± 0.9	1.2 ± 0.1	0.9 ± 0.2	2.3 ± 0.3	2.8 ± 0.4	32.0 ± 6.1	7.0 ± 1.5
S283N (SEQ ID NO:188)	13.5 ± 1.4	2.1 ± 0.4	0.5 ± 0.1	0.3 ± 0.5	7.9 ± 1.0	14.4 ± 3.9	0.9 ± 0.4
Q23H+H155L (SEQ ID NO:217)	12.4 ± 1.1	1.4 ± 0.3	0.8 ± 0.1	1.9 ± 0.5	4.0 ± 0.4	22.4 ± 5.9	8.4 ± 3.4
T146G+H155L (SEQ ID NO:218)	13.8 ± 1.3	1.4 ± 0.2	0.8 ± 0.1	2.2 ± 0.1	3.4 ± 0.4	26.5 ± 2.5	9.5 ± 1.9
L257G+H155L (SEQ ID NO:219)	14.1 ± 1.3	0.9 ± 0.4	1.0 ± 0.1	3.1 ± 0.5	1.8 ± 0.5	23.8 ± 5.2	15.9 ± 1.5
S283N+H155L (SEQ ID NO:220)	13.4 ± 2.6	2.3 ± 0.5	0.5 ± 0.3	0.3 ± 0.5	7.2 ± 1.8	10.1 ± 4.3	1.2 ± 0.6

Table 9B. Accumulation of steviol glycosides, glycosylated ent-kaurenoic acid, or glycosylated kaurenol (in AUC) in a host comprising wild-type UGT76G1 or a UGT76G1 variant.

	KA+2Glc (#7)	KA+3Glc (isomer 1)	KA+3Glc (isomer 2)	KL+2Glc (#8)	KL+3Glc (isomer 1 and isomer 2)	1,2-stevioside	steviol+3Glc (#1)
Wild-type (SEQ ID NO:9)	N/A	N/A	859 ± 1089	N/A	N/A	887 ± 668	N/A
H155L (SEQ ID NO:184)	N/A	N/A	1862 ± 1825	N/A	550 ± 1035	874 ± 754	N/A
Q23H (SEQ ID NO:181)	3118 ± 1068	592 ± 1165	N/A	N/A	N/A	6716 ± 966	466 ± 500
T146G (SEQ ID NO:183)	3109 ± 1441	1355 ± 951	N/A	N/A	N/A	8313 ± 1498	1243 ± 601
L257G (SEQ ID NO:185)	2562 ± 1267	1062 ± 1199	N/A	N/A	N/A	5716 ± 837	N/A
S283N (SEQ ID NO:188)	3872 ± 1086	1200 ± 1929	N/A	N/A	N/A	8572 ± 1325	1162 ± 644
Q23H+H155L (SEQ ID NO:217)	2690 ± 423	N/A	236 ± 668	N/A	N/A	6690 ± 734	110 ± 311
T146G+H155L (SEQ ID NO:218)	2416 ± 555	N/A	N/A	N/A	N/A	6172 ± 524	208 ± 385
L257G+H155L (SEQ ID NO:219)	1634 ± 1227	212 ± 600	1524 ± 1318	N/A	222 ± 628	5458 ± 1068	N/A
S283N+H155L (SEQ ID NO:220)	3886 ± 750	496 ± 929	N/A	408 ± 1154	N/A	8036 ± 1601	1118 ± 614

–KA:ent-kaurenoic acid

–KL:ent-kaurenol

Table 9C. Accumulation of steviol glycosides (in AUC) in a host comprising wild-type UGT76G1 or a UGT76G1 variant.

	steviol +3 Glc (#34)	steviol+4 Glc (#26)	steviol+4 Glc (#33)	steviol+5 Glc (#22)	steviol+5 Glc (#25)	steviol +6 Glc (isomer 1)	steviol+7 Glc (isomer 2)
Wild-type (SEQ ID NO:9)	N/A	2443 ± 1164	N/A	N/A	N/A	N/A	N/A
H155L (SEQ ID NO:184)	N/A	1020 ± 731	N/A	N/A	938 ± 1039	N/A	N/A
Q23H (SEQ ID	472 ± 507	818 ± 726	N/A	19804 ± 4600	N/A	7350 ± 4013	N/A

NO:181)							
T146G (SEQ ID NO:183)	1262 ± 605	1509 ± 376	114 ± 302	38469 ± 8953	N/A	7365 ± 3483	N/A
L257G (SEQ ID NO:185)	104 ± 294	1038 ± 459	N/A	11638± 2268	N/A	10722 ± 1871	3870 ± 2463
S283N (SEQ ID NO:188)	1168 ± 655	1572 ± 625	104 ± 294	44460 ± 11455	N/A	12174 ± 5214	N/A
Q23H+H155L (SEQ ID NO:217)	122 ± 345	964 ± 459	N/A	16600 ± 3617	N/A	4404 ± 2744	5230 ± 3262
T146G+H155L (SEQ ID NO:218)	212 ± 383	1114 ± 192	N/A	14362 ± 1802	N/A	2498 ± 2743	4840 ± 2053
L257G+H155L (SEQ ID NO:219)	N/A	782 ± 725	N/A	6354 ± 4578	N/A	2408 ± 2584	5780 ± 977
S283N+H155L (SEQ ID NO:220)	1186 ± 673	1020 ± 739	N/A	38410 ± 17463	N/A	3864 ± 3520	N/A

[00217] The double UGT76G1 variants were also tested. The double variants were: UGT76G1 Q23H H155L (SEQ ID NO:217), UGT76G1 T146G H155L (SEQ ID NO:218), UGT76G1 L257G H155L (SEQ ID NO:219), and UGT76G1 S283N H155L (SEQ ID NO:220). Double variants UGT76G1 Q23H H155L (SEQ ID NO:217), UGT76G1 T146G H155L (SEQ ID NO:218), and UGT76G1 L257G H155L (SEQ ID NO:219) resulted in increased RebM accumulation, as compared to the three single variants UGT76G1 Q23H (SEQ ID NO:181), UGT76G1 T146G (SEQ ID NO:183), and UGT76G1 L257G (SEQ ID NO:185). *See* Tables 9A-9C. Specifically, expression of UGT76G1 Q23H H155L (SEQ ID NO:217) increased the amount of RebM and steviol+7Glc (isomer 2), compared to the UGT76G1 Q23H (SEQ ID NO:181) variant. Expression of UGT76G1 T146G H155L (SEQ ID NO:218) increased accumulation of RebA, RebD, RebM, and steviol+7Glc (isomer 2) and decreased accumulation of ent-kaurenoic acid+3Glc (isomer1), 1,2-bioside, 1,2-stevioside, steviol+3Glc (#1), Stev3Glc (#34), RebE, and steviol+5Glc (#22), as compared to the UGT76G1 T146G (SEQ ID NO:183) variant. Expression of UGT76G1 L257G H155L (SEQ ID NO:219) increased accumulation of ent-kaurenoic acid+3Glc (isomer 2), RebA, and RebM and decreased accumulation of RebE and steviol+6Glc (isomer 1), as compared to the UGT76G1 L257G (SEQ ID NO:185) variant. *See* Tables 9A-9C. Thus, synergistic effects were observed for UGT76G1 double variants.

[00218] UGT76G1 variants were also analyzed in a modified version of the strain described above, which comprised a higher copy number of UGT91D2e (SEQ ID NO:10, SEQ ID NO:11), UGT74G1 (SEQ ID NO:3, SEQ ID NO:4), and ATR2 (SEQ ID NO:91, SEQ ID NO:92). Steviol glycoside-producing *S. cerevisiae* strains expressing UGT76G1 variants that resulted in increased RebD levels, including UGT76G1 Q23H, UGT76G T146G, and S283N, also increased accumulation of ent-kaurenoic acid+2Glc (#7) and ent-kaurenoic acid+2Glc (isomer 1) but decreased accumulation of ent-kaurenoic acid+3Glc (isomer 2), compared to steviol glycoside-producing *S. cerevisiae* strains expressing wild-type UGT76G1. *See* Figure 9A. UGT76G1 variants that increased RebD levels also increased accumulation of ent-kaurenol+2Glc (#8) but decreased accumulation of ent-kaurenol+3Glc (isomer 1) co-eluted with ent-kaurenol+3Glc (#6) (Figure 9B).

[00219] Expression of the UGT76G1 H155L variant (SEQ ID NO:184), a variant that increased levels of RebM, resulted in decreased accumulation of ent-kaurenoic acid+2Glc (#7) and ent-kaurenoic acid+3Glc (isomer 1) (Figure 9A). Levels of ent-kaurenol glycosides were not significantly altered upon expression of UGT76G1 variants that increased levels of RebM, compared to strains expressing wild-type UGT76G1 (Figure 9B).

[00220] Levels of 13-SMG, 1,2-bioside, rubusoside, RebA, RebB, RebD, RebE, RebM, RebG (1,3-stevioside), steviol+3Glc (#1), steviol+4Glc (#26), steviol+5Glc (#22), steviol+5Glc (#24), steviol+5Glc (#25), steviol+6Glc (isomer 1), and steviol+6Glc (#23) produced in the steviol glycoside-producing strain are shown in Figures 10A-10C. Expression of UGT variants that resulted in increased RebD levels also increased accumulation of steviol+5Glc (#22), 1,2-stevioside, steviol+6Glc (isomer 1), and Stevio+3Glc (#1) but decreased accumulation of steviol+4Glc (#26), steviol+5Glc (#24), and RebG (1,3-stevioside) (Figure 10A). Expression of UGT76G1 H155L (SEQ ID NO:184) resulted in increased accumulation of steviol+5Glc (#25) but decreased accumulation of 1,2-stevioside, steviol+3Glc (#1), steviol+4Glc (#26), steviol+5Glc (#22), steviol+6Glc (isomer 1), and steviol+6Glc (#23) (Figure 10B). Expression of UGT76G1 S253W (SEQ ID NO:186) resulted in decreased accumulation of 1,2-stevioside and steviol+6Glc (isomer 1) (Figure 10B). Expression of UGT76G1 284G resulted in increased accumulation of 1,2-stevioside and steviol+6Glc (isomer 1) but decreased accumulation of RebG, steviol+4Glc (#26), steviol+5Glc (#25), and steviol+6Glc (#23) (Figure 10B). Figure 10C shows accumulation of 13-SMG, 1,2-bioside, rubusoside, RebA, RebB, RebD, RebE, and RebM in *S. cerevisiae* expressing wild-type UGT76G1 (SEQ ID NO:9) or a UGT76G1 variant that increases accumulation of RebD or RebM.

[00221] The steviol glycoside-producing strain comprising a higher copy number of UGT91D2e (SEQ ID NO:10, SEQ ID NO:11), UGT74G1 (SEQ ID NO:3, SEQ ID NO:4), and ATR2 (SEQ ID NO:91, SEQ ID NO:92) was further tested in a separate experiment. As shown in Tables 9D-9F, expression of UGT76G1 H155L (SEQ ID NO:184) resulted in increased accumulation of steviol+5Glc (#25), increased the ratio of RebM/RebD produced, and decreased accumulation of 1,2-bioside, steviol+3Glc (#1), RebE, steviol+6Glc (isomer 1), and steviol+6Glc (#23), as compared to wild-type UGT76G1. Expression of UGT76G1 Q23H (SEQ ID NO:181), UGT76G1 T146G (SEQ ID NO:183), UGT76G1 L257G (SEQ ID NO:185), or UGT76G1 S283N (SEQ ID NO:188) increased accumulation of 1,2-bioside, 1,2-stevioside, steviol+3Glc (#1), Stev+3Glc (#34), RebE, and steviol+5Glc (#22), increased the ratio of RebD/RebM produced, and decreased accumulation of RebG, RebA, steviol+5Glc (#25), steviol+7Glc (isomer 2), and steviol+7Glc (isomer 5). Specifically, expression of UGT76G1 Q23H (SEQ ID NO:181) resulted in increased accumulation of rubusoside, steviol+6Glc (isomer 1) and decreased accumulation of RebB and steviol+5Glc (#24). Expression of UGT76G1 T146G (SEQ ID NO:183) resulted in increased accumulation of rubusoside and decreased accumulation of RebB, steviol+5Glc (#24) and steviol+6Glc (#23). Expression of UGT76G1 L257G (SEQ ID NO:185) resulted in increased accumulation of steviol+6Glc (isomer 1). Expression of UGT76G1 S283N (SEQ ID NO:188) resulted in increased accumulation of rubusoside and decreased accumulation of RebB, steviol+5Glc (#24) and steviol+6Glc (#23). *See* Tables 9D-F.

Table 9D. Accumulation of steviol glycosides (in µM) in a host comprising wild-type UGT76G1 or a UGT76G1 variant.

	13-SMG	**1,2-bioside**	**Rubu**	**RebG**	**RebB**	**RebA**	**RebE**	**RebD**	**RebM**
Wild-type (SEQ ID NO:9)	37.6 ± 8.8	1.3 ± 0.5	1.2 ± 0.2	0.2 ± 0.2	8.4 ± 2.3	32.5 ± 7.5	0.4 ± 0.1	30.4 ± 12.5	43.0 ± 9.6
H155L (SEQ ID NO:184)	35.3 ± 7.0	0.4 ± 0.1	1.3 ± 0.1	0.2 ± 0.2	8.9 ± 2.1	35.2 ± 9.3	0.1 ± 0.1	5.7 ± 1.8	64.5 ± 7.1
Q23H (SEQ ID NO:181)	40.8 ± 6.9	11.1 ± 1.5	2.4 ± 0.4	N/A	4.3 ± 1.3	7.2 ± 2.0	11.8 ± 4.5	35.1 ± 6.5	1.0 ± 0.4
T146G (SEQ ID NO:183)	41.4 ± 6.9	16.1 ± 1.4	3.1 ± 0.4	N/A	1.5 ± 0.5	2.4 ± 1.1	19.2 ± 3.2	15.0 ± 5.3	0.2 ± 0.2
L257G (SEQ ID NO:185)	32.4 ± 6.2	6.9 ± 1.0	1.8 ± 0.5	N/A	5.2 ± 1.8	12.1 ± 4.8	4.7 ± 1.6	41.7 ± 10.4	2.3 ± 0.9

S283N (SEQ ID NO:188)	39.8 ± 7.2	15.1 ± 2.8	2.6 ± 0.4	N/A	1.5 ± 0.5	2.9 ± 1.2	16.2 ± 4.8	19.2 ± 6.9	0.3 ± 0.1
Q23H+H155L (SEQ ID NO:217)	39.4 ± 4.5	9.0 ± 1.3	2.1 ± 0.2	N/A	4.7 ± 0.9	8.3 ± 2.6	8.8 ± 1.6	34.1 ± 4.5	3.0 ± 1.2
T146G+H155L (SEQ ID NO:218)	33.0 ± 8.0	8.5 ± 2.0	1.9 ± 0.7	N/A	3.8 ± 1.0	9.2 ± 2.9	6.6 ± 1.7	36.5 ± 4.7	3.1 ± 0.9
L257G+H155L (SEQ ID NO:219)	44.4 ± 6.6	4.9 ± 0.9	1.5 ± 0.3	N/A	8.2 ± 1.2	19.2 ± 4.0	3.4 ± 1.0	47.8 ± 4.5	12.3 ± 3.3
S283N+H155L (SEQ ID NO:220)	42.9 ± 6.6	14.5 ± 1.1	2.8 ± 0.2	N/A	2.1 ± 0.7	2.7 ± 0.9	16.7 ± 1.9	17.2 ± 3.7	0.7 ± 0.3

Table 9E. Accumulation of steviol glycosides, glycosylated ent-kaurenoic acid, or glycosylated kaurenol (in AUC) in a host comprising wild-type UGT76G1 or a UGT76G1 variant.

	KA+2 Glc (#7)	**KA+3 Glc (isomer 1)**	**KA+3 Glc (isomer 2)**	**KL+2 Glc (#8)**	**KL+3 Glc (isomer 1 and isomer 2)**	**19-SMG**	**1,3-bioside**	**1,2-stevioside**	**steviol+3Glc (#1)**	**steviol+3Glc (#34)**
Wild-type (SEQ ID NO:9)	14444 ± 5537	2472 ± 1360	47650 ± 20783	8102 ± 4937	123288 ± 20872	2174 ± 1054	274 ± 775	23410 ± 10331	2226 ± 1961	1512 ± 2135
H155L (SEQ ID NO:184)	1096 ± 1570	N/A	48264 ± 17847	1770 ± 1118	105904 ± 33369	2072 ± 940	N/A	13466 ± 2764	N/A	N/A
Q23H (SEQ ID NO:181)	140332 ± 26599	10386 ± 2233	2914 ± 2162	183464 ± 22523	53058 ± 11295	2364 ± 520	N/A	199500 ± 50824	21436 ± 6924	21436 ± 6924
T146G (SEQ ID NO:183)	158245 ± 18966	7339 ± 2016	N/A	266539 ± 21693	21515 ± 3812	1961 ± 1049	N/A	237205 ± 38885	27438 ± 6704	27438 ± 6704
L257G (SEQ ID NO:185)	111152 ± 39204	9732 ± 3604	7486 ± 3428	100144 ± 34855	67696 ± 22294	2010 ± 480	N/A	123746 ± 31888	13040 ± 2074	13070 ± 2086
S283N (SEQ ID NO:188)	149050 ± 55275	8722 ± 3756	N/A	222832 ± 63472	19864 ± 6586	1980 ± 875	N/A	205128 ± 58796	28660 ± 10712	28660 ± 10712
Q23H+H155L (SEQ ID NO:217)	107934 ± 18511	9230 ± 944	15348 ± 3586	86190 ± 13792	84080 ± 7629	2712 ± 674	N/A	162262 ± 12368	19104 ± 3180	19148 ± 3184
T146G+H155L	104146 ±	9346 ± 1964	13674 ± 4859	98980 ±	81762 ±	2034 ± 768	N/A	138510 ±	18846 ± 4723	18900

(SEQ ID NO:218)	17815			30306	19834			32208		± 4624
L257G+H155L (SEQ ID NO:219)	68986 ± 17561	7974 ± 1665	34450 ± 6021	34730 ± 9050	99436 ± 7792	2800 ± 1291	N/A	118750 ± 15972	10356 ± 1814	10376 ± 1838
S283N+H155L (SEQ ID NO:220)	146704 ± 15045	8168 ± 1243	1706 ± 1880	191804 ± 25165	31296 ± 6636	2694 ± 574	N/A	200156 ± 11694	25406 ± 6048	25406 ± 6048

–KA:ent-kaurenoic acid

–KL:ent-kaurenol

Table 9F. Accumulation of steviol glycosides (in AUC) in a host comprising wild-type UGT76G1 or a UGT76G1 variant.

	steviol+ 4Glc (#26)	**steviol+ 5Glc (#22)**	**steviol+ 5Glc (#24)**	**steviol+ 5Glc (#25)**	**steviol+ 6Glc (isomer 1)**	**steviol+ 6Glc (#23)**	**steviol+ 7Glc (isomer 2)**	**steviol+ 7Glc (isomer 5)**	**Steviol**
Wild-type (SEQ ID NO:9)	38936 ± 21188	3288 ± 3892	2194 ± 2020	9068 ± 3994	12294 ± 10105	5838 ± 2979	13784 ± 4806	7630 ± 3054	N/A
H155L (SEQ ID NO:184)	20000 ± 4629	178 ± 503	1530 ± 2310	29526 ± 15999	122 ± 345	2000 ± 830	6494 ± 2530	10782 ± 2519	N/A
Q23H (SEQ ID NO:181)	26366 ± 7357	161044 ± 57250	N/A	N/A	26590 ± 3671	3108 ± 1514	2964 ± 1547	918 ± 1268	N/A
T146G (SEQ ID NO:183)	25070 ± 6192	224315 ± 53331	N/A	N/A	10320 ± 3647	304 ± 804	322 ± 853	286 ± 756	N/A
L257G (SEQ ID NO:185)	17638 ± 5814	81252 ± 31941	258 ± 730	N/A	31616 ± 5164	5088 ± 1171	5154 ± 1398	1590 ± 1335	1246 ± 3524
S283N (SEQ ID NO:188)	24980 ± 8098	219964 ± 61935	N/A	N/A	19666 ± 5418	846 ± 1170	264 ± 747	296 ± 837	N/A
Q23H+H155L (SEQ ID NO:217)	23100 ± 2234	142460 ± 24407	N/A	N/A	15108 ± 1958	3582 ± 819	5996 ± 1705	596 ± 1121	N/A
T146G+H155L (SEQ ID NO:218)	19064 ± 3666	120990 ± 34224	N/A	N/A	13048 ± 2270	4288 ± 889	4640 ± 1866	1306 ± 1449	N/A

L257G+ H155L (SEQ ID NO:219)	17126 ± 2237	56416 ± 15937	928 ± 1293	N/A	17756 ± 2361	5856 ± 960	15114 ± 1900	2230 ± 985	N/A
S283N+ H155L (SEQ ID NO:220)	23536 ± 2818	213846 ± 31505	N/A	N/A	11222 ± 2649	1162 ± 1288	1042 ± 1117	N/A	N/A

[00222] Expression of UGT76G1 Q23H H155L (SEQ ID NO:217) increased accumulation of ent-kaurenoic acid+3Glc (isomer 2) and ent-kaurenol+3Glc (isomer 1) and decreased accumulation of ent-kaurenol+2Glc (#8) and steviol+6Glc (isomer 1), as compared to UGT76G1 Q23H (SEQ ID NO:181). UGT76G1 T146G H155L (SEQ ID NO:218) increased accumulation of ent-kaurenoic acid+3Glc (isomer 2), ent-kaurenol+3Glc (isomer 1), RebB, RebA, RebD, steviol+6Glc (#23), and steviol+7Glc (isomer 2) and decreased accumulation of ent-kaurenoic acid+2Glc (#7), ent-kaurenol+2Glc (#8), 1,2-bioside, rubusoside, 1,2-stevioside, RebE, steviol+5Glc (#22), as compared to UGT76G1 T146G (SEQ ID NO:183). Expression of UGT76G1 L257G H155L (SEQ ID NO:219) increased accumulation of ent-kaurenoic acid+3Glc (isomer 2), ent-kaurenol+3Glc (isomer 1), and steviol+7Glc (isomer 2) and decreased accumulation of ent-kaurenol+2Glc (#8), 1,2-bioside, and steviol+6Glc (isomer 1), as compared to UGT76G1 L257G (SEQ ID NO:185). As well, UGT76G1 L257G H155L (SEQ ID NO:219) increased accumulation of RebD, as compared to wild-type UGT76G1. Expression of UGT76G1 S283N H155L (SEQ ID NO:220) decreased accumulation of steviol+6Glc (isomer 1), as compared to UGT76G1 S283N (SEQ ID NO:188). *See* Tables 9D-F.

[00223] UGT76G1 variants were also expressed in a steviol glycoside-producing strain comprising an extra copy of CPR1 (SEQ ID NO:77, SEQ ID NO:78), an extra copy of SrKAHe1 (SEQ ID NO:93, SEQ ID NO:94), and an extra copy of a UGT76G1 (SEQ ID NO:8, SEQ ID NO:9) or a UGT76G1 variant. Accumulation of steviol glycosides, tri-glycosylated ent-kaurenol, and tri-glycosylated ent-kaurenoic acid levels were measured. *See* Figure 11.

[00224] UGT76G1 variants that increased accumulation of RebD or RebM were also expressed in a steviol glycoside production *S. cerevisiae* strain comprising an extra copy of CPR1 (SEQ ID NO:77, SEQ ID NO:78) and an extra copy of SrKAHe1 (SEQ ID NO:93, SEQ ID NO:94). The control steviol glycoside production strain comprised three copies of wild-type UGT76G1 (SEQ ID NO:9), and the variant-comprising strains comprised two copies of wild-type UGT76G1 (SEQ ID NO:9) and one copy of a UGT76G1 variant. Figure 11A shows levels of ent-kaurenoic acid+2Glc (#7), ent-kaurenoic acid+3Glc (isomer 1), ent-kaurenoic acid+3Glc (isomer 2), ent-kaurenol+2Glc (#8), and ent-kaurenol+3Glc (isomer 1) co-eluted with ent-kaurenol+3Glc (#6) in production strains expressing wild-type UGT76G1 (SEQ ID NO:9), UGT76G1 Q23H (SEQ ID NO:181), UGT76G1 I26W (SEQ ID NO:182), UGT76G1 T146G (SEQ ID NO:183), UGT76G1 H155L (SEQ ID NO:184), UGT76G1 L257G (SEQ ID NO:185), or UGT76G1 S283N (SEQ ID NO:188). Total levels of glycosylated ent-kaurenoic acid (ent-kaurenoic acid+2Glc (#7) + ent-kaurenoic acid+3Glc (isomer 1) + ent-kaurenoic acid+3Glc (isomer 2)) were most significantly increased in production strains expressing UGT76G1 Q23H (SEQ ID NO:181), UGT76G1 I26W (SEQ ID NO:182), and UGT76G1 L257G (SEQ ID NO:185) (Figure 11B), and total levels of glycosylated ent-kaurenol (ent-kaurenol+3Glc (isomer 1) co-eluted with ent-kaurenol+3Glc (#6) and ent-kaurenol+2Glc (#8) were most significantly affected for production strains expressing UGT76G1 Q23H (SEQ ID NO:181), UGT76G1 I26W (SEQ ID NO:182), and UGT76G1 T146G (SEQ ID NO:183) (Figure 11C).

[00225] Figure 11D and 11E show accumulation of 1,2-bioside, 1,2-stevioside, steviol+3Glc (#1), steviol+4Glc (#26), steviol+5Glc (#22), steviol+5Glc (#24), steviol+5Glc (#25), steviol+6Glc (isomer 1), steviol+6Glc (#23), steviol+7Glc (isomer 2), steviol+7Glc (isomer 5), 13-SMG, rubusoside, RebG (1,3-stevioside), RebA, RebB, RebD, RebE, and RebM in production strains expressing wild-type UGT76G1 (SEQ ID NO:9), UGT76G1 Q23H (SEQ ID NO:181), UGT76G1 I26W (SEQ ID NO:182), UGT76G1 T146G (SEQ ID NO:183), UGT76G1 H155L (SEQ ID NO:184), UGT76G1 L257G (SEQ ID NO:185), or UGT76G1 S283N (SEQ ID NO:188).

[00226] All UGT76G1 variants tested in Figure 11D showed decreased accumulation of steviol+4Glc (#26). Expression of UGT76G1 Q23H (SEQ ID NO:181), UGT76G1 I26W (SEQ ID NO:182), UGT76G1 T146G (SEQ ID NO:183), UGT76G1 L257G (SEQ ID NO:185), or UGT76G1 S283N (SEQ ID NO:188), all of which increased production of RebD, resulted in decreased accumulation of steviol+5Glc (#25), compared to a control strain expressing wild-type UGT76G1 (Figure 11D). However, expression of the UGT76G1 H155L (SEQ ID NO:184) variant, which increased RebM production, resulted in increased accumulation of steviol+5Glc (#25) (Figure 11D).

[00227] Expression of UGT76G1 Q23H (SEQ ID NO:181), UGT76G1 I26W (SEQ ID NO:182), UGT76G1 T146G (SEQ ID NO:183), UGT76G1 L257G (SEQ ID NO:185), or UGT76G1 S283N (SEQ ID NO:188) resulted in increased accumulation of steviol+6Glc (#23), compared to a control strain expressing wild-type UGT76G1, whereas expression of the UGT76G1 H155L (SEQ ID NO:184) variant resulted in decreased accumulation of steviol+6Glc

(#23) (Figure 11D). Expression of UGT76G1 Q23H (SEQ ID NO:181), UGT76G1 I26W (SEQ ID NO:182), UGT76G1 T146G (SEQ ID NO:183), UGT76G1 L257G (SEQ ID NO:185), or UGT76G1 S283N (SEQ ID NO:188) resulted in increased accumulation of steviol+7Glc (isomer 2), compared to a control strain expressing wild-type UGT76G1, whereas expression of the UGT76G1 H155L (SEQ ID NO:184) variant resulted in decreased accumulation of steviol+7Glc (isomer 2) (Figure 11D). Expression of UGT76G1 Q23H (SEQ ID NO:181), UGT76G1 I26W (SEQ ID NO:182), UGT76G1 T146G (SEQ ID NO:183), UGT76G1 L257G (SEQ ID NO:185), or UGT76G1 S283N (SEQ ID NO:188) resulted in increased accumulation of steviol+7Glc (isomer 5) (Figure 11D).

[00228] The steviol glycoside-producing strain comprising a higher copy number of CPR1 (SEQ ID NO:77, SEQ ID NO:78) and SrKAHe1 (SEQ ID NO:93, SEQ ID NO:94) was further tested in a separate experiment. As shown in Tables 9G-9I, expression of UGT76G1 H155L (SEQ ID NO:184) reduced the levels of ent-kaurenoic acid+3Glc (isomer 1), RebD, steviol+6Glc (#23), steviol+7Glc (isomer 2), as compared to wild-type UGT76G1. Expression of UGT76G1 Q23H (SEQ ID NO:181), UGT76G1 T146G (SEQ ID NO:183), UGT76G1 L257G (SEQ ID NO:185), or UGT76G1 S283N (SEQ ID NO:188) each reduced accumulation of steviol+4Glc (#26) and steviol+5Glc (#24), as compared to wild-type UGT76G1. Specifically, expression UGT76G1 T146G (SEQ ID NO:183) increased the amount of ent-kaurenoic acid+2Glc (#7), ent-kaurenoic acid+3Glc (isomer 1), RebD, steviol+6Glc (#23), and steviol+7Glc (isomer 2) and reduced the amount of RebG, steviol+5Glc #25, as compared to wild-type UGT76G1. Expression of UGT76G1 L257G (SEQ ID NO:185) increased accumulation of ent-kaurenoic acid+3Glc (isomer 1) and reduced accumulation of ent-kaurenoic acid+3Glc (isomer 2) and steviol+5Glc (#25), as compared to wild-type UGT76G1. Expression of UGT76G1 S283N (SEQ ID NO:188) increased accumulation of ent-kaurenoic acid+3Glc (isomer 1), RebD, steviol+6Glc (isomer 1), and steviol+7Glc (isomer 2) and reduced accumulation of RebG and steviol+5Gl (#25), as compared to wild-type UGT76G1. Expression of UGT76G1 L257G H155L reduced accumulation of ent-kaurenoic acid+3Glc (isomer 1), as compared to the single variant UGT76G1 L257G. Expression of the double variant UGT76G1 Q23H H155L reduced accumulation of steviol+5Glc (#25), as compared to wild-type UGT76G1. Expression of the double variant UGT76G1 S283N H155L reduced accumulation of ent-kaurenoic acid+3Glc (isomer 2), as compared to wild-type UGT76G1. *See* Tables 9G-9I.

Table 9G. Accumulation of steviol glycosides (in µM) in a host comprising wild-type UGT76G1 or a UGT76G1 variant.

	13-SMG	1,2-bioside	Rubu	RebG	RebB	RebA	RebE	RebD	RebM
Wild-type (SEQ ID NO:9)	66.9 ± 4.7	0.4 ± 0.1	1.2 ± 0.2	0.7 ± 0.3	5.6 ± 0.4	30.3 ± 2.4	0.5 ± 0.4	31.0 ± 6.7	199.3 ± 14.2
H155L (SEQ ID NO:184)	63.1 ± 4.6	0.3 ± 0.1	1.3 ± 0.3	0.9 ± 0.3	5.5 ± 0.5	29.6 ± 1.9	0.1 ± 0.2	12.0 ± 10.8	210.0 ± 19.3
Q23H (SEQ ID NO:181)	62.2 ± 13.9	0.4 ± 0.1	0.8 ± 0.3	0.2 ± 0.3	5.2 ± 0.9	27.7 ± 3.3	0.6 ± 0.2	42.0 ± 9.8	179.2 ±19.6
T146G (SEQ ID NO:183)	64.8 ±5.2	0.5 ± 0.2	1.0 ± 0.1	0.1 ± 0.2	5.3 ± 0.8	27.9 ± 3.1	0.8 ± 0.1	46.2 ± 6.7	180.4 ± 24.2
L257G (SEQ ID NO:185)	68.7 ±9.2	0.4 ± 0.1	0.6 ± 0.4	0.2 ± 0.3	5.5 ± 0.6	29.6 ± 3.4	0.6 ± 0.4	45.6 ± 9.3	187.3 ± 14.7
S283N (SEQ ID NO:188)	67.4 ± 13.3	0.4 ± 0.1	0.7 ± 0.5	0.1 ± 0.2	5.7 ± 0.7	32.0 ± 4.2	0.8 ± 0.4	52.7 ± 7.4	189.2 ± 14.1
Q23H+H155L (SEQ ID NO:217)	65.2 ±4.3	0.3 ± 0.0	0.8 ± 0.4	0.3 ± 0.3	5.3 ± 0.3	27.1 ± 2.8	0.7 ± 0.3	37.5 ± 5.4	187.5 ± 10.8
T146G+H155L (SEQ ID NO:218)	64.3 ± 9.8	0.5 ± 0.1	0.8 ± 0.3	0.1 ± 0.2	5.4 ± 0.6	27.3 ± 4.3	0.7 ± 0.4	40.0 ± 8.7	171.2 ± 29.8
L257G+H155L (SEQ ID NO:219)	58.5 ± 15.9	0.3 ± 0.1	0.5 ± 0.5	0.3 ± 0.3	5.2 ± 1.5	25.1 ± 7.9	0.7 ± 0.3	30.4 ± 13.3	167.6 ± 33.6
S283N+H155L (SEQ ID NO:220)	61.2 ± 11.8	0.4 ± 0.1	0.6 ± 0.5	0.0 ± 0.0	5.2 ± 1.0	25.0 ± 5.5	0.6 ± 0.5	37.5 ± 12.0	152.5 ± 35.2

Table 9H. Accumulation of steviol glycosides, glycosylated ent-kaurenoic acid, or glycosylated kaurenol (in AUC) in a host comprising wild-type UGT76G1 or a UGT76G1 variant.

	KA+2Glc (#7)	KA+3Glc (isomer 1)	KA+3Glc (isomer 2)	KL+3Glc (isomer 1 and isomer 2)	19-SMG	1,2-steviosi de	RebI	steviol+ 4Glc (#26)
Wild-type (SEQ ID NO:9)	2422 ± 419	1962 ± 383	40290 ± 3139	11500 ± 1169	422 ± 270	4712 ± 656	N/A	11194 ± 2466
H155L (SEQ	2894 ±	418 ±	40350 ±	10326 ±	376 ±	4466 ±	512 ±	9086 ±

ID NO:184)	401	841	2392	759	316	359	992	1374
Q23H (SEQ ID NO:181)	3340 ± 1018	3044 ± 747	41140 ± 5158	11404 ± 1306	476 ± 317	4452 ± 595	N/A	6550 ± 771
T146G (SEQ ID NO:183)	3362 ± 509	2934 ± 399	40636 ± 5193	10880 ± 872	400 ± 350	4600 ± 511	N/A	6996 ± 695
L257G (SEQ ID NO:185)	2816 ± 240	2712 ± 264	34402 ± 2377	10820 ± 708	254 ± 272	4770 ± 642	N/A	5884 ± 674
S283N (SEQ ID NO:188)	3114 ± 585	2914 ± 346	35830 ± 2929	11430 ± 641	188 ± 348	4986 ± 562	N/A	5734 ± 442
Q23H+H155L (SEQ ID NO:217)	2622 ± 286	2250 ± 408	37176 ± 3860	10376 ± 1049	264 ± 283	4404 ± 416	N/A	6036 ± 906
T146G+H155L (SEQ ID NO:218)	2884 ± 354	2424 ± 324	34100 ± 5312	10026 ± 1326	248 ± 347	4438 ± 1060	N/A	5836 ± 10777
L257G+H155L (SEQ ID NO:219)	2364 ± 691	1798 ± 368	32044 ± 5509	9472 ± 1812	256 ± 363	3690 ± 1217	N/A	5254 ± 1189
S283N+H155L (SEQ ID NO:220)	3162 ± 1250	2656 ± 980	31504 ± 4414	9386 ± 1425	384 ± 331	4014 ± 925	N/A	5638 ± 1696

–KA:ent-kaurenoic acid

–KL:ent-kaurenol

Table 9I. Accumulation of steviol glycosides (in AUC) in a host comprising wild-type UGT76G1 or a UGT76G1 variant.

	steviol+ 4Glc (#33)	**steviol+ 5Glc (#22)**	**steviol+ 5Glc (#24)**	**steviol+ 5Glc (#25)**	**steviol+ 6Glc (isomer 1)**	**steviol+ 6Glc (#23)**	**steviol+ 7Glc (isomer 2)**	**steviol+ 7Glc (isomer 5)**
Wild-type (SEQ ID NO:9)	N/A	N/A	7416 ± 1103	5230 ± 789	1572 ± 1044	3622 ± 590	7078 ± 912	4474 ± 2521
H155L (SEQ ID NO:184)	122 ± 345	N/A	7452 ± 2166	9450 ± 4068	320 ± 905	1868 ± 825	3894 ± 1243	4760 ± 1318
Q23H (SEQ ID NO:181)	N/A	108 ± 305	4382 ± 1490	3412 ± 1176	2792 ± 1053	4520 ± 985	9388 ± 1677	4158 ± 1528
T146G (SEQ ID NO:183)	N/A	114 ± 322	3598 ± 1630	2996 ± 745	3356 ± 1047	5438 ± 636	10406 ± 910	3700 ± 1726
L257G	N/A	N/A	4336 ±	3484 ±	2860 ±	4158 ±	9348 ±	4420 ±

(SEQ ID NO:185)			1158	754	842	1149	1429	1036
S283N (SEQ ID NO:188)	N/A	N/A	4834 ± 1338	3358 ± 546	3566 ± 784	4350 ± 909	9796 ± 1619	3924 ± 1203
Q23H+H 155L (SEQ ID NO:217)	N/A	N/A	4468 ± 1172	3668 ± 679	1932 ± 380	3798 ± 619	8764 ± 1384	3528 ± 2244
T146G+ H155L (SEQ ID NO:218)	N/A	N/A	3682 ± 1715	3008 ± 775	2176 ± 698	4022 ± 898	8712 ± 879	3284 ± 1803
L257G+ H155L (SEQ ID NO:219)	N/A	N/A	3566 ± 1693	2974 ± 781	956 ± 1073	2988 ± 772	7046 ± 1660	3072 ± 1631
S283N+ H155L (SEQ ID NO:220)	N/A	N/A	2670 ± 1807	2554 ± 444	2430 ± 1647	3874 ± 1837	9450 ± 3268	2758 ± 1204

Example 9: Further characterization of UGT76G1 H155L Variant

[00229] UGT76G1 H155L (SEQ ID NO:184) was expressed in the steviol glycoside-producing *S. cerevisiae* strain described in Examples 2 and 8. As shown in Figure 6A, the strain expressing UGT76G1 H155L (gray bars) produced higher levels of RebM, RebA, RebB, 13-SMG, and rubusoside, compared to the control strain expressing wild-type UGT76G1 (black bars). The steviol glycoside-producing strain expressing UGT76G1 H155L produced higher titers of RebM than RebD (Figure 6A).

[00230] The strain expressing UGT76G1 H155L (SEQ ID NO:184) produced greater total levels of steviol glycosides (13-SMG + 1,2-bioside + rubusoside + RebG + RebB + RebA + RebE + RebD + RebM) and RebD + RebM (gray bars), compared to the control strain expressing wild-type UGT76G1 (black bars) (Figure 6B). Thus, the steviol glycoside-producing strain expressing UGT76G1 H155L (gray bars) demonstrated a 20% increase in steviol glycoside production and a 10% increase in RebD and RebM titers, compared to the control strain expressing wild-type UGT76G1 (black bars) (Figure 6C).

[00231] The strain expressing UGT76G1 H155L (gray bars) also produced lesser amounts of a 1,2-bioside, 1,2-stevioside, a tri-glycosylated steviol molecule (steviol+3Glc (#1)), a penta-glycosylated steviol molecule (steviol+5Glc (#22), two hexa-glycosylated steviol molecules (steviol+6Glc (isomer 1 and #23)), and a hepta-glycosylated steviol molecule (steviol+7Glc (isomer 2)) but increased amounts of a tetra-glycosylated molecule (steviol+4Glc (#26)) and two penta-glycosylated steviol molecules (Steviol+5Glc (#24 and #25)), compared to the control strain expressing wild-type UGT76G1 (black bars) (Figure 6D). *See* Figures 1, 7, and 8 for structures of particular steviol glycosides detected.

[00232] Having described the invention in detail and by reference to specific embodiments thereof, it will be apparent that modifications and variations are possible without departing from the scope of the invention defined in the appended claims. More specifically, although some aspects of the present invention are identified herein as particularly advantageous, it is contemplated that the present invention is not necessarily limited to these particular aspects of the invention.

Table 10. Sequences disclosed herein.

SEQ ID NO:1

```
MATSDSIVDD RKQLHVATFP WLAFGHILPY LQLSKLIAEK GHKVSFLSTT RNIQRLSSHI    60
SPLINVVQLT LPRVQELPED AEATTDVHPE DIPYLKKASD GLQPEVTRFL EQHSPDWIIY   120
DYTHYWLPSI AASLGISRAH FSVTTPWAIA YMGPSADAMI NGSDGRTTVE DLTTPPKWFP   180
FPTKVCWRKH DLARLVPYKA PGISDGYRMG LVLKGSDCLL SKCYHEFGTQ WLPLLETLHQ   240
VPVVPVGLLP PEIPGDEKDE TWVSIKKWLD GKQKGSVVYV ALGSECLVSQ TEVVELALGL   300
ELSGLPFVWA YRKPKGPAKS DSVELPDGFV ERTRDRGLVW TSWAPQLRIL SHESVCGFLT   360
HCGSGSIVEG LMFGHPLIML PIFGDQPLNA RLLEDKQVGI EIPRNEEDGC LTKESVARSL   420
RSVVVEKEGE IYKANARELS KIYNDTKVEK EYVSQFVDYL EKNARAVAID HES          473
```

SEQ ID NO:2

```
MATSDSIVDD RKQLHVATFP WLAFGHILPY LQLSKLIAEK GHKVSFLSTT RNIQRLSSHI    60
SPLINVVQLT LPRVQELPED AEATTDVHPE DIPYLKKASD GLQPEVTRFL EQHSPDWIIY   120
DYTHYWLPSI AASLGISRAH FSVTTPWAIA YMGPSADAMI NGSDGRTTVE DLTTPPKWFP   180
FPTKVCWRKH DLARLVPYKA PGISDGYRMG LVLKGSDCLL SKCYHEFGTQ WLPLLETLHQ   240
VPVVPVGLLP PEIPGDEKDE TWVSIKKWLD GKQKGSVVYV ALGSEVLVSQ TEVVELALGL   300
ELSGLPFVWA YRKPKGPAKS DSVELPDGFV ERTRDRGLVW TSWAPQLRIL SHESVCGFLT   360
HCGSGSIVEG LMFGHPLIML PIFWDQPLNA RLLEDKQVGI EIPRNEEDGC LTKESVARSL   420
RSVVVEKEGE IYKANARELS KIYNDTKVEK EYVSQFVDYL EKNARAVAID HES          473
```

SEQ ID NO:3

```
atggcagagc aacaaaagat caaaaagtca cctcacgtct tacttattcc atttcctctg    60
caaggacata tcaacccatt catacaattt gggaaaagat tgattagtaa gggtgtaaag   120
acaacactgg taaccactat ccacactttg aattctactc tgaaccactc aaatactact   180
actacaagta tagaaattca agctatatca gacggatgcg atgagggtgg ctttatgtct   240
gccggtgaat cttacttgga aacattcaag caagtgggat ccaagtctct ggccgatcta   300
atcaaaaagt tacagagtga aggcaccaca attgacgcca taatctacga ttctatgaca   360
gagtgggttt tagacgttgc tatcgaattt ggtattgatg gaggttcctt tttcacacaa   420
gcatgtgttg tgaattctct atactaccat gtgcataaag ggttaatctc tttaccattg   480
```

```
ggtgaaactg tttcagttcc aggttttcca gtgttacaac gttgggaaac cccattgatc   540
ttacaaaatc atgaacaaat acaatcacct tggtcccaga tgttgtttgg tcaattcgct   600
aacatcgatc aagcaagatg ggtctttact aattcattct ataagttaga ggaagaggta   660
attgaatgga ctaggaagat ctggaatttg aaagtcattg gtccaacatt gccatcaatg   720
tatttggaca aaagacttga tgatgataaa gataatggtt tcaatttgta caaggctaat   780
catcacgaat gtatgaattg gctggatgac aaaccaaagg aatcagttgt atatgttgct   840
ttcggctctc ttgttaaaca tggtccagaa caagttgagg agattacaag agcacttata   900
gactctgacg taaacttttt gtgggtcatt aagcacaaag aggaggggaa actgccagaa   960
aacctttctg aagtgataaa gaccggaaaa ggtctaatcg ttgcttggtg taaacaattg  1020
gatgttttag ctcatgaatc tgtaggctgt tttgtaacac attgcggatt caactctaca  1080
ctagaagcca tttccttagg cgtacctgtc gttgcaatgc ctcagttctc cgatcagaca  1140
accaacgcta aacttttgga cgaaatacta ggggtgggtg tcagagttaa agcagacgag  1200
aatggtatcg tcagaagagg gaacctagct tcatgtatca aaatgatcat ggaagaggaa  1260
agaggagtta tcataaggaa aaacgcagtt aagtggaagg atcttgcaaa ggttgccgtc  1320
catgaaggcg gctcttcaga taatgatatt gttgaatttg tgtccgaact aatcaaagcc  1380
taa                                                                1383
```

SEQ ID NO:4

```
MAEQQKIKKS PHVLLIPFPL QGHINPFIQF GKRLISKGVK TTLVTTIHTL NSTLNHSNTT    60
TTSIEIQAIS DGCDEGGFMS AGESYLETFK QVGSKSLADL IKKLQSEGTT IDAIIYDSMT   120
EWVLDVAIEF GIDGGSFFTQ ACVVNSLYYH VHKGLISLPL GETVSVPGFP VLQRWETPLI   180
LQNHEQIQSP WSQMLFGQFA NIDQARWVFT NSFYKLEEEV IEWTRKIWNL KVIGPTLPSM   240
YLDKRLDDDK DNGFNLYKAN HHECMNWLDD KPKESVVYVA FGSLVKHGPE QVEEITRALI   300
DSDVNFLWVI KHKEEGKLPE NLSEVIKTGK GLIVAWCKQL DVLAHESVGC FVTHCGFNST   360
LEAISLGVPV VAMPQFSDQT TNAKLLDEIL GVGVRVKADE NGIVRRGNLA SCIKMIMEEE   420
RGVIIRKNAV KWKDLAKVAV HEGGSSDNDI VEFVSELIKA                         460
```

SEQ ID NO:5

```
atggatgcaa tggctacaac tgagaagaaa ccacacgtca tcttcatacc atttccagca    60
caaagccaca ttaaagccat gctcaaacta gcacaacttc tccaccacaa aggactccag   120
ataaccttcg tcaacaccga cttcatccac aaccagtttc ttgaatcatc gggcccacat   180
tgtctagacg gtgcaccggg tttccggttc gaaaccattc cggatggtgt ttctcacagt   240
ccggaagcga gcatcccaat cagagaatca ctcttgagat ccattgaaac caacttcttg   300
gatcgtttca ttgatcttgt aaccaaactt ccggatcctc cgacttgtat tatctcagat   360
gggttcttgt cggttttcac aattgacgct gcaaaaaagc ttggaattcc ggtcatgatg   420
tattggacac ttgctgcctg tgggttcatg ggtttttacc atattcattc tctcattgag   480
aaaggatttg caccacttaa agatgcaagt tacttgacaa atgggtattt ggacaccgtc   540
attgattggg ttccgggaat ggaaggcatc cgtctcaagg atttcccgct ggactggagc   600
actgacctca atgacaaagt tttgatgttc actacggaag ctcctcaaag gtcacacaag   660
gtttcacatc atattttcca cacgttcgat gagttggagc ctagtattat aaaaactttg   720
tcattgaggt ataatcacat ttacaccatc ggcccactgc aattacttct tgatcaaata   780
cccgaagaga aaaagcaaac tggaattacg agtctccatg gatacagttt agtaaaagaa   840
gaaccagagt gtttccagtg gcttcagtct aaagaaccaa attccgtcgt ttatgtaaat   900
tttggaagta ctacagtaat gtctttagaa gacatgacgg aatttggttg gggacttgct   960
aatagcaacc attatttcct ttggatcatc cgatcaaact tggtgatagg ggaaaatgca  1020
gttttgcccc ctgaacttga ggaacatata aagaaaagag gctttattgc tagctggtgt  1080
tcacaagaaa aggtcttgaa gcacccttcg gttggagggt tcttgactca ttgtgggtgg  1140
ggatcgacca tcgagagctt gtctgctggg gtgccaatga tatgctggcc ttattcgtgg  1200
gaccagctga ccaactgtag gtatatatgc aaagaatggg aggttggggct cgagatggga  1260
accaaagtga aacgagatga agtcaagagg cttgtacaag agttgatggg agaaggaggt  1320
cacaaaatga ggaacaaggc taaagattgg aaagaaaagg ctcgcattgc aatagctcct  1380
aacggttcat cttctttgaa catagacaaa atggtcaagg aaatcaccgt gctagcaaga  1440
aactagttac aaagttgttt cacattgtgc tttctattta agatgtaact ttgttctaat  1500
ttaatattgt ctagatgtat tgaaccataa gtttagttgg tctcaggaat tgatttttaa  1560
tgaaataatg gtcattaggg gtgagt                                       1586
```

SEQ ID NO:6

```
atggatgcaa tggcaactac tgagaaaaag cctcatgtga tcttcattcc atttcctgca     60
caatctcaca taaaggcaat gctaaagtta gcacaactat tacaccataa gggattacag    120
ataactttcg tgaataccga cttcatccat aatcaatttc tggaatctag tggccctcat    180
tgtttggacg gagccccagg gtttagattc gaaacaattc ctgacggtgt ttcacattcc    240
ccagaggcct ccatcccaat aagagagagt ttactgaggt caatagaaac caactttttg    300
gatcgtttca ttgacttggt cacaaaactt ccagacccac caacttgcat aatctctgat    360
ggctttctgt cagtgtttac tatcgacgct gccaaaaagt tgggtatccc agttatgatg    420
tactggactc ttgctgcatg cggtttcatg ggtttctatc acatccattc tcttatcgaa    480
aagggttttg ctccactgaa agatgcatca tacttaacca acggctacct ggatactgtt    540
attgactggg taccaggtat ggaaggtata agacttaaag attttccttt ggattggtct    600
acagacctta atgataaagt attgatgttt actacagaag ctccacaaag atctcataag    660
gtttcacatc atatctttca cacctttgat gaattggaac catcaatcat caaaaccttg    720
tctctaagat acaatcatat ctacactatt ggtccattac aattacttct agatcaaatt    780
cctgaagaga aaaagcaaac tggtattaca tccttacacg gctactcttt agtgaaagag    840
gaaccagaat gttttcaatg gctacaaagt aaagagccta attctgtggt ctacgtcaac    900
ttcggaagta caacagtcat gtccttggaa gatatgactg aatttggttg ggcccttgct    960
aattcaaatc attactttct atggattatc aggtccaatt tggtaatagg ggaaaacgcc   1020
gtattacctc cagaattgga ggaacacatc aaaaagagag gtttcattgc ttcctggtgt   1080
tctcaggaaa aggtattgaa acatccttct gttggtggtt tccttactca ttgcggttgg   1140
ggctctacaa tcgaatcact aagtgcagga gttccaatga tttgttggcc atattcatgg   1200
gaccaactta caaattgtag gtatatctgt aaagagtggg aagttggatt agaaatggga   1260
acaaaggtta aacgtgatga agtgaaaaga ttggttcagg agttgatggg ggaaggtggc   1320
cacaagatga gaaacaaggc caaagattgg aaggaaaaag ccagaattgc tattgctcct   1380
aacgggtcat cctctctaaa cattgataag atggtcaaag agattacagt cttagccaga   1440
aactaa                                                              1446
```

SEQ ID NO:7

```
MDAMATTEKK PHVIFIPFPA QSHIKAMLKL AQLLHHKGLQ ITFVNTDFIH NQFLESSGPH     60
CLDGAPGFRF ETIPDGVSHS PEASIPIRES LLRSIETNFL DRFIDLVTKL PDPPTCIISD    120
GFLSVFTIDA AKKLGIPVMM YWTLAACGFM GFYHIHSLIE KGFAPLKDAS YLTNGYLDTV    180
IDWVPGMEGI RLKDFPLDWS TDLNDKVLMF TTEAPQRSHK VSHHIFHTFD ELEPSIIKTL    240
SLRYNHIYTI GPLQLLLDQI PEEKKQTGIT SLHGYSLVKE EPECFQWLQS KEPNSVVYVN    300
FGSTTVMSLE DMTEFGWGLA NSNHYFLWII RSNLVIGENA VLPPELEEHI KKRGFIASWC    360
SQEKVLKHPS VGGFLTHCGW GSTIESLSAG VPMICWPYSW DQLTNCRYIC KEWEVGLEMG    420
TKVKRDEVKR LVQELMGEGG HKMRNKAKDW KEKARIAIAP NGSSSLNIDK MVKEITVLAR    480
N                                                                    481
```

SEQ ID NO:8

```
atggaaaaca agaccgaaac aacagttaga cgtaggcgta gaatcattct gtttccagta     60
ccttttcaag ggcacatcaa tccaatacta caactagcca acgttttgta ctctaaaggt    120
ttttctatta caatctttca caccaatttc aacaaaccaa aaacatccaa ttacccacat    180
ttcacattca gattcatact tgataatgat ccacaagatg aacgtatttc aaacttacct    240
acccacggtc ctttagctgg aatgagaatt ccaatcatca atgaacatgg tgccgatgag    300
cttagaagag aattagagtt acttatgttg gcatccgaag aggacgagga agtctcttgt    360
ctgattactg acgctctatg gtactttgcc caatctgtgg ctgatagttt gaatttgagg    420
agattggtac taatgacatc cagtctgttt aactttcacg ctcatgttag tttaccacaa    480
tttgacgaat tgggatactt ggaccctgat gacaagacta ggttagagga acaggcctct    540
ggttttccta tgttgaaagt caaagatatc aagtctgcct attctaattg gcaaatcttg    600
aaagagatct taggaaagat gatcaaacag acaaaggctt catctggagt gatttggaac    660
agtttcaaag agttagaaga gtctgaattg gagactgtaa tcagagaaat tccagcacct    720
tcattcctga taccattacc aaaacatttg actgcttcct cttcctcttt gttggatcat    780
gacagaacag tttttcaatg gttggaccaa caaccaccta gttctgtttt gtacgtgtca    840
tttggtagta cttctgaagt cgatgaaaag gacttccttg aaatcgcaag aggcttagtc    900
gatagtaagc agtcattcct ttgggtcgtg cgtccaggtt tcgtgaaagg ctcaacatgg    960
gtcgaaccac ttccagatgg ttttctaggc gaaagaggta gaatagtcaa atgggttcct   1020
caacaggaag ttttagctca tggcgctatt ggggcattct ggactcattc cggatggaat   1080
tcaactttag aatcagtatg cgaaggggta cctatgatct tttcagattt tggtcttgat   1140
```

caaccactga acgcaagata catgtctgat gttttgaaag tgggtgtata tctagaaaat 1200
ggctgggaaa ggggtgaaat agctaatgca ataagacgtg ttatggttga tgaagagggg 1260
gagtatatca gacaaaacgc aagagtgctg aagcaaaagg ccgacgtttc tctaatgaag 1320
ggaggctctt catacgaatc cttagaatct cttgtttcct acatttcatc actgtaa 1377

SEQ ID NO:9
MENKTETTVR RRRRIILFPV PFQGHINPIL QLANVLYSKG FSITIFHTNF NKPKTSNYPH 60
FTFRFILDND PQDERISNLP THGPLAGMRI PIINEHGADE LRRELELLML ASEEDEEVSC 120
LITDALWYFA QSVADSLNLR RLVLMTSSLF NFHAHVSLPQ FDELGYLDPD DKTRLEEQAS 180
GFPMLKVKDI KSAYSNWQIL KEILGKMIKQ TKASSGVIWN SFKELEESEL ETVIREIPAP 240
SFLIPLPKHL TASSSSLLDH DRTVFQWLDQ QPPSSVLYVS FGSTSEVDEK DFLEIARGLV 300
DSKQSFLWVV RPGFVKGSTW VEPLPDGFLG ERGRIVKWVP QQEVLAHGAI GAFWTHSGWN 360
STLESVCEGV PMIFSDFGLD QPLNARYMSD VLKVGVYLEN GWERGEIANA IRRVMVDEEG 420
EYIRQNARVL KQKADVSLMK GGSSYESLES LVSYISSL 458

SEQ ID NO:10
atggctacat ctgattctat tgttgatgac aggaagcagt tgcatgtggc tactttccct 60
tggcttgctt tcggtcatat actgccttac ctacaactat caaaactgat agctgaaaaa 120
ggacataaag tgtcattcct ttcaacaact agaaacattc aaagattatc ttcccacata 180
tcaccattga ttaacgtcgt tcaattgaca cttccaagag tacaggaatt accagaagat 240
gctgaagcta caacagatgt gcatcctgaa gatatccctt acttgaaaaa ggcatccgat 300
ggattacagc ctgaggtcac tagattcctt gagcaacaca gtccagattg gatcatatac 360
gactacactc actattggtt gccttcaatt gcagcatcac taggcatttc tagggcacat 420
ttcagtgtaa ccacaccttg ggccattgct tacatgggtc catccgctga tgctatgatt 480
aacggcagtg atggtagaac taccgttgaa gatttgacaa ccccaccaaa gtggtttcca 540
tttccaacta aagtctgttg gagaaaacac gacttagcaa gactggttcc atacaaggca 600
ccaggaatct cagacggcta tagaatgggt ttagtcctta aagggtctga ctgcctattg 660
tctaagtgtt accatgagtt tgggacacaa tggctaccac ttttggaaac attacaccaa 720
gttcctgtcg taccagttgg tctattacct ccagaaatcc ctggtgatga gaaggacgag 780
acttgggttt caatcaaaaa gtggttagac gggaagcaaa aaggctcagt ggtatatgtg 840
gcactgggtt ccgaagtttt agtatctcaa acagaagttg tggaacttgc cttaggtttg 900
gaactatctg gattgccatt tgtctgggcc tacagaaaac caaaaggccc tgcaaagtcc 960
gattcagttg aattgccaga cggctttgtc gagagaacta gagatagagg gttggtatgg 1020
acttcatggg ctccacaatt gagaatcctg agtcacgaat ctgtgtgcgg tttcctaaca 1080
cattgtggtt ctggttctat agttgaagga ctgatgtttg gtcatccact tatcatgttg 1140
ccaatctttg gtgaccagcc tttgaatgca cgtctgttag aagataaaca agttggaatt 1200
gaaatcccac gtaatgagga agatggatgt ttaaccaagg agtctgtggc cagatcatta 1260
cgttccgttg tcgttgaaaa ggaaggcgaa atctacaagg ccaatgcccg tgaactttca 1320
aagatctaca atgacacaaa agtagagaag gaatatgttt ctcaatttgt agattaccta 1380
gagaaaaacg ctagagccgt agctattgat catgaatcct aa 1422

SEQ ID NO:11
MATSDSIVDD RKQLHVATFP WLAFGHILPY LQLSKLIAEK GHKVSFLSTT RNIQRLSSHI 60
SPLINVVQLT LPRVQELPED AEATTDVHPE DIPYLKKASD GLQPEVTRFL EQHSPDWIIY 120
DYTHYWLPSI AASLGISRAH FSVTTPWAIA YMGPSADAMI NGSDGRTTVE DLTTPPKWFP 180
FPTKVCWRKH DLARLVPYKA PGISDGYRMG LVLKGSDCLL SKCYHEFGTQ WLPLLETLHQ 240
VPVVPVGLLP PEIPGDEKDE TWVSIKKWLD GKQKGSVVYV ALGSEVLVSQ TEVVELALGL 300
ELSGLPFVWA YRKPKGPAKS DSVELPDGFV ERTRDRGLVW TSWAPQLRIL SHESVCGFLT 360
HCGSGSIVEG LMFGHPLIML PIFGDQPLNA RLLEDKQVGI EIPRNEEDGC LTKESVARSL 420
RSVVVEKEGE IYKANARELS KIYNDTKVEK EYVSQFVDYL EKNARAVAID HES 473

SEQ ID NO:12
atggctactt ctgattccat cgttgacgat agaaagcaat tgcatgttgc tacttttcca 60
tggttggctt tcggtcatat tttgccatac ttgcaattgt ccaagttgat tgctgaaaag 120
ggtcacaagg tttcattctt gtctaccacc agaaacatcc aaagattgtc ctctcatatc 180
tccccattga tcaacgttgt tcaattgact ttgccaagag tccaagaatt gccagaagat 240
gctgaagcta ctactgatgt tcatccagaa gatatccctt acttgaaaaa ggcttccgat 300

```
ggtttacaac cagaagttac tagattcttg gaacaacatt ccccagattg gatcatctac      360
gattatactc attactggtt gccatccatt gctgcttcat tgggtatttc tagagcccat      420
ttctctgtta ctactccatg ggctattgct tatatgggtc catctgctga tgctatgatt      480
aacggttctg atggtagaac taccgttgaa gatttgacta ctccaccaaa gtggtttcca      540
tttccaacaa aagtctgttg gagaaaacac gatttggcta gattggttcc atacaaagct      600
ccaggtattt ctgatggtta cagaatgggt atggttttga aaggttccga ttgcttgttg      660
tctaagtgct atcatgaatt cggtactcaa tggttgcctt tgttggaaac attgcatcaa      720
gttccagttg ttccagtagg tttgttgcca ccagaaattc caggtgacga aaaagacgaa      780
acttgggttt ccatcaaaaa gtggttggat ggtaagcaaa agggttctgt tgtttatgtt      840
gctttgggtt ccgaagcttt ggtttctcaa accgaagttg ttgaattggc tttgggtttg      900
gaattgtctg gtttgccatt tgtttgggct tacagaaaac ctaaaggtcc agctaagtct      960
gattctgttg aattgccaga tggtttcgtt gaaagaacta gagatagagg tttggtttgg     1020
acttcttggg ctccacaatt gagaattttg tctcatgaat ccgtctgtgg tttcttgact     1080
cattgtggtt ctggttctat cgttgaaggt ttgatgtttg gtcacccatt gattatgttg     1140
ccaatctttg gtgaccaacc attgaacgct agattattgg aagataagca agtcggtatc     1200
gaaatcccaa gaaatgaaga agatggttgc ttgaccaaag aatctgttgc tagatctttg     1260
agatccgttg tcgttgaaaa agaaggtgaa atctacaagg ctaacgctag agaattgtcc     1320
aagatctaca acgataccaa ggtcgaaaaa gaatacgttt cccaattcgt tgactacttg     1380
gaaaagaatg ctagagctgt tgccattgat catgaatctt ga                        1422
```

SEQ ID NO:13

```
MATSDSIVDD RKQLHVATFP WLAFGHILPY LQLSKLIAEK GHKVSFLSTT RNIQRLSSHI       60
SPLINVVQLT LPRVQELPED AEATTDVHPE DIPYLKKASD GLQPEVTRFL EQHSPDWIIY      120
DYTHYWLPSI AASLGISRAH FSVTTPWAIA YMGPSADAMI NGSDGRTTVE DLTTPPKWFP      180
FPTKVCWRKH DLARLVPYKA PGISDGYRMG MVLKGSDCLL SKCYHEFGTQ WLPLLETLHQ      240
VPVVPVGLLP PEIPGDEKDE TWVSIKKWLD GKQKGSVVYV ALGSEALVSQ TEVVELALGL      300
ELSGLPFVWA YRKPKGPAKS DSVELPDGFV ERTRDRGLVW TSWAPQLRIL SHESVCGFLT      360
HCGSGSIVEG LMFGHPLIML PIFGDQPLNA RLLEDKQVGI EIPRNEEDGC LTKESVARSL      420
RSVVVEKEGE IYKANARELS KIYNDTKVEK EYVSQFVDYL EKNARAVAID HES              473
```

SEQ ID NO:14

```
atggactccg gctactcctc ctcctacgcc gccgccgccg ggatgcacgt cgtgatctgc       60
ccgtggctcg ccttcggcca cctgctcccg tgcctcgacc tcgcccagcg cctcgcgtcg      120
cggggccacc gcgtgtcgtt cgtctccacg ccgcggaaca tatcccgcct cccgccggtg      180
cgccccgcgc tcgcgccgct cgtcgccttc gtggcgctgc cgctcccgcg cgtcgagggg      240
ctccccgacg gcgccgagtc caccaacgac gtcccccacg acaggccgga catggtcgag      300
ctccaccgga gggccttcga cgggctcgcc gcgcccttct cggagttctt gggcaccgcg      360
tgcgccgact gggtcatcgt cgacgtcttc caccactggg ccgcagccgc cgctctcgag      420
cacaaggtgc catgtgcaat gatgttgttg ggctctgcac atatgatcgc ttccatagca      480
gacagacggc tcgagcgcgc ggagacagag tcgcctgcgg ctgccgggca gggacgccca      540
gcggcggcgc caacgttcga ggtggcgagg atgaagttga tacgaaccaa aggctcatcg      600
ggaatgtccc tcgccgagcg cttctccttg acgctctcga ggagcagcct cgtcgtcggg      660
cggagctgcg tggagttcga gccggagacc gtcccgctcc tgtcgacgct ccgcggtaag      720
cctattacct tccttggcct tatgccgccg ttgcatgaag gccgccgcga ggacggcgag      780
gatgccaccg tccgctggct cgacgcgcag ccggccaagt ccgtcgtgta cgtcgcgcta      840
ggcagcgagg tgccactggg agtggagaag gtccacgagc tcgcgctcgg gctggagctc      900
gccgggacgc gcttcctctg ggctcttagg aagcccactg gcgtctccga cgccgacctc      960
ctccccgccg gcttcgagga gcgcacgcgc ggccgcggcg tcgtggcgac gagatgggtt     1020
cctcagatga gcatactggc gcacgccgcc gtgggcgcgt tcctgaccca ctgcggctgg     1080
aactcgacca tcgaggggct catgttcggc cacccgctta tcatgctgcc gatcttcggc     1140
gaccagggac cgaacgcgcg gctaatcgag gcgaagaacg ccggattgca ggtggcaaga     1200
aacgacggcg atggatcgtt cgaccgagaa ggcgtcgcgg cggcgattcg tgcagtcgcg     1260
gtggaggaag aaagcagcaa agtgtttcaa gccaaagcca agaagctgca ggagatcgtc     1320
gcggacatgg cctgccatga gaggtacatc gacggattca ttcagcaatt gagatcttac     1380
aaggattga                                                             1389
```

SEQ ID NO:15

```
atggatagtg gctactcctc atcttatgct gctgccgctg gtatgcacgt tgtgatctgc      60
ccttggttgg cctttggtca cctgttacca tgtctggatt tagcccaaag actggcctca     120
agaggccata gagtatcatt tgtgtctact cctagaaata tctctcgttt accaccagtc     180
agacctgctc tagctcctct agttgcattc gttgctcttc cacttccaag agtagaagga     240
ttgccagacg gcgctgaatc tactaatgac gtaccacatg atagacctga catggtcgaa     300
ttgcatagaa gagcctttga tggattggca gctccatttt ctgagttcct gggcacagca     360
tgtgcagact gggttatagt cgatgtattt catcactggg ctgctgcagc cgcattggaa     420
cataaggtgc cttgtgctat gatgttgtta gggtcagcac acatgatcgc atccatagct     480
gatagaagat tggaaagagc tgaaacagaa tccccagccg cagcaggaca aggtaggcca     540
gctgccgccc caacctttga agtggctaga atgaaattga ttcgtactaa aggtagttca     600
gggatgagtc ttgctgaaag gttttctctg acattatcta gatcatcatt agttgtaggt     660
agatcctgcg tcgagttcga acctgaaaca gtacctttac tatctacttt gagaggcaaa     720
cctattactt tccttggtct aatgcctcca ttacatgaag gaaggagaga agatggtgaa     780
gatgctactg ttaggtggtt agatgcccaa cctgctaagt ctgttgttta cgttgcattg     840
ggttctgagg taccactagg ggtggaaaag gtgcatgaat tagcattagg acttgagctg     900
gccggaacaa gattcctttg ggctttgaga aaaccaaccg gtgtttctga cgccgacttg     960
ctaccagctg ggttcgaaga gagaacaaga ggccgtggtg tcgttgctac tagatgggtc    1020
ccacaaatga gtattctagc tcatgcagct gtaggggcct ttctaaccca ttgcggttgg    1080
aactcaacaa tagaaggact gatgtttggt catccactta ttatgttacc aatctttggc    1140
gatcagggac ctaacgcaag attgattgag gcaaagaacg caggtctgca ggttgcacgt    1200
aatgatggtg atggttcctt tgatagagaa ggcgttgcag ctgccatcag agcagtcgcc    1260
gttgaggaag agtcatctaa agttttccaa gctaaggcca aaaaattaca agagattgtg    1320
gctgacatgg cttgtcacga aagatacatc gatggtttca tccaacaatt gagaagttat    1380
aaagactaa                                                            1389
```

SEQ ID NO:16

```
MDSGYSSSYA AAAGMHVVIC PWLAFGHLLP CLDLAQRLAS RGHRVSFVST PRNISRLPPV      60
RPALAPLVAF VALPLPRVEG LPDGAESTND VPHDRPDMVE LHRRAFDGLA APFSEFLGTA     120
CADWVIVDVF HHWAAAAALE HKVPCAMMLL GSAHMIASIA DRRLERAETE SPAAAGQGRP     180
AAAPTFEVAR MKLIRTKGSS GMSLAERFSL TLSRSSLVVG RSCVEFEPET VPLLSTLRGK     240
PITFLGLMPP LHEGRREDGE DATVRWLDAQ PAKSVVYVAL GSEVPLGVEK VHELALGLEL     300
AGTRFLWALR KPTGVSDADL LPAGFEERTR GRGVVATRWV PQMSILAHAA VGAFLTHCGW     360
NSTIEGLMFG HPLIMLPIFG DQGPNARLIE AKNAGLQVAR NDGDGSFDRE GVAAAIRAVA     420
VEEESSKVFQ AKAKKLQEIV ADMACHERYI DGFIQQLRSY KD                       462
```

SEQ ID NO:17

```
MDSGYSSSYA AAAGMHVVIC PWLAFGHLLP CLDLAQRLAS RGHRVSFVST PRNISRLPPV      60
RPALAPLVAF VALPLPRVEG LPDGAESTND VPHDRPDMVE LHRRAFDGLA APFSEFLGTA     120
CADWVIVDVF HHWAAAAALE HKVPCAMMLL GSAHMIASIA DRRLERAETE SPAAAGQGRP     180
AAAPTFEVAR MKLIRTKGSS GMSLAERFSL TLSRSSLVVG RSCVEFEPET VPLLSTLRGK     240
PITFLGLLPP EIPGDEKDET WVSIKKWLDG KQKGSVVYVA LGSEALVSQT EVVELALGLE     300
LSGLPFVWAY RKPKGPAKSD SVELPDGFVE RTRDRGLVWT SWAPQLRILS HESVCGFLTH     360
CGSGSIVEGL MFGHPLIMLP IFGDQPLNAR LLEDKQVGIE IARNDGDGSF DREGVAAAIR     420
AVAVEEESSK VFQAKAKKLQ EIVADMACHE RYIDGFIQQL RSYKD                    465
```

SEQ ID NO:18

```
MATSDSIVDD RKQLHVATFP WLAFGHILPY LQLSKLIAEK GHKVSFLSTT RNIQRLSSHI      60
SPLINVVQLT LPRVQELPED AEATTDVHPE DIPYLKKASD GLQPEVTRFL EQHSPDWIIY     120
DYTHYWLPSI AASLGISRAH FSVTTPWAIA YMGPSADAMI NGSDGRTTVE DLTTPPKWFP     180
FPTKVCWRKH DLARLVPYKA PGISDGYRMG MVLKGSDCLL SKCYHEFGTQ WLPLLETLHQ     240
VPVVPVGLMP PLHEGRREDG EDATVRWLDA QPAKSVVYVA LGSEVPLGVE KVHELALGLE     300
LAGTRFLWAL RKPTGVSDAD LLPAGFEERT RGRGVVATRW VPQMSILAHA AVGAFLTHCG     360
WNSTIEGLMF GHPLIMLPIF GDQGPNARLI EAKNAGLQVP RNEEDGCLTK ESVARSLRSV     420
VVEKEGEIYK ANARELSKIY NDTKVEKEYV SQFVDYLEKN ARAVAIDHES                470
```

SEQ ID NO:19

```
atggctttgg taaacccaac cgctcttttc tatggtacct ctatcagaac aagacctaca      60
```

```
aacttactaa atccaactca aaagctaaga ccagtttcat catcttcctt accttctttc      120
tcatcagtta gtgcgattct tactgaaaaa catcaatcta atccttctga gaacaacaat      180
ttgcaaactc atctagaaac tcctttcaac tttgatagtt atatgttgga aaaagtcaac      240
atggttaacg aggcgcttga tgcatctgtc ccactaaaag acccaatcaa aatccatgaa      300
tccatgagat actctttatt ggcaggcggt aagagaatca gaccaatgat gtgtattgca      360
gcctgcgaaa tagtcggagg taatatcctt aacgccatgc cagccgcatg tgccgtggaa      420
atgattcata ctatgtcttt ggtgcatgac gatcttccat gtatggataa tgatgacttc      480
agaagaggta aacctatttc acacaaggtc tacggggagg aaatggcagt attgaccggc      540
gatgctttac taagtttatc tttcgaacat atagctactg ctacaaaggg tgtatcaaag      600
gatagaatcg tcagagctat aggggagttg gcccgttcag ttggctccga aggtttagtg      660
gctggacaag ttgtagatat cttgtcagag ggtgctgatg ttggattaga tcacctagaa      720
tacattcaca tccacaaaac agcaatgttg cttgagtcct cagtagttat tggcgctatc      780
atgggaggag gatctgatca gcagatcgaa aagttgagaa aattcgctag atctattggt      840
ctactattcc aagttgtgga tgacattttg gatgttacaa aatctaccga agagttgggg      900
aaaacagctg gtaaggattt gttgacagat aagacaactt acccaaagtt gttaggtata      960
gaaaagtcca gagaatttgc cgaaaaactt aacaaggaag cacaagagca attaagtggc     1020
tttgatagac gtaaggcagc tcctttgatc gcgttagcca actacaatgc gtaccgtcaa     1080
aattga                                                                1086
```

SEQ ID NO:20

```
MALVNPTALF YGTSIRTRPT NLLNPTQKLR PVSSSSLPSF SSVSAILTEK HQSNPSENNN       60
LQTHLETPFN FDSYMLEKVN MVNEALDASV PLKDPIKIHE SMRYSLLAGG KRIRPMMCIA      120
ACEIVGGNIL NAMPAACAVE MIHTMSLVHD DLPCMDNDDF RRGKPISHKV YGEEMAVLTG      180
DALLSLSFEH IATATKGVSK DRIVRAIGEL ARSVGSEGLV AGQVVDILSE GADVGLDHLE      240
YIHIHKTAML LESSVVIGAI MGGGSDQQIE KLRKFARSIG LLFQVVDDIL DVTKSTEELG      300
KTAGKDLLTD KTTYPKLLGI EKSREFAEKL NKEAQEQLSG FDRRKAAPLI ALANYNAYRQ      360
N                                                                      361
```

SEQ ID NO:21

```
atggctgagc aacaaatatc taacttgctg tctatgtttg atgcttcaca tgctagtcag       60
aaattagaaa ttactgtcca aatgatggac acataccatt acagagaaac gcctccagat      120
tcctcatctt ctgaaggcgg ttcattgtct agatacgacg agagaagagt ctctttgcct      180
ctcagtcata atgctgcctc tccagatatt gtatcacaac tatgtttttc cactgcaatg      240
tcttcagagt tgaatcacag atggaaatct caaagattaa aggtggccga ttctccttac      300
aactatatcc taacattacc atcaaaagga attagaggtg cctttatcga ttccctgaac      360
gtatggttgg aggttccaga ggatgaaaca tcagtcatca aggaagttat tggtatgctc      420
cacaactctt cattaatcat tgatgacttc caagataatt ctccacttag aagaggaaag      480
ccatctaccc atacagtctt cggccctgcc caggctatca atactgctac ttacgttata      540
gttaaagcaa tcgaaaagat acaagacata gtgggacacg atgcattggc agatgttacg      600
ggtactatta caactatttt ccaaggtcag gccatggact tgtggtggac agcaaatgca      660
atcgttccat caatacagga atacttactt atggtaaacg ataaaaccgg tgctctcttt      720
agactgagtt tggagttgtt agctctgaat tccgaagcca gtatttctga ctctgcttta      780
gaaagtttat ctagtgctgt ttccttgcta ggtcaatact tccaaatcag agacgactat      840
atgaacttga tcgataacaa gtatacagat cagaaaggct tctgcgaaga tcttgatgaa      900
ggcaagtact cactaacact tattcatgcc ctccaaactg attcatccga tctactgacc      960
aacatccttt caatgagaag agtgcaagga aagttaacgg cacaaaagag atgttggttc     1020
tggaaatga                                                             1029
```

SEQ ID NO:22

```
MAEQQISNLL SMFDASHASQ KLEITVQMMD TYHYRETPPD SSSSEGGSLS RYDERRVSLP       60
LSHNAASPDI VSQLCFSTAM SSELNHRWKS QRLKVADSPY NYILTLPSKG IRGAFIDSLN      120
VWLEVPEDET SVIKEVIGML HNSSLIIDDF QDNSPLRRGK PSTHTVFGPA QAINTATYVI      180
VKAIEKIQDI VGHDALADVT GTITTIFQGQ AMDLWWTANA IVPSIQEYLL MVNDKTGALF      240
RLSLELLALN SEASISDSAL ESLSSAVSLL GQYFQIRDDY MNLIDNKYTD QKGFCEDLDE      300
GKYSLTLIHA LQTDSSDLLT NILSMRRVQG KLTAQKRCWF WK                          342
```

SEQ ID NO:23

```
atggaaaaga ctaaggagaa agcagaacgt atcttgctgg agccatacag atacttatta      60
caactaccag gaaagcaagt ccgttctaaa ctatcacaag cgttcaatca ctggttaaaa     120
gttcctgaag ataagttaca aatcattatt gaagtcacag aaatgctaca caatgcttct     180
ttactgatcg atgatataga ggattcttcc aaactgagaa gaggttttcc tgtcgctcat     240
tccatatacg gggtaccaag tgtaatcaac tcagctaatt acgtctactt cttgggattg     300
gaaaaagtat tgacattaga tcatccagac gctgtaaagc tattcaccag acaacttctt     360
gaattgcatc aaggtcaagg tttggatatc tattggagag acacttatac ttgcccaaca     420
gaagaggagt acaaagcaat ggttctacaa aagactggcg gtttgttcgg acttgccgtt     480
ggtctgatgc aacttttctc tgattacaag gaggacttaa agcctctgtt ggataccttg     540
ggcttgtttt tccagattag agatgactac gctaacttac attcaaagga atattcagaa     600
aacaaatcat tctgtgaaga tttgactgaa gggaagttta gttttccaac aatccacgcc     660
atttggtcaa gaccagaatc tactcaagtg caaaacattc tgcgtcagag aacagagaat     720
attgacatca aaaagtattg tgttcagtac ttggaagatg ttggttcttt tgcttacaca     780
agacatacac ttagagaatt agaggcaaaa gcatacaagc aaatagaagc ctgtggaggc     840
aatccttctc tagtggcatt ggttaaacat ttgtccaaaa tgttcaccga ggaaaacaag     900
taa                                                                  903
```

SEQ ID NO:24

```
MEKTKEKAER ILLEPYRYLL QLPGKQVRSK LSQAFNHWLK VPEDKLQIII EVTEMLHNAS      60
LLIDDIEDSS KLRRGFPVAH SIYGVPSVIN SANYVYFLGL EKVLTLDHPD AVKLFTRQLL     120
ELHQGQGLDI YWRDTYTCPT EEEYKAMVLQ KTGGLFGLAV GLMQLFSDYK EDLKPLLDTL     180
GLFFQIRDDY ANLHSKEYSE NKSFCEDLTE GKFSFPTIHA IWSRPESTQV QNILRQRTEN     240
IDIKKYCVQY LEDVGSFAYT RHTLRELEAK AYKQIEACGG NPSLVALVKH LSKMFTEENK     300
```

SEQ ID NO:25

```
atggcaagat tctattttct taacgcacta ttgatggtta tctcattaca atcaactaca      60
gccttcactc cagctaaact tgcttatcca acaacaacaa cagctctaaa tgtcgcctcc     120
gccgaaactt ctttcagtct agatgaatac ttggcctcta agataggacc tatagagtct     180
gccttggaag catcagtcaa atccagaatt ccacagaccg ataagatctg cgaatctatg     240
gcctactctt tgatggcagg aggcaagaga attagaccag tgttgtgtat cgctgcatgt     300
gagatgttcg gtggatccca agatgtcgct atgcctactg ctgtggcatt agaaatgata     360
cacacaatgt ctttgattca tgatgatttg ccatccatgg ataacgatga cttgagaaga     420
ggtaaaccaa caaaccatgt cgttttcggc gaagatgtag ctattcttgc aggtgactct     480
ttattgtcaa cttccttcga gcacgtcgct agagaaacaa aaggagtgtc agcagaaaag     540
atcgtggatg ttatcgctag attaggcaaa tctgttggtg ccgagggcct tgctggcggt     600
caagttatgg acttagaatg tgaagctaaa ccaggtacca cattagacga cttgaaatgg     660
attcatatcc ataaaaccgc tacattgtta caagttgctg tagcttctgg tgcagttcta     720
ggtggtgcaa ctcctgaaga ggttgctgca tgcgagttgt ttgctatgaa tataggtctt     780
gcctttcaag ttgccgacga tatccttgat gtaaccgctt catcagaaga tttgggtaaa     840
actgcaggca aagatgaagc tactgataag acaacttacc caaagttatt aggattagaa     900
gagagtaagg catacgcaag acaactaatc gatgaagcca aggaaagttt ggctcctttt     960
ggagatagag ctgccccttt attggccatt gcagatttca ttattgatag aaagaattga    1020
```

SEQ ID NO:26

```
MARFYFLNAL LMVISLQSTT AFTPAKLAYP TTTTALNVAS AETSFSLDEY LASKIGPIES      60
ALEASVKSRI PQTDKICESM AYSLMAGGKR IRPVLCIAAC EMFGGSQDVA MPTAVALEMI     120
HTMSLIHDDL PSMDNDDLRR GKPTNHVVFG EDVAILAGDS LLSTSFEHVA RETKGVSAEK     180
IVDVIARLGK SVGAEGLAGG QVMDLECEAK PGTTLDDLKW IHIHKTATLL QVAVASGAVL     240
GGATPEEVAA CELFAMNIGL AFQVADDILD VTASSEDLGK TAGKDEATDK TTYPKLLGLE     300
ESKAYARQLI DEAKESLAPF GDRAAPLLAI ADFIIDRKN                            339
```

SEQ ID NO:27

```
atgcacttag caccacgtag agtccctaga ggtagaagat caccacctga cagagttcct      60
gaaagacaag gtgccttggg tagaagacgt ggagctggct ctactggctg tgcccgtgct     120
gctgctggtg ttcaccgtag aagaggagga ggcgaggctg atccatcagc tgctgtgcat     180
agaggctggc aagccggtgg tggcaccggt ttgcctgatg aggtggtgtc taccgcagcc     240
gccttagaaa tgtttcatgc ttttgcttta atccatgatg atatcatgga tgatagtgca     300
```

```
actagaagag gctccccaac tgttcacaga gccctagctg atcgtttagg cgctgctctg      360
gacccagatc aggccggtca actaggagtt tctactgcta tcttggttgg agatctggct      420
ttgacatggt ccgatgaatt gttatacgct ccattgactc cacatagact ggcagcagta      480
ctaccattgg taacagctat gagagctgaa accgttcatg gccaatatct tgatataact      540
agtgctagaa gacctgggac cgatacttct cttgcattga gaatagccag atataagaca      600
gcagcttaca caatggaacg tccactgcac attggtgcag ccctggctgg ggcaagacca      660
gaactattag cagggctttc agcatacgcc ttgccagctg gagaagcctt ccaattggca      720
gatgacctgc taggcgtctt cggtgatcca agacgtacag ggaaacctga cctagatgat      780
cttagaggtg gaaagcatac tgtcttagtc gccttggcaa gagaacatgc cactccagaa      840
cagagacaca cattggatac attattgggt acaccaggtc ttgatagaca aggcgcttca      900
agactaagat gcgtattggt agcaactggt gcaagagccg aagccgaaag acttattaca      960
gagagaagag atcaagcatt aactgcattg aacgcattaa cactgccacc tcctttagct     1020
gaggcattag caagattgac attagggtct acagctcatc ctgcctaa                  1068
```

SEQ ID NO:28

```
MHLAPRRVPR GRRSPPDRVP ERQGALGRRR GAGSTGCARA AAGVHRRRGG GEADPSAAVH       60
RGWQAGGGTG LPDEVVSTAA ALEMFHAFAL IHDDIMDDSA TRRGSPTVHR ALADRLGAAL      120
DPDQAGQLGV STAILVGDLA LTWSDELLYA PLTPHRLAAV LPLVTAMRAE TVHGQYLDIT      180
SARRPGTDTS LALRIARYKT AAYTMERPLH IGAALAGARP ELLAGLSAYA LPAGEAFQLA      240
DDLLGVFGDP RRTGKPDLDD LRGGKHTVLV ALAREHATPE QRHTLDTLLG TPGLDRQGAS      300
RLRCVLVATG ARAEAERLIT ERRDQALTAL NALTLPPPLA EALARLTLGS TAHPA            355
```

SEQ ID NO:29

```
atgtcatatt tcgataacta cttcaatgag atagttaatt ccgtgaacga catcattaag       60
tcttacatct ctggcgacgt accaaaacta tacgaagcct cctaccattt gtttacatca      120
ggaggaaaga gactaagacc attgatcctt acaatttctt ctgatctttt cggtggacag      180
agagaaagag catactatgc tggcgcagca atcgaagttt tgcacacatt cactttggtt      240
cacgatgata tcatggatca agataacatt cgtagaggtc ttcctactgt acatgtcaag      300
tatggcctac ctttggccat tttagctggt gacttattgc atgcaaaagc ctttcaattg      360
ttgactcagg cattgagagg tctaccatct gaaactatca tcaaggcgtt tgatatcttt      420
acaagatcta tcattatcat atcagaaggt caagctgtcg atatggaatt cgaagataga      480
attgatatca aggaacaaga gtatttggat atgatatctc gtaaaaccgc tgccttattc      540
tcagcttctt cttccattgg ggcgttgata gctggagcta atgataacga tgtgagatta      600
atgtccgatt tcggtacaaa tcttgggatc gcatttcaaa ttgtagatga tatacttggt      660
ttaacagctg atgaaaaaga gctaggaaaa cctgttttca gtgatatcag agaaggtaaa      720
aagaccatat tagtcattaa gactttagaa ttgtgtaagg aagacgagaa aaagattgtg      780
ttaaaagcgc taggcaacaa gtcagcatca aaggaagagt tgatgagttc tgctgacata      840
atcaaaaagt actcattgga ttacgcctac aacttagctg agaaatacta caaaaacgcc      900
atcgattctc taaatcaagt ttcaagtaaa agtgatattc cagggaaggc attgaaatat      960
cttgctgaat tcaccatcag aagacgtaag taa                                   993
```

SEQ ID NO:30

```
MSYFDNYFNE IVNSVNDIIK SYISGDVPKL YEASYHLFTS GGKRLRPLIL TISSDLFGGQ       60
RERAYYAGAA IEVLHTFTLV HDDIMDQDNI RRGLPTVHVK YGLPLAILAG DLLHAKAFQL      120
LTQALRGLPS ETIIKAFDIF TRSIIIISEG QAVDMEFEDR IDIKEQEYLD MISRKTAALF      180
SASSSIGALI AGANDNDVRL MSDFGTNLGI AFQIVDDILG LTADEKELGK PVFSDIREGK      240
KTILVIKTLE LCKEDEKKIV LKALGNKSAS KEELMSSADI IKKYSLDYAY NLAEKYYKNA      300
IDSLNQVSSK SDIPGKALKY LAEFTIRRRK                                        330
```

SEQ ID NO:31

```
atggtcgcac aaactttcaa cctggatacc tacttatccc aaagacaaca acaagttgaa       60
gaggccctaa gtgctgctct tgtgccagct tatcctgaga gaatatacga agctatgaga      120
tactccctcc tggcaggtgg caaaagatta agacctatct tatgtttagc tgcttgcgaa      180
ttggcaggtg gttctgttga acaagccatg ccaactgcgt gtgcacttga aatgatccat      240
acaatgtcac taattcatga tgacctgcca gccatggata acgatgattt cagaagagga      300
aagccaacta atcacaaggt gttcggggaa gatatagcca tcttagcggg tgatgcgctt      360
ttagcttacg cttttgaaca tattgcttct caaacaagag gagtaccacc tcaattggtg      420
```

ctacaagtta ttgctagaat cggacacgcc gttgctgcaa caggcctcgt tggaggccaa 480
gtcgtagacc ttgaatctga aggtaaagct atttccttag aaacattgga gtatattcac 540
tcacataaga ctggagcctt gctggaagca tcagttgtct caggcggtat tctcgcaggg 600
gcagatgaag agcttttggc cagattgtct cattacgcta gagatatagg cttggctttt 660
caaatcgtcg atgatatcct ggatgttact gctacatctg aacagttggg gaaaaccgct 720
ggtaaagacc aggcagccgc aaaggcaact tatccaagtc tattgggttt agaagcctct 780
agacagaaag cggaagagtt gattcaatct gctaaggaag ccttaagacc ttacggttca 840
caagcagagc cactcctagc gctggcagac ttcatcacac gtcgtcagca ttaa 894

SEQ ID NO:32
MVAQTFNLDT YLSQRQQQVE EALSAALVPA YPERIYEAMR YSLLAGGKRL RPILCLAACE 60
LAGGSVEQAM PTACALEMIH TMSLIHDDLP AMDNDDFRRG KPTNHKVFGE DIAILAGDAL 120
LAYAFEHIAS QTRGVPPQLV LQVIARIGHA VAATGLVGGQ VVDLESEGKA ISLETLEYIH 180
SHKTGALLEA SVVSGGILAG ADEELLARLS HYARDIGLAF QIVDDILDVT ATSEQLGKTA 240
GKDQAAAKAT YPSLLGLEAS RQKAEELIQS AKEALRPYGS QAEPLLALAD FITRRQH 297

SEQ ID NO:33
atgaaaaccg ggtttatctc accagcaaca gtatttcatc acagaatctc accagcgacc 60
actttcagac atcacttatc acctgctact acaaactcta caggcattgt cgccttaaga 120
gacatcaact tcagatgtaa agcagtttct aaagagtact ctgatctgtt gcagaaagat 180
gaggcttctt tcacaaaatg ggacgatgac aaggtgaaag atcatcttga taccaacaaa 240
aacttatacc caaatgatga gattaaggaa tttgttgaat cagtaaaggc tatgttcggt 300
agtatgaatg acggggagat aaacgtctct gcatacgata ctgcatgggt tgctttggtt 360
caagatgtcg atggatcagg tagtcctcag ttcccttctt ctttagaatg gattgccaac 420
aatcaattgt cagatggatc atggggagat catttgctgt tctcagctca cgatagaatc 480
atcaacacat tagcatgcgt tattgcactt acaagttgga atgttcatcc ttctaagtgt 540
gaaaaaggtt tgaattttct gagagaaaac atttgcaaat tagaagatga aaacgcagaa 600
catatgccaa ttggttttga agtaacattc ccatcactaa ttgatatcgc gaaaaagttg 660
aacattgaag tacctgagga tactccagca cttaaagaga tctacgcacg tagagatatc 720
aagttaacta agatcccaat ggaagttctt cacaaggtac ctactacttt gttacattct 780
ttggaaggaa tgcctgattt ggagtgggaa aaactgttaa agctacaatg taaagatggt 840
agtttcttgt tttccccatc tagtaccgca ttcgccctaa tgcaaacaaa agatgagaaa 900
tgcttacagt atctaacaaa tatcgtcact aagttcaacg gtggcgtgcc taatgtgtac 960
ccagtcgatt tgtttgaaca tatttgggtt gttgatagac tgcagagatt ggggattgcc 1020
agatacttca aatcagagat aaaagattgt gtagagtata tcaataagta ctggaccaaa 1080
aatggaattt gttgggctag aaatactcac gttcaagata tcgatgatac agccatggga 1140
ttcagagtgt tgagagcgca cggttatgac gtcactccag atgtttttag acaatttgaa 1200
aaagatggta aattcgtttg ctttgcaggg caatcaacac aagccgtgac aggaatgttt 1260
aacgtttaca gagcctctca aatgttgttc ccaggggaga gaattttgga agatgccaaa 1320
aagttctctt acaattactt aaaggaaaag caaagtacca acgaattgct ggataaatgg 1380
ataatcgcta aagatctacc tggtgaagtt ggttatgctc tggatatccc atggtatgct 1440
tccttaccaa gattggaaac tcgttattac cttgaacaat acggcggtga agatgatgtc 1500
tggataggca agacattata cagaatgggt tacgtgtcca ataacacata tctagaaatg 1560
gcaaagctgg attacaataa ctatgttgca gtccttcaat tagaatggta cacaatacaa 1620
caatggtacg tcgatattgg tatagagaag ttcgaatctg acaacatcaa gtcagtcctg 1680

SEQ ID NO:34
MKTGFISPAT VFHHRISPAT TFRHHLSPAT TNSTGIVALR DINFRCKAVS KEYSDLLQKD 60
EASFTKWDDD KVKDHLDTNK NLYPNDEIKE FVESVKAMFG SMNDGEINVS AYDTAWVALV 120
QDVDGSGSPQ FPSSLEWIAN NQLSDGSWGD HLLFSAHDRI INTLACVIAL TSWNVHPSKC 180
EKGLNFLREN ICKLEDENAE HMPIGFEVTF PSLIDIAKKL NIEVPEDTPA LKEIYARRDI 240
KLTKIPMEVL HKVPTTLLHS LEGMPDLEWE KLLKLQCKDG SFLFSPSSTA FALMQTKDEK 300
CLQYLTNIVT KFNGGVPNVY PVDLFEHIWV VDRLQRLGIA RYFKSEIKDC VEYINKYWTK 360
NGICWARNTH VQDIDDTAMG FRVLRAHGYD VTPDVFRQFE KDGKFVCFAG QSTQAVTGMF 420
NVYRASQMLF PGERILEDAK KFSYNYLKEK QSTNELLDKW IIAKDLPGEV GYALDIPWYA 480
SLPRLETRYY LEQYGGEDDV WIGKTLYRMG YVSNNTYLEM AKLDYNNYVA VLQLEWYTIQ 540
QWYVDIGIEK FESDNIKSVL VSYYLAAASI FEPERSKERI AWAKTTILVD KITSIFDSSQ 600

```
SSKEDITAFI DKFRNKSSSK KHSINGEPWH EVMVALKKTL HGFALDALMT HSQDIHPQLH     660
QAWEMWLTKL QDGVDVTAEL MVQMINMTAG RWVSKELLTH PQYQRLSTVT NSVCHDITKL     720
HNFKENSTTV DSKVQELVQL VFSDTPDDLD QDMKQTFLTV MKTFYYKAWC DPNTINDHIS     780
KVFEIVI                                                               787
```

SEQ ID NO:35

```
atgcctgatg cacacgatgc tccacctcca caaataagac agagaacact agtagatgag      60
gctacccaac tgctaactga gtccgcagaa gatgcatggg gtgaagtcag tgtgtcagaa     120
tacgaaacag caaggctagt tgcccatgct acatggttag gtggacacgc cacaagagtg     180
gccttccttc tggagagaca acacgaagac gggtcatggg gtccaccagg tggatatagg     240
ttagtcccta cattatctgc tgttcacgca ttattgacat gtcttgcctc tcctgctcag     300
gatcatggcg ttccacatga tagactttta agagctgttg acgcaggctt gactgccttg     360
agaagattgg ggacatctga ctccccacct gatactatag cagttgagct ggttatccca     420
tctttgctag agggcattca acacttactg gaccctgctc atcctcatag tagaccagcc     480
ttctctcaac atagaggctc tcttgtttgt cctggtggac tagatgggag aactctagga     540
gctttgagat cacacgccgc agcaggtaca ccagtaccag gaaaagtctg gcacgcttcc     600
gagactttgg gcttgagtac cgaagctgct tctcacttgc aaccagccca aggtataatc     660
ggtggctctg ctgctgccac agcaacatgg ctaaccaggg ttgcaccatc tcaacagtca     720
gattctgcca gaagatacct tgaggaatta caacacagat actctggccc agttccttcc     780
attaccccta tcacatactt cgaaagagca tggttattga acaattttgc agcagccggt     840
gttccttgtg aggctccagc tgctttgttg gattccttag aagcagcact tacaccacaa     900
ggtgctcctg ctggagcagg attgcctcca gatgctgatg atacagccgc tgtgttgctt     960
gcattggcaa cacatgggag aggtagaaga ccagaagtac tgatggatta caggactgac    1020
gggtatttcc aatgctttat tggggaaagg actccatcaa tttcaacaaa cgctcacgta    1080
ttggaaacat tagggcatca tgtggcccaa catccacaag atagagccag atacggatca    1140
gccatggata ccgcatcagc ttggctgctg gcagctcaaa agcaagatgg ctcttggtta    1200
gataaatggc atgcctcacc atactacgct actgtttgtt gcacacaagc cctagccgct    1260
catgcaagtc ctgcaactgc accagctaga cagagagctg tcagatgggt tttagccaca    1320
caaagatccg atggcggttg gggtctatgg cattcaactg ttgaagagac tgcttatgcc    1380
ttacagatct tggccccacc ttctggtggt ggcaatatcc cagtccaaca agcacttact    1440
agaggcagag caagattgtg tggagccttg ccactgactc ctttatggca tgataaggat    1500
ttgtatactc cagtaagagt agtcagagct gccagagctg ctgctctgta cactaccaga    1560
gatctattgt taccaccatt gtaa                                           1584
```

SEQ ID NO:36

```
MPDAHDAPPP QIRQRTLVDE ATQLLTESAE DAWGEVSVSE YETARLVAHA TWLGGHATRV      60
AFLLERQHED GSWGPPGGYR LVPTLSAVHA LLTCLASPAQ DHGVPHDRLL RAVDAGLTAL     120
RRLGTSDSPP DTIAVELVIP SLLEGIQHLL DPAHPHSRPA FSQHRGSLVC PGGLDGRTLG     180
ALRSHAAAGT PVPGKVWHAS ETLGLSTEAA SHLQPAQGII GGSAAATATW LTRVAPSQQS     240
DSARRYLEEL QHRYSGPVPS ITPITYFERA WLLNNFAAAG VPCEAPAALL DSLEAALTPQ     300
GAPAGAGLPP DADDTAAVLL ALATHGRGRR PEVLMDYRTD GYFQCFIGER TPSISTNAHV     360
LETLGHHVAQ HPQDRARYGS AMDTASAWLL AAQKQDGSWL DKWHASPYYA TVCCTQALAA     420
HASPATAPAR QRAVRWVLAT QRSDGGWGLW HSTVEETAYA LQILAPPSGG GNIPVQQALT     480
RGRARLCGAL PLTPLWHDKD LYTPVRVVRA ARAAALYTTR DLLLPPL                   527
```

SEQ ID NO:37

```
atgaacgccc tatccgaaca cattttgtct gaattgagaa gattattgtc tgaaatgagt      60
gatggcggat ctgttggtcc atctgtgtat gatacggccc aggccctaag attccacggt     120
aacgtaacag gtagacaaga tgcatatgct tggttgatcg cccagcaaca agcagatgga     180
ggttggggct ctgccgactt tccactcttt agacatgctc caacatgggc tgcacttctc     240
gcattacaaa gagctgatcc acttcctggc gcagcagacg cagttcagac cgcaacaaga     300
ttcttgcaaa gacaaccaga tccatacgct catgccgttc ctgaggatgc ccctattggt     360
gctgaactga tcttgcctca gttttgtgga gaggctgctt ggttgttggg aggtgtggcc     420
ttccctagac acccagccct attaccatta agacaggctt gtttagtcaa actgggtgca     480
gtcgccatgt tgccttcagg acacccattg ctccactcct gggaggcatg ggggtacttct   540
ccaacaacag cctgtccaga cgatgatggt tctataggta tctcaccagc agctacagcc     600
gcctggagag cccaggctgt gaccagaggc tcaactcctc aagtgggcag agctgacgca     660
```

tacttacaaa tggcttcaag agcaacgaga tcaggcatag aaggagtctt ccctaatgtt 720
tggcctataa acgtattcga accatgctgg tcactgtaca ctctccatct tgccggtctg 780
ttcgcccatc cagcactggc tgaggctgta agagttatcg ttgctcaact tgaagcaaga 840
ttgggagtgc atggcctcgg accagcttta cattttgctg ccgacgctga tgatactgca 900
gttgccttat gcgttctgca tttggctggc agagatcctg cagttgacgc attgagacat 960
tttgaaattg gtgagctctt tgttacattc ccaggagaga gaaatgctag tgtctctacg 1020
aacattcacg ctcttcatgc tttgagattg ttaggtaaac cagctgccgg agcaagtgca 1080
tacgtcgaag caaatagaaa tccacatggt ttgtgggaca acgaaaaatg gcacgtttca 1140
tggctttatc caactgcaca cgccgttgca gctctagctc aaggcaagcc tcaatggaga 1200
gatgaaagag cactagccgc tctactacaa gctcaaagag atgatggtgg ttggggagct 1260
ggtagaggat ccactttcga ggaaaccgcc tacgctcttt tcgctttaca cgttatggac 1320
ggatctgagg aagccacagg cagaagaaga atcgctcaag tcgtcgcaag agccttagaa 1380
tggatgctag ctagacatgc cgcacatgga ttaccacaaa caccactctg gattggtaag 1440
gaattgtact gtcctactag agtcgtaaga gtagctgagc tagctggcct gtggttagca 1500
ttaagatggg gtagaagagt attagctgaa ggtgctggtg ctgcacctta a 1551

SEQ ID NO:38
MNALSEHILS ELRRLLSEMS DGGSVGPSVY DTAQALRFHG NVTGRQDAYA WLIAQQQADG 60
GWGSADFPLF RHAPTWAALL ALQRADPLPG AADAVQTATR FLQRQPDPYA HAVPEDAPIG 120
AELILPQFCG EAAWLLGGVA FPRHPALLPL RQACLVKLGA VAMLPSGHPL LHSWEAWGTS 180
PTTACPDDDG SIGISPAATA AWRAQAVTRG STPQVGRADA YLQMASRATR SGIEGVFPNV 240
WPINVFEPCW SLYTLHLAGL FAHPALAEAV RVIVAQLEAR LGVHGLGPAL HFAADADDTA 300
VALCVLHLAG RDPAVDALRH FEIGELFVTF PGERNASVST NIHALHALRL LGKPAAGASA 360
YVEANRNPHG LWDNEKWHVS WLYPTAHAVA ALAQGKPQWR DERALAALLQ AQRDDGGWGA 420
GRGSTFEETA YALFALHVMD GSEEATGRRR IAQVVARALE WMLARHAAHG LPQTPLWIGK 480
ELYCPTRVVR VAELAGLWLA LRWGRRVLAE GAGAAP 516

SEQ ID NO:39
atggttttgt cttcttcttg tactacagta ccacacttat cttcattagc tgtcgtgcaa 60
cttggtcctt ggagcagtag gattaaaaag aaaaccgata ctgttgcagt accagccgct 120
gcaggaaggt ggagaagggc cttggctaga gcacagcaca catcagaatc cgcagctgtc 180
gcaaagggca gcagtttgac ccctatagtg agaactgacg ctgagtcaag gagaacaaga 240
tggccaaccg atgacgatga cgccgaacct ttagtggatg agatcagggc aatgcttact 300
tccatgtctg atggtgacat ttccgtgagc gcatacgata cagcctgggt cggattggtt 360
ccaagattag acggcggtga aggtcctcaa tttccagcag ctgtgagatg gataagaaat 420
aaccagttgc ctgacggaag ttggggcgat gccgcattat tctctgccta tgacaggctt 480
atcaataccc ttgcctgcgt tgtaactttg acaaggtggt ccctagaacc agagatgaga 540
ggtagaggac tatctttttt gggtaggaac atgtggaaat tagcaactga agatgaagag 600
tcaatgccta ttggcttcga attagcattt ccatctttga tagagcttgc taagagccta 660
ggtgtccatg acttccctta tgatcaccag gccctacaag gaatctactc ttcaagagag 720
atcaaaatga agaggattcc aaaagaagtg atgcataccg ttccaacatc aatattgcac 780
agtttggagg gtatgcctgg cctagattgg gctaaactac ttaaactaca gagcagcgac 840
ggaagttttt tgttctcacc agctgccact gcatatgctt taatgaatac cggagatgac 900
aggtgtttta gctacatcga tagaacagta aagaaattca acggcggcgt ccctaatgtt 960
tatccagtgg atctatttga acatatttgg gccgttgata gacttgaaag attaggaatc 1020
tccaggtact tccaaaagga gatcgaacaa tgcatggatt atgtaaacag gcattggact 1080
gaggacggta tttgttgggc aaggaactct gatgtcaaag aggtggacga cacagctatg 1140
gcctttagac ttcttaggtt gcacggctac agcgtcagtc ctgatgtgtt taaaaacttc 1200
gaaaaggacg gtgaattttt cgcatttgtc ggacagtcta atcaagctgt taccggtatg 1260
tacaacttaa acagagcaag ccagatatcc ttcccaggcg aggatgtgct tcatagagct 1320
ggtgccttct catatgagtt cttgaggaga aaagaagcag agggagcttt gagggacaag 1380
tggatcattt ctaaagatct acctggtgaa gttgtgtata ctttggattt tccatggtac 1440
ggcaacttac ctagagtcga ggccagagac tacctagagc aatacggagg tggtgatgac 1500
gtttggattg gcaagacatt gtataggatg ccacttgtaa acaatgatgt atatttggaa 1560
ttggcaagaa tggatttcaa ccactgccag gctttgcatc agttagagtg gcaaggacta 1620
aaaagatggt atactgaaaa taggttgatg gactttggtg tcgcccaaga agatgccctt 1680
agagcttatt ttcttgcagc cgcatctgtt tacgagcctt gtagagctgc cgagaggctt 1740

gcatgggcta gagccgcaat actagctaac gccgtgagca cccacttaag aaatagccca 1800
tcattcagag aaaggttaga gcattctctt aggtgtagac ctagtgaaga gacagatggc 1860
tcctggttta actcctcaag tggctctgat gcagttttag taaaggctgt cttaagactt 1920
actgattcat tagccaggga agcacagcca atccatggag gtgacccaga agatattata 1980
cacaagttgt taagatctgc ttgggccgag tgggttaggg aaaaggcaga cgctgccgat 2040
agcgtgtgca atggtagttc tgcagtagaa caagagggat caagaatggt ccatgataaa 2100
cagacctgtc tattattggc tagaatgatc gaaatttctg ccggtagggc agctggtgaa 2160
gcagccagtg aggacggcga tagaagaata attcaattaa caggctccat ctgcgacagt 2220
cttaagcaaa aaatgctagt ttcacaggac cctgaaaaaa atgaagagat gatgtctcac 2280
gtggatgacg aattgaagtt gaggattaga gagttcgttc aatatttgct tagactaggt 2340
gaaaaaaaga ctggatctag cgaaaccagg caaacatttt taagtatagt gaaatcatgt 2400
tactatgctg ctcattgccc acctcatgtc gttgatagac acattagtag agtgattttc 2460
gagccagtaa gtgccgcaaa gtaaccgcgg 2490

SEQ ID NO:40
MVLSSSCTTV PHLSSLAVVQ LGPWSSRIKK KTDTVAVPAA AGRWRRALAR AQHTSESAAV 60
AKGSSLTPIV RTDAESRRTR WPTDDDDAEP LVDEIRAMLT SMSDGDISVS AYDTAWVGLV 120
PRLDGGEGPQ FPAAVRWIRN NQLPDGSWGD AALFSAYDRL INTLACVVTL TRWSLEPEMR 180
GRGLSFLGRN MWKLATEDEE SMPIGFELAF PSLIELAKSL GVHDFPYDHQ ALQGIYSSRE 240
IKMKRIPKEV MHTVPTSILH SLEGMPGLDW AKLLKLQSSD GSFLFSPAAT AYALMNTGDD 300
RCFSYIDRTV KKFNGGVPNV YPVDLFEHIW AVDRLERLGI SRYFQKEIEQ CMDYVNRHWT 360
EDGICWARNS DVKEVDDTAM AFRLLRLHGY SVSPDVFKNF EKDGEFFAFV GQSNQAVTGM 420
YNLNRASQIS FPGEDVLHRA GAFSYEFLRR KEAEGALRDK WIISKDLPGE VVYTLDFPWY 480
GNLPRVEARD YLEQYGGGDD VWIGKTLYRM PLVNNDVYLE LARMDFNHCQ ALHQLEWQGL 540
KRWYTENRLM DFGVAQEDAL RAYFLAAASV YEPCRAAERL AWARAAILAN AVSTHLRNSP 600
SFRERLEHSL RCRPSEETDG SWFNSSSGSD AVLVKAVLRL TDSLAREAQP IHGGDPEDII 660
HKLLRSAWAE WVREKADAAD SVCNGSSAVE QEGSRMVHDK QTCLLLARMI EISAGRAAGE 720
AASEDGDRRI IQLTGSICDS LKQKMLVSQD PEKNEEMMSH VDDELKLRIR EFVQYLLRLG 780
EKKTGSSETR QTFLSIVKSC YYAAHCPPHV VDRHISRVIF EPVSAAK 827

SEQ ID NO:41
cttcttcact aaatacttag acagagaaaa cagagctttt taaagccatg tctcttcagt 60
atcatgttct aaactccatt ccaagtacaa cctttctcag ttctactaaa acaacaatat 120
cttcttcttt ccttaccatc tcaggatctc ctctcaatgt cgctagagac aaatccagaa 180
gcggttccat acattgttca aagcttcgaa ctcaagaata cattaattct caagaggttc 240
aacatgattt gcctctaata catgagtggc aacagcttca aggagaagat gctcctcaga 300
ttagtgttgg aagtaatagt aatgcattca aagaagcagt gaagagtgtg aaaacgatct 360
tgagaaacct aacggacggg gaaattacga tatcggctta cgatacagct tgggttgcat 420
tgatcgatgc cggagataaa actccggcgt tccctccgc cgtgaaatgg atcgccgaga 480
accaactttc cgatggttct tggggagatg cgtatctctt ctcttatcat gatcgtctca 540
tcaataccct tgcatgcgtc gttgctctaa gatcatggaa tctctttcct catcaatgca 600
acaaaggaat cacgtttttc cgggaaaata ttgggaagct agaagacgaa aatgatgagc 660
atatgccaat cggattcgaa gtagcattcc catcgttgct tgagatagct cgaggaataa 720
acattgatgt accgtacgat tctccggtct taaaagatat atacgccaag aaagagctaa 780
agcttacaag gataccaaaa gagataatgc acaagatacc aacaacattg ttgcatagtt 840
tggaggggat gcgtgattta gattgggaaa agctcttgaa acttcaatct caagacggat 900
ctttcctctt ctctccttcc tctaccgctt ttgcattcat gcagacccga gacagtaact 960
gcctcgagta tttgcgaaat gccgtcaaac gtttcaatgg aggagttccc aatgtctttc 1020
ccgtggatct tttcgagcac atatggatag tggatcggtt acaacgttta gggatatcga 1080
gatactttga agaagagatt aaagagtgtc ttgactatgt ccacagatat tggaccgaca 1140
atggcatatg ttgggctaga tgttcccatg tccaagacat cgatgataca gccatggcat 1200
ttaggctctt aagacaacat ggataccaag tgtccgcaga tgtattcaag aactttgaga 1260
aagagggaga gtttttctgc tttgtggggc aatcaaacca agcagtaacc ggtatgttca 1320
acctataccg ggcatcacaa ttggcgtttc caagggaaga gatattgaaa aacgccaaag 1380
agttttctta taattatctg ctagaaaaac gggagagaga ggagttgatt gataagtgga 1440
ttataatgaa agacttacct ggcgagattg ggtttgcgtt agagattcca tggtacgcaa 1500
gcttgcctcg agtagagacg agattctata ttgatcaata tggtggagaa aacgacgttt 1560

```
ggattggcaa gactctttat aggatgccat acgtgaacaa taatggatat ctggaattag      1620
caaaacaaga ttacaacaat tgccaagctc agcatcagct cgaatgggac atattccaaa      1680
agtggtatga agaaaatagg ttaagtgagt ggggtgtgcg cagaagtgag cttctcgagt      1740
gttactactt agcggctgca actatatttg aatcagaaag gtcacatgag agaatggttt      1800
gggctaagtc aagtgtattg gttaaagcca tttcttcttc ttttggggaa tcctctgact      1860
ccagaagaag cttctccgat cagtttcatg aatacattgc caatgctcga cgaagtgatc      1920
atcactttaa tgacaggaac atgagattgg accgaccagg atcggttcag gccagtcggc      1980
ttgccggagt gttaatcggg actttgaatc aaatgtcttt tgaccttttc atgtctcatg      2040
gccgtgacgt taacaatctc ctctatctat cgtggggaga ttggatggaa aaatggaaac      2100
tatatggaga tgaaggagaa ggagagctca tggtgaagat gataattcta atgaagaaca      2160
atgacctaac taacttcttc acccacactc acttcgttcg tctcgcggaa atcatcaatc      2220
gaatctgtct tcctcgccaa tacttaaagg caaggagaaa cgatgagaag gagaagacaa      2280
taaagagtat ggagaaggag atggggaaaa tggttgagtt agcattgtcg gagagtgaca      2340
catttcgtga cgtcagcatc acgtttcttg atgtagcaaa agcattttac tactttgctt      2400
tatgtggcga tcatctccaa actcacatct ccaaagtctt gtttcaaaaa gtctagtaac      2460
ctcatcatca tcatcgatcc attaacaatc agtggatcga tgtatccata gatgcgtgaa      2520
taatatttca tgtagagaag gagaacaaat tagatcatgt agggttatca                 2570
```

SEQ ID NO:42

```
MSLQYHVLNS IPSTTFLSST KTTISSSFLT ISGSPLNVAR DKSRSGSIHC SKLRTQEYIN        60
SQEVQHDLPL IHEWQQLQGE DAPQISVGSN SNAFKEAVKS VKTILRNLTD GEITISAYDT       120
AWVALIDAGD KTPAFPSAVK WIAENQLSDG SWGDAYLFSY HDRLINTLAC VVALRSWNLF       180
PHQCNKGITF FRENIGKLED ENDEHMPIGF EVAFPSLLEI ARGINIDVPY DSPVLKDIYA       240
KKELKLTRIP KEIMHKIPTT LLHSLEGMRD LDWEKLLKLQ SQDGSFLFSP SSTAFAFMQT       300
RDSNCLEYLR NAVKRFNGGV PNVFPVDLFE HIWIVDRLQR LGISRYFEEE IKECLDYVHR       360
YWTDNGICWA RCSHVQDIDD TAMAFRLLRQ HGYQVSADVF KNFEKEGEFF CFVGQSNQAV       420
TGMFNLYRAS QLAFPREEIL KNAKEFSYNY LLEKREREEL IDKWIIMKDL PGEIGFALEI       480
PWYASLPRVE TRFYIDQYGG ENDVWIGKTL YRMPYVNNNG YLELAKQDYN NCQAQHQLEW       540
DIFQKWYEEN RLSEWGVRRS ELLECYYLAA ATIFESERSH ERMVWAKSSV LVKAISSSFG       600
ESSDSRRSFS DQFHEYIANA RRSDHHFNDR NMRLDRPGSV QASRLAGVLI GTLNQMSFDL       660
FMSHGRDVNN LLYLSWGDWM EKWKLYGDEG EGELMVKMII LMKNNDLTNF FTHTHFVRLA       720
EIINRICLPR QYLKARRNDE KEKTIKSMEK EMGKMVELAL SESDTFRDVS ITFLDVAKAF       780
YYFALCGDHL QTHISKVLFQ KV                                                802
```

SEQ ID NO:43

```
atgaatttga gtttgtgtat agcatctcca ctattgacca aatctaatag accagctgct        60
ttatcagcaa ttcatacagc tagtacatcc catggtggcc aaaccaaccc tacgaatctg       120
ataatcgata cgaccaagga gagaatacaa aaacaattca aaaatgttga aatttcagtt       180
tcttcttatg atactgcgtg ggttgccatg gttccatcac ctaattctcc aaagtctcca       240
tgtttcccag aatgtttgaa ttggctgatt aacaaccagt tgaatgatgg atcttggggt       300
ttagtcaatc acacgcacaa tcacaaccat ccacttttga aagattcttt atcctcaact       360
ttggcttgca tcgtggccct aaagagatgg aacgtaggtg aggatcagat taacaagggg       420
cttagtttca ttgaatctaa cttggcttcc gcgactgaaa aatctcaacc atctccaata       480
ggattcgata tcatctttcc aggtctgtta gagtacgcca aaaatctaga tatcaactta       540
ctgtctaagc aaactgattt ctcactaatg ttacacaaga gagaattaga acaaaagaga       600
tgtcattcaa acgaaatgga tggttaccta gcttatatct ctgaaggtct tggtaatctt       660
tacgattgga atatggtgaa aaagtaccag atgaaaaatg gctcagtttt caattcccct       720
tctgcaactg cggcagcatt cattaaccat caaaatccag gatgcctgaa ctatttgaat       780
tcactactag acaaattcgg caacgcagtt ccaactgtat accctcacga tttgtttatc       840
agattgagta tggtggatac aattgaaaga cttggtatat cccaccactt tagagtcgag       900
atcaaaaatg ttttggatga gacataccgt tgttgggtgg agagagatga acaaatcttt       960
atggatgttg tgacgtgcgc gttggccttt agattgttgc gtattaacgg ttacgaagtt      1020
agtccagatc cacttgccga aattacaaac gaattagctt taaaggatga atacgccgct      1080
cttgaaacat atcatgcgtc acatatcctt taccaagagg acttatcatc tggaaaacaa      1140
attcttaaat ctgctgattt cctgaaggaa atcatatcca ctgatagtaa tagactgtcc      1200
aaactgatcc ataaagaggt tgaaaatgca cttaagttcc ctattaacac cggcttagaa      1260
cgtattaaca caagacgtaa catccagctt tacaacgtag acaatactag aatcttgaaa      1320
```

```
accacttacc attcttccaa catatcaaac actgattacc taagattagc tgttgaagat      1380
ttctacacat gtcagtctat ctatagagaa gagctgaaag gattagagag atgggtcgtt      1440
gagaataagc tagatcaatt gaaatttgcc agacaaaaga cagcttattg ttacttctca      1500
gttgccgcca ctttatcaag tccagaattg tcagatgcac gtatttcttg ggctaaaaac      1560
ggaattttga caactgttgt tgatgatttc tttgatattg gcgggacaat cgacgaattg      1620
acaaacctga ttcaatgcgt tgaaaagtgg aatgtcgatg tcgataaaga ctgttgctca      1680
gaacatgtta gaatactgtt cttggctctg aaagatgcta tctgttggat cggggatgag      1740
gctttcaaat ggcaagctag agatgtgacg tctcacgtca ttcaaacctg gctagaactg      1800
atgaactcta tgttgagaga agcaatttgg actagagatg catacgttcc tacattaaac      1860
gagtatatgg aaaacgctta tgtctccttt gctttgggtc ctatcgttaa gcctgccata      1920
tactttgtag gaccaaagct atccgaggaa atcgtcgaat catcagaata ccataacttg      1980
ttcaagttaa tgtccacaca aggcagatta cttaatgata ttcattcttt caaaagagag      2040
tttaaggaag gaaagttaaa tgctgttgct ctgcatcttt ctaatggcga aagtggtaaa      2100
gtcgaagagg aagtagttga ggaaatgatg atgatgatca aaaacaagag aaaggagttg      2160
atgaaactaa tcttcgaaga gaacggttca attgttccta gagcatgtaa ggatgcattt      2220
tggaacatgt gtcatgtgct aaactttttc tacgcaaacg acgatggttt tactgggaac      2280
acaatactag atacagtaaa agacatcata tacaaccctt tggtcttagt aaacgaaaac      2340
gaggagcaaa gataa                                                       2355
```

SEQ ID NO:44

```
MNLSLCIASP LLTKSNRPAA LSAIHTASTS HGGQTNPTNL IIDTTKERIQ KQFKNVEISV        60
SSYDTAWVAM VPSPNSPKSP CFPECLNWLI NNQLNDGSWG LVNHTHNHNH PLLKDSLSST       120
LACIVALKRW NVGEDQINKG LSFIESNLAS ATEKSQPSPI GFDIIFPGLL EYAKNLDINL       180
LSKQTDFSLM LHKRELEQKR CHSNEMDGYL AYISEGLGNL YDWNMVKKYQ MKNGSVFNSP       240
SATAAAFINH QNPGCLNYLN SLLDKFGNAV PTVYPHDLFI RLSMVDTIER LGISHHFRVE       300
IKNVLDETYR CWVERDEQIF MDVVTCALAF RLLRINGYEV SPDPLAEITN ELALKDEYAA       360
LETYHASHIL YQEDLSSGKQ ILKSADFLKE IISTDSNRLS KLIHKEVENA LKFPINTGLE       420
RINTRRNIQL YNVDNTRILK TTYHSSNISN TDYLRLAVED FYTCQSIYRE ELKGLERWVV       480
ENKLDQLKFA RQKTAYCYFS VAATLSSPEL SDARISWAKN GILTTVVDDF FDIGGTIDEL       540
TNLIQCVEKW NVDVDKDCCS EHVRILFLAL KDAICWIGDE AFKWQARDVT SHVIQTWLEL       600
MNSMLREAIW TRDAYVPTLN EYMENAYVSF ALGPIVKPAI YFVGPKLSEE IVESSEYHNL       660
FKLMSTQGRL LNDIHSFKRE FKEGKLNAVA LHLSNGESGK VEEEVVEEMM MMIKNKRKEL       720
MKLIFEENGS IVPRACKDAF WNMCHVLNFF YANDDGFTGN TILDTVKDII YNPLVLVNEN       780
EEQR                                                                    784
```

SEQ ID NO:45

```
atgaatctgt ccctttgtat agctagtcca ctgttgacaa aatcttctag accaactgct        60
ctttctgcaa ttcatactgc cagtactagt catggaggtc aaacaaaccc aacaaatttg       120
ataatcgata ctactaagga gagaatccaa aagctattca aaaatgttga aatctcagta       180
tcatcttatg acaccgcatg ggttgcaatg gtgccatcac ctaattcccc aaaaagtcca       240
tgttttccag agtgcttgaa ttggttaatc aataatcagt taaacgatgg ttcttggggt       300
ttagtcaacc acactcataa ccacaatcat ccattattga aggactcttt atcatcaaca       360
ttagcctgta ttgttgcatt gaaaagatgg aatgtaggtg aagatcaaat caacaagggt       420
ttatcattca tagaatccaa tctagcttct gctaccgaca aatcacaacc atctccaatc       480
gggttcgaca taatcttccc tggtttgctg gagtatgcca aaaaccttga tatcaactta       540
ctgtctaaac aaacagattt ctctttgatg ctacacaaaa gagagttaga gcagaaaaga       600
tgccattcta acgaaattga cgggtactta gcatatatct cagaaggttt gggtaatttg       660
tatgactgga acatggtcaa aaagtatcag atgaaaaatg gatccgtatt caattctcct       720
tctgcaactg ccgcagcatt cattaatcat caaaaccctg ggtgtcttaa ctacttgaac       780
tcactattag ataagtttgg aaatgcagtt ccaacagtct atcctttgga cttgtacatc       840
agattatcta tggttgacac tatagagaga ttaggtattt ctcatcattt cagagttgag       900
atcaaaaatg ttttggacga gacatacaga tgttgggtcg aaagagatga gcaaatcttt       960
atggatgtcg tgacctgcgc tctggctttt agattgctaa ggatacacgg atacaaagta      1020
tctcctgatc aactggctga gattacaaac gaactggctt tcaaagacga atacgccgca      1080
ttagaaacat accatgcatc ccaaatactt taccaggaag acctaagttc aggaaaacaa      1140
atcttgaagt ctgcagattt cctgaaaggc attctgtcta cagatagtaa taggttgtct      1200
aaattgatac acaaggaagt agaaaacgca ctaaagtttc ctattaacac tggtttagag      1260
```

```
agaatcaata ctaggagaaa cattcagctg tacaacgtag ataatacaag gattcttaag      1320
accacctacc atagttcaaa catttccaac acctattact taagattagc tgtcgaagac      1380
ttttacactt gtcaatcaat ctacagagag gagttaaagg gcctagaaag atgggtagtt      1440
caaaacaagt tggatcaact gaagtttgct agacagaaga cagcatactg ttatttctct      1500
gttgctgcta ccctttcatc cccagaattg tctgatgcca gaataagttg ggccaaaaat      1560
ggtattctta caactgtagt cgatgatttc tttgatattg gaggtactat tgatgaactg      1620
acaaatctta ttcaatgtgt tgaaaagtgg aacgtggatg tagataagga ttgctgcagt      1680
gaacatgtga gaatactttt cctggctcta aaagatgcaa tatgttggat tggcgacgag      1740
gccttcaagt ggcaagctag agatgttaca tctcatgtca tccaaacttg gcttgaactg      1800
atgaactcaa tgctaagaga agcaatctgg acaagagatg catacgttcc aacattgaac      1860
gaatacatgg aaaacgctta cgtctcattt gccttgggtc ctattgttaa gccagccata      1920
tactttgttg ggccaaagtt atccgaagag attgttgagt cttccgaata tcataaccta      1980
ttcaagttaa tgtcaacaca aggcagactt ctgaacgata tccactcctt caaaagagaa      2040
ttcaaggaag gtaagctaaa cgctgttgct ttgcacttgt ctaatggtga atctggcaaa      2100
gtggaagagg aagtcgttga ggaaatgatg atgatgatca aaaacaagag aaaggaattg      2160
atgaaattga ttttcgagga aaatggttca atcgtaccta gagcttgtaa agatgctttt      2220
tggaatatgt gccatgttct taacttcttt tacgctaatg atgatggctt cactggaaat      2280
acaatattgg atacagttaa agatatcatc tacaacccac ttgttttggt caatgagaac      2340
gaggaacaaa gataa                                                       2355
```

SEQ ID NO:46

```
MNLSLCIASP LLTKSSRPTA LSAIHTASTS HGGQTNPTNL IIDTTKERIQ KLFKNVEISV        60
SSYDTAWVAM VPSPNSPKSP CFPECLNWLI NNQLNDGSWG LVNHTHNHNH PLLKDSLSST       120
LACIVALKRW NVGEDQINKG LSFIESNLAS ATDKSQPSPI GFDIIFPGLL EYAKNLDINL       180
LSKQTDFSLM LHKRELEQKR CHSNEIDGYL AYISEGLGNL YDWNMVKKYQ MKNGSVFNSP       240
SATAAAFINH QNPGCLNYLN SLLDKFGNAV PTVYPLDLYI RLSMVDTIER LGISHHFRVE       300
IKNVLDETYR CWVERDEQIF MDVVTCALAF RLLRIHGYKV SPDQLAEITN ELAFKDEYAA       360
LETYHASQIL YQEDLSSGKQ ILKSADFLKG ILSTDSNRLS KLIHKEVENA LKFPINTGLE       420
RINTRRNIQL YNVDNTRILK TTYHSSNISN TYYLRLAVED FYTCQSIYRE ELKGLERWVV       480
QNKLDQLKFA RQKTAYCYFS VAATLSSPEL SDARISWAKN GILTTVVDDF FDIGGTIDEL       540
TNLIQCVEKW NVDVDKDCCS EHVRILFLAL KDAICWIGDE AFKWQARDVT SHVIQTWLEL       600
MNSMLREAIW TRDAYVPTLN EYMENAYVSF ALGPIVKPAI YFVGPKLSEE IVESSEYHNL       660
FKLMSTQGRL LNDIHSFKRE FKEGKLNAVA LHLSNGESGK VEEEVVEEMM MMIKNKRKEL       720
MKLIFEENGS IVPRACKDAF WNMCHVLNFF YANDDGFTGN TILDTVKDII YNPLVLVNEN       780
EEQR                                                                    784
```

SEQ ID NO:47

```
atggctatgc cagtgaagct aacacctgcg tcattatcct taaaagctgt gtgctgcaga        60
ttctcatccg gtggccatgc tttgagattc gggagtagtc tgccatgttg gagaaggacc       120
cctacccaaa gatctacttc ttcctctact actagaccag ctgccgaagt gtcatcaggt       180
aagagtaaac aacatgatca ggaagctagt gaagcgacta tcagacaaca attacaactt       240
gtggatgtcc tggagaatat gggaatatcc agacattttg ctgcagagat aaagtgcata       300
ctagacagaa cttacagatc ttggttacaa agacacgagg aaatcatgct ggacactatg       360
acatgtgcta tggcttttag aatcctaaga ttgaacggat acaacgtttc atcagatgaa       420
ctataccacg ttgtagaggc atctggtctg cataattctt tgggtgggta tcttaacgat       480
accagaacac tacttgaatt acacaaggct tcaacagtta gtatctctga ggatgaatct       540
atcttagatt caattggctc tagatccaga acattgctta gagaacaatt ggagtctggt       600
ggcgcactga gaaagccttc tttattcaaa gaggttgaac atgcactgga tggacctttt       660
tacaccacac ttgatagact tcatcatagg tggaatattg aaaacttcaa cattattgag       720
caacacatgt tggagactcc atacttatct aaccagcata catcaaggga tatcctagca       780
ttgtcaatta gagattttc ctcctcacaa ttcacttatc aacaagagct acagcatctg        840
gagagttggg ttaaggaatg tagattagat caactacagt tcgcaagaca gaaattagcg       900
tacttttacc tatcagccgc aggcaccatg ttttctcctg agctttctga tgcgagaaca       960
ttatgggcca aaaacggggt gttgacaact attgttgatg atttctttga tgttgccggt      1020
tctaaagagg aattggaaaa cttagtcatg ctggtcgaaa tgtgggatga acatcacaaa      1080
gttgaattct attctgagca ggtcgaaatc atcttctctt ccatctacga ttctgtcaac      1140
caattgggtg agaaggcctc tttggttcaa gacagatcaa ttacaaaaca ccttgttgaa      1200
```

```
atatggttag acttgttaaa gtccatgatg acggaagttg aatggagact gtcaaaatac      1260
gtgcctacag aaaaggaata catgattaat gcctctctta tcttcggcct aggtccaatc      1320
gttttaccag ctttgtattt cgttggtcca aagatttcag aaagtatagt aaaggaccca      1380
gaatatgatg aattgttcaa actaatgtca acatgtggta gattgttgaa tgacgtgcaa      1440
acgttcgaaa gagaatacaa tgagggtaaa ctgaattctg tcagtctatt ggttcttcac      1500
ggaggcccaa tgtctatttc agacgcaaag aggaaattac aaaagcctat tgatacgtgt      1560
agaagagatc ttctttcttt ggtccttaga gaagagtctg tagtaccaag accatgtaag      1620
gaactattct ggaaaatgtg taaagtgtgc tatttctttt actcaacaac tgatgggttt      1680
tctagtcaag tcgaaagagc aaaagaggta gacgctgtca taaatgagcc actgaagttg      1740
caaggttctc atacactggt atctgatgtt taa                                   1773
```

SEQ ID NO:48

```
MAMPVKLTPA SLSLKAVCCR FSSGGHALRF GSSLPCWRRT PTQRSTSSST TRPAAEVSSG        60
KSKQHDQEAS EATIRQQLQL VDVLENMGIS RHFAAEIKCI LDRTYRSWLQ RHEEIMLDTM       120
TCAMAFRILR LNGYNVSSDE LYHVVEASGL HNSLGGYLND TRTLLELHKA STVSISEDES       180
ILDSIGSRSR TLLREQLESG GALRKPSLFK EVEHALDGPF YTTLDRLHHR WNIENFNIIE       240
QHMLETPYLS NQHTSRDILA LSIRDFSSSQ FTYQQELQHL ESWVKECRLD QLQFARQKLA       300
YFYLSAAGTM FSPELSDART LWAKNGVLTT IVDDFFDVAG SKEELENLVM LVEMWDEHHK       360
VEFYSEQVEI IFSSIYDSVN QLGEKASLVQ DRSITKHLVE IWLDLLKSMM TEVEWRLSKY       420
VPTEKEYMIN ASLIFGLGPI VLPALYFVGP KISESIVKDP EYDELFKLMS TCGRLLNDVQ       480
TFEREYNEGK LNSVSLLVLH GGPMSISDAK RKLQKPIDTC RRDLLSLVLR EESVVPRPCK       540
ELFWKMCKVC YFFYSTTDGF SSQVERAKEV DAVINEPLKL QGSHTLVSDV                  590
```

SEQ ID NO:49

```
atgcagaact tccatggtac aaaggaaagg atcaaaaaga tgtttgacaa gattgaattg        60
tccgtttctt cttatgatac agcctgggtt gcaatggtcc catcccctga ttgcccagaa       120
acaccttgtt ttccagaatg tactaaatgg atcctagaaa atcagttggg tgatggtagt       180
tggtcacttc ctcatggcaa tccacttcta gttaaagatg cattatcttc cactcttgct       240
tgtattctgg ctcttaaaag atggggaatc ggtgaggaac agattaacaa aggactgaga       300
ttcatagaac tcaactctgc tagtgtaacc gataacgaac aacacaaacc aattggattt       360
gacattatct ttccaggtat gattgaatac gctatagact tagacctgaa tctaccacta       420
aaaccaactg acattaactc catgttgcat cgtagagccc ttgaattgac atcaggtgga       480
ggcaaaaatc tagaaggtag aagagcttac ttggcctacg tctctgaagg aatcggtaag       540
ctgcaagatt gggaaatggc tatgaaatac caacgtaaaa acggatctct gttcaatagt       600
ccatcaacaa ctgcagctgc attcatccat atacaagatg ctgaatgcct ccactatatt       660
cgttctcttc tccagaaatt tggaaacgca gtccctacaa tataccctct cgatatctat       720
gccagacttt caatggtaga tgccctggaa cgtcttggta ttgatagaca tttcagaaag       780
gagagaaagt tcgttctgga tgaaacatac agattttggt tgcaaggaga agaggagatt       840
ttctccgata acgcaacctg tgctttggcc ttcagaatat tgagacttaa tggttacgat       900
gtctctcttg aagatcactt ctctaactct ctgggcggtt acttaaagga ctcaggagca       960
gctttagaac tgtacagagc cctccaattg tcttacccag acgagtccct cctggaaaag      1020
caaaattcta gaacttctta cttcttaaaa caaggtttat ccaatgtctc cctctgtggt      1080
gacagattgc gtaaaaacat aattggagag gtgcatgatg ctttaaactt ttccgaccac      1140
gctaacttac aaagattagc tattcgtaga aggattaagc attacgctac tgacgataca      1200
aggattctaa aaacttccta cagatgctca acaatcggta accaagattt tctaaaactt      1260
gcagtggaag atttcaatat ctgtcaatca atacaaagag aggaattcaa gcatattgaa      1320
agatgggtcg ttgaaagacg tctagacaag ttaaagttcg ctagacaaaa agaggcctat      1380
tgctatttct cagccgcagc aacattgttt gcccctgaat tgtctgatgc tagaatgtct      1440
tgggccaaaa atggtgtatt gacaactgtg gttgatgatt tcttcgatgt cggaggctct      1500
gaagaggaat tagttaactt gatagaattg atcgagcgtt gggatgtgaa tggcagtgca      1560
gatttttgta gtgaggaagt tgagattatc tattctgcta tccactcaac tatctctgaa      1620
ataggtgata agtcatttgg ctggcaaggt agagatgtaa agtctcaagt tatcaagatc      1680
tggctggact tattgaaatc aatgttaact gaagctcaat ggtcttcaaa caagtctgtt      1740
cctaccctag atgagtatat gacaaccgcc catgtttcat tcgcacttgg tccaattgta      1800
cttccagcct tatacttcgt tggcccaaag ttgtcagaag aggttgcagg tcatcctgaa      1860
ctactaaacc tctacaaagt cacatctact tgtggcagac tactgaatga ttggagaagt      1920
tttaagagag aatccgagga aggtaagctc aacgctatta gtttatacat gatccactcc      1980
```

```
ggtggtgctt ctacagaaga ggaaacaatc gaacatttca aaggtttgat tgattctcag      2040
agaaggcaac tgttacaatt ggtgttgcaa gagaaggata gtatcatacc tagaccatgt      2100
aaagatctat tttggaatat gattaagtta ttacacactt tctacatgaa agatgatggc      2160
ttcacctcaa atgagatgag gaatgtagtt aaggcaatca ttaacgaacc aatctcactg      2220
gatgaattat ga                                                          2232
```

SEQ ID NO:50

```
MSCIRPWFCP SSISATLTDP ASKLVTGEFK TTSLNFHGTK ERIKKMFDKI ELSVSSYDTA       60
WVAMVPSPDC PETPCFPECT KWILENQLGD GSWSLPHGNP LLVKDALSST LACILALKRW      120
GIGEEQINKG LRFIELNSAS VTDNEQHKPI GFDIIFPGMI EYAKDLDLNL PLKPTDINSM      180
LHRRALELTS GGGKNLEGRR AYLAYVSEGI GKLQDWEMAM KYQRKNGSLF NSPSTTAAAF      240
IHIQDAECLH YIRSLLQKFG NAVPTIYPLD IYARLSMVDA LERLGIDRHF RKERKFVLDE      300
TYRFWLQGEE EIFSDNATCA LAFRILRLNG YDVSLEDHFS NSLGGYLKDS GAALELYRAL      360
QLSYPDESLL EKQNSRTSYF LKQGLSNVSL CGDRLRKNII GEVHDALNFP DHANLQRLAI      420
RRRIKHYATD DTRILKTSYR CSTIGNQDFL KLAVEDFNIC QSIQREEFKH IERWVVERRL      480
DKLKFARQKE AYCYFSAAAT LFAPELSDAR MSWAKNGVLT TVVDDFFDVG GSEEELVNLI      540
ELIERWDVNG SADFCSEEVE IIYSAIHSTI SEIGDKSFGW QGRDVKSHVI KIWLDLLKSM      600
LTEAQWSSNK SVPTLDEYMT TAHVSFALGP IVLPALYFVG PKLSEEVAGH PELLNLYKVM      660
STCGRLLNDW RSFKRESEEG KLNAISLYMI HSGGASTEEE TIEHFKGLID SQRRQLLQLV      720
LQEKDSIIPR PCKDLFWNMI KLLHTFYMKD DGFTSNEMRN VVKAIINEPI SLDEL            775
```

SEQ ID NO:51

```
atgtctatca accttcgctc ctccggttgt tcgtctccga tctcagctac tttggaacga        60
ggattggact cagaagtaca gacaagagct aacaatgtga gctttgagca aacaaaggag       120
aagattagga agatgttgga gaaagtggag ctttctgttt cggcctacga tactagttgg       180
gtagcaatgg ttccatcacc gagctcccaa aatgctccac ttttcccaca gtgtgtgaaa       240
tggttattgg ataatcaaca tgaagatgga tcttggggac ttgataacca tgaccatcaa       300
tctcttaaga aggatgtgtt atcatctaca ctggctagta tcctcgcgtt aaagaagtgg       360
ggaattggtg aaagacaaat aaacaagggt ctccagttta ttgagctgaa ttctgcatta       420
gtcactgatg aaaccataca gaaaccaaca gggtttgata ttatatttcc tgggatgatt       480
aaatatgcta gagatttgaa tctgacgatt ccattgggct cagaagtggt ggatgacatg       540
atacgaaaaa gagatctgga tcttaaatgt gatagtgaaa agttttcaaa gggaagagaa       600
gcatatctgg cctatgtttt agaggggaca agaaacctaa aagattggga tttgatagtc       660
aaatatcaaa ggaaaaatgg gtcactgttt gattctccag ccacaacagc agctgctttt       720
actcagtttg ggaatgatgg ttgtctccgt tatctctgtt ctctccttca gaaattcgag       780
gctgcagttc cttcagttta tccatttgat caatatgcac gccttagtat aattgtcact       840
cttgaaagct taggaattga tagagatttc aaaaccgaaa tcaaaagcat attggatgaa       900
acctatagat attggcttcg tggggatgaa gaaatatgtt tggacttggc cacttgtgct       960
ttggctttcc gattattgct tgctcatggc tatgatgtgt cttacgatcc gctaaaacca      1020
tttgcagaag aatctggttt ctctgatact ttggaaggat atgttaagaa tacgttttct      1080
gtgttagaat tatttaaggc tgctcaaagt tatccacatg aatcagcttt gaagaagcag      1140
tgttgttgga ctaaacaata tctggagatg gaattgtcca gctgggttaa gacctctgtt      1200
cgagataaat acctcaagaa agaggtcgag gatgctcttg cttttccctc ctatgcaagc      1260
ctagaaagat cagatcacag gagaaaaata ctcaatggtt ctgctgtgga aaacaccaga      1320
gttacaaaaa cctcatatcg tttgcacaat atttgcacct ctgatatcct gaagttagct      1380
gtggatgact tcaatttctg ccagtccata caccgtgaag aaatggaacg tcttgatagg      1440
tggattgtgg agaatagatt gcaggaactg aaatttgcca gacagaagct ggcttactgt      1500
tatttctctg ggctgcaac tttattttct ccagaactat ctgatgctcg tatatcgtgg       1560
gccaaaggtg gagtacttac aacggttgta gacgacttct ttgatgttgg agggtccaaa      1620
gaagaactgg aaaacctcat acacttggtc gaaaagtggg atttgaacgg tgttcctgag      1680
tacagctcag aacatgttga gatcatattc tcagttctaa gggacaccat tctcgaaaca      1740
ggagacaaag cattcaccta tcaaggacgc aatgtgacac accacattgt gaaaatttgg      1800
ttggatctgc tcaagtctat gttgagagaa gccgagtggt ccagtgacaa gtcaacacca      1860
agcttggagg attacatgga aaatgcgtac atatcatttg cattaggacc aattgtcctc      1920
ccagctacct atctgatcgg acctccactt ccagagaaga cagtcgatag ccaccaatat      1980
aatcagctct acaagctcgt gagcactatg ggtcgtcttc taaatgacat acaaggtttt      2040
aagagagaaa gcgcggaagg gaagctgaat gcggtttcat tgcacatgaa acacgagaga      2100
```

gacaatcgca gcaaagaagt gatcatagaa tcgatgaaag gtttagcaga gagaaagagg 2160
gaagaattgc ataagctagt tttggaggag aaaggaagtg tggttccaag ggaatgcaaa 2220
gaagcgttct tgaaaatgag caaagtgttg aacttatttt acaggaagga cgatggattc 2280
acatcaaatg atctgatgag tcttgttaaa tcagtgatct acgagcctgt tagcttacag 2340
aaagaatctt taacttga 2358

SEQ ID NO:52
MSINLRSSGC SSPISATLER GLDSEVQTRA NNVSFEQTKE KIRKMLEKVE LSVSAYDTSW 60
VAMVPSPSSQ NAPLFPQCVK WLLDNQHEDG SWGLDNHDHQ SLKKDVLSST LASILALKKW 120
GIGERQINKG LQFIELNSAL VTDETIQKPT GFDIIFPGMI KYARDLNLTI PLGSEVVDDM 180
IRKRDLDLKC DSEKFSKGRE AYLAYVLEGT RNLKDWDLIV KYQRKNGSLF DSPATTAAAF 240
TQFGNDGCLR YLCSLLQKFE AAVPSVYPFD QYARLSIIVT LESLGIDRDF KTEIKSILDE 300
TYRYWLRGDE EICLDLATCA LAFRLLLAHG YDVSYDPLKP FAEESGFSDT LEGYVKNTFS 360
VLELFKAAQS YPHESALKKQ CCWTKQYLEM ELSSWVKTSV RDKYLKKEVE DALAFPSYAS 420
LERSDHRRKI LNGSAVENTR VTKTSYRLHN ICTSDILKLA VDDFNFCQSI HREEMERLDR 480
WIVENRLQEL KFARQKLAYC YFSGAATLFS PELSDARISW AKGGVLTTVV DDFFDVGGSK 540
EELENLIHLV EKWDLNGVPE YSSEHVEIIF SVLRDTILET GDKAFTYQGR NVTHHIVKIW 600
LDLLKSMLRE AEWSSDKSTP SLEDYMENAY ISFALGPIVL PATYLIGPPL PEKTVDSHQY 660
NQLYKLVSTM GRLLNDIQGF KRESAEGKLN AVSLHMKHER DNRSKEVIIE SMKGLAERKR 720
EELHKLVLEE KGSVVPRECK EAFLKMSKVL NLFYRKDDGF TSNDLMSLVK SVIYEPVSLQ 780
KESLT 785

SEQ ID NO:53
atggaatttg atgaaccatt ggttgacgaa gcaagatctt tagtgcagcg tactttacaa 60
gattatgatg acagatacgg cttcggtact atgtcatgtg ctgcttatga tacagcctgg 120
gtgtctttag ttacaaaaac agtcgatggg agaaaacaat ggcttttccc agagtgtttt 180
gaatttctac tagaaacaca atctgatgcc ggaggatggg aaatcgggaa ttcagcacca 240
atcgacggta tattgaatac agctgcatcc ttacttgctc taaaacgtca cgttcaaact 300
gagcaaatca tccaacctca acatgaccat aaggatctag caggtagagc tgaacgtgcc 360
gctgcatctt tgagagcaca attggctgca ttggatgtgt ctacaactga acacgtcggt 420
tttgagataa ttgttcctgc aatgctagac ccattagaag ccgaagatcc atctctagtt 480
ttcgattttc cagctaggaa acctttgatg aagattcatg atgctaagat gagtagattc 540
aggccagaat acttgtatgg caaacaacca atgaccgcct tacattcatt agaggctttc 600
ataggcaaaa tcgacttcga taaggtaaga caccaccgta cccatgggtc tatgatgggt 660
tctccttcat ctaccgcagc ctacttaatg cacgcttcac aatgggatgg tgactcagag 720
gcttacctta gacacgtgat taaacacgca gcagggcagg gaactggtgc tgtaccatct 780
gctttcccat caacacattt tgagtcatct tggattctta ccacattgtt tagagctgga 840
ttttcagctt ctcatcttgc ctgtgatgag ttgaacaagt tggtcgagat acttgagggc 900
tcattcgaga aggaaggtgg ggcaatcggt tacgctccag ggtttcaagc agatgttgat 960
gatactgcta aaacaataag tacattagca gtccttggaa gagatgctac accaagacaa 1020
atgatcaagg tatttgaagc taatacacat tttagaacat accctggtga aagagatcct 1080
tctttgacag ctaattgtaa tgctctatca gccttactac accaaccaga tgcagcaatg 1140
tatggatctc aaattcaaaa gattaccaaa tttgtctgtg actattggtg gaagtctgat 1200
ggtaagatta aagataagtg gaacacttgc tacttgtacc catctgtctt attagttgag 1260
gttttggttg atcttgttag tttattggag cagggtaaat tgcctgatgt tttggatcaa 1320
gagcttcaat acagagtcgc catcacattg ttccaagcat gtttaaggcc attactagac 1380
caagatgccg aaggatcatg gaacaagtct atcgaagcca cagcctacgg catccttatc 1440
ctaactgaag ctaggagagt ttgtttcttc gacagattgt ctgagccatt gaatgaggca 1500
atccgtagag gtatcgcttt cgccgactct atgtctggaa ctgaagctca gttgaactac 1560
atttggatcg aaaaggttag ttacgcacct gcattattga ctaaatccta tttgttagca 1620
gcaagatggg ctgctaagtc tcctttaggc gcttccgtag gctcttcttt gtggactcca 1680
ccaagagaag gattggataa gcatgtcaga ttattccatc aagctgagtt attcagatcc 1740
cttccagaat gggaattaag agcctccatg attgaagcag ctttgttcac accacttcta 1800
agagcacata gactagacgt tttccctaga caagatgtag gtgaagacaa atatcttgat 1860
gtagttccat tcttttggac tgccgctaac aacagagata gaacttacgc ttccactcta 1920
ttcctttacg atatgtgttt tatcgcaatg ttaaacttcc agttagacga attcatggag 1980
gccacagccg gtatcttatt cagagatcat atggatgatt tgaggcaatt gattcatgat 2040

```
ctttggcag agaaaacttc cccaaagagt tctggtagaa gtagtcaggg cacaaaagat      2100
gctgactcag gtatagagga agacgtgtca atgtccgatt cagcttcaga ttcccaggat      2160
agaagtccag aatacgactt ggttttcagt gcattgagta cctttacaaa acatgtcttg      2220
caacacccat ctatacaaag tgcctctgta tgggatagaa aactacttgc tagagagatg      2280
aaggcttact tacttgctca tatccaacaa gcagaagatt caactccatt gtctgaattg      2340
aaagatgtgc ctcaaaagac tgatgtaaca agagtttcta catctactac taccttcttt      2400
aactgggtta gaacaacttc cgcagaccat atatcctgcc catactcctt ccactttgta      2460
gcatgccatc taggcgcagc attgtcacct aaagggtcta acggtgattg ctatccttca      2520
gctggtgaga agttcttggc agctgcagtc tgcagacatt tggccaccat gtgtagaatg      2580
tacaacgatc ttggatcagc tgaacgtgat tctgatgaag gtaatttgaa ctcccttggac     2640
ttccctgaat tcgccgattc cgcaggaaac ggagggatag aaattcagaa ggccgctcta      2700
ttaaggttag ctgagtttga gagagattca tacttagagg ccttccgtcg tttacaagat      2760
gaatccaata gagttcacgg tccagccggt ggtgatgaag ccagattgtc cagaaggaga      2820
atggcaatcc ttgaattctt cgcccagcag gtagatttgt acggtcaagt atacgtcatt      2880
agggatattt ccgctcgtat tcctaaaaac gaggttgaga aaaagagaaa attggatgat      2940
gctttcaatt ga                                                          2952
```

SEQ ID NO:54

```
MEFDEPLVDE ARSLVQRTLQ DYDDRYGFGT MSCAAYDTAW VSLVTKTVDG RKQWLFPECF       60
EFLLETQSDA GGWEIGNSAP IDGILNTAAS LLALKRHVQT EQIIQPQHDH KDLAGRAERA      120
AASLRAQLAA LDVSTTEHVG FEIIVPAMLD PLEAEDPSLV FDFPARKPLM KIHDAKMSRF      180
RPEYLYGKQP MTALHSLEAF IGKIDFDKVR HHRTHGSMMG SPSSTAAYLM HASQWDGDSE      240
AYLRHVIKHA AGQGTGAVPS AFPSTHFESS WILTTLFRAG FSASHLACDE LNKLVEILEG      300
SFEKEGGAIG YAPGFQADVD DTAKTISTLA VLGRDATPRQ MIKVFEANTH FRTYPGERDP      360
SLTANCNALS ALLHQPDAAM YGSQIQKITK FVCDYWWKSD GKIKDKWNTC YLYPSVLLVE      420
VLVDLVSLLE QGKLPDVLDQ ELQYRVAITL FQACLRPLLD QDAEGSWNKS IEATAYGILI      480
LTEARRVCFF DRLSEPLNEA IRRGIAFADS MSGTEAQLNY IWIEKVSYAP ALLTKSYLLA      540
ARWAAKSPLG ASVGSSLWTP PREGLDKHVR LFHQAELFRS LPEWELRASM IEAALFTPLL      600
RAHRLDVFPR QDVGEDKYLD VVPFFWTAAN NRDRTYASTL FLYDMCFIAM LNFQLDEFME      660
ATAGILFRDH MDDLRQLIHD LLAEKTSPKS SGRSSQGTKD ADSGIEEDVS MSDSASDSQD      720
RSPEYDLVFS ALSTFTKHVL QHPSIQSASV WDRKLLAREM KAYLLAHIQQ AEDSTPLSEL      780
KDVPQKTDVT RVSTSTTTFF NWVRTTSADH ISCPYSFHFV ACHLGAALSP KGSNGDCYPS      840
AGEKFLAAAV CRHLATMCRM YNDLGSAERD SDEGNLNSLD FPEFADSAGN GGIEIQKAAL      900
LRLAEFERDS YLEAFRRLQD ESNRVHGPAG GDEARLSRRR MAILEFFAQQ VDLYGQVYVI      960
RDISARIPKN EVEKKRKLDD AFN                                             983
```

SEQ ID NO:55

```
atggcttcta gtacacttat ccaaaacaga tcatgtggcg tcacatcatc tatgtcaagt        60
tttcaaatct tcagaggtca accactaaga tttcctggca ctagaacccc agctgcagtt       120
caatgcttga aaaagaggag atgccttagg ccaaccgaat ccgtactaga atcatctcct       180
ggctctggtt catatagaat agtaactggc ccttctggaa ttaaccctag ttctaacggg       240
cacttgcaag agggttcctt gactcacagg ttaccaatac caatggaaaa atctatcgat       300
aacttccaat ctactctata tgtgtcagat atttggtctg aaacactaca gagaactgaa       360
tgtttgctac aagtaactga aaacgtccag atgaatgagt ggattgagga aattagaatg       420
tactttagaa atatgacttt aggtgaaatt tccatgtccc cttacgacac tgcttgggtg       480
gctagagttc cagcgttgga cggttctcat gggcctcaat tccacagatc tttgcaatgg       540
attatcgaca accaattacc agatggggac tggggcgaac cttctctttt cttgggttac       600
gatagagttt gtaatacttt agcctgtgtg attgcgttga aaacatgggg tgttggggca       660
caaaacgttg aaagaggaat tcagttccta caatctaaca tatacaagat ggaggaagat       720
gacgctaatc atatgccaat aggattcgaa atcgtattcc ctgctatgat ggaagatgcc       780
aaagcattag gtttggattt gccatacgat gctactattt tgcaacagat ttcagccgaa       840
agagagaaaa agatgaaaaa gatcccaatg gcaatggtgt acaaataccc aaccacttta       900
cttcactcct tagaaggctt gcatagagaa gttgattgga ataagttgtt acaattacaa       960
tctgaaaatg gtagttttct ttattcacct gcttcaaccg catgcgcctt aatgtacact      1020
aaggacgtta aatgttttga ttacttaaac cagttgttga tcaagttcga ccacgcatgc      1080
ccaaatgtat atccagtcga tctattcgaa agattatgga tggttgacag attgcagaga      1140
ttagggatct ccagatactt tgaaagagag attagagatt gtttacaata cgtctacaga      1200
```

```
tattggaaag attgtggaat cggatgggct tctaactctt ccgtacaaga tgttgatgat      1260
acagccatgg cgtttagact tttaaggact catggtttcg acgtaaagga agattgcttt      1320
agacagtttt tcaaggacgg agaattcttc tgcttcgcag gccaatcatc tcaagcagtt      1380
acaggcatgt ttaatctttc aagagccagt caaacattgt ttccaggaga atctttattg      1440
aaaaaggcta gaaccttctc tagaaacttc ttgagaacaa agcatgagaa caacgaatgt      1500
ttcgataaat ggatcattac taaagatttg gctggtgaag tcgagtataa cttgaccttc      1560
ccatggtatg cctctttgcc tagattagaa cataggacat acttagatca atatggaatc      1620
gatgatatct ggataggcaa atctttatac aaaatgcctg ctgttaccaa cgaagttttc      1680
ctaaagttgg caaaggcaga ctttaacatg tgtcaagctc tacacaaaaa ggaattggaa      1740
caagtgataa agtggaacgc gtcctgtcaa ttcagagatc ttgaattcgc cagacaaaaa      1800
tcagtagaat gctattttgc tggtgcagcc acaatgttcg aaccagaaat ggttcaagct      1860
agattagtct gggcaagatg ttgtgtattg acaactgtct tagacgatta ctttgaccac      1920
gggacacctg ttgaggaact tagagtgttt gttcaagctg tcagaacatg gaatccagag      1980
ttgatcaacg gtttgccaga gcaagctaaa atcttgttta tgggcttata caaaacagtt      2040
aacacaattg cagaggaagc attcatggca cagaaaagag acgtccatca tcatttgaaa      2100
cactattggg acaagttgat aacaagtgcc ctaaaggagg ccgaatgggc agagtcaggt      2160
tacgtcccaa catttgatga atacatggaa gtagctgaaa tttctgttgc tctagaacca      2220
attgtctgta gtaccttgtt ctttgcgggt catagactag atgaggatgt tctagatagt      2280
tacgattacc atctagttat gcatttggta aacagagtcg gtagaatctt gaatgatata      2340
caaggcatga agagggaggc ttcacaaggt aagatctcat cagttcaaat ctacatggag      2400
gaacatccat ctgttccatc tgaggccatg gcgatcgctc atcttcaaga gttagttgat      2460
aattcaatgc agcaattgac atacgaagtt cttaggttca ctgcggttcc aaaaagttgt      2520
aagagaatcc acttgaatat ggctaaaatc atgcatgcct tctacaagga tactgatgga      2580
ttctcatccc ttactgcaat gacaggattc gtcaaaaagg ttcttttcga acctgtgcct      2640
gagtaa                                                                 2646
```

SEQ ID NO:56

```
MASSTLIQNR SCGVTSSMSS FQIFRGQPLR FPGTRTPAAV QCLKKRRCLR PTESVLESSP        60
GSGSYRIVTG PSGINPSSNG HLQEGSLTHR LPIPMEKSID NFQSTLYVSD IWSETLQRTE       120
CLLQVTENVQ MNEWIEEIRM YFRNMTLGEI SMSPYDTAWV ARVPALDGSH GPQFHRSLQW       180
IIDNQLPDGD WGEPSLFLGY DRVCNTLACV IALKTWGVGA QNVERGIQFL QSNIYKMEED       240
DANHMPIGFE IVFPAMMEDA KALGLDLPYD ATILQQISAE REKKMKKIPM AMVYKYPTTL       300
LHSLEGLHRE VDWNKLLQLQ SENGSFLYSP ASTACALMYT KDVKCFDYLN QLLIKFDHAC       360
PNVYPVDLFE RLWMVDRLQR LGISRYFERE IRDCLQYVYR YWKDCGIGWA SNSSVQDVDD       420
TAMAFRLLRT HGFDVKEDCF RQFFKDGEFF CFAGQSSQAV TGMFNLSRAS QTLFPGESLL       480
KKARTFSRNF LRTKHENNEC FDKWIITKDL AGEVEYNLTF PWYASLPRLE HRTYLDQYGI       540
DDIWIGKSLY KMPAVTNEVF LKLAKADFNM CQALHKKELE QVIKWNASCQ FRDLEFARQK       600
SVECYFAGAA TMFEPEMVQA RLVWARCCVL TTVLDDYFDH GTPVEELRVF VQAVRTWNPE       660
LINGLPEQAK ILFMGLYKTV NTIAEEAFMA QKRDVHHHLK HYWDKLITSA LKEAEWAESG       720
YVPTFDEYME VAEISVALEP IVCSTLFFAG HRLDEDVLDS YDYHLVMHLV NRVGRILNDI       780
QGMKREASQG KISSVQIYME EHPSVPSEAM AIAHLQELVD NSMQQLTYEV LRFTAVPKSC       840
KRIHLNMAKI MHAFYKDTDG FSSLTAMTGF VKKVLFEPVP E                           881
```

SEQ ID NO:57

```
atgcctggta aaattgaaaa tggtacccca aaggacctca agactggaaa tgattttgtt        60
tctgctgcta agagtttact agatcgagct ttcaaaagtc atcattccta ctacggatta       120
tgctcaactt catgtcaagt ttatgataca gcttgggttg caatgattcc aaaaacaaga       180
gataatgtaa aacagtggtt gtttccagaa tgtttccatt acctcttaaa aacacaagcc       240
gcagatggct catggggttc attgcctaca acacagacag cgggtatcct agatacagcc       300
tcagctgtgc tggcattatt gtgccacgca caagagcctt tacaaatatt ggatgtatct       360
ccagatgaaa tggggttgag aatagaacac ggtgtcacat ccttgaaacg tcaattagca       420
gtttggaatg atgtggagga caccaaccat attggcgtcg agtttatcat accagcctta       480
ctttccatgc tagaaaagga attagatgtt ccatcttttg aatttccatg taggtccatc       540
ttagagagaa tgcacgggga gaaattaggt catttcgacc tggaacaagt ttacggcaag       600
ccaagctcat tgttgcactc attggaagca tttctcggta agctagattt tgatcgacta       660
tcacatcacc tataccacgg cagtatgatg gcatctccat cttcaacggc tgcttatctt       720
attggggcta caaaatggga tgacgaagcc gaagattacc taagacatgt aatgcgtaat       780
```

```
ggtgcaggac atgggaatgg aggtatttct ggtacatttc caactactca tttcgaatgt    840
agctggatta tagcaacgtt gttaaaggtt ggctttactt tgaagcaaat tgacggcgat    900
ggcttaagag gtttatcaac catcttactt gaggcgcttc gtgatgagaa tggtgtcata    960
ggctttgccc ctagaacagc agatgtagat gacacagcca aagctctatt ggccttgtca   1020
ttggtaaacc agccagtgtc acctgatatc atgattaagg tctttgaggg caaagaccat   1080
tttaccactt ttggttcaga aagagatcca tcattgactt ccaacctgca cgtcctttta   1140
tctttactta aacaatctaa cttgtctcaa taccatcctc aaatcctcaa aacaacatta   1200
ttcacttgta gatggtggtg ggttccgat cattgtgtca aagacaaatg gaatttgagt   1260
cacctatatc caactatgtt gttggttgaa gccttcactg aagtgctcca tctcattgac   1320
ggtggtgaat tgtctagtct gtttgatgaa tcctttaagt gtaagattgg tcttagcatc   1380
tttcaagcgg tacttagaat aatcctcacc caagacaacg acggctcttg gagaggatac   1440
agagaacaga cgtgttacgc aatattggct ttagttcaag cgagacatgt atgctttttc   1500
actcacatgg ttgacagact gcaatcatgt gttgatcgag gtttctcatg gttgaaatct   1560
tgctcttttc attctcaaga cctgacttgg acctctaaaa cagcttatga agtgggtttc   1620
gtagctgaag catataaact agctgcttta caatctgctt ccctggaggt tcctgctgcc   1680
accattggac attctgtcac gtctgccgtt ccatcaagtg atcttgaaaa atacatgaga   1740
ttggtgagaa aaactgcgtt attctctcca ctggatgagt ggggtctaat ggcttctatc   1800
atcgaatctt catttttcgt accattactg caggcacaaa gagttgaaat ataccctaga   1860
gataatatca aggtggacga agataagtac ttgtctatta tcccattcac atgggtcgga   1920
tgcaataata ggtctagaac tttcgcaagt aacagatggc tatacgatat gatgtacctt   1980
tcattactcg gctatcaaac cgacgagtac atggaagctg tagctggcc agtgtttggg   2040
gatgtttcct tgttacatca aacaattgat aaggtgattg ataatacaat gggtaacctt   2100
gcgagagcca atggaacagt acacagtggt aatggacatc agcacgaatc tcctaatata   2160
ggtcaagtcg aggacacctt gactcgtttc acaaattcag tcttgaatca caaagacgtc   2220
cttaactcta gctcatctga tcaagatact ttgagaagag agtttagaac attcatgcac   2280
gctcatataa cacaaatcga agataactca cgattcagta agcaagcctc atccgatgcg   2340
ttttcctctc ctgaacaatc ttactttcaa tgggtgaact caactggtgg ctcacatgtc   2400
gcttgcgcct attcatttgc cttctctaat tgcctcatgt ctgcaaattt gttgcagggt   2460
aaagacgcat ttccaagcgg aacgcaaaag tacttaatct cctctgttat gagacatgcc   2520
acaaacatgt gtagaatgta taacgacttt ggctctattg ccagagacaa cgctgagaga   2580
aatgttaata gtattcattt tcctgagttt actctctgta acggaacttc tcaaaaccta   2640
gatgaaagga aggaaagact tctgaaaatc gcaacttacg aacaagggta tttggataga   2700
gcactagagg ccttggaaag acagagtaga gatgatgccg gagacagagc tggatctaaa   2760
gatatgagaa agttgaaaat cgttaagtta ttctgtgatg ttacggactt atacgatcag   2820
ctctacgtta tcaaagattt gtcatcctct atgaagtaa                          2859
```

SEQ ID NO:58

```
MPGKIENGTP KDLKTGNDFV SAAKSLLDRA FKSHHSYYGL CSTSCQVYDT AWVAMIPKTR     60
DNVKQWLFPE CFHYLLKTQA ADGSWGSLPT TQTAGILDTA SAVLALLCHA QEPLQILDVS    120
PDEMGLRIEH GVTSLKRQLA VWNDVEDTNH IGVEFIIPAL LSMLEKELDV PSFEFPCRSI    180
LERMHGEKLG HFDLEQVYGK PSSLLHSLEA FLGKLDFDRL SHHLYHGSMM ASPSSTAAYL    240
IGATKWDDEA EDYLRHVMRN GAGHGNGGIS GTFPTTHFEC SWIIATLLKV GFTLKQIDGD    300
GLRGLSTILL EALRDENGVI GFAPRTADVD DTAKALLALS LVNQPVSPDI MIKVFEGKDH    360
FTTFGSERDP SLTSNLHVLL SLLKQSNLSQ YHPQILKTTL FTCRWWWGSD HCVKDKWNLS    420
HLYPTMLLVE AFTEVLHLID GGELSSLFDE SFKCKIGLSI FQAVLRIILT QDNDGSWRGY    480
REQTCYAILA LVQARHVCFF THMVDRLQSC VDRGFSWLKS CSFHSQDLTW TSKTAYEVGF    540
VAEAYKLAAL QSASLEVPAA TIGHSVTSAV PSSDLEKYMR LVRKTALFSP LDEWGLMASI    600
IESSFFVPLL QAQRVEIYPR DNIKVDEDKY LSIIPFTWVG CNNRSRTFAS NRWLYDMMYL    660
SLLGYQTDEY MEAVAGPVFG DVSLLHQTID KVIDNTMGNL ARANGTVHSG NGHQHESPNI    720
GQVEDTLTRF TNSVLNHKDV LNSSSSDQDT LRREFRTFMH AHITQIEDNS RFSKQASSDA    780
FSSPEQSYFQ WVNSTGGSHV ACAYSFAFSN CLMSANLLQG KDAFPSGTQK YLISSVMRHA    840
TNMCRMYNDF GSIARDNAER NVNSIHFPEF TLCNGTSQNL DERKERLLKI ATYEQGYLDR    900
ALEALERQSR DDAGDRAGSK DMRKLKIVKL FCDVTDLYDQ LYVIKDLSSS MK               952
```

SEQ ID NO:59

```
atggatgctg tgacgggttt gttaactgtc ccagcaaccg ctataactat tggtggaact     60
gctgtagcat tggcggtagc gctaatcttt tggtacctga aatcctacac atcagctaga    120
```

```
agatcccaat caaatcatct tccaagagtg cctgaagtcc caggtgttcc attgttagga      180
aatctgttac aattgaagga gaaaaagcca tacatgactt ttacgagatg ggcagcgaca      240
tatggaccta tctatagtat caaaactggg gctacaagta tggttgtggt atcatctaat      300
gagatagcca aggaggcatt ggtgaccaga ttccaatcca tatctacaag gaacttatct      360
aaagccctga aagtacttac agcagataag acaatggtcg caatgtcaga ttatgatgat      420
tatcataaaa cagttaagag acacatactg accgccgtct tgggtcctaa tgcacagaaa      480
aagcatagaa ttcacagaga tatcatgatg gataacatat ctactcaact tcatgaattc      540
gtgaaaaaca acccagaaca ggaagaggta gaccttagaa aaatctttca atctgagtta      600
ttcggcttag ctatgagaca agccttagga aaggatgttg aaagtttgta cgttgaagac      660
ctgaaaatca ctatgaatag agacgaaatc tttcaagtcc ttgttgttga tccaatgatg      720
ggagcaatcg atgttgattg gagagacttc tttccatacc taaagtgggt cccaaacaaa      780
aagttcgaaa atactattca acaaatgtac atcagaagag aagctgttat gaaatcttta      840
atcaaagagc acaaaaagag aatagcgtca ggcgaaaagc taaatagtta tatcgattac      900
cttttatctg aagctcaaac tttaaccgat cagcaactat tgatgtcctt gtgggaacca      960
atcattgaat cttcagatac aacaatggtc acaacagaat gggcaatgta cgaattagct     1020
aaaaacccta aattgcaaga taggttgtac agagacatta agtccgtctg tggatctgaa     1080
aagataaccg aagagcatct atcacagctg ccttacatta cagctatttt ccacgaaaca     1140
ctgagaagac actcaccagt tcctatcatt cctctaagac atgtacatga agataccgtt     1200
ctaggcggct accatgttcc tgctggcaca gaacttgccg ttaacatcta cggttgcaac     1260
atggacaaaa acgtttggga aaatccagag gaatggaacc cagaaagatt catgaaagag     1320
aatgagacaa ttgattttca aaagacgatg gccttcggtg gtggtaagag agtttgtgct     1380
ggttccttgc aagccctttt aactgcatct attgggattg ggagaatggt tcaagagttc     1440
gaatggaaac tgaaggatat gactcaagag gaagtgaaca cgataggcct aactacacaa     1500
atgttaagac cattgagagc tattatcaaa cctaggatct aa                        1542
```

SEQ ID NO:60

```
MDAVTGLLTV PATAITIGGT AVALAVALIF WYLKSYTSAR RSQSNHLPRV PEVPGVPLLG       60
NLLQLKEKKP YMTFTRWAAT YGPIYSIKTG ATSMVVVSSN EIAKEALVTR FQSISTRNLS      120
KALKVLTADK TMVAMSDYDD YHKTVKRHIL TAVLGPNAQK KHRIHRDIMM DNISTQLHEF      180
VKNNPEQEEV DLRKIFQSEL FGLAMRQALG KDVESLYVED LKITMNRDEI FQVLVVDPMM      240
GAIDVDWRDF FPYLKWVPNK KFENTIQQMY IRREAVMKSL IKEHKKRIAS GEKLNSYIDY      300
LLSEAQTLTD QQLLMSLWEP IIESSDTTMV TTEWAMYELA KNPKLQDRLY RDIKSVCGSE      360
KITEEHLSQL PYITAIFHET LRRHSPVPII PLRHVHEDTV LGGYHVPAGT ELAVNIYGCN      420
MDKNVWENPE EWNPERFMKE NETIDFQKTM AFGGGKRVCA GSLQALLTAS IGIGRMVQEF      480
EWKLKDMTQE EVNTIGLTTQ MLRPLRAIIK PRI                                  513
```

SEQ ID NO:61

```
aagcttacta gtaaaatgga cggtgtcatc gatatgcaaa ccattccatt gagaaccgct       60
attgctattg gtggtactgc tgttgctttg gttgttgcat tatacttttg gttcttgaga      120
tcctacgctt ccccatctca tcattctaat catttgccac cagtacctga agttccaggt      180
gttccagttt tgggtaattt gttgcaattg aaagaaaaaa agccttacat gaccttcacc      240
aagtgggctg aaatgtatgg tccaatctac tctattagaa ctggtgctac ttccatggtt      300
gttgtctctt ctaacgaaat cgccaaagaa gttgttgtta ccagattccc atctatctct      360
accagaaaat tgtcttacgc cttgaaggtt ttgaccgaag ataagtctat ggttgccatg      420
tctgattatc acgattacca taagaccgtc aagagacata ttttgactgc tgttttgggt      480
ccaaacgccc aaaaaaagtt tagagcacat agagacacca tgatggaaaa cgtttccaat      540
gaattgcatg ccttcttcga aaagaaccca aatcaagaag tcaacttgag aaagatcttc      600
caatcccaat tattcggttt ggctatgaag caagccttgg gtaaagatgt tgaatccatc      660
tacgttaagg atttggaaac caccatgaag agagaagaaa tcttcgaagt tttggttgtc      720
gatccaatga tgggtgctat tgaagttgat tggagagact tttcccata cttgaaatgg       780
gttccaaaca agtccttcga aaacatcatc catagaatgt acactagaag agaagctgtt      840
atgaaggcct tgatccaaga acacaagaaa agaattgcct ccggtgaaaa cttgaactcc      900
tacattgatt acttgttgtc tgaagcccaa accttgaccg ataagcaatt attgatgtct      960
ttgtgggaac ctattatcga atcttctgat accactatgg ttactactga atgggctatg     1020
tacgaattgg ctaagaatcc aaacatgcaa gacagattat acgaagaaat ccaatccgtt     1080
tgcggttccg aaaagattac tgaagaaaac ttgtcccaat tgccatactt gtacgctgtt     1140
ttccaagaaa ctttgagaaa gcactgtcca gttcctatta tgccattgag atatgttcac     1200
```

```
gaaaacaccg ttttgggtgg ttatcatgtt ccagctggta ctgaagttgc tattaacatc      1260
tacggttgca acatggataa gaaggtctgg gaaaatccag aagaatggaa tccagaaaga      1320
ttcttgtccg aaaaagaatc catggacttg tacaaaacta tggcttttgg tggtggtaaa      1380
agagtttgcg ctggttcttt acaagccatg gttatttctt gcattggtat cggtagattg      1440
gtccaagatt ttgaatggaa gttgaaggat gatgccgaag aagatgttaa cactttgggt      1500
ttgactaccc aaaagttgca tccattattg gccttgatta acccaagaaa gtaactcgag      1560
ccgcgg                                                                 1566
```

SEQ ID NO:62

```
MDGVIDMQTI PLRTAIAIGG TAVALVVALY FWFLRSYASP SHHSNHLPPV PEVPGVPVLG        60
NLLQLKEKKP YMTFTKWAEM YGPIYSIRTG ATSMVVVSSN EIAKEVVVTR FPSISTRKLS       120
YALKVLTEDK SMVAMSDYHD YHKTVKRHIL TAVLGPNAQK KFRAHRDTMM ENVSNELHAF       180
FEKNPNQEVN LRKIFQSQLF GLAMKQALGK DVESIYVKDL ETTMKREEIF EVLVVDPMMG       240
AIEVDWRDFF PYLKWVPNKS FENIIHRMYT RREAVMKALI QEHKKRIASG ENLNSYIDYL       300
LSEAQTLTDK QLLMSLWEPI IESSDTTMVT TEWAMYELAK NPNMQDRLYE EIQSVCGSEK       360
ITEENLSQLP YLYAVFQETL RKHCPVPIMP LRYVHENTVL GGYHVPAGTE VAINIYGCNM       420
DKKVWENPEE WNPERFLSEK ESMDLYKTMA FGGGKRVCAG SLQAMVISCI GIGRLVQDFE       480
WKLKDDAEED VNTLGLTTQK LHPLLALINP RK                                     512
```

SEQ ID NO:63

```
atggccaccc tccttgagca tttccaagct atgccctttg ccatccctat tgcactggct        60
gctctgtctt ggctgttcct cttttacatc aaagtttcat tcttttccaa caagagtgct       120
caggctaagc tccctcctgt gccagtggtt cctgggctgc cggtgattgg gaatttactg       180
caactcaagg agaagaaacc ctaccagact tttacaaggt gggctgagga gtatggacca       240
atctattcta tcaggactgg tgcttccacc atggtcgttc tcaataccac ccaagttgca       300
aaagaggcca tggtgaccag atatttatcc atctcaacca gaaagctatc aaacgcacta       360
aagattctta ctgctgataa atgtatggtt gcaataagtg actacaacga ttttcacaag       420
atgataaagc gatacatact ctcaaatgtt cttggaccta gtgctcagaa gcgtcaccgg       480
agcaacagag ataccttgag agctaatgtc tgcagccgat tgcattctca agtaaagaac       540
tctcctcgag aagctgtgaa tttcagaaga gtttttgagt gggaactctt tggaattgca       600
ttgaagcaag cctttggaaa ggacatagaa aagcccattt atgtggagga acttggcact       660
acactgtcaa gagatgagat ctttaaggtt ctagtgcttg acataatgga gggtgcaatt       720
gaggttgatt ggagagattt cttcccttac ctgagatgga ttccgaatac gcgcatggaa       780
acaaaaattc agcgactcta tttccgcagg aaagcagtga tgactgccct gatcaacgag       840
cagaagaagc gaattgcttc aggagaggaa atcaactgtt atatcgactt cttgcttaag       900
gaagggaaga cactgacaat ggaccaaata agtatgttgc tttgggagac ggttattgaa       960
acagcagata ctacaatggt aacgacagaa tgggctatgt atgaagttgc taaagactca      1020
aagcgtcagg atcgtctcta tcaggaaatc caaaaggttt gtggatcgga gatggttaca      1080
gaggaatact tgtcccaact gccgtacctg aatgcagttt tccatgaaac gctaaggaag      1140
cacagtccgg ctgcgttagt tcctttaaga tatgcacatg aagataccca actaggaggt      1200
tactacattc cagctggaac tgagattgct ataaacatat acgggtgtaa catggacaag      1260
catcaatggg aaagccctga ggaatggaaa ccggagagat tttggaccc gaaatttgat      1320
cctatggatt tgtacaagac catggctttt ggggctggaa agagggtatg tgctggttct      1380
cttcaggcaa tgttaatagc gtgcccgacg attggtaggc tggtgcagga gtttgagtgg      1440
aagctgagag atggagaaga agaaaatgta gatactgttg ggctcaccac tcacaaacgc      1500
tatccaatgc atgcaatcct gaagccaaga agtta                                 1535
```

SEQ ID NO:64

```
atggctacct tgttggaaca ttttcaagct atgccattcg ctattccaat tgctttggct        60
gctttgtctt ggttgttttt gttctacatc aaggtttctt tcttctccaa caaatccgct       120
caagctaaat tgccaccagt tccagttgtt ccaggtttgc cagttattgg taatttgttg       180
caattgaaag aaaagaagcc ataccaaacc ttcactagat gggctgaaga atatggtcca       240
atctactcta ttagaactgg tgcttctact atggttgtct tgaacactac tcaagttgcc       300
aaagaagcta tggttaccag atacttgtct atctctacca gaaagttgtc caacgccttg       360
aaaattttga ccgctgataa gtgcatggtt gccatttctg attacaacga tttccacaag       420
atgatcaaga gatatatctt gtctaacgtt ttgggtccat ctgcccaaaa aagacataga       480
tctaacagag ataccttgag agccaacgtt tgttctagat tgcattccca agttaagaac       540
```

tctccaagag aagctgtcaa ctttagaaga gttttcgaat gggaattatt cggtatcgct 600
ttgaaacaag ccttcggtaa ggatattgaa aagccaatct acgtcgaaga attgggtact 660
actttgtcca gagatgaaat cttcaaggtt ttggtcttgg acattatgga aggtgccatt 720
gaagttgatt ggagagattt tttcccatac ttgcgttgga ttccaaacac cagaatggaa 780
actaagatcc aaagattata ctttagaaga aaggccgtta tgaccgcctt gattaacgaa 840
caaaagaaaa gaattgcctc cggtgaagaa atcaactgct acatcgattt cttgttgaaa 900
gaaggtaaga ccttgaccat ggaccaaatc tctatgttgt tgtgggaaac cgttattgaa 960
actgctgata ccacaatggt tactactgaa tgggctatgt acgaagttgc taaggattct 1020
aaaagacaag acagattata ccaagaaatc caaaaggtct gcggttctga aatggttaca 1080
gaagaatact tgtcccaatt gccatacttg aatgctgttt tccacgaaac tttgagaaaa 1140
cattctccag ctgctttggt tccattgaga tatgctcatg aagatactca attgggtggt 1200
tattacattc cagccggtac tgaaattgcc attaacatct acggttgcaa catggacaaa 1260
caccaatggg aatctccaga agaatggaag ccagaaagat tttggatcc taagtttgac 1320
ccaatggact tgtacaaaac tatggctttt ggtgctggta aaagagtttg cgctggttct 1380
ttacaagcta tgttgattgc ttgtccaacc atcggtagat tggttcaaga atttgaatgg 1440
aagttgagag atggtgaaga agaaaacgtt gatactgttg gtttgaccac ccataagaga 1500
tatccaatgc atgctatttt gaagccaaga tcttaa 1536

SEQ ID NO:65

aagcttacta gtaaaatggc ctccatcacc catttcttac aagattttca agctactcca 60
ttcgctactg cttttgctgt tggtggtgtt tctttgttga tattcttctt cttcatccgt 120
ggtttccact ctactaagaa aaacgaatat tacaagttgc caccagttcc agttgttcca 180
ggtttgccag ttgttggtaa tttgttgcaa ttgaaagaaa agaagccata caagactttc 240
ttgagatggg ctgaaattca tggtccaatc tactctatta gaactggtgc ttctaccatg 300
gttgttgtta actctactca tgttgccaaa gaagctatgg ttaccagatt ctcttcaatc 360
tctaccagaa agttgtccaa ggctttggaa ttattgacct ccaacaaatc tatggttgcc 420
acctctgatt acaacgaatt tcacaagatg gtcaagaagt acatcttggc cgaattattg 480
ggtgctaatg ctcaaaagag acacagaatt catagagaca ccttgatcga aaacgtcttg 540
aacaaattgc atgcccatac caagaattct ccattgcaag ctgttaactt cagaaagatc 600
ttcgaatctg aattattcgg tttggctatg aagcaagcct tgggttatga tgttgattcc 660
ttgttcgttg aagaattggg tactaccttg tccagagaag aaatctacaa cgttttggtc 720
agtgacatgt tgaagggtgc tattgaagtt gattggagag actttttccc atacttgaaa 780
tggatcccaa acaagtcctt cgaaatgaag attcaaagat tggcctctag aagacaagcc 840
gttatgaact ctattgtcaa agaacaaaag aagtccattg cctctggtaa gggtgaaaac 900
tgttacttga attacttgtt gtccgaagct aagactttga ccgaaaagca aatttccatt 960
ttggcctggg aaaccattat tgaaactgct gatacaactg ttgttaccac tgaatgggct 1020
atgtacgaat tggctaaaaa cccaaagcaa caagacagat tatacaacga aatccaaaac 1080
gtctgcggta ctgataagat taccgaagaa catttgtcca agttgcctta cttgtctgct 1140
gtttttcacg aaaccttgag aaagtattct ccatctccat tggttccatt gagatacgct 1200
catgaagata ctcaattggg tggttattat gttccagccg gtactgaaat tgctgttaat 1260
atctacggtt gcaacatgga caagaatcaa tgggaaactc cagaagaatg gaagccagaa 1320
agatttttgg acgaaaagta cgatccaatg gacatgtaca agactatgtc ttttggttcc 1380
ggtaaaagag tttgcgctgg ttctttacaa gctagtttga ttgcttgtac ctccatcggt 1440
agattggttc aagaatttga atggagattg aaagacggtg aagttgaaaa cgttgatacc 1500
ttgggtttga ctacccataa gttgtatcca atgcaagcta tcttgcaacc tagaaactga 1560
ctcgagccgc gg 1572

SEQ ID NO:66

MASITHFLQD FQATPFATAF AVGGVSLLIF FFFIRGFHST KKNEYYKLPP VPVVPGLPVV 60
GNLLQLKEKK PYKTFLRWAE IHGPIYSIRT GASTMVVVNS THVAKEAMVT RFSSISTRKL 120
SKALELLTSN KSMVATSDYN EFHKMVKKYI LAELLGANAQ KRHRIHRDTL IENVLNKLHA 180
HTKNSPLQAV NFRKIFESEL FGLAMKQALG YDVDSLFVEE LGTTLSREEI YNVLVSDMLK 240
GAIEVDWRDF FPYLKWIPNK SFEMKIQRLA SRRQAVMNSI VKEQKKSIAS GKGENCYLNY 300
LLSEAKTLTE KQISILAWET IIETADTTVV TTEWAMYELA KNPKQQDRLY NEIQNVCGTD 360
KITEEHLSKL PYLSAVFHET LRKYSPSPLV PLRYAHEDTQ LGGYYVPAGT EIAVNIYGCN 420
MDKNQWETPE EWKPERFLDE KYDPMDMYKT MSFGSGKRVC AGSLQASLIA CTSIGRLVQE 480
FEWRLKDGEV ENVDTLGLTT HKLYPMQAIL QPRN 514

SEQ ID NO:67
atgatttcct tgttgttggg ttttgttgtc tcctccttct tgtttatctt cttcttgaaa 60
aaattgttgt tcttcttcag tcgtcacaaa atgtccgaag tttctagatt gccatctgtt 120
ccagttccag gttttccatt gattggtaac ttgttgcaat tgaaagaaaa gaagccacac 180
aagactttca ccaagtggtc tgaattatat ggtccaatct actctatcaa gatgggttcc 240
tcttctttga tcgtcttgaa ctctattgaa accgccaaag aagctatggt cagtagattc 300
tcttcaatct ctaccagaaa gttgtctaac gctttgactg ttttgacctg caacaaatct 360
atggttgcta cctctgatta cgatgacttt cataagttcg tcaagagatg cttgttgaac 420
ggtttgttgg gtgctaatgc tcaagaaaga aaaagacatt acagagatgc cttgatcgaa 480
aacgttacct ctaaattgca tgcccatacc agaaatcatc cacaagaacc agttaacttc 540
agagccattt tcgaacacga attattcggt gttgctttga aacaagcctt cggtaaagat 600
gtcgaatcca tctatgtaaa agaattgggt gtcaccttgt ccagagatga aattttcaag 660
gttttggtcc acgacatgat ggaaggtgct attgatgttg attggagaga tttcttccca 720
tacttgaaat ggatcccaaa caactctttc gaagccagaa ttcaacaaaa gcacaagaga 780
agattggctg ttatgaacgc cttgatccaa gacagattga atcaaaacga ttccgaatcc 840
gatgatgact gctacttgaa tttcttgatg tctgaagcta agaccttgac catggaacaa 900
attgctattt tggtttggga aaccattatc gaaactgctg ataccacttt ggttactact 960
gaatgggcta tgtacgaatt ggccaaacat caatctgttc aagatagatt attcaaagaa 1020
atccaatccg tctgcggtgg tgaaaagatc aaagaagaac aattgccaag attgccttac 1080
gtcaatggtg tttttcacga aaccttgaga aagtattctc cagctccatt ggttccaatt 1140
agatacgctc atgaagatac ccaaattggt ggttatcata ttccagccgg ttctgaaatt 1200
gccattaaca tctacggttg caacatggat aagaagagat gggaaagacc tgaagaatgg 1260
tggccagaaa gatttttgga agatagatac gaatcctccg acttgcataa gactatggct 1320
tttggtgctg gtaaaagagt ttgtgctggt gctttacaag ctagtttgat ggctggtatt 1380
gctatcggta gattggttca agaattcgaa tggaagttga gagatggtga agaagaaaac 1440
gttgatactt acggtttgac ctcccaaaag ttgtatccat tgatggccat tatcaaccca 1500
agaagatctt aa 1512

SEQ ID NO:68
MASMISLLLG FVVSSFLFIF FLKKLLFFFS RHKMSEVSRL PSVPVPGFPL IGNLLQLKEK 60
KPHKTFTKWS ELYGPIYSIK MGSSSLIVLN SIETAKEAMV SRFSSISTRK LSNALTVLTC 120
NKSMVATSDY DDFHKFVKRC LLNGLLGANA QERKRHYRDA LIENVTSKLH AHTRNHPQEP 180
VNFRAIFEHE LFGVALKQAF GKDVESIYVK ELGVTLSRDE IFKVLVHDMM EGAIDVDWRD 240
FFPYLKWIPN NSFEARIQQK HKRRLAVMNA LIQDRLNQND SESDDDCYLN FLMSEAKTLT 300
MEQIAILVWE TIIETADTTL VTTEWAMYEL AKHQSVQDRL FKEIQSVCGG EKIKEEQLPR 360
LPYVNGVFHE TLRKYSPAPL VPIRYAHEDT QIGGYHIPAG SEIAINIYGC NMDKKRWERP 420
EEWWPERFLE DRYESSDLHK TMAFGAGKRV CAGALQASLM AGIAIGRLVQ EFEWKLRDGE 480
EENVDTYGLT SQKLYPLMAI INPRRS 506

SEQ ID NO:69
aagcttacta gtaaaatgga catgatgggt attgaagctg ttccatttgc tactgctgtt 60
gttttgggtg gtatttcctt ggttgttttg atcttcatca gaagattcgt ttccaacaga 120
aagagatccg ttgaaggttt gccaccagtt ccagatattc caggtttacc attgattggt 180
aacttgttgc aattgaaaga aaagaagcca cataagacct ttgctagatg ggctgaaact 240
tacggtccaa ttttctctat tagaactggt gcttctacca tgatcgtctt gaattcttct 300
gaagttgcca aagaagctat ggtcactaga ttctcttcaa tctctaccag aaagttgtcc 360
aacgccttga agattttgac cttcgataag tgtatggttg ccacctctga ttacaacgat 420
tttcacaaaa tggtcaaggg tttcatcttg agaaacgttt taggtgctcc agcccaaaaa 480
agacatagat gtcatagaga taccttgatc gaaaacatct ctaagtactt gcatgcccat 540
gttaagactt ctccattgga accagttgtc ttgaagaaga ttttcgaatc cgaaattttc 600
ggtttggctt tgaaacaagc cttgggtaag gatatcgaat ccatctatgt tgaagaattg 660
ggtactacct tgtccagaga agaaattttt gccgttttgg ttgttgatcc aatggctggt 720
gctattgaag ttgattggag agatttttttc ccatacttgt cctggattcc aaacaagtct 780
atggaaatga agatccaaag aatggatttt agaagaggtg ctttgatgaa ggccttgatt 840
ggtgaacaaa agaaaagaat cggttccggt gaagaaaaga actcctacat tgatttcttg 900
ttgtctgaag ctaccacttt gaccgaaaag caaattgcta tgttgatctg ggaaaccatc 960

atcgaaattt ccgatacaac tttggttacc tctgaatggg ctatgtacga attggctaaa 1020
gacccaaata gacaagaaat cttgtacaga gaaatccaca aggtttgcgg ttctaacaag 1080
ttgactgaag aaaacttgtc caagttgcca tacttgaact ctgttttcca cgaaaccttg 1140
agaaagtatt ctccagctcc aatggttcca gttagatatg ctcatgaaga tactcaattg 1200
ggtggttacc atattccagc tggttctcaa attgccatta acatctacgg ttgcaacatg 1260
aacaaaaagc aatgggaaaa tcctgaagaa tggaagccag aaagattctt ggacgaaaag 1320
tatgacttga tggacttgca taagactatg gcttttggtg gtggtaaaag agtttgtgct 1380
ggtgctttac aagcaatgtt gattgcttgc acttccatcg gtagattcgt tcaagaattt 1440
gaatggaagt tgatgggtgg tgaagaagaa aacgttgata ctgttgcttt gacctcccaa 1500
aaattgcatc caatgcaagc cattattaag gccagagaat gactcgagcc gcgg 1554

SEQ ID NO:70
MDMMGIEAVP FATAVVLGGI SLVVLIFIRR FVSNRKRSVE GLPPVPDIPG LPLIGNLLQL 60
KEKKPHKTFA RWAETYGPIF SIRTGASTMI VLNSSEVAKE AMVTRFSSIS TRKLSNALKI 120
LTFDKCMVAT SDYNDFHKMV KGFILRNVLG APAQKRHRCH RDTLIENISK YLHAHVKTSP 180
LEPVVLKKIF ESEIFGLALK QALGKDIESI YVEELGTTLS REEIFAVLVV DPMAGAIEVD 240
WRDFFPYLSW IPNKSMEMKI QRMDFRRGAL MKALIGEQKK RIGSGEEKNS YIDFLLSEAT 300
TLTEKQIAML IWETIIEISD TTLVTSEWAM YELAKDPNRQ EILYREIHKV CGSNKLTEEN 360
LSKLPYLNSV FHETLRKYSP APMVPVRYAH EDTQLGGYHI PAGSQIAINI YGCNMNKKQW 420
ENPEEWKPER FLDEKYDLMD LHKTMAFGGG KRVCAGALQA MLIACTSIGR FVQEFEWKLM 480
GGEEENVDTV ALTSQKLHPM QAIIKARE 508

SEQ ID NO:71
aagcttaaaa tgagtaagtc taatagtatg aattctacat cacacgaaac ccttttttcaa 60
caattggtct tgggtttgga ccgtatgcca ttgatggatg ttcactggtt gatctacgtt 120
gctttcggcg catggttatg ttcttatgtg atacatgttt tatcatcttc ctctacagta 180
aaagtgccag ttgttggata caggtctgta ttcgaaccta catggttgct tagacttaga 240
ttcgtctggg aaggtggctc tatcataggt caagggtaca ataagtttaa agactctatt 300
ttccaagtta ggaaattggg aactgatatt gtcattatac cacctaacta tattgatgaa 360
gtgagaaaat tgtcacagga caagactaga tcagttgaac ctttcattaa tgattttgca 420
ggtcaataca caagaggcat ggttttcttg caatctgact tacaaaaccg tgttatacaa 480
caaagactaa ctccaaaatt ggtttccttg accaaggtca tgaaggaaga gttggattat 540
gctttaacaa aagagatgcc tgatatgaaa aatgacgaat gggtagaagt agatatcagt 600
agtataatgg tgagattgat ttccaggatc tccgccagag tctttctagg gcctgaacac 660
tgtcgtaacc aggaatggtt gactactaca gcagaatatt cagaatcact tttcattaca 720
gggtttatct taagagttgt acctcatatc ttaagaccat tcatcgcccc tctattacct 780
tcatacagga ctctacttag aaacgtttca agtggtagaa gagtcatcgg tgacatcata 840
agatctcagc aaggggatgg taacgaagat atactttcct ggatgagaga tgctgccaca 900
ggagaggaaa agcaaatcga taacattgct cagagaatgt taattctttc tttagcatca 960
atccacacta ctgcgatgac catgacacat gccatgtacg atctatgtgc ttgccctgag 1020
tacattgaac cattaagaga tgaagttaaa tctgttgttg gggcttctgg ctgggacaag 1080
acagcgttaa acagatttca taagttggac tccttcctaa aagagtcaca aagattcaac 1140
ccagtattct tattgacatt caatagaatc taccatcaat ctatgacctt atcagatggc 1200
actaacattc catctggaac acgtattgct gttccatcac acgcaatgtt gcaagattct 1260
gcacatgtcc caggtccaac cccacctact gaatttgatg gattcagata tagtaagata 1320
cgttctgata gtaactacgc acaaaagtac ctattctcca tgaccgattc ttcaaacatg 1380
gctttcggat acggcaagta tgcttgtcca ggtagatttt acgcgtctaa tgagatgaaa 1440
ctaacattag ccattttgtt gctacaattt gagttcaaac taccagatgg taaaggtcgt 1500
cctagaaata tcactatcga ttctgatatg attccagacc caagagctag actttgcgtc 1560
agaaaaagat cacttagaga tgaatgaccg cgg 1593

SEQ ID NO:72
MSKSNSMNST SHETLFQQLV LGLDRMPLMD VHWLIYVAFG AWLCSYVIHV LSSSSTVKVP 60
VVGYRSVFEP TWLLRLRFVW EGGSIIGQGY NKFKDSIFQV RKLGTDIVII PPNYIDEVRK 120
LSQDKTRSVE PFINDFAGQY TRGMVFLQSD LQNRVIQQRL TPKLVSLTKV MKEELDYALT 180
KEMPDMKNDE WVEVDISSIM VRLISRISAR VFLGPEHCRN QEWLTTTAEY SESLFITGFI 240
LRVVPHILRP FIAPLLPSYR TLLRNVSSGR RVIGDIIRSQ QGDGNEDILS WMRDAATGEE 300

```
KQIDNIAQRM LILSLASIHT TAMTMTHAMY DLCACPEYIE PLRDEVKSVV GASGWDKTAL    360
NRFHKLDSFL KESQRFNPVF LLTFNRIYHQ SMTLSDGTNI PSGTRIAVPS HAMLQDSAHV    420
PGPTPPTEFD GFRYSKIRSD SNYAQKYLFS MTDSSNMAFG YGKYACPGRF YASNEMKLTL    480
AILLLQFEFK LPDGKGRPRN ITIDSDMIPD PRARLCVRKR SLRDE                    525
```

SEQ ID NO:73

```
aagcttaaaa tggaagatcc tactgtctta tatgcttgtc ttgccattgc agttgcaact      60
ttcgttgtta gatggtacag agatccattg agatccatcc caacagttgg tggttccgat     120
ttgcctattc tatcttacat cggcgcacta agatggacaa gacgtggcag agagatactt     180
caagagggat atgatggcta cagaggatct acattcaaaa tcgcgatgtt agaccgttgg     240
atcgtgatcg caaatggtcc taaactagct gatgaagtca gacgtagacc agatgaagag     300
ttaaacttta tggacggatt aggagcattc gtccaaacta agtacacctt aggtgaagct     360
attcataacg atccatacca tgtcgatatc ataagagaaa aactaacaag aggccttcca     420
gccgtgcttc ctgatgtcat tgaagagttg acacttgcgg ttagacagta cattccaaca     480
gaaggtgatg aatgggtgtc cgtaaactgt tcaaaggccg caagagatat tgttgctaga     540
gcttctaata gagtctttgt aggtttgcct gcttgcagaa accaaggtta cttagatttg     600
gcaatagact ttacattgtc tgttgtcaag gatagagcca tcatcaatat gtttccagaa     660
ttgttgaagc caatagttgg cagagttgta ggtaacgcca ccagaaatgt tcgtagagct     720
gttccttttg ttgctccatt ggtggaggaa agacgtagac ttatggaaga gtacggtgaa     780
gactggtctg aaaaacctaa tgatatgtta cagtggataa tggatgaagc tgcatccaga     840
gatagttcag tgaaggcaat cgcagagaga ttgttaatgg tgaacttcgc ggctattcat     900
acctcatcaa acactatcac tcatgctttg taccaccttg ccgaaatgcc tgaaactttg     960
caaccactta gagaagagat cgaaccatta gtcaaagagg agggctggac caaggctgct    1020
atgggaaaaa tgtggtggtt agattcattt ctaagagaat ctcaaagata caatggcatt    1080
aacatcgtat ctttaactag aatggctgac aaagatatta cattgagtga tggcacattt    1140
ttgccaaaag gtactctagt ggccgttcca gcgtattcta ctcatagaga tgatgctgtc    1200
tacgctgatg ccttagtatt cgatcctttc agattctcac gtatgagagc gagagaaggt    1260
gaaggtacaa agcaccagtt cgttaatact tcagtcgagt acgttccatt tggtcacgga    1320
aagcatgctt gtccaggaag attcttcgcc gcaaacgaat tgaaagcaat gttggcttac    1380
attgttctaa actatgatgt aaagttgcct ggtgacggta aacgtccatt gaacatgtat    1440
tggggtccaa cagttttgcc tgcaccagca ggccaagtat tgttcagaaa gagacaagtt    1500
agtctataac cgcgg                                                     1515
```

SEQ ID NO:74

```
MEDPTVLYAC LAIAVATFVV RWYRDPLRSI PTVGGSDLPI LSYIGALRWT RRGREILQEG     60
YDGYRGSTFK IAMLDRWIVI ANGPKLADEV RRRPDEELNF MDGLGAFVQT KYTLGEAIHN    120
DPYHVDIIRE KLTRGLPAVL PDVIEELTLA VRQYIPTEGD EWVSVNCSKA ARDIVARASN    180
RVFVGLPACR NQGYLDLAID FTLSVVKDRA IINMFPELLK PIVGRVVGNA TRNVRRAVPF    240
VAPLVEERRR LMEEYGEDWS EKPNDMLQWI MDEAASRDSS VKAIAERLLM VNFAAIHTSS    300
NTITHALYHL AEMPETLQPL REEIEPLVKE EGWTKAAMGK MWWLDSFLRE SQRYNGINIV    360
SLTRMADKDI TLSDGTFLPK GTLVAVPAYS THRDDAVYAD ALVFDPFRFS RMRAREGEGT    420
KHQFVNTSVE YVPFGHGKHA CPGRFFAANE LKAMLAYIVL NYDVKLPGDG KRPLNMYWGP    480
TVLPAPAGQV LFRKRQVSL                                                 499
```

SEQ ID NO:75

```
atggcatttt tctctatgat ttcaattttg ttgggatttg ttatttcttc tttcatcttc      60
atctttttct tcaaaaagtt acttagtttt agtaggaaaa acatgtcaga agtttctact     120
ttgccaagtg ttccagtagt gcctggtttt ccagttattg ggaatttgtt gcaactaaag     180
gagaaaaagc ctcataaaac tttcactaga tggtcagaga tatatggacc tatctactct     240
ataaagatgg gttcttcatc tcttattgta ttgaacagta cagaaactgc taaggaagca     300
atggtcacta gattttcatc aatatctacc agaaaattgt caaacgccct aacagttcta     360
acctgcgata agtctatggt cgccacttct gattatgatg acttccacaa attagttaag     420
agatgtttgc taaatggact tcttggtgct aatgctcaaa agagaaaaag acactacaga     480
gatgctttga ttgaaaatgt gagttccaag ctacatgcac acgctagaga tcatccacaa     540
gagccagtta actttagagc aattttcgaa cacgaattgt ttggtgtagc attaaagcaa     600
gccttcggta aagacgtaga atccatatac gtcaaggagt taggcgtaac attatcaaaa     660
gatgaaatct ttaaggtgct tgtacatgat atgatggagg gtgcaattga tgtagattgg     720
```

```
agagatttct tcccatattt gaaatggatc cctaataagt cttttgaagc taggatacaa      780
caaaagcaca agagaagact agctgttatg aacgcactta tacaggacag attgaagcaa      840
aatgggtctg aatcagatga tgattgttac cttaacttct taatgtctga ggctaaaaca      900
ttgactaagg aacagatcgc aatccttgtc tgggaaacaa tcattgaaac agcagatact      960
accttagtca caactgaatg ggccatatac gagctagcca aacatccatc tgtgcaagat     1020
aggttgtgta aggagatcca gaacgtgtgt ggtggagaga aattcaagga agagcagttg     1080
tcacaagttc cttaccttaa cggcgttttc catgaaacct tgagaaaata ctcacctgca     1140
ccattagttc ctattagata cgcccacgaa gatacacaaa tcggtggcta ccatgttcca     1200
gctgggtccg aaattgctat aaacatctac gggtgcaaca tggacaaaaa gagatgggaa     1260
agaccagaag attggtggcc agaaagattc ttagatgatg gcaaatatga aacatctgat     1320
ttgcataaaa caatggcttt cggagctggc aaaagagtgt gtgccggtgc tctacaagcc     1380
tccctaatgg ctggtatcgc tattggtaga ttggtccaag agttcgaatg gaaacttaga     1440
gatggtgaag aggaaaatgt cgatacttat gggttaacat ctcaaaagtt atacccacta     1500
atggcaatca tcaatcctag aagatcctaa                                      1530
```

SEQ ID NO:76

```
MAFFSMISIL LGFVISSFIF IFFFKKLLSF SRKNMSEVST LPSVPVVPGF PVIGNLLQLK       60
EKKPHKTFTR WSEIYGPIYS IKMGSSSLIV LNSTETAKEA MVTRFSSIST RKLSNALTVL      120
TCDKSMVATS DYDDFHKLVK RCLLNGLLGA NAQKRKRHYR DALIENVSSK LHAHARDHPQ      180
EPVNFRAIFE HELFGVALKQ AFGKDVESIY VKELGVTLSK DEIFKVLVHD MMEGAIDVDW      240
RDFFPYLKWI PNKSFEARIQ QKHKRRLAVM NALIQDRLKQ NGSESDDDCY LNFLMSEAKT      300
LTKEQIAILV WETIIETADT TLVTTEWAIY ELAKHPSVQD RLCKEIQNVC GGEKFKEEQL      360
SQVPYLNGVF HETLRKYSPA PLVPIRYAHE DTQIGGYHVP AGSEIAINIY GCNMDKKRWE      420
RPEDWWPERF LDDGKYETSD LHKTMAFGAG KRVCAGALQA SLMAGIAIGR LVQEFEWKLR      480
DGEEENVDTY GLTSQKLYPL MAIINPRRS                                        509
```

SEQ ID NO:77

```
atgcaatcag attcagtcaa agtctctcca tttgatttgg tttccgctgc tatgaatggc       60
aaggcaatgg aaaagttgaa cgctagtgaa tctgaagatc caacaacatt gcctgcacta      120
aagatgctag ttgaaaatag agaattgttg acactgttca caacttcctt cgcagttctt      180
attgggtgtc ttgtatttct aatgtggaga cgttcatcct ctaaaaagct ggtacaagat      240
ccagttccac aagttatcgt tgtaaagaag aaagagaagg agtcagaggt tgatgacggg      300
aaaaagaaag tttctatttt ctacggcaca caaacaggaa ctgccgaagg ttttgctaaa      360
gcattagtcg aggaagcaaa agtgagatat gaaaagacct ctttcaaggt tatcgatcta      420
gatgactacg ctgcagatga tgatgaatat gaggaaaaac tgaaaaagga atccttagcc      480
ttcttcttct tggccacata cggtgatggt gaacctactg ataatgctgc taacttctac      540
aagtggttca cagaaggcga cgataaaggt gaatggctga aaaagttaca atacggagta      600
tttggtttag gtaacagaca atatgaacat ttcaacaaga tcgctattgt agttgatgat      660
aaacttactg aaatgggagc caaaagatta gtaccagtag gattagggga tgatgatcag      720
tgtatagaag atgacttcac cgcctggaag gaattggtat ggccagaatt ggatcaactt      780
ttaagggacg aagatgatac ttctgtgact accccataca ctgcagccgt attggagtac      840
agagtggttt accatgataa accagcagac tcatatgctg aagatcaaac ccatacaaac      900
ggtcatgttg ttcatgatgc acagcatcct tcaagatcta atgtggcttt caaaaaggaa      960
ctacacacct ctcaatcaga taggtcttgt actcacttag aattcgatat ttctcacaca     1020
ggactgtctt acgaaactgg cgatcacgtt ggcgtttatt ccgagaactt gtccgaagtt     1080
gtcgatgaag cactaaaact gttagggtta tcaccagaca catacttctc agtccatgct     1140
gataaggagg atgggacacc tatcggtggt gcttcactac caccaccttt tcctccttgc     1200
acattgagag acgctctaac cagatacgca gatgtcttat cctcacctaa aaaggtagct     1260
ttgctggcat tggctgctca tgctagtgat cctagtgaag ccgataggtt aaagttcctg     1320
gcttcaccag ccggaaaaga tgaatatgca caatggatcg tcgccaacca acgttctttg     1380
ctagaagtga tgcaaagttt tccatctgcc aagcctccat taggtgtgtt cttcgcagca     1440
gtagctccac gtttacaacc aagatactac tctatcagtt catctcctaa gatgtctcct     1500
aacagaatac atgttacatg tgctttggtg tacgagacta ctccagcagg cagaattcac     1560
agaggattgt gttcaacctg gatgaaaaat gctgtccctt taacagagtc acctgattgc     1620
tctcaagcat ccattttcgt tagaacatca aatttcagac ttccagtgga tccaaaagtt     1680
ccagtcatta tgataggacc aggcactggt cttgccccat tcaggggctt tcttcaagag     1740
agattggcct tgaaggaatc tggtacagaa ttgggttctt ctatcttttt ctttggttgc     1800
```

```
cgtaatagaa aagttgactt tatctacgag gacgagctta acaattttgt tgagacagga      1860
gcattgtcag aattgatcgt cgcattttca agagaaggga ctgccaaaga gtacgttcag      1920
cacaagatga gtcaaaaagc ctccgatata tggaaacttc taagtgaagg tgcctatctt      1980
tatgtctgtg gcgatgcaaa gggcatggcc aaggatgtcc atagaactct gcatacaatt      2040
gttcaggaac aagggagtct ggattcttcc aaggctgaat tgtacgtcaa aaacttacag      2100
atgtctggaa gatacttaag agatgtttgg taa                                   2133
```

SEQ ID NO:78

```
MQSDSVKVSP FDLVSAAMNG KAMEKLNASE SEDPTTLPAL KMLVENRELL TLFTTSFAVL        60
IGCLVFLMWR RSSSKKLVQD PVPQVIVVKK KEKESEVDDG KKKVSIFYGT QTGTAEGFAK       120
ALVEEAKVRY EKTSFKVIDL DDYAADDDEY EEKLKKESLA FFFLATYGDG EPTDNAANFY       180
KWFTEGDDKG EWLKKLQYGV FGLGNRQYEH FNKIAIVVDD KLTEMGAKRL VPVGLGDDDQ       240
CIEDDFTAWK ELVWPELDQL LRDEDDTSVT TPYTAAVLEY RVVYHDKPAD SYAEDQTHTN       300
GHVVHDAQHP SRSNVAFKKE LHTSQSDRSC THLEFDISHT GLSYETGDHV GVYSENLSEV       360
VDEALKLLGL SPDTYFSVHA DKEDGTPIGG ASLPPPFPPC TLRDALTRYA DVLSSPKKVA       420
LLALAAHASD PSEADRLKFL ASPAGKDEYA QWIVANQRSL LEVMQSFPSA KPPLGVFFAA       480
VAPRLQPRYY SISSSPKMSP NRIHVTCALV YETTPAGRIH RGLCSTWMKN AVPLTESPDC       540
SQASIFVRTS NFRLPVDPKV PVIMIGPGTG LAPFRGFLQE RLALKESGTE LGSSIFFFGC       600
RNRKVDFIYE DELNNFVETG ALSELIVAFS REGTAKEYVQ HKMSQKASDI WKLLSEGAYL       660
YVCGDAKGMA KDVHRTLHTI VQEQGSLDSS KAELYVKNLQ MSGRYLRDVW                  710
```

SEQ ID NO:79

```
atgaaggtca gtccattcga attcatgtcc gctattatca agggtagaat ggacccatct        60
aactcctcat ttgaatctac tggtgaagtt gcctccgtta tctttgaaaa cagagaattg       120
gttgccatct tgaccacttc tattgctgtt atgattggtt gcttcgttgt cttgatgtgg       180
agaagagctg gttctagaaa ggttaagaat gtcgaattgc caaagccatt gattgtccat       240
gaaccagaac ctgaagttga agatggtaag aagaaggttt ccatcttctt cggtactcaa       300
actggtactg ctgaaggttt tgctaaggct ttggctgatg aagctaaagc tagatacgaa       360
aaggctacct tcagagttgt tgatttggat gattatgctg ccgatgatga ccaatacgaa       420
gaaaaattga agaacgaatc cttcgccgtt ttcttgttgg ctacttatgg tgatggtgaa       480
cctactgata atgctgctag attttacaag tggttcgccg aaggtaaaga aagaggtgaa       540
tggttgcaaa acttgcacta tgctgttttt ggtttgggta acagacaata cgaacacttc       600
aacaagattg ctaaggttgc cgacgaatta ttggaagctc aaggtggtaa tagattggtt       660
aaggttggtt taggtgatga cgatcaatgc atcgaagatg atttttctgc ttggagagaa       720
tctttgtggc cagaattgga tatgttgttg agagatgaag atgatgctac tactgttact       780
actccatata ctgctgctgt cttggaatac agagttgtct ttcatgattc tgctgatgtt       840
gctgctgaag ataagtcttg gattaacgct aatggtcatg ctgttcatga tgctcaacat       900
ccattcagat ctaacgttgt cgtcagaaaa gaattgcata cttctgcctc tgatagatcc       960
tgttctcatt tggaattcaa catttccggt tccgctttga attacgaaac tggtgatcat      1020
gttggtgtct actgtgaaaa cttgactgaa actgttgatg aagccttgaa cttgttgggt      1080
ttgtctccag aaacttactt ctctatctac accgataacg aagatggtac tccattgggt      1140
ggttcttcat tgccaccacc atttccatca tgtactttga gaactgcttt gaccagatac      1200
gctgatttgt tgaactctcc aaaaaagtct gctttgttgg ctttagctgc tcatgcttct      1260
aatccagttg aagctgatag attgagatac ttggcttctc cagctggtaa agatgaatat      1320
gcccaatctg ttatcggttc ccaaaagtct ttgttggaag ttatggctga attcccatct      1380
gctaaaccac cattaggtgt ttttttttgct gctgttgctc caagattgca acctagattc      1440
tactccattt catcctctcc aagaatggct ccatctagaa tccatgttac ttgtgctttg      1500
gtttacgata agatgccaac tggtagaatt cataagggtg tttgttctac ctggatgaag      1560
aattctgttc caatggaaaa gtcccatgaa tgttcttggg ctccaatttt cgttagacaa      1620
tccaatttta agttgccagc cgaatccaag gttccaatta tcatggttgg tccaggtact      1680
ggtttggctc cttttagagg tttttacaa gaaagattgg ccttgaaaga atccggtgtt       1740
gaattgggtc catccatttt gtttttcggt tgcagaaaca gaagaatgga ttacatctac      1800
gaagatgaat tgaacaactt cgttgaaacc ggtgctttgt ccgaattggt tattgctttt      1860
tctagagaag gtcctaccaa agaatacgtc caacataaga tggctgaaaa ggcttctgat      1920
atctggaact tgatttctga aggtgcttac ttgtacgttt gtggtgatgc taaaggtatg      1980
gctaaggatg ttcatagaac cttgcatacc atcatgcaag aacaaggttc tttggattct      2040
tccaaagctg aatccatggt caagaacttg caaatgaatg gtagatactt aagagatgtt      2100
```

tggtaa 2106

SEQ ID NO:80
MKVSPFEFMS AIIKGRMDPS NSSFESTGEV ASVIFENREL VAILTTSIAV MIGCFVVLMW 60
RRAGSRKVKN VELPKPLIVH EPEPEVEDGK KKVSIFFGTQ TGTAEGFAKA LADEAKARYE 120
KATFRVVDLD DYAADDDQYE EKLKNESFAV FLLATYGDGE PTDNAARFYK WFAEGKERGE 180
WLQNLHYAVF GLGNRQYEHF NKIAKVADEL LEAQGGNRLV KVGLGDDDQC IEDDFSAWRE 240
SLWPELDMLL RDEDDATTVT TPYTAAVLEY RVVFHDSADV AAEDKSWINA NGHAVHDAQH 300
PFRSNVVVRK ELHTSASDRS CSHLEFNISG SALNYETGDH VGVYCENLTE TVDEALNLLG 360
LSPETYFSIY TDNEDGTPLG GSSLPPPFPS CTLRTALTRY ADLLNSPKKS ALLALAAHAS 420
NPVEADRLRY LASPAGKDEY AQSVIGSQKS LLEVMAEFPS AKPPLGVFFA AVAPRLQPRF 480
YSISSSPRMA PSRIHVTCAL VYDKMPTGRI HKGVCSTWMK NSVPMEKSHE CSWAPIFVRQ 540
SNFKLPAESK VPIIMVGPGT GLAPFRGFLQ ERLALKESGV ELGPSILFFG CRNRRMDYIY 600
EDELNNFVET GALSELVIAF SREGPTKEYV QHKMAEKASD IWNLISEGAY LYVCGDAKGM 660
AKDVHRTLHT IMQEQGSLDS SKAESMVKNL QMNGRYLRDV W 701

SEQ ID NO:81
atggcagaat tagatacact tgatatagta gtattaggtg ttatcttttt gggtactgtg 60
gcatacttta ctaagggtaa attgtggggt gttaccaagg atccatacgc taacggattc 120
gctgcaggtg gtgcttccaa gcctggcaga actagaaaca tcgtcgaagc tatggaggaa 180
tcaggtaaaa actgtgttgt tttctacggc agtcaaacag gtacagcgga ggattacgca 240
tcaagacttg caaaggaagg aaagtccaga ttcggtttga acactatgat cgccgatcta 300
gaagattatg acttcgataa cttagacact gttccatctg ataacatcgt tatgtttgta 360
ttggctactt acggtgaagg cgaaccaaca gataacgccg tggatttcta tgagttcatt 420
actggcgaag atgcctcttt caatgagggc aacgatcctc cactaggtaa cttgaattac 480
gttgcgttcg gtctgggcaa caatacctac gaacactaca actcaatggt caggaacgtt 540
aacaaggctc tagaaaagtt aggagctcat agaattggag aagcaggtga gggtgacgac 600
ggagctggaa ctatggaaga ggacttttta gcttggaaag atccaatgtg ggaagccttg 660
gctaaaaaga tgggcttgga ggaaagagaa gctgtatatg aacctatttt cgctatcaat 720
gagagagatg atttgacccc tgaagcgaat gaggtatact tgggagaacc taataagcta 780
cacttggaag gtacagcgaa aggtccattc aactcccaca acccatatat cgcaccaatt 840
gcagaatcat acgaactttt ctcagctaag gatagaaatt gtctgcatat ggaaattgat 900
atttctggta gtaatctaaa gtatgaaaca ggcgaccata tcgcgatctg gcctaccaac 960
ccaggtgaag aggtcaacaa atttcttgac attctagatc tgtctggtaa gcaacattcc 1020
gtcgtaacag tgaaagcctt agaacctaca gccaaagttc cttttccaaa tccaactacc 1080
tacgatgcta tattgagata ccatctggaa atatgcgctc cagtttctag acagtttgtc 1140
tcaactttag cagcattcgc ccctaatgat gatatcaaag ctgagatgaa ccgtttggga 1200
tcagacaaag attacttcca cgaaaagaca ggaccacatt actacaatat cgctagattt 1260
ttggcctcag tctctaaagg tgaaaaatgg acaaagatac cattttctgc tttcatagaa 1320
ggccttacaa aactacaacc aagatactat tctatctctt cctctagttt agttcagcct 1380
aaaaagatta gtattactgc tgttgtcgaa tctcagcaaa ttccaggtag agatgaccca 1440
ttcagaggtg tagcgactaa ctacttgttc gctttgaagc agaaacaaaa cggtgatcca 1500
aatccagctc cttttggcca atcatacgag ttgacaggac caaggaataa gtatgatggt 1560
atacatgttc cagtccatgt aagacattct aactttaagc taccatctga tccaggcaaa 1620
cctattatca tgatcggtcc aggtaccggt gttgcccctt ttagaggctt cgtccaagag 1680
agggcaaaac aagccagaga tggtgtagaa gttggtaaaa cactgctgtt ctttggatgt 1740
agaaagagta cagaagattt catgtatcaa aaagagtggc aagagtacaa ggaagctctt 1800
ggcgacaaat tcgaaatgat tacagctttt tcaagagaag gatctaaaaa ggtttatgtt 1860
caacacagac tgaaggaaag atcaaaggaa gtttctgatc ttctatccca aaaagcatac 1920
ttctacgttt gcggagacgc cgcacatatg gcacgtgaag tgaacactgt gttagcacag 1980
atcatagcag aaggccgtgg tgtatcagaa gccaagggtg aggaaattgt caaaaacatg 2040
agatcagcaa atcaatacca agtgtgttct gatttcgtaa ctttacactg taaagagaca 2100
acatacgcga attcagaatt gcaagaggat gtctggagtt aa 2142

SEQ ID NO:82
MAELDTLDIV VLGVIFLGTV AYFTKGKLWG VTKDPYANGF AAGGASKPGR TRNIVEAMEE 60
SGKNCVVFYG SQTGTAEDYA SRLAKEGKSR FGLNTMIADL EDYDFDNLDT VPSDNIVMFV 120

```
LATYGEGEPT DNAVDFYEFI TGEDASFNEG NDPPLGNLNY VAFGLGNNTY EHYNSMVRNV    180
NKALEKLGAH RIGEAGEGDD GAGTMEEDFL AWKDPMWEAL AKKMGLEERE AVYEPIFAIN    240
ERDDLTPEAN EVYLGEPNKL HLEGTAKGPF NSHNPYIAPI AESYELFSAK DRNCLHMEID    300
ISGSNLKYET GDHIAIWPTN PGEEVNKFLD ILDLSGKQHS VVTVKALEPT AKVPFPNPTT    360
YDAILRYHLE ICAPVSRQFV STLAAFAPND DIKAEMNRLG SDKDYFHEKT GPHYYNIARF    420
LASVSKGEKW TKIPFSAFIE GLTKLQPRYY SISSSSLVQP KKISITAVVE SQQIPGRDDP    480
FRGVATNYLF ALKQKQNGDP NPAPFGQSYE LTGPRNKYDG IHVPVHVRHS NFKLPSDPGK    540
PIIMIGPGTG VAPFRGFVQE RAKQARDGVE VGKTLLFFGC RKSTEDFMYQ KEWQEYKEAL    600
GDKFEMITAF SREGSKKVYV QHRLKERSKE VSDLLSQKAY FYVCGDAAHM AREVNTVLAQ    660
IIAEGRGVSE AKGEEIVKNM RSANQYQVCS DFVTLHCKET TYANSELQED VWS           713
```

SEQ ID NO:83

```
atgcaatcgg aatccgttga agcatcgacg attgatttga tgactgctgt tttgaaggac      60
acagtgatcg atacagcgaa cgcatctgat aacggagact caaagatgcc gccggcgttg     120
gcgatgatgt tcgaaattcg tgatctgttg ctgattttga ctacgtcagt tgctgttttg     180
gtcggatgtt tcgttgtttt ggtgtggaag agatcgtccg ggaagaagtc cggcaaggaa     240
ttggagccgc cgaagatcgt tgtgccgaag aggcggctgg agcaggaggt tgatgatggt     300
aagaagaagg ttacgatttt cttcggaaca caaactggaa cggctgaagg tttcgctaag     360
gcacttttcg aagaagcgaa agcgcgatat gaaaaggcag cgtttaaagt gattgatttg     420
gatgattatg ctgctgattt ggatgagtat gcagagaagc tgaagaagga aacatatgct     480
ttcttcttct tggctacata tggagatggt gagccaactg ataatgctgc caaattttat     540
aaatggttta ctgagggaga cgagaaaggc gtttggcttc aaaaacttca atatggagta     600
tttggtcttg gcaacagaca atatgaacat ttcaacaaga ttggaatagt ggttgatgat     660
ggtctcaccg agcagggtgc aaaacgcatt gttcccgttg gtcttggaga cgacgatcaa     720
tcaattgaag acgatttttc ggcatggaaa gagttagtgt ggcccgaatt ggatctattg     780
cttcgcgatg aagatgacaa agctgctgca actccttaca cagctgcaat ccctgaatac     840
cgcgtcgtat ttcatgacaa acccgatgcg ttttctgatg atcatactca aaccaatggt     900
catgctgttc atgatgctca acatccatgc agatccaatg tggctgttaa aaaagagctt     960
catactcctg aatccgatcg ttcatgcaca catcttgaat ttgacatttc tcacactgga    1020
ttatcttatg aaactgggga tcatgttggt gtatactgtg aaaacctaat tgaagtagtg    1080
gaagaagctg ggaaattgtt aggattatca acagatactt atttctcgtt acatattgat    1140
aacgaagatg gttcaccact tggtggacct tcattacaac ctccttttcc tccttgtact    1200
ttaagaaaag cattgactaa ttatgcagat ctgttaagct ctcccaaaaa gtcaactttg    1260
cttgctctag ctgctcatgc ttccgatccc actgaagctg atcgtttaag atttcttgca    1320
tctcgcgagg gcaaggatga atatgctgaa tgggttgttg caaaccaaag aagtcttctt    1380
gaagtcatgg aagctttccc gtcagctaga ccgccacttg gtgttttctt tgcagcggtt    1440
gcaccgcgtt tacagcctcg ttactactct atttcttcct ccccaaagat ggaaccaaac    1500
aggattcatg ttacttgcgc gttggtttat gaaaaaactc ccgcaggtcg tatccacaaa    1560
ggaatctgct caacctggat gaagaacgct gtacctttga ccgaaagtca agattgcagt    1620
tgggcaccga tttttgttag aacatcaaac ttcagacttc caattgaccc gaaagtcccg    1680
gttatcatga ttggtcctgg aaccgggttg gctccattta ggggttttct tcaagaaaga    1740
ttggctctta aagaatccgg aaccgaactc gggtcatcta ttttattctt cggttgtaga    1800
aaccgcaaag tggattacat atatgagaat gaactcaaca actttgttga aaatggtgcg    1860
ctttctgagc ttgatgttgc tttctcccgc gatggcccga cgaaagaata cgtgcaacat    1920
aaaatgaccc aaaaggcttc tgaaatatgg aatatgcttt ctgagggagc atatttatat    1980
gtatgtggtg atgctaaagg catggctaaa gatgtacacc gtacacttca caccattgtg    2040
caagaacagg gaagtttgga ctcgtctaaa gcggagttgt atgtgaagaa tctacaaatg    2100
tcaggaagat acctccgtga tgtttggtaa                                     2130
```

SEQ ID NO:84

```
MQSESVEAST IDLMTAVLKD TVIDTANASD NGDSKMPPAL AMMFEIRDLL LILTTSVAVL     60
VGCFVVLVWK RSSGKKSGKE LEPPKIVVPK RRLEQEVDDG KKKVTIFFGT QTGTAEGFAK    120
ALFEEAKARY EKAAFKVIDL DDYAADLDEY AEKLKKETYA FFFLATYGDG EPTDNAAKFY    180
KWFTEGDEKG VWLQKLQYGV FGLGNRQYEH FNKIGIVVDD GLTEQGAKRI VPVGLGDDDQ    240
SIEDDFSAWK ELVWPELDLL LRDEDDKAAA TPYTAAIPEY RVVFHDKPDA FSDDHTQTNG    300
HAVHDAQHPC RSNVAVKKEL HTPESDRSCT HLEFDISHTG LSYETGDHVG VYCENLIEVV    360
EEAGKLLGLS TDTYFSLHID NEDGSPLGGP SLQPPFPPCT LRKALTNYAD LLSSPKKSTL    420
```

```
LALAAHASDP TEADRLRFLA SREGKDEYAE WVVANQRSLL EVMEAFPSAR PPLGVFFAAV    480
APRLQPRYYS ISSSPKMEPN RIHVTCALVY EKTPAGRIHK GICSTWMKNA VPLTESQDCS    540
WAPIFVRTSN FRLPIDPKVP VIMIGPGTGL APFRGFLQER LALKESGTEL GSSILFFGCR    600
NRKVDYIYEN ELNNFVENGA LSELDVAFSR DGPTKEYVQH KMTQKASEIW NMLSEGAYLY    660
VCGDAKGMAK DVHRTLHTIV QEQGSLDSSK AELYVKNLQM SGRYLRDVW               709
```

SEQ ID NO:85

```
atgcaatcta actccgtgaa gatttcgccg cttgatctgg taactgcgct gtttagcggc      60
aaggttttgg acacatcgaa cgcatcggaa tcgggagaat ctgctatgct gccgactata     120
gcgatgatta tggagaatcg tgagctgttg atgatactca caacgtcggt tgctgtattg     180
atcggatgcg ttgtcgtttt ggtgtggcgg agatcgtcta cgaagaagtc ggcgttggag     240
ccaccggtga ttgtggttcc gaagagagtg caagaggagg aagttgatga tggtaagaag     300
aaagttacgg ttttcttcgg cacccaaact ggaacagctg aaggcttcgc taaggcactt     360
gttgaggaag ctaaagctcg atatgaaaag gctgtcttta aagtaattga tttggatgat     420
tatgctgctg atgacgatga gtatgaggag aaactaaaga aagaatcttt ggcctttttc     480
tttttggcta cgtatggaga tggtgagcca acagataatg ctgccagatt ttataaatgg     540
tttactgagg gagatgcgaa aggagaatgg cttaataagc ttcaatatgg agtatttggt     600
ttgggtaaca gacaatatga acattttaac aagatcgcaa aagtggttga tgatggtctt     660
gtagaacagg gtgcaaagcg tcttgttcct gttggacttg gagatgatga tcaatgtatt     720
gaagatgact tcaccgcatg gaaagagtta gtatggccgg agttggatca attacttcgt     780
gatgaggatg acacaactgt tgctactcca tacacagctg ctgttgcaga atatcgcgtt     840
gtttttcatg aaaaaccaga cgcgctttct gaagattata gttatacaaa tggccatgct     900
gttcatgatg ctcaacatcc atgcagatcc aacgtggctg tcaaaaagga acttcatagt     960
cctgaatctg accggtcttg cactcatctt gaatttgaca tctcgaacac cggactatca    1020
tatgaaactg ggaccatgt tggagtttac tgtgaaaact tgagtgaagt tgtgaatgat    1080
gctgaaagat tagtaggatt accaccagac acttactcct ccatccacac tgatagtgaa    1140
gacgggtcgc cacttggcgg agcctcattg ccgcctcctt tcccgccatg cactttaagg    1200
aaagcattga cgtgttatgc tgatgttttg agttctccca agaagtcggc tttgcttgca    1260
ctagctgctc atgccaccga tcccagtgaa gctgatagat tgaaatttct tgcatccccc    1320
gccggaaagg atgaatattc tcaatggata gttgcaagcc aaagaagtct ccttgaagtc    1380
atggaagcat tcccgtcagc taagccttca cttggtgttt tctttgcatc tgttgccccg    1440
cgcttacaac caagatacta ctctatttct tcctcaccca agatggcacc ggataggatt    1500
catgttacat gtgcattagt ctatgagaaa acacctgcag gccgcatcca caaaggagtt    1560
tgttcaactt ggatgaagaa cgcagtgcct atgaccgaga gtcaagattg cagttgggcc    1620
ccaatatacg tccgaacatc caatttcaga ctaccatctg accctaaggt cccggttatc    1680
atgattggac ctggcactgg tttggctcct tttagaggtt tccttcaaga gcggttagct    1740
ttaaaggaag ccggaactga cctcggttta tccattttat tcttcggatg taggaatcgc    1800
aaagtggatt tcatatatga aaacgagctt aacaactttg tggagactgg tgctctttct    1860
gagcttattg ttgctttctc ccgtgaaggc ccgactaagg aatatgtgca acacaagatg    1920
agtgagaagg cttcggatat ctggaacttg ctttctgaag gagcatattt atacgtatgt    1980
ggtgatgcca aaggcatggc caaagatgta catcgaaccc tccacacaat tgtgcaagaa    2040
cagggatctc ttgactcgtc aaaggcagaa ctctacgtga agaatctaca aatgtcagga    2100
agatacctcc gtgacgtttg gtaa                                           2124
```

SEQ ID NO:86

```
MQSNSVKISP LDLVTALFSG KVLDTSNASE SGESAMLPTI AMIMENRELL MILTTSVAVL     60
IGCVVVLVWR RSSTKKSALE PPVIVVPKRV QEEEVDDGKK KVTVFFGTQT GTAEGFAKAL    120
VEEAKARYEK AVFKVIDLDD YAADDDEYEE KLKKESLAFF FLATYGDGEP TDNAARFYKW    180
FTEGDAKGEW LNKLQYGVFG LGNRQYEHFN KIAKVVDDGL VEQGAKRLVP VGLGDDDQCI    240
EDDFTAWKEL VWPELDQLLR DEDDTTVATP YTAAVAEYRV VFHEKPDALS EDYSYTNGHA    300
VHDAQHPCRS NVAVKKELHS PESDRSCTHL EFDISNTGLS YETGDHVGVY CENLSEVVND    360
AERLVGLPPD TYSSIHTDSE DGSPLGGASL PPPFPPCTLR KALTCYADVL SSPKKSALLA    420
LAAHATDPSE ADRLKFLASP AGKDEYSQWI VASQRSLLEV MEAFPSAKPS LGVFFASVAP    480
RLQPRYYSIS SSPKMAPDRI HVTCALVYEK TPAGRIHKGV CSTWMKNAVP MTESQDCSWA    540
PIYVRTSNFR LPSDPKVPVI MIGPGTGLAP FRGFLQERLA LKEAGTDLGL SILFFGCRNR    600
KVDFIYENEL NNFVETGALS ELIVAFSREG PTKEYVQHKM SEKASDIWNL LSEGAYLYVC    660
GDAKGMAKDV HRTLHTIVQE QGSLDSSKAE LYVKNLQMSG RYLRDVW                  707
```

SEQ ID NO:87
atgtcctcca actccgattt ggtcagaaga ttggaatctg ttttgggtgt ttctttcggt 60
ggttctgtta ctgattccgt tgttgttatt gctaccacct ctattgcttt ggttatcggt 120
gttttggttt tgttgtggag aagatcctct gacagatcta gagaagttaa gcaattggct 180
gttccaaagc cagttactat cgttgaagaa gaagatgaat tcgaagttgc ttctggtaag 240
accagagttt ctattttcta cggtactcaa actggtactg ctgaaggttt tgctaaggct 300
ttggctgaag aaatcaaagc cagatacgaa aaagctgccg ttaaggttat tgatttggat 360
gattacacag ccgaagatga caaatacggt gaaaagttga agaaagaaac tatggccttc 420
ttcatgttgg ctacttatgg tgatggtgaa cctactgata atgctgctag attttacaag 480
tggttcaccg aaggtactga tagaggtgtt tggttggaac atttgagata cggtgtattc 540
ggtttgggta acagacaata cgaacacttc aacaagattg ccaaggttgt tgatgatttg 600
ttggttgaac aaggtgccaa gagattggtt actgttggtt tgggtgatga tgatcaatgc 660
atcgaagatg atttctccgc ttggaaagaa gccttgtggc cagaattgga tcaattattg 720
caagatgata ccaacaccgt ttctactcca tacactgctg ttattccaga atacagagtt 780
gttatccacg atccatctgt tacctcttat gaagatccat actctaacat ggctaacggt 840
aatgcctctt acgatattca tcatccatgt agagctaacg ttgccgtcca aaaagaattg 900
cataagccag aatctgacag aagttgcatc catttggaat tcgatatttt cgctactggt 960
ttgacttacg aaaccggtga tcatgttggt gtttacgctg ataattgtga tgatactgta 1020
gaagaagccg ctaagttgtt gggtcaacca ttggatttgt tgttctccat tcataccgat 1080
aacaacgacg gtacttcttt gggttcttct ttgccaccac catttccagg tccatgtact 1140
ttgagaactg ctttggctag atatgccgat ttgttgaatc caccaaaaaa ggctgctttg 1200
attgctttag ctgctcatgc tgatgaacca tctgaagctg aaagattgaa gttcttgtca 1260
tctccacaag gtaaggacga atattctaaa tgggttgtcg gttcccaaag atccttggtt 1320
gaagttatgg ctgaatttcc atctgctaaa ccaccattgg gtgtattttt tgctgctgtt 1380
gttcctagat tgcaacctag atattactcc atctcttcca gtccaagatt tgctccacat 1440
agagttcatg ttacttgcgc tttggtttat ggtccaactc caactggtag aattcacaga 1500
ggtgtatgtt cattctggat gaagaatgtt gtcccattgg aaaagtctca aaactgttct 1560
tgggccccaa ttttcatcag acaatctaat ttcaagttgc cagccgatca ttctgttcca 1620
atagttatgg ttggtccagg tactggttta gctcctttta gaggtttctt acaagaaaga 1680
ttggccttga aagaagaagg tgctcaagtt ggtcctgctt tgttgttttt tggttgcaga 1740
aacagacaaa tggacttcat ctacgaagtc gaattgaaca actttgtcga acaaggtgct 1800
ttgtccgaat tgatcgttgc tttttcaaga gaaggtccat ccaaagaata cgtccaacat 1860
aagatggttg aaaaggcagc ttacatgtgg aacttgattt ctcaaggtgg ttacttctac 1920
gtttgtggtg atgctaaagg tatggctaga gatgttcata gaacattgca taccatcgtc 1980
caacaagaag aaaaggttga ttctaccaag gccgaatcca tcgttaagaa attgcaaatg 2040
gacggtagat acttgagaga tgtttggtga 2070

SEQ ID NO:88
MSSNSDLVRR LESVLGVSFG GSVTDSVVVI ATTSIALVIG VLVLLWRRSS DRSREVKQLA 60
VPKPVTIVEE EDEFEVASGK TRVSIFYGTQ TGTAEGFAKA LAEEIKARYE KAAVKVIDLD 120
DYTAEDDKYG EKLKKETMAF FMLATYGDGE PTDNAARFYK WFTEGTDRGV WLEHLRYGVF 180
GLGNRQYEHF NKIAKVVDDL LVEQGAKRLV TVGLGDDDQC IEDDFSAWKE ALWPELDQLL 240
QDDTNTVSTP YTAVIPEYRV VIHDPSVTSY EDPYSNMANG NASYDIHHPC RANVAVQKEL 300
HKPESDRSCI HLEFDIFATG LTYETGDHVG VYADNCDDTV EEAAKLLGQP LDLLFSIHTD 360
NNDGTSLGSS LPPPFPGPCT LRTALARYAD LLNPPKKAAL IALAAHADEP SEAERLKFLS 420
SPQGKDEYSK WVVGSQRSLV EVMAEFPSAK PPLGVFFAAV VPRLQPRYYS ISSSPRFAPH 480
RVHVTCALVY GPTPTGRIHR GVCSFWMKNV VPLEKSQNCS WAPIFIRQSN FKLPADHSVP 540
IVMVGPGTGL APFRGFLQER LALKEEGAQV GPALLFFGCR NRQMDFIYEV ELNNFVEQGA 600
LSELIVAFSR EGPSKEYVQH KMVEKAAYMW NLISQGGYFY VCGDAKGMAR DVHRTLHTIV 660
QQEEKVDSTK AESIVKKLQM DGRYLRDVW 689

SEQ ID NO:89
atgacttctg cactttatgc ctccgatctt ttcaaacaat tgaaaagtat catgggaacg 60
gattctttgt ccgatgatgt tgtattagtt attgctacaa cttctctggc actggttgct 120
ggtttcgttg tcttattgtg gaaaaagacc acggcagatc gttccggcga gctaaagcca 180
ctaatgatcc ctaagtctct gatggcgaaa gatgaggatg atgacttaga tctaggttct 240

```
ggaaaaacga gagtctctat cttcttcggc acacaaaccg gaacagccga aggattcgct 300
aaagcacttt cagaagagat caaagcaaga tacgaaaagg cggctgtaaa agtaatcgat 360
ttggatgatt acgctgccga tgatgaccaa tatgaggaaa agttgaaaaa ggaaacattg 420
gctttctttt gtgtagccac gtatggtgat ggtgaaccaa ccgataacgc cgcaagattc 480
tacaagtggt ttactgaaga gaacgaaaga gatatcaagt tgcagcaact tgcttacggc 540
gtttttgcct taggtaacag acaatacgag cactttaaca agataggtat tgtcttagat 600
gaagagttat gcaaaaaggg tgcgaagaga ttgattgaag tcggtttagg agatgatgat 660
caatctatcg aggatgactt taatgcatgg aaggaatctt tgtggtctga attagataag 720
ttacttaagg acgaagatga taaatccgtt gccactccat acacagccgt cattccagaa 780
tatagagtag ttactcatga tccaagattc acaacacaga aatcaatgga aagtaatgtg 840
gctaatggta atactaccat cgatattcat catccatgta gagtagacgt tgcagttcaa 900
aaggaattgc acactcatga atcagacaga tcttgcatac atcttgaatt tgatatatca 960
cgtactggta tcacttacga aacaggtgat cacgtgggtg tctacgctga aaaccatgtt 1020
gaaattgtag aggaagctgg aaagttgttg ggccatagtt tagatcttgt tttctcaatt 1080
catgccgata aagaggatgg ctcaccacta gaaagtgcag tgcctccacc atttccagga 1140
ccatgcaccc taggtaccgg tttagctcgt tacgcggatc tgttaaatcc tccacgtaaa 1200
tcagctctag tggccttggc tgcgtacgcc acagaacctt ctgaggcaga aaaactgaaa 1260
catctaactt caccagatgg taaggatgaa tactcacaat ggatagtagc tagtcaacgt 1320
tctttactag aagttatggc tgctttccca tccgctaaac ctcctttggg tgttttcttc 1380
gccgcaatag cgcctagact gcaaccaaga tactattcaa tttcatcctc acctagactg 1440
gcaccatcaa gagttcatgt cacatccgct ttagtgtacg gtccaactcc tactggtaga 1500
atccataagg gcgtttgttc aacatggatg aaaaacgcgg ttccagcaga gaagtctcac 1560
gaatgttctg gtgctccaat ctttatcaga gcctccaact tcaaactgcc ttccaatcct 1620
tctactccta ttgtcatggt cggtcctggt acaggtcttg ctccattcag aggtttctta 1680
caagagagaa tggccttaaa ggaggatggt gaagagttgg gatcttcttt gttgtttttc 1740
ggctgtagaa acagacaaat ggatttcatc tacgaagatg aactgaataa ctttgtagat 1800
caaggagtta tttcagagtt gataatggct tttctagag aaggtgctca gaaggagtac 1860
gtccaacaca aaatgatgga aaaggccgca caagtttggg acttaatcaa agaggaaggc 1920
tatctatatg tctgtggtga tgcaaagggt atggcaagag atgttcacag aacacttcat 1980
actatagtcc aggaacagga aggcgttagt tcttctgaag cggaagcaat tgtgaaaaag 2040
ttacaaacag agggaagata cttgagagat gtgtggtaa 2079
```

SEQ ID NO:90

```
MTSALYASDL FKQLKSIMGT DSLSDDVVLV IATTSLALVA GFVVLLWKKT TADRSGELKP 60
LMIPKSLMAK DEDDDLDLGS GKTRVSIFFG TQTGTAEGFA KALSEEIKAR YEKAAVKVID 120
LDDYAADDDQ YEEKLKKETL AFFCVATYGD GEPTDNAARF YKWFTEENER DIKLQQLAYG 180
VFALGNRQYE HFNKIGIVLD EELCKKGAKR LIEVGLGDDD QSIEDDFNAW KESLWSELDK 240
LLKDEDDKSV ATPYTAVIPE YRVVTHDPRF TTQKSMESNV ANGNTTIDIH HPCRVDVAVQ 300
KELHTHESDR SCIHLEFDIS RTGITYETGD HVGVYAENHV EIVEEAGKLL GHSLDLVFSI 360
HADKEDGSPL ESAVPPPFPG PCTLGTGLAR YADLLNPPRK SALVALAAYA TEPSEAEKLK 420
HLTSPDGKDE YSQWIVASQR SLLEVMAAFP SAKPPLGVFF AAIAPRLQPR YYSISSSPRL 480
APSRVHVTSA LVYGPTPTGR IHKGVCSTWM KNAVPAEKSH ECSGAPIFIR ASNFKLPSNP 540
STPIVMVGPG TGLAPFRGFL QERMALKEDG EELGSSLLFF GCRNRQMDFI YEDELNNFVD 600
QGVISELIMA FSREGAQKEY VQHKMMEKAA QVWDLIKEEG YLYVCGDAKG MARDVHRTLH 660
TIVQEQEGVS SSEAEAIVKK LQTEGRYLRD VW 692
```

SEQ ID NO:91

```
atgtcttcct cttcctcttc cagtacctct atgattgatt tgatggctgc tattattaaa 60
ggtgaaccag ttatcgtctc cgacccagca aatgcctctg cttatgaatc agttgctgca 120
gaattgtctt caatgttgat cgaaaacaga caattcgcca tgatcgtaac tacatcaatc 180
gctgttttga tcggttgtat tgtcatgttg gtatggagaa gatccggtag tggtaattct 240
aaaagagtcg aacctttgaa accattagta attaagccaa gagaagaaga aatagatgac 300
ggtagaaaga aagttacaat atttttcggt acccaaactg gtacagctga aggttttgca 360
aaagccttag gtgaagaagc taaggcaaga tacgaaaaga ctagattcaa gatagtcgat 420
ttggatgact atgccgctga tgacgatgaa tacgaagaaa agttgaagaa agaagatgtt 480
gcatttttct tttggcaac ctatggtgac ggtgaaccaa ctgacaatgc agccagattc 540
tacaaatggt ttacagaggg taatgatcgt ggtgaatggt tgaaaaactt aaagtacggt 600
```

gttttcggtt tgggtaacag acaatacgaa catttcaaca aagttgcaaa ggttgtcgac 660
gatattttgg tcgaacaagg tgctcaaaga ttagtccaag taggtttggg tgacgatgac 720
caatgtatag aagatgactt tactgcctgg agagaagctt tgtggcctga attagacaca 780
atcttgagag aagaaggtga caccgccgtt gctaccccat atactgctgc agtattagaa 840
tacagagttt ccatccatga tagtgaagac gcaaagttta atgatatcac tttggccaat 900
ggtaacggtt atacagtttt cgatgcacaa cacccttaca aagctaacgt tgcagtcaag 960
agagaattac atacaccaga atccgacaga agttgtatac acttggaatt tgatatcgct 1020
ggttccggtt taaccatgaa gttgggtgac catgtaggtg ttttatgcga caatttgtct 1080
gaaactgttg atgaagcatt gagattgttg gatatgtccc ctgacactta ttttagtttg 1140
cacgctgaaa aagaagatgg tacaccaatt tccagttctt taccacctcc attccctcca 1200
tgtaacttaa gaacagcctt gaccagatac gcttgcttgt tatcatcccc taaaaagtcc 1260
gccttggttg ctttagccgc tcatgctagt gatcctactg aagcagaaag attgaaacac 1320
ttagcatctc cagccggtaa agatgaatat tcaaagtggg tagttgaatc tcaaagatca 1380
ttgttagaag ttatggcaga atttccatct gccaagcctc cattaggtgt cttctttgct 1440
ggtgtagcac ctagattgca accaagattc tactcaatca gttcttcacc taagatcgct 1500
gaaactagaa ttcatgttac atgtgcatta gtctacgaaa agatgccaac cggtagaatt 1560
cacaagggtg tatgctctac ttggatgaaa aatgctgttc cttacgaaaa atcagaaaag 1620
ttgttcttag gtagaccaat cttcgtaaga caatcaaact tcaagttgcc ttctgattca 1680
aaggttccaa taatcatgat aggtcctggt acaggtttag ccccattcag aggtttcttg 1740
caagaaagat tggctttagt tgaatctggt gtcgaattag gtccttcagt tttgttcttt 1800
ggttgtagaa acagaagaat ggatttcatc tatgaagaag aattgcaaag attcgtcgaa 1860
tctggtgcat tggccgaatt atctgtagct tttcaagag aaggtccaac taaggaatac 1920
gttcaacata agatgatgga taaggcatcc gacatatgga acatgatcag tcaaggtgct 1980
tatttgtacg tttgcggtga cgcaaagggt atggccagag atgtccatag atctttgcac 2040
acaattgctc aagaacaagg ttccatggat agtaccaaag ctgaaggttt cgtaaagaac 2100
ttacaaactt ccggtagata cttgagagat gtctggtga 2139

SEQ ID NO:92
MSSSSSSSTS MIDLMAAIIK GEPVIVSDPA NASAYESVAA ELSSMLIENR QFAMIVTTSI 60
AVLIGCIVML VWRRSGSGNS KRVEPLKPLV IKPREEEIDD GRKKVTIFFG TQTGTAEGFA 120
KALGEEAKAR YEKTRFKIVD LDDYAADDDE YEEKLKKEDV AFFFLATYGD GEPTDNAARF 180
YKWFTEGNDR GEWLKNLKYG VFGLGNRQYE HFNKVAKVVD DILVEQGAQR LVQVGLGDDD 240
QCIEDDFTAW REALWPELDT ILREEGDTAV ATPYTAAVLE YRVSIHDSED AKFNDITLAN 300
GNGYTVFDAQ HPYKANVAVK RELHTPESDR SCIHLEFDIA GSGLTMKLGD HVGVLCDNLS 360
ETVDEALRLL DMSPDTYFSL HAEKEDGTPI SSSLPPPFPP CNLRTALTRY ACLLSSPKKS 420
ALVALAAHAS DPTEAERLKH LASPAGKDEY SKWVVESQRS LLEVMAEFPS AKPPLGVFFA 480
GVAPRLQPRF YSISSSPKIA ETRIHVTCAL VYEKMPTGRI HKGVCSTWMK NAVPYEKSEK 540
LFLGRPIFVR QSNFKLPSDS KVPIIMIGPG TGLAPFRGFL QERLALVESG VELGPSVLFF 600
GCRNRRMDFI YEEELQRFVE SGALAELSVA FSREGPTKEY VQHKMMDKAS DIWNMISQGA 660
YLYVCGDAKG MARDVHRSLH TIAQEQGSMD STKAEGFVKN LQTSGRYLRD VW 712

SEQ ID NO:93
atggaagcct cttacctata catttctatt ttgcttttac tggcatcata cctgttcacc 60
actcaactta gaaggaagag cgctaatcta ccaccaaccg tgtttccatc aataccaatc 120
attggacact tatacttact caaaaagcct ctttatagaa ctttagcaaa aattgccgct 180
aagtacggac caatactgca attacaactc ggctacagac gtgttctggt gatttcctca 240
ccatcagcag cagaagagtg ctttaccaat aacgatgtaa tcttcgcaaa tagacctaag 300
acattgtttg gcaaaatagt gggtggaaca tcccttggca gtttatccta cggcgatcaa 360
tggcgtaatc taaggagagt agcttctatc gaaatcctat cagttcatag gttgaacgaa 420
tttcatgata tcagagtgga tgagaacaga ttgttaatta gaaaacttag aagttcatct 480
tctcctgtta ctcttataac agtcttttat gctctaacat tgaacgtcat tatgagaatg 540
atctctggca aaagatattt cgacagtggg gatagagaat tggaggagga aggtaagaga 600
tttcgagaaa tcttagacga aacgttgctt ctagccggtg cttctaatgt tggcgactac 660
ttaccaatat tgaactggtt gggagttaag tctcttgaaa agaaattgat cgctttgcag 720
aaaaagagag atgacttttt ccagggtttg attgaacagg ttagaaaatc tcgtggtgct 780
aaagtaggca aaggtagaaa aacgatgatc gaactcttat tatctttgca agagtcagaa 840
cctgagtact atacagatgc tatgataaga tcttttgtcc taggtctgct ggctgcaggt 900

```
agtgatactt cagcgggcac tatggaatgg gccatgagct tactggtcaa tcacccacat      960
gtattgaaga aagctcaagc tgaaatcgat agagttatcg gtaataacag attgattgac     1020
gagtcagaca ttggaaatat cccttacatc gggtgtatta tcaatgaaac tctaagactc     1080
tatccagcag ggccattgtt gttcccacat gaaagttctg ccgactgcgt tatttccggt     1140
tacaatatac ctagaggtac aatgttaatc gtaaaccaat gggcgattca tcacgatcct     1200
aaagtctggg atgatcctga aacctttaaa cctgaaagat ttcaaggatt agaaggaact     1260
agagatggtt tcaaacttat gccattcggt tctgggagaa gaggatgtcc aggtgaaggt     1320
ttggcaataa ggctgttagg gatgacacta ggctcagtga tccaatgttt tgattgggag     1380
agagtaggag atgagatggt tgacatgaca gaaggtttgg gtgtcacact tcctaaggcc     1440
gttccattag ttgccaaatg taagccacgt tccgaaatga ctaatctcct atccgaactt     1500
taa                                                                    1503
```

SEQ ID NO:94

```
MEASYLYISI LLLLASYLFT TQLRRKSANL PPTVFPSIPI IGHLYLLKKP LYRTLAKIAA       60
KYGPILQLQL GYRRVLVISS PSAAEECFTN NDVIFANRPK TLFGKIVGGT SLGSLSYGDQ      120
WRNLRRVASI EILSVHRLNE FHDIRVDENR LLIRKLRSSS SPVTLITVFY ALTLNVIMRM      180
ISGKRYFDSG DRELEEEGKR FREILDETLL LAGASNVGDY LPILNWLGVK SLEKKLIALQ      240
KKRDDFFQGL IEQVRKSRGA KVGKGRKTMI ELLLSLQESE PEYYTDAMIR SFVLGLLAAG      300
SDTSAGTMEW AMSLLVNHPH VLKKAQAEID RVIGNNRLID ESDIGNIPYI GCIINETLRL      360
YPAGPLLFPH ESSADCVISG YNIPRGTMLI VNQWAIHHDP KVWDDPETFK PERFQGLEGT      420
RDGFKLMPFG SGRRGCPGEG LAIRLLGMTL GSVIQCFDWE RVGDEMVDMT EGLGVTLPKA      480
VPLVAKCKPR SEMTNLLSEL                                                  500
```

SEQ ID NO:95

```
atggaagtaa cagtagctag tagtgtagcc ctgagcctgg tctttattag catagtagta       60
agatgggcat ggagtgtggt gaattgggtg tggtttaagc cgaagaagct ggaaagattt      120
ttgagggagc aaggccttaa aggcaattcc tacaggtttt tatatggaga catgaaggag      180
aactctatcc tgctcaaaca agcaagatcc aaacccatga acctctccac ctcccatgac      240
atagcacctc aagtcacccc ttttgtcgac caaaccgtga aagcttacgg taagaactct      300
tttaattggg ttggccccat accaagggtg aacataatga atccagaaga tttgaaggac      360
gtcttaacaa aaaatgttga ctttgttaag ccaatatcaa acccacttat caagttgcta      420
gctacaggta ttgcaatcta tgaaggtgag aaatggacta aacacagaag gattatcaac      480
ccaacattcc attcggagag gctaaagcgt atgttacctt catttcacca aagttgtaat      540
gagatggtca aggaatggga gagcttggtg tcaaaagagg gttcatcatg tgagttggat      600
gtctggcctt ttcttgaaaa tatgtcggca gatgtgatct cgagaacagc atttggaact      660
agctacaaaa aaggacagaa aatctttgaa ctcttgagag agcaagtaat atatgtaacg      720
aaaggctttc aaagttttta cattccagga tggaggtttc tcccaactaa gatgaacaag      780
aggatgaatg agattaacga agaaataaaa ggattaatca ggggtattat aattgacaga      840
gagcaaatca ttaaggcagg tgaagaaacc aacgatgact tattaggtgc acttatggag      900
tcaaacttga aggacattcg ggaacatggg aaaaacaaca aaaatgttgg gatgagtatt      960
gaagatgtaa ttcaggagtg taagctgttt tactttgctg ggcaagaaac cacttcagtg     1020
ttgctggctt ggacaatggt tttacttggt caaaatcaga actggcaaga tcgagcaaga     1080
caagaggttt tgcaagtctt tggaagcagc aagccagatt ttgatggtct agctcacctt     1140
aaagtcgtaa ccatgatttt gcttgaagtt cttcgattat acccaccagt cattgaactt     1200
attcgaacca ttcacaagaa aacacaactt gggaagctct cactaccaga aggagttgaa     1260
gtccgcttac caacactgct cattcaccat gacaaggaac tgtggggtga tgatgcaaac     1320
cagttcaatc cagagaggtt ttcggaagga gtttccaaag caacaaagaa ccgactctca     1380
ttcttcccct tcggagccgg tccacgcatt tgcattggac agaacttttc tatgatggaa     1440
gcaaagttgg ccttagcatt gatcttgcaa cacttcacct ttgagctttc tccatctcat     1500
gcacatgctc cttcccatcg tataaccctt caaccacagt atggtgttcg tatcatttta     1560
catcgacgtt ag                                                         1572
```

SEQ ID NO:96

```
atggaagtca ctgtcgcctc ttctgtcgct ttatccttag tcttcatttc cattgtcgtc       60
agatgggctt ggtccgttgt caactgggtt tggttcaaac caaagaagtt ggaaagattc      120
ttgagagagc aaggtttgaa gggtaattct tatagattct tgtacggtga catgaaggaa      180
aattctattt tgttgaagca agccagatcc aaaccaatga acttgtctac ctctcatgat      240
```

```
attgctccac aagttactcc attcgtcgat caaactgtta aagcctacgg taagaactct     300
ttcaattggg ttggtccaat tcctagagtt aacatcatga acccagaaga tttgaaggat     360
gtcttgacca agaacgttga cttcgttaag ccaatttcca acccattgat taaattgttg     420
gctactggta ttgccattta cgaaggtgaa aagtggacta agcatagaag aatcatcaac     480
cctaccttcc actctgaaag attgaagaga atgttaccat ctttccatca atcctgtaat     540
gaaatggtta aggaatggga atccttggtt tctaaagaag gttcttcttg cgaattggat     600
gtttggccat tcttggaaaa tatgtctgct gatgtcattt ccagaaccgc tttcggtacc     660
tcctacaaga agggtcaaaa gattttcgaa ttgttgagag agcaagttat ttacgttacc     720
aagggtttcc aatccttcta catcccaggt tggagattct tgccaactaa aatgaacaag     780
cgtatgaacg agatcaacga agaaattaaa ggtttgatca gaggtattat tatcgacaga     840
gaacaaatta ttaaagctgg tgaagaaacc aacgatgatt tgttgggtgc tttgatggag     900
tccaacttga aggatattag agaacatggt aagaacaaca agaatgttgg tatgtctatt     960
gaagatgtta ttcaagaatg taagttattc tacttcgctg gtcaagagac cacttctgtt    1020
ttgttagcct ggactatggt cttgttaggt caaaaccaaa attggcaaga tagagctaga    1080
caagaagttt tgcaagtctt cggttcttcc aagccagact ttgatggttt ggcccacttg    1140
aaggttgtta ctatgatttt gttagaagtt ttgagattgt acccaccagt cattgagtta    1200
atcagaacca ttcataaaaa gactcaattg ggtaaattat ctttgccaga aggtgttgaa    1260
gtcagattac caaccttgtt gattcaccac gataaggaat tatggggtga cgacgctaat    1320
caatttaatc cagaaagatt ttccgaaggt gtttccaagg ctaccaaaaa ccgtttgtcc    1380
ttcttcccat ttggtgctgg tccacgtatt tgtatcggtc aaaacttttc catgatggaa    1440
gccaagttgg ctttggcttt aatcttgcaa cacttcactt tcgaattgtc tccatcccat    1500
gcccacgctc cttctcatag aatcacttta caaccacaat acggtgtcag aatcatctta    1560
cacagaagat aa                                                        1572
```

SEQ ID NO:97

```
MEVTVASSVA LSLVFISIVV RWAWSVVNWV WFKPKKLERF LREQGLKGNS YRFLYGDMKE      60
NSILLKQARS KPMNLSTSHD IAPQVTPFVD QTVKAYGKNS FNWVGPIPRV NIMNPEDLKD     120
VLTKNVDFVK PISNPLIKLL ATGIAIYEGE KWTKHRRIIN PTFHSERLKR MLPSFHQSCN     180
EMVKEWESLV SKEGSSCELD VWPFLENMSA DVISRTAFGT SYKKGQKIFE LLREQVIYVT     240
KGFQSFYIPG WRFLPTKMNK RMNEINEEIK GLIRGIIIDR EQIIKAGEET NDDLLGALME     300
SNLKDIREHG KNNKNVGMSI EDVIQECKLF YFAGQETTSV LLAWTMVLLG QNQNWQDRAR     360
QEVLQVFGSS KPDFDGLAHL KVVTMILLEV LRLYPPVIEL IRTIHKKTQL GKLSLPEGVE     420
VRLPTLLIHH DKELWGDDAN QFNPERFSEG VSKATKNRLS FFPFGAGPRI CIGQNFSMME     480
AKLALALILQ HFTFELSPSH AHAPSHRITL QPQYGVRIIL HRR                      523
```

SEQ ID NO:98

```
atggaagcat caagggctag ttgtgttgcg ctatgtgttg tttgggtgag catagtaatt      60
acattggcat ggagggtgct gaattgggtg tggttgaggc caaagaaact agaaagatgc     120
ttgagggagc aaggccttac aggcaattct tacaggcttt tgtttggaga caccaaggat     180
ctctcgaaga tgctggaaca aacacaatcc aaacccatca aactctccac ctcccatgat     240
atagcgccac gagtcacccc atttttccat cgaactgtga actctaatgg caagaattct     300
tttgtttgga tgggccctat accaagagtg cacatcatga atccagaaga tttgaaagat     360
gccttcaaca gacatgatga ttttcataag acagtaaaaa atcctatcat gaagtctcca     420
ccaccgggca ttgtaggcat tgaaggtgag caatgggcta aacacagaaa gattatcaac     480
ccagcattcc atttagagaa gctaaagggt atggtaccaa tattttacca aagttgtagc     540
gagatgatta acaaatggga gagcttggtg tccaaagaga gttcatgtga gttggatgtg     600
tggccttatc ttgaaaattt taccagcgat gtgatttccc gagctgcatt tggaagtagc     660
tatgaagagg gaaggaaaat atttcaacta ctaagagagg aagcaaaagt ttattcggta     720
gctctacgaa gtgtttacat tccaggatgg aggtttctac caaccaagca gaacaagaag     780
acgaaggaaa ttcacaatga aattaaaggc ttacttaagg gcattataaa taaaagggaa     840
gaggcgatga aggcagggga agccactaaa gatgacttac taggaatact tatggagtcc     900
aacttcaggg aaattcagga acatgggaac aacaaaaatg ctggaatgag tattgaagat     960
gtaattggag agtgtaagtt gttttacttt gctgggcaag agaccacttc ggtgttgctt    1020
gtttggacaa tgattttact aagccaaaat caggattggc aagctcgtgc aagagaagag    1080
gtcttgaaag tctttggaag caacatccca acctatgaag agctaagtca cctaaaagtt    1140
gtgaccatga ttttacttga agttcttcga ttatacccat cagtcgttgc gcttcctcga    1200
accactcaca agaaaacaca gcttggaaaa ttatcattac cagctggagt ggaagtctcc    1260
```

ttgcccatac tgcttgttca ccatgacaaa gagttgtggg gtgaggatgc aaatgagttc 1320
aagccagaga ggttttcaga gggagtttca aaggcaacaa agaacaaatt tacatactta 1380
cctttcggag ggggtccaag gatttgcatt ggacaaaact ttgccatggt ggaagctaaa 1440
ttggccttgg ccctgatttt acaacacttt gcctttgagc tttctccatc ctatgctcat 1500
gctccttctg cagttataac ccttcaacct caatttggtg ctcatatcat tttgcataaa 1560
cgttga 1566

SEQ ID NO:99
atggaagctt ctagagcatc ttgtgttgct ttgtgtgttg tttgggtttc catcgttatt 60
actttggctt ggagagtttt gaattgggtc tggttaagac caaaaaagtt ggaaagatgc 120
ttgagagaac aaggtttgac tggtaactct tacagattgt tgttcggtga taccaaggac 180
ttgtctaaga tgttggaaca aactcaatcc aagcctatca agttgtctac ctctcatgat 240
attgctccaa gagttactcc attcttccat agaactgtta actccaacgg taagaactct 300
tttgtttgga tgggtccaat tccaagagtc catattatga accctgaaga tttgaaggac 360
gctttcaaca gacatgatga tttccataag accgtcaaga acccaattat gaagtctcca 420
ccaccaggta tagttggtat tgaaggtgaa caatgggcca aacatagaaa gattattaac 480
ccagccttcc acttggaaaa gttgaaaggt atggttccaa tcttctacca atcctgctct 540
gaaatgatta acaagtggga atccttggtt tccaaagaat cttcctgtga attggatgtc 600
tggccatatt tggaaaactt cacctccgat gttatttcca gagctgcttt tggttcttct 660
tacgaagaag gtagaaagat cttccaatta ttgagagaag aagccaaggt ttactccgtt 720
gctttgagat ctgtttacat tccaggttgg agattcttgc caactaagca aaacaaaaag 780
accaaagaaa tccacaacga aatcaagggt ttgttgaagg gtatcatcaa caagagagaa 840
gaagctatga aggctggtga agctacaaaa gatgatttgt tgggtatctt gatggaatcc 900
aacttcagag aaatccaaga acacggtaac aacaagaatg ccggtatgtc tattgaagat 960
gttatcggtg aatgcaagtt gttctacttt gctggtcaag aaactacctc cgttttgttg 1020
gtttggacca tgattttgtt gtcccaaaat caagattggc aagctagagc tagagaagaa 1080
gtcttgaaag ttttcggttc taacatccca acctacgaag aattgtctca cttgaaggtt 1140
gtcactatga tcttgttgga agtattgaga ttatacccat ccgttgttgc attgccaaga 1200
actactcata agaaaactca attgggtaaa ttgtccttgc cagctggtgt tgaagtttct 1260
ttgccaattt tgttagtcca ccacgacaaa gaattgtggg gtgaagatgc taatgaattc 1320
aagccagaaa gattctccga aggtgtttct aaagctacca agaacaagtt cacttacttg 1380
ccatttggtg gtggtccaag aatatgtatt ggtcaaaatt tcgctatggt cgaagctaaa 1440
ttggctttgg ctttgatctt gcaacatttc gctttcgaat tgtcaccatc ttatgctcat 1500
gctccatctg ctgttattac attgcaacca caatttggtg cccatatcat cttgcataag 1560
agataac 1567

SEQ ID NO:100
MEASRASCVA LCVVWVSIVI TLAWRVLNWV WLRPKKLERC LREQGLTGNS YRLLFGDTKD 60
LSKMLEQTQS KPIKLSTSHD IAPRVTPFFH RTVNSNGKNS FVWMGPIPRV HIMNPEDLKD 120
AFNRHDDFHK TVKNPIMKSP PPGIVGIEGE QWAKHRKIIN PAFHLEKLKG MVPIFYQSCS 180
EMINKWESLV SKESSCELDV WPYLENFTSD VISRAAFGSS YEEGRKIFQL LREEAKVYSV 240
ALRSVYIPGW RFLPTKQNKK TKEIHNEIKG LLKGIINKRE EAMKAGEATK DDLLGILMES 300
NFREIQEHGN NKNAGMSIED VIGECKLFYF AGQETTSVLL VWTMILLSQN QDWQARAREE 360
VLKVFGSNIP TYEELSHLKV VTMILLEVLR LYPSVVALPR TTHKKTQLGK LSLPAGVEVS 420
LPILLVHHDK ELWGEDANEF KPERFSEGVS KATKNKFTYL PFGGGPRICI GQNFAMVEAK 480
LALALILQHF AFELSPSYAH APSAVITLQP QFGAHIILHK R 521

SEQ ID NO:101
ASWVAVLSVV WVSMVIAWAW RVLNWVWLRP KKLEKCLREQ GLAGNSYRLL FGDTKDLSKM 60
LEQTQSKPIK LSTSHDIAPH VTPFFHQTVN SYGKNSFVWM GPIPRVHIMN PEDLKDTFNR 120
HDDFHKVVKN PIMKSLPQGI VGIEGEQWAK HRKIINPAFH LEKLKGMVPI FYRSCSEMIN 180
KWESLVSKES SCELDVWPYL ENFTSDVISR AAFGSSYEEG RKIFQLLREE AKIYTVAMRS 240
VYIPGWRFLP TKQNKKAKEI HNEIKGLLKG IINKREEAMK AGEATKDDLL GILMESNFRE 300
IQEHGNNKNA GMSIEDVIGE CKLFYFAGQE TTSVLLVWTM VLLSQNQDWQ ARAREEVLQV 360
FGSNIPTYEE LSQLKVVTMI LLEVLRLYPS VVALPRTTHK KTQLGKLSLP AGVEVSLPIL 420
LVHHDKELWG EDANEFKPER FSEGVSKATK NQFTYFPFGG GPRICIGQNF AMMEAKLALS 480
LILRHFALEL SPLYAHAPSV TITLQPQYGA HIILHKR 517

SEQ ID NO:102

MEASRPSCVA LSVVLVSIVI AWAWRVLNWV WLRPNKLERC LREQGLTGNS YRLLFGDTKE 60
ISMMVEQAQS KPIKLSTTHD IAPRVIPFSH QIVYTYGRNS FVWMGPTPRV TIMNPEDLKD 120
AFNKSDEFQR AISNPIVKSI SQGLSSLEGE KWAKHRKIIN PAFHLEKLKG MLPTFYQSCS 180
EMINKWESLV FKEGSREMDV WPYLENLTSD VISRAAFGSS YEEGRKIFQL LREEAKFYTI 240
AARSVYIPGW RFLPTKQNKR MKEIHKEVRG LLKGIINKRE DAIKAGEAAK GNLLGILMES 300
NFREIQEHGN NKNAGMSIED VIGECKLFYF AGQETTSVLL VWTLVLLSQN QDWQARAREE 360
VLQVFGTNIP TYDQLSHLKV VTMILLEVLR LYPAVVELPR TTYKKTQLGK FLLPAGVEVS 420
LHIMLAHHDK ELWGEDAKEF KPERFSEGVS KATKNQFTYF PFGAGPRICI GQNFAMLEAK 480
LALSLILQHF TFELSPSYAH APSVTITLHP QFGAHFILHK R 521

SEQ ID NO:103

CVALSVVLVS IVIAWAWRVL NWVWLRPNKL ERCLREQGLT GNSYRLLFGD TKEISMMVEQ 60
AQSKPIKLST THDIAPRVIP FSHQIVYTYG RNSFVWMGPT PRVTIMNPED LKDAFNKSDE 120
FQRAISNPIV KSISQGLSSL EGEKWAKHRK IINPAFHLEK LKGMLPTFYQ SCSEMINKWE 180
SLVFKEGSRE MDVWPYLENL TSDVISRAAF GSSYEEGRKI FQLLREEAKF YTIAARSVYI 240
PGWRFLPTKQ NKRMKEIHKE VRGLLKGIIN KREDAIKAGE AAKGNLLGIL MESNFREIQE 300
HGNNKNAGMS IEDVIGECKL FYFAGQETTS VLLVWTLVLL SQNQDWQARA REEVLQVFGT 360
NIPTYDQLSH LKVVTMILLE VLRLYPAVVE LPRTTYKKTQ LGKFLLPAGV EVSLHIMLAH 420
HDKELWGEDA KEFKPERFSE GVSKATKNQF TYFPFGAGPR ICIGQNFAML EAKLALSLIL 480
QHFTFELSPS YAHAPSVTIT LHPQFGAHFI LHKR 514

SEQ ID NO:104

MGPIPRVHIM NPEDLKDTFN RHDDFHKVVK NPIMKSLPQG IVGIEGDQWA KHRKIINPAF 60
HLEKLKGMVP IFYQSCSEMI NIWKSLVSKE SSCELDVWPY LENFTSDVIS RAAFGSSYEE 120
GRKIFQLLRE EAKVYTVAVR SVYIPGWRFL PTKQNKKTKE IHNEIKGLLK GIINKREEAM 180
KAGEATKDDL LGILMESNFR EIQEHGNNKN AGMSIEDVIG ECKLFYFAGQ ETTSVLLVWT 240
MVLLSQNQDW QARAREEVLQ VFGSNIPTYE ELSHLKVVTM ILLEVLRLYP SVVALPRTTH 300
KKTQLGKLSL PAGVEVSLPI LLVHHDKELW GEDANEFKPE RFSEGVSKAT KNQFTYFPFG 360
GGPRICIGQN FAMMEAKLAL SLILQHFTFE LSPQYSHAPS VTITLQPQYG AHLILHKR 418

SEQ ID NO:105

atgggtttgt tcccattaga ggattcctac gcgctggtct ttgaaggact agcaataaca 60
ctggctttgt actatctact gtctttcatc tacaaaacat ctaaaaagac atgtacacct 120
cctaaagcat ctggtgaaat cattccaatt acaggaatca tattgaatct gctatctggc 180
tcaagtggtc tacctattat cttagcactt gcctctttag cagacagatg tggtcctatt 240
ttcaccatta ggctgggtat taggagagtg ctagtagtat caaattggga aatcgctaag 300
gagattttca ctacccacga tttgatagtt tctaatagac caaaatactt agccgctaag 360
attcttggtt tcaattatgt ttcattctct ttcgctccat acggcccata ttgggtcgga 420
atcagaaaga ttattgctac aaaactaatg tcttcttcca gacttcagaa gttgcaattt 480
gtaagagttt ttgaactaga aaactctatg aaatctatca gagaatcatg gaaggagaaa 540
aaggatgaag agggaaaggt attagttgag atgaaaaagt ggttctggga actgaatatg 600
aacatagtgt taaggacagt tgctggtaaa caatacactg gtacagttga tgatgccgat 660
gcaaagcgta tctccgagtt attcagagaa tggtttcact acactggcag atttgtcgtt 720
ggagacgctt ttccttttct aggttggttg gacctgggcg gatacaaaaa gacaatggaa 780
ttagttgcta gtagattgga ctcaatggtc agtaaatggt tagatgagca tcgtaaaaag 840
caagctaacg atgacaaaaa ggaggatatg gatttcatgg atatcatgat ctccatgaca 900
gaagcaaatt caccacttga aggatacggc actgatacta ttatcaagac cacatgtatg 960
actttgattg tttcaggagt tgatacaacc tcaatcgtac ttacttgggc cttatcactt 1020
ttgttaaaca acagagatac tttgaaaaag gcacaagagg aattagatat gtgcgtaggt 1080
aaaggaagac aagtcaacga gtctgatctt gttaacttga tatacttgga agcagtgctt 1140
aaagaggctt taagacttta cccagcagcg ttcttaggcg gaccaagagc attcttggaa 1200
gattgtactg ttgctggtta tagaattcca aagggcacct gcttgttgat taacatgtgg 1260
aaactgcata gagatccaaa catttggagt gatccttgcg aattcaagcc agaaagattt 1320
ttgacaccta atcaaaagga tgttgatgtg atcggtatgg atttcgaatt gataccattt 1380
ggtgccggca gaagatattg tccaggtact agattggctt tacagatgtt gcatatcgta 1440

```
ttagcgacat tgctgcaaaa cttcgaaatg tcaacaccaa acgatgcgcc agtcgatatg      1500
actgcttctg ttggcatgac aaatgccaaa gcatcacctt tagaagtctt gctatcacct      1560
cgtgttaaat ggtcctaa                                                    1578
```

SEQ ID NO:106

```
MGLFPLEDSY ALVFEGLAIT LALYYLLSFI YKTSKKTCTP PKASGEHPIT GHLNLLSGSS        60
GLPHLALASL ADRCGPIFTI RLGIRRVLVV SNWEIAKEIF TTHDLIVSNR PKYLAAKILG       120
FNYVSFSFAP YGPYWVGIRK IIATKLMSSS RLQKLQFVRV FELENSMKSI RESWKEKKDE       180
EGKVLVEMKK WFWELNMNIV LRTVAGKQYT GTVDDADAKR ISELFREWFH YTGRFVVGDA       240
FPFLGWLDLG GYKKTMELVA SRLDSMVSKW LDEHRKKQAN DDKKEDMDFM DIMISMTEAN       300
SPLEGYGTDT IIKTTCMTLI VSGVDTTSIV LTWALSLLLN NRDTLKKAQE ELDMCVGKGR       360
QVNESDLVNL IYLEAVLKEA LRLYPAAFLG GPRAFLEDCT VAGYRIPKGT CLLINMWKLH       420
RDPNIWSDPC EFKPERFLTP NQKDVDVIGM DFELIPFGAG RRYCPGTRLA LQMLHIVLAT       480
LLQNFEMSTP NDAPVDMTAS VGMTNAKASP LEVLLSPRVK WS                         522
```

SEQ ID NO:107

```
atgatacaag ttttaactcc aattctactc ttcctcatct tcttcgtttt ctggaaagtc        60
tacaaacatc aaaagactaa aatcaatcta ccaccaggtt ccttcggctg gccatttttg       120
ggtgaaacct tagccttact tagagcaggc tgggattctg agccagaaag attcgtaaga       180
gagcgtatca aaaagcatgg atctccactt gttttcaaga catcactatt tggagacaga       240
ttcgctgttc tttgcggtcc agctggtaat aagtttttgt tctgcaacga aaacaaatta       300
gtggcatctt ggtggccagt ccctgtaagg aagttgttcg gtaaaagttt actcacaata       360
agaggagatg aagcaaaatg gatgagaaaa atgctattgt cttacttggg tccagatgca       420
tttgccacac attatgccgt tactatggat gttgtaacac gtagacatat tgatgtccat       480
tggaggggca aggaggaagt taatgtattt caaacagtta agttgtacgc attcgaatta       540
gcttgtagat tattcatgaa cctagatgac ccaaaccaca tcgcgaaact cggtagtctt       600
ttcaacattt tcctcaaagg gatcatcgag cttcctatag acgttcctgg aactagattt       660
tactccagta aaaaggccgc agctgccatt agaattgaat tgaaaaagct cattaaagct       720
agaaaactcg aattgaagga gggtaaggcg tcttcttcac aggacttgct ttctcatcta       780
ttaacatcac ctgatgagaa tgggatgttc ttgacagaag aggaaatagt cgataacatt       840
ctacttttgt tattcgctgg tcacgatacc tctgcactat caataacact tttgatgaaa       900
accttaggtg aacacagtga tgtgtacgac aaggttttga aggaacaatt agaaatttcc       960
aaaacaaagg aggcttggga atcactaaag tgggaagata tccagaagat gaagtactca      1020
tggtcagtaa tctgtgaagt catgagattg aatcctcctg tcatagggac atacagagag      1080
gcgttggttg atatcgacta tgctggttac actatcccaa aggatggaa gttgcattgg       1140
tcagctgttt ctactcaaag agacgaagcc aatttcgaag atgtaactag attcgatcca      1200
tccagatttg aaggggcagg ccctactcca ttcacatttg tgcctttcgg tggaggtcct      1260
agaatgtgtt taggcaaaga gtttgccagg ttagaagtgt tagcatttct ccacaacatt      1320
gttaccaact ttaagtggga tcttctaatc cctgatgaga agatcgaata tgatccaatg      1380
gctactccag ctaagggctt gccaattaga cttcatccac accaagtcta a               1431
```

SEQ ID NO:108

```
MIQVLTPILL FLIFFVFWKV YKHQKTKINL PPGSFGWPFL GETLALLRAG WDSEPERFVR        60
ERIKKHGSPL VFKTSLFGDR FAVLCGPAGN KFLFCNENKL VASWWPVPVR KLFGKSLLTI       120
RGDEAKWMRK MLLSYLGPDA FATHYAVTMD VVTRRHIDVH WRGKEEVNVF QTVKLYAFEL       180
ACRLFMNLDD PNHIAKLGSL FNIFLKGIIE LPIDVPGTRF YSSKKAAAAI RIELKKLIKA       240
RKLELKEGKA SSSQDLLSHL LTSPDENGMF LTEEEIVDNI LLLLFAGHDT SALSITLLMK       300
TLGEHSDVYD KVLKEQLEIS KTKEAWESLK WEDIQKMKYS WSVICEVMRL NPPVIGTYRE       360
ALVDIDYAGY TIPKGWKLHW SAVSTQRDEA NFEDVTRFDP SRFEGAGPTP FTFVPFGGGP       420
RMCLGKEFAR LEVLAFLHNI VTNFKWDLLI PDEKIEYDPM ATPAKGLPIR LHPHQV           476
```

SEQ ID NO:109

```
atggagtctt tagtggttca tacagtaaat gctatctggt gtattgtaat cgtcgggatt        60
ttctcagttg gttatcacgt ttacggtaga gctgtggtcg aacaatggag aatgagaaga       120
tcactgaagc tacaaggtgt taaaggccca ccaccatcca tcttcaatgg taacgtctca       180
gaaatgcaac gtatccaatc cgaagctaaa cactgctctg gcgataacat tatctcacat       240
gattattctt cttcattatt cccacacttc gatcactgga gaaaacagta cggcagaatc       300
```

```
tacacatact ctactggatt aaagcaacac ttgtacatca atcatccaga aatggtgaag      360
gagctatctc agactaacac attgaacttg ggtagaatca cccatataac caaaagattg      420
aatcctatct taggtaacgg aatcataacc tctaatggtc ctcattgggc ccatcagcgt      480
agaattatcg cctacgagtt tactcatgat aagatcaagg gtatggttgg tttgatggtt      540
gagtctgcta tgcctatgtt gaataagtgg gaggagatgg taaagagagg cggagaaatg      600
ggatgcgaca taagagttga tgaggacttg aaagatgttt cagcagatgt gattgcaaaa      660
gcctgtttcg gatcctcatt ttctaaaggt aaggctattt tctctatgat aagagatttg      720
cttacagcta tcacaaagag aagtgttcta ttcagattca acggattcac tgatatggtc      780
tttgggagta aaaagcatgg tgacgttgat atagacgctt tagaaatgga attggaatca      840
tccatttggg aaactgtcaa ggaacgtgaa atagaatgta aagatactca caaaaaggat      900
ctgatgcaat tgattttgga aggggcaatg cgttcatgtg acggtaacct ttgggataaa      960
tcagcatata gaagatttgt tgtagataat tgtaaatcta tctacttcgc agggcatgat     1020
agtacagctg tctcagtgtc atggtgtttg atgttactgg ccctaaaccc atcatggcaa     1080
gttaagatcc gtgatgaaat tctgtcttct tgcaaaaatg gtattccaga tgccgaaagt     1140
atcccaaacc ttaaaacagt gactatggtt attcaagaga caatgagatt ataccctcca     1200
gcaccaatcg tcgggagaga agcctctaaa gatatcagat tgggcgatct agttgttcct     1260
aaaggcgtct gtatatggac actaatacca gctttacaca gagatcctga gatttgggga     1320
ccagatgcaa acgatttcaa accagaaaga ttttctgaag gaatttcaaa ggcttgtaag     1380
tatcctcaaa gttacattcc atttggtctg ggtcctagaa catgcgttgg taaaaacttt     1440
ggcatgatgg aagtaaaggt tcttgtttcc ctgattgtct ccaagttctc tttcactcta     1500
tctcctacct accaacatag tcctagtcac aaacttttag tagaaccaca acatggggtg     1560
gtaattagag tggtttaa                                                   1578
```

SEQ ID NO:110

```
MESLVVHTVN AIWCIVIVGI FSVGYHVYGR AVVEQWRMRR SLKLQGVKGP PPSIFNGNVS       60
EMQRIQSEAK HCSGDNIISH DYSSSLFPHF DHWRKQYGRI YTYSTGLKQH LYINHPEMVK      120
ELSQTNTLNL GRITHITKRL NPILGNGIIT SNGPHWAHQR RIIAYEFTHD KIKGMVGLMV      180
ESAMPMLNKW EEMVKRGGEM GCDIRVDEDL KDVSADVIAK ACFGSSFSKG KAIFSMIRDL      240
LTAITKRSVL FRFNGFTDMV FGSKKHGDVD IDALEMELES SIWETVKERE IECKDTHKKD      300
LMQLILEGAM RSCDGNLWDK SAYRRFVVDN CKSIYFAGHD STAVSVSWCL MLLALNPSWQ      360
VKIRDEILSS CKNGIPDAES IPNLKTVTMV IQETMRLYPP APIVGREASK DIRLGDLVVP      420
KGVCIWTLIP ALHRDPEIWG PDANDFKPER FSEGISKACK YPQSYIPFGL GPRTCVGKNF      480
GMMEVKVLVS LIVSKFSFTL SPTYQHSPSH KLLVEPQHGV VIRVV                    525
```

SEQ ID NO:111

```
atgtacttcc tactacaata cctcaacatc acaaccgttg gtgtctttgc cacattgttt       60
ctctcttatt gtttacttct ctggagaagt agagcgggta acaaaaagat tgccccagaa      120
gctgccgctg catggcctat tatcggccac ctccacttac ttgcaggtgg atcccatcaa      180
ctaccacata ttacattggg taacatggca gataagtacg gtcctgtatt cacaatcaga      240
ataggcttgc atagagctgt agttgtctca tcttgggaaa tggcaaagga atgttcaaca      300
gctaatgatc aagtgtcttc ttcaagacct gaactattag cttctaagtt gttgggttat      360
aactacgcca tgtttggttt ttcaccatac ggttcatact ggagagaaat gagaaagatc      420
atctctctcg aattactatc taattccaga ttggaactat tgaaagatgt tagagcctca      480
gaagttgtca catctattaa ggaactatac aaattgtggg cggaaaagaa gaatgagtca      540
ggattggttt ctgtcgagat gaaacaatgg ttcggagatt tgactttaaa cgtgatcttg      600
agaatggtgg ctggtaaaag atacttctcc gcgagtgacg cttcagaaaa caaacaggcc      660
cagcgttgta gaagagtctt cagagaattc ttccatctct ccggcttgtt tgtggttgct      720
gatgctatac cttttcttgg atggctcgat tggggaagac acgagaagac cttgaaaaag      780
accgccatag aaatggattc catcgcccag gagtggcttg aggaacatag acgtagaaaa      840
gattctggag atgataattc tacccaagat ttcatggacg ttatgcaatc tgtgctagat      900
ggcaaaaatc taggcggata cgatgctgat acgattaaca aggctacatg cttaactctt      960
atatcaggtg gcagtgatac tactgtagtt tctttgacat gggctcttag tcttgtgtta     1020
aacaatagag atactttgaa aaaggcacag gaagagttag acatccaagt cggtaaggaa     1080
agattggtta acgagcaaga catcagtaag ttagtttact tgcaagcaat agtaaaagag     1140
acactcagac tttatccacc aggtcctttg ggtggtttga gacaattcac tgaagattgt     1200
acactaggtg gctatcacgt ttcaaaagga actagattaa tcatgaactt atccaagatt     1260
caaaaagatc cacgtatttg gtctgatcct actgaattcc aaccagagag attccttacg     1320
```

actcataaag atgtcgatcc acgtggtaaa cactttgaat tcattccatt cggtgcagga 1380
agacgtgcat gtcctggtat cacattcgga ttacaagtac tacatctaac attggcatct 1440
ttcttgcatg cgtttgaatt ttcaacacca tcaaatgagc aggttaacat gagagaatca 1500
ttaggtctta cgaatatgaa atctacccca ttagaagttt tgatttctcc aagactatcc 1560
cttaattgct tcaaccttat gaaaatttga 1590

SEQ ID NO:112
MYFLLQYLNI TTVGVFATLF LSYCLLLWRS RAGNKKIAPE AAAAWPIIGH LHLLAGGSHQ 60
LPHITLGNMA DKYGPVFTIR IGLHRAVVVS SWEMAKECST ANDQVSSSRP ELLASKLLGY 120
NYAMFGFSPY GSYWREMRKI ISLELLSNSR LELLKDVRAS EVVTSIKELY KLWAEKKNES 180
GLVSVEMKQW FGDLTLNVIL RMVAGKRYFS ASDASENKQA QRCRRVFREF FHLSGLFVVA 240
DAIPFLGWLD WGRHEKTLKK TAIEMDSIAQ EWLEEHRRRK DSGDDNSTQD FMDVMQSVLD 300
GKNLGGYDAD TINKATCLTL ISGGSDTTVV SLTWALSLVL NNRDTLKKAQ EELDIQVGKE 360
RLVNEQDISK LVYLQAIVKE TLRLYPPGPL GGLRQFTEDC TLGGYHVSKG TRLIMNLSKI 420
QKDPRIWSDP TEFQPERFLT THKDVDPRGK HFEFIPFGAG RRACPGITFG LQVLHLTLAS 480
FLHAFEFSTP SNEQVNMRES LGLTNMKSTP LEVLISPRLS SCSLYN 526

SEQ ID NO:113
atggaaccta acttttactt gtcattacta ttgttgttcg tgaccttcat ttctttaagt 60
ctgtttttca tcttttacaa acaaaagtcc ccattgaatt tgccaccagg gaaaatgggt 120
taccctatca taggtgaaag tttagaattc ctatccacag gctggaaggg acatcctgaa 180
aagttcatat ttgatagaat gcgtaagtac agtagtgagt tattcaagac ttctattgta 240
ggcgaatcca cagttgtttg ctgtggggca gctagtaaca aattcctatt ctctaacgaa 300
aacaaactgg taactgcctg gtggccagat tctgttaaca aaatcttccc aacaacttca 360
ctggattcta atttgaagga ggaatctata aagatgagaa agttgctgcc acagttcttc 420
aaaccagaag cacttcaaag atacgtcggc gttatggatg taatcgcaca aagacatttt 480
gtcactcact gggacaacaa aaatgagatc acagtttatc cacttgctaa aagatacact 540
ttcttgcttg cgtgtagact gttcatgtct gttgaggatg aaaatcatgt ggcgaaattc 600
tcagacccat tccaactaat cgctgcaggc atcatttcac ttcctatcga tcttcctggt 660
actccattca acaaggccat aaaggcttca aatttcatta gaaaagagct gataaagatt 720
atcaaacaaa gacgtgttga tctggcagag ggtacagcat ctccaaccca ggatatcttg 780
tcacatatgc tattaacatc tgatgaaaac ggtaaatcta tgaacgagtt gaacattgcc 840
gacaagattc ttggactatt gataggaggc cacgatacag cttcagtagc ttgcacattt 900
ctagtgaagt acttaggaga attaccacat atctacgata aagtctacca agagcaaatg 960
gaaattgcca agtccaaacc tgctggggaa ttgttgaatt gggatgactt gaaaaagatg 1020
aagtattcat ggaatgtggc atgtgaggta atgagattgt caccaccttt acaaggtggt 1080
tttagagagg ctataactga ctttatgttt aacggtttct ctattccaaa agggtggaag 1140
ttatactggt ccgccaactc tacacacaaa aatgcagaat gtttcccaat gcctgagaaa 1200
ttcgatccta ccagatttga aggtaatggt ccagcgcctt atacatttgt accattcggt 1260
ggaggcccta gaatgtgtcc tggaaaggaa tacgctagat tagaaatctt ggttttcatg 1320
cataatctgg tcaaacgttt taagtgggaa aaggttattc cagacgaaaa gattattgtc 1380
gatccattcc caatcccagc taaagatctt ccaatccgtt tgtatcctca caaagcttaa 1440

SEQ ID NO:114
MEPNFYLSLL LLFVTFISLS LFFIFYKQKS PLNLPPGKMG YPIIGESLEF LSTGWKGHPE 60
KFIFDRMRKY SSELFKTSIV GESTVVCCGA ASNKFLFSNE NKLVTAWWPD SVNKIFPTTS 120
LDSNLKEESI KMRKLLPQFF KPEALQRYVG VMDVIAQRHF VTHWDNKNEI TVYPLAKRYT 180
FLLACRLFMS VEDENHVAKF SDPFQLIAAG IISLPIDLPG TPFNKAIKAS NFIRKELIKI 240
IKQRRVDLAE GTASPTQDIL SHMLLTSDEN GKSMNELNIA DKILGLLIGG HDTASVACTF 300
LVKYLGELPH IYDKVYQEQM EIAKSKPAGE LLNWDDLKKM KYSWNVACEV MRLSPPLQGG 360
FREAITDFMF NGFSIPKGWK LYWSANSTHK NAECFPMPEK FDPTRFEGNG PAPYTFVPFG 420
GGPRMCPGKE YARLEILVFM HNLVKRFKWE KVIPDEKIIV DPFPIPAKDL PIRLYPHKA 479

SEQ ID NO:115
atggcctctg ttactttggg ttcctggatc gtcgtccacc accataacca tcaccatcca 60
tcatctatcc taactaaatc tcgttcaaga tcctgtccta ttacactaac caaaccaatc 120
tcttttcgtt caaagagaac agtttcctct agtagttcta tcgtgtcctc tagtgtcgtc 180

```
actaaggaag acaatctgag acagtctgaa ccttcttcct ttgatttcat gtcatatatc      240
attactaagg cagaactagt gaataaggct cttgattcag cagttccatt aagagagcca      300
ttgaaaatcc atgaagcaat gagatactct cttctagctg gcgggaagag agtcagacct      360
gtactctgca tagcagcgtg cgaattagtt ggtggcgagg aatcaaccgc tatgcctgcc      420
gcttgtgctg tagaaatgat tcatacaatg tcactgatac acgatgattt gccatgtatg      480
gataacgatg atctgagaag ggtaagcca actaaccata aggttttcgg cgaagatgtt      540
gccgtcttag ctggtgatgc tttgttatct ttcgcgttcg aacatttggc atccgcaaca      600
tcaagtgatg ttgtgtcacc agtaagagta gttagagcag ttggagaact ggctaaagct      660
attggaactg agggtttagt tgcaggtcaa gtcgtcgata tctcttccga aggtcttgat      720
ttgaatgatg taggtcttga acatctcgaa ttcatccatc ttcacaagac agctgcactt      780
ttagaagcca gtgcggttct cggcgcaatt gttggcggag ggagtgatga cgaaattgag      840
agattgagga agtttgctag atgtatagga ttactgttcc aagtagtaga cgatatacta      900
gatgtgacaa agtcttccaa agagttggga aaaacagctg gtaaagattt gattgccgac      960
aaattgacct accctaagat tatggggcta gaaaaatcaa gagaatttgc cgagaaactc     1020
aatagagagg cgcgtgatca actgttgggt ttcgattctg ataaagttgc accactctta     1080
gccttagcca actacatcgc ttacagacaa aactaa                               1116
```

SEQ ID NO:116

```
MASVTLGSWI VVHHHNHHHP SSILTKSRSR SCPITLTKPI SFRSKRTVSS SSSIVSSSVV       60
TKEDNLRQSE PSSFDFMSYI ITKAELVNKA LDSAVPLREP LKIHEAMRYS LLAGGKRVRP      120
VLCIAACELV GGEESTAMPA ACAVEMIHTM SLIHDDLPCM DNDDLRRGKP TNHKVFGEDV      180
AVLAGDALLS FAFEHLASAT SSDVVSPVRV VRAVGELAKA IGTEGLVAGQ VVDISSEGLD      240
LNDVGLEHLE FIHLHKTAAL LEASAVLGAI VGGGSDDEIE RLRKFARCIG LLFQVVDDIL      300
DVTKSSKELG KTAGKDLIAD KLTYPKIMGL EKSREFAEKL NREARDQLLG FDSDKVAPLL      360
ALANYIAYRQ N                                                           371
```

SEQ ID NO:117

```
MATLLEHFQA MPFAIPIALA ALSWLFLFYI KVSFFSNKSA QAKLPPVPVV PGLPVIGNLL       60
QLKEKKPYQT FTRWAEEYGP IYSIRTGAST MVVLNTTQVA KEAMVTRYLS ISTRKLSNAL      120
KILTADKCMV AISDYNDFHK MIKRYILSNV LGPSAQKRHR SNRDTLRANV CSRLHSQVKN      180
SPREAVNFRR VFEWELFGIA LKQAFGKDIE KPIYVEELGT TLSRDEIFKV LVLDIMEGAI      240
EVDWRDFFPY LRWIPNTRME TKIQRLYFRR KAVMTALINE QKKRIASGEE INCYIDFLLK      300
EGKTLTMDQI SMLLWETVIE TADTTMVTTE WAMYEVAKDS KRQDRLYQEI QKVCGSEMVT      360
EEYLSQLPYL NAVFHETLRK HSPAALVPLR YAHEDTQLGG YYIPAGTEIA INIYGCNMDK      420
HQWESPEEWK PERFLDPKFD PMDLYKTMAF GAGKRVCAGS LQAMLIACPT IGRLVQEFEW      480
KLRDGEEENV DTVGLTTHKR YPMHAILKPR S                                     511
```

SEQ ID NO:118

```
MATSDSIVDD RKQLHVATFP WLAFGHILPY LQLSKLIAEK GHKVSFLSTT RNIQRLSSHI       60
SPLINVVQLT LPRVQELPED AEATTDVHPE DIPYLKKASD GLQPEVTRFL EQHSPDWIIY      120
DYTHYWLPSI AASLGISRAH FSVTTPWAIA YMGPSADAMI NGSDGRTTVE DLTTPPKWFP      180
FPTKVCWRKH DLARLVPYKA PGISDGYRMG MVLKGSDCLL SKCYHEFGTQ WLPLLETLHQ      240
VPVVPVGLLP PEIPGDEKDE TWVSIKKWLD GKQKGSVVYV ALGSEVLVSQ TEVVELALGL      300
ELSGLPFVWA YRKPKGPAKS DSVELPDGFV ERTRDRGLVW TSWAPQLRIL SHESVCGFLT      360
HCGSGSIVEG LMFGHPLIML PIFGDQPLNA RLLEDKQVGI EIPRNEEDGC LTKESVARSL      420
RSVVVEKEGE IYKANARELS KIYNDTKVEK EYVSQFVDYL EKNARAVAID HES              473
```

SEQ ID NO:119

```
MATSDSIVDD RKQLHVATFP WLAFGHILPY LQLSKLIAEK GHKVSFLSTT RNIQRLSSHI       60
SPLINVVQLT LPRVQELPED AEATTDVHPE DIPYLKKASD GLQPEVTRFL EQHSPDWIIY      120
DYTHYWLPSI AASLGISRAH FSVTTPWAIA YMGPSADAMI NGSDGRTTVE DLTTPPKWFP      180
FPTKVCWRKH DLARGVPYKA PGISDGYRMG LVLKGSDCLL SKCYHEFGTQ WLPLLETLHQ      240
VPVVPVGLLP PEIPGDEKDE TWVSIKKWLD GKQKGSVVYV ALGSEVLVSQ TEVVELALGL      300
ELSGLPFVWA YRKPKGPAKS DSVELPDGFV ERTRDRGLVW TSWAPQLRIL SHESVCGFLT      360
HCGSGSIVEG LMFGHPLIML PIFGDQPLNA RLLEDKQVGI EIPRNEEDGC LTKESVARSL      420
RSVVVEKEGE IYKANARELS KIYNDTKVEK EYVSQFVDYL EKNARAVAID HES              473
```

SEQ ID NO:120

```
MATSDSIVDD RKQLHVATFP WLAFGHILPY LQLSKLIAEK GHKVSFLSTT RNIQRLSSHI   60
SPLINVVQLT LPRVQELPED AEATTDVHPE DIPYLKKASD GLQPEVTRFL EQHSPDWIIY  120
DYTHYWLPSI AASLGISRAH FSVTTPWAIA YMGPSADAMI NGSDGRTTVE DLTTPPKWFP  180
FPTKVCWRKH DLARLPPYKA PGISDGYRMG LVLKGSDCLL SKCYHEFGTQ WLPLLETLHQ  240
VPVVPVGLLP PEIPGDEKDE TWVSIKKWLD GKQKGSVVYV ALGSEVLVSQ TEVVELALGL  300
ELSGLPFVWA YRKPKGPAKS DSVELPDGFV ERTRDRGLVW TSWAPQLRIL SHESVCGFLT  360
HCGSGSIVEG LMFGHPLIML PIFGDQPLNA RLLEDKQVGI EIPRNEEDGC LTKESVARSL  420
RSVVVEKEGE IYKANARELS KIYNDTKVEK EYVSQFVDYL EKNARAVAID HES          473
```

SEQ ID NO:121

```
MATSDSIVDD RKQLHVATFP WLAFGHILPY LQLSKLIAEK GHKVSFLSTT RNIQRLSSHI   60
SPLINVVQLT LPRVQELPED AEATTDVHPE DIPYLKKASD GLQPEVTRFL EQHSPDWIIY  120
DYTHYWLPSI AASLGISRAH FSVTTPWAIA YMGPSADAMI NGSDGRTTVE DLTTPPKWFP  180
FPTKVCWRKH DLARLVPYKA PGISDGYRMG HVLKGSDCLL SKCYHEFGTQ WLPLLETLHQ  240
VPVVPVGLLP PEIPGDEKDE TWVSIKKWLD GKQKGSVVYV ALGSEVLVSQ TEVVELALGL  300
ELSGLPFVWA YRKPKGPAKS DSVELPDGFV ERTRDRGLVW TSWAPQLRIL SHESVCGFLT  360
HCGSGSIVEG LMFGHPLIML PIFGDQPLNA RLLEDKQVGI EIPRNEEDGC LTKESVARSL  420
RSVVVEKEGE IYKANARELS KIYNDTKVEK EYVSQFVDYL EKNARAVAID HES          473
```

SEQ ID NO:122

```
MDSGYSSSYA AAAGMHVVIC PWLAFGHLLP CLDLAQRLAS RGHRVSFVST PRNISRLPPV   60
RPALAPLVAF VALPLPRVEG LPDGAESTND VPHDRPDMVE LHRRAFDGLA APFSEFLGTA  120
CADWVIVDVF HHWAAAAALE HKVPCAMMLL GSAHMIASIA DRRLERAETE SPAAAGQGRP  180
AAAPTFEVAR MKLIRTKGSS GMSLAERFSL TLSRSSLVVG RSCVEFEPET VPLLSTLRGK  240
PITFLGLMPP LHEGRREDGE DATVRWLDAQ PAKSVVYVAL GSEVPLGVEK VHELALGLEL  300
AGTRFLWALR KPTGVSDADL LPAGFEERTR GRGVVATRWV PQMSILAHAA VGAFLTHCGW  360
NSTIEGLMFG HPLIMLPIFG DQGPNARLIE AKNAGLQVPR NEEDGCLTKE SVARSLRSVV  420
VEKEGEIYKA NARELSKIYN DTKVEKEYVS QFVDYLEKNA RAVAIDHES            469
```

SEQ ID NO:123

```
MATSDSIVDD RKQLHVATFP WLAFGHILPY LQLSKLIAEK GHKVSFLSTT RNIQRLSSHI   60
SPLINVVQLT LPRVQELPED AEATTDVHPE DIPYLKKASD GLQPEVTRFL EQHSPDWIIY  120
DYTHYWLPSI AASLGISRAH FSVTTPWAIA YMGPSADAMI NGSDGRTTVE DLTTPPKWFP  180
FPTKVCWRKH DLARCVPYKA PGISDGYRMG LVLKGSDCLL SKCYHEFGTQ WLPLLETLHQ  240
VPVVPVGLLP PEIPGDEKDE TWVSIKKWLD GKQKGSVVYV ALGSEVLVSQ TEVVELALGL  300
ELSGLPFVWA YRKPKGPAKS DSVELPDGFV ERTRDRGLVW TSWAPQLRIL SHESVCGFLT  360
HCGSGSIVEG LMFGHPLIML PIFGDQPLNA RLLEDKQVGI EIPRNEEDGC LTKESVARSL  420
RSVVVEKEGE IYKANARELS KIYNDTKVEK EYVSQFVDYL EKNARAVAID HES          473
```

SEQ ID NO:124

```
MDSGYSSSYA AAAGMHVVIC PWLAFGHLLP CLDLAQRLAS RGHRVSFVST PRNISRLPPV   60
RPALAPLVAF VALPLPRVEG LPDGAESTND VPHDRPDMVE LHRRAFDGLA APFSEFLGTA  120
CADWVIVDVF HHWLPSIAAS LGISRAHFSV TTPWAIAYMG PSADAMINGS DGRTTVEDLT  180
TPPKWFPFPT KVCWRKHDLA RLVPYKAPGI SDGYRMGMVL KGSDCLLSKC YHEFGTQWLP  240
LLETLHQVPV VPVGLMPPLH EGRREDGEDA TVRWLDAQPA KSVVYVALGS EVPLGVEKVH  300
ELALGLELAG TRFLWALRKP TGVSDADLLP AGFEERTRGR GVVATRWVPQ MSILAHAAVG  360
AFLTHCGWNS TIEGLMFGHP LIMLPIFGDQ GPNARLIEAK NAGLQVARND GDGSFDREGV  420
AAAIRAVAVE EESSKVFQAK AKKLQEIVAD MACHERYIDG FIQQLRSYKD             470
```

SEQ ID NO:125

```
MATSDSIVDD RKQLHVATFP WLAFGHILPY LQLSKLIAEK GHKVSFLSTT RNIQRLSSHI   60
SPLINVVQLT LPRVQELPED AEATTDVHPE DIPYLKKASD GLQPEVTRFL EQHSPDWIIY  120
DYTHYWAAAA ALEHKVPCAM MLLGSAHMIA SIADRRLERA ETESPAAAGQ GRPAAAPTFE  180
VARMKLIRTK GSSGMSLAER FSLTLSRSSL VVGRSCVEFE PETVPLLSTL RGKPITFLGL  240
MPPLHEGRRE DGEDATVRWL DAQPAKSVVY VALGSEVPLG VEKVHELALG LELAGTRFLW  300
ALRKPTGVSD ADLLPAGFEE RTRGRGVVAT RWVPQMSILA HAAVGAFLTH CGWNSTIEGL  360
```

MFGHPLIMLP IFGDQGPNAR LIEAKNAGLQ VARNDGDGSF DREGVAAAIR AVAVEEESSK 420
VFQAKAKKLQ EIVADMACHE RYIDGFIQQL RSYKD 455

SEQ ID NO:126
MATSDSIVDD RKQLHVATFP WLAFGHILPY LQLSKLIAEK GHKVSFLSTT RNIQRLSSHI 60
SPLINVVQLT LPRVQELPED AEATTDVHPE DIPYLKKASD GLQPEVTRFL EQHSPDWIIY 120
DYTHYWLPSI AASLGISRAH FSVTTPWAIA YMGPSADAMI NGSDGRTTVE DLTTPPKWFP 180
FPTKVCWRKH DLARLVPYKA PGISDGYRMG MVLKGSDCLL SKCYHEFGTQ WLPLLETLHQ 240
VPVVPVGLLP PEIPGDEKDE TWVSIKKWLD GKQKGSVVYV ALGSEALVSQ TEVVELALGL 300
ELSGLPFVWA YRKPKGPAKS DSVELPDGFV ERTRDRGLVW TSWAPQLRIL SHESVCGFLT 360
HCGSGSIVEG LMFGHPLIML PIFGDQPLNA RLLEDKQVGI EIARNDGDGS FDREGVAAAI 420
RAVAVEEESS KVFQAKAKKL QEIVADMACH ERYIDGFIQQ LRSYKD 466

SEQ ID NO:127
MDAMATTEKK PHVIFIPFPA QSHIKAMLKL AQLLHHKGLQ ITFVNTDFIH NQFLESSGPH 60
CLDGAPGFRF ETIPDGVSHS PEASIPIRES LLRSIETNFL DRFIDLVTKL PDPPTCIISD 120
GFLSVFTIDA AKKLGIPVMM YWTLAACGFM GFYHIHSLIE KGFAPLKDAS YLTNGYLDTV 180
IDWVPGMEGI RLKDFPLDWS TDLNDKVLMF TTEAPQRSHK VSHHIFHTFD ELEPSIIKTL 240
SLRYNHIYTI GPLQLLLDQI PEEKKQTGIT SLHGYSLVKE EPECFQWLQS KEPNSVVYVN 300
FGSSTVMSLE DMTEFGWGLA NSNHYFLWII RSNLVIGENA VLPPELEEHI KKRGFIASWC 360
SQEKVLKHPS VGGFLTHCGW GSTIESLSAG VPMICWPYSW DQLTNCRYIC KEWEVGLEMG 420
TKVKRDEVKR LVQELMGEGG HKMRNKAKDW KEKARIAIAP NGSSSLNIDK MVKEITVLAR 480
N 481

SEQ ID NO:128
MATSDSIVDD RKQLHVATFP WLAFGHILPY LQLSKLIAEK GHKVSFLSTT RNIQRLSSHI 60
SPLINVVQLT LPRVQELPED AEATTDVHPE DIPYLKKASD GLQPEVTRFL EQHSPDWIIY 120
DYTHYWAAAA ALEHKVPCAM MLLGSAHMIA SIADRRLERA ETESPAAAGQ GRPAAAPTFE 180
VARMKLIRTK GSSGMSLAER FSLTLSRSSL VVGRSCVEFE PETVPLLSTL RGKPITFLGL 240
LPPEIPGDEK DETWVSIKKW LDGKQKGSVV YVALGSEALV SQTEVVELAL GLELSGLPFV 300
WAYRKPKGPA KSDSVELPDG FVERTRDRGL VWTSWAPQLR ILSHESVCGF LTHCGSGSIV 360
EGLMFGHPLI MLPIFGDQPL NARLLEDKQV GIEIPRNEED GCLTKESVAR SLRSVVVEKE 420
GEIYKANARE LSKIYNDTKV EKEYVSQFVD YLEKNARAVA IDHES 465

SEQ ID NO:129
MDSGYSSSYA AAAGMHVVIC PWLAFGHLLP CLDLAQRLAS RGHRVSFVST PRNISRLPPV 60
RPALAPLVAF VALPLPRVEG LPDGAESTND VPHDRPDMVE LHRRAFDGLA APFSEFLGTA 120
CADWVIVDVF HHWLPSIAAS LGISRAHFSV TTPWAIAYMG PSADAMINGS DGRTTVEDLT 180
TPPKWFPFPT KVCWRKHDLA RLVPYKAPGI SDGYRMGMVL KGSDCLLSKC YHEFGTQWLP 240
LLETLHQVPV VPVGLLPPEI PGDEKDETWV SIKKWLDGKQ KGSVVYVALG SEALVSQTEV 300
VELALGLELS GLPFVWAYRK PKGPAKSDSV ELPDGFVERT RDRGLVWTSW APQLRILSHE 360
SVCGFLTHCG SGSIVEGLMF GHPLIMLPIF GDQPLNARLL EDKQVGIEIP RNEEDGCLTK 420
ESVARSLRSV VVEKEGEIYK ANARELSKIY NDTKVEKEYV SQFVDYLEKN ARAVAIDHES 480

SEQ ID NO:130
MDSGYSSSYA AAAGMHVVIC PWLAFGHLLP CLDLAQRLAS RGHRVSFVST PRNISRLPPV 60
RPALAPLVAF VALPLPRVEG LPDGAESTND VPHDRPDMVE LHRRAFDGLA APFSEFLGTA 120
CADWVIVDVF HHWAAAAALE HKVPCAMMLL GSAHMIASIA DRRLERAETE SPAAAGQGRP 180
AAAPTFEVAR MKLIRTKGSS GMSLAERFSL TLSRSSLVVG RSCVEFEPET VPLLSTLRGK 240
PITFLGLLPP EIPGDEKDET WVSIKKWLDG KQKGSVVYVA LGSEALVSQT EVVELALGLE 300
LSGLPFVWAY RKPKGPAKSD SVELPDGFVE RTRDRGLVWT SWAPQLRILS HESVCGFLTH 360
CGSGSIVEGL MFGHPLIMLP IFGDQPLNAR LLEDKQVGIE IPRNEEDGCL TKESVARSLR 420
SVVVEKEGEI YKANARELSK IYNDTKVEKE YVSQFVDYLE KNARAVAIDH ES 472

SEQ ID NO:131
MDSGYSSSYA AAAGMHVVIC PWLAFGHLLP CLDLAQRLAS RGHRVSFVST PRNISRLPPV 60
RPALAPLVAF VALPLPRVEG LPDGAESTND VPHDRPDMVE LHRRAFDGLA APFSEFLGTA 120

CADWVIVDVF HHWLPSIAAS LGISRAHFSV TTPWAIAYMG PSADAMINGS DGRTTVEDLT 180
TPPKWFPFPT KVCWRKHDLA RLVPYKAPGI SDGYRMGMVL KGSDCLLSKC YHEFGTQWLP 240
LLETLHQVPV VPVGLLPPEI PGDEKDETWV SIKKWLDGKQ KGSVVYVALG SEALVSQTEV 300
VELALGLELS GLPFVWAYRK PKGPAKSDSV ELPDGFVERT RDRGLVWTSW APQLRILSHE 360
SVCGFLTHCG SGSIVEGLMF GHPLIMLPIF GDQPLNARLL EDKQVGIEIA RNDGDGSFDR 420
EGVAAAIRAV AVEEESSKVF QAKAKKLQEI VADMACHERY IDGFIQQLRS YKD 473

SEQ ID NO:132
MATSDSIVDD RKQLHVATFP WLAFGHILPY LQLSKLIAEK GHKVSFLSTT RNIQRLSSHI 60
SPLINVVQLT LPRVQELPED AEATTDVHPE DIPYLKKASD GLQPEVTRFL EQHSPDWIIY 120
DYTHYWLPSI AASLGISRAH FSVTTPWAIA YMGPSADAMI NGSDGRTTVE DLTTPPKWFP 180
FPTKVCWRKH DLARLVPYKA PGISDGYRMG MVLKGSDCLL SKCYHEFGTQ WLPLLETLHQ 240
VPVVPVGLMP PLHEGRREDG EDATVRWLDA QPAKSVVYVA LGSEVPLGVE KVHELALGLE 300
LAGTRFLWAL RKPTGVSDAD LLPAGFEERT RGRGVVATRW VPQMSILAHA AVGAFLTHCG 360
WNSTIEGLMF GHPLIMLPIF GDQGPNARLI EAKNAGLQVA RNDGDGSFDR EGVAAAIRAV 420
AVEEESSKVF QAKAKKLQEI VADMACHERY IDGFIQQLRS YKD 463

SEQ ID NO:133
MATSDSIVDD RKQLHVATFP WLAFGHILPY LQLSKLIAEK GHKVSFLSTT RNIQRLSSHI 60
SPLINVVQLT LPRVQELPED AEATTDVHPE DIPYLKKASD GLQPEVTRFL EQHSPDWIIY 120
DYTHYWAAAA ALEHKVPCAM MLLGSAHMIA SIADRRLERA ETESPAAAGQ GRPAAAPTFE 180
VARMKLIRTK GSSGMSLAER FSLTLSRSSL VVGRSCVEFE PETVPLLSTL RGKPITFLGL 240
MPPLHEGRRE DGEDATVRWL DAQPAKSVVY VALGSEVPLG VEKVHELALG LELAGTRFLW 300
ALRKPTGVSD ADLLPAGFEE RTRGRGVVAT RWVPQMSILA HAAVGAFLTH CGWNSTIEGL 360
MFGHPLIMLP IFGDQGPNAR LIEAKNAGLQ VPRNEEDGCL TKESVARSLR SVVVEKEGEI 420
YKANARELSK IYNDTKVEKE YVSQFVDYLE KNARAVAIDH ES 462

SEQ ID NO:134
MATSDSIVDD RKQLHVATFP WLAFGHILPY LQLSKLIAEK GHKVSFLSTT RNIQRLSSHI 60
SPLINVVQLT LPRVQELPED AEATTDVHPE DIPYLKKASD GLQPEVTRFL EQHSPDWIIY 120
DYTHYWAAAA ALEHKVPCAM MLLGSAHMIA SIADRRLERA ETESPAAAGQ GRPAAAPTFE 180
VARMKLIRTK GSSGMSLAER FSLTLSRSSL VVGRSCVEFE PETVPLLSTL RGKPITFLGL 240
LPPEIPGDEK DETWVSIKKW LDGKQKGSVV YVALGSEALV SQTEVVELAL GLELSGLPFV 300
WAYRKPKGPA KSDSVELPDG FVERTRDRGL VWTSWAPQLR ILSHESVCGF LTHCGSGSIV 360
EGLMFGHPLI MLPIFGDQPL NARLLEDKQV GIEIARNDGD GSFDREGVAA AIRAVAVEEE 420
SSKVFQAKAK KLQEIVADMA CHERYIDGFI QQLRSYKD 458

SEQ ID NO:135
ggcaagccac gtttggtg 18

SEQ ID NO:136
ggagctgcat gtgtcagagg 20

SEQ ID NO:137
cgatgtattt catcactggt tgccatccat cgcggct 37

SEQ ID NO:138
agccgcgatg gatggcaacc agtgatgaaa tacatcg 37

SEQ ID NO:139
ttatgattat actcactact gggctgctgc agccgcattg 40

SEQ ID NO:140
agccgcgatg gatggcaacc agtgatgaaa tacatcg 37

SEQ ID NO:141

caaacctatt actttccttg gtttactgcc accggaaata c 41

SEQ ID NO:142
gtatttccgg tggcagtaaa ccaaggaaag taataggttt g 41

SEQ ID NO:143
ccggtggttc cggtgggact aatgcctcca ttacatga 38

SEQ ID NO:144
tcatgtaatg gaggcattag tcccaccgga accaccgg 38

SEQ ID NO:145
gaacgcaggt ctgcaggttc caagaaatga ggaagatgg 39

SEQ ID NO:146
ccatcttcct catttcttgg aacctgcaga cctgcgttc 39

SEQ ID NO:147
MDAMATTEKK PHVIFIPFPA LSHIKAMLKL AQLLHHKGLQ ITFVNTDFIH NQFLESSGPH 60
CLDGAPGFRF ETIPDGVSHS PEASIPIRES LLRSIETNFL DRFIDLVTKL PDPPTCIISD 120
GFLSVFTIDA AKKLGIPVMM YWTLAACGFM GFYHIHSLIE KGFAPLKDAS YLTNGYLDTV 180
IDWVPGMEGI RLKDFPLDWS TDLNDKVLMF TTEAPQRSHK VSHHIFHTFD ELEPSIIKTL 240
SLRYNHIYTI GPLQLLLDQI PEEKKQTGIT SLHGYSLVKE EPECFQWLQS KEPNSVVYVN 300
FGSTTVMSLE DMTEFGWGLA NSNHYFLWII RSNLVIGENA VLPPELEEHI KKRGFIASWC 360
SQEKVLKHPS VGGFLTHCGW GSTIESLSAG VPMICWPYSW DQLTNCRYIC KEWEVGLEMG 420
TKVKRDEVKR LVQELMGEGG HKMRNKAKDW KEKARIAIAP NGSSSLNIDK MVKEITVLAR 480
N 481

SEQ ID NO:148
MDAMATTEKK PHVIFIPFPA TSHIKAMLKL AQLLHHKGLQ ITFVNTDFIH NQFLESSGPH 60
CLDGAPGFRF ETIPDGVSHS PEASIPIRES LLRSIETNFL DRFIDLVTKL PDPPTCIISD 120
GFLSVFTIDA AKKLGIPVMM YWTLAACGFM GFYHIHSLIE KGFAPLKDAS YLTNGYLDTV 180
IDWVPGMEGI RLKDFPLDWS TDLNDKVLMF TTEAPQRSHK VSHHIFHTFD ELEPSIIKTL 240
SLRYNHIYTI GPLQLLLDQI PEEKKQTGIT SLHGYSLVKE EPECFQWLQS KEPNSVVYVN 300
FGSTTVMSLE DMTEFGWGLA NSNHYFLWII RSNLVIGENA VLPPELEEHI KKRGFIASWC 360
SQEKVLKHPS VGGFLTHCGW GSTIESLSAG VPMICWPYSW DQLTNCRYIC KEWEVGLEMG 420
TKVKRDEVKR LVQELMGEGG HKMRNKAKDW KEKARIAIAP NGSSSLNIDK MVKEITVLAR 480
N 481

SEQ ID NO:149
MDAMATTEKK PHVIFIPFPA VSHIKAMLKL AQLLHHKGLQ ITFVNTDFIH NQFLESSGPH 60
CLDGAPGFRF ETIPDGVSHS PEASIPIRES LLRSIETNFL DRFIDLVTKL PDPPTCIISD 120
GFLSVFTIDA AKKLGIPVMM YWTLAACGFM GFYHIHSLIE KGFAPLKDAS YLTNGYLDTV 180
IDWVPGMEGI RLKDFPLDWS TDLNDKVLMF TTEAPQRSHK VSHHIFHTFD ELEPSIIKTL 240
SLRYNHIYTI GPLQLLLDQI PEEKKQTGIT SLHGYSLVKE EPECFQWLQS KEPNSVVYVN 300
FGSTTVMSLE DMTEFGWGLA NSNHYFLWII RSNLVIGENA VLPPELEEHI KKRGFIASWC 360
SQEKVLKHPS VGGFLTHCGW GSTIESLSAG VPMICWPYSW DQLTNCRYIC KEWEVGLEMG 420
TKVKRDEVKR LVQELMGEGG HKMRNKAKDW KEKARIAIAP NGSSSLNIDK MVKEITVLAR 480
N 481

SEQ ID NO:150
MDAMATTEKK PHVIFIPFPA QSHIKAMLKL AQLLHHKGLQ ITFVNTDSIH NQFLESSGPH 60
CLDGAPGFRF ETIPDGVSHS PEASIPIRES LLRSIETNFL DRFIDLVTKL PDPPTCIISD 120
GFLSVFTIDA AKKLGIPVMM YWTLAACGFM GFYHIHSLIE KGFAPLKDAS YLTNGYLDTV 180
IDWVPGMEGI RLKDFPLDWS TDLNDKVLMF TTEAPQRSHK VSHHIFHTFD ELEPSIIKTL 240
SLRYNHIYTI GPLQLLLDQI PEEKKQTGIT SLHGYSLVKE EPECFQWLQS KEPNSVVYVN 300

```
FGSTTVMSLE DMTEFGWGLA NSNHYFLWII RSNLVIGENA VLPPELEEHI KKRGFIASWC    360
SQEKVLKHPS VGGFLTHCGW GSTIESLSAG VPMICWPYSW DQLTNCRYIC KEWEVGLEMG    420
TKVKRDEVKR LVQELMGEGG HKMRNKAKDW KEKARIAIAP NGSSSLNIDK MVKEITVLAR    480
N                                                                   481
```

SEQ ID NO:151

```
MDAMATTEKK PHVIFIPFPA QSHIKAMLKL AQLLHHKGLQ ITFVNTDHIH NQFLESSGPH     60
CLDGAPGFRF ETIPDGVSHS PEASIPIRES LLRSIETNFL DRFIDLVTKL PDPPTCIISD    120
GFLSVFTIDA AKKLGIPVMM YWTLAACGFM GFYHIHSLIE KGFAPLKDAS YLTNGYLDTV    180
IDWVPGMEGI RLKDFPLDWS TDLNDKVLMF TTEAPQRSHK VSHHIFHTFD ELEPSIIKTL    240
SLRYNHIYTI GPLQLLLDQI PEEKKQTGIT SLHGYSLVKE EPECFQWLQS KEPNSVVYVN    300
FGSTTVMSLE DMTEFGWGLA NSNHYFLWII RSNLVIGENA VLPPELEEHI KKRGFIASWC    360
SQEKVLKHPS VGGFLTHCGW GSTIESLSAG VPMICWPYSW DQLTNCRYIC KEWEVGLEMG    420
TKVKRDEVKR LVQELMGEGG HKMRNKAKDW KEKARIAIAP NGSSSLNIDK MVKEITVLAR    480
N                                                                   481
```

SEQ ID NO:152

```
MDAMATTEKK PHVIFIPFPA QSHIKAMLKL AQLLHHKGLQ ITFVNTDYIH NQFLESSGPH     60
CLDGAPGFRF ETIPDGVSHS PEASIPIRES LLRSIETNFL DRFIDLVTKL PDPPTCIISD    120
GFLSVFTIDA AKKLGIPVMM YWTLAACGFM GFYHIHSLIE KGFAPLKDAS YLTNGYLDTV    180
IDWVPGMEGI RLKDFPLDWS TDLNDKVLMF TTEAPQRSHK VSHHIFHTFD ELEPSIIKTL    240
SLRYNHIYTI GPLQLLLDQI PEEKKQTGIT SLHGYSLVKE EPECFQWLQS KEPNSVVYVN    300
FGSTTVMSLE DMTEFGWGLA NSNHYFLWII RSNLVIGENA VLPPELEEHI KKRGFIASWC    360
SQEKVLKHPS VGGFLTHCGW GSTIESLSAG VPMICWPYSW DQLTNCRYIC KEWEVGLEMG    420
TKVKRDEVKR LVQELMGEGG HKMRNKAKDW KEKARIAIAP NGSSSLNIDK MVKEITVLAR    480
N                                                                   481
```

SEQ ID NO:153

```
MDAMATTEKK PHVIFIPFPA QSHIKAMLKL AQLLHHKGLQ ITFVNTDRIH NQFLESSGPH     60
CLDGAPGFRF ETIPDGVSHS PEASIPIRES LLRSIETNFL DRFIDLVTKL PDPPTCIISD    120
GFLSVFTIDA AKKLGIPVMM YWTLAACGFM GFYHIHSLIE KGFAPLKDAS YLTNGYLDTV    180
IDWVPGMEGI RLKDFPLDWS TDLNDKVLMF TTEAPQRSHK VSHHIFHTFD ELEPSIIKTL    240
SLRYNHIYTI GPLQLLLDQI PEEKKQTGIT SLHGYSLVKE EPECFQWLQS KEPNSVVYVN    300
FGSTTVMSLE DMTEFGWGLA NSNHYFLWII RSNLVIGENA VLPPELEEHI KKRGFIASWC    360
SQEKVLKHPS VGGFLTHCGW GSTIESLSAG VPMICWPYSW DQLTNCRYIC KEWEVGLEMG    420
TKVKRDEVKR LVQELMGEGG HKMRNKAKDW KEKARIAIAP NGSSSLNIDK MVKEITVLAR    480
N                                                                   481
```

SEQ ID NO:154

```
MDAMATTEKK PHVIFIPFPA QSHIKAMLKL AQLLHHKGLQ ITFVNTDQIH NQFLESSGPH     60
CLDGAPGFRF ETIPDGVSHS PEASIPIRES LLRSIETNFL DRFIDLVTKL PDPPTCIISD    120
GFLSVFTIDA AKKLGIPVMM YWTLAACGFM GFYHIHSLIE KGFAPLKDAS YLTNGYLDTV    180
IDWVPGMEGI RLKDFPLDWS TDLNDKVLMF TTEAPQRSHK VSHHIFHTFD ELEPSIIKTL    240
SLRYNHIYTI GPLQLLLDQI PEEKKQTGIT SLHGYSLVKE EPECFQWLQS KEPNSVVYVN    300
FGSTTVMSLE DMTEFGWGLA NSNHYFLWII RSNLVIGENA VLPPELEEHI KKRGFIASWC    360
SQEKVLKHPS VGGFLTHCGW GSTIESLSAG VPMICWPYSW DQLTNCRYIC KEWEVGLEMG    420
TKVKRDEVKR LVQELMGEGG HKMRNKAKDW KEKARIAIAP NGSSSLNIDK MVKEITVLAR    480
N                                                                   481
```

SEQ ID NO:155

```
MDAMATTEKK PHVIFIPFPA QSHIKAMLKL AQLLHHKGLQ ITFVNTDWIH NQFLESSGPH     60
CLDGAPGFRF ETIPDGVSHS PEASIPIRES LLRSIETNFL DRFIDLVTKL PDPPTCIISD    120
GFLSVFTIDA AKKLGIPVMM YWTLAACGFM GFYHIHSLIE KGFAPLKDAS YLTNGYLDTV    180
IDWVPGMEGI RLKDFPLDWS TDLNDKVLMF TTEAPQRSHK VSHHIFHTFD ELEPSIIKTL    240
SLRYNHIYTI GPLQLLLDQI PEEKKQTGIT SLHGYSLVKE EPECFQWLQS KEPNSVVYVN    300
FGSTTVMSLE DMTEFGWGLA NSNHYFLWII RSNLVIGENA VLPPELEEHI KKRGFIASWC    360
SQEKVLKHPS VGGFLTHCGW GSTIESLSAG VPMICWPYSW DQLTNCRYIC KEWEVGLEMG    420
```

```
TKVKRDEVKR LVQELMGEGG HKMRNKAKDW KEKARIAIAP NGSSSLNIDK MVKEITVLAR      480
N                                                                     481
```

SEQ ID NO:156

```
MDAMATTEKK PHVIFIPFPA QSHIKAMLKL AQLLHHKGLQ ITFVNTDTIH NQFLESSGPH       60
CLDGAPGFRF ETIPDGVSHS PEASIPIRES LLRSIETNFL DRFIDLVTKL PDPPTCIISD      120
GFLSVFTIDA AKKLGIPVMM YWTLAACGFM GFYHIHSLIE KGFAPLKDAS YLTNGYLDTV      180
IDWVPGMEGI RLKDFPLDWS TDLNDKVLMF TTEAPQRSHK VSHHIFHTFD ELEPSIIKTL      240
SLRYNHIYTI GPLQLLLDQI PEEKKQTGIT SLHGYSLVKE EPECFQWLQS KEPNSVVYVN      300
FGSTTVMSLE DMTEFGWGLA NSNHYFLWII RSNLVIGENA VLPPELEEHI KKRGFIASWC      360
SQEKVLKHPS VGGFLTHCGW GSTIESLSAG VPMICWPYSW DQLTNCRYIC KEWEVGLEMG      420
TKVKRDEVKR LVQELMGEGG HKMRNKAKDW KEKARIAIAP NGSSSLNIDK MVKEITVLAR      480
N                                                                     481
```

SEQ ID NO:157

```
MDAMATTEKK PHVIFIPFPA QSHIKAMLKL AQLLHHKGLQ ITFVNTDFVH NQFLESSGPH       60
CLDGAPGFRF ETIPDGVSHS PEASIPIRES LLRSIETNFL DRFIDLVTKL PDPPTCIISD      120
GFLSVFTIDA AKKLGIPVMM YWTLAACGFM GFYHIHSLIE KGFAPLKDAS YLTNGYLDTV      180
IDWVPGMEGI RLKDFPLDWS TDLNDKVLMF TTEAPQRSHK VSHHIFHTFD ELEPSIIKTL      240
SLRYNHIYTI GPLQLLLDQI PEEKKQTGIT SLHGYSLVKE EPECFQWLQS KEPNSVVYVN      300
FGSTTVMSLE DMTEFGWGLA NSNHYFLWII RSNLVIGENA VLPPELEEHI KKRGFIASWC      360
SQEKVLKHPS VGGFLTHCGW GSTIESLSAG VPMICWPYSW DQLTNCRYIC KEWEVGLEMG      420
TKVKRDEVKR LVQELMGEGG HKMRNKAKDW KEKARIAIAP NGSSSLNIDK MVKEITVLAR      480
N                                                                     481
```

SEQ ID NO:158

```
MDAMATTEKK PHVIFIPFPA QSHIKAMLKL AQLLHHKGLQ ITFVNTDFIH NQFLESSGPH       60
CLDGAPGFRF ETIPDGVSHS PEAGIPIRES LLRSIETNFL DRFIDLVTKL PDPPTCIISD      120
GFLSVFTIDA AKKLGIPVMM YWTLAACGFM GFYHIHSLIE KGFAPLKDAS YLTNGYLDTV      180
IDWVPGMEGI RLKDFPLDWS TDLNDKVLMF TTEAPQRSHK VSHHIFHTFD ELEPSIIKTL      240
SLRYNHIYTI GPLQLLLDQI PEEKKQTGIT SLHGYSLVKE EPECFQWLQS KEPNSVVYVN      300
FGSTTVMSLE DMTEFGWGLA NSNHYFLWII RSNLVIGENA VLPPELEEHI KKRGFIASWC      360
SQEKVLKHPS VGGFLTHCGW GSTIESLSAG VPMICWPYSW DQLTNCRYIC KEWEVGLEMG      420
TKVKRDEVKR LVQELMGEGG HKMRNKAKDW KEKARIAIAP NGSSSLNIDK MVKEITVLAR      480
N                                                                     481
```

SEQ ID NO:159

```
MDAMATTEKK PHVIFIPFPA QSHIKAMLKL AQLLHHKGLQ ITFVNTDFIH NQFLESSGPH       60
CLDGAPGFRF ETIPDGVSHS PEAAIPIRES LLRSIETNFL DRFIDLVTKL PDPPTCIISD      120
GFLSVFTIDA AKKLGIPVMM YWTLAACGFM GFYHIHSLIE KGFAPLKDAS YLTNGYLDTV      180
IDWVPGMEGI RLKDFPLDWS TDLNDKVLMF TTEAPQRSHK VSHHIFHTFD ELEPSIIKTL      240
SLRYNHIYTI GPLQLLLDQI PEEKKQTGIT SLHGYSLVKE EPECFQWLQS KEPNSVVYVN      300
FGSTTVMSLE DMTEFGWGLA NSNHYFLWII RSNLVIGENA VLPPELEEHI KKRGFIASWC      360
SQEKVLKHPS VGGFLTHCGW GSTIESLSAG VPMICWPYSW DQLTNCRYIC KEWEVGLEMG      420
TKVKRDEVKR LVQELMGEGG HKMRNKAKDW KEKARIAIAP NGSSSLNIDK MVKEITVLAR      480
N                                                                     481
```

SEQ ID NO:160

```
MDAMATTEKK PHVIFIPFPA QSHIKAMLKL AQLLHHKGLQ ITFVNTDFIH NQFLESSGPH       60
CLDGAPGFRF ETIPDGVSHS PEATIPIRES LLRSIETNFL DRFIDLVTKL PDPPTCIISD      120
GFLSVFTIDA AKKLGIPVMM YWTLAACGFM GFYHIHSLIE KGFAPLKDAS YLTNGYLDTV      180
IDWVPGMEGI RLKDFPLDWS TDLNDKVLMF TTEAPQRSHK VSHHIFHTFD ELEPSIIKTL      240
SLRYNHIYTI GPLQLLLDQI PEEKKQTGIT SLHGYSLVKE EPECFQWLQS KEPNSVVYVN      300
FGSTTVMSLE DMTEFGWGLA NSNHYFLWII RSNLVIGENA VLPPELEEHI KKRGFIASWC      360
SQEKVLKHPS VGGFLTHCGW GSTIESLSAG VPMICWPYSW DQLTNCRYIC KEWEVGLEMG      420
TKVKRDEVKR LVQELMGEGG HKMRNKAKDW KEKARIAIAP NGSSSLNIDK MVKEITVLAR      480
N                                                                     481
```

SEQ ID NO:161

```
MDAMATTEKK PHVIFIPFPA QSHIKAMLKL AQLLHHKGLQ ITFVNTDFIH NQFLESSGPH    60
CLDGAPGFRF ETIPDGVSHS PEACIPIRES LLRSIETNFL DRFIDLVTKL PDPPTCIISD   120
GFLSVFTIDA AKKLGIPVMM YWTLAACGFM GFYHIHSLIE KGFAPLKDAS YLTNGYLDTV   180
IDWVPGMEGI RLKDFPLDWS TDLNDKVLMF TTEAPQRSHK VSHHIFHTFD ELEPSIIKTL   240
SLRYNHIYTI GPLQLLLDQI PEEKKQTGIT SLHGYSLVKE EPECFQWLQS KEPNSVVYVN   300
FGSTTVMSLE DMTEFGWGLA NSNHYFLWII RSNLVIGENA VLPPELEEHI KKRGFIASWC   360
SQEKVLKHPS VGGFLTHCGW GSTIESLSAG VPMICWPYSW DQLTNCRYIC KEWEVGLEMG   420
TKVKRDEVKR LVQELMGEGG HKMRNKAKDW KEKARIAIAP NGSSSLNIDK MVKEITVLAR   480
N                                                                  481
```

SEQ ID NO:162

```
MDAMATTEKK PHVIFIPFPA QSHIKAMLKL AQLLHHKGLQ ITFVNTDFIH NQFLESSGPH    60
CLDGAPGFRF ETIPDGVSHS PEAPIPIRES LLRSIETNFL DRFIDLVTKL PDPPTCIISD   120
GFLSVFTIDA AKKLGIPVMM YWTLAACGFM GFYHIHSLIE KGFAPLKDAS YLTNGYLDTV   180
IDWVPGMEGI RLKDFPLDWS TDLNDKVLMF TTEAPQRSHK VSHHIFHTFD ELEPSIIKTL   240
SLRYNHIYTI GPLQLLLDQI PEEKKQTGIT SLHGYSLVKE EPECFQWLQS KEPNSVVYVN   300
FGSTTVMSLE DMTEFGWGLA NSNHYFLWII RSNLVIGENA VLPPELEEHI KKRGFIASWC   360
SQEKVLKHPS VGGFLTHCGW GSTIESLSAG VPMICWPYSW DQLTNCRYIC KEWEVGLEMG   420
TKVKRDEVKR LVQELMGEGG HKMRNKAKDW KEKARIAIAP NGSSSLNIDK MVKEITVLAR   480
N                                                                  481
```

SEQ ID NO:163

```
MDAMATTEKK PHVIFIPFPA QSHIKAMLKL AQLLHHKGLQ ITFVNTDFIH NQFLESSGPH    60
CLDGAPGFRF ETIPDGVSHS PEANIPIRES LLRSIETNFL DRFIDLVTKL PDPPTCIISD   120
GFLSVFTIDA AKKLGIPVMM YWTLAACGFM GFYHIHSLIE KGFAPLKDAS YLTNGYLDTV   180
IDWVPGMEGI RLKDFPLDWS TDLNDKVLMF TTEAPQRSHK VSHHIFHTFD ELEPSIIKTL   240
SLRYNHIYTI GPLQLLLDQI PEEKKQTGIT SLHGYSLVKE EPECFQWLQS KEPNSVVYVN   300
FGSTTVMSLE DMTEFGWGLA NSNHYFLWII RSNLVIGENA VLPPELEEHI KKRGFIASWC   360
SQEKVLKHPS VGGFLTHCGW GSTIESLSAG VPMICWPYSW DQLTNCRYIC KEWEVGLEMG   420
TKVKRDEVKR LVQELMGEGG HKMRNKAKDW KEKARIAIAP NGSSSLNIDK MVKEITVLAR   480
N                                                                  481
```

SEQ ID NO:164

```
MDAMATTEKK PHVIFIPFPA QSHIKAMLKL AQLLHHKGLQ ITFVNTDFIH NQFLESSGPH    60
CLDGAPGFRF ETIPDGVSHS PEAVIPIRES LLRSIETNFL DRFIDLVTKL PDPPTCIISD   120
GFLSVFTIDA AKKLGIPVMM YWTLAACGFM GFYHIHSLIE KGFAPLKDAS YLTNGYLDTV   180
IDWVPGMEGI RLKDFPLDWS TDLNDKVLMF TTEAPQRSHK VSHHIFHTFD ELEPSIIKTL   240
SLRYNHIYTI GPLQLLLDQI PEEKKQTGIT SLHGYSLVKE EPECFQWLQS KEPNSVVYVN   300
FGSTTVMSLE DMTEFGWGLA NSNHYFLWII RSNLVIGENA VLPPELEEHI KKRGFIASWC   360
SQEKVLKHPS VGGFLTHCGW GSTIESLSAG VPMICWPYSW DQLTNCRYIC KEWEVGLEMG   420
TKVKRDEVKR LVQELMGEGG HKMRNKAKDW KEKARIAIAP NGSSSLNIDK MVKEITVLAR   480
N                                                                  481
```

SEQ ID NO:165

```
MDAMATTEKK PHVIFIPFPA QSHIKAMLKL AQLLHHKGLQ ITFVNTDFIH NQFLESSGPH    60
CLDGAPGFRF ETIPDGVSHS PEASIRIRES LLRSIETNFL DRFIDLVTKL PDPPTCIISD   120
GFLSVFTIDA AKKLGIPVMM YWTLAACGFM GFYHIHSLIE KGFAPLKDAS YLTNGYLDTV   180
IDWVPGMEGI RLKDFPLDWS TDLNDKVLMF TTEAPQRSHK VSHHIFHTFD ELEPSIIKTL   240
SLRYNHIYTI GPLQLLLDQI PEEKKQTGIT SLHGYSLVKE EPECFQWLQS KEPNSVVYVN   300
FGSTTVMSLE DMTEFGWGLA NSNHYFLWII RSNLVIGENA VLPPELEEHI KKRGFIASWC   360
SQEKVLKHPS VGGFLTHCGW GSTIESLSAG VPMICWPYSW DQLTNCRYIC KEWEVGLEMG   420
TKVKRDEVKR LVQELMGEGG HKMRNKAKDW KEKARIAIAP NGSSSLNIDK MVKEITVLAR   480
N                                                                  481
```

SEQ ID NO:166

```
MDAMATTEKK PHVIFIPFPA QSHIKAMLKL AQLLHHKGLQ ITFVNTDFIH NQFLESSGPH     60
CLDGAPGFRF ETIPDGVSHS PEASIGIRES LLRSIETNFL DRFIDLVTKL PDPPTCIISD    120
GFLSVFTIDA AKKLGIPVMM YWTLAACGFM GFYHIHSLIE KGFAPLKDAS YLTNGYLDTV    180
IDWVPGMEGI RLKDFPLDWS TDLNDKVLMF TTEAPQRSHK VSHHIFHTFD ELEPSIIKTL    240
SLRYNHIYTI GPLQLLLDQI PEEKKQTGIT SLHGYSLVKE EPECFQWLQS KEPNSVVYVN    300
FGSTTVMSLE DMTEFGWGLA NSNHYFLWII RSNLVIGENA VLPPELEEHI KKRGFIASWC    360
SQEKVLKHPS VGGFLTHCGW GSTIESLSAG VPMICWPYSW DQLTNCRYIC KEWEVGLEMG    420
TKVKRDEVKR LVQELMGEGG HKMRNKAKDW KEKARIAIAP NGSSSLNIDK MVKEITVLAR    480
N                                                                    481
```

SEQ ID NO:167

```
MDAMATTEKK PHVIFIPFPA QSHIKAMLKL AQLLHHKGLQ ITFVNTDFIH NQFLESSGPH     60
CLDGAPGFRF ETIPDGVSHS PEASIPHRES LLRSIETNFL DRFIDLVTKL PDPPTCIISD    120
GFLSVFTIDA AKKLGIPVMM YWTLAACGFM GFYHIHSLIE KGFAPLKDAS YLTNGYLDTV    180
IDWVPGMEGI RLKDFPLDWS TDLNDKVLMF TTEAPQRSHK VSHHIFHTFD ELEPSIIKTL    240
SLRYNHIYTI GPLQLLLDQI PEEKKQTGIT SLHGYSLVKE EPECFQWLQS KEPNSVVYVN    300
FGSTTVMSLE DMTEFGWGLA NSNHYFLWII RSNLVIGENA VLPPELEEHI KKRGFIASWC    360
SQEKVLKHPS VGGFLTHCGW GSTIESLSAG VPMICWPYSW DQLTNCRYIC KEWEVGLEMG    420
TKVKRDEVKR LVQELMGEGG HKMRNKAKDW KEKARIAIAP NGSSSLNIDK MVKEITVLAR    480
N                                                                    481
```

SEQ ID NO:168

```
MDAMATTEKK PHVIFIPFPA QSHIKAMLKL AQLLHHKGLQ ITFVNTDFIH NQFLESSGPH     60
CLDGAPGFRF ETIPDGVSHS PEASIPPRES LLRSIETNFL DRFIDLVTKL PDPPTCIISD    120
GFLSVFTIDA AKKLGIPVMM YWTLAACGFM GFYHIHSLIE KGFAPLKDAS YLTNGYLDTV    180
IDWVPGMEGI RLKDFPLDWS TDLNDKVLMF TTEAPQRSHK VSHHIFHTFD ELEPSIIKTL    240
SLRYNHIYTI GPLQLLLDQI PEEKKQTGIT SLHGYSLVKE EPECFQWLQS KEPNSVVYVN    300
FGSTTVMSLE DMTEFGWGLA NSNHYFLWII RSNLVIGENA VLPPELEEHI KKRGFIASWC    360
SQEKVLKHPS VGGFLTHCGW GSTIESLSAG VPMICWPYSW DQLTNCRYIC KEWEVGLEMG    420
TKVKRDEVKR LVQELMGEGG HKMRNKAKDW KEKARIAIAP NGSSSLNIDK MVKEITVLAR    480
N                                                                    481
```

SEQ ID NO:169

```
MDAMATTEKK PHVIFIPFPA QSHIKAMLKL AQLLHHKGLQ ITFVNTDFIH NQFLESSGPH     60
CLDGAPGFRF ETIPDGVSHS PEASIPMRES LLRSIETNFL DRFIDLVTKL PDPPTCIISD    120
GFLSVFTIDA AKKLGIPVMM YWTLAACGFM GFYHIHSLIE KGFAPLKDAS YLTNGYLDTV    180
IDWVPGMEGI RLKDFPLDWS TDLNDKVLMF TTEAPQRSHK VSHHIFHTFD ELEPSIIKTL    240
SLRYNHIYTI GPLQLLLDQI PEEKKQTGIT SLHGYSLVKE EPECFQWLQS KEPNSVVYVN    300
FGSTTVMSLE DMTEFGWGLA NSNHYFLWII RSNLVIGENA VLPPELEEHI KKRGFIASWC    360
SQEKVLKHPS VGGFLTHCGW GSTIESLSAG VPMICWPYSW DQLTNCRYIC KEWEVGLEMG    420
TKVKRDEVKR LVQELMGEGG HKMRNKAKDW KEKARIAIAP NGSSSLNIDK MVKEITVLAR    480
N                                                                    481
```

SEQ ID NO:170

```
MDAMATTEKK PHVIFIPFPA QSHIKAMLKL AQLLHHKGLQ ITFVNTDFIH NQFLESSGPH     60
CLDGAPGFRF ETIPDGVSHS PEASIPYRES LLRSIETNFL DRFIDLVTKL PDPPTCIISD    120
GFLSVFTIDA AKKLGIPVMM YWTLAACGFM GFYHIHSLIE KGFAPLKDAS YLTNGYLDTV    180
IDWVPGMEGI RLKDFPLDWS TDLNDKVLMF TTEAPQRSHK VSHHIFHTFD ELEPSIIKTL    240
SLRYNHIYTI GPLQLLLDQI PEEKKQTGIT SLHGYSLVKE EPECFQWLQS KEPNSVVYVN    300
FGSTTVMSLE DMTEFGWGLA NSNHYFLWII RSNLVIGENA VLPPELEEHI KKRGFIASWC    360
SQEKVLKHPS VGGFLTHCGW GSTIESLSAG VPMICWPYSW DQLTNCRYIC KEWEVGLEMG    420
TKVKRDEVKR LVQELMGEGG HKMRNKAKDW KEKARIAIAP NGSSSLNIDK MVKEITVLAR    480
N                                                                    481
```

SEQ ID NO:171

```
MDAMATTEKK PHVIFIPFPA QSHIKAMLKL AQLLHHKGLQ ITFVNTDFIH NQFLESSGPH     60
```

CLDGAPGFRF ETIPDGVSHS PEASIPIRES KLRSIETNFL DRFIDLVTKL PDPPTCIISD 120
GFLSVFTIDA AKKLGIPVMM YWTLAACGFM GFYHIHSLIE KGFAPLKDAS YLTNGYLDTV 180
IDWVPGMEGI RLKDFPLDWS TDLNDKVLMF TTEAPQRSHK VSHHIFHTFD ELEPSIIKTL 240
SLRYNHIYTI GPLQLLLDQI PEEKKQTGIT SLHGYSLVKE EPECFQWLQS KEPNSVVYVN 300
FGSTTVMSLE DMTEFGWGLA NSNHYFLWII RSNLVIGENA VLPPELEEHI KKRGFIASWC 360
SQEKVLKHPS VGGFLTHCGW GSTIESLSAG VPMICWPYSW DQLTNCRYIC KEWEVGLEMG 420
TKVKRDEVKR LVQELMGEGG HKMRNKAKDW KEKARIAIAP NGSSSLNIDK MVKEITVLAR 480
N 481

SEQ ID NO:172
MDAMATTEKK PHVIFIPFPA QSHIKAMLKL AQLLHHKGLQ ITFVNTDFIH NQFLESSGPH 60
CLDGAPGFRF ETIPDGVSHS PEASIPIRES RLRSIETNFL DRFIDLVTKL PDPPTCIISD 120
GFLSVFTIDA AKKLGIPVMM YWTLAACGFM GFYHIHSLIE KGFAPLKDAS YLTNGYLDTV 180
IDWVPGMEGI RLKDFPLDWS TDLNDKVLMF TTEAPQRSHK VSHHIFHTFD ELEPSIIKTL 240
SLRYNHIYTI GPLQLLLDQI PEEKKQTGIT SLHGYSLVKE EPECFQWLQS KEPNSVVYVN 300
FGSTTVMSLE DMTEFGWGLA NSNHYFLWII RSNLVIGENA VLPPELEEHI KKRGFIASWC 360
SQEKVLKHPS VGGFLTHCGW GSTIESLSAG VPMICWPYSW DQLTNCRYIC KEWEVGLEMG 420
TKVKRDEVKR LVQELMGEGG HKMRNKAKDW KEKARIAIAP NGSSSLNIDK MVKEITVLAR 480
N 481

SEQ ID NO:173
MDAMATTEKK PHVIFIPFPA QSHIKAMLKL AQLLHHKGLQ ITFVNTDFIH NQFLESSGPH 60
CLDGAPGFRF ETIPDGVSHS PEASIPIRES TLRSIETNFL DRFIDLVTKL PDPPTCIISD 120
GFLSVFTIDA AKKLGIPVMM YWTLAACGFM GFYHIHSLIE KGFAPLKDAS YLTNGYLDTV 180
IDWVPGMEGI RLKDFPLDWS TDLNDKVLMF TTEAPQRSHK VSHHIFHTFD ELEPSIIKTL 240
SLRYNHIYTI GPLQLLLDQI PEEKKQTGIT SLHGYSLVKE EPECFQWLQS KEPNSVVYVN 300
FGSTTVMSLE DMTEFGWGLA NSNHYFLWII RSNLVIGENA VLPPELEEHI KKRGFIASWC 360
SQEKVLKHPS VGGFLTHCGW GSTIESLSAG VPMICWPYSW DQLTNCRYIC KEWEVGLEMG 420
TKVKRDEVKR LVQELMGEGG HKMRNKAKDW KEKARIAIAP NGSSSLNIDK MVKEITVLAR 480
N 481

SEQ ID NO:174
MDAMATTEKK PHVIFIPFPA QSHIKAMLKL AQLLHHKGLQ ITFVNTDFIH NQFLESSGPH 60
CLDGAPGFRF ETIPDGVSHS PEASIPIRES LFRSIETNFL DRFIDLVTKL PDPPTCIISD 120
GFLSVFTIDA AKKLGIPVMM YWTLAACGFM GFYHIHSLIE KGFAPLKDAS YLTNGYLDTV 180
IDWVPGMEGI RLKDFPLDWS TDLNDKVLMF TTEAPQRSHK VSHHIFHTFD ELEPSIIKTL 240
SLRYNHIYTI GPLQLLLDQI PEEKKQTGIT SLHGYSLVKE EPECFQWLQS KEPNSVVYVN 300
FGSTTVMSLE DMTEFGWGLA NSNHYFLWII RSNLVIGENA VLPPELEEHI KKRGFIASWC 360
SQEKVLKHPS VGGFLTHCGW GSTIESLSAG VPMICWPYSW DQLTNCRYIC KEWEVGLEMG 420
TKVKRDEVKR LVQELMGEGG HKMRNKAKDW KEKARIAIAP NGSSSLNIDK MVKEITVLAR 480
N 481

SEQ ID NO:175
MDAMATTEKK PHVIFIPFPA QSHIKAMLKL AQLLHHKGLQ ITFVNTDFIH NQFLESSGPH 60
CLDGAPGFRF ETIPDGVSHS PEASIPIRES LIRSIETNFL DRFIDLVTKL PDPPTCIISD 120
GFLSVFTIDA AKKLGIPVMM YWTLAACGFM GFYHIHSLIE KGFAPLKDAS YLTNGYLDTV 180
IDWVPGMEGI RLKDFPLDWS TDLNDKVLMF TTEAPQRSHK VSHHIFHTFD ELEPSIIKTL 240
SLRYNHIYTI GPLQLLLDQI PEEKKQTGIT SLHGYSLVKE EPECFQWLQS KEPNSVVYVN 300
FGSTTVMSLE DMTEFGWGLA NSNHYFLWII RSNLVIGENA VLPPELEEHI KKRGFIASWC 360
SQEKVLKHPS VGGFLTHCGW GSTIESLSAG VPMICWPYSW DQLTNCRYIC KEWEVGLEMG 420
TKVKRDEVKR LVQELMGEGG HKMRNKAKDW KEKARIAIAP NGSSSLNIDK MVKEITVLAR 480
N 481

SEQ ID NO:176
MDAMATTEKK PHVIFIPFPA QSHIKAMLKL AQLLHHKGLQ ITFVNTDFIH NQFLESSGPH 60
CLDGAPGFRF ETIPDGVSHS PEASIPIRES LMRSIETNFL DRFIDLVTKL PDPPTCIISD 120
GFLSVFTIDA AKKLGIPVMM YWTLAACGFM GFYHIHSLIE KGFAPLKDAS YLTNGYLDTV 180

```
IDWVPGMEGI RLKDFPLDWS TDLNDKVLMF TTEAPQRSHK VSHHIFHTFD ELEPSIIKTL    240
SLRYNHIYTI GPLQLLLDQI PEEKKQTGIT SLHGYSLVKE EPECFQWLQS KEPNSVVYVN    300
FGSTTVMSLE DMTEFGWGLA NSNHYFLWII RSNLVIGENA VLPPELEEHI KKRGFIASWC    360
SQEKVLKHPS VGGFLTHCGW GSTIESLSAG VPMICWPYSW DQLTNCRYIC KEWEVGLEMG    420
TKVKRDEVKR LVQELMGEGG HKMRNKAKDW KEKARIAIAP NGSSSLNIDK MVKEITVLAR    480
N                                                                   481
```

SEQ ID NO:177

```
MDAMATTEKK PHVIFIPFPA QSHIKAMLKL AQLLHHKGLQ ITFVNTDFIH NQFLESSGPH     60
CLDGAPGFRF ETIPDGVSHS PEASIPIRES LLRSKETNFL DRFIDLVTKL PDPPTCIISD    120
GFLSVFTIDA AKKLGIPVMM YWTLAACGFM GFYHIHSLIE KGFAPLKDAS YLTNGYLDTV    180
IDWVPGMEGI RLKDFPLDWS TDLNDKVLMF TTEAPQRSHK VSHHIFHTFD ELEPSIIKTL    240
SLRYNHIYTI GPLQLLLDQI PEEKKQTGIT SLHGYSLVKE EPECFQWLQS KEPNSVVYVN    300
FGSTTVMSLE DMTEFGWGLA NSNHYFLWII RSNLVIGENA VLPPELEEHI KKRGFIASWC    360
SQEKVLKHPS VGGFLTHCGW GSTIESLSAG VPMICWPYSW DQLTNCRYIC KEWEVGLEMG    420
TKVKRDEVKR LVQELMGEGG HKMRNKAKDW KEKARIAIAP NGSSSLNIDK MVKEITVLAR    480
N                                                                   481
```

SEQ ID NO:178

```
MDAMATTEKK PHVIFIPFPA QSHIKAMLKL AQLLHHKGLQ ITFVNTDFIH NQFLESSGPH     60
CLDGAPGFRF ETIPDGVSHS PEASIPIRES LLRSIETNFL DRFIDLVTKL PDPPTCIISD    120
GSLSVFTIDA AKKLGIPVMM YWTLAACGFM GFYHIHSLIE KGFAPLKDAS YLTNGYLDTV    180
IDWVPGMEGI RLKDFPLDWS TDLNDKVLMF TTEAPQRSHK VSHHIFHTFD ELEPSIIKTL    240
SLRYNHIYTI GPLQLLLDQI PEEKKQTGIT SLHGYSLVKE EPECFQWLQS KEPNSVVYVN    300
FGSTTVMSLE DMTEFGWGLA NSNHYFLWII RSNLVIGENA VLPPELEEHI KKRGFIASWC    360
SQEKVLKHPS VGGFLTHCGW GSTIESLSAG VPMICWPYSW DQLTNCRYIC KEWEVGLEMG    420
TKVKRDEVKR LVQELMGEGG HKMRNKAKDW KEKARIAIAP NGSSSLNIDK MVKEITVLAR    480
N                                                                   481
```

SEQ ID NO:179

```
MDAMATTEKK PHVIFIPFPA QSHIKAMLKL AQLLHHKGLQ ITFVNTDFIH NQFLESSGPH     60
CLDGAPGFRF ETIPDGVSHS PEASIPIRES LLRSIETNFL DRFIDLVTKL PDPPTCIISD    120
GFLSVFTIDA AKKLGIPVMM YWTLAACGFM GFYHIHSLIE KGFAPLKDAS YLTNGYLDTV    180
IDWVPGMEGI RLKDFPLDWS TDLNDKVLMF TTEAPQRSHK VSHHIFHTFD ELEPSIIKTL    240
SLRYNHIYTI GPLQLLLDQI PEEKKQTGIT SLHGYSLVKE EPECFQWLQS KEPNSVVYVN    300
FGSTTVMSLE DMTEFGWGLA NSNHYFLWII RSNSVIGENA VLPPELEEHI KKRGFIASWC    360
SQEKVLKHPS VGGFLTHCGW GSTIESLSAG VPMICWPYSW DQLTNCRYIC KEWEVGLEMG    420
TKVKRDEVKR LVQELMGEGG HKMRNKAKDW KEKARIAIAP NGSSSLNIDK MVKEITVLAR    480
N                                                                   481
```

SEQ ID NO:180

```
MDAMATTEKK PHVIFIPFPA QSHIKAMLKL AQLLHHKGLQ ITFVNTDFIH NQFLESSGPH     60
CLDGAPGFRF ETIPDGVSHS PEASIPIRES LLRSIETNFL DRFIDLVTKL PDPPTCIISD    120
GFLSVFTIDA AKKLGIPVMM YWTLAACGFM GFYHIHSLIE KGFAPLKDAS YLTNGYLDTV    180
IDWVPGMEGI RLKDFPLDWS TDLNDKVLMF TTEAPQRSHK VSHHIFHTFD ELEPSIIKTL    240
SLRYNHIYTI GPLQLLLDQI PEEKKQTGIT SLHGYSLVKE EPECFQWLQS KEPNSVVYVN    300
FGSTTVMSLE DMTEFGWGLA NSNHYFLWII RSNMVIGENA VLPPELEEHI KKRGFIASWC    360
SQEKVLKHPS VGGFLTHCGW GSTIESLSAG VPMICWPYSW DQLTNCRYIC KEWEVGLEMG    420
TKVKRDEVKR LVQELMGEGG HKMRNKAKDW KEKARIAIAP NGSSSLNIDK MVKEITVLAR    480
N                                                                   481
```

SEQ ID NO:181

```
MENKTETTVR RRRRIILFPV PFHGHINPIL QLANVLYSKG FSITIFHTNF NKPKTSNYPH     60
FTFRFILDND PQDERISNLP THGPLAGMRI PIINEHGADE LRRELELLML ASEEDEEVSC    120
LITDALWYFA QSVADSLNLR RLVLMTSSLF NFHAHVSLPQ FDELGYLDPD DKTRLEEQAS    180
GFPMLKVKDI KSAYSNWQIL KEILGKMIKQ TKASSGVIWN SFKELEESEL ETVIREIPAP    240
SFLIPLPKHL TASSSSLLDH DRTVFQWLDQ QPPSSVLYVS FGSTSEVDEK DFLEIARGLV    300
```

DSKQSFLWVV RPGFVKGSTW VEPLPDGFLG ERGRIVKWVP QQEVLAHGAI GAFWTHSGWN 360
STLESVCEGV PMIFSDFGLD QPLNARYMSD VLKVGVYLEN GWERGEIANA IRRVMVDEEG 420
EYIRQNARVL KQKADVSLMK GGSSYESLES LVSYISSL 458

SEQ ID NO:182
MENKTETTVR RRRRIILFPV PFQGHWNPIL QLANVLYSKG FSITIFHTNF NKPKTSNYPH 60
FTFRFILDND PQDERISNLP THGPLAGMRI PIINEHGADE LRRELELLML ASEEDEEVSC 120
LITDALWYFA QSVADSLNLR RLVLMTSSLF NFHAHVSLPQ FDELGYLDPD DKTRLEEQAS 180
GFPMLKVKDI KSAYSNWQIL KEILGKMIKQ TKASSGVIWN SFKELEESEL ETVIREIPAP 240
SFLIPLPKHL TASSSSLLDH DRTVFQWLDQ QPPSSVLYVS FGSTSEVDEK DFLEIARGLV 300
DSKQSFLWVV RPGFVKGSTW VEPLPDGFLG ERGRIVKWVP QQEVLAHGAI GAFWTHSGWN 360
STLESVCEGV PMIFSDFGLD QPLNARYMSD VLKVGVYLEN GWERGEIANA IRRVMVDEEG 420
EYIRQNARVL KQKADVSLMK GGSSYESLES LVSYISSL 458

SEQ ID NO:183
MENKTETTVR RRRRIILFPV PFQGHINPIL QLANVLYSKG FSITIFHTNF NKPKTSNYPH 60
FTFRFILDND PQDERISNLP THGPLAGMRI PIINEHGADE LRRELELLML ASEEDEEVSC 120
LITDALWYFA QSVADSLNLR RLVLMGSSLF NFHAHVSLPQ FDELGYLDPD DKTRLEEQAS 180
GFPMLKVKDI KSAYSNWQIL KEILGKMIKQ TKASSGVIWN SFKELEESEL ETVIREIPAP 240
SFLIPLPKHL TASSSSLLDH DRTVFQWLDQ QPPSSVLYVS FGSTSEVDEK DFLEIARGLV 300
DSKQSFLWVV RPGFVKGSTW VEPLPDGFLG ERGRIVKWVP QQEVLAHGAI GAFWTHSGWN 360
STLESVCEGV PMIFSDFGLD QPLNARYMSD VLKVGVYLEN GWERGEIANA IRRVMVDEEG 420
EYIRQNARVL KQKADVSLMK GGSSYESLES LVSYISSL 458

SEQ ID NO:184
MENKTETTVR RRRRIILFPV PFQGHINPIL QLANVLYSKG FSITIFHTNF NKPKTSNYPH 60
FTFRFILDND PQDERISNLP THGPLAGMRI PIINEHGADE LRRELELLML ASEEDEEVSC 120
LITDALWYFA QSVADSLNLR RLVLMTSSLF NFHALVSLPQ FDELGYLDPD DKTRLEEQAS 180
GFPMLKVKDI KSAYSNWQIL KEILGKMIKQ TKASSGVIWN SFKELEESEL ETVIREIPAP 240
SFLIPLPKHL TASSSSLLDH DRTVFQWLDQ QPPSSVLYVS FGSTSEVDEK DFLEIARGLV 300
DSKQSFLWVV RPGFVKGSTW VEPLPDGFLG ERGRIVKWVP QQEVLAHGAI GAFWTHSGWN 360
STLESVCEGV PMIFSDFGLD QPLNARYMSD VLKVGVYLEN GWERGEIANA IRRVMVDEEG 420
EYIRQNARVL KQKADVSLMK GGSSYESLES LVSYISSL 458

SEQ ID NO:185
MENKTETTVR RRRRIILFPV PFQGHINPIL QLANVLYSKG FSITIFHTNF NKPKTSNYPH 60
FTFRFILDND PQDERISNLP THGPLAGMRI PIINEHGADE LRRELELLML ASEEDEEVSC 120
LITDALWYFA QSVADSLNLR RLVLMTSSLF NFHAHVSLPQ FDELGYLDPD DKTRLEEQAS 180
GFPMLKVKDI KSAYSNWQIL KEILGKMIKQ TKASSGVIWN SFKELEESEL ETVIREIPAP 240
SFLIPLPKHL TASSSSGLDH DRTVFQWLDQ QPPSSVLYVS FGSTSEVDEK DFLEIARGLV 300
DSKQSFLWVV RPGFVKGSTW VEPLPDGFLG ERGRIVKWVP QQEVLAHGAI GAFWTHSGWN 360
STLESVCEGV PMIFSDFGLD QPLNARYMSD VLKVGVYLEN GWERGEIANA IRRVMVDEEG 420
EYIRQNARVL KQKADVSLMK GGSSYESLES LVSYISSL 458

SEQ ID NO:186
MENKTETTVR RRRRIILFPV PFQGHINPIL QLANVLYSKG FSITIFHTNF NKPKTSNYPH 60
FTFRFILDND PQDERISNLP THGPLAGMRI PIINEHGADE LRRELELLML ASEEDEEVSC 120
LITDALWYFA QSVADSLNLR RLVLMTSSLF NFHAHVSLPQ FDELGYLDPD DKTRLEEQAS 180
GFPMLKVKDI KSAYSNWQIL KEILGKMIKQ TKASSGVIWN SFKELEESEL ETVIREIPAP 240
SFLIPLPKHL TAWSSSLLDH DRTVFQWLDQ QPPSSVLYVS FGSTSEVDEK DFLEIARGLV 300
DSKQSFLWVV RPGFVKGSTW VEPLPDGFLG ERGRIVKWVP QQEVLAHGAI GAFWTHSGWN 360
STLESVCEGV PMIFSDFGLD QPLNARYMSD VLKVGVYLEN GWERGEIANA IRRVMVDEEG 420
EYIRQNARVL KQKADVSLMK GGSSYESLES LVSYISSL 458

SEQ ID NO:187
MENKTETTVR RRRRIILFPV PFQGHINPIL QLANVLYSKG FSITIFHTNF NKPKTSNYPH 60
FTFRFILDND PQDERISNLP THGPLAGMRI PIINEHGADE LRRELELLML ASEEDEEVSC 120

LITDALWYFA QSVADSLNLR RLVLMTSSLF NFHAHVSLPQ FDELGYLDPD DKTRLEEQAS 180
GFPMLKVKDI KSAYSNWQIL KEILGKMIKQ TKASSGVIWN SFKELEESEL ETVIREIPAP 240
SFLIPLPKHL TASSSSLLDH DRTVFQWLDQ QPPSSVLYVS FGSGSEVDEK DFLEIARGLV 300
DSKQSFLWVV RPGFVKGSTW VEPLPDGFLG ERGRIVKWVP QQEVLAHGAI GAFWTHSGWN 360
STLESVCEGV PMIFSDFGLD QPLNARYMSD VLKVGVYLEN GWERGEIANA IRRVMVDEEG 420
EYIRQNARVL KQKADVSLMK GGSSYESLES LVSYISSL 458

SEQ ID NO:188
MENKTETTVR RRRRIILFPV PFQGHINPIL QLANVLYSKG FSITIFHTNF NKPKTSNYPH 60
FTFRFILDND PQDERISNLP THGPLAGMRI PIINEHGADE LRRELELLML ASEEDEEVSC 120
LITDALWYFA QSVADSLNLR RLVLMTSSLF NFHAHVSLPQ FDELGYLDPD DKTRLEEQAS 180
GFPMLKVKDI KSAYSNWQIL KEILGKMIKQ TKASSGVIWN SFKELEESEL ETVIREIPAP 240
SFLIPLPKHL TASSSSLLDH DRTVFQWLDQ QPPSSVLYVS FGNTSEVDEK DFLEIARGLV 300
DSKQSFLWVV RPGFVKGSTW VEPLPDGFLG ERGRIVKWVP QQEVLAHGAI GAFWTHSGWN 360
STLESVCEGV PMIFSDFGLD QPLNARYMSD VLKVGVYLEN GWERGEIANA IRRVMVDEEG 420
EYIRQNARVL KQKADVSLMK GGSSYESLES LVSYISSL 458

SEQ ID NO:189
MENKTETTVR RRRRIILFPV PFQGHINPIL QLANVLYSKG FSITIFHTNF NKPKTSNYPH 60
FTFRFILDND PQDERISNLP THGPLAGMRI PIINEHGADE LRRELELLML ASEEDEEVSC 120
LITDALWYFA QSVADSLNLR RLVLMTSSLF NFHAHVSLPQ FDELGYLDPD DKTRLEEQAS 180
GFPMLKVKDI KSAYSNWQIL KEILGKMIKQ TKASSGVIWN SFKELEESEL ETVIREIPAP 240
SFLIPLPKHL TASSSSLLDH DRTVFQWLDQ QPPSSVLYVS FGSTSEVDEK DFLEIARGLV 300
DSKQSFLWVV RPGFVKGSTW VEPLPDGFLG ERGRIVPWVP QQEVLAHGAI GAFWTHSGWN 360
STLESVCEGV PMIFSDFGLD QPLNARYMSD VLKVGVYLEN GWERGEIANA IRRVMVDEEG 420
EYIRQNARVL KQKADVSLMK GGSSYESLES LVSYISSL 458

SEQ ID NO:190
MENKTETTVR RRRRIILFPV PFQGHINPIL QLANVLYSKG FSITIFHTNF NKPKKSNYPH 60
FTFRFILDND PQDERISNLP THGPLAGMRI PIINEHGADE LRRELELLML ASEEDEEVSC 120
LITDALWYFA QSVADSLNLR RLVLMTSSLF NFHAHVSLPQ FDELGYLDPD DKTRLEEQAS 180
GFPMLKVKDI KSAYSNWQIL KEILGKMIKQ TKASSGVIWN SFKELEESEL ETVIREIPAP 240
SFLIPLPKHL TASSSSLLDH DRTVFQWLDQ QPPSSVLYVS FGSTSEVDEK DFLEIARGLV 300
DSKQSFLWVV RPGFVKGSTW VEPLPDGFLG ERGRIVKWVP QQEVLAHGAI GAFWTHSGWN 360
STLESVCEGV PMIFSDFGLD QPLNARYMSD VLKVGVYLEN GWERGEIANA IRRVMVDEEG 420
EYIRQNARVL KQKADVSLMK GGSSYESLES LVSYISSL 458

SEQ ID NO:191
MATSDSIVDD RKQLHVATFP WLAFGHILPY LQLSKLIAEK GHKVSFLSTT RNIQRLSSHI 60
SPLINVVQLT LPRVQELPED AEATTDVHPE DIPYLKKASD GLQPEVTRFL EQHSPDWIIY 120
DYTHYWLPSI AASLGISRAH FSVTTPWAIA YMGPSADAMI NGSDGRTTVE DLTTPPKWFP 180
FPTKVCWRKH DLARLVPYKA PGISDGYRMG LVEKGSDCLL SKCYHEFGTQ WLPLLETLHQ 240
VPVVPVGLLP PEIPGDEKDE TWVSIKKWLD GKQKGSVVYV ALGSEVLVSQ TEVVELALGL 300
ELSGLPFVWA YRKPKGPAKS DSVELPDGFV ERTRDRGLVW TSWAPQLRIL SHESVCGFLT 360
HCGSGSIVEG LMFGHPLIML PIFGDQPLNA RLLEDKQVGI EIPRNEEDGC LTKESVARSL 420
RSVVVEKEGE IYKANARELS KIYNDTKVEK EYVSQFVDYL EKNARAVAID HES 473

SEQ ID NO:192
MATSDSIVDD RKQLHVATFP WLAFGHILPY LQLSKLIAEK GHKVSFLSTT RNIQRLSSHI 60
SPLINVVQLT LPRVQELPED AEATTDVHPE DIPYLKKASD GLQPEVTRFL EQHSPDWIIY 120
DYTHYWLPSI AASLGISRAH FSVTTPWAIA YMGPSADAMI NGSDGRTTVE DLTTPPKWFP 180
FPTKVCWRKH DLARLVPYKA PGISDGYRMG LVLKGSDCLL YKCYHEFGTQ WLPLLETLHQ 240
VPVVPVGLLP PEIPGDEKDE TWVSIKKWLD GKQKGSVVYV ALGSEVLVSQ TEVVELALGL 300
ELSGLPFVWA YRKPKGPAKS DSVELPDGFV ERTRDRGLVW TSWAPQLRIL SHESVCGFLT 360
HCGSGSIVEG LMFGHPLIML PIFGDQPLNA RLLEDKQVGI EIPRNEEDGC LTKESVARSL 420
RSVVVEKEGE IYKANARELS KIYNDTKVEK EYVSQFVDYL EKNARAVAID HES 473

SEQ ID NO:193

```
MATSDSIVDD RKQLHVATFP WLAFGHILPY LQLSKLIAEK GHKVSFLSTT RNIQRLSSHI    60
SPLINVVQLT LPRVQELPED AEATTDVHPE DIPYLKKASD GLQPEVTRFL EQHSPDWIIY   120
DYTHYWLPSI AASLGISRAH FSVTTPWAIA YMGPSADAMI NGSDGRTTVE DLTTPPKWFP   180
FPTKVCWRKH DLARLVPYKA PGISDGYRMG LVLKGSDCLL SKCYHEFGTQ WLPLLETLHQ   240
VPVVPVGLLP PEIPGDEKDE TWVSIKKWLD GKQKGSVVYV ALGSEVLVSQ TEVVELALGL   300
ELSGLPFVWA YRKPKGPAKS DSVELPDGFV ERTRDRGLVW TSWAPQLRIL SHESVCGFLT   360
HCGSGSIVEG LMFGHPLIML PIFGDQPLNA RLLEDKQVGI EIPRNEEDGC LTKESVARSL   420
RSVVVEKEGE IYKANARHLS KIYNDTKVEK EYVSQFVDYL EKNARAVAID HES          473
```

SEQ ID NO:194

```
MATSDSIVDD RKQLHVATFP WLAFGHILPY LQLSKLIAEK GHKVSFLSTT RNIQRLSSHI    60
SPLINVVQLT LPRVQELPED AEATTDVHPE DIPYLKKASD GLQPEVTRFL EQHSPDWIIY   120
DYTHYWLPSI AASLGISRAH FSVTTPWAIA YTGPSADAMI NGSDGRTTVE DLTTPPKWFP   180
FPTKVCWRKH DLARLVPYKA PGISDGYRMG LVLKGSDCLL SKCYHEFGTQ WLPLLETLHQ   240
VPVVPVGLLP PEIPGDEKDE TWVSIKKWLD GKQKGSVVYV ALGSEVLVSQ TEVVELALGL   300
ELSGLPFVWA YRKPKGPAKS DSVELPDGFV ERTRDRGLVW TSWAPQLRIL SHESVCGFLT   360
HCGSGSIVEG LMFGHPLIML PIFGDQPLNA RLLEDKQVGI EIPRNEEDGC LTKESVARSL   420
RSVVVEKEGE IYKANARELS KIYNDTKVEK EYVSQFVDYL EKNARAVAID HES          473
```

SEQ ID NO:195

```
MATSDSIVDD RKQLHVATFP WLAFGHILPY LQLSKLIAEK GHKVSFLSTT RNIQRLSSHI    60
SPLINVVQLT LPRVQELPED AEATTDVHPE DIPYLKKASD GLQPEVTRFL EQHSPDWIIY   120
DYTHYWLPSI AASLGISRAH FSVTTPWAIA YMGPSADAMI NGSDGRTTVE DLTTPPKWFP   180
FPTKVCWRKH DLARLVPYKA PGISDGYRMG CVLKGSDCLL SKCYHEFGTQ WLPLLETLHQ   240
VPVVPVGLLP PEIPGDEKDE TWVSIKKWLD GKQKGSVVYV ALGSEVLVSQ TEVVELALGL   300
ELSGLPFVWA YRKPKGPAKS DSVELPDGFV ERTRDRGLVW TSWAPQLRIL SHESVCGFLT   360
HCGSGSIVEG LMFGHPLIML PIFGDQPLNA RLLEDKQVGI EIPRNEEDGC LTKESVARSL   420
RSVVVEKEGE IYKANARELS KIYNDTKVEK EYVSQFVDYL EKNARAVAID HES          473
```

SEQ ID NO:196

```
MATSDSIVDD RKQLHVATFP WLAFGHILPY LQLSKLIAEK GHKVSFLSTT RNIQRLSSHI    60
SPLINVVQLT LPRVQELPED AEATTDVHPE DIPYLKKASD GLQPEVTRFL EQHSPDWIIY   120
DYTHYWLPSI AASLGISRAH FSVTTPWAIA YMGPSADAMI NGSDGRTTVE DLTTPPKWFP   180
FPTKVCWRKH DLARSVPYKA PGISDGYRMG LVLKGSDCLL SKCYHEFGTQ WLPLLETLHQ   240
VPVVPVGLLP PEIPGDEKDE TWVSIKKWLD GKQKGSVVYV ALGSEVLVSQ TEVVELALGL   300
ELSGLPFVWA YRKPKGPAKS DSVELPDGFV ERTRDRGLVW TSWAPQLRIL SHESVCGFLT   360
HCGSGSIVEG LMFGHPLIML PIFGDQPLNA RLLEDKQVGI EIPRNEEDGC LTKESVARSL   420
RSVVVEKEGE IYKANARELS KIYNDTKVEK EYVSQFVDYL EKNARAVAID HES          473
```

SEQ ID NO:197

```
MATSDSIVDD RKQLHVATFP WLAFGHILPY LQLSKLIAEK GHKVSFLSTT RNIQRLSSHI    60
SPLINVVQLT LPRVQELPED AEATTDVHPE DIPYLKKASD GLQPEVTRFL EQHSPDWIIY   120
DYTHYWLPSI AASLGISRAH FSVTTPWAIA YMGPSADAMI NGSDGRTTVE DLTTPPKWFP   180
FPTKVCWRKH DLARVVPYKA PGISDGYRMG LVLKGSDCLL SKCYHEFGTQ WLPLLETLHQ   240
VPVVPVGLLP PEIPGDEKDE TWVSIKKWLD GKQKGSVVYV ALGSEVLVSQ TEVVELALGL   300
ELSGLPFVWA YRKPKGPAKS DSVELPDGFV ERTRDRGLVW TSWAPQLRIL SHESVCGFLT   360
HCGSGSIVEG LMFGHPLIML PIFGDQPLNA RLLEDKQVGI EIPRNEEDGC LTKESVARSL   420
RSVVVEKEGE IYKANARELS KIYNDTKVEK EYVSQFVDYL EKNARAVAID HES          473
```

SEQ ID NO:198

```
MATSDSIVDD RKQLHVATFP WLAFGHILPY LQLSKLIAEK GHKVSFLSTT RNIQRLSSHI    60
SPLINVVQLT LPRVQELPED AEATTDVHPE DIPYLKKASD GLQPEVTRFL EQHSPDWIIY   120
DYTHYWLPSI AASLGISRAH FSVTTPWAIA YMGPSADAMI NGSDGRTTVE DLTTPPKWFP   180
FPTKVCWRKH DLARLVPYKA PGISDGYRMG LVLKGSDCLL SKCYHEFGTQ WLPLLETLHQ   240
VPVVPVGLLP PEIPGDEKDE TWVSIKKWLD GKQKGSVVYV ALGSESLVSQ TEVVELALGL   300
ELSGLPFVWA YRKPKGPAKS DSVELPDGFV ERTRDRGLVW TSWAPQLRIL SHESVCGFLT   360
```

HCGSGSIVEG LMFGHPLIML PIFGDQPLNA RLLEDKQVGI EIPRNEEDGC LTKESVARSL 420
RSVVVEKEGE IYKANARELS KIYNDTKVEK EYVSQFVDYL EKNARAVAID HES 473

SEQ ID NO:199
MATSDSIVDD RKQLHVATFP WLAFGHILPY LQLSKLIAEK GHKVSFLSTT RNIQRLSSHI 60
SPLINVVQLT LPRVQELPED AEATTDVHPE DIPYLKKASD GLQPEVTRFL EQHSPDWIIY 120
DYTHYWLPSI AASLGISRAH FSVTTPWAIA YMGPSADAMI NGSDGRTTVE DLTTPPKWFP 180
FPTKVCWRKH DLARLVPYKA PGISDGYRMG LVLKGSDCLL SKCYHEFGTQ WLPLLETLHQ 240
VPVVPVGLLP PEIPGDEKDE TWVSIKKWLD GKQKGSVVYV ALGSEVLVSQ TEVVELALGL 300
ELSGLPFVWA YRKPKGPAKS DSVELPDGFV ERTRDRGLVW TSWAPQLRIL SHESVCGFLT 360
HCGSGSIVEG LMFGHPLIML PIFGDQPLNA RLLEDKQVGI EIPRNEEDGC LTKESVARSL 420
RSVVVEKEGE IYKANARELS KIYNDTKVEK EYVSQFVDYL EKNARAVAID HES 473

SEQ ID NO:200
MATSDSIVDD RKQLHVATFP WLAFGHILPY LQLSKLIAEK GHKVSFLSTT RNIQRLSSHI 60
SPLINVVQLT LPRVQELPED AEATTDVHPE DIVYLKKASD GLQPEVTRFL EQHSPDWIIY 120
DYTHYWLPSI AASLGISRAH FSVTTPWAIA YGGPSADAMI NGSDGRTTVE DLTTPPKWFP 180
FPTKVCWRKH DLARLVPYKA PGISDGYRMG LVLKGSDCLL SKCYHEFGTQ WLPLLETLHQ 240
VPVVPVGLLP PEIPGDEKDE TWVSIKKWLD GKQKGSVVYV ALGSEVLVSQ TEVVELALGL 300
ELSGLPFVWA YRKPKGPAKS DSVELPDGFV ERTRDRGLVW TSWAPQLRIL SHESVCGFLT 360
HCGSGSIVEG LMFGHPLIML PIFGDQPLNA RLLEDKQVGI EIPRNEEDGC LTKESVARSL 420
RSVVVEKEGE IYKANARELS KIYNDTKVEK EYVSQFVDYL EKNARAVAID HES 473

SEQ ID NO:201
MATSDSIVDD RKQLHVATFP WLAFGHILPY LQLSKLIAEK GHKVSFLSTT RNIQRLSSHI 60
SPLINVVQLT LPRVQELPED AEATTDVHPE DIPYLKKAID GLQPEVTRFL EQHSPDWIIY 120
DYTHYWLPSI AASLGISRAH FSVTTPWAIA YMGPSADAMI NGSDGRTTVE DLTTPPKWFP 180
FPTKVCWRKH DLARLVPYKA PGISDGYRMG LVLKGSDCLL SKCYHEFGTQ WLPLLETLHQ 240
VPVVPVGLLP PEIPGDEKDE TWVSIKKWLD GKQKGSVVYV ALGSEVLVSQ TEVVELALGL 300
ELSGLPFVWA YRKPKGPAKS DSVELPDGFV ERTRDRGLVW TSWAPQLRIL SHESVCGFLT 360
HCGSGSIVEG LMFGHPLIML PIFGDQPLNA RLLEDKQVGI EIPRNEEDGC LTKESVARSL 420
RSVVVEKEGE IYKANARELS KIYNDTKVEK EYVSQFVDYL EKNARAVAID HES 473

SEQ ID NO:202
MATSDSIVDD RKQLHVATFP WLAFGHILPY LQLSKLIAEK GHKVSFLSTT RNIQRLSSHI 60
SPLINVVQLT LPRVQELPED AEATTDVHPE DIPYLKKASD GLQPEVTRFL EQHSPDWIIY 120
DYTHYWLPSI AASLGISRAH FSVKTPWAIA YMGPSADAMI NGSDGRTTVE DLTTPPKWFP 180
FPTKVCWRKH DLARLVPYKA PGISDGYRMG LVLKGSDCLL SKCYHEFGTQ WLPLLETLHQ 240
VPVVPVGLLP PEIPGDEKDE TWVSIKKWLD GKQKGSVVYV ALGSEVLVSQ TEVVELALGL 300
ELSGLPFVWA YRKPKGPAKS DSVELPDGFV ERTRDRGLVW TSWAPQLRIL SHESVCGFLT 360
HCGSGSIVEG LMFGHPLIML PIFGDQPLNA RLLEDKQVGI EIPRNEEDGC LTKESVARSL 420
RSVVVEKEGE IYKANARELS KIYNDTKVEK EYVSQFVDYL EKNARAVAID HES 473

SEQ ID NO:203
MATSDSIVDD RKQLHVATFP WLAFGHILPY LQLSKLIAEK GHKVSFLSTT RNIQRLSSHI 60
SPLINVVQLT LPRVQELPED AEATTDVHPE DIPYLKKASD GLQPEVTRFL EQHSPDWIIY 120
DYTHYWLPSI AASLGISRAH FSVLTPWAIA YMGPSADAMI NGSDGRTTVE DLTTPPKWFP 180
FPTKVCWRKH DLARLVPYKA PGISDGYRMG LVLKGSDCLL SKCYHEFGTQ WLPLLETLHQ 240
VPVVPVGLLP PEIPGDEKDE TWVSIKKWLD GKQKGSVVYV ALGSEVLVSQ TEVVELALGL 300
ELSGLPFVWA YRKPKGPAKS DSVELPDGFV ERTRDRGLVW TSWAPQLRIL SHESVCGFLT 360
HCGSGSIVEG LMFGHPLIML PIFGDQPLNA RLLEDKQVGI EIPRNEEDGC LTKESVARSL 420
RSVVVEKEGE IYKANARELS KIYNDTKVEK EYVSQFVDYL EKNARAVAID HES 473

SEQ ID NO:204
MATSDSIVDD RKQLHVATFP WLAFGHILPY LQLSKLIAEK GHKVSFLSTT RNIQRLSSHI 60
SPLINVVQLT LPRVQELPED AEATTDVHPE DIPYLKKASD GLQPEVTRFL EQHSPDWIIY 120
DYTHYWLPSI AASLGISRAH FSVMTPWAIA YMGPSADAMI NGSDGRTTVE DLTTPPKWFP 180

FPTKVCWRKH DLARLVPYKA PGISDGYRMG LVLKGSDCLL SKCYHEFGTQ WLPLLETLHQ 240
VPVVPVGLLP PEIPGDEKDE TWVSIKKWLD GKQKGSVVYV ALGSEVLVSQ TEVVELALGL 300
ELSGLPFVWA YRKPKGPAKS DSVELPDGFV ERTRDRGLVW TSWAPQLRIL SHESVCGFLT 360
HCGSGSIVEG LMFGHPLIML PIFGDQPLNA RLLEDKQVGI EIPRNEEDGC LTKESVARSL 420
RSVVVEKEGE IYKANARELS KIYNDTKVEK EYVSQFVDYL EKNARAVAID HES 473

SEQ ID NO:205
MATSDSIVDD RKQLHVATFP WLAFGHILPY LQLSKLIAEK GHKVSFLSTT RNIQRLSSHI 60
SPLINVVQLT LPRVQELPED AEATTDVHPE DIPYLKKASD GLQPEVTRFL EQHSPDWIIY 120
DYTHYWLPSI AASLGISRAH FSVTTPWKIA YMGPSADAMI NGSDGRTTVE DLTTPPKWFP 180
FPTKVCWRKH DLARLVPYKA PGISDGYRMG IVLKGSDCLL SKCYHEFGTQ WLPLLETLHQ 240
VPVVPVGLLP PEIPGDEKDE TWVSIKKWLD GKQKGSVVYV ALGSEVLVSQ TEVVELALGL 300
ELSGLPFVWA YRKPKGPAKS DSVELPDGFV ERTRDRGLVW TSWAPQLRIL SHESVCGFLT 360
HCGSGSIVEG LMFGHPLIML PIFGDQPLNA RLLEDKQVGI EIPRNEEDGC LTKESVARSL 420
RSVVVEKEGE IYKANARELS KIYNDTKVEK EYVSQFVDYL EKNARAVAID HES 473

SEQ ID NO:206
MATSDSIVDD RKQLHVATFP WLAFGHILPY LQLSKLIAEK GHKVSFLSTT RNIQRLSSHI 60
SPLINVVQLT LPRVQELPED AEATTDVHPE DIPYLKKASD GLQPEVTRFL EQHSPDWIIY 120
DYTHYWLPSI AASLGISRAH FSVTTPWAIA YMGPSADAMI NGSDGRTTVE DLTTPPKWFP 180
FPTKVCWRKH DLARNVPYKA PGISDGYRMG LVLKGSDCLL SKCYHEFGTQ WLPLLETLHQ 240
VPVVPVGLLP PEIPGDEKDE TWVSIKKWLD GKQKGSVVYV ALGSEVLVSQ TEVVELALGL 300
ELSGLPFVWA YRKPKGPAKS DSVELPDGFV ERTRDRGLVW TSWAPQLRIL SHESVCGFLT 360
HCGSGSIVEG LMFGHPLIML PIFGDQPLNA RLLEDKQVGI EIPRNEEDGC LTKESVARSL 420
RSVVVEKEGE IYKANARELS KIYNDTKVEK EYVSQFVDYL EKNARAVAID HES 473

SEQ ID NO:207
MATSDSIVDD RKQLHVATFP WLAFGHILPY LQLSKLIAEK GHKVSFLSTT RNIQRLSSHI 60
SPLINVVQLT LPRVQELPED AEATTDVHPE DIPYLKKASD GLQPEVTRFL EQHSPDWIIY 120
DYTHYWLPSI AASLGISRAH FSVTTPWAIA YMGPSADAMI NGSDGRTTVE DLTTPPKWFP 180
FPTKVCWRKH DLARLVPYCA PGISDGYRMG LVLKGSDCLL SKCYHEFGTQ WLPLLETLHQ 240
VPVVPVGLLP PEIPGDEKDE TWVSIKKWLD GKQKGSVVYV ALGSEVLVSQ TEVVELALGL 300
ELSGLPFVWA YRKPKGPAKS DSVELPDGFV ERTRDRGLVW TSWAPQLRIL SHESVCGFLT 360
HCGSGSIVEG LMFGHPLIML PIFGDQPLNA RLLEDKQVGI EIPRNEEDGC LTKESVARSL 420
RSVVVEKEGE IYKANARELS KIYNDTKVEK EYVSQFVDYL EKNARAVAID HES 473

SEQ ID NO:208
MATSDSIVDD RKQLHVATFP WLAFGHILPY LQLSKLIAEK GHKVSFLSTT RNIQRLSSHI 60
SPLINVVQLT LPRVQELPED AEATTDVHPE DIPYLKKASD GLQPEVTRFL EQHSPDWIIY 120
DYTHYWLPSI AASLGISRAH FSVTTPWAIA YMGPSADAMI NGSDGRTTVE DLTTPPKWFP 180
FPTKVCWRKH DLARLVPYKA PGISDGYRMG MVLKGSDCLL SKCYHEFGTQ WLPLLETLHQ 240
VPVVPVGLLP PEIPGDEKDE TWVSIKKWLD GKQKGSVVYV ALGSEVLVSQ TEVVELALGL 300
ELSGLPFVWA YRKPKGPAKS DSVELPDGFV ERTRDRGLVW TSWAPQLRIL SHESVCGFLT 360
HCGSGSIVEG LMFGHPLIML PIFGDQPLNA RLLEDKQVGI EIPRNEEDGC LTKESVARSL 420
RSVVVGKEGE IYKANARELS KIYNDTKVEK EYVSQFVDYL EKNARVVAID HES 473

SEQ ID NO:209
MATSDSIVDD RKQLHVATFP WLAFGHILPY LQLSKLIAEK GHKVSFLSTT RNIQRLSSHI 60
SPLINVVQLT LPRVQELPED AEATTDVHPE DIPYLKKASD GLQPEVTRFL EQHSPDWIIY 120
DYTHYWLPSI AASLGISRAH FSVTTPWAIA YMGPSADAMI NGSDGRTTVE DLTTPPKWFP 180
FPTKVCWRKH DLARLVPYKA PGISDGYRMG TVLKGSDCLL SKCYHEFGTQ WLPLLETLHQ 240
VPVVPVGLLP PEIPGDEKDE TWVSIKKWLD GKQKGSVVYV ALGSEVLVSQ TEVVELALGL 300
ELSGLPFVWA YRKPKGPAKS DSVELPDGFV ERTRDRGLVW TSWAPQLRIL SHESVCGFLT 360
HCGSGSIVEG LMFGHPLIML PIFGDQPLNA RLLEDKQVGI EIPRNEEDGC LTKESVARSL 420
RSVVVEKEGE IYKANARELS KIYNDTKVEK EYVSQFVDYL EKNARAVAID HES 473

SEQ ID NO:210

MATSDSIVDD RKQLHVATFP WLAFGHILPY LQLSKLIAEK GHKVSFLSTT RNIQRLSSHI 60
SPLINVVQLT LPRVQELPED AEATTDVHPE DIPYLKKASD GLQPEVTRFL EQHSPDWIIY 120
DYTHYWLPSI AASLGISRAH FSVTTPWAIA YMGPSADAMI NGSDGRTTVE DLTTPPKWFP 180
FPTKVCWRKH DLARLVPYKA PGISDGYRMG LVLKGSDCLL SKCYHEFGTQ WLPLLETLHQ 240
VPVVPVGLLP PEIPGDEKDE TWVSIKKWLD GKQKGSVVYV ALGSENLVSQ TEVVELALGL 300
ELSGLPFVWA YRKPKGPAKS DSVELPDGFV ERTRDRGLVW TSWAPQLRIL SHESVCGFLT 360
HCGSGSIVEG LMFGHPLIML PIFGDQPLNA RLLEDKQVGI EIPRNEEDGC LTKESVARSL 420
RSVVVEKEGE IYKANARELS KIYNDTKVEK EYVSQFVDYL EKNARAVAID HES 473

SEQ ID NO:211
MATSDSIVDD RKQLHVATFP WLAFGHILPY LQLSKLIAEK GHKVSFLSTT RNIQRLSSHI 60
SPLINVVQLT LPRVQELPED AEATTDVHPE DIPYLKKASD GLQPEVTRFL EQHFPDWIIY 120
DYTHYWLPSI AASLGISRAH FSVTTPWAIA YMGPSADAMI NGSDGRTTVE DLTTPPKWFP 180
FPTKVCWRKH DLARLVPYKA PGISDGYRMG LVLKGSDCLL SKCYHEFGTQ WLPLLETLHQ 240
VPVVPVGLLP PEIPGDEKDE TWVSIKKWLD GKQKGSVVYV ALGSESLVSQ TEVVELALGL 300
ELSGLPFVWA YRKPKGPAKS DSVELPDGFV ERTRDRGLVW TSWAPQLRIL SHESVCGFLT 360
HCGSGSIVEG LMFGHPLIML PIFGDQPLNA RLLEDKQVGI EIPRNEEDGC LTKESVARSL 420
RSVVVEKEGE IYKANARELS KIYNDTKVEK EYVSQFVDYL EKNARAVAID HES 473

SEQ ID NO:212
MATSDSIVDD RKQLHVATFP WLAFGHILPY LQLSKLIAEK GHKVSFLSTT RNIQRLSSHI 60
SPLINVVQLT LPRVQELPED AEATTDVHPE DIPYLKKASD GLQPEVTRFL EQHSPDWIIY 120
DYTHYWLPSI AASLGISRAH FSVTTPWAIA YMGPSADAMI NGSDGRTTVE DLTTPPKWFP 180
FPTKVCWRKH DLARLVPYKA PGISDGYRMG LVLKGSDCLL SKCYHEFGTQ WLPLLETLHQ 240
VPVVPVGLLP PEIPGDEKDE TWVSIKKWLD GKQKGSVVYV ALGSEVLVSQ TEVVELALGL 300
ELSGLPFVWA YRKPKGPAKS DSVELPDGFV ERTRDRGLVW TSWAPQLRIL SHESVCGFLT 360
HCGSGSIVEG LMFGHPLIML PIFKDQPLNA RLLEDKQVGI EIPRNEEDGC LTKESVARSL 420
RSVVVEKEGE IYKANARELS KIYNDTKVEK EYVSQFVDYL EKNARAVAID HES 473

SEQ ID NO:213
MATSDSIVDD RKQLHVATFP WLAFGHILPY LQLSKLIAEK GHKVSFLSTT RNIQRLSSHI 60
SPLINVVQLT LPRVQELPED AEATTDVHPE DIPYLKKASD GLQPEVTRFL EQHSPDWIIY 120
DYTHYWLPSI AASLGISRAH FSVTTPWAIA YMGPSADAMI NGSDGRTTVE DLTTPPKWFP 180
FPTKVCWRKH DLARLVPYKA PGISDGYRMG LVLKGSDCLL SKCYHEFGTQ WLPLLETLHQ 240
VPVVPVGLLP PEIPGDEKDE TWVSIKKWLD GKQKGSVVYV ALGSEVLVSQ TEVVELALGL 300
ELSGLPFVWA YRKPKGPAKS DSVELPDGFV ERTRDRGLVW TSWAPQLRIL SHESVCGFLT 360
HCGSGSIVEG LMFGHPLIML PIFYDQPLNA RLLEDKQVGI EIPRNEEDGC LTKESVARSL 420
RSVVVEKEGE IYKANARELS KIYNDTKVEK EYVSQFVDYL EKNARAVAID HES 473

SEQ ID NO:214
MATSDSIVDD RKQLHVATFP WLAFGHILPY LQLSKLIAEK GHKVSFLSTT RNIQRLSSHI 60
SPLINVVQLT LPRVQELPED AEATTDVHPE DIPYLKKASD GLQPEVTRFL EQHSPDWIIY 120
DYTHYWLPSI AASLGISRAH FSVTTPWAIA YMGPSADAMI NGSDGRTTVE DLTTPPKWFP 180
FPTKVCWRKH DLARLVPYKA PGISDGYRMG LVLKGSDCLL SKCYHEFGTQ WLPLLETLHQ 240
VPVVPVGLLP PEIPGDEKDE TWVSIKKWLD GKQKGSVVYV ALGSEVLVSQ TEVVELALGL 300
ELSGLPFVWA YRKPKGPAKS DSVELPDGFV ERTRDRGLVW TSWAPQLRIL SHESVCGFLT 360
HCGSGSIVEG LMFGHPLIML PIFGDQPLNA RLLEDKQVGI EIPRNEEDGC LTKESVARSL 420
RSVVVEKEGE IYKANARMLS KIYNDTKVEK EYVSQFVDYL EKNARAVAID HES 473

SEQ ID NO:215
ATCAACGGGUAAAATGGATGCTATGGCTACCACCG

SEQ ID NO:216
CGTGCGAUTCAGTTTCTGGCCAAAACGGTGATT

SEQ ID NO:217

```
MENKTETTVR RRRRIILFPV PFHGHINPIL QLANVLYSKG FSITIFHTNF NKPKTSNYPH    60
FTFRFILDND PQDERISNLP THGPLAGMRI PIINEHGADE LRRELELLML ASEEDEEVSC   120
LITDALWYFA QSVADSLNLR RLVLMTSSLF NFHALVSLPQ FDELGYLDPD DKTRLEEQAS   180
GFPMLKVKDI KSAYSNWQIL KEILGKMIKQ TKASSGVIWN SFKELEESEL ETVIREIPAP   240
SFLIPLPKHL TASSSSLLDH DRTVFQWLDQ QPPSSVLYVS FGSTSEVDEK DFLEIARGLV   300
DSKQSFLWVV RPGFVKGSTW VEPLPDGFLG ERGRIVKWVP QQEVLAHGAI GAFWTHSGWN   360
STLESVCEGV PMIFSDFGLD QPLNARYMSD VLKVGVYLEN GWERGEIANA IRRVMVDEEG   420
EYIRQNARVL KQKADVSLMK GGSSYESLES LVSYISSL                           458
```

SEQ ID NO:218

```
MENKTETTVR RRRRIILFPV PFQGHINPIL QLANVLYSKG FSITIFHTNF NKPKTSNYPH    60
FTFRFILDND PQDERISNLP THGPLAGMRI PIINEHGADE LRRELELLML ASEEDEEVSC   120
LITDALWYFA QSVADSLNLR RLVLMGSSLF NFHALVSLPQ FDELGYLDPD DKTRLEEQAS   180
GFPMLKVKDI KSAYSNWQIL KEILGKMIKQ TKASSGVIWN SFKELEESEL ETVIREIPAP   240
SFLIPLPKHL TASSSSLLDH DRTVFQWLDQ QPPSSVLYVS FGSTSEVDEK DFLEIARGLV   300
DSKQSFLWVV RPGFVKGSTW VEPLPDGFLG ERGRIVKWVP QQEVLAHGAI GAFWTHSGWN   360
STLESVCEGV PMIFSDFGLD QPLNARYMSD VLKVGVYLEN GWERGEIANA IRRVMVDEEG   420

EYIRQNARVL KQKADVSLMK GGSSYESLES LVSYISSL                           458
```

SEQ ID NO:219

```
MENKTETTVR RRRRIILFPV PFQGHINPIL QLANVLYSKG FSITIFHTNF NKPKTSNYPH    60
FTFRFILDND PQDERISNLP THGPLAGMRI PIINEHGADE LRRELELLML ASEEDEEVSC   120
LITDALWYFA QSVADSLNLR RLVLMTSSLF NFHALVSLPQ FDELGYLDPD DKTRLEEQAS   180
GFPMLKVKDI KSAYSNWQIL KEILGKMIKQ TKASSGVIWN SFKELEESEL ETVIREIPAP   240
SFLIPLPKHL TASSSSGLDH DRTVFQWLDQ QPPSSVLYVS FGSTSEVDEK DFLEIARGLV   300
DSKQSFLWVV RPGFVKGSTW VEPLPDGFLG ERGRIVKWVP QQEVLAHGAI GAFWTHSGWN   360
STLESVCEGV PMIFSDFGLD QPLNARYMSD VLKVGVYLEN GWERGEIANA IRRVMVDEEG   420

EYIRQNARVL KQKADVSLMK GGSSYESLES LVSYISSL                           458
```

SEQ ID NO:220

```
MENKTETTVR RRRRIILFPV PFQGHINPIL QLANVLYSKG FSITIFHTNF NKPKTSNYPH    60
FTFRFILDND PQDERISNLP THGPLAGMRI PIINEHGADE LRRELELLML ASEEDEEVSC   120
LITDALWYFA QSVADSLNLR RLVLMTSSLF NFHALVSLPQ FDELGYLDPD DKTRLEEQAS   180
GFPMLKVKDI KSAYSNWQIL KEILGKMIKQ TKASSGVIWN SFKELEESEL ETVIREIPAP   240
SFLIPLPKHL TASSSSLLDH DRTVFQWLDQ QPPSSVLYVS FGNTSEVDEK DFLEIARGLV   300
DSKQSFLWVV RPGFVKGSTW VEPLPDGFLG ERGRIVKWVP QQEVLAHGAI GAFWTHSGWN   360
STLESVCEGV PMIFSDFGLD QPLNARYMSD VLKVGVYLEN GWERGEIANA IRRVMVDEEG   420

EYIRQNARVL KQKADVSLMK GGSSYESLES LVSYISSL                           458
```

WHAT IS CLAIMED IS:

1. A recombinant host cell, comprising at least one recombinant gene that is:
   (a) a gene encoding a UGT91D2e polypeptide having at least 90% sequence identity to the amino acid sequence set forth in SEQ ID NO:11;
   (b) a gene encoding a chimeric polypeptide having at least 70% sequence identity to the amino acid sequence set forth in SEQ ID NO:17 or SEQ ID NO:18;
   (c) a gene encoding a UGT85C2 polypeptide having at least 55% sequence identity to the amino acid sequence set forth in SEQ ID NO:7; and/or
   (d) a gene encoding a UGT76G1 polypeptide having at least 50% sequence identity to the amino acid sequence set forth in SEQ ID NO:9;

   wherein the recombinant host cell is capable of producing a steviol glycoside, glycosylated ent-kaurenol compound, and/or a glycosylated ent-kaurenoic acid compound in a cell culture broth.

2. The recombinant host cell of claim 1, wherein the UGT91D2e polypeptide comprises a UGT91D2e polypeptide having at least one amino acid substitution at residues 93, 99, 114, 144, 148, 152, 195, 196, 199, 211, 213, 221, 286, 384, 426, 438, or 466 of SEQ ID NO:11.

3. The recombinant host cell of claim 1, wherein the UGT85C2 polypeptide comprises a UGT85C2 polypeptide having at least one amino acid substitution at residues 21, 48, 49, 84, 86, 87, 91, 92, 95, 122, 334, or 334 of SEQ ID NO:7.

4. The recombinant host cell of claim 1, wherein the UGT76G1 polypeptide comprises a UGT76G1 polypeptide having at least one amino acid substitution at residues 23, 26, 55, 146, 257, 283, and 337 of SEQ ID NO:9.

5. The recombinant host cell of claim 1, wherein the UGT91D2e polypeptide comprises one or more of the UGT91D2e polypeptide variants comprising: P93V, S99I, S114F, T144K, T144L, T144M, A148K, M152T, L195G, L195C, L195S, L195N, L195V, V196P, K199C, L211H, L211M, L211I, L211C, L211T, L213E, S221I, V286C, V286N, V286S, G384W, G384K, G384Y, E426G, E438H, 3438M or A466V of SEQ ID NO:11.

6. The recombinant host cell of claim 1, wherein the UGT85C2 polypeptide comprises one or more of the UGT85C2 polypeptide variants comprising: Q21L, Q21T, Q21V, F48S, F48H, F48Y, F48R, F48Q, F48W, F48T, I49V, S84G, S84A, S84T, S84C, S84P, S84N, S84V, P86R, P86G, I87H, I87P, I87M, I87Y, L91K, L91R, L91T, L92F, L92I, L92M, I95K, F122S, L334S or L334M of SEQ ID NO:7.

7. The recombinant host cell of claim 1, wherein the UGT76G1 polypeptide comprises one or more of the UGT76G1 polypeptide variants comprising: Q23H, I26W, T146G, H155L, L257G, S253W, T284G, S283N, K337P or T55K of SEQ ID NO:9.

8. The recombinant host cell of any one of claims 1-7, further comprising at least one recombinant gene that is:
   (a) a gene encoding a geranylgeranyl diphosphate synthase (GGPPS) polypeptide;
   (b) a gene encoding an ent-copalyl diphosphate synthase (CDPS) polypeptide;
   (c) a gene encoding an ent-kaurene synthase (KS) polypeptide;
   (d) a gene encoding an ent-kaurene oxidase (KO) polypeptide;
   (e) a gene encoding a cytochrome P450 reductase (CPR) polypeptide; and
   (f) a gene encoding an ent-kaurenoic acid hydroxylase (KAH) polypeptide;
   (g) a gene encoding a UGT74G1 polypeptide; and/or
   (h) a gene encoding an EUGT11 polypeptide;

   wherein the recombinant host cell capable of producing a steviol glycoside, glycosylated ent-kaurenol compound, and/or a glycosylated ent-kaurenoic acid compound in a cell culture broth.

9. The recombinant host cell of claim 8, wherein:
   (a) the GGPPS polypeptide comprises a polypeptide having at least 70% identity to an amino acid sequence set forth in SEQ ID NO:20, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:26, SEQ ID NO:28, SEQ ID NO:30, SEQ ID NO:32, or SEQ ID NO:116;

(b) the CDPS polypeptide comprises a polypeptide having at least 70% identity to an amino acid sequence set forth in SEQ ID NO:34, SEQ ID NO:36, SEQ ID NO:38, SEQ ID NO:40, or SEQ ID NO:42;

(c) the KS polypeptide comprises a polypeptide having at least 70% identity to an amino acid sequence set forth in SEQ ID NO:44, SEQ ID NO:46, SEQ ID NO:48, SEQ ID NO:50, or SEQ ID NO:52;

(d) the KO polypeptide comprises a polypeptide having at least 70% identity to an amino acid sequence set forth in SEQ ID NO:60, SEQ ID NO:62, SEQ ID NO:117, SEQ ID NO:66, SEQ ID NO:68, SEQ ID NO:70, SEQ ID NO:72, SEQ ID NO:74, or SEQ ID NO:76;

(e) the CPR polypeptide comprises a polypeptide having at least 70% identity to an amino acid sequence set forth in SEQ ID NO:78, SEQ ID NO:80, SEQ ID NO:82, SEQ ID NO:84, SEQ ID NO:86, SEQ ID NO:88, SEQ ID NO:90, SEQ ID NO:92;

(f) the KAH polypeptide comprises a polypeptide having at least 70% identity to an amino acid sequence set forth in SEQ ID NO:94, SEQ ID NO:97, SEQ ID NO:100, SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:103, SEQ ID NO:104, SEQ ID NO:106, SEQ ID NO:108, SEQ ID NO:110, SEQ ID NO:112, or SEQ ID NO:114;

(g) the UGT74G1 polypeptide comprises a polypeptide having at least 55% identity to an amino acid sequence set forth in SEQ ID NO:4;

(h) the EUGT11 polypeptide comprises a polypeptide having at least 65% identity to an amino acid sequence set forth in SEQ ID NO:16.

10. The recombinant host cell of any one of claims 1-9, wherein the cell culture broth comprises:

(a) the steviol glycoside, glycosylated ent-kaurenol compound, and/or the glycosylated ent-kaurenoic acid compound produced by the recombinant host cell,

(b) glucose, fructose and/or sucrose; and/or

(c) supplemental nutrients comprising trace metals, vitamins, salts, yeast nitrogen base (YNB), and/or amino acids.

11. The recombinant host cell of any one of claims 1-10, wherein the recombinant host comprises a plant cell, a mammalian cell, an insect cell, a fungal cell, an algal cell, or a bacterial cell.

12. The recombinant host cell of claim 11, wherein the bacterial cell comprises *Escherichia* cells, *Lactobacillus* cells, *Lactococcus* cells, *Cornebacterium* cells, *Acetobacter* cells, *Acinetobacter* cells, or *Pseudomonas* cells.

13. The recombinant host cell of claim 11, wherein the fungal cell comprises a yeast cell.

14. The recombinant host cell of claim 13, wherein the yeast cell is a cell from *Saccharomyces cerevisiae*, *Schizosaccharomyces pombe*, *Yarrowia lipolytica*, *Candida glabrata*, *Ashbya gossypii*, *Cyberlindnera jadinii*, *Pichia pastoris*, *Kluyveromyces lactis*, *Hansenula polymorpha*, *Candida boidinii*, *Arxula adeninivorans*, *Xanthophyllomyces dendrorhous*, or *Candida albicans* species.

15. The recombinant host cell of claim 14, wherein the yeast cell is a *Saccharomycete*.

16. The recombinant host cell of claim 15, wherein the yeast cell is a cell from the *Saccharomyces cerevisiae* species.

17. A method of producing a steviol glycoside, glycosylated ent-kaurenol compound, and/or glycosylated ent-kaurenoic acid compound in a cell culture broth, comprising growing the recombinant host cell of any one of claims 1-16 in a culture medium, under conditions in which one or more of the genes are expressed;

wherein at least one of the genes is a recombinant gene;

wherein the steviol glycoside, glycosylated ent-kaurenol compound, and/or the glycosylated ent-kaurenoic acid compound is produced by the recombinant host cell.

18. The method of claim 17, wherein one or more of the genes is constitutively expressed and/or expression of one or more of the genes is induced.

19. A method for producing a steviol glycoside, glycosylated ent-kaurenol compound, and/or the glycosylated ent-kaurenoic acid compound comprising whole-cell bioconversion of plant-derived components or synthetic steviol or steviol glycosides using one or more of:
    (a) a UGT91D2e polypeptide having at least 90% sequence identity to the amino acid sequence set forth in SEQ ID NO:11;
    (b) a chimeric polypeptide having at least 70% sequence identity to the amino acid sequence set forth in SEQ ID NO:17 or SEQ ID NO:18;
    (c) a UGT85C2 polypeptide having at least 55% sequence identity to the amino acid sequence set forth in SEQ ID NO:7; and/or
    (d) a UGT76G1 polypeptide having at least 50% sequence identity to the amino acid sequence set forth in SEQ ID NO:9;

    wherein at least one of the polypeptides is a recombinant polypeptide.

20. The method of claim 19, wherein the whole cell is the recombinant host cell of any one of claims 1-16.

21. The method of any one of claims 17-20, wherein the recombinant host cell is grown in a fermentor at a temperature for a period of time, wherein the temperature and period of time facilitate the production of the steviol glycoside, glycosylated ent-kaurenol compound, and/or glycosylated ent-kaurenoic acid compound.

22. An *in vitro* method for producing a steviol glycoside, glycosylated ent-kaurenol compound, and/or the glycosylated ent-kaurenoic acid compound, comprising adding one or more of:
    (a) a UGT91D2e polypeptide having at least 90% sequence identity to the amino acid sequence set forth in SEQ ID NO:11;
    (b) a chimeric polypeptide having at least 70% sequence identity to the amino acid sequence set forth in SEQ ID NO:17 or SEQ ID NO:18;
    (c) a UGT85C2 polypeptide having at least 55% sequence identity to the amino acid sequence set forth in SEQ ID NO:7; and/or
    (d) a UGT76G1 polypeptide having at least 50% sequence identity to the amino acid sequence set forth in SEQ ID NO:9,

    and plant-derived components or synthetic steviol or steviol glycosides to a reaction mixture;

wherein at least one of the polypeptides is a recombinant polypeptide; and synthesizing the steviol glycoside, glycosylated ent-kaurenol compound, and/or the glycosylated ent-kaurenoic acid compound in the reaction mixture.

23. The method of any one of claims 17-22, that further comprises isolating the steviol glycoside, glycosylated ent-kaurenol compound, and/or the glycosylated ent-kaurenoic acid compound, alone or in combination from the cell culture broth.

24. The method of claim 23, wherein the isolating step comprises:
   (a) providing the cell culture broth comprising the steviol glycoside, glycosylated ent-kaurenol compound, and/or the glycosylated ent-kaurenoic acid compound alone or in combination;
   (b) separating a liquid phase of the cell culture broth from a solid phase of the cell culture broth to obtain a supernatant comprising the steviol glycoside, glycosylated ent-kaurenol compound, and/or the glycosylated ent-kaurenoic acid compound alone or in combination;
   (c) providing one or more adsorbent resins, comprising providing the adsorbent resins in a packed column; and
   (d) contacting the supernatant of step (b) with the one or more adsorbent resins in order to obtain at least a portion of the steviol glycoside, glycosylated ent-kaurenol compound, and/or the glycosylated ent-kaurenoic acid compound alone or in combination thereby isolating the steviol glycoside, glycosylated ent-kaurenol compound, and/or the glycosylated ent-kaurenoic acid compound alone or in combination.

25. The method of any one of claims 17-22, that further comprises recovering the the steviol glycoside, glycosylated ent-kaurenol compound, and/or the glycosylated ent-kaurenoic acid compound alone or a composition comprising the steviol glycoside, glycosylated ent-kaurenol compound, and/or the glycosylated ent-kaurenoic acid compound.

26. The method of claim 25, wherein the recovered composition is enriched for the steviol glycoside, glycosylated ent-kaurenol compound, and/or the glycosylated ent-kaurenoic acid compound relative to a steviol glycoside composition of Stevia plant and has a

reduced level of non-steviol glycoside Stevia plant-derived components relative to a plant-derived stevia extract.

27. The method of any one of claims 17-22, wherein the cell culture broth comprises:
    (a) one or more steviol glycosides, glycosylated ent-kaurenol compounds, and/or glycosylated ent-kaurenoic acid compounds produced by the recombinant host cell of any one of claims 1-12,
    (b) glucose, fructose, and/or sucrose; and/or
    (c) supplemental nutrients comprising trace metals, vitamins, salts, YNB, and/or amino acids.

28. The method of claim 22, wherein the reaction mixture comprising:
    (a) one or more steviol glycosides, glycosylated ent-kaurenol compounds, and/or a glycosylated ent-kaurenoic acid compounds produced in the reaction mixture;
    (b) a UGT polypeptide;
    (c) UDP-glucose, UDP-rhamnose, UDP-xylose, and/or N-acetyl-glucosamine; and/or
    (d) reaction buffer and/or salts.

29. The method of any one of claims 17-28, wherein the recombinant host cell comprises a plant cell, a mammalian cell, an insect cell, a fungal cell, an algal cell, or a bacterial cell.

30. The method of claim 29, wherein the bacterial cell comprises *Escherichia* cells, *Lactobacillus* cells, *Lactococcus* cells, *Cornebacterium* cells, *Acetobacter* cells, *Acinetobacter* cells, or *Pseudomonas* cells.

31. The method of claim 29, wherein the fungal cell comprises a yeast cell.

32. The method of claim 31, wherein the yeast cell is a cell from *Saccharomyces cerevisiae*, *Schizosaccharomyces pombe*, *Yarrowia lipolytica*, *Candida glabrata*, *Ashbya gossypii*, *Cyberlindnera jadinii*, *Pichia pastoris*, *Kluyveromyces lactis*, *Hansenula polymorpha*, *Candida boidinii*, *Arxula adeninivorans*, *Xanthophyllomyces dendrorhous*, or *Candida albicans* species.

33. The method of claim 31, wherein the yeast cell is a *Saccharomycete*.

34. The method of claim 33, wherein the yeast cell is a cell from the *Saccharomyces cerevisiae* species.

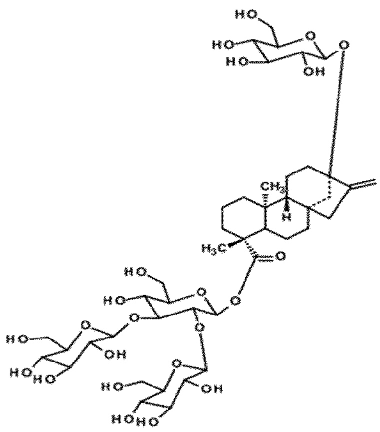
35. The recombinant host cell of any one of claims 1-16 or the method of any one of claims 17-34, wherein:
    (a) the steviol glycoside comprises 13-SMG, 19-SMG, Steviol-1,2-bioside, Steviol-1,3-bioside, 1,2-stevioside, 1,3-stevioside, rubusoside, RebA, RebB, RebD, RebE, RebM, di-glycosylated tri-glycosylated steviol, tetra-glycosylated steviol, penta-glycosylated steviol, hexa-glycosylated steviol, hepta-glycosylated steviol, and/or isomers thereof;
    (b) the glycosylated ent-kaurenol compound comprises di-glycosylated ent-kaurenol, tri-glycosylated ent-kaurenol, and/or isomers thereof; and/or
    (c) the glycosylated ent-kaurenoic acid compound comprises di-glycosylated ent-kaurenoic acid, tri-glycosylated ent-kaurenoic acid, and/or isomers thereof.

36. The recombinant host cell or the method of claim 35, wherein:
    (a) the di-glycosylated steviol comprises compound 2.23 of Table 1;
    (b) the tri-glycosylated steviol comprises compound 3.1 and/or compound 3.34 of Table 1;
    (c) the tetra-glycosylated steviol comprises compound 4.26 and/or compound 4.33 of Table 1;
    (d) the penta-glycosylated steviol comprises compound 5.22, compound 5.24, and/or compound 5.25 of Table 1;
    (e) the hexa-glycosylated steviol comprises compound 6.1 and/or compound 6.23 of Table 1;
    (f) the hepta-glycosylated steviol comprises compound 7.2, compound 7.5, and/or compound 7.13 of Table 1;
    (g) the glycosylated ent-kaurenoic acid compound comprises compound KA3.1, compound KA3.2, and/or compound KA2.7 of Table 1; and/or

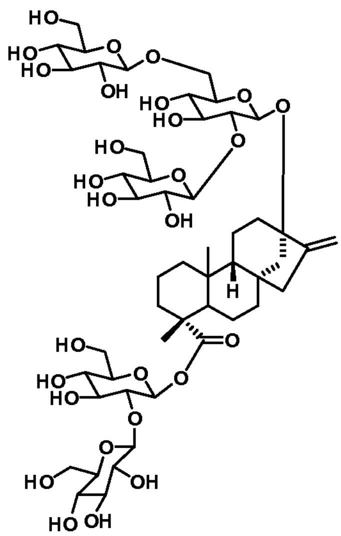
(h) the glycosylated ent-kaurenol compound comprises compound KL2.8 and/or compound KL3.1 co-eluted with compound KL3.6 of Table 1.

37. The recombinant host cell or method of claim 36, wherein:

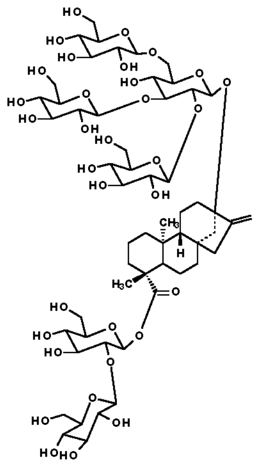
(a) compound 4.26 has the structure:



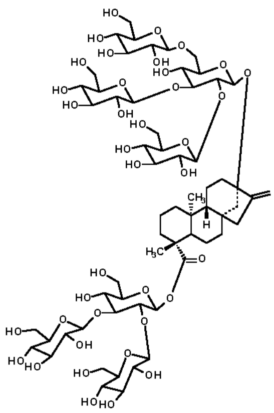
(b) compound 5.22 has the structure:



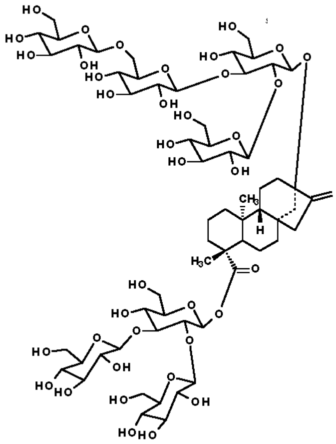
(c) compound 6.1 has the structure:



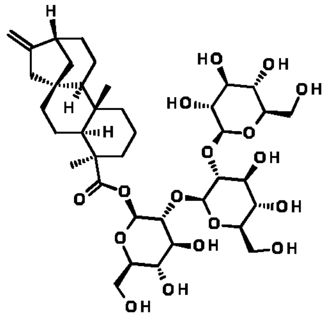
(d) compound 7.2 has the structure:



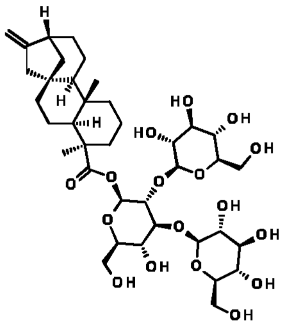
(e) compound 7.5 has the structure:



(f) compound KA3.1 has the structure:

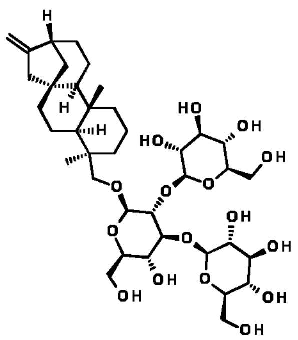


(g) compound KA3.2 has the structure:



; and

(h) compound KL3.1 has the structure:



.

38. A steviol glycoside composition produced by the recombinant host cell of any one of claims 1-16 or the method of any one of claims 17-34, wherein the composition has a steviol glycoside composition enriched for RebD, RebM, or isomers thereof relative to a steviol glycoside composition of Stevia plant and has a reduced level of non-steviol glycoside Stevia plant-derived components relative to a plant-derived stevia extract.

39. A cell culture broth comprising:

(a) the recombinant host cell of any one of claims 1-16; and

(b) one or more steviol glycosides, glycosylated ent-kaurenol compounds, and/or glycosylated ent-kaurenoic acid compounds produced by the recombinant host cell;

wherein one or more steviol glycosides is present at a concentration of at least 1 mg/liter of the culture broth.

40. A cell culture broth comprising:

(a) one or more steviol glycosides, glycosylated ent-kaurenol compounds, and/or glycosylated ent-kaurenoic acid compounds produced by the recombinant host cell of any one of claims 1-16,

(b) glucose, fructose, sucrose, xylose, ethanol, and/or glycerol; and/or

(c) supplemental nutrients comprising trace metals, vitamins, salts, YNB, and/or amino acids.

41. A cell lysate comprising:

(a) one or more steviol glycosides, glycosylated ent-kaurenol compounds, and/or glycosylated ent-kaurenoic acid compounds produced by the recombinant host cell of any one of claims 1-16,

(b) glucose, fructose, sucrose, xylose, ethanol, glycerol, uridine diphosphate (UDP)-glucose, UDP-rhamnose, UDP-xylose, and/or N-acetyl-glucosamine; and/or

(c) supplemental nutrients comprising trace metals, vitamins, salts, YNB, and/or amino acids.

42. A reaction mixture comprising:

(a) one or more steviol glycosides, glycosylated ent-kaurenol compounds, and/or a glycosylated ent-kaurenoic acid compounds produced in the reaction mixture;

(b) a UGT polypeptide;

(c) glucose, fructose, sucrose, xylose, ethanol, glycerol, uridine diphosphate (UDP)-glucose, UDP-rhamnose, UDP-xylose, and/or N-acetyl-glucosamine; and/or

(d) reaction buffer and/or salts.

Figure 1

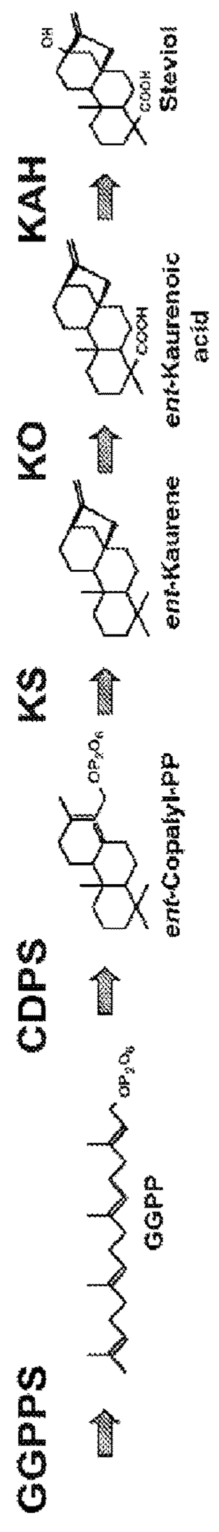

GGPPS
GGPP
CDPS
ent-Copalyl-PP
KS
ent-Kaurene
KO
ent-Kaurenoic acid
KAH
Steviol

Figure 2

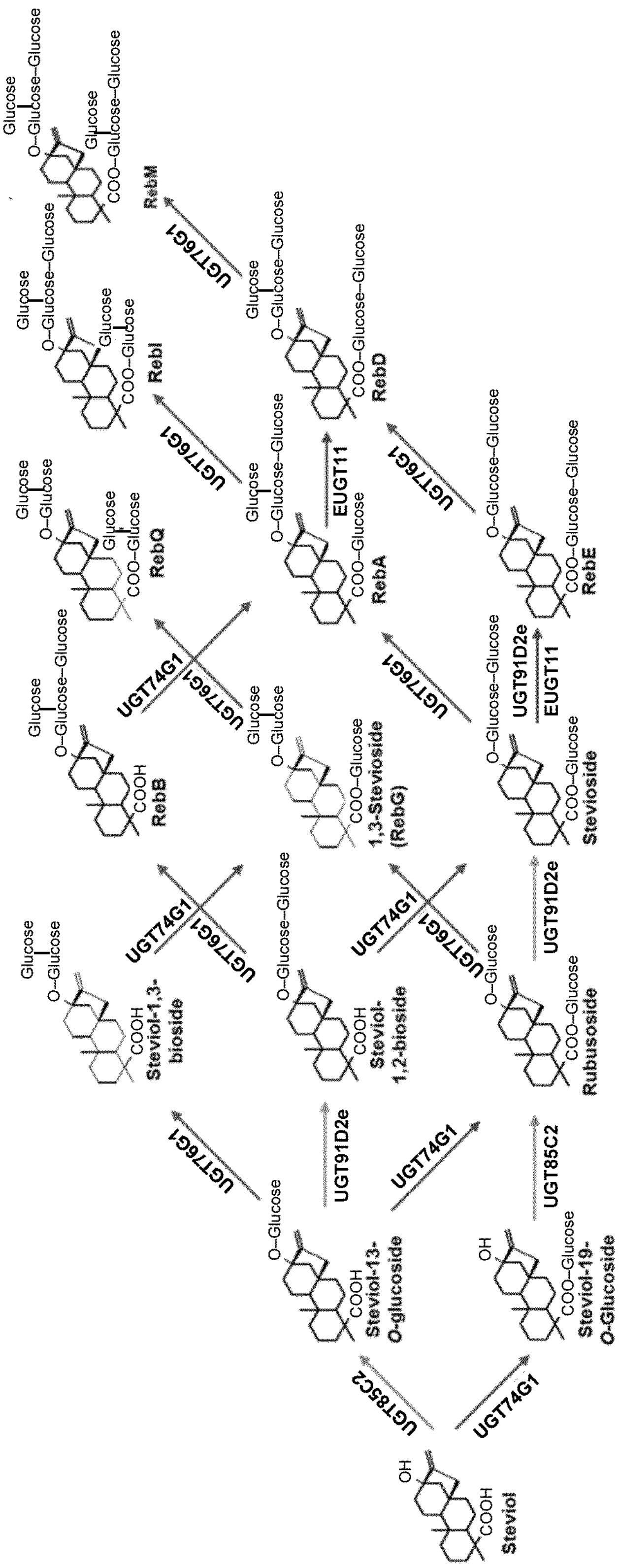
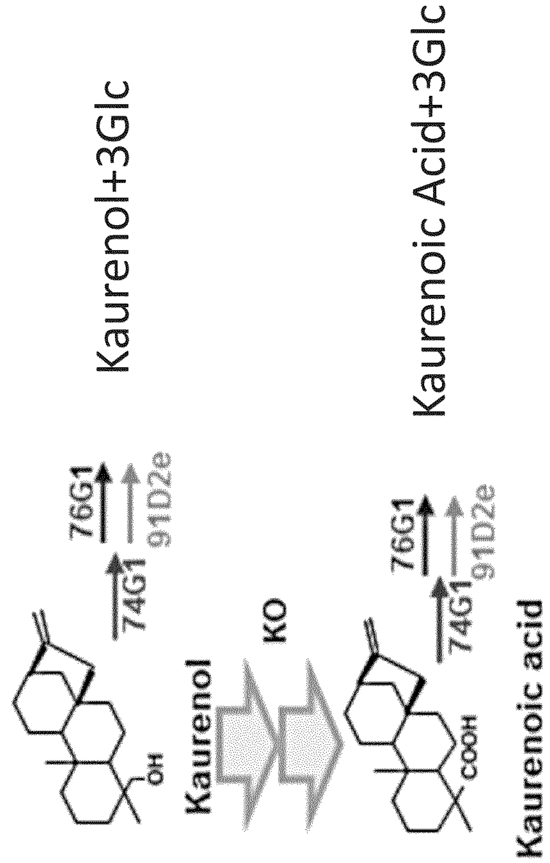

Steviol
UGT85C2
UGT74G1
Steviol-13-O-glucoside
Steviol-19-O-Glucoside
UGT76G1
UGT91D2e
UGT74G1
UGT85C2
Steviol-1,3-bioside
Steviol-1,2-bioside
Rubusoside
UGT74G1
UGT76G1
UGT91D2e
RebB
1,3-Stevioside (RebG)
Stevioside
EUGT11
RebQ
RebA
RebE
RebI
RebD
RebM

Figure 3



Kaurenol
OH
74G1
76G1
91D2e
Kaurenol+3Glc
KO
Kaurenoic acid
COOH
74G1
76G1
91D2e
Kaurenoic Acid+3Glc

Figure 4A

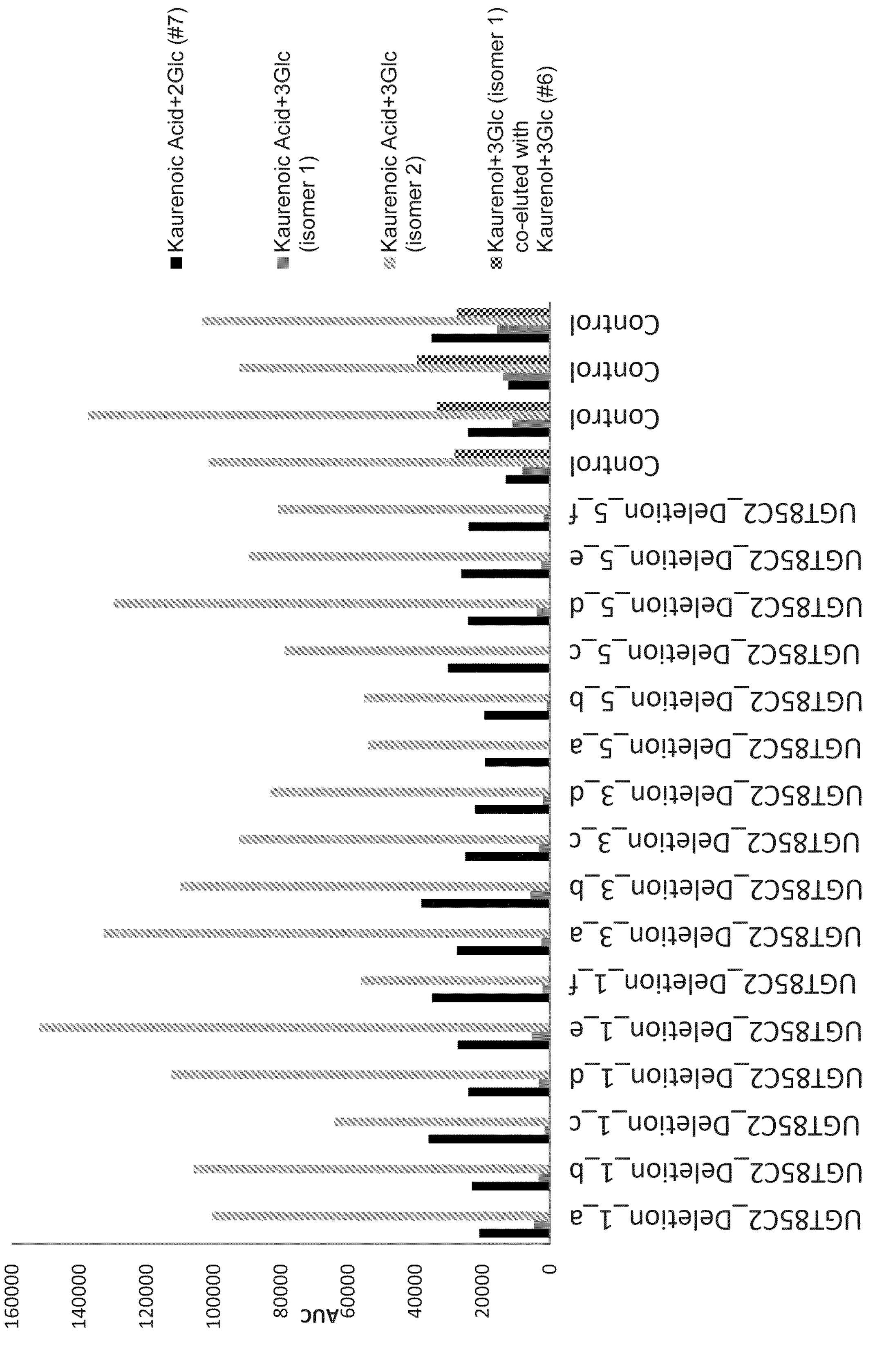

Kaurenoic Acid+2Glc (#7)
Kaurenoic Acid+3Glc (isomer 1)
Kaurenoic Acid+3Glc (isomer 2)
Kaurenol+3Glc (isomer 1) co-eluted with Kaurenol+3Glc (#6)
AUC
160000
140000
120000
100000
80000
60000
40000
20000
0
UGT85C2_Deletion_1_a
UGT85C2_Deletion_1_b
UGT85C2_Deletion_1_c
UGT85C2_Deletion_1_d
UGT85C2_Deletion_1_e
UGT85C2_Deletion_1_f
UGT85C2_Deletion_3_a
UGT85C2_Deletion_3_b
UGT85C2_Deletion_3_c
UGT85C2_Deletion_3_d
UGT85C2_Deletion_5_a
UGT85C2_Deletion_5_b
UGT85C2_Deletion_5_c
UGT85C2_Deletion_5_d
UGT85C2_Deletion_5_e
UGT85C2_Deletion_5_f
Control
Control
Control
Control

Figure 4B

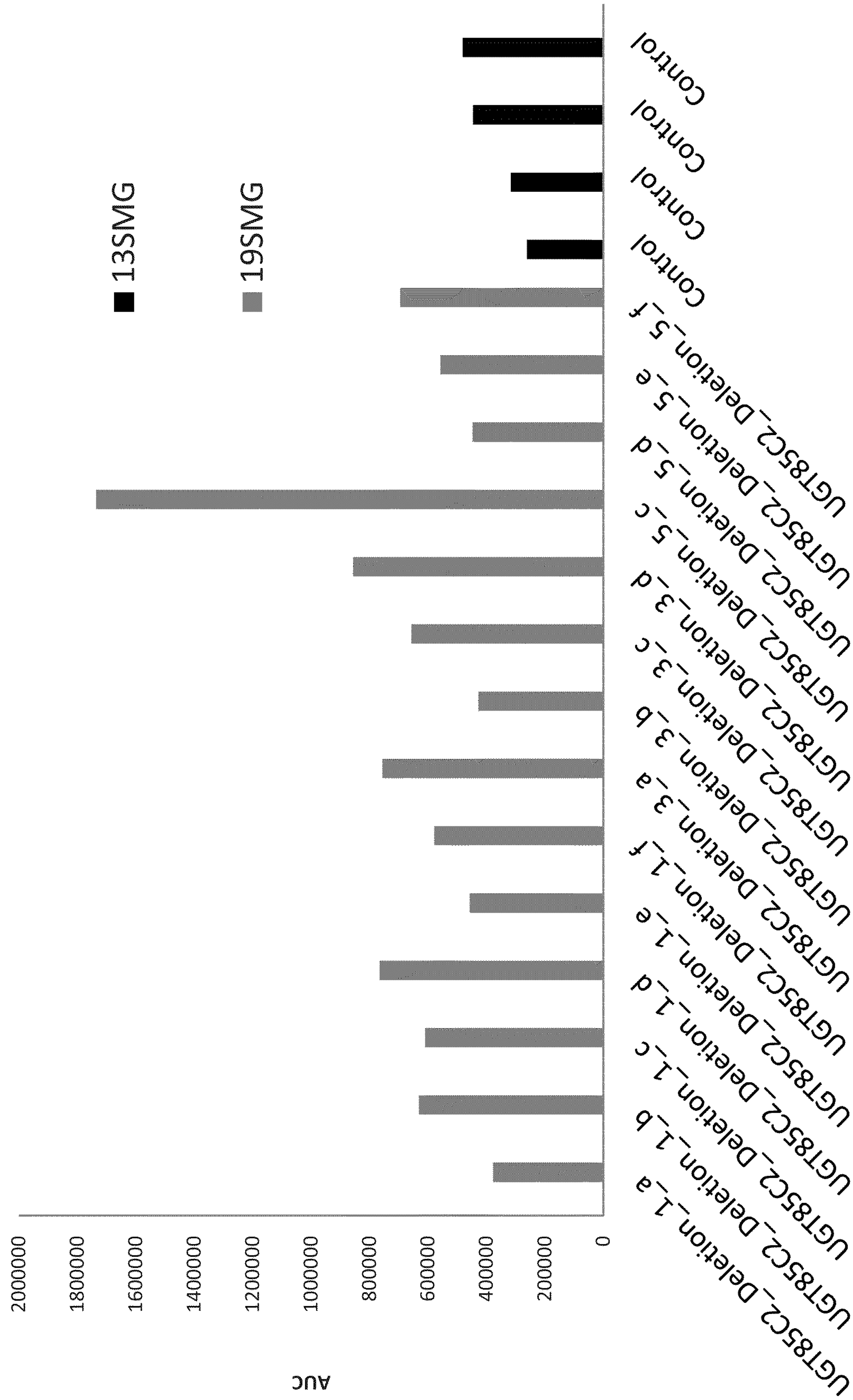

13SMG
19SMG
AUC
2000000
1800000
1600000
1400000
1200000
1000000
800000
600000
400000
200000
0
UGT85C2_Deletion_1_a
UGT85C2_Deletion_1_b
UGT85C2_Deletion_1_c
UGT85C2_Deletion_1_d
UGT85C2_Deletion_1_e
UGT85C2_Deletion_1_f
UGT85C2_Deletion_3_a
UGT85C2_Deletion_3_b
UGT85C2_Deletion_3_c
UGT85C2_Deletion_3_d
UGT85C2_Deletion_5_c
UGT85C2_Deletion_5_d
UGT85C2_Deletion_5_e
UGT85C2_Deletion_5_f
Control
Control
Control
Control

Figure 4C

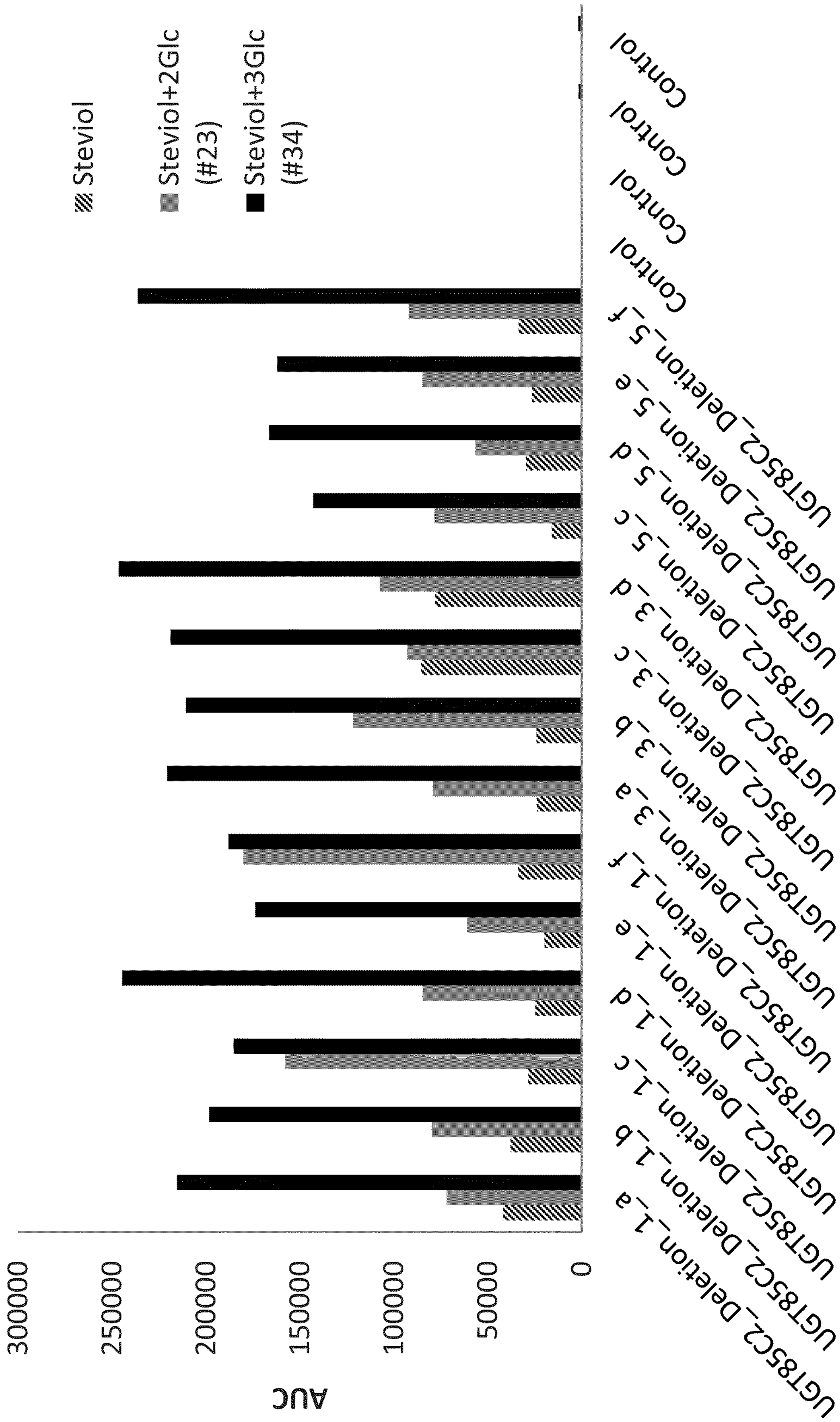

Steviol
Steviol+2Glc (#23)
Steviol+3Glc (#34)
AUC
300000
250000
200000
150000
100000
50000
0
UGT85C2_Deletion_1_a
UGT85C2_Deletion_1_b
UGT85C2_Deletion_1_c
UGT85C2_Deletion_1_d
UGT85C2_Deletion_1_e
UGT85C2_Deletion_1_f
UGT85C2_Deletion_3_a
UGT85C2_Deletion_3_b
UGT85C2_Deletion_3_c
UGT85C2_Deletion_3_d
UGT85C2_Deletion_5_c
UGT85C2_Deletion_5_d
UGT85C2_Deletion_5_e
UGT85C2_Deletion_5_f
Control
Control
Control
Control

Figure 5

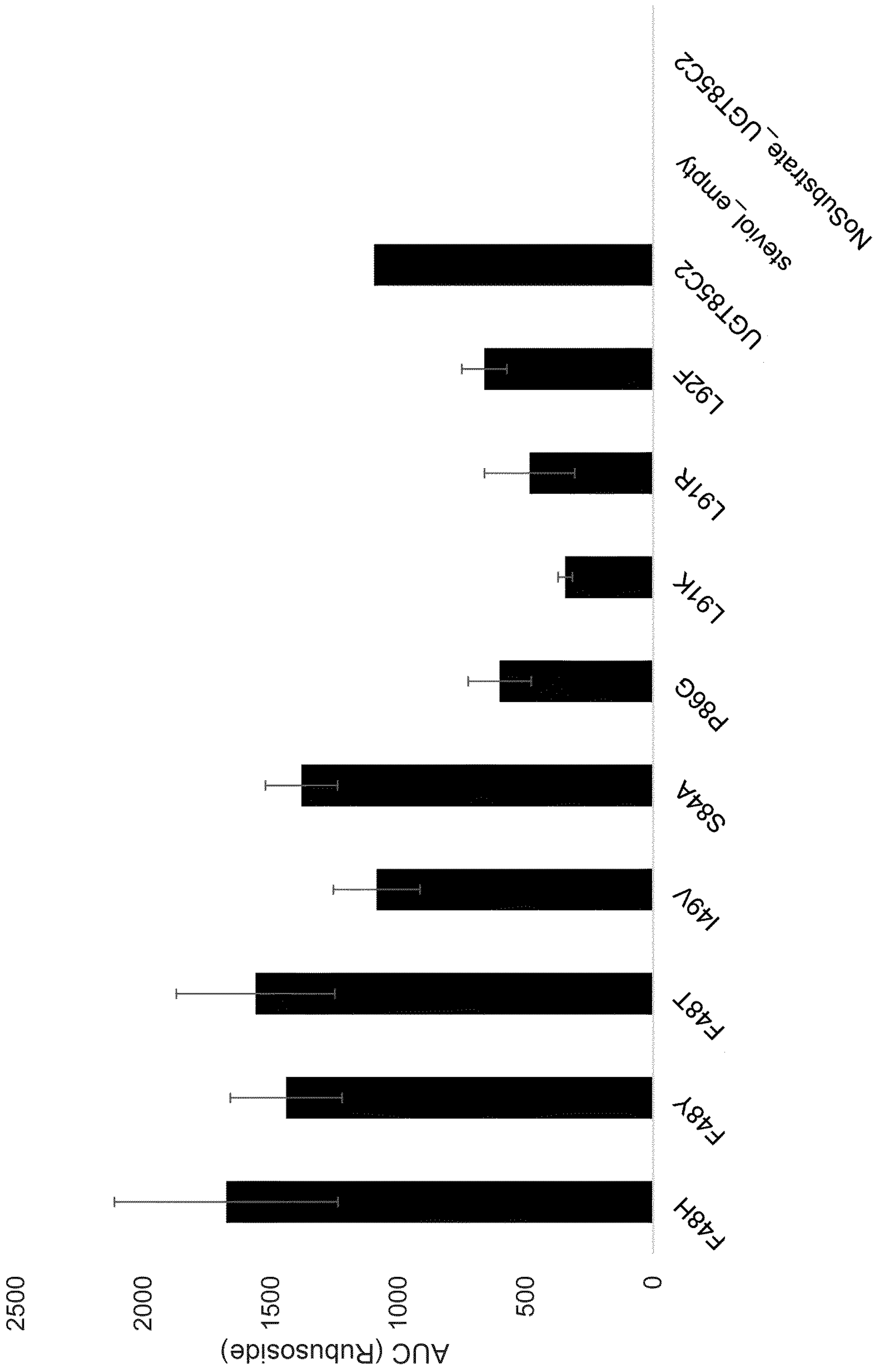

AUC (Rubusoside)
0
500
1000
1500
2000
2500
F48H
F48Y
F48T
I49V
S84A
P86G
L91K
L91R
L92F
UGT85C2
steviol_empty
NoSubstrate_UGT85C2

Figure 6A

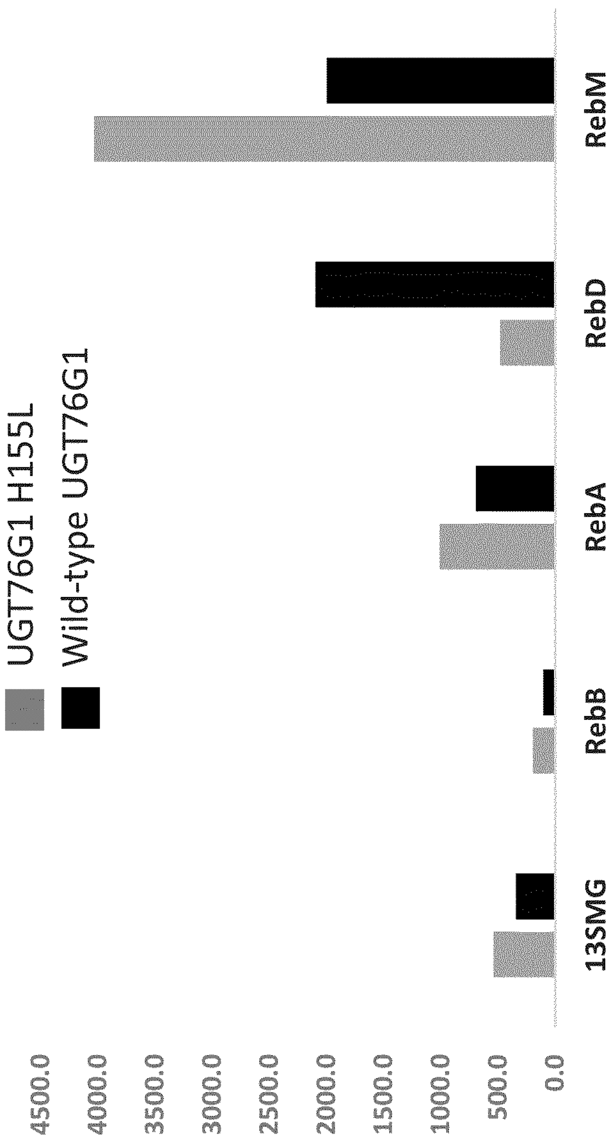

UGT76G1 H155L
Wild-type UGT76G1
mg/L
4500.0
4000.0
3500.0
3000.0
2500.0
2000.0
1500.0
1000.0
500.0
0.0
13SMG
RebB
RebA
RebD
RebM

Figure 6B

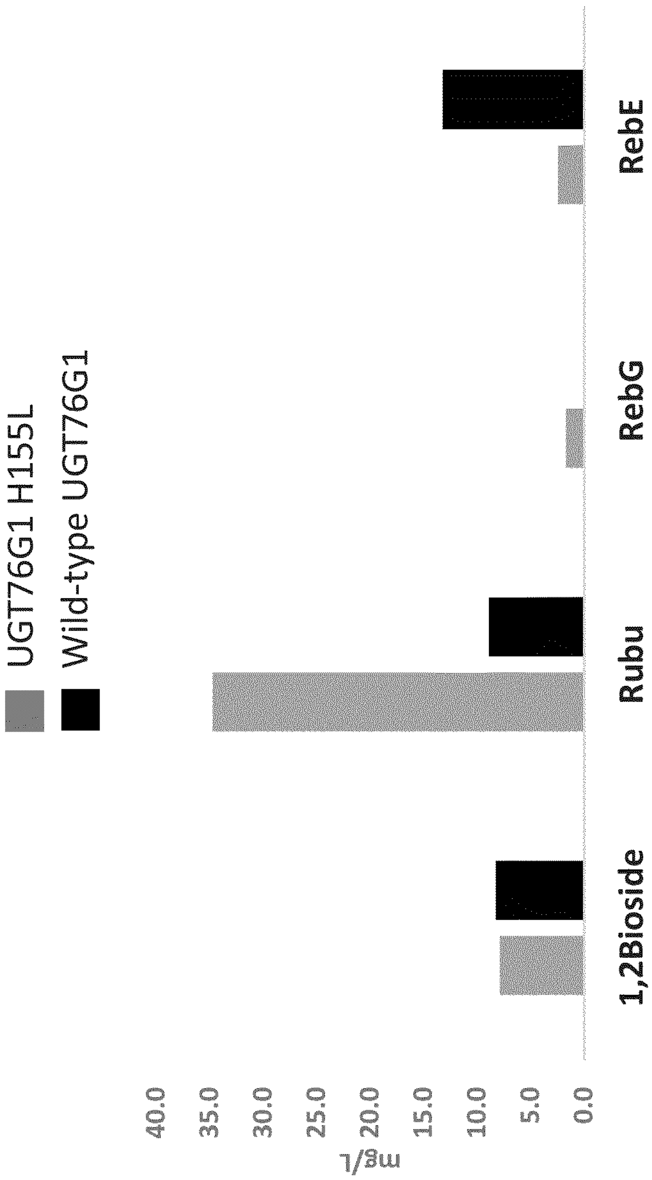

UGT76G1 H155L
Wild-type UGT76G1
mg/L
40.0
35.0
30.0
25.0
20.0
15.0
10.0
5.0
0.0
1,2Bioside
Rubu
RebG
RebE

Figure 6C

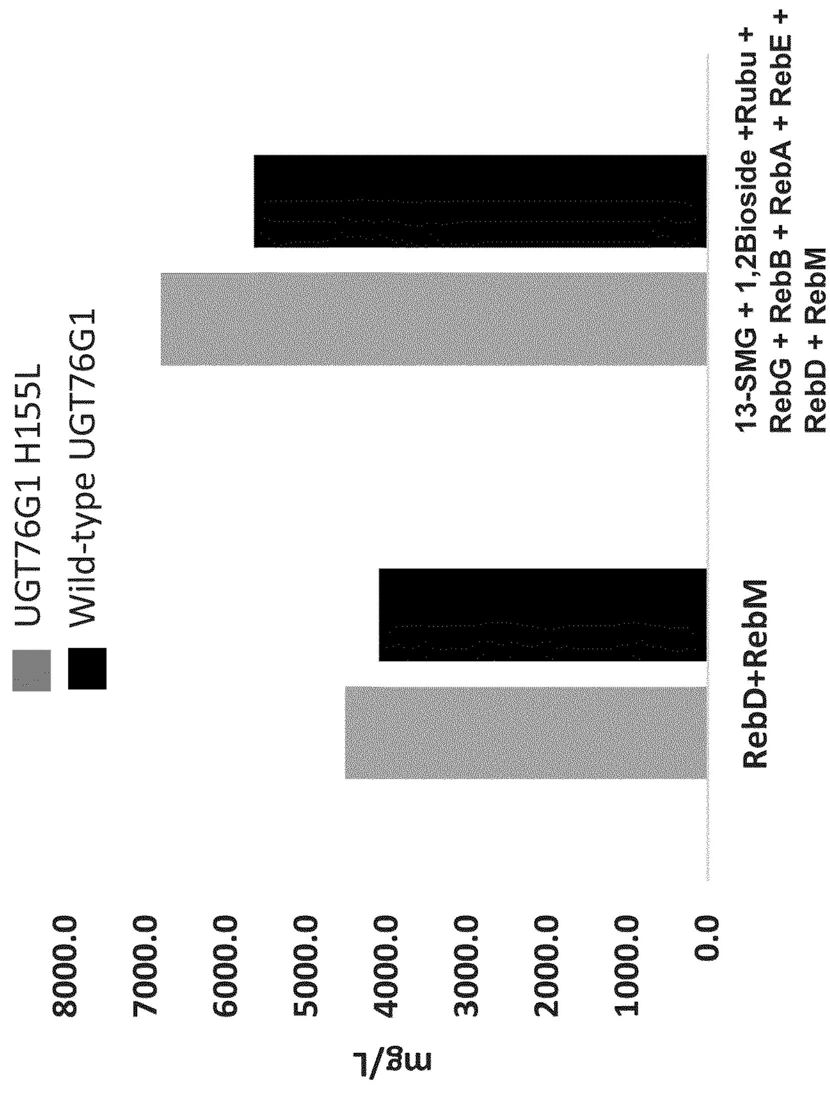

UGT76G1 H155L
Wild-type UGT76G1
mg/L
8000.0
7000.0
6000.0
5000.0
4000.0
3000.0
2000.0
1000.0
0.0
RebD+RebM
13-SMG + 1,2Bioside +Rubu + RebG + RebB + RebA + RebE + RebD + RebM

Figure 6D

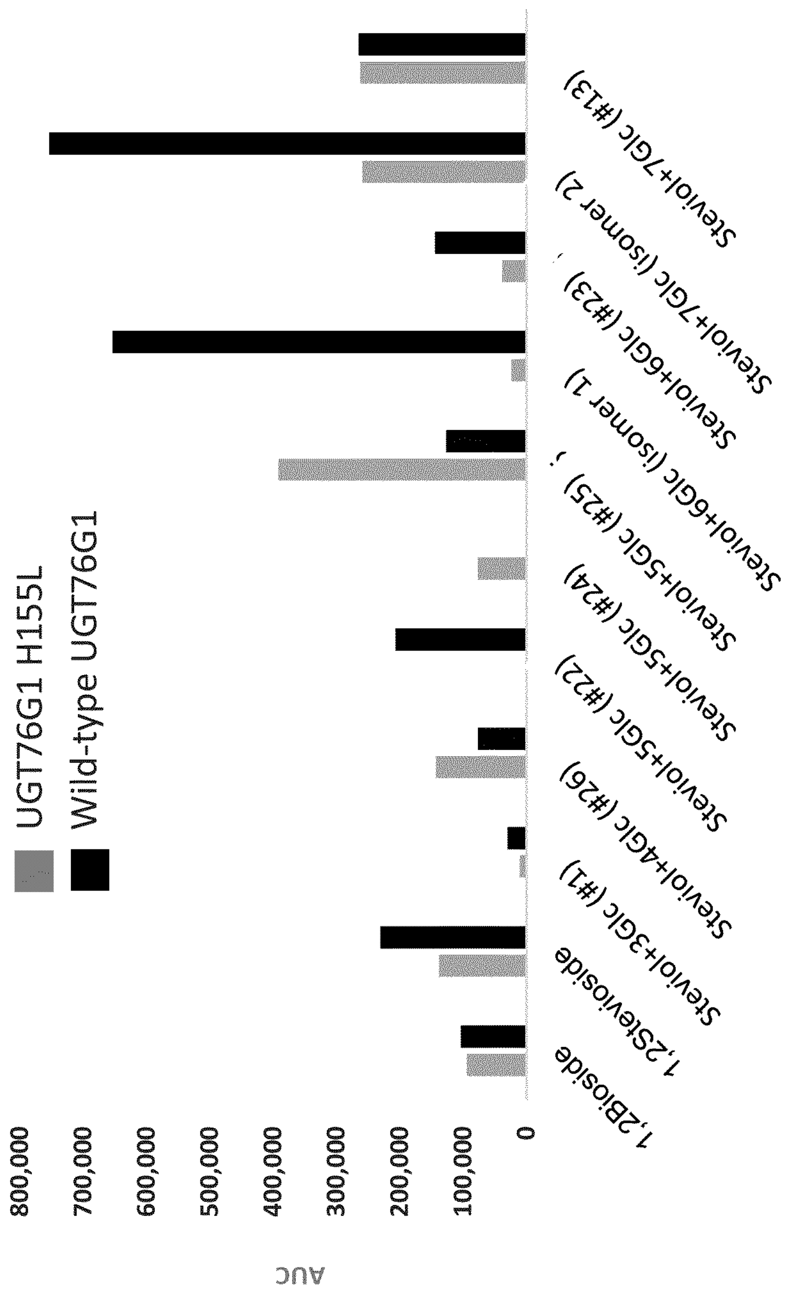
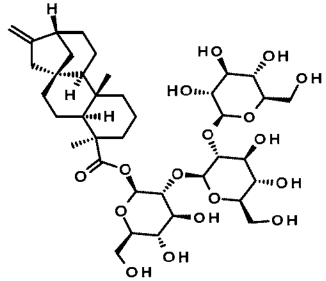

UGT76G1 H155L
Wild-type UGT76G1
AUC
800,000
700,000
600,000
500,000
400,000
300,000
200,000
100,000
0
1,2Bioside
1,2Stevioside
Steviol+3Glc (#1)
Steviol+4Glc (#26)
Steviol+5Glc (#22)
Steviol+5Glc (#24)
Steviol+5Glc (#25)
Steviol+6Glc (isomer 1)
Steviol+6Glc (#23)
Steviol+7Glc (isomer 2)
Steviol+7Glc (#13)

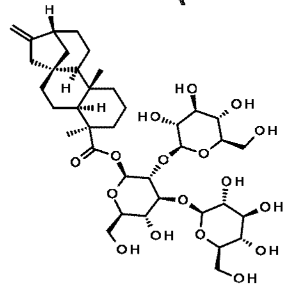
Figure 7A

Kaurenoic acid+3Glc (isomer 1)



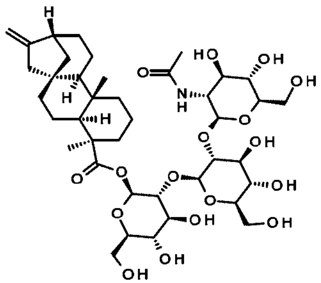
Formula Weight : 788.87(3)
Exact Mass : 788.38305050(3)
Formula : $C_{38}H_{60}O_{17}$

Kaurenoic acid+3Glc (isomer 2)



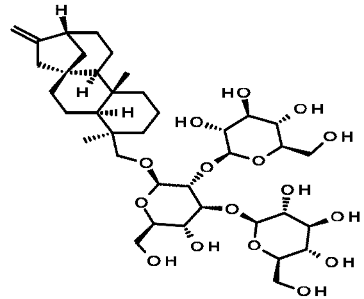
Formula Weight : 788.87(3)
Exact Mass : 788.38305050(3)
Formula : $C_{38}H_{60}O_{17}$

Kaurenoic acid+2Glc+1GlcNAc



Formula Weight : 829.92(3)
Exact Mass : 829.40959960(4)
Formula : $C_{40}H_{63}NO_{17}$

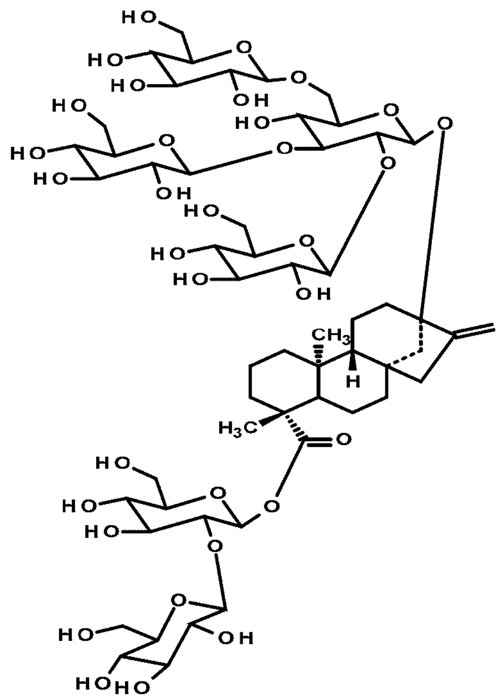
Kaurenol+3Glc (isomer 1)



Formula Weight : 774.89(3)
Exact Mass : 774.40378594(3)
Formula : $C_{38}H_{62}O_{16}$

Figure 7B

Steviol+6Glc (isomer 1)



Steviol+7Glc (isomer 2)

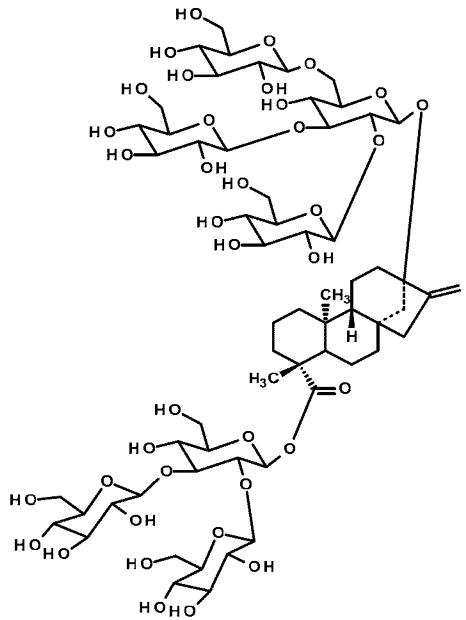
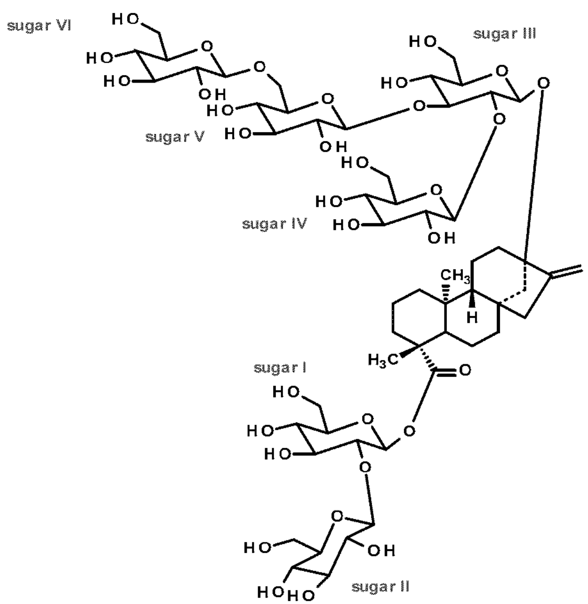


Figure 7C

Steviol+6Glc (isomer 4)



Steviol+7Glc (isomer 5)

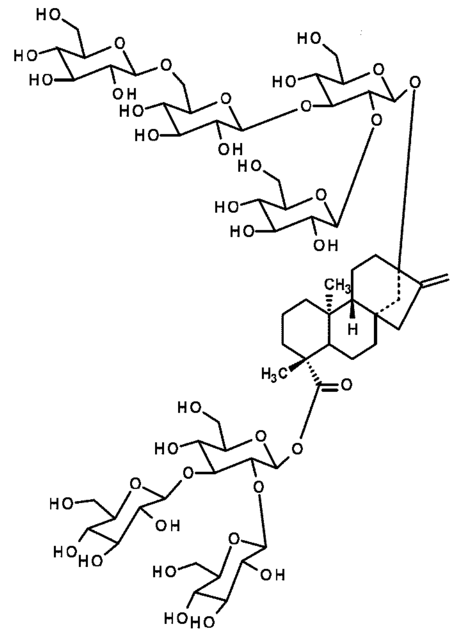
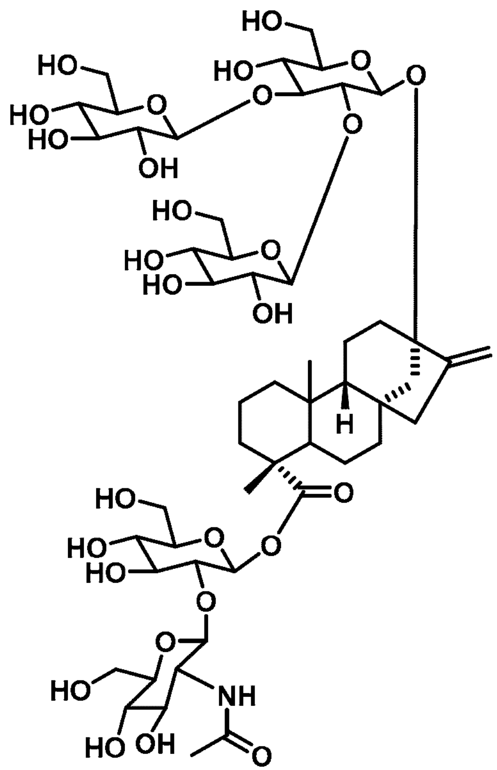


Figure 7D

Steviol+4Glc+1GlcNAc (#11)



Steviol+4Glc (#26)

Formula Weight : 967.01(4)
Exact Mass : 966.43078856(4)
Formula : $C_{44}H_{70}O_{23}$

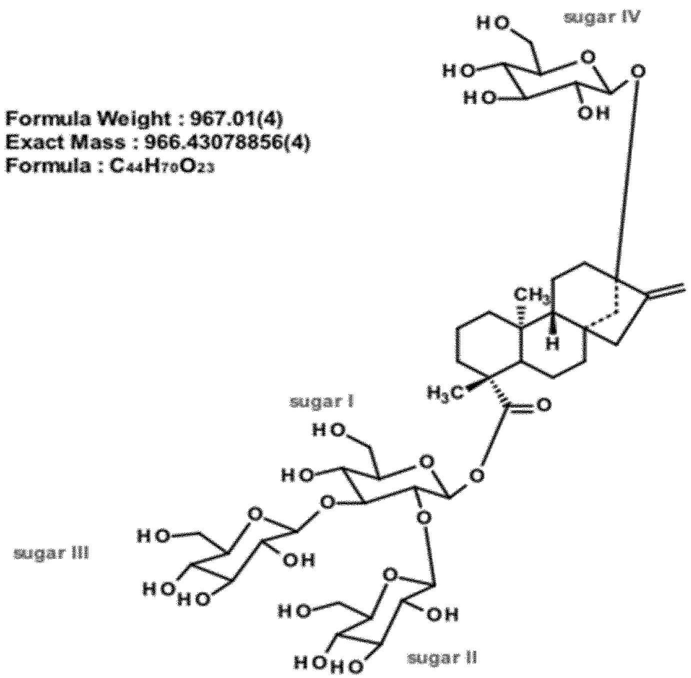
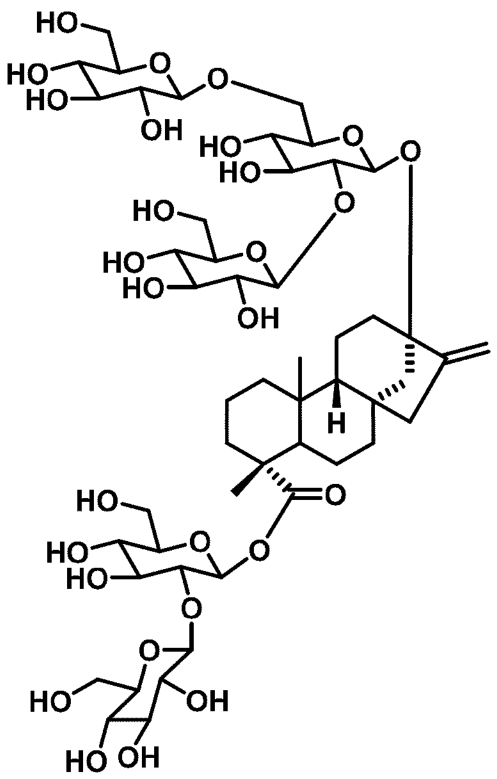


Figure 7E

Steviol+5Glc (#22)



Steviol+7Glc (#14)

Formula Weight : 1453.43(5)
Exact Mass : 1452.58925885(7)
Formula : $C_{62}H_{100}O_{38}$

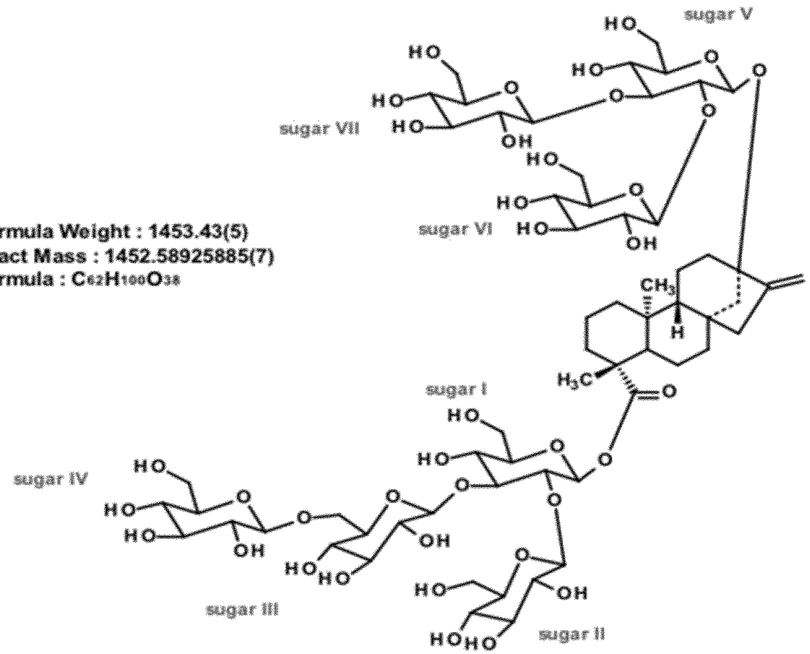


Figure 8A

Kaurenoic Acid+3Glc (isomer 1)

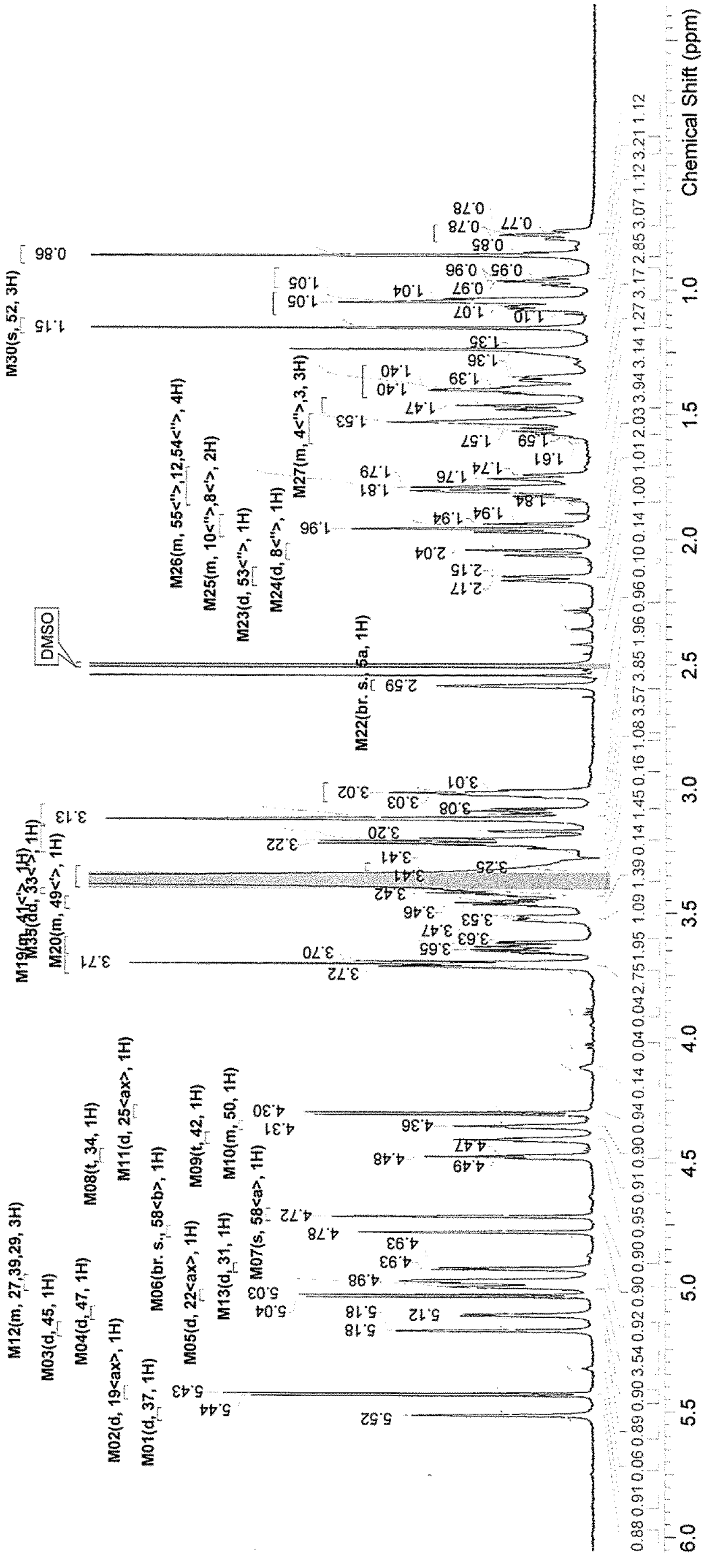


Figure 8B

Atom1	Shift1 (ppm	H's	Type	J (Hz)	Multiplet1	(ppm)
55<'>	0.78	1	m	-	M34	[0.74 .. 0.81]
57	0.86	3	m	-	M33	[0.83 .. 0.90]
53<'>	0.97	1	td	13.33, 4.16	M32	[0.92 .. 1.00]
13a, 2a, 10<'>	1.07	3	m	-	M31	[1.02 .. 1.10]
52	1.15	3	s	-	M30	[1.12 .. 1.18]
11<'>, 4<'>, 54<'>	1.38	3	m	-	M29	[1.30 .. 1.44]
11<">	1.47	1	m	-	M28	[1.44 .. 1.50]
4<">, 3	1.56	3	m	-	M27	[1.50 .. 1.62]
55<">, 12, 54<">	1.79	4	m	-	M26	[1.72 .. 1.87]
10<">, 8<'>	1.95	2	m	-	M25	[1.91 .. 1.99]
8<">	2.06	1	d	17.12	M24	[2.02 .. 2.08]
53<">	2.16	1	d	12.72	M23	[2.12 .. 2.19]
5a	2.59	1	br. s.	-	M22	[2.57 .. 2.61]
38<ax>, 26<ax>	3.02	2	m	-	M14	[2.98 .. 3.06]
30<ax>, 40<ax>, 28<ax>, 32<ax	3.10	4	m	-	M15	[3.07 .. 3.15]
46<ax>, 23<ax>, 48<ax>	3.22	3	m	-	M16	[3.16 .. 3.26]
36<ax>	3.32	1	m	-	M21	[3.30 .. 3.33]
33<'>	3.42	1	dd	11.00, 5.14	M35	[3.41 .. 3.43]
49<'>	3.46	1	m	-	M20	[3.44 .. 3.49]
41<'>	3.52	1	m	-	M19	[3.50 .. 3.55]
44<ax>, 49<">	3.64	2	m	-	M18	[3.60 .. 3.67]
41<">, 33<">, 20<ax>	3.71	3	m	-	M17	[3.68 .. 3.75]
25<ax>	4.31	1	d	7.82	M11	[4.28 .. 4.33]
50	4.35	1	m	-	M10	[4.34 .. 4.37]
42	4.41	1	t	5.38	M09	[4.39 .. 4.43]
34	4.48	1	t	5.62	M08	[4.45 .. 4.51]
58<a>	4.72	1	s	-	M07	[4.69 .. 4.74]
58<b>	4.78	1	br. s.	-	M06	[4.76 .. 4.81]
31	4.93	1	d	5.38	M13	[4.91 .. 4.95]
27, 39, 29	4.99	3	m	-	M12	[4.96 .. 5.02]
22<ax>	5.04	1	d	7.83	M05	[5.02 .. 5.06]
47	5.12	1	d	5.38	M04	[5.09 .. 5.14]
45	5.18	1	d	2.45	M03	[5.15 .. 5.21]
19<ax>	5.43	1	d	7.83	M02	[5.40 .. 5.46]
37	5.52	1	d	2.45	M01	[5.49 .. 5.54]

Kaurenoic Acid+3Glc (isomer 1)

^{1}H NMR (800 MHz, *DMSO* d_6) δ ppm 0.74 - 0.81 (m, 1 H) 0.83 - 0.90 (m, 3 H) 0.97 (td, *J*=13.33, 4.16 Hz, 1 H) 1.02 - 1.10 (m, 3 H) 1.15 (s, 3 H) 1.30 - 1.44 (m, 3 H) 1.44 - 1.50 (m, 1 H) 1.50 - 1.62 (m, 3 H) 1.72 - 1.87 (m, 4 H) 1.91 - 1.99 (m, 2 H) 2.06 (d, *J*=17.12 Hz, 1 H) 2.16 (d, *J*=12.72 Hz, 1 H) 2.59 (br. s., 1 H) 2.98 - 3.06 (m, 2 H) 3.07 - 3.15 (m, 4 H) 3.16 - 3.26 (m, 3 H) 3.30 - 3.33 (m, 1 H) 3.42 (dd, *J*=11.00, 5.14 Hz, 1 H) 3.44 - 3.49 (m, 1 H) 3.50 - 3.55 (m, 1 H) 3.60 - 3.67 (m, 2 H) 3.68 - 3.75 (m, 3 H) 4.31 (d, *J*=7.82 Hz, 1 H) 4.34 - 4.37 (m, 1 H) 4.41 (t, *J*=5.38 Hz, 1 H) 4.48 (t, *J*=5.62 Hz, 1 H) 4.72 (s, 1 H) 4.78 (br. s., 1 H) 4.93 (d, *J*=5.38 Hz, 1 H) 4.96 - 5.02 (m, 3 H) 5.04 (d, *J*=7.83 Hz, 1 H) 5.12 (d, *J*=5.38 Hz, 1 H) 5.18 (d, *J*=2.45 Hz, 1 H) 5.43 (d, *J*=7.83 Hz, 1 H) 5.52 (d, *J*=2.45 Hz, 1 H)

^{13}C NMR (201.21 MHz, *DMSO* d_6) δ ppm 175.4 (1C), 155.3 (1C), 104.6 (1C), 103.6 (1C), 99.8 (1C), 92.4 (1C), 83.4 (1C), 77.6 (1C), 77.5 (1C), 77.2 (1C), 76.9 (1C), 76.2 (1C), 76.1 (1C), 75.8 (1C), 75.2 (1C), 70.8 (1C), 70.0 (1C), 69.8 (1C), 61.5 (1C), 61.4 (1C), 60.6 (1C), 56.7 (1C), 54.6 (1C), 48.7 (1C), 43.9 (1C), 43.4 (1C), 43.3 (1C), 41.2 (1C), 40.4 (1C), 40.0 (1C), 39.4 (1C), 37.8 (1C), 32.9 (1C), 28.5 (1C), 21.6 (1C), 19.1 (1C), 18.5 (1C), 16.1 (1C)

Figure 8C

Kaurenoic Acid+3Glc (isomer 1)

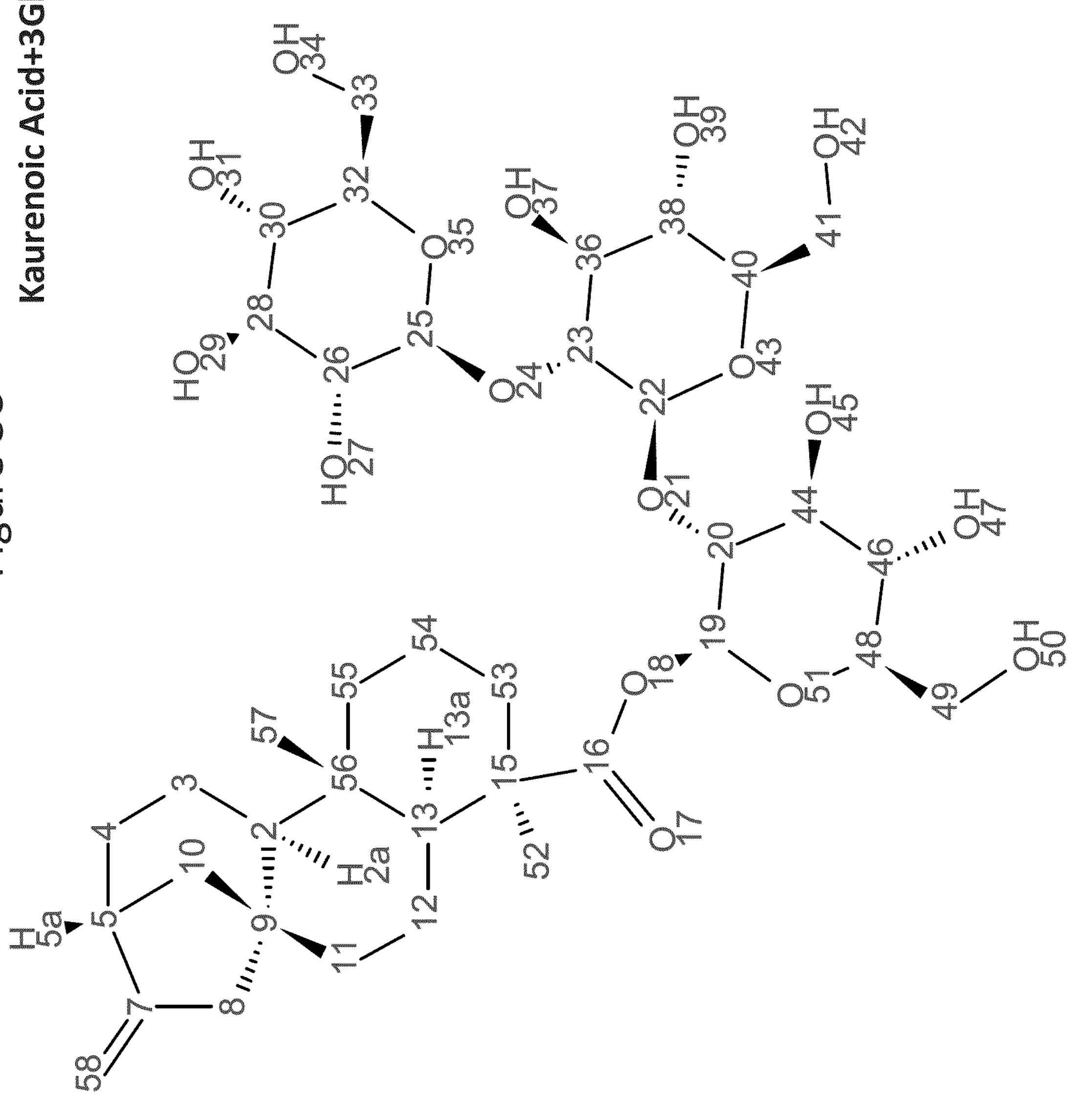


Figure 8D

Kaurenoic Acid+3Glc (isomer 2)

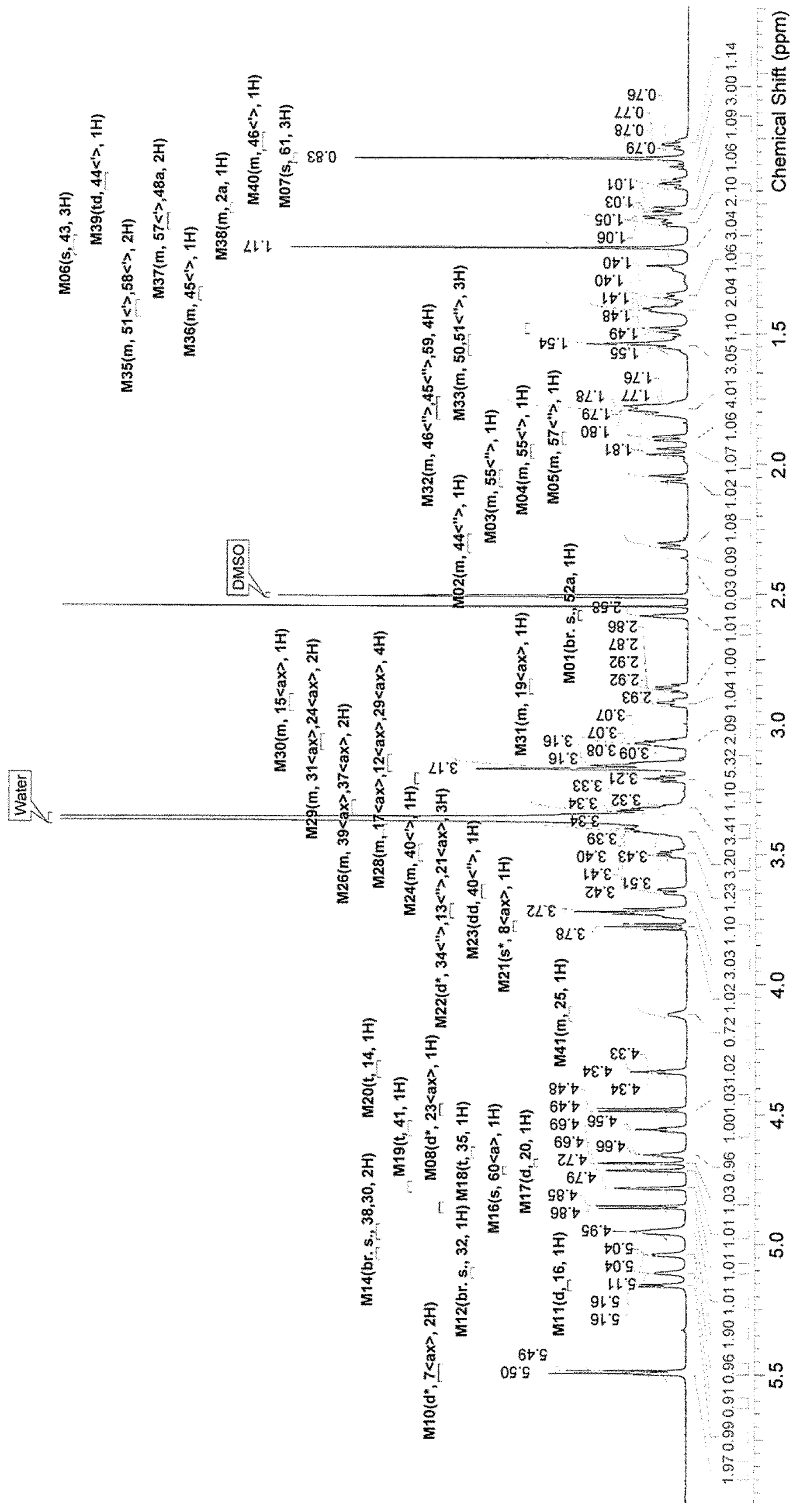


Figure 8E

Atom1	Shift1 (ppm	H's	Type	J (Hz)	Multiplet1	(ppm)
46<'>	0.77	1	m	-	M40	[0.73 .. 0.80]
61	0.83	3	s	-	M07	[0.81 .. 0.85]
44<'>	0.92	1	td	13.33, 4.16	M39	[0.89 .. 0.96]
2a	1.03	1	m	-	M38	[1.00 .. 1.04]
57<'>, 48a	1.07	2	m	-	M37	[1.04 .. 1.10]
43	1.17	3	s	-	M06	[1.13 .. 1.21]
45<'>	1.36	1	m	-	M36	[1.33 .. 1.38]
51<'>, 58<'>	1.40	2	m	-	M35	
58<">	1.49	1	d	12.72	M34	
50, 51<">	1.54	3	m	-	M33	
46<">, 45<">, 59	1.78	4	m	-	M32	
57<">	1.90	1	m	-	M05	
55<'>	1.95	1	m	-	M04	
55<">	2.06	1	m	-	M03	
44<">	2.31	1	m	-	M02	
52a	2.58	1	br. s.	-	M01	
19<ax>	2.86	1	m	-	M31	
15<ax>	2.92	1	m	-	M30	
31<ax>, 24<ax>	3.07	2	m	-	M29	
17<ax>, 12<ax>, 29<ax>	3.16	4	m	-	M28	
33<ax>	3.21	1	m	-	M27	
39<ax>, 37<ax>	3.32	2	m	-	M26	
34<'>, 13<'>	3.41	2	m	-	M25	
40<'>	3.50	1	m	-	M24	
40<">	3.64	1	dd	10.51, 4.16	M23	
34<">, 13<">, 21<ax>	3.73	3	d	7.83	M22	
8<ax>	3.78	1	s	-	M21	
25	4.12	1	m	-	M41	
14	4.34	1	t	5.14	M20	
23<ax>	4.48	1	d	7.83	M08	
41	4.56	1	t	5.62	M19	
35	4.66	1	t	4.89	M18	
20	4.69	1	d	2.45	M17	
60<a>	4.72	1	s	-	M16	
60<b>	4.79	1	br. s.	-	M15	
10<ax>	4.86	1	d	7.83	M09	[4.84 .. 4.88]
38, 30	4.95	2	br. s.	-	M14	[4.93 .. 4.99]
18	5.04	1	d	4.89	M13	[5.02 .. 5.06]
32	5.11	1	br. s.	-	M12	[5.09 .. 5.13]
16	5.16	1	d	6.36	M11	[5.14 .. 5.18]
7<ax>	5.49	2	d	8.31	M10	[5.46 .. 5.53]

Kaurenoic Acid+3Glc (isomer 2)

^{1}H NMR (800 MHz, *DMSO d_6*) δ ppm 0.73 - 0.80 (m, 1 H) 0.83 (s, 3 H) 0.92 (td, *J*=13.33, 4.16 Hz, 1 H) 1.00 - 1.04 (m, 1 H) 1.04 - 1.10 (m, 2 H) 1.17 (s, 3 H) 1.33 - 1.38 (m, 1 H) 1.38 - 1.44 (m, 2 H) 1.49 (d, *J*=12.72 Hz, 1 H) 1.51 - 1.59 (m, 3 H) 1.75 - 1.83 (m, 4 H) 1.88 - 1.93 (m, 1 H) 1.93 - 1.98 (m, 1 H) 2.03 - 2.09 (m, 1 H) 2.27 - 2.34 (m, 1 H) 2.58 (br. s., 1 H) 2.83 - 2.88 (m, 1 H) 2.89 - 2.95 (m, 1 H) 3.04 - 3.10 (m, 2 H) 3.12 - 3.19 (m, 4 H) 3.19 - 3.23 (m, 1 H) 3.30 - 3.35 (m, 2 H) 3.39 - 3.44 (m, 2 H) 3.4 - 3.53 (m, 1 H) 3.64 (dd, *J*=10.51, 4.16 Hz, 1 H) 3.73 (d, *J*=7.83 Hz, 3 H) 3.78 (s, 1 H) 4.09 - 4.14 (m, 1 H) 4.34 (t, *J*=5.14 Hz, 1 H) 4.48 (d, *J*=7.83 Hz, 1 H) 4.56 (t, *J*=5.62 Hz, 1 H) 4.66 (t, *J*=4.89 Hz, 1 H) 4.69 (d, *J*=2.45 Hz, 1 H) 4.72 (s, 1 H) 4.79 (br. s., 1 H) 4.86 (d, *J*=7.83 Hz, 1 H) 4.95 (br. s., 2 H) 5.04 (d, *J*=4.89 Hz, 1 H) 5.11 (br. s., 1 H) 5.16 (d, *J*=6.36 Hz, 1 H) 5.49 (d, *J*=8.31 Hz, 2 H)

^{13}C NMR (201.21 MHz, *DMSO d_6*) δ ppm 175.1 (1C), 155.4 (1C), 103.7 (1C), 103.2 (1C), 101.5 (1C), 92.1 (1C), 86.8 (1C), 77.9 (1C), 77.3 (1C), 77.1 (1C), 77.0 (1C), 76.8 (1C), 76.7 (1C), 74.4 (1C), 73.9 (1C), 71.2 (1C), 70.2 (1C), 68.2 (1C), 61.8 (1C), 61.1 (1C), 60.6 (1C), 56.7 (1C), 54.6 (1C), 48.8 (1C), 44.0 (1C), 43.6 (1C), 43.4 (1C), 41.1 (1C), 40.0 (1C), 39.5 (1C), 39.4 (1C), 37.1 (1C), 32.8 (1C), 28.4 (1C), 21.6 (1C), 19.3 (1C), 18.2 (1C), 16.2 (1C)

Figure 8F

Kaurenoic Acid+3Glc (isomer 2)

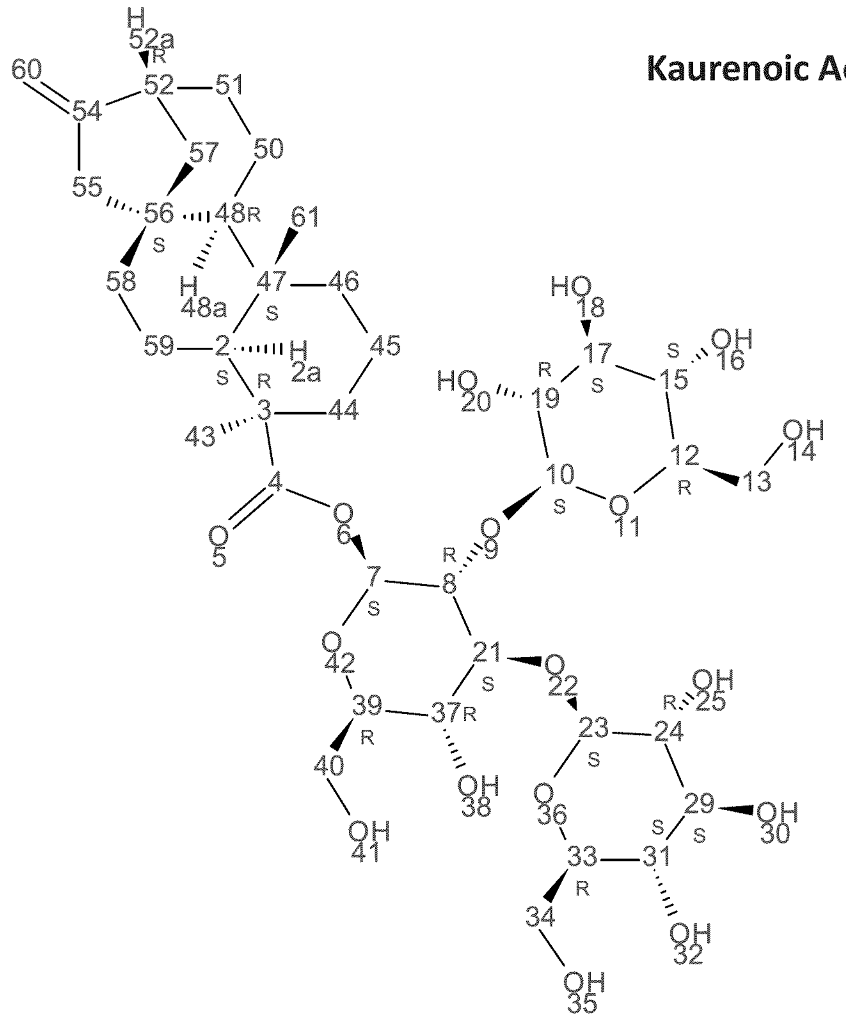


Figure 8G

Kaurenoic Acid+2Glc+1GlcNAc

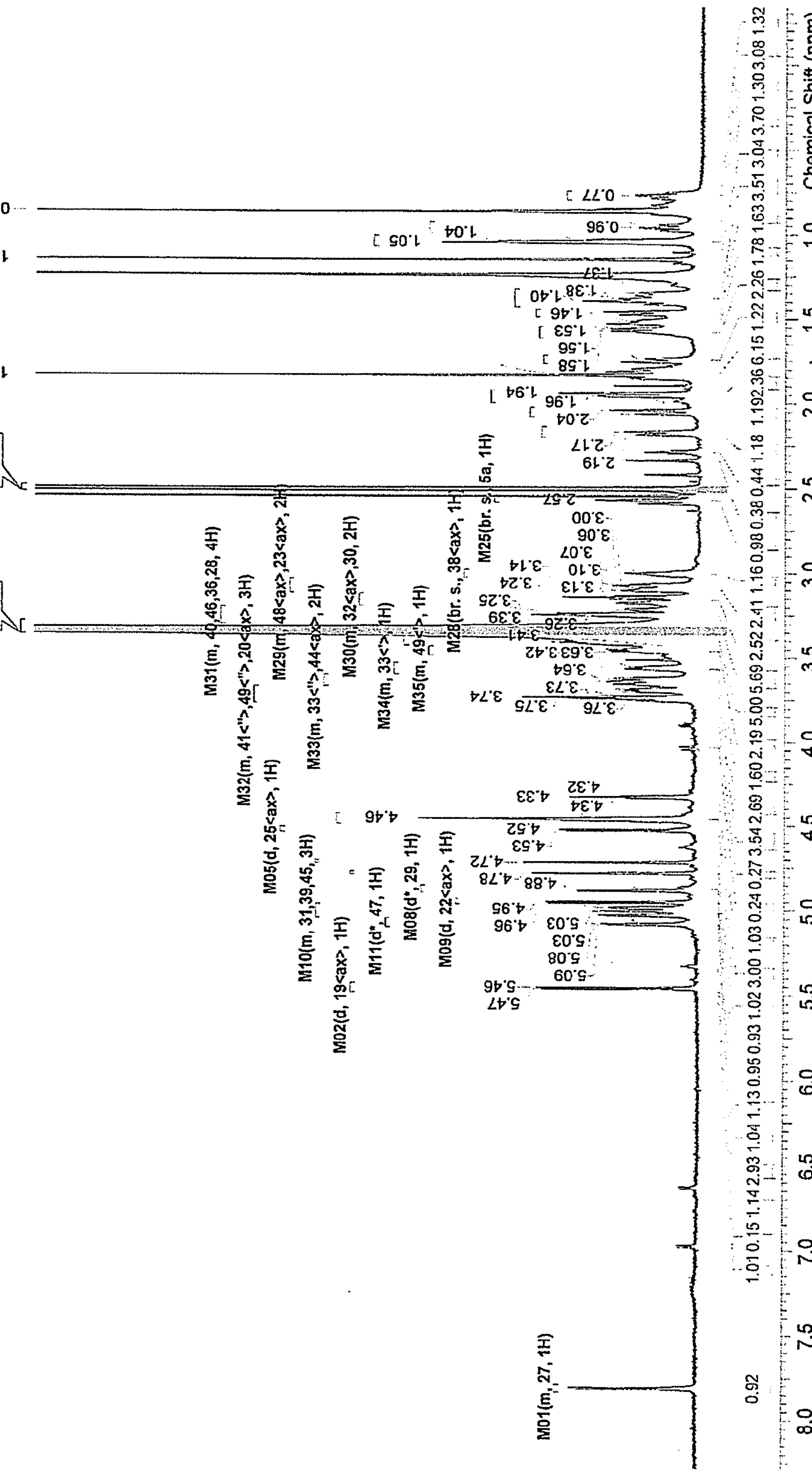


Figure 8H

Kaurenoic Acid+2Glc+1GlcNAc

Atom1	Shift1 (ppm	H's	Type	J (Hz)	Multiplet1	(ppm)
55<'>	0.77	1	br. s.	-	M12	[0.75 .. 0.80]
57	0.87	3	s	-	M14	[0.86 .. 0.88]
53<'>	0.96	1	m	-	M13	[0.93 .. 1.00]
2a, 13a, 10<'>	1.05	3	m	-	M15	[1.01 .. 1.08]
52	1.15	3	s	-	M16	[1.13 .. 1.17]
54<'>, 4<'>, 11<'>	1.38	3	m	-	M17	[1.33 .. 1.43]
11<">	1.47	1	d	13.20	M18	[1.45 .. 1.49]
3<'>	1.53	1	d	10.27	M19	[1.50 .. 1.55]
3<">, 4<">	1.57	2	d	11.74	M20	[1.55 .. 1.62]
12<'>	1.76	1	br. s.	-	M21	[1.72 .. 1.77]
12<">, 55<">, 54<">, 3	1.82	6	m	-	M37	[1.77 .. 1.87]
10<">, 8<'>	1.95	2	d	14.18	M22	[1.93 .. 2.00]
8<">	2.05	1	d	17.12	M23	[2.03 .. 2.08]
53<">	2.18	1	d	12.23	M24	[2.14 .. 2.20]
5a	2.57	1	br. s.	-	M25	[2.56 .. 2.59]
38<ax>	3.00	1	br. s.	-	M28	[2.98 .. 3.03]
48<ax>, 23<ax>	3.08	2	m	-	M29	[3.04 .. 3.12]
32<ax>, 30	3.15	2	m	-	M30	[3.13 .. 3.19]
40, 46, 36, 28	3.24	4	m	-	M31	[3.20 .. 3.31]
41<'>, 26	3.41	2	m	-	M36	[3.38 .. 3.43]
49<'>	3.46	1	m	-	M35	[3.43 .. 3.49]
33<'>	3.56	1	m	-	M34	[3.53 .. 3.60]
33<">, 44<ax>	3.65	2	m	-	M33	[3.60 .. 3.67]
41<">, 49<">, 20<ax>	3.72	3	m	-	M32	[3.67 .. 3.77]
50	4.33	1	t	5.38	M03	[4.31 .. 4.35]
37, 34, 42	4.47	3	m	-	M04	[4.43 .. 4.49]
25<ax>	4.53	1	d	8.31	M05	[4.51 .. 4.54]
58<a>	4.72	1	br. s.	-	M06	[4.71 .. 4.73]
58<b>	4.78	1	br. s.	-	M07	[4.78 .. 4.79]
29	4.89	1	d	5.38	M08	[4.86 .. 4.90]
22<ax>	4.95	1	d	7.83	M09	[4.93 .. 4.97]
31, 39, 45	5.01	3	m	-	M10	[4.97 .. 5.05]
47	5.08	1	d	5.38	M11	[5.05 .. 5.10]
19<ax>	5.46	1	d	7.82	M02	[5.43 .. 5.49]
27	7.82	1	m	-	M01	[7.79 .. 7.84]

^{1}H NMR (800 MHz, *DMSO* d_6) δ ppm 0.77 (br. s., 1 H) 0.87 (s, 3 H) 0.93 - 1.00 (m, 1 H) 1.01 - 1.08 (m, 3 H) 1.15 (s, 3 H) 1.33 - 1.43 (m, 3 H) 1.47 (d, *J*=13.20 Hz, 1 H) 1.53 (d, *J*=10.27 Hz, 1 H) 1.57 (d, *J*=11.74 Hz, 2 H) 1.76 (br. s., 1 H) 1.77 - 1.87 (m, 6 H) 1.95 (d, *J*=14.18 Hz, 2 H) 2.05 (d, *J*=17.12 Hz, 1 H) 2.18 (d, *J*=12.23 Hz, 1 H) 2.57 (br. s., 1 H) 3.00 (br. s., 1 H) 3.04 - 3.12 (m, 2 H) 3.13 - 3.19 (m, 2 H) 3.20 - 3.31 (m, 4 H) 3.38 - 3.43 (m, 2 H) 3.43 - 3.49 (m, 1 H) 3.53 - 3.60 (m, 1 H) 3.60 - 3.67 (m, 2 H) 3.67 - 3.77 (m, 3 H) 4.33 (t, *J*=5.38 Hz, 1 H) 4.43 - 4.49 (m, 3 H) 4.53 (d, *J*=8.31 Hz, 1 H) 4.72 (br. s., 1 H) 4.78 (br. s., 1 H) 4.89 (d, *J*=5.38 Hz, 1 H) 4.95 (d, *J*=7.83 Hz, 1 H) 4.97 - 5.05 (m, 3 H) 5.08 (d, *J*=5.38 Hz, 1 H) 5.46 (d, *J*=7.82 Hz, 1 H) 7.79 - 7.84 (m, 1 H)

^{13}C NMR (201.21 MHz, *DMSO* d_6) δ ppm 175.6 (1C), 171.6 (1C), 155.5 (1C), 103.6 (1C), 101.9 (1C), 99.9 (1C), 92.5 (1C), 82.1 (1C), 77.6 (1C), 77.3 (1C), 77.0 (1C), 77.0 (1C), 76.1 (1C), 75.9 (1C), 74.0 (1C), 70.5 (1C), 70.3 (1C), 69.9 (1C), 61.8 (1C), 61.0 (1C), 60.9 (1C), 57.2 (1C), 56.7 (1C), 54.6 (1C), 48.8 (1C), 44.1 (1C), 43.8 (1C), 43.4 (1C), 41.3 (1C), 40.4 (1C), 39.9 (1C), 39.5 (1C), 37.6 (1C), 32.9 (1C), 28.5 (1C), 23.4 (1C), 21.6 (1C), 19.2 (1C), 18.4 (1C), 16.2 (1C)

Figure 8I

Kaurenoic Acid+2Glc+1GlcNAc

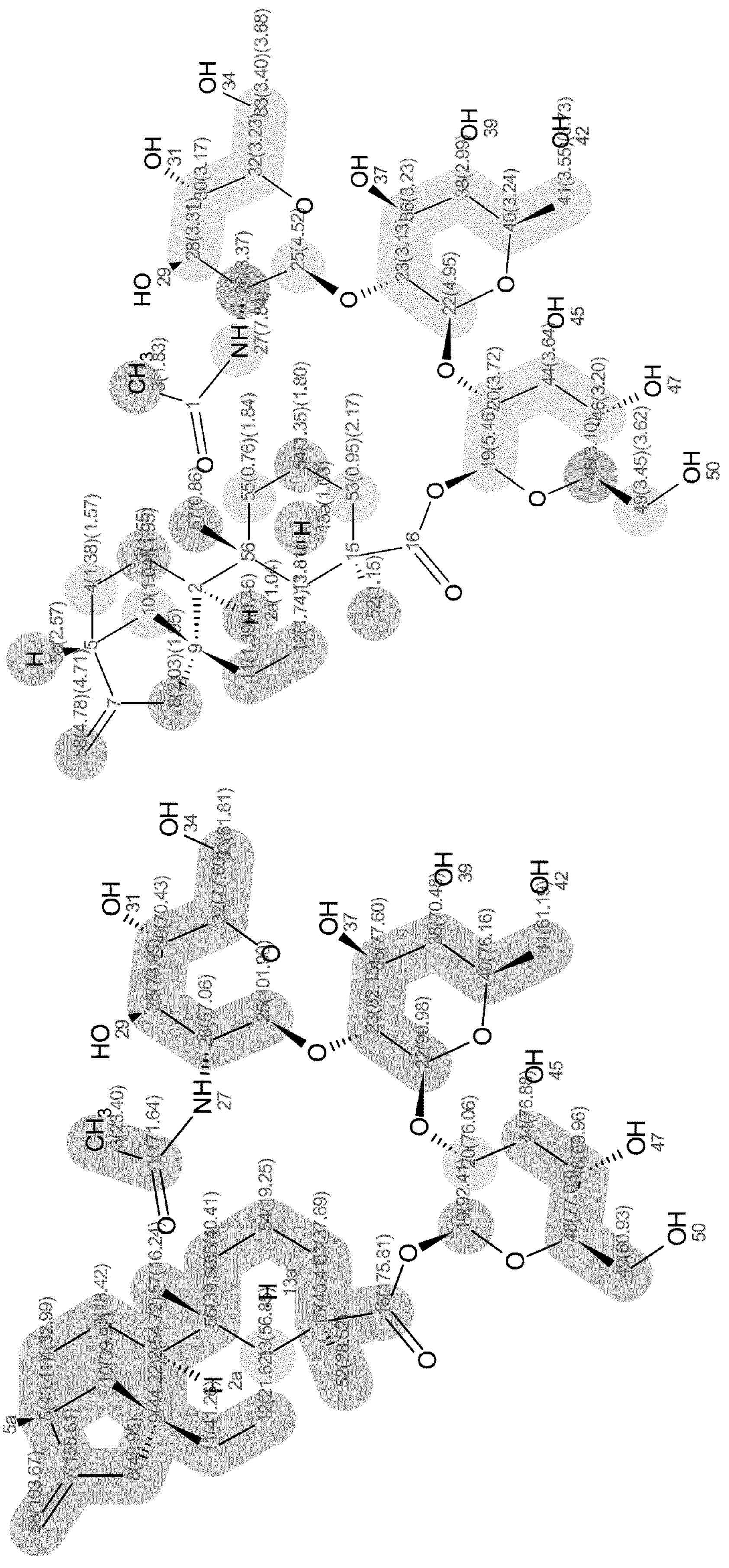


Figure 8J

Kaurenol+3Glc (isomer 1)

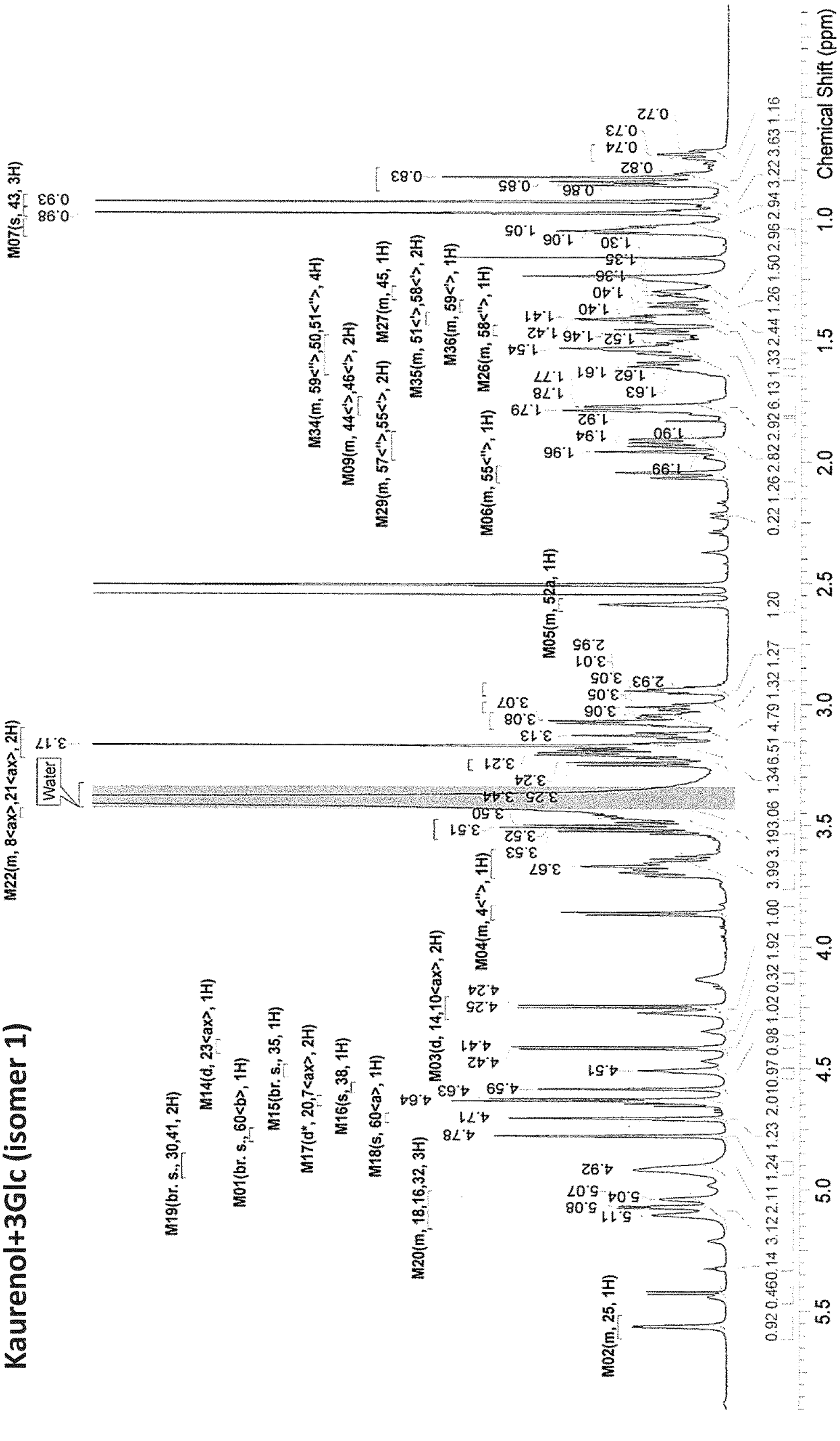


Figure 8K

Kaurenol+3Glc (isomer 1)

Atom1	Shift1 (ppm	H's	Type	J (Hz)	Multiplet1	(ppm)
46<">	0.74	1	m	-	M32	[0.70 .. 0.76]
44<">, 2a	0.84	2	m	-	M25	[0.79 .. 0.89]
61	0.93	3	s	-	M08	[0.91 .. 0.96]
43	0.98	3	s	-	M07	[0.96 .. 1.00]
48a, 57<'>	1.04	2	m	-	M28	[1.01 .. 1.08]
45	1.32	1	m	-	M27	[1.28 .. 1.34]
59<'>	1.36	1	m	-	M36	[1.34 .. 1.39]
51<'>, 58<'>	1.41	2	m	-	M35	[1.39 .. 1.44]
58<">	1.46	1	m	-	M26	[1.44 .. 1.48]
59<">, 50, 51<">	1.56	4	m	-	M34	[1.48 .. 1.65]
44<'>, 46<'>	1.78	2	m	-	M09	[1.74 .. 1.82]
57<">, 55<'>	1.94	2	m	-	M29	[1.88 .. 2.00]
55<">	2.06	1	m	-	M06	[2.02 .. 2.09]
52a	2.59	1	m	-	M05	[2.57 .. 2.62]
19<ax>	2.94	1	m	-	M24	[2.91 .. 2.97]
37<ax>	3.02	1	m	-	M23	[2.99 .. 3.04]
31<ax>, 24<ax>	3.07	2	m	-	M30	[3.04 .. 3.11]
15<ax>	3.13	1	t	9.05	M11	[3.11 .. 3.15]
17<ax>, 29<ax>, 12<ax>, 33<ax>, 39<ax>	3.19	5	m	-	M31	[3.15 .. 3.23]
4<'>	3.24	1	m	-	M33	[3.23 .. 3.28]
8<ax>, 21<ax>	3.46	2	m	-	M22	[3.44 .. 3.48]
13<'>, 34<'>, 40<'>	3.51	3	dd	11.74, 7.82	M21	[3.48 .. 3.56]
13<">, 34<">, 40<">	3.67	3	br. s.	-	M12	[3.60 .. 3.72]
4<">	3.86	1	m	-	M04	[3.83 .. 3.89]
14, 10<ax>	4.25	2	d	7.34	M03	[4.21 .. 4.30]
23<ax>	4.42	1	d	7.83	M14	[4.39 .. 4.45]
35	4.51	1	br. s.	-	M15	[4.49 .. 4.54]
38	4.59	1	s	-	M16	[4.56 .. 4.61]
20, 7<ax>	4.63	2	d	8.31	M17	[4.62 .. 4.66]
60<a>	4.71	1	s	-	M18	[4.69 .. 4.73]
60<b>	4.78	1	br. s.	-	M01	[4.75 .. 4.81]
30, 41	4.92	2	br. s.	-	M19	[4.86 .. 4.96]
18, 16, 32	5.07	3	m	-	M20	[5.01 .. 5.17]
25	5.57	1	m	-	M02	[5.52 .. 5.62]

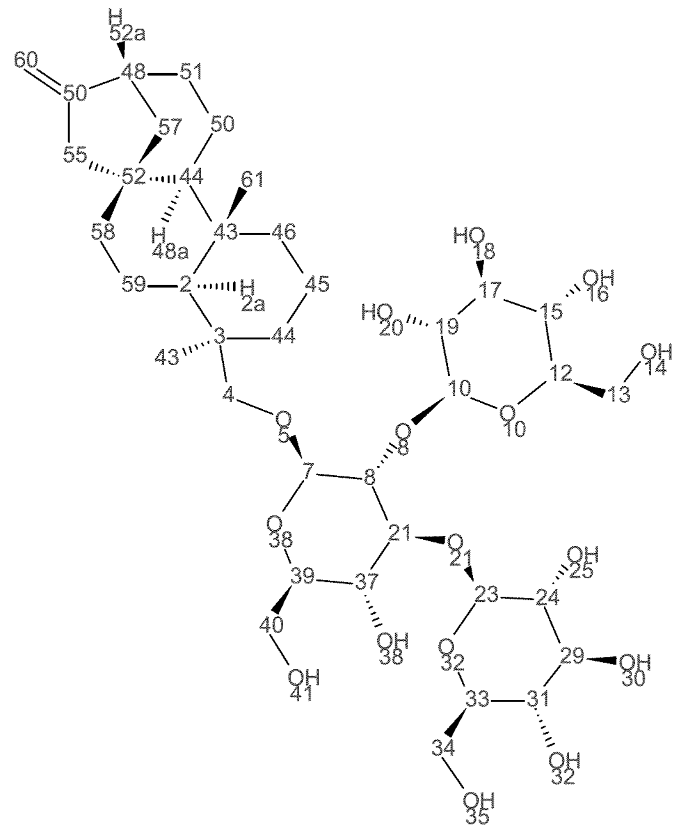


Figure 8L

Kaurenol+3Glc (isomer 1)

^{1}H NMR (800 MHz, *DMSO d_6*) δ ppm 0.70 - 0.76 (m, 1 H) 0.79 - 0.89 (m, 2 H) 0.93 (s, 3 H) 0.98 (s, 3 H) 1.01 - 1.08 (m, 2 H) 1.28 - 1.34 (m, 1 H) 1.34 - 1.39 (m, 1 H) 1.39 - 1.44 (m, 2 H) 1.44 - 1.48 (m, 1 H) 1.48 - 1.65 (m, 4 H) 1.74 - 1.82 (m, 2 H) 1.88 - 2.00 (m, 2 H) 2.02 - 2.09 (m, 1 H) 2.57 - 2.62 (m, 1 H) 2.91 - 2.97 (m, 1 H) 2.99 - 3.04 (m, 1 H) 3.04 - 3.11 (m, 2 H) 3.13 (t, *J*=9.05 Hz, 1 H) 3.15 - 3.23 (m, 5 H) 3.23 - 3.28 (m, 1 H) 3.44 - 3.48 (m, 2 H) 3.51 (dd, *J*=11.74, 7.82 Hz, 3 H) 3.67 (br. s., 3 H) 3.83 - 3.89 (m, 1 H) 4.25 (d, *J*=7.34 Hz, 2 H) 4.42 (d, *J*=7.83 Hz, 1 H) 4.51 (br. s., 1 H) 4.59 (s, 1 H) 4.63 (d, *J*=8.31 Hz, 2 H) 4.71 (s, 1 H) 4.78 (br. s., 1 H) 4.92 (br. s., 2 H) 5.01 - 5.17 (m, 3 H) 5.52 - 5.62 (m, 1 H)

^{13}C NMR (201.21 MHz, *DMSO d_6*) δ ppm 155.8 (1C), 103.6 (1C), 103.4 (1C), 102.3 (1C), 102.1 (1C), 86.7 (1C), 78.6 (1C), 77.1 (1C), 77.0 (1C), 76.5 (1C), 76.4 (1C), 76.2 (1C), 74.7 (1C), 73.8 (1C), 72.2 (1C), 70.5 (1C), 70.2 (1C), 68.8 (1C), 61.5 (1C), 61.3 (1C), 61.1 (1C), 56.7 (1C), 55.9 (1C), 48.9 (1C), 44.1 (1C), 43.6 (1C), 41.4 (1C), 40.4 (1C), 39.4 (1C), 39.1 (1C), 37.7 (1C), 36.4 (1C), 33.1 (1C), 28.0 (1C), 20.4 (1C), 18.4 (1C), 18.2 (1C), 18.1 (1C)

Figure 8M

Steviol+6Glc (isomer 1)

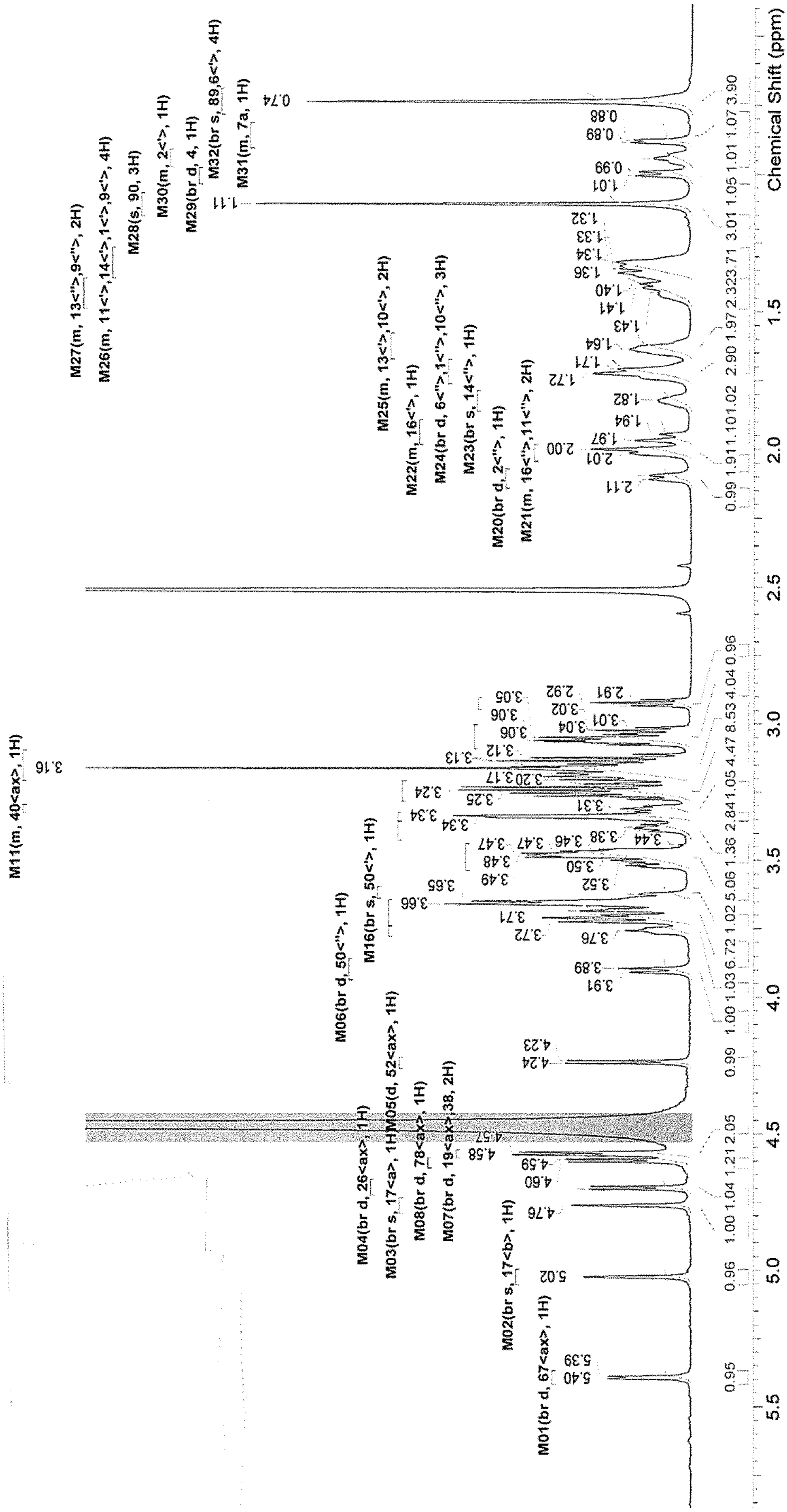
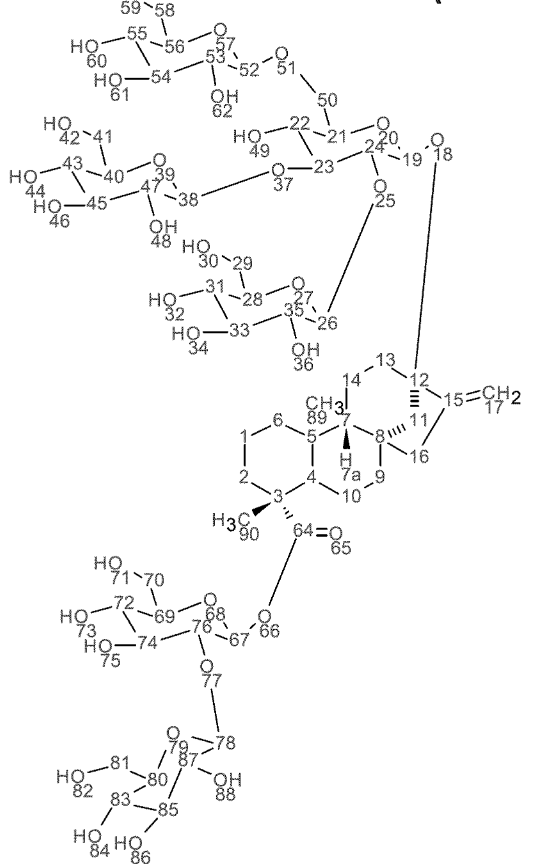


Figure 8N

Steviol+6Glc (isomer 1)

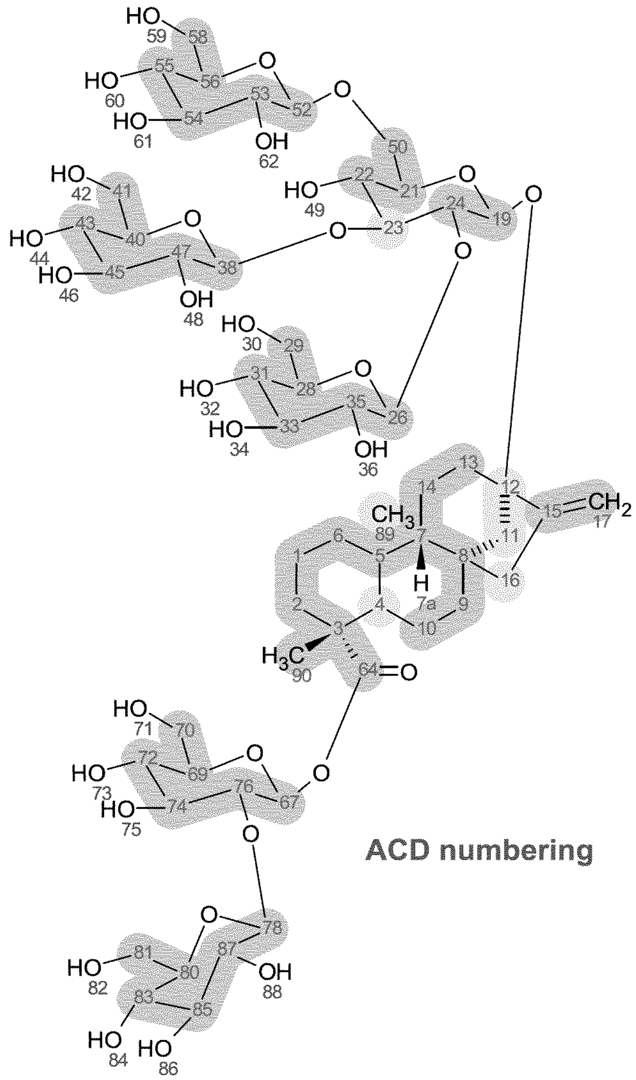


No.	Atom1	Shift1 (ppm)	H's	Type	J (Hz)	Multiplet1	(ppm)
1	89, 6<'>	0.74	4	br s	-	M32	[0.69 .. 0.78]
2	7a	0.88	1	m	-	M31	[0.81 .. 0.91]
3	2<'>	0.94	1	m	-	M30	[0.91 .. 0.98]
4	4	1.00	1	br d	12.72	M29	[0.98 .. 1.04]
5	90	1.11	3	s	-	M28	[1.07 .. 1.15]
6	11<'>, 14<'>, 1<'>, 9<'>	1.34	4	m	-	M26	[1.27 .. 1.38]
7	13<">, 9<">	1.42	2	m	-	M27	[1.38 .. 1.49]
8	13<'>, 10<'>	1.64	2	m	-	M25	[1.58 .. 1.67]
9	6<">, 1<">, 10<">	1.72	3	br d	12.23	M24	[1.67 .. 1.76]
10	14<">	1.82	1	br s	-	M23	[1.79 .. 1.86]
11	16<'>	1.96	1	m	-	M22	[1.89 .. 1.98]
12	16<">, 11<">	2.00	2	m	-	M21	[1.98 .. 2.04]
13	2<">	2.10	1	br d	11.49	M20	[2.07 .. 2.14]
14	31<ax>	2.92	1	m	-	M15	[2.90 .. 2.95]
15	85<ax>, 87<ax>, 35<ax>, 53<ax>	3.05	4	m	-	M14	[3.00 .. 3.09]
16	80<ax>, 83<ax>, 43<ax>, 55<ax>, 56<ax>, 28<ax>, 47<ax>, 33<ax	3.16	8	m	-	M13	[3.10 .. 3.21]
17	45<ax>, 54<ax>, 74<ax>, 72<ax>	3.25	4	br dd	17.24, 8.93	M19	[3.21 .. 3.28]
18	40<ax>	3.31	1	m	-	M11	[3.30 .. 3.32]
19	69<ax>, 21<ax>, 22<ax>	3.34	3	br d	4.65	M18	[3.32 .. 3.35]
20	29<'>	3.38	1	m	-	M12	[3.36 .. 3.43]
21	81<'>, 41<'>, 58<'>, 70<'>, 24<ax>	3.48	5	m	-	M10	[3.44 .. 3.54]
22	50<'>	3.62	1	br s	-	M16	[3.59 .. 3.64]
23	81<">, 41<">, 58<">, 76<ax>, 70<">, 29<">	3.68	6	m	-	M09	[3.64 .. 3.74]
24	23<ax>	3.75	1	br d	8.56	M17	[3.74 .. 3.78]
25	50<">	3.90	1	br d	11.25	M06	[3.86 .. 3.94]
26	52<ax>	4.24	1	d	7.82	M05	[4.22 .. 4.26]
27	19<ax>, 38	4.57	2	br d	7.83	M07	[4.56 .. 4.59]
28	78<ax>	4.60	1	br d	7.58	M08	[4.59 .. 4.63]
29	26<ax>	4.70	1	br d	7.82	M04	[4.67 .. 4.72]
30	17<a>	4.76	1	br s	-	M03	[4.73 .. 4.79]
31	17<b>	5.02	1	br s	-	M02	[5.00 .. 5.05]
32	67<ax>	5.39	1	br d	7.34	M01	[5.37 .. 5.42]

^{1}H NMR (800 MHz, *DMSO-d_6*) δ ppm 0.74 (br s, 4 H) 0.81 - 0.91 (m, 1 H) 0.91 - 0.98 (m, 1 H) 1.00 (br d, *J*=12.72 Hz, 1 H) 1.11 (s, 3 H) 1.27 - 1.38 (m, 4 H) 1.38 - 1.49 (m, 2 H) 1.58 - 1.67 (m, 2 H) 1.72 (br d, *J*=12.23 Hz, 3 H) 1.82 (br s, 1 H) 1.89 - 1.98 (m, 1 H) 1.98 - 2.04 (m, 2 H) 2.10 (br d, *J*=11.49 Hz, 1 H) 2.90 - 2.95 (m, 1 H) 3.00 - 3.09 (m, 4 H) 3.10 - 3.21 (m, 8 H) 3.25 (br dd, *J*=17.24, 8.93 Hz, 4 H) 3.30 - 3.32 (m, 1 H) 3.34 (br d, *J*=4.65 Hz, 3 H) 3.36 - 3.43 (m, 1 H) 3.44 - 3.54 (m, 5 H) 3.62 (br s, 1 H) 3.64 - 3.74 (m, 6 H) 3.75 (br d, *J*=8.56 Hz, 1 H) 3.90 (br d, *J*=11.25 Hz, 1 H) 4.24 (d, *J*=7.82 Hz, 1 H) 4.57 (br d, *J*=7.83 Hz, 2 H) 4.60 (br d, *J*=7.58 Hz, 1 H) 4.70 (br d, *J*=7.82 Hz, 1 H) 4.76 (br s, 1 H) 5.02 (br s, 1 H) 5.39 (br d, *J*=7.34 Hz, 1 H)

Figure 8O

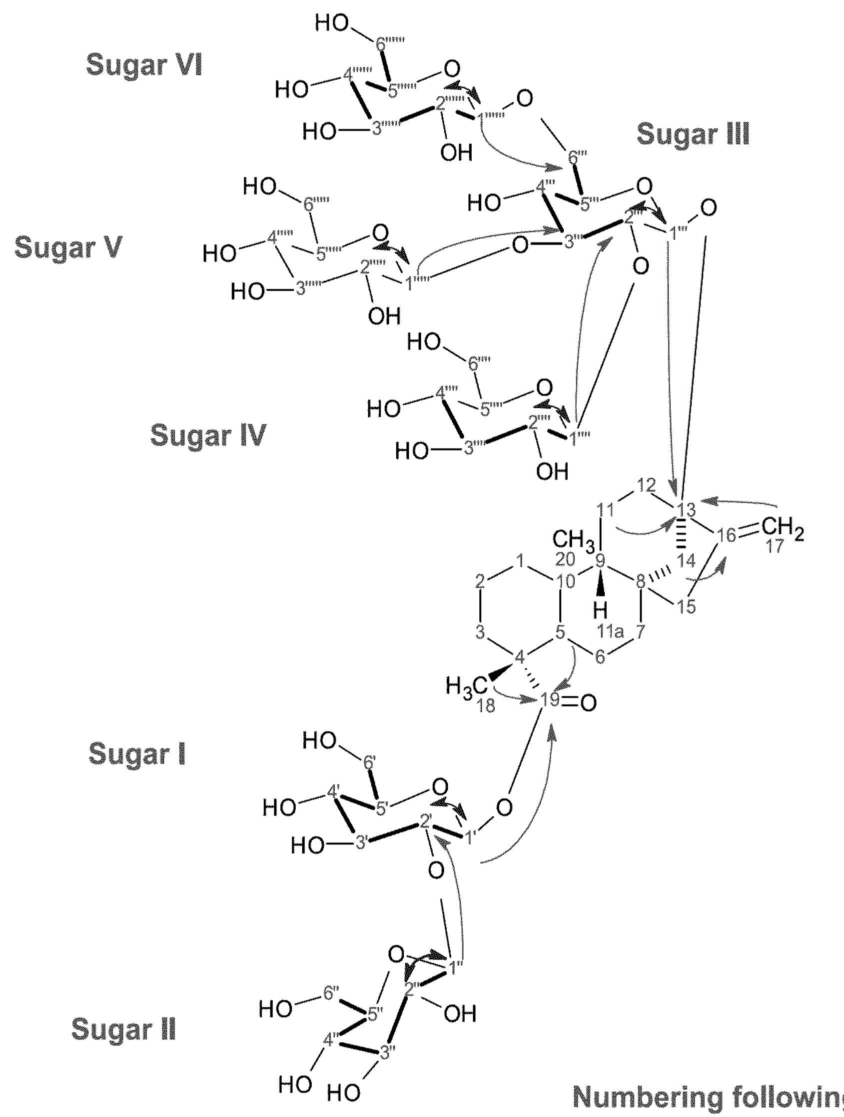
Steviol+6Glc (isomer 1)



F2 Atom	F2 (ppm)	F2 Atom	F2 (ppm)	F1 Atom	F1 (ppm)	F1 Atom	F1 (ppm)
1<">	1.71	31<ax>	2.91	1	19.9	31	71.5
1<'>	1.31	33<ax>	3.18			33	77.2
2<">	2.09	35<ax>	3.01	2	37.7	35	75.4
2<'>	0.93	38<ax>	4.56			38	103.3
		40<ax>	3.33	3	44.8	40	77.8
4	0.99	41<">	3.69	4	57.4	41	61.9
		41<'>	3.46	5	40.3		
6<">	1.71	43<ax>	3.24	6	40.8	43	70.3
6<'>	0.73	45<ax>	3.23			45	76.9
7a	0.87	47<ax>	3.12	7	54	47	74.4
		50<">	3.89	8	42.2	50	69.3
9<">	1.39	50<'>	3.62	9	42.1		
9<'>	1.31	52<ax>	4.23			52	103.9
10<">	1.72	53<ax>	3.04	10	22.7	53	74.2
10<'>	1.62	54<ax>	3.18			54	77.2
11<">	2	55<ax>	3.33	11	44.4	55	69.1
11<'>	1.34	56<ax>	3.3			56	77.2
		58<">	3.68	12	88.4	58	62
13<">	1.81	58<'>	3.46	13	38.3		
13<'>	1.36					64	178
14<">	1.62	67<ax>	5.38	14	20.6	67	93.6
14<'>	1.43	69<ax>	3.23			69	76.9
		70<">	3.64	15	153.2	70	61.6
16<">	1.99	70<'>	3.5	16	47.4		
16<'>	1.94	72<ax>	3.15			72	70.8
17<a>	4.75	74<ax>	3.65	17	105.8	74	77.2
17<b>	5.02	76	3.65			76	78.4
19<ax>	4.57	78<ax>	4.59	19	96.4	78	103.3
21<ax>	3.15	80<ax>	3.33	21	77.6	80	75.6
22<ax>	3.12	81<">	3.66	22	70.8	81	62.7
23<ax>	3.75	81<'>	3.37	23	86.5		
24<ax>	3.48	83<ax>	3.06	24	79.6	83	71.3
26<ax>	4.69	85<ax>	3.18	26	103	85	77.2
28<ax>	3.3	87<ax>	3.05	28	77.2	87	75.1
29<">	3.71	89	0.73	29	62.1	89	17.1
29<'>	3.69	90	1.1			90	29.2

^{13}C NMR (201 MHz, *DMSO-d_6*) δ ppm 17.1, 19.9, 20.6, 22.7, 29.2, 37.7, 38.3, 40.3, 40.8, 42.1, 42.2, 44.4, 44.8, 47.4, 54.0, 57.4, 61.6, 61.9, 62.0, 62.1, 62.7, 69.1, 69.3, 70.3, 70.8, 70.8, 71.3, 71.5, 74.2, 74.4, 75.1, 75.4, 75.6, 76.9, 76.9, 77.2, 77.2, 77.2, 77.2, 77.2, 77.2, 77.6, 77.8, 78.4, 79.6, 86.5, 88.4, 93.6, 96.4, 103.0, 103.3, 103.3, 103.9, 105.8, 153.2, 178.0

Figure 8P



= ^{1}H-^{13}C HMBC

= ^{1}H-^{1}H COSY

= ^{1}H-^{1}H TOCSY spin system

Assigments were made on the basis of ^{1}H-^{1}H COSY, ^{1}H-^{1}H TOCSY, ^{1}H-^{13}C HSQC-DEPT, ^{1}H-^{13}C HMBC.

Steviol+6Glc (isomer 1)

Numbering following IUPAC

Figure 8Q

Steviol+7Glc (isomer 2)

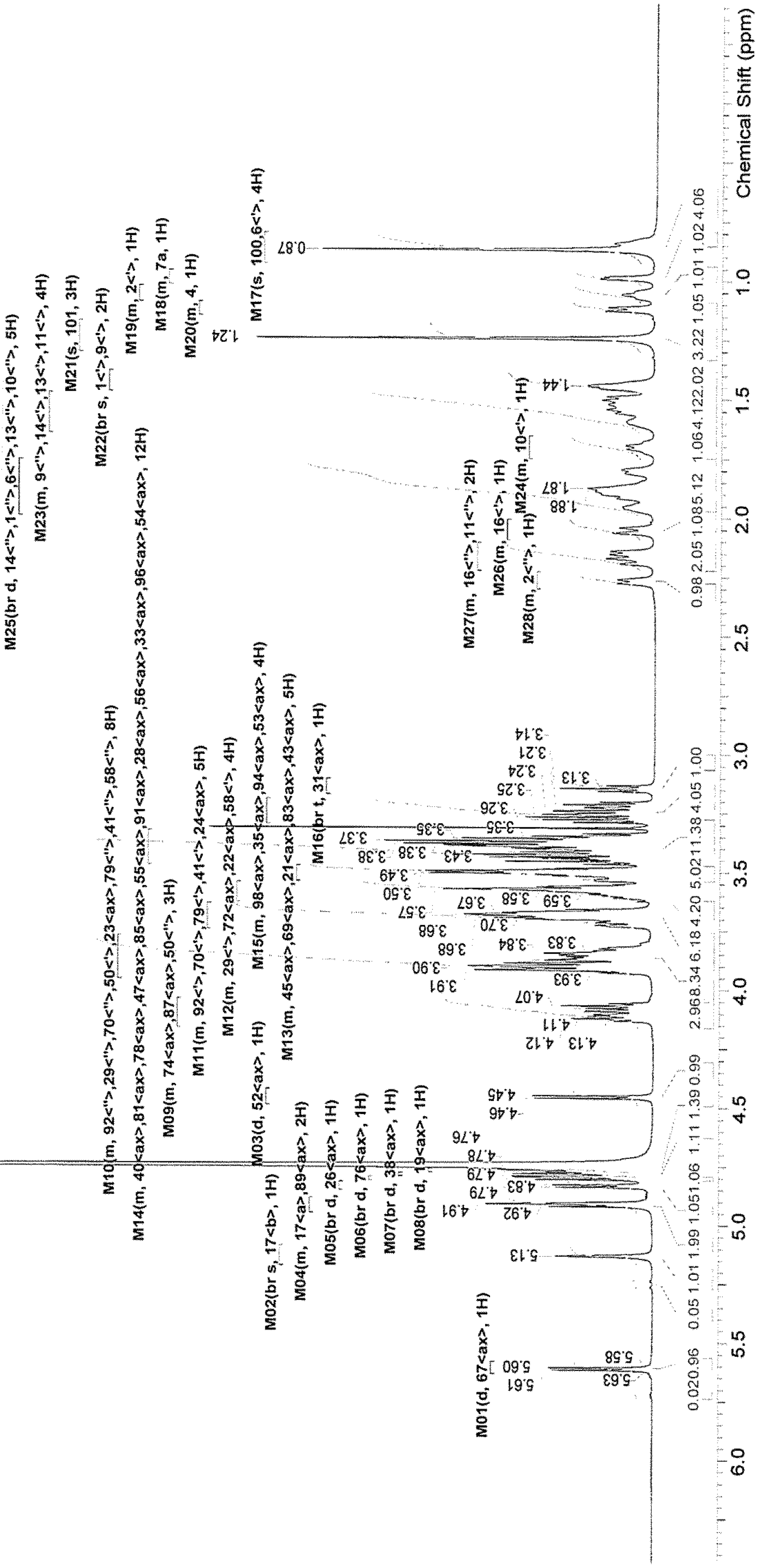
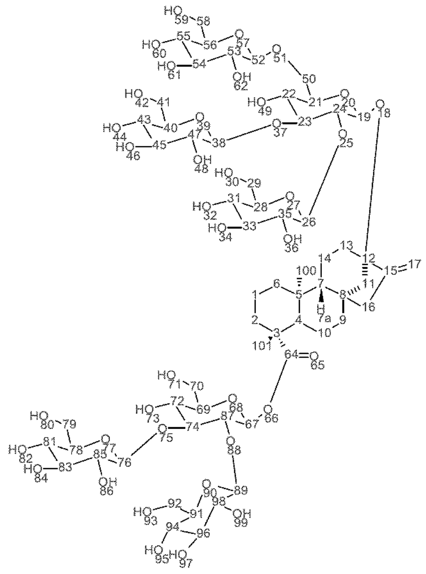


Figure 8R

Steviol+7Glc (isomer 2)

No.	Atom1	Shift1 (ppm)	H's	Type	J (Hz)	Multiplet1	(ppm)
1	100, 6<'>	0.87	4	s	-	M17	[0.80 .. 0.93]
2	7a	0.99	1	m	-	M18	[0.96 .. 1.02]
3	2<'>	1.06	1	m	-	M19	[1.02 .. 1.09]
4	4	1.12	1	m	-	M20	[1.09 .. 1.15]
5	101	1.24	3	s	-	M21	[1.17 .. 1.30]
6	1<'>, 9<'>	1.44	2	br s	-	M22	[1.38 .. 1.47]
7	9<">, 14<'>, 13<'>, 11<'>	1.56	4	m	-	M23	[1.47 .. 1.65]
8	10<'>	1.70	1	m	-	M24	[1.65 .. 1.75]
9	14<">, 1<">, 6<">, 13<">, 10<">	1.88	5	br d	10.51	M25	[1.76 .. 1.99]
10	16<'>	2.05	1	m	-	M26	[2.00 .. 2.09]
11	16<">, 11<">	2.16	2	m	-	M27	[2.10 .. 2.22]
12	2<">	2.26	1	m	-	M28	[2.23 .. 2.30]
13	31<ax>	3.14	1	br t	9.41	M16	[3.10 .. 3.17]
14	98<ax>, 35<ax>, 94<ax>, 53<ax>	3.24	4	m	-	M15	[3.19 .. 3.30]
15	40<ax>, 81<ax>, 78<ax>, 47<ax>, 85<ax>, 55<ax>, 91<ax>, 28<ax>, 56<ax>, 33<ax>, 96<ax>, 54<	3.40	12	m	-	M14	[3.32 .. 3.47]
16	45<ax>, 69<ax>, 21<ax>, 83<ax>, 43<ax>	3.50	5	m	-	M13	[3.47 .. 3.54]
17	29<'>, 72<ax>, 22<ax>, 58<'>	3.58	4	m	-	M12	[3.54 .. 3.63]
18	92<'>, 70<'>, 79<'>, 41<'>, 24<ax>	3.69	5	m	-	M11	[3.63 .. 3.74]
19	92<">, 29<">, 70<">, 50<'>, 23<ax>, 79<">, 41<">, 58<">	3.86	8	m	-	M10	[3.77 .. 3.95]
20	74<ax>, 87<ax>, 50<">	4.09	3	m	-	M09	[4.04 .. 4.16]
21	52<ax>	4.45	1	d	7.82	M03	[4.42 .. 4.49]
22	19<ax>	4.77	1	br d	8.07	M08	[4.76 .. 4.77]
23	38<ax>	4.78	1	br d	8.07	M07	[4.78 .. 4.79]
24	76<ax>	4.80	1	br d	8.07	M06	[4.79 .. 4.81]
25	26<ax>	4.83	1	br d	7.83	M05	[4.81 .. 4.85]
26	17<a>, 89<ax>	4.91	2	m	-	M04	[4.88 .. 4.95]
27	17<b>	5.13	1	br s	-	M02	[5.09 .. 5.17]
28	67<ax>	5.61	1	d	7.83	M01	[5.58 .. 5.63]



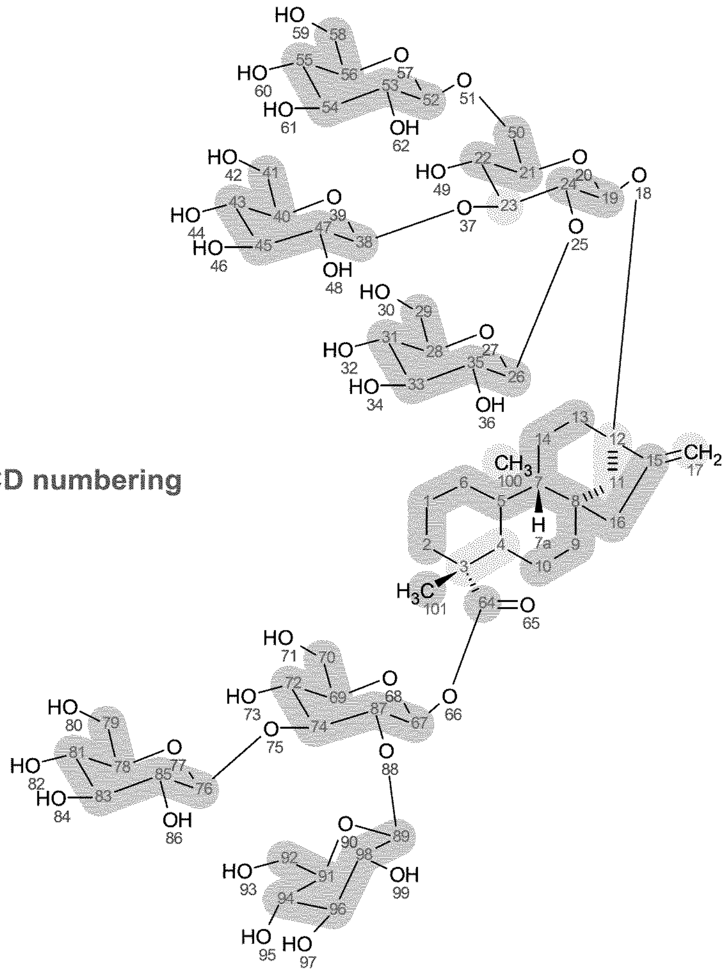
[1]H NMR (800 MHz, *DEUTERIUM OXIDE*) δ ppm 0.87 (s, 4 H) 0.96 - 1.02 (m, 1 H) 1.02 - 1.09 (m, 1 H) 1.09 - 1.15 (m, 1 H) 1.24 (s, 3 H) 1.44 (br s, 2 H) 1.47 - 1.65 (m, 4 H) 1.65 - 1.75 (m, 1 H) 1.88 (br d, *J*=10.51 Hz, 5 H) 2.00 - 2.09 (m, 1 H) 2.10 - 2.22 (m, 2 H) 2.23 - 2.30 (m, 1 H) 3.14 (br t, *J*=9.41 Hz, 1 H) 3.19 - 3.30 (m, 4 H) 3.32 - 3.47 (m, 12 H) 3.47 - 3.54 (m, 5 H) 3.54 - 3.63 (m, 4 H) 3.63 - 3.74 (m, 5 H) 3.77 - 3.95 (m, 8 H) 4.04 - 4.16 (m, 3 H) 4.45 (d, *J*=7.82 Hz, 1 H) 4.77 (br d, *J*=8.07 Hz, 1 H) 4.78 (br d, *J*=8.07 Hz, 1 H) 4.80 (br d, *J*=8.07 Hz, 1 H) 4.83 (br d, *J*=7.83 Hz, 1 H) 4.88 - 4.95 (m, 2 H) 5.13 (br s, 1 H) 5.61 (d, *J*=7.83 Hz, 1 H)

Figure 8S

Steviol+7Glc (isomer 2)

F2 Atom	F2 (ppm)	F1 Atom	F1 (ppm)
1<">	1.87	1	19.3
1<'>	1.45		
2<">	2.27	2	37.1
2<'>	1.06		
		3	44.3
4	1.12	4	57.1
		5	39.8
6<">	1.88	6	40.3
6<'>	0.84		
7a	0.99	7	53.5
		8	42
9<">	1.55	9	41.5
9<'>	1.44		
10<">	1.91	10	22.1
10<'>	1.7		
11<">	2.15	11	44
11<'>	1.5		
		12	88.6
13<">	1.96	13	37.5
13<'>	1.52		
14<">	1.81	14	20.3
14<'>	1.6		
		15	153.1
16<">	2.19	16	47
16<'>	2.06		
17<a>	4.91	17	104.9
17<b>	5.14		
19<ax>	4.77	19	95.7
21<ax>	3.54	21	74.8
22<ax>	3.57	22	68.5
23<ax>	3.92	23	85.4
24<ax>	3.68	24	78.9
26<ax>	4.84	26	102.4
28<ax>	3.39	28	76.6
29<">	3.87	29	62
29<'>	3.6		
31<ax>	3.15	31	70.9
33<ax>	3.44	33	76.2
35<ax>	3.25	35	74.6
38<ax>	4.79	38	102.4

F2 Atom	F2 (ppm)	F1 Atom	F1 (ppm)
40<ax>	3.44	40	76.2
41<">	3.89	41	61.1
41<'>	3.7		
43<ax>	3.51	43	69.9
45<ax>	3.51	45	76.3
47<ax>	3.35	47	73.8
50<">	4.1	50	68.9
50<'>	3.83		
52<ax>	4.46	52	103.1
53<ax>	3.28	53	73.5
54<ax>	3.44	54	76.2
55<ax>	3.39	55	69.9
56<ax>	3.44	56	76.2
58<">	3.89	58	61.1
58<'>	3.7		
		64	178.8
67<ax>	5.62	67	92.9
69<ax>	3.51	69	76.3
70<">	3.89	70	61.1
70<'>	3.7		
72<ax>	3.54	72	68.5
74<ax>	4.13	74	85.1
76<ax>	4.8	76	102.4
78<ax>	3.39	78	76.6
79<">	3.89	79	61.1
79<'>	3.7		
81<ax>	3.39	81	69.9
83<ax>	3.51	83	76.3
85<ax>	3.37	85	73.8
87<ax>	4.07	87	76.3
89<ax>	4.92	89	101.9
91<ax>	3.39	91	76.6
92<">	3.92	92	62
92<'>	3.67		
94<ax>	3.26	94	70.9
96<ax>	3.44	96	76.2
98<ax>	3.22	98	74.2
100	0.87	100	16.4
101	1.25	101	28.6

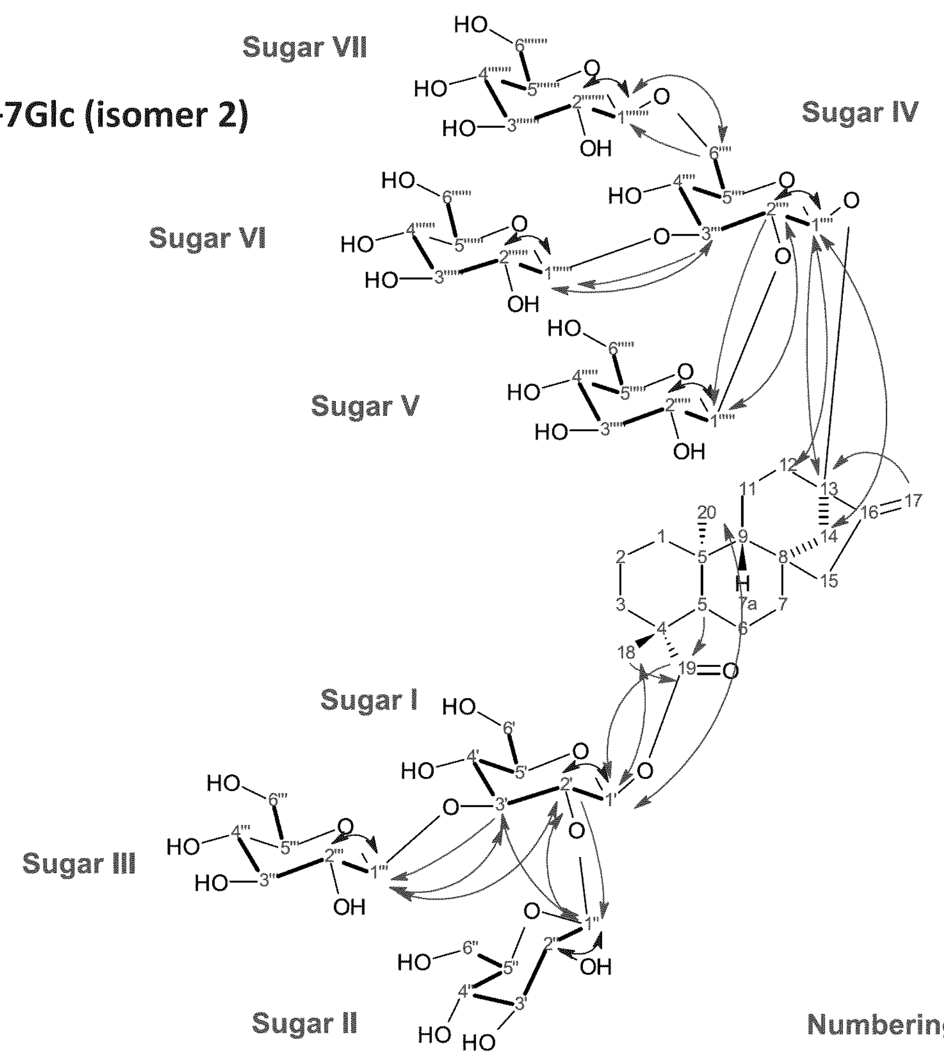


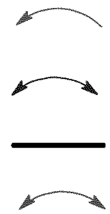
ACD numbering

^{13}C NMR (201 MHz, *DEUTERIUM OXIDE*) δ ppm 16.4, 19.3, 20.3, 22.1, 28.6, 37.1, 37.5, 39.8, 40.3, 41.5, 42.0, 44.0, 44.3, 47.0, 53.5, 57.1, 61.1, 61.1, 61.1, 61.1, 62.0, 62.0, 68.5, 68.5, 68.9, 69.9, 69.9, 69.9, 70.9, 70.9, 73.5, 73.8, 73.8, 74.2, 74.6, 74.8, 76.2, 76.2, 76.2, 76.2, 76.2, 76.3, 76.3, 76.3, 76.3, 76.6, 76.6, 76.6, 78.9, 85.1, 85.4, 88.6, 92.9, 95.7, 101.9, 102.4, 102.4, 102.4, 103.1, 104.9, 153.1, 178.8

Figure 8T

Steviol+7Glc (isomer 2)





= ^{1}H-^{13}C HMBC

= ^{1}H-^{1}H COSY

= ^{1}H-^{1}H TOCSY spin system

= ^{1}H-^{1}H dipolar correlation (ROESY)

Assigments were made on the basis of ^{1}H-^{1}H COSY, ^{1}H-^{1}H TOCSY, ^{1}H-^{13}C HSQC-DEPT, ^{1}H-^{13}C HMBC and ^{1}H-^{1}H ROESY.

Numbering following IUPAC

Figure 8U

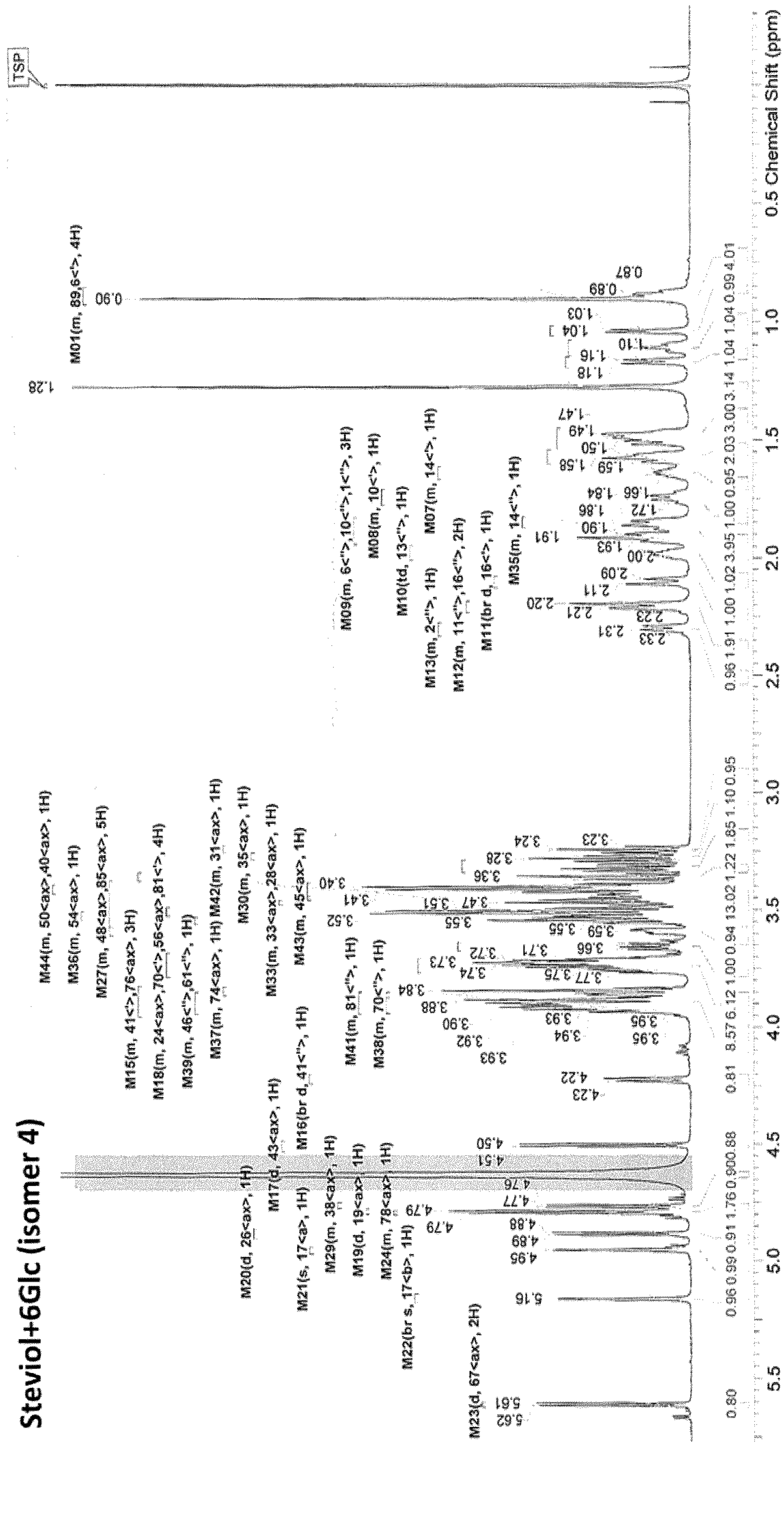

Steviol+6Glc (isomer 4)
TSP
M01(m, 89,6<>, 4H)
M09(m, 6<">,10<">,1<">, 3H)
M08(m, 10<>, 1H)
M10(td, 13<">, 1H)
M07(m, 14<>, 1H)
M13(m, 2<">, 1H)
M12(m, 11<">,16<">, 2H)
M11(br d, 16<>, 1H)
M35(m, 14<">, 1H)
M44(m, 50<ax>,40<ax>, 1H)
M36(m, 54<ax>, 1H)
M27(m, 48<ax>,85<ax>, 5H)
M15(m, 41<>,76<ax>, 3H)
M18(m, 24<ax>,70<>,56<ax>,81<>, 4H)
M39(m, 46<">,61<">, 1H)
M37(m, 74<ax>, 1H)
M42(m, 31<ax>, 1H)
M30(m, 35<ax>, 1H)
M33(m, 33<ax>,28<ax>, 1H)
M43(m, 45<ax>, 1H)
M16(br d, 41<">, 1H)
M41(m, 81<">, 1H)
M38(m, 70<">, 1H)
M17(d, 43<ax>, 1H)
M20(d, 26<ax>, 1H)
M21(s, 17<a>, 1H)
M29(m, 38<ax>, 1H)
M19(d, 19<ax>, 1H)
M24(m, 78<ax>, 1H)
M22(br s, 17<b>, 1H)
M23(d, 67<ax>, 2H)
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5 Chemical Shift (ppm)

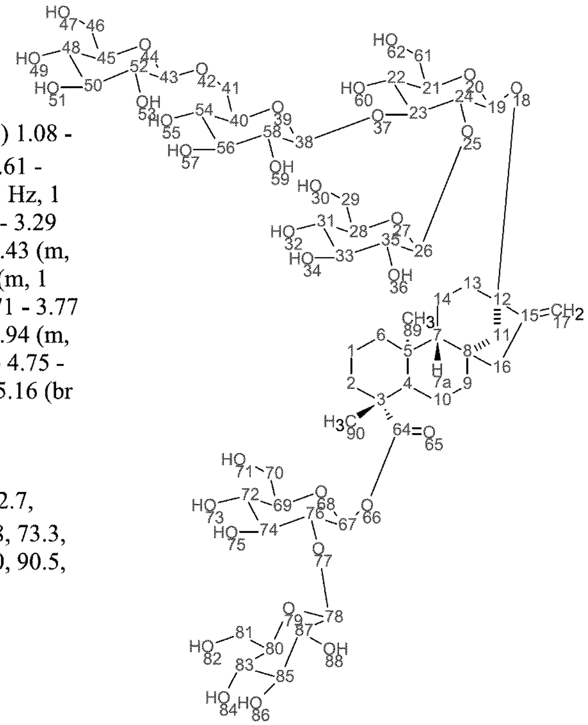
Figure 8V

Steviol+6Glc (isomer 4)

Multiplet1	Shift1 (ppm)	Atom1	H's	Type	J (Hz)	(ppm)
M01	0.90	89, 6<'>	4	m	-	[0.85 .. 0.93]
M02	1.04	7a	1	br d	8.07	[1.02 .. 1.06]
M03	1.11	2<'>	1	m	-	[1.08 .. 1.14]
M04	1.17	4	1	br d	12.47	[1.15 .. 1.20]
M05	1.28	90	3	s	-	[1.25 .. 1.30]
M06	1.49	11<'>, 9<'>, 1<'>	3	m	-	[1.45 .. 1.54]
M51	1.57	13<'>, 9<">	2	m	-	[1.54 .. 1.61]
M07	1.64	14<'>	1	m	-	[1.61 .. 1.67]
M08	1.74	10<'>	1	m	-	[1.71 .. 1.78]
M35	1.85	14<">	1	m	-	[1.83 .. 1.87]
M09	1.89	6<">, 10<">, 1<">	3	m	-	[1.83 .. 1.94]
M10	1.98	13<">	1	td	12.10, 6.11	[1.95 .. 2.01]
M11	2.10	16<'>	1	br d	17.12	[2.08 .. 2.13]
M12	2.20	11<">, 16<">	2	m	-	[2.18 .. 2.24]
M13	2.30	2<">	1	m	-	[2.28 .. 2.33]
M42	3.24	31<ax>	1	m	-	[3.23 .. 3.26]
M30	3.27	35<ax>	1	m	-	[3.26 .. 3.29]
M14	3.32	87<ax>, 52<ax>	2	m	-	[3.29 .. 3.34]
M28	3.36	83<ax>	1	m	-	[3.34 .. 3.38]
M44	3.41	50<ax>, 40<ax>	2	m	-	[3.39 .. 3.43]
M32	3.42	22<ax>, 58<ax>	3	m	-	[3.38 .. 3.46]
M43	3.45	45<ax>	1	m	-	[3.44 .. 3.46]
M33	3.47	33<ax>, 28<ax>	2	m	-	[3.46 .. 3.48]
M27	3.48	48<ax>, 85<ax>	3	m	-	[3.38 .. 3.57]
M31	3.51	72<ax>	1	m	-	[3.49 .. 3.53]
M36	3.53	54<ax>	1	m	-	[3.51 .. 3.55]
M34	3.55	80<ax>	1	m	-	[3.53 .. 3.56]
M26	3.59	69<ax>	1	ddd	9.72, 5.07, 2.32	[3.57 .. 3.61]
M25	3.66	29<'>	1	dd	12.23, 7.09	[3.64 .. 3.68]
M18	3.73	24<ax>, 70<'>, 56<ax>, 81<'>	4	m	-	[3.68 .. 3.79]
M47	3.74	46<'>	1	m	-	[3.71 .. 3.77]
M49	3.76	61<'>	1	m	-	[3.74 .. 3.78]
M37	3.85	74<ax>	1	m	-	[3.83 .. 3.87]
M15	3.89	41<'>, 76<ax>	2	m	-	[3.82 .. 3.96]
M40	3.90	23<ax>, 29<">	2	m	-	[3.85 .. 3.94]
M39	3.90	46<">, 61<">	2	m	-	[3.85 .. 3.94]
M41	3.90	81<">	1	m	-	[3.85 .. 3.94]
M38	3.91	70<">	1	m	-	[3.87 .. 3.94]
M16	4.22	41<">	1	br d	9.54	[4.20 .. 4.24]
M17	4.50	43<ax>	1	d	7.83	[4.49 .. 4.53]
M29	4.77	38<ax>	1	m	-	[4.75 .. 4.78]
M19	4.79	19<ax>	1	d	7.83	[4.78 .. 4.80]
M24	4.79	78<ax>	1	m	-	[4.78 .. 4.80]
M20	4.88	26<ax>	1	d	8.07	[4.86 .. 4.90]
M21	4.95	17<a>	1	s	-	[4.94 .. 4.97]
M22	5.16	17<b>	1	br s	-	[5.14 .. 5.18]
M23	5.61	67<ax>	1	d	7.82	[5.60 .. 5.62]

Figure 8W

Steviol+6Glc (isomer 4)

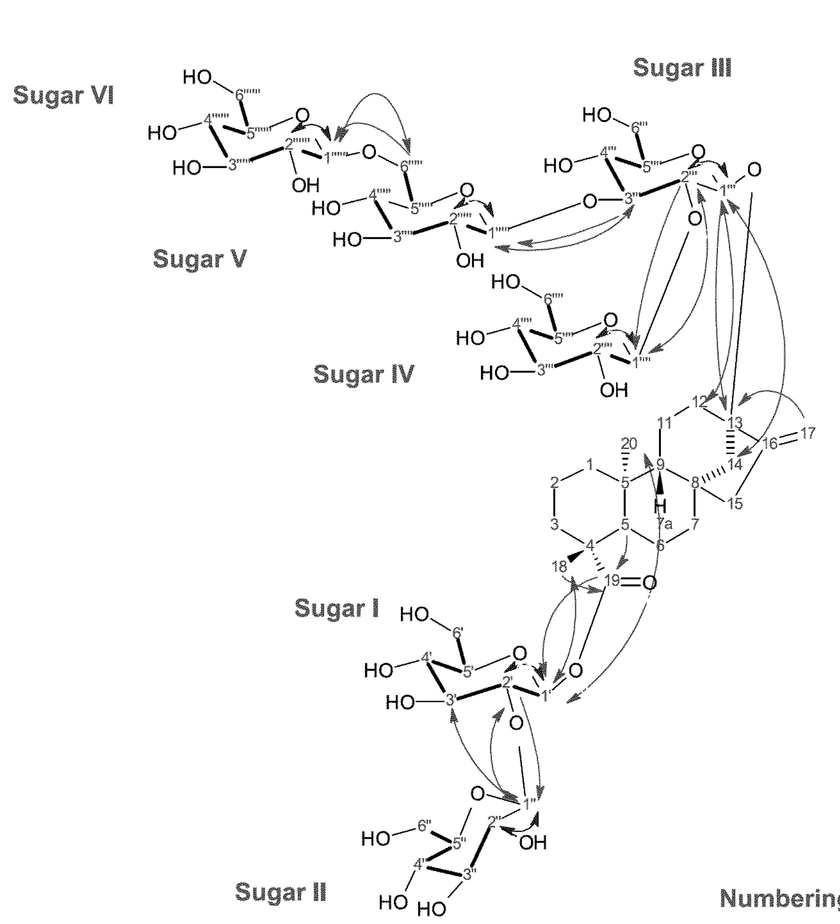


^{1}H NMR (800 MHz, *DEUTERIUM OXIDE*) δ ppm 0.85 - 0.93 (m, 4 H) 1.04 (br d, *J*=8.07 Hz, 1 H) 1.08 - 1.14 (m, 1 H) 1.17 (br d, *J*=12.47 Hz, 1 H) 1.28 (s, 3 H) 1.45 - 1.54 (m, 3 H) 1.54 - 1.61 (m, 2 H) 1.61 - 1.67 (m, 1 H) 1.71 - 1.78 (m, 1 H) 1.83 - 1.87 (m, 1 H) 1.83 - 1.94 (m, 3 H) 1.98 (td, *J*=12.10, 6.11 Hz, 1 H) 2.10 (br d, *J*=17.12 Hz, 1 H) 2.18 - 2.24 (m, 2 H) 2.28 - 2.33 (m, 1 H) 3.23 - 3.26 (m, 1 H) 3.26 - 3.29 (m, 1 H) 3.29 - 3.34 (m, 2 H) 3.34 - 3.38 (m, 1 H) 3.38 - 3.57 (m, 3 H) 3.38 - 3.46 (m, 3 H) 3.39 - 3.43 (m, 2 H) 3.44 - 3.46 (m, 1 H) 3.46 - 3.48 (m, 2 H) 3.49 - 3.53 (m, 1 H) 3.51 - 3.55 (m, 1 H) 3.53 - 3.56 (m, 1 H) 3.59 (ddd, *J*=9.72, 5.07, 2.32 Hz, 1 H) 3.66 (dd, *J*=12.23, 7.09 Hz, 1 H) 3.68 - 3.79 (m, 4 H) 3.71 - 3.77 (m, 1 H) 3.74 - 3.78 (m, 1 H) 3.82 - 3.96 (m, 2 H) 3.83 - 3.87 (m, 1 H) 3.85 - 3.94 (m, 2 H) 3.85 - 3.94 (m, 2 H) 3.85 - 3.94 (m, 1 H) 3.87 - 3.94 (m, 1 H) 4.22 (br d, *J*=9.54 Hz, 1 H) 4.50 (d, *J*=7.83 Hz, 1 H) 4.75 - 4.78 (m, 1 H) 4.79 (d, *J*=7.83 Hz, 1 H) 4.78 - 4.80 (m, 1 H) 4.88 (d, *J*=8.07 Hz, 1 H) 4.95 (s, 1 H) 5.16 (br s, 1 H) 5.61 (d, *J*=7.82 Hz, 1 H)

^{13}C NMR (201 MHz, *DEUTERIUM OXIDE*) δ ppm 18.8, 21.8, 22.6, 24.2, 31.1, 39.6, 39.6, 42.0, 42.7, 43.7, 44.1, 46.8, 46.8, 49.5, 55.8, 59.5, 63.3, 63.5, 63.7, 64.3, 64.3, 71.3, 71.5, 72.2, 72.3, 72.5, 72.8, 73.3, 75.9, 76.1, 77.0, 77.5, 78.0, 78.4, 78.4, 78.5, 78.6, 78.7, 78.7, 78.8, 79.0, 79.0, 79.3, 80.8, 81.3, 89.0, 90.5, 95.4, 98.4, 104.8, 105.2, 105.3, 105.3, 107.1, 155.9, 181.1

Figure 8X

Steviol+6Glc (isomer 4)



= ^{1}H-^{13}C HMBC

= ^{1}H-^{1}H COSY

= ^{1}H-^{1}H TOCSY spin system

= ^{1}H-^{1}H dipolar correlation (ROESY)

Assigments were made on the basis of ^{1}H-^{1}H COSY, ^{1}H-^{1}H TOCSY, ^{1}H-^{13}C HSQC-DEPT, ^{1}H-^{13}C HMBC and ^{1}H-^{1}H ROESY.

Numbering following IUPAC

Steviol+7Glc (isomer 5)

Figure 8Y

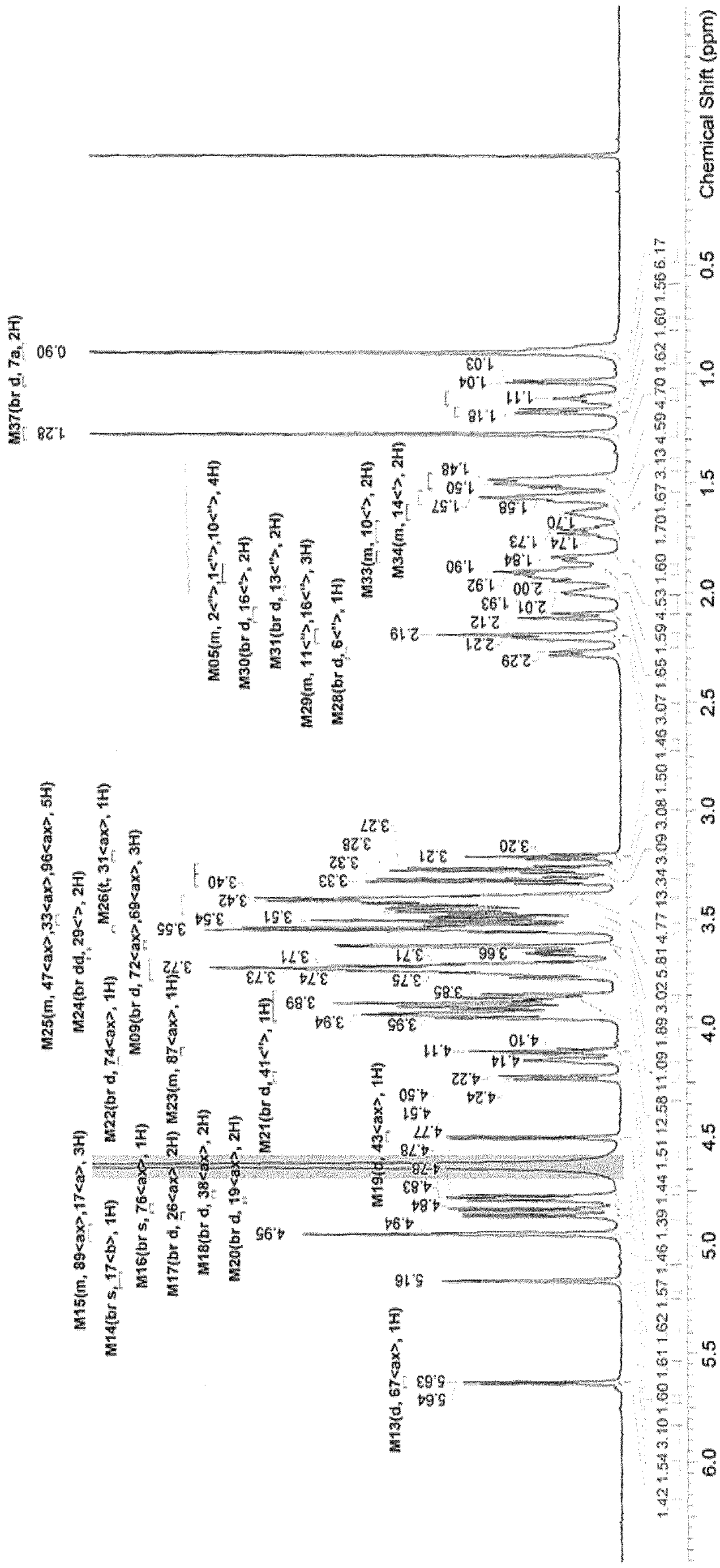


Figure 8Z

Steviol+7Glc (isomer 5)

Multiplet1	Shift1 (ppm)	Atom1	H's	Type	J (Hz)	(ppm)
M01	0.90	100, 6<'>	4	s	-	[0.86 .. 0.94]
M37	1.04	7a	1	br d	7.83	[1.01 .. 1.06]
M36	1.11	2<'>	1	m	-	[1.08 .. 1.14]
M35	1.17	4	1	br d	12.23	[1.15 .. 1.20]
M02	1.28	101	3	s	-	[1.25 .. 1.31]
M03	1.50	11<'>, 1<'>, 9<'>	3	m	-	[1.46 .. 1.53]
M04	1.57	13<'>, 9<">	2	m	-	[1.54 .. 1.60]
M34	1.63	14<'>	1	m	-	[1.60 .. 1.67]
M33	1.72	10<'>	1	m	-	[1.67 .. 1.77]
M32	1.84	14<">	1	br d	9.29	[1.81 .. 1.86]
M05	1.92	10<">, 1<">, 2<">	3	m	-	[1.87 .. 1.96]
M31	2.00	13<">	1	br d	6.36	[1.97 .. 2.04]
M30	2.11	16<'>	1	br d	16.14	[2.07 .. 2.14]
M29	2.20	16<">, 11<">	2	m	-	[2.17 .. 2.23]
M28	2.28	6<">	1	br d	12.72	[2.25 .. 2.30]
M26	3.21	31<ax>	1	t	9.29	[3.19 .. 3.23]
M06	3.27	98<ax>, 35<ax>	2	q	8.31	[3.25 .. 3.30]
M27	3.32	44<ax>, 94<ax>	2	m	-	[3.30 .. 3.35]
M07	3.43	46<ax>, 21<ax>, 23<ax>, 58<ax>, 28<ax>, 91<ax>, 78<ax>, 83<ax>, 85<ax	9	m	-	[3.39 .. 3.48]
M25	3.50	96<ax>, 33<ax>, 47<ax>	3	m	-	[3.48 .. 3.53]
M08	3.54	56<ax>, 81<ax>, 54<ax>, 45<ax>	4	m	-	[3.53 .. 3.56]
M09	3.62	69<ax>, 72<ax>	2	br d	4.40	[3.60 .. 3.64]
M24	3.66	29<'>	1	br dd	12.23, 7.34	[3.64 .. 3.68]
M10	3.73	70<'>, 40<ax>, 24<ax>, 61<'>, 79<'>, 92<'>, 49<'>	7	m	-	[3.69 .. 3.78]
M11	3.90	41<'>, 49<">, 79<">, 22<ax>, 70<">, 92<">, 61<">, 29<">	8	m	-	[3.83 .. 3.97]
M23	4.11	87<ax>	1	m	-	[4.09 .. 4.13]
M22	4.15	74<ax>	1	br d	3.91	[4.13 .. 4.17]
M21	4.23	41<">	1	br d	10.76	[4.20 .. 4.25]
M19	4.50	43<ax>	1	d	7.83	[4.48 .. 4.52]
M18	4.77	38<ax>	1	br d	7.83	[4.75 .. 4.78]
M20	4.79	19<ax>	1	br d	8.31	[4.78 .. 4.80]
M16	4.81	76<ax>	1	br s	-	[4.81 .. 4.85]
M17	4.86	26<ax>	1	br d	7.82	[4.85 .. 4.88]
M15	4.95	17<a>, 89<ax>	2	m	-	[4.90 .. 4.98]
M14	5.16	17<b>	1	br s	-	[5.13 .. 5.20]
M13	5.63	67<ax>	1	d	7.34	[5.61 .. 5.66]

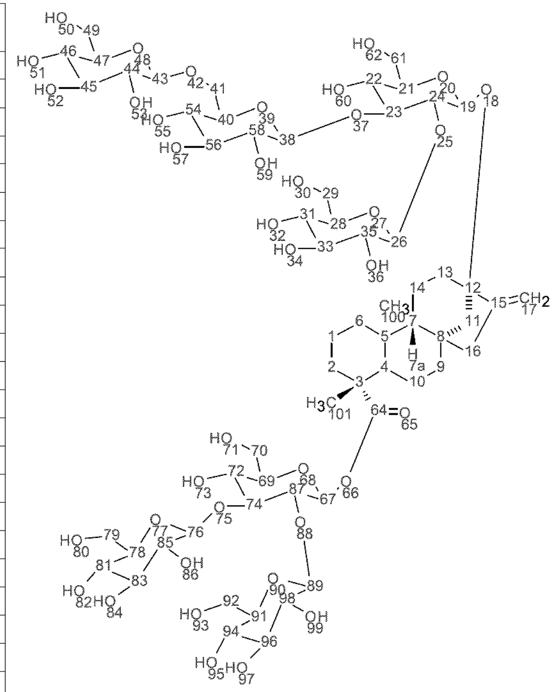
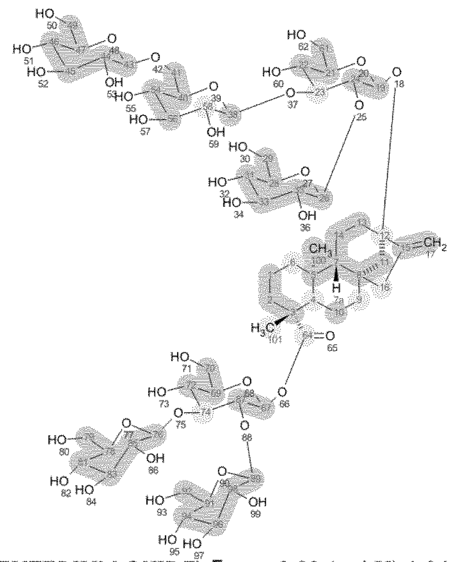


Figure 8AA

Steviol+7Glc (isomer 5)

F2 Atom	F2 (ppm)	F1 Atom	F1 (ppm)
1<">	1.9	1	21.7
1<'>	1.49		
2<">	2.28	2	39.7
2<'>	1.11		
		3	46.8
4	1.17	4	59.5
		5	41.9
6<">	1.91	6	42.7
6<'>	0.89		
7a	1.04	7	55.9
		8	44.1
9<">	1.57	9	43.9
9<'>	1.48		
10<">	1.94	10	24.5
10<'>	1.72		
11<">	2.2	11	46.7
11<'>	1.51		
		12	90.7
13<">	2	13	39.9
13<'>	1.56		
14<">	1.84	14	22.7
14<'>	1.63		
		15	155.7
16<">	2.2	16	49.4
16<'>	2.11		
17<a>	4.95	17	107.1
17<b>	5.16		
19<ax>	4.79	19	98.3
21<ax>	3.72	21	77.6
22<ax>	3.54	22	71.5
23<ax>	3.93	23	89.2
24<ax>	3.71	24	81.4
26<ax>	4.87	26	105
28<ax>	3.47	28	78.8
29<">	3.9	29	64.5
29<'>	3.65		
31<ax>	3.21	31	73.4
33<ax>	3.39	33	78
35<ax>	3.27	35	77
38<ax>	4.77	38	105.2
40<ax>	3.47	40	78.8
41<">	4.23	41	71.6
41<'>	3.87		
43<ax>	4.5	43	105.4
44<ax>	3.33	44	76
45<ax>	3.55	45	78.8
46<ax>	3.41	46	72.5
47<ax>	3.5	47	78.6
49<">	3.92	49	63.6
49<'>	3.95		
54<ax>	3.51	54	72.4
56<ax>	3.5	56	78.6
58<ax>	3.42	58	79.1
61<'>	3.73	61	63.7
61<">	3.85		
		64	181.2
67<ax>	5.63	67	95.6
69<ax>	3.62	69	79.1
70<">	3.74	70	63.6
70<'>	3.73		

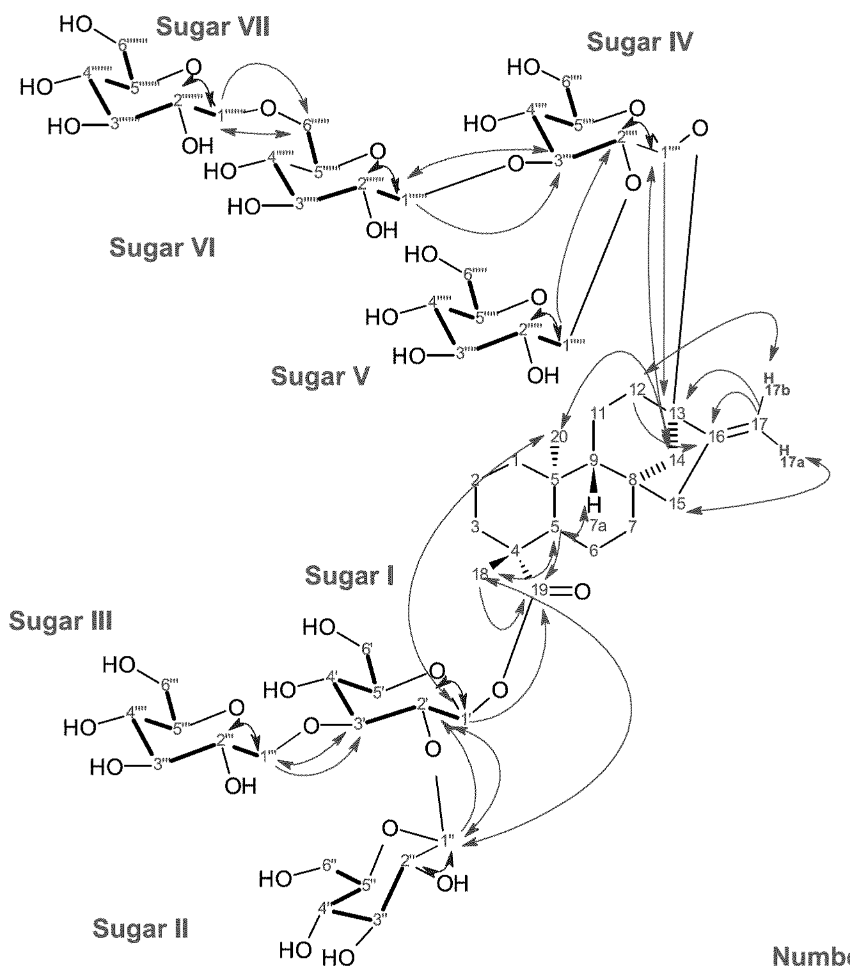


[1]H NMR (800 MHz, *DEUTERIUM OXIDE*) δ ppm 0.90 (s, 4 H) 1.04 (br d, J=7.83 Hz, 1 H) 1.08 - 1.14 (m, 1 H) 1.17 (br d, J=12.23 Hz, 1 H) 1.28 (s, 3 H) 1.46 - 1.53 (m, 3 H) 1.54 - 1.60 (m, 2 H) 1.60 - 1.67 (m, 1 H) 1.67 - 1.77 (m, 1 H) 1.84 (br d, J=9.29 Hz, 1 H) 1.87 - 1.96 (m, 3 H) 2.00 (br d, J=6.36 Hz, 1 H) 2.11 (br d, J=16.14 Hz, 1 H) 2.17 - 2.23 (m, 2 H) 2.28 (br d, J=12.72 Hz, 1 H) 3.21 (t, J=9.29 Hz, 1 H) 3.27 (q, J=8.31 Hz, 2 H) 3.30 - 3.35 (m, 2 H) 3.39 - 3.48 (m, 9 H) 3.48 - 3.53 (m, 3 H) 3.53 - 3.56 (m, 4 H) 3.62 (br d, J=4.40 Hz, 2 H) 3.66 (br dd, J=12.23, 7.34 Hz, 1 H) 3.69 - 3.78 (m, 7 H) 3.83 - 3.97 (m, 8 H) 4.09 - 4.13 (m, 1 H) 4.15 (br d, J=3.91 Hz, 1 H) 4.23 (br d, J=10.76 Hz, 1 H) 4.50 (d, J=7.83 Hz, 1 H) 4.77 (br d, J=7.83 Hz, 1 H) 4.79 (br d, J=8.31 Hz, 1 H) 4.81 (br s, 1 H) 4.86 (br d, J=7.82 Hz, 1 H) 4.90 - 4.98 (m, 2 H) 5.16 (br s, 1 H) 5.63 (d, J=7.34 Hz, 1 H)

[13]C NMR (201 MHz, *DEUTERIUM OXIDE*) δ ppm 18.8, 21.7, 22.7, 24.5, 31.0, 39.7, 39.9, 41.9, 42.7, 43.9, 44.1, 46.7, 46.8, 49.4, 55.9, 59.5, 63.5, 63.6, 63.6, 63.7, 64.5, 64.5, 71.0, 71.5, 71.6, 72.4, 72.5, 72.5, 73.4, 73.4, 76.0, 76.3, 76.8, 77.0, 77.6, 78.0, 78.6, 78.6, 78.8, 78.8, 78.8, 78.8, 78.8, 79.1, 79.1, 79.1, 81.4, 87.5, 89.2, 90.7, 95.6, 98.3, 104.5, 104.9, 105.0, 105.2, 105.4, 107.1, 155.7, 181.2

Figure 8AB

Steviol+7Glc (isomer 5)



= ^{1}H-^{13}C HMBC

= ^{1}H-^{1}H COSY

= ^{1}H-^{1}H TOCSY spin system

= ^{1}H-^{1}H dipolar correlation (ROESY)

Assigments were made on the basis of ^{1}H-^{1}H COSY, ^{1}H-^{1}H TOCSY, ^{1}H-^{13}C HSQC-DEPT, ^{1}H-^{13}C HMBC and ^{1}H-^{1}H ROESY.

Numbering following IUPAC

Figure 8AC

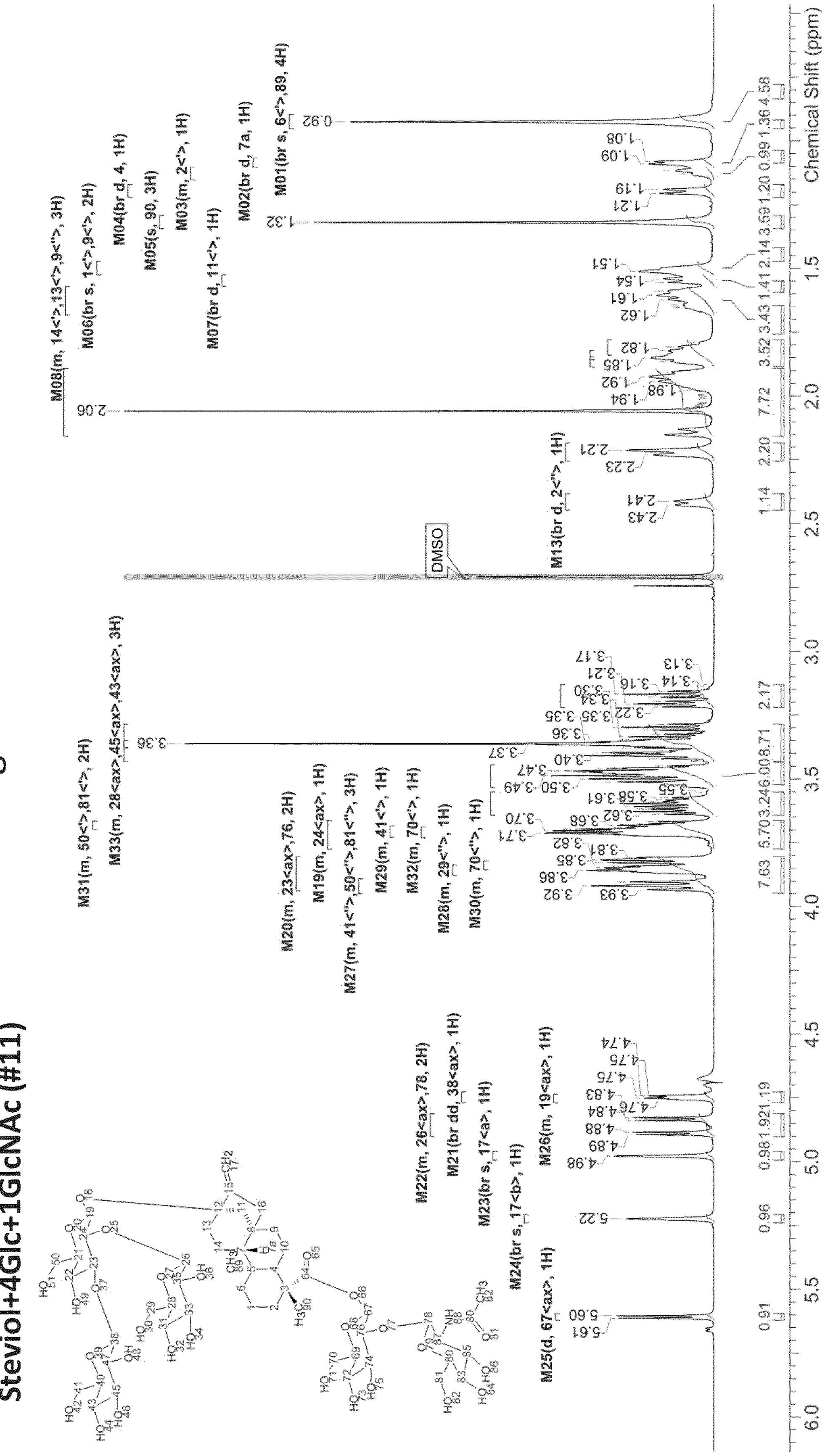
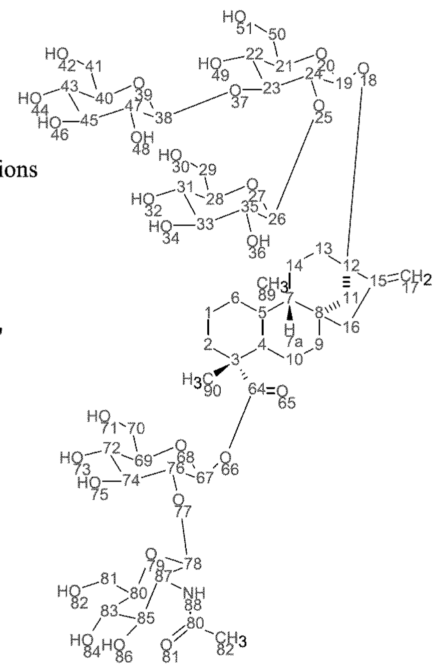


Figure 8AD

Steviol+4Glc+1GlcNAc (#11)

Multiplet1	Shift1 (ppm)	Atom1	H's	Type	J (Hz)	(ppm)
M25	5.61	67<ax>	1	d	7.43	[5.60 .. 5.62]
M24	5.22	17<b>	1	br s	-	[5.21 .. 5.24]
M23	4.98	17<a>	1	br s	-	[4.96 .. 4.99]
M22	4.86	26<ax>, 78	2	m	-	[4.81 .. 4.90]
M26	4.75	19<ax>	1	m	-	[4.73 .. 4.77]
M21	4.75	38<ax>	1	br dd	7.63, 4.11	[4.73 .. 4.77]
M27	3.92	41<">, 50<">, 81<">	3	m	-	[3.89 .. 3.95]
M20	3.86	23<ax>, 76	2	m	-	[3.80 .. 3.94]
M28	3.86	29<">	1	m	-	[3.84 .. 3.88]
M30	3.84	70<">	1	m	-	[3.82 .. 3.86]
M32	3.71	70<'>	1	m	-	[3.69 .. 3.73]
M29	3.71	41<'>	1	m	-	[3.68 .. 3.73]
M19	3.70	24<ax>	1	m	-	[3.66 .. 3.77]
M31	3.68	50<'>, 81<'>	2	m	-	[3.67 .. 3.70]
M18	3.61	29<'>, 74, 87<ax>	3	m	-	[3.55 .. 3.64]
M17	3.48	21<ax>, 40<ax>, 85<ax>, 72<ax>, 69<ax>, 22	6	m	-	[3.45 .. 3.53]
M34	3.40	80<ax>, 33<ax>	2	m	-	[3.38 .. 3.42]
M33	3.36	28<ax>, 45<ax>, 43<ax>	3	m	-	[3.35 .. 3.38]
M16	3.36	83<ax>, 47<ax>	2	m	-	[3.29 .. 3.43]
M15	3.19	31<ax>, 35<ax>	2	m	-	[3.13 .. 3.22]
M13	2.42	2<">	1	br d	12.52	[2.38 .. 2.45]
M12	2.22	11<">, 16<">	2	br d	13.69	[2.18 .. 2.25]
M11	2.03	10<">, 13<">, 16<'>, 6<">, 82	7	m	-	[1.89 .. 2.16]
M10	1.86	14<">	1	br d	10.95	[1.85 .. 1.89]
M35	1.84	1<">	1	m	-	[1.82 .. 1.86]
M09	1.81	10<'>	1	m	-	[1.78 .. 1.84]
M08	1.62	14<'>, 13<'>, 9<">	3	m	-	[1.57 .. 1.68]
M07	1.55	11<'>	1	br d	10.95	[1.53 .. 1.57]
M06	1.51	1<'>, 9<'>	2	br s	-	[1.47 .. 1.53]
M05	1.32	90	3	s	-	[1.29 .. 1.34]
M04	1.20	4	1	br d	12.13	[1.17 .. 1.22]
M03	1.12	2<'>	1	m	-	[1.10 .. 1.15]
M02	1.09	7a	1	br d	7.82	[1.07 .. 1.10]
M01	0.92	6<'>, 89	4	br s	-	[0.90 .. 0.95]



Homonuclear dipolar correlations between:
H-38 and H-23
H-26 and H-24
H-78 and H-76
H-67 and Me-90, Me-89
H-19 and H-11', H-13", H-16"
H-17a and H-16', H-16"
H-17b and H-13'
H-4 and H-7a, Me-90
Me-89 and H-11"
H-7a and H-16'

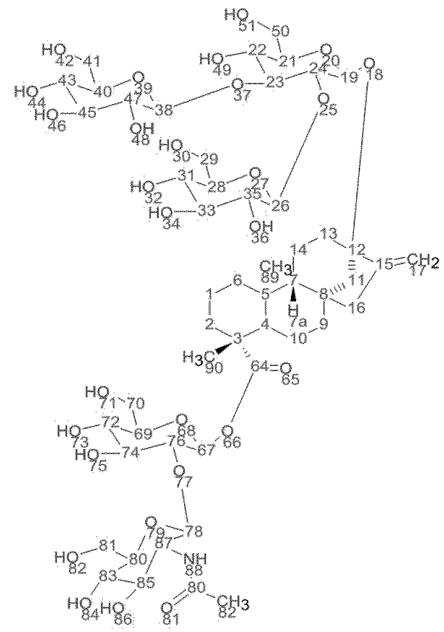
[1]H NMR (800 MHz, *Solvent*) δ ppm 0.92 (br s, 4 H) 1.09 (br d, =7.82 Hz, 1 H) 1.10 - 1.15 (m, 1 H) 1.20 (br d, =12.13 Hz, 1 H) 1.32 (s, 3 H) 1.51 (br s, 2 H) 1.55 (br d, =10.95 Hz, 1 H) 1.57 - 1.68 (m, 3 H) 1.78 - 1.84 (m, 1 H) 1.82 - 1.86 (m, 1 H) 1.86 (br d, =10.95 Hz, 1 H) 1.89 - 2.16 (m, 7 H) 2.22 (br d, =13.69 Hz, 2 H) 2.42 (br d, =12.52 Hz, 1 H) 3.13 - 3.22 (m, 2 H) 3.29 - 3.43 (m, 2 H) 3.35 - 3.38 (m, 3 H) 3.38 - 3.42 (m, 2 H) 3.45 - 3.53 (m, 6 H) 3.55 - 3.64 (m, 3 H) 3.66 - 3.77 (m, 1 H) 3.67 - 3.70 (m, 2 H) 3.68 - 3.73 (m, 1 H) 3.69 - 3.73 (m, 1 H) 3.80 - 3.94 (m, 2 H) 3.82 - 3.86 (m, 1 H) 3.84 - 3.88 (m, 1 H) 3.89 - 3.95 (m, 3 H) 4.75 (br dd, =7.63, 4.11 Hz, 1 H) 4.73 - 4.77 (m, 1 H) 4.81 - 4.90 (m, 2 H) 4.98 (br s, 1 H) 5.22 (br s, 1 H) 5.61 (d, =7.43 Hz, 1 H)

Figure 8AE

Steviol+4Glc+1GlcNAc (#11)

F2 Atom	δ(1H) (ppm)	F1 Atom	δ(13C) (ppm)
1<">	1.84	1	20.2
1<'>	1.51		
2<">	2.42	2	37.6
2<'>	1.12		
		3	45.1
4	1.2	4	57.6
		5	40.1
6<">	1.91	6	41.1
6<'>	0.92		
7a	1.08	7	53.9
		8	42.5
9<">	1.62	9	42
9<'>	1.51		
10<">	1.93	10	22.4
10<'>	1.81		
11<">	2.22	11	45
11<'>	1.55		
		12	88.4
13<">	1.96	13	38.1
13<'>	1.59		
14<">	1.86	14	21
14<'>	1.65		
16<">	2.22	16	47.9
16<'>	2.14		
17<a>	4.98	17	105.7
17<b>	5.22		
19<ax>	4.75	19	96.7
21<ax>	3.5	21	75.2

22	3.49	22	69.3
23<ax>	3.86	23	86.7
24<ax>	3.72	24	79.5
26<ax>	4.89	26	103
28<ax>	3.37	28	77.7
29<">	3.86	29	62.6
29<'>	3.58	29	62.6
31<ax>	3.17	31	71.6
33<ax>	3.41	33	77.2
35<ax>	3.2	35	75.4
38<ax>	4.75	38	103.4
40<ax>	3.47	40	77.2
41<">	3.93	41	62.4
41<'>	3.71	41	62.4
43<ax>	3.37	43	70.8
45<ax>	3.36	45	76.6
47<ax>	3.33	47	74.6
50<">	3.92	50	61.8
50<'>	3.69		
		64	178.1
67<ax>	5.61	67	93.2
69<ax>	3.52	69	77.7
70<">	3.84	70	61.7
70<'>	3.71		
72<ax>	3.46	72	70.5
74	3.63	74	77.6
76	3.82	76	78.4
78	4.83	78	101.7
80<ax>	3.41	80	77.2
81<">	3.92	81	61.8
81<'>	3.69		
82	2.06	82	23.7

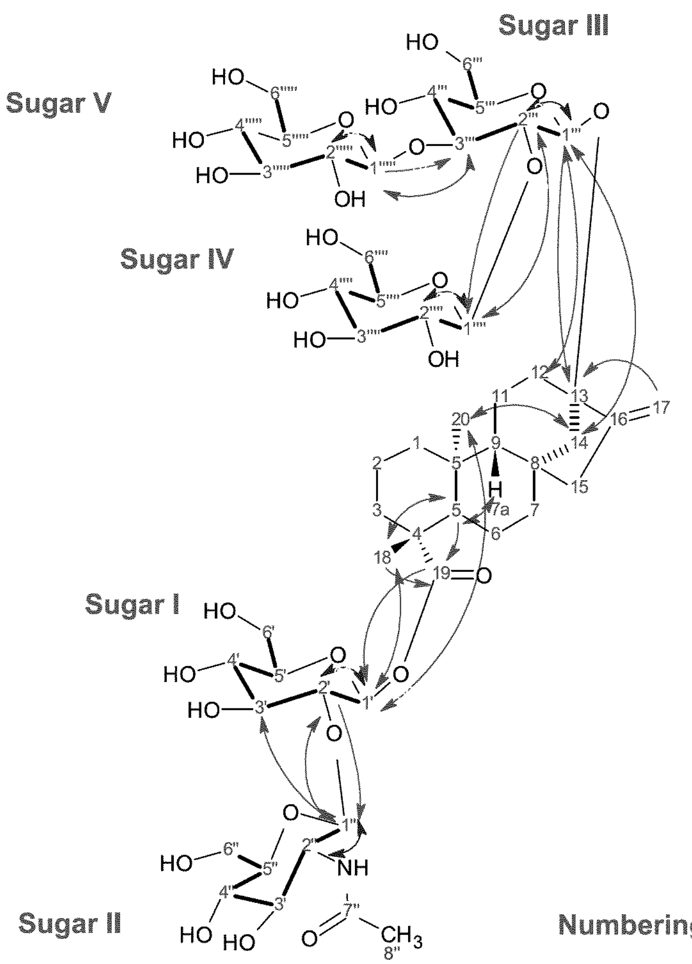


Heteronuclear scalar correlations between:
C=O(64) and H-67, Me-90, H-4
C-12 and H-19, H-17a/b
H-26 and C-24 (C-26 and H-24)
H-38 and C-23 (C-38 and H-23)
H-78 and C-76 (C-78 and H-76)
C=O(80) and H-87, Me-82

^{13}C NMR (201 MHz, *Solvent*) δ ppm 178.1 (1C), 105.7 (1C), 103.4 (1C), 103.0 (1C), 101.7 (1C), 96.7 (1C), 93.2 (1C), 88.4 (1C), 86.7 (1C), 79.5 (1C), 78.4 (1C), 77.7 (1C), 77.7 (1C), 77.6 (1C), 77.2 (1C), 77.2 (1C), 77.2 (1C), 76.6 (1C), 75.4 (1C), 75.2 (1C), 74.6 (1C), 71.6 (1C), 71.6 (1C), 70.8 (1C), 70.5 (1C), 70.5 (1C), 69.3 (1C), 62.6 (1C), 62.6 (1C), 62.4 (1C), 62.4 (1C), 61.8 (1C), 61.8 (1C), 61.7 (1C), 57.6 (1C), 57.1 (1C), 53.9 (1C), 47.9 (1C), 45.1 (1C), 45.0 (1C), 42.5 (1C), 42.0 (1C), 41.1 (1C), 40.1 (1C), 38.1 (1C), 37.6 (1C), 29.7 (1C), 23.7 (1C), 22.4 (1C), 21.0 (1C), 20.2 (1C), 17.3 (1C),

Figure 8AF

Steviol+4Glc+1GlcNAc (#11)



= ^{1}H-^{13}C HMBC

= ^{1}H-^{1}H COSY

= ^{1}H-^{1}H TOCSY spin system

= ^{1}H-^{1}H dipolar correlation (ROESY)

Assigments were made on the basis of ^{1}H-^{1}H COSY, ^{1}H-^{1}H TOCSY, ^{1}H-^{13}C HSQC-DEPT, ^{1}H-^{13}C HMBC and ^{1}H-^{1}H ROESY.

Numbering following IUPAC

Figure 8AG

Steviol+4Glc (#26)

Homonuclear diploar correlations between:
H-2 and Me-53, Me-54
H-11 and H-3, H-18
H-18 and H-4
H-68 and H-28, Me-53, H-38'
H-28 and H-38', Me-53
Me-54 and H-32"

Heteronuclear scalar correlations between:
C=O(-8) and H-2, Me-53, H-28
H-11 and C-3 (H-3 and C-11)
H-18 and C-4 (H-4 and C18)
H-56 and C-33

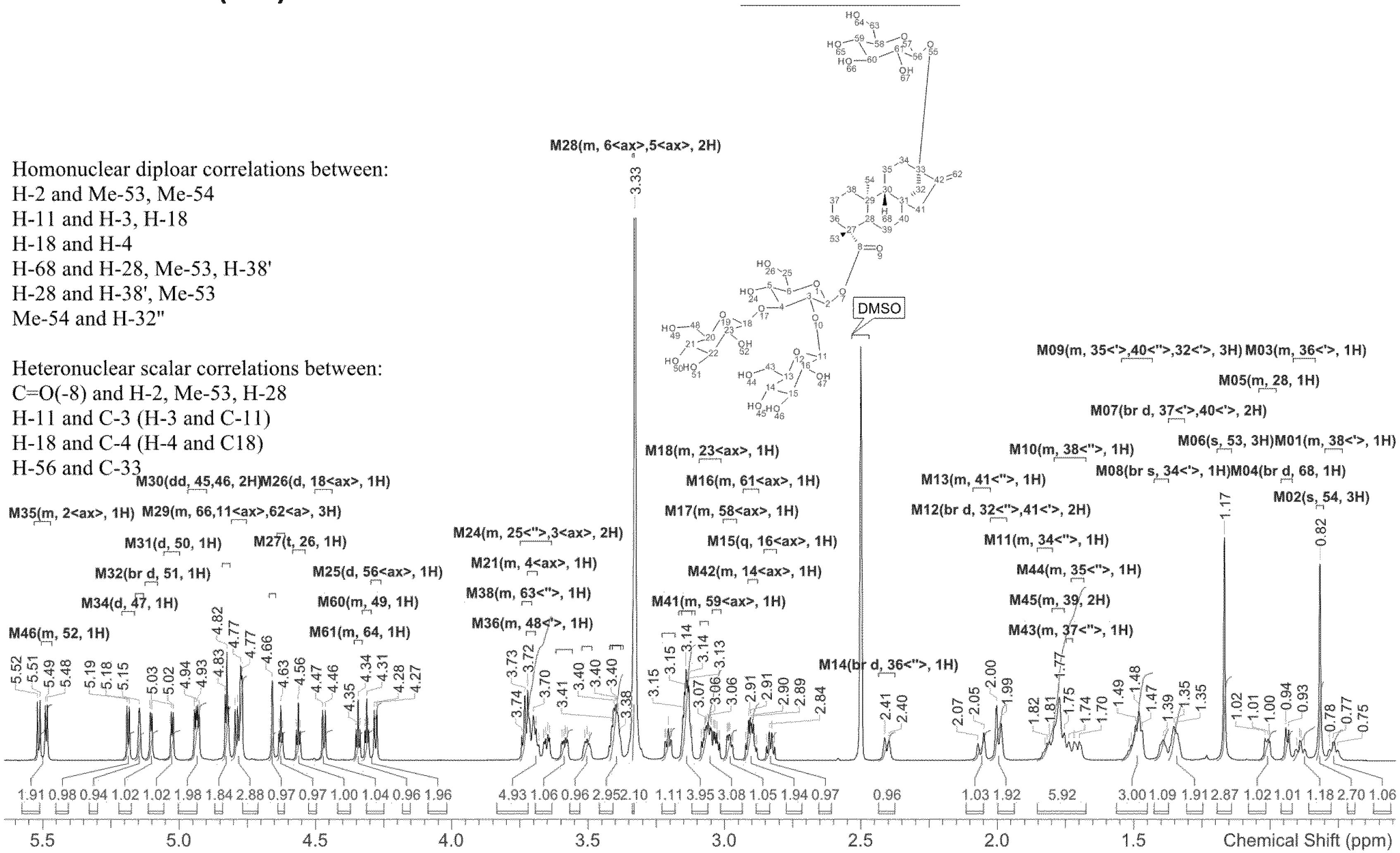
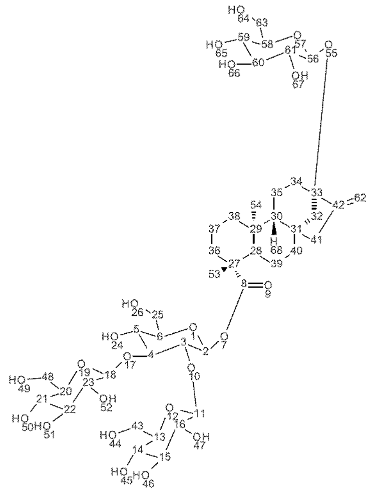


Figure 8AH

Steviol+4Glc (#26)

Multiplet1	Shift1 (ppm	Atom1	H's	Type	J (Hz)	(ppm)
M35	5.50	2<ax>	1	m	-	[5.47 .. 5.53]
M46	5.49	52	1	m	-	[5.47 .. 5.50]
M34	5.19	47	1	d	6.60	[5.16 .. 5.21]
M33	5.15	62<b>	1	br s	-	[5.13 .. 5.16]
M32	5.10	51	1	br d	4.89	[5.08 .. 5.13]
M31	5.03	50	1	d	5.38	[5.00 .. 5.06]
M30	4.93	45, 46	2	dd	8.80, 4.89	[4.90 .. 4.97]
M58	4.83	65, 67	2	m	-	[4.81 .. 4.84]
M29	4.78	66, 11<ax>, 62<a>	3	m	-	[4.75 .. 4.81]
M59	4.66	24	1	m	-	[4.65 .. 4.67]
M62	4.63	44	1	m	-	[4.61 .. 4.64]
M27	4.56	26	1	t	5.50	[4.54 .. 4.58]
M26	4.47	18<ax>	1	d	7.83	[4.44 .. 4.50]
M61	4.34	64	1	m	-	[4.33 .. 4.36]
M60	4.31	49	1	m	-	[4.30 .. 4.33]
M25	4.28	56<ax>	1	d	7.82	[4.26 .. 4.30]
M38	3.73	63<">	1	m	-	[3.71 .. 3.74]
M36	3.71	48<'>	1	m	-	[3.69 .. 3.73]
M21	3.71	4<ax>	1	m	-	[3.69 .. 3.72]
M24	3.70	25<">, 3<ax>	2	m	-	[3.63 .. 3.75]
M23	3.59	43<">	1	br dd	9.90, 5.50	[3.56 .. 3.62]
M22	3.50	25<'>	1	m	-	[3.49 .. 3.52]
M47	3.40	43<'>	1	m	-	[3.38 .. 3.42]
M37	3.40	48<">	1	m	-	[3.38 .. 3.42]
M39	3.39	63<'>	1	m	-	[3.37 .. 3.41]
M28	3.33	6<ax>, 5<ax>	2	m	-	[3.33 .. 3.34]
M20	3.21	20<ax>	1	m	-	[3.18 .. 3.23]
M19	3.14	60<ax>, 15<ax>, 22<ax>	3	m	-	[3.11 .. 3.17]
M48	3.14	13<ax>	1	m	-	[3.12 .. 3.16]
M40	3.07	21<ax>	1	m	-	[3.06 .. 3.09]
M18	3.05	23<ax>	1	m	-	[3.01 .. 3.09]
M41	3.03	59<ax>	1	m	-	[3.01 .. 3.05]
M17	2.98	58<ax>	1	m	-	[2.96 .. 3.00]
M16	2.90	61<ax>	1	m	-	[2.87 .. 2.93]
M42	2.90	14<ax>	1	m	-	[2.88 .. 2.91]
M15	2.83	16<ax>	1	q	7.99	[2.81 .. 2.85]
M14	2.40	36<">	1	br d	12.47	[2.38 .. 2.43]
M13	2.06	41<">	1	m	-	[2.03 .. 2.09]
M12	1.99	32<">, 41<'>	2	br d	13.45	[1.96 .. 2.03]
M11	1.82	34<">	1	m	-	[1.80 .. 1.85]
M45	1.78	39	2	m	-	[1.75 .. 1.80]
M10	1.75	38<">	1	m	-	[1.68 .. 1.79]
M43	1.74	37<">	1	m	-	[1.72 .. 1.75]
M44	1.71	35<">	1	m	-	[1.68 .. 1.73]
M09	1.49	35<'>, 40<">, 32<'>	3	m	-	[1.43 .. 1.54]
M08	1.39	34<'>	1	br s	-	[1.37 .. 1.42]
M07	1.35	37<'>, 40<'>	2	br d	4.40	[1.31 .. 1.37]
M06	1.17	53	3	s	-	[1.14 .. 1.19]
M05	1.01	28	1	m	-	[0.98 .. 1.04]
M04	0.94	68	1	br d	8.07	[0.92 .. 0.96]
M03	0.89	36<'>	1	m	-	[0.83 .. 0.91]
M02	0.82	54	3	s	-	[0.80 .. 0.83]
M01	0.77	38<'>	1	m	-	[0.73 .. 0.80]

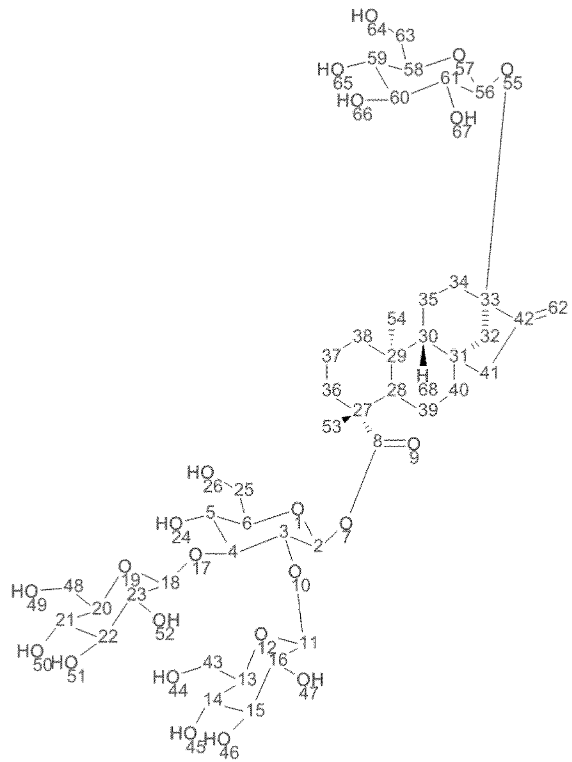


^{1}H NMR (800 MHz, *DMSO d_6*) δ ppm 0.73 - 0.80 (m, 1 H) 0.82 (s, 3 H) 0.83 - 0.91 (m, 1 H) 0.94 (br d, *J*=8.07 Hz, 1 H) 0.98 - 1.04 (m, 1 H) 1.17 (s, 3 H) 1.35 (br d, *J*=4.40 Hz, 2 H) 1.39 (br s, 1 H) 1.43 - 1.54 (m, 3 H) 1.68 - 1.79 (m, 1 H) 1.68 - 1.73 (m, 1 H) 1.72 - 1.75 (m, 1 H) 1.75 - 1.80 (m, 2 H) 1.80 - 1.85 (m, 1 H) 1.99 (br d, *J*=13.45 Hz, 2 H) 2.03 - 2.09 (m, 1 H) 2.40 (br d, *J*=12.47 Hz, 1 H) 2.83 (q, *J*=7.99 Hz, 1 H) 2.87 - 2.93 (m, 1 H) 2.88 - 2.91 (m, 1 H) 2.96 - 3.00 (m, 1 H) 3.01 - 3.09 (m, 1 H) 3.01 - 3.05 (m, 1 H) 3.06 - 3.09 (m, 1 H) 3.11 - 3.17 (m, 3 H) 3.12 - 3.16 (m, 1 H) 3.18 - 3.23 (m, 1 H) 3.33 - 3.34 (m, 2 H) 3.37 - 3.41 (m, 1 H) 3.38 - 3.42 (m, 1 H) 3.38 - 3.42 (m, 1 H) 3.49 - 3.52 (m, 1 H) 3.59 (br dd, *J*=9.90, 5.50 Hz, 1 H) 3.63 - 3.75 (m, 2 H) 3.69 - 3.72 (m, 1 H) 3.69 - 3.73 (m, 1 H) 3.71 - 3.74 (m, 1 H) 4.28 (d, *J*=7.82 Hz, 1 H) 4.30 - 4.33 (m, 1 H) 4.33 - 4.36 (m, 1 H) 4.47 (d, *J*=7.83 Hz, 1 H) 4.56 (t, *J*=5.50 Hz, 1 H) 4.61 - 4.64 (m, 1 H) 4.65 - 4.67 (m, 1 H) 4.75 - 4.81 (m, 3 H) 4.81 - 4.84 (m, 2 H) 4.93 (dd, *J*=8.80, 4.89 Hz, 2 H) 5.03 (d, *J*=5.38 Hz, 1 H) 5.10 (br d, *J*=4.89 Hz, 1 H) 5.15 (br s, 1 H) 5.19 (d, *J*=6.60 Hz, 1 H) 5.47 - 5.50 (m, 1 H) 5.47 - 5.53 (m, 1 H)

Figure 8AI

Steviol+4Glc (#26)

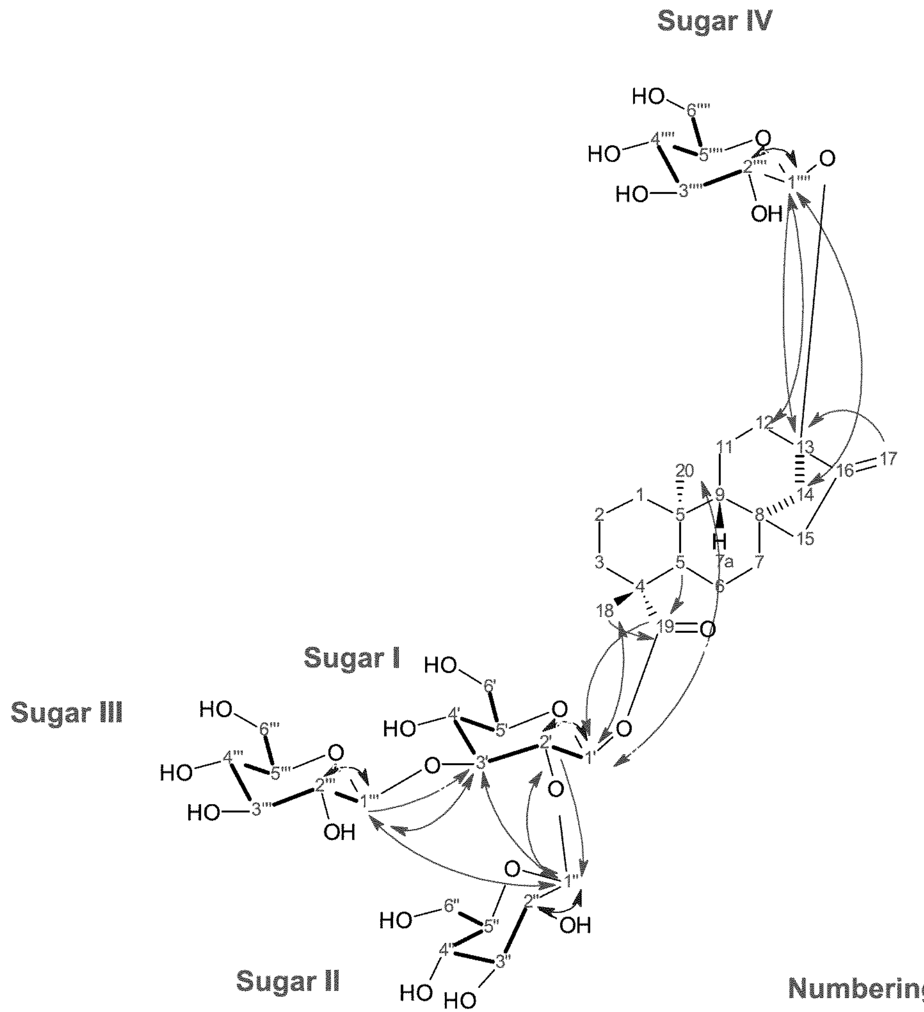
F2 Atom	δ(1H) (ppm)	F1 Atom	δ(13C) (ppm)
2<ax>	5.52	2	91.9
3<ax>	3.73	3	75.5
4<ax>	3.69	4	87
5<ax>	3.34	5	68.3
6<ax>	3.33	6	77.8
		8	174.9
11<ax>	4.79	11	101.8
13<ax>	3.14	13	77.3
14<ax>	2.89	14	71.4
15<ax>	3.14	15	77
16<ax>	2.83	16	74.3
18<ax>	4.47	18	103.3
20<ax>	3.21	20	77.3
21<ax>	3.07	21	70.3
22<ax>	3.14	22	77
23<ax>	3.06	23	74
25<''>	3.65	25	60.7
25<'>	3.5		
		27	43.6
28	1.01	28	56.7
		29	39.1
		31	41.6
32<''>	2	32	43.6
32<'>	1.48		
		33	85.8
34<''>	1.82	34	37.9
34<'>	1.39		
35<''>	1.7	35	20.1
35<'>	1.5		
36<''>	2.4	36	36.6
36<'>	0.89		
37<''>	1.74	37	19.5
37<'>	1.35		
38<''>	1.78	38	40.2
38<'>	0.77		
39	1.78	39	21.4
40<''>	1.49	40	41.3
40<'>	1.35		
41<''>	2.06	41	47.8
41<'>	2		
		42	152.6
43<''>	3.59	43	61.4
43<'>	3.39		
48<''>	3.4	48	61.3
48<'>	3.71		
53	1.17	53	28.5
54	0.82	54	16.4
56<ax>	4.28	56	98.1
58<ax>	2.98	58	76.9
59<ax>	3.03	59	70.5
60<ax>	3.14	60	77
61<ax>	2.91	61	74
62<a>	4.77	62	104.8
62<b>	5.15		
63<''>	3.73	63	62
63<'>	3.39		
68	0.94	30	53.4



^{13}C NMR (201 MHz, *DMSO d_6*) δ ppm 174.9 (1C), 152.6 (1C), 104.8 (1C), 103.3 (1C), 101.8 (1C), 98.1 (1C), 91.9 (1C), 87.0 (1C), 85.8 (1C), 77.8 (1C), 77.3 (2C), 77.0 (3C), 76.9 (1C), 75.5 (1C), 74.3 (1C), 74.0 (2C), 71.4 (1C), 70.5 (1C), 70.3 (1C), 68.3 (1C), 62.0 (1C), 61.4 (1C), 61.3 (1C), 60.7 (1C), 56.7 (1C), 53.4 (1C), 47.8 (1C), 43.6 (2C), 41.6 (1C), 41.3 (1C), 40.2 (1C), 39.1 (1C), 37.9 (1C), 36.6 (1C), 28.5 (1C), 21.4 (1C), 20.1 (1C), 19.5 (1C), 16.4 (1C)

Figure 8AJ

Steviol+4Glc (#26)



= $^{1}H-^{13}C$ HMBC

= $^{1}H-^{1}H$ COSY

= $^{1}H-^{1}H$ TOCSY spin system

= $^{1}H-^{1}H$ dipolar correlation (ROESY)

Assigments were made on the basis of $^{1}H-^{1}H$ COSY, $^{1}H-^{1}H$ TOCSY, $^{1}H-^{13}C$ HSQC-DEPT, $^{1}H-^{13}C$ HMBC and $^{1}H-^{1}H$ ROESY.

Numbering following IUPAC

Figure 8AK

Steviol+5Glc (#22)

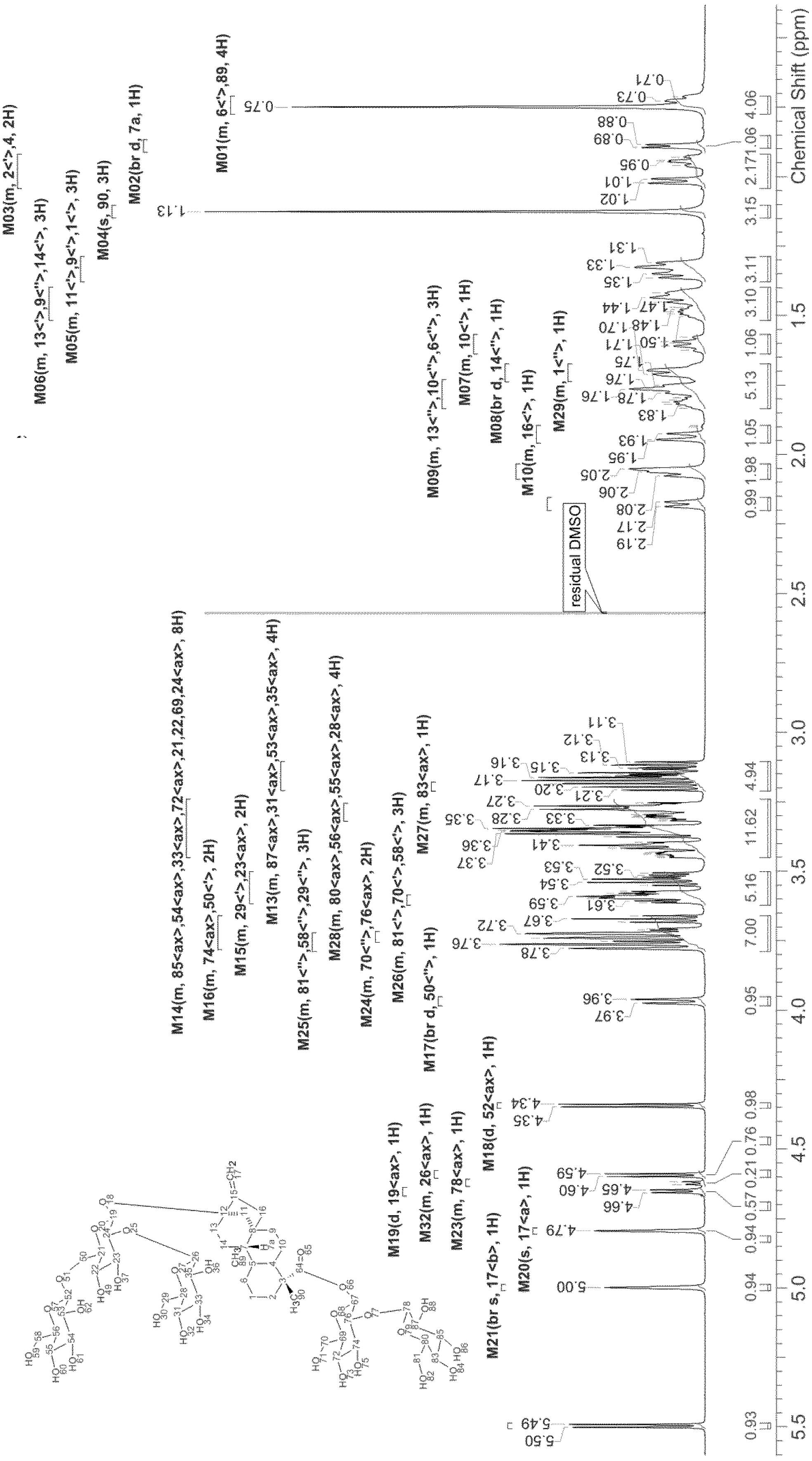
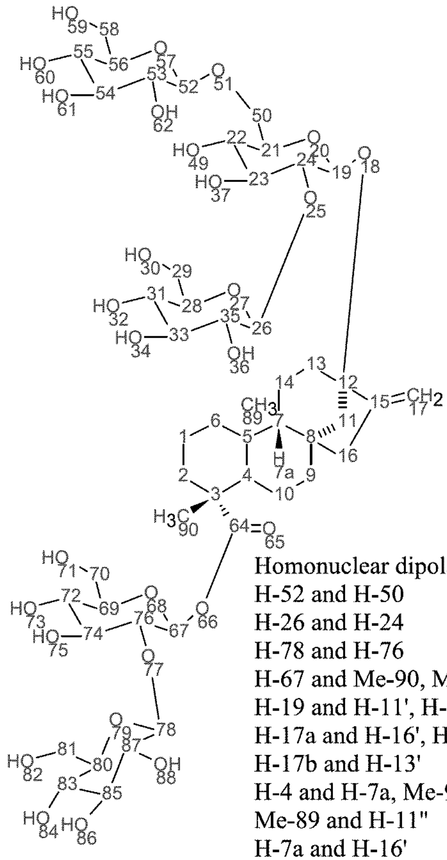


Figure 8AL

Steviol+5Glc (#22)

Multiplet1	Shift1 (ppm)	Atom1	H's	Type	J (Hz)	(ppm)
M22	5.50	67<ax>	1	d	7.82	[5.49 .. 5.51]
M21	5.00	17<b>	1	br s	-	[4.99 .. 5.01]
M20	4.79	17<a>	1	s	-	[4.78 .. 4.81]
M19	4.65	19<ax>	1	d	7.82	[4.64 .. 4.67]
M23	4.62	78<ax>	1	m	-	[4.61 .. 4.64]
M32	4.59	26<ax>	1	m	-	[4.58 .. 4.61]
M18	4.34	52<ax>	1	d	8.07	[4.33 .. 4.35]
M17	3.97	50<">	1	br d	10.51	[3.95 .. 3.98]
M25	3.76	81<">, 58<">, 29<">	3	m	-	[3.72 .. 3.79]
M24	3.74	70<">, 76<ax>	2	m	-	[3.72 .. 3.76]
M16	3.73	74<ax>, 50<'>	2	m	-	[3.66 .. 3.78]
M26	3.60	81<'>, 70<'>, 58<'>	3	m	-	[3.58 .. 3.62]
M15	3.57	29<'>, 23<ax>	2	m	-	[3.50 .. 3.62]
M14	3.34	85<ax>, 54<ax>, 33<ax>, 72<ax>, 21, 22, 69, 24<ax>	8	m	-	[3.24 .. 3.45]
M28	3.29	80<ax>, 56<ax>, 55<ax>, 28<ax>	4	m	-	[3.26 .. 3.32]
M27	3.20	83<ax>	1	m	-	[3.18 .. 3.21]
M13	3.16	87<ax>, 31<ax>, 53<ax>, 35<ax>	4	m	-	[3.11 .. 3.21]
M12	2.18	2<">	1	br d	13.20	[2.16 .. 2.20]
M11	2.06	11<">, 16<">	2	m	-	[2.03 .. 2.09]
M10	1.93	16<'>	1	m	-	[1.90 .. 1.96]
M09	1.78	13<">, 10<">, 6<">	3	m	-	[1.73 .. 1.84]
M29	1.71	1<">	1	m	-	[1.67 .. 1.74]
M08	1.70	14<">	1	br d	10.51	[1.67 .. 1.74]
M07	1.60	10<'>	1	m	-	[1.57 .. 1.64]
M06	1.46	13<'>, 9<">, 14<'>	3	m	-	[1.40 .. 1.52]
M05	1.34	11<'>, 9<'>, 1<'>	3	m	-	[1.29 .. 1.38]
M04	1.13	90	3	s	-	[1.10 .. 1.15]
M03	0.98	2<'>, 4	2	m	-	[0.92 .. 1.04]
M02	0.89	7a	1	br d	7.83	[0.87 .. 0.91]
M01	0.75	6<'>, 89	4	m	-	[0.71 .. 0.77]



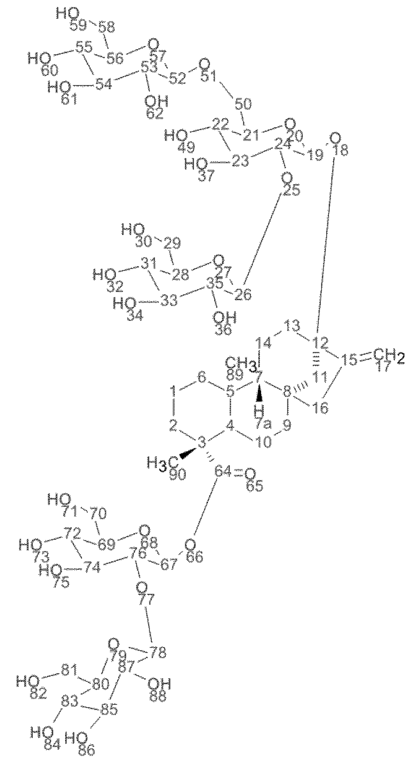
Homonuclear dipolar correlations between:
H-52 and H-50
H-26 and H-24
H-78 and H-76
H-67 and Me-90, Me-89
H-19 and H-11', H-13", H-16"
H-17a and H-16', H-16"
H-17b and H-13'
H-4 and H-7a, Me-90
Me-89 and H-11"
H-7a and H-16'

[1]H NMR (800 MHz, *DEUTERIUM OXIDE*) δ ppm 0.71 - 0.77 (m, 4 H) 0.89 (br d, J=7.83 Hz, 1 H) 0.92 - 1.04 (m, 2 H) 1.13 (s, 3 H) 1.29 - 1.38 (m, 3 H) 1.40 - 1.52 (m, 3 H) 1.57 - 1.64 (m, 1 H) 1.70 (br d, J=10.51 Hz, 1 H) 1.67 - 1.74 (m, 1 H) 1.73 - 1.84 (m, 3 H) 1.90 - 1.96 (m, 1 H) 2.03 - 2.09 (m, 2 H) 2.18 (br d, J=13.20 Hz, 1 H) 3.11 - 3.21 (m, 4 H) 3.18 - 3.21 (m, 1 H) 3.24 - 3.45 (m, 8 H) 3.26 - 3.32 (m, 4 H) 3.50 - 3.62 (m, 2 H) 3.58 - 3.62 (m, 3 H) 3.66 - 3.78 (m, 2 H) 3.72 - 3.76 (m, 2 H) 3.72 - 3.79 (m, 3 H) 3.97 (br d, J=10.51 Hz, 1 H) 4.34 (d, J=8.07 Hz, 1 H) 4.58 - 4.61 (m, 1 H) 4.61 - 4.64 (m, 1 H) 4.65 (d, J=7.82 Hz, 1 H) 4.79 (s, 1 H) 5.00 (br s, 1 H) 5.50 (d, J=7.82 Hz, 1 H)

Figure 8AM

Steviol+5Glc (#22)

F2 Atom	δ(1H) (ppm)	F1 Atom	δ(13C) (ppm)
1<">	1.71	1	18.9
1<'>	1.32		
2<">	2.18	2	36.6
2<'>	0.95		
		3	44
4	1.02	4	56.6
		5	39
6<">	1.76	6	39.8
6<'>	0.73		
7a	0.89	7	52.9
9<">	1.44	9	40.7
9<'>	1.33		
10<">	1.77	10	21.2
10<'>	1.6		
11<">	2.06	11	44
11<'>	1.36		
		12	87.4
13<">	1.81	13	36.6
13<'>	1.42		
14<">	1.71	14	19.9
14<'>	1.49		
		15	153.1
16<">	2.07	16	46.8
16<'>	1.93		
17<a>	4.79	17	104.3
17<b>	5		
19<ax>	4.65	19	95.5
21	3.41	21	74.5
22	3.36	22	69
23<ax>	3.54	23	76
24<ax>	3.41	24	74.5
26<ax>	4.59	26	102.7
28<ax>	3.28	28	76.1
29<">	3.73	29	61
29<'>	3.52	29	61
31<ax>	3.15	31	69.9
33<ax>	3.35	33	75.3
35<ax>	3.16	35	74.1
50<">	3.97	50	68.2
50<'>	3.72		
52<ax>	4.34	52	102.5
53<ax>	3.17	53	72.9
54<ax>	3.35	54	75.3
55<ax>	3.27	55	69.4
56<ax>	3.3	56	75.8
58<">	3.77	58	60.7
58<'>	3.59		
		64	178
67<ax>	5.5	67	92.2
69	3.44	69	76.4
70<">	3.73	70	60.4
70<'>	3.6		
72<ax>	3.36	72	69
74<ax>	3.67	74	75.8
76<ax>	3.75	76	78
78<ax>	4.62	78	102.4
80<ax>	3.28	80	76.1
81<">	3.77	81	60.7
81<'>	3.59		
83<ax>	3.2	83	69.7

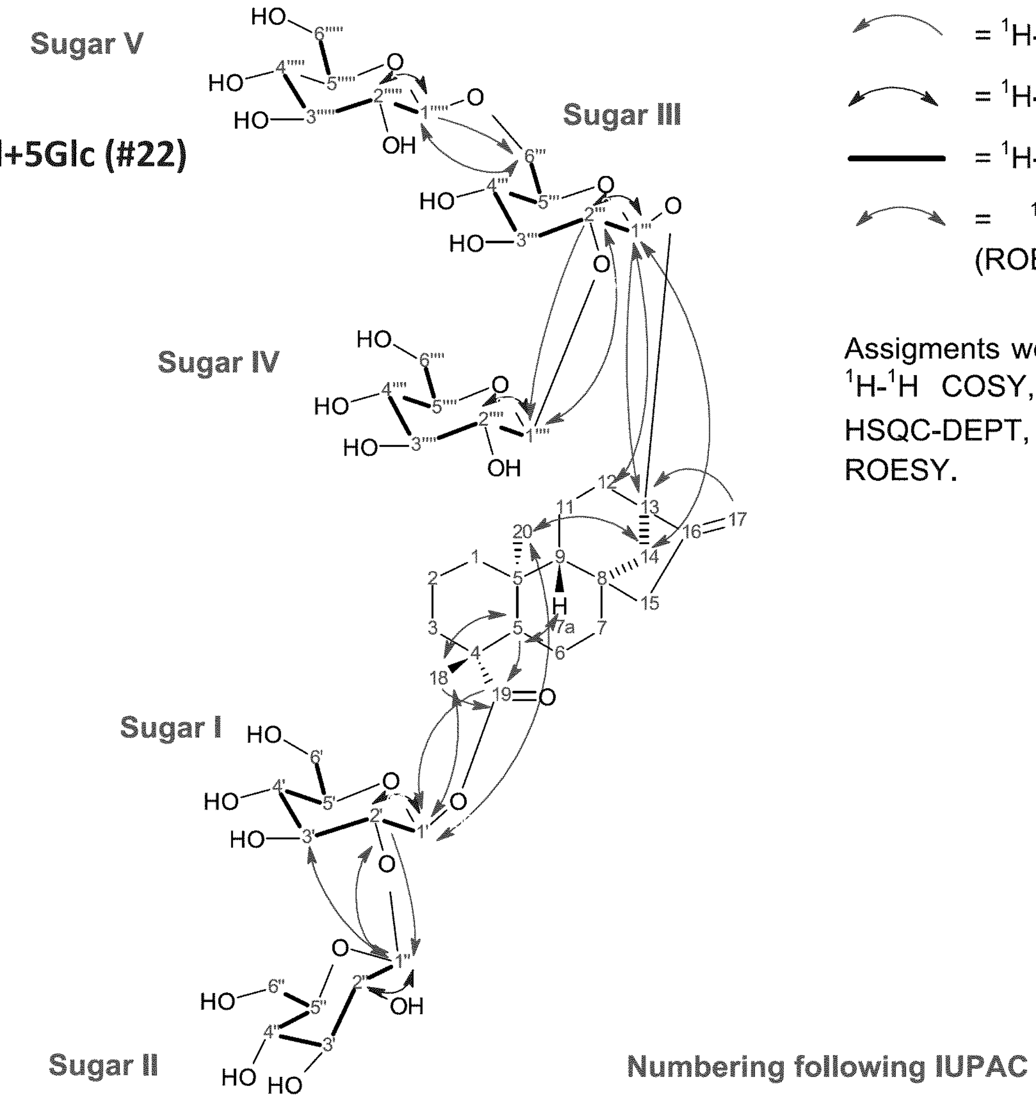


Heteronuclear scalar correlations between:
C=O(64) and H-67, Me-90, H-4
C-12 and H-19, H-17a/b
H-26 and C-24 (C-26 and H-24)
H-52 and C-50 (C-52 and H-50)
H-78 and C-76 (C-78 and H-76)

^{13}C NMR (201 MHz, *DEUTERIUM OXIDE*) δ ppm 178.0 (1C), 153.1 (1C), 104.3 (1C), 102.7 (1C), 102.5 (1C), 102.4 (1C), 95.5 (1C), 92.2 (1C), 87.4 (1C), 78.0 (1C), 76.4 (1C), 76.1 (2C), 76.0 (1C), 75.8 (2C), 75.3 (3C), 74.5 (2C), 74.1 (1C), 73.8 (1C), 72.9 (1C), 69.9 (1C), 69.7 (1C), 69.4 (1C), 69.0 (2C), 68.2 (1C), 61.0 (2C), 60.7 (2C), 60.4 (1C), 56.6 (1C), 52.9 (1C), 46.8 (1C), 44.0 (2C), 40.7 (1C), 39.8 (1C), 39.0 (1C), 36.6 (1C), 36.6 (1C), 28.4 (1C), 21.2 (1C), 19.9 (1C), 18.9 (1C), 15.8 (1C)

Figure 8AN

Steviol+5Glc (#22)



= ^{1}H-^{13}C HMBC

= ^{1}H-^{1}H COSY

= ^{1}H-^{1}H TOCSY spin system

= ^{1}H-^{1}H dipolar correlation (ROESY)

Assigments were made on the basis of ^{1}H-^{1}H COSY, ^{1}H-^{1}H TOCSY, ^{1}H-^{13}C HSQC-DEPT, ^{1}H-^{13}C HMBC and ^{1}H-^{1}H ROESY.

Figure 8AO

Steviol+7Glc (#14)

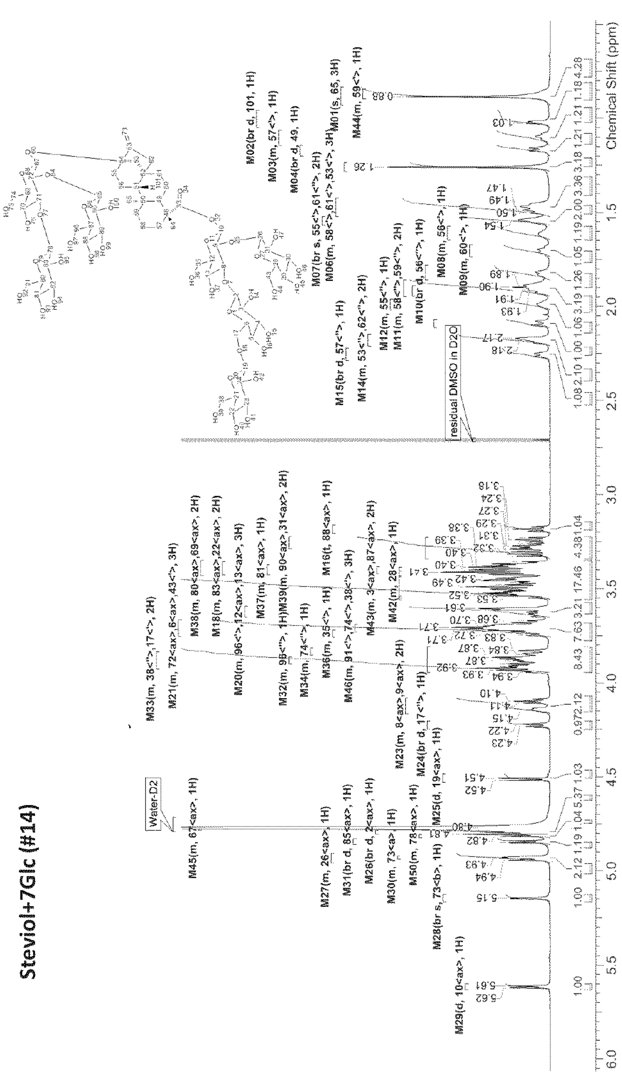


Figure 8AP

Steviol+7Glc (#14)

Multiplet1	Shift1 (ppm)	Atom1	H's	Type	J (Hz)	(ppm)
M29	5.62	10<ax>	1	d	7.83	[5.60 .. 5.63]
M28	5.15	73<b>	1	br s	-	[5.13 .. 5.17]
M27	4.93	26<ax>	1	m	-	[4.91 .. 4.96]
M30	4.93	73<a>	1	m	-	[4.92 .. 4.94]
M31	4.85	85<ax>	1	br d	7.83	[4.83 .. 4.86]
M50	4.82	78<ax>	1	m	-	[4.81 .. 4.82]
M26	4.80	2<ax>	1	br d	8.56	[4.78 .. 4.81]
M45	4.78	67<ax>	1	m	-	[4.78 .. 4.79]
M25	4.51	19<ax>	1	d	8.07	[4.49 .. 4.53]
M24	4.23	17<">	1	br d	10.03	[4.20 .. 4.25]
M23	4.12	8<ax>, 9<ax>	2	m	-	[4.08 .. 4.17]
M22	3.89	71<ax>, 43<">	2	m	-	[3.81 .. 3.95]
M35	3.88	91<">, 35<">	2	m	-	[3.84 .. 3.93]
M33	3.88	38<">, 17<'>	2	m	-	[3.84 .. 3.93]
M32	3.88	96<">	1	m	-	[3.86 .. 3.90]
M34	3.83	74<">	1	m	-	[3.82 .. 3.85]
M36	3.74	35<'>	1	m	-	[3.72 .. 3.76]
M46	3.71	91<'>, 74<'>, 38<'>	3	m	-	[3.69 .. 3.73]
M21	3.71	72<ax>, 6<ax>, 43<'>	3	m	-	[3.67 .. 3.75]
M20	3.62	96<'>, 12<ax>, 13<ax>	3	m	-	[3.59 .. 3.65]
M19	3.49	5<ax>	1	m	-	[3.44 .. 3.54]
M40	3.47	82<ax>, 70<ax>, 23<ax>	3	m	-	[3.39 .. 3.56]
M41	3.47	89<ax>, 21<ax>, 4<ax>, 30<ax	4	m	-	[3.39 .. 3.55]
M42	3.42	28<ax>	1	m	-	[3.41 .. 3.43]
M43	3.40	3<ax>, 87<ax>	2	m	-	[3.38 .. 3.42]
M37	3.40	81<ax>	1	m	-	[3.37 .. 3.43]
M18	3.39	83<ax>, 22<ax>	2	m	-	[3.36 .. 3.43]
M38	3.39	80<ax>, 69<ax>	2	m	-	[3.35 .. 3.43]
M17	3.28	24<ax>, 29<ax>	2	m	-	[3.23 .. 3.34]
M39	3.26	90<ax>, 31<ax>	2	m	-	[3.22 .. 3.29]
M16	3.18	88<ax>	1	t	9.41	[3.16 .. 3.21]
M15	2.26	57<">	1	br d	12.23	[2.22 .. 2.29]
M14	2.18	53<">, 62<">	2	m	-	[2.15 .. 2.21]
M13	2.09	62<'>	1	br d	17.12	[2.07 .. 2.11]
M12	1.99	55<">	1	m	-	[1.96 .. 2.02]
M47	1.92	60<">	1	m	-	[1.89 .. 1.95]
M11	1.90	58<">, 59<">	2	m	-	[1.86 .. 1.95]
M10	1.82	56<">	1	br d	9.78	[1.78 .. 1.86]
M09	1.70	60<'>	1	m	-	[1.67 .. 1.73]
M08	1.61	56<'>	1	m	-	[1.57 .. 1.65]
M07	1.54	55<'>, 61<">	2	br s	-	[1.52 .. 1.57]
M06	1.48	58<'>, 61<'>, 53<'>	3	m	-	[1.42 .. 1.52]
M05	1.26	64	3	s	-	[1.24 .. 1.28]
M04	1.16	49	1	br d	12.72	[1.14 .. 1.20]
M03	1.10	57<'>	1	m	-	[1.06 .. 1.14]
M02	1.02	101	1	br d	7.58	[0.96 .. 1.05]
M01	0.88	65	3	s	-	[0.83 .. 0.93]
M44	0.87	59<'>	1	m	-	[0.84 .. 0.90]

H

Homonuclear dipolar correlations between:
H-26 and H-9
H-2 and H-8
H-19 and H-17
H-85 and H-72
H-78 and H-71
H-10 and Me-65, Me-64
H-67 and H-53', H-55"
H-101 and H-49
H-49 and H-59', H-101, Me-64
Me-65 and H-60', H-53", H-53' (indirect)
Me-64 and H-60"

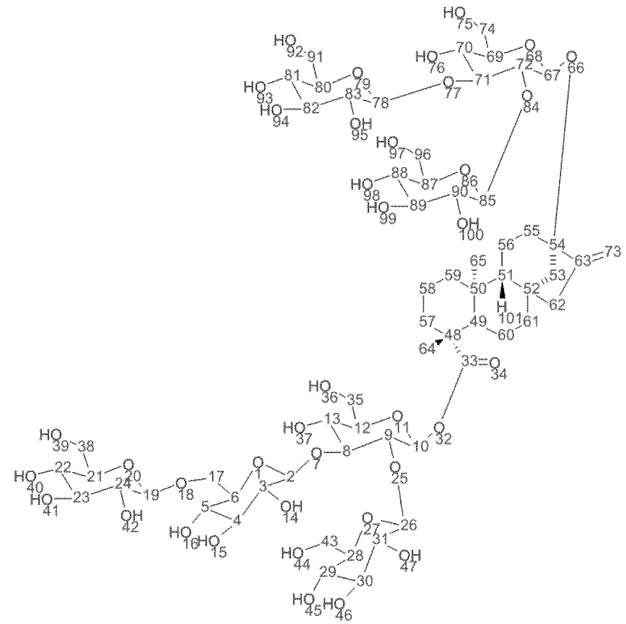
[1]H NMR (800 MHz, *DEUTERIUM OXIDE*) δ ppm 0.88 (s, 3 H) 0.84 - 0.90 (m, 1 H) 1.02 (br d, *J*=7.58 Hz, 1 H) 1.06 - 1.14 (m, 1 H) 1.16 (br d, *J*=12.72 Hz, 1 H) 1.26 (s, 3 H) 1.42 - 1.52 (m, 3 H) 1.54 (br s, 2 H) 1.57 - 1.65 (m, 1 H) 1.67 - 1.73 (m, 1 H) 1.82 (br d, *J*=9.78 Hz, 1 H) 1.86 - 1.95 (m, 2 H) 1.89 - 1.95 (m, 1 H) 1.96 - 2.02 (m, 1 H) 2.09 (br d, *J*=17.12 Hz, 1 H) 2.15 - 2.21 (m, 2 H) 2.26 (br d, *J*=12.23 Hz, 1 H) 3.18 (t, *J*=9.41 Hz, 1 H) 3.22 - 3.29 (m, 2 H) 3.23 - 3.34 (m, 2 H) 3.35 - 3.43 (m, 2 H) 3.36 - 3.43 (m, 2 H) 3.37 - 3.43 (m, 1 H) 3.38 - 3.42 (m, 2 H) 3.39 - 3.56 (m, 3 H) 3.39 - 3.55 (m, 4 H) 3.41 - 3.43 (m, 1 H) 3.44 - 3.54 (m, 1 H) 3.59 - 3.65 (m, 3 H) 3.67 - 3.75 (m, 3 H) 3.69 - 3.73 (m, 3 H) 3.72 - 3.76 (m, 1 H) 3.81 - 3.95 (m, 2 H) 3.82 - 3.85 (m, 1 H) 3.84 - 3.93 (m, 2 H) 3.84 - 3.93 (m, 2 H) 3.86 - 3.90 (m, 1 H) 4.08 - 4.17 (m, 2 H) 4.23 (br d, *J*=10.03 Hz, 1 H) 4.51 (d, *J*=8.07 Hz, 1 H) 4.78 - 4.79 (m, 1 H) 4.80 (br d, *J*=8.56 Hz, 1 H) 4.81 - 4.82 (m, 1 H) 4.85 (br d, *J*=7.83 Hz, 1 H) 4.91 - 4.96 (m, 1 H) 4.92 - 4.94 (m, 1 H) 5.15 (br s, 1 H) 5.62 (d, *J*=7.83 Hz, 1 H)

Figure 8AQ

Steviol+7Glc (#14)

F2 Atom	δ(1H) (ppm)	F1 Atom	δ(13C) (ppm)
2<ax>	4.8	2	102.9
3<ax>	3.4	3	77.1
4<ax>	3.52	4	76.7
5<ax>	3.49	5	70.4
6<ax>	3.71	6	75.6
8<ax>	4.14	8	86.3
9<ax>	4.1	9	76.6
10<ax>	5.62	10	93.4
12<ax>	3.61	12	76.9
13<ax>	3.61	13	69
17<">	4.23	17	69.5
17<'>	3.86		
19<ax>	4.51	19	103.4
21<ax>	3.45	21	76.7
22<ax>	3.39	22	70.3
23<ax>	3.49	23	76.4
24<ax>	3.32	24	73.9
26<ax>	4.94	26	102.4
28<ax>	3.41	28	76.9
29<ax>	3.29	29	71.3
30<ax>	3.45	30	76.7
31<ax>	3.24	31	74.7
		33	179.3
35<">	3.87	35	61.3
35<'>	3.74		
38<">	3.91		
38<'>	3.71	38	61.4
43<">	3.93	43	62.4
43<'>	3.7		

		48	44.7
49	1.16	49	57.4
		50	39.8
		52	41.9
53<">	2.17	53	44.6
53<'>	1.49		
		54	88.8
55<">	1.99	55	37.8
55<'>	1.54		
56<">	1.82	56	20.5
56<'>	1.61		
57<">	2.26	57	37.5
57<'>	1.1		
58<">	1.88	58	19.7
58<'>	1.46		
59<">	1.89	59	40.5
59<'>	0.87		
60<">	1.92	60	22.5
60<'>	1.7		
61<">	1.55	61	41.8
61<'>	1.47		
62<">	2.18	62	47.2
62<'>	2.09		
		63	153.5
64	1.26	64	28.8
65	0.88	65	16.8
67<ax>	4.78	67	96.1
69<ax>	3.37	69	74.3
70<ax>	3.5	70	69.2
71<ax>	3.93	71	86
72<ax>	3.68	72	79.5



Heteronuclear scalar correlations between:
C=O(33) and H-10
C-54 and H-67
H-26 and C-9 (C-26 and H-9)
H-2 and C-8 (C-2 and H-8)
H-19 and C-17 (C-19 and H-17)
H-85 and C-72 (C-85 and H-72)
H-78 and C-71 (C-78 and H-71)

^{13}C NMR (201 MHz, *DEUTERIUM OXIDE*) δ ppm 179.3 (1C), 153.5 (1C), 105.1 (1C), 103.4 (1C), 103.0 (1C), 102.9 (2C), 102.4 (1C), 96.1 (1C), 93.4 (1C), 88.8 (1C), 86.3 (1C), 86.0 (1C), 79.5 (1C), 77.1 (2C), 76.9 (2C), 76.7 (4C), 76.6 (1C), 76.4 (2C), 76.0 (1C), 75.6 (1C), 75.0 (1C), 74.7 (1C), 74.3 (1C), 74.1 (1C), 73.9 (1C), 71.4 (1C), 71.3 (1C), 70.4 (1C), 70.3 (2C), 69.5 (1C), 69.2 (1C), 69.0 (1C), 62.4 (1C), 62.3 (1C), 61.4 (2C), 61.3 (2C), 57.4 (1C), 53.8 (1C), 47.2 (1C), 44.7 (1C), 44.6 (1C), 41.9 (1C), 41.8 (1C), 40.5 (1C), 39.8 (1C), 37.8 (1C), 37.5 (1C), 28.8 (1C), 22.5 (1C), 20.5 (1C), 19.7 (1C), 16.8 (1C)

Figure 8AR

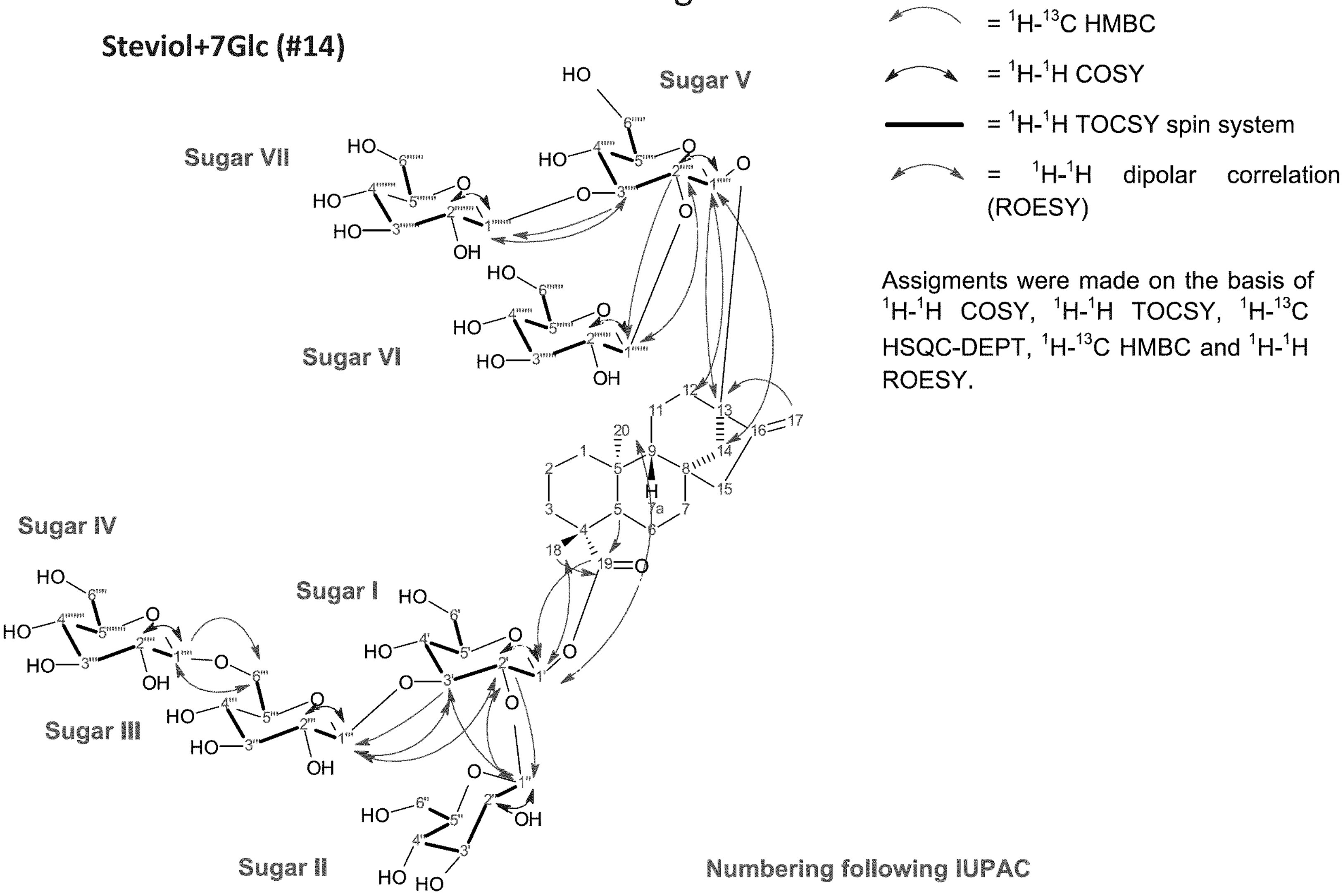

Steviol+7Glc (#14)
Sugar I
Sugar II
Sugar III
Sugar IV
Sugar V
Sugar VI
Sugar VII
= ^1H-^{13}C HMBC
= ^1H-^1H COSY
= ^1H-^1H TOCSY spin system
= ^1H-^1H dipolar correlation (ROESY)
Assigments were made on the basis of ^1H-^1H COSY, ^1H-^1H TOCSY, ^1H-^{13}C HSQC-DEPT, ^1H-^{13}C HMBC and ^1H-^1H ROESY.
Numbering following IUPAC

Figure 9A

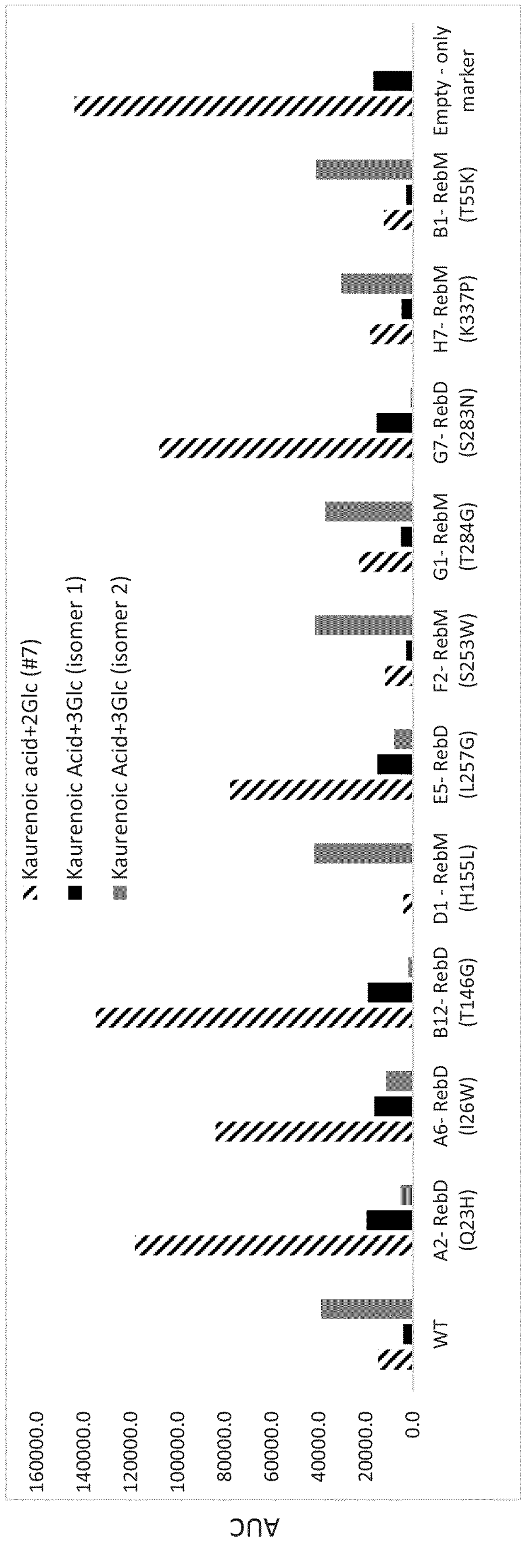

Kaurenoic acid+2Glc (#7)
Kaurenoic Acid+3Glc (isomer 1)
Kaurenoic Acid+3Glc (isomer 2)
AUC
160000.0
140000.0
120000.0
100000.0
80000.0
60000.0
40000.0
20000.0
0.0
WT
A2- RebD (Q23H)
A6- RebD (I26W)
B12- RebD (T146G)
D1 - RebM (H155L)
E5- RebD (L257G)
F2- RebM (S253W)
G1- RebM (T284G)
G7- RebD (S283N)
H7- RebM (K337P)
B1- RebM (T55K)
Empty - only marker

Figure 9B

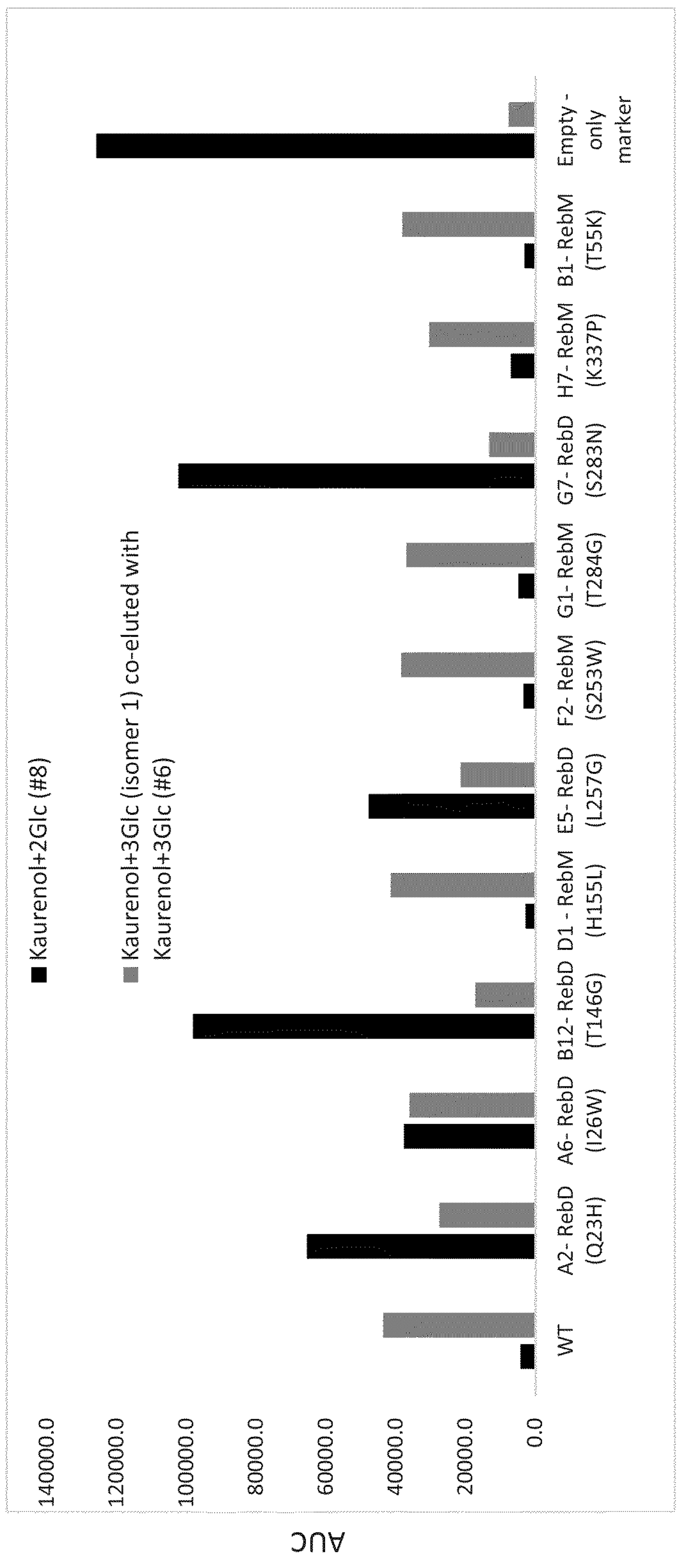

Kaurenol+2Glc (#8)
Kaurenol+3Glc (isomer 1) co-eluted with Kaurenol+3Glc (#6)
AUC
140000.0
120000.0
100000.0
80000.0
60000.0
40000.0
20000.0
0.0
WT
A2- RebD (Q23H)
A6- RebD (I26W)
B12- RebD (T146G)
D1 - RebM (H155L)
E5- RebD (L257G)
F2- RebM (S253W)
G1- RebM (T284G)
G7- RebD (S283N)
H7- RebM (K337P)
B1- RebM (T55K)
Empty - only marker

Figure 10A

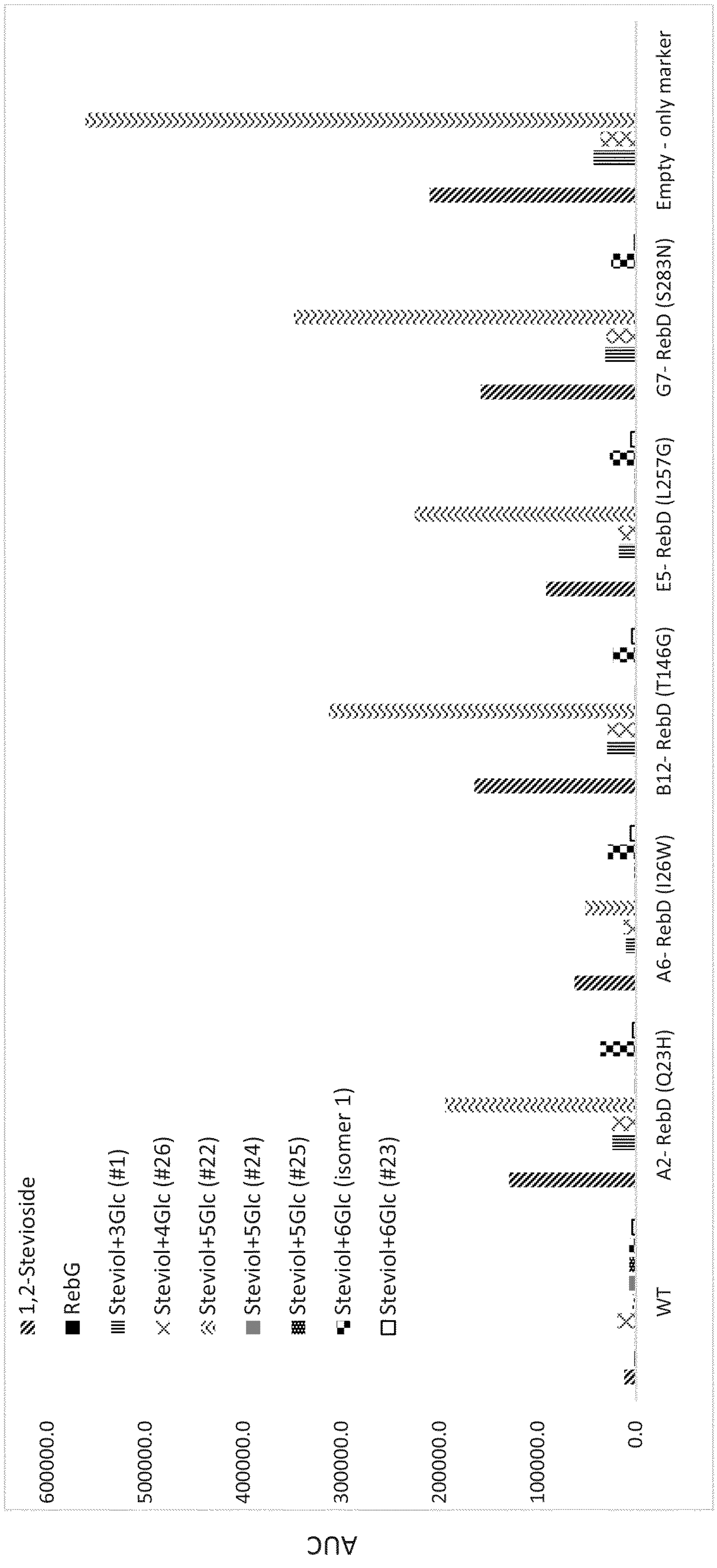

1,2-Stevioside
RebG
Steviol+3Glc (#1)
Steviol+4Glc (#26)
Steviol+5Glc (#22)
Steviol+5Glc (#24)
Steviol+5Glc (#25)
Steviol+6Glc (isomer 1)
Steviol+6Glc (#23)
600000.0
500000.0
400000.0
300000.0
200000.0
100000.0
0.0
AUC
WT
A2- RebD (Q23H)
A6- RebD (I26W)
B12- RebD (T146G)
E5- RebD (L257G)
G7- RebD (S283N)
Empty - only marker

Figure 10B

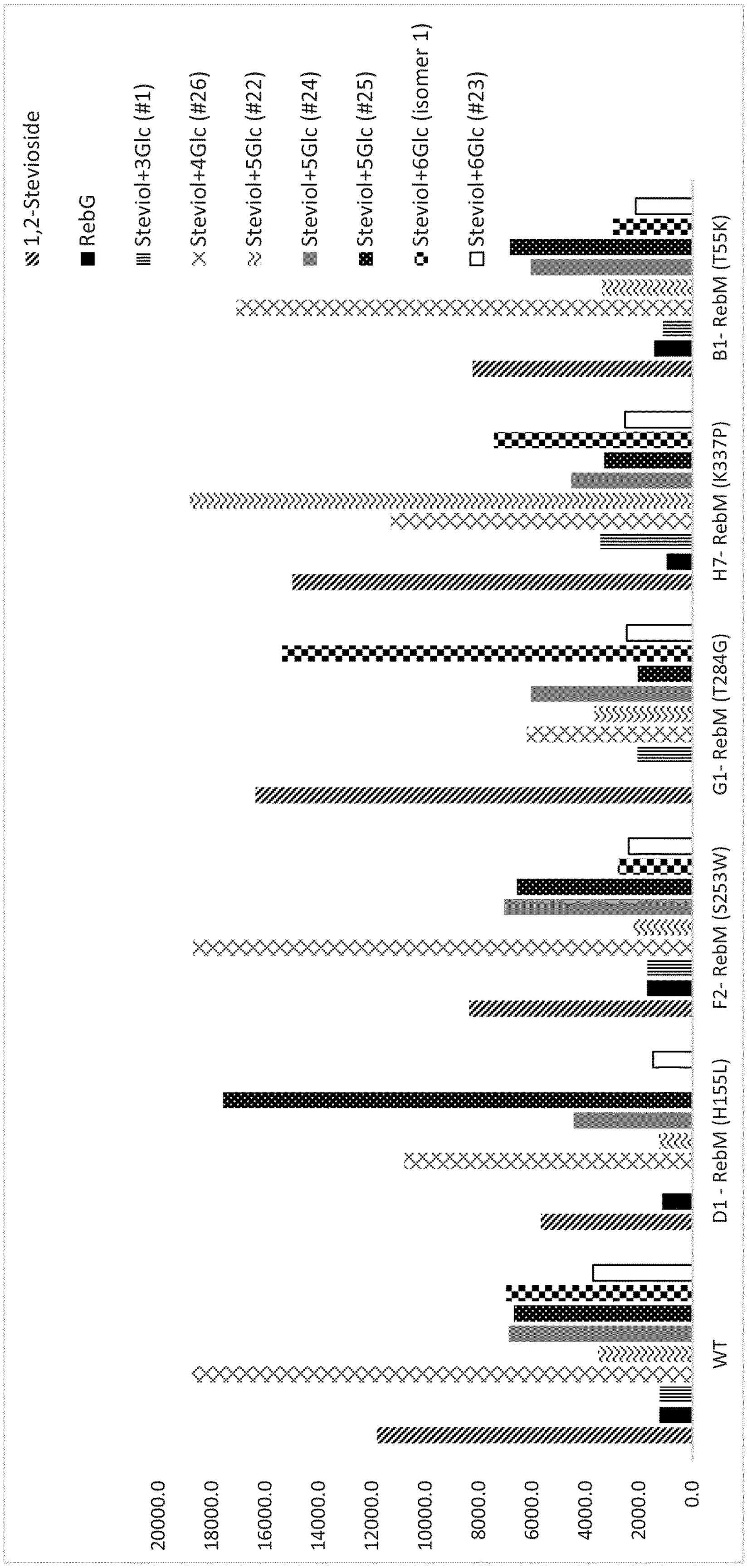

1,2-Stevioside
RebG
Steviol+3Glc (#1)
Steviol+4Glc (#26)
Steviol+5Glc (#22)
Steviol+5Glc (#24)
Steviol+5Glc (#25)
Steviol+6Glc (isomer 1)
Steviol+6Glc (#23)
WT
D1 - RebM (H155L)
F2- RebM (S253W)
G1- RebM (T284G)
H7- RebM (K337P)
B1- RebM (T55K)
20000.0
18000.0
16000.0
14000.0
12000.0
10000.0
8000.0
6000.0
4000.0
2000.0
0.0
AUC

Figure 10C

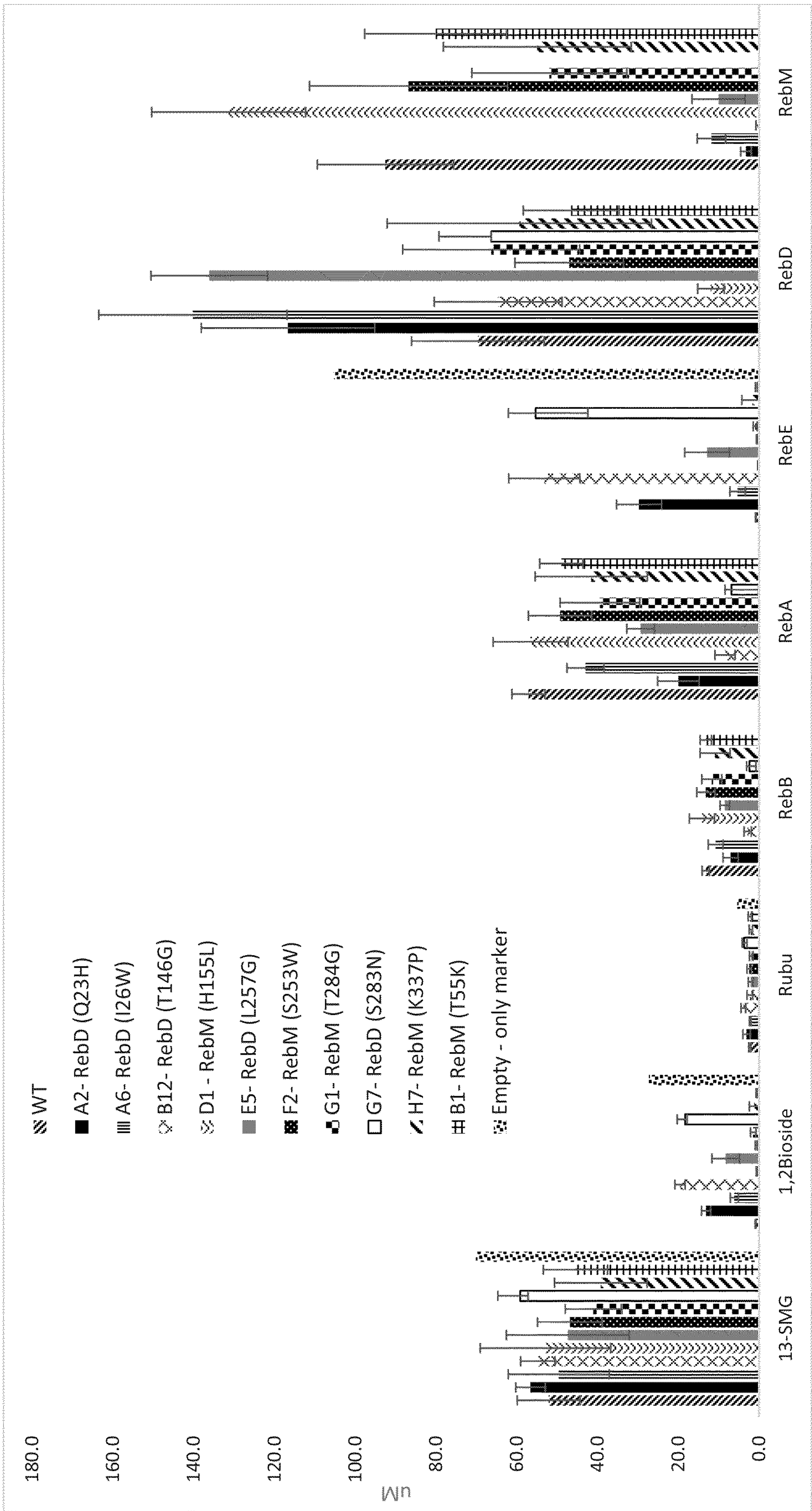

WT
A2- RebD (Q23H)
A6- RebD (I26W)
B12- RebD (T146G)
D1 - RebM (H155L)
E5- RebD (L257G)
F2- RebM (S253W)
G1- RebM (T284G)
G7- RebD (S283N)
H7- RebM (K337P)
B1- RebM (T55K)
Empty - only marker
uM
180.0
160.0
140.0
120.0
100.0
80.0
60.0
40.0
20.0
0.0
13-SMG
1,2Bioside
Rubu
RebB
RebA
RebE
RebD
RebM

Figure 11A

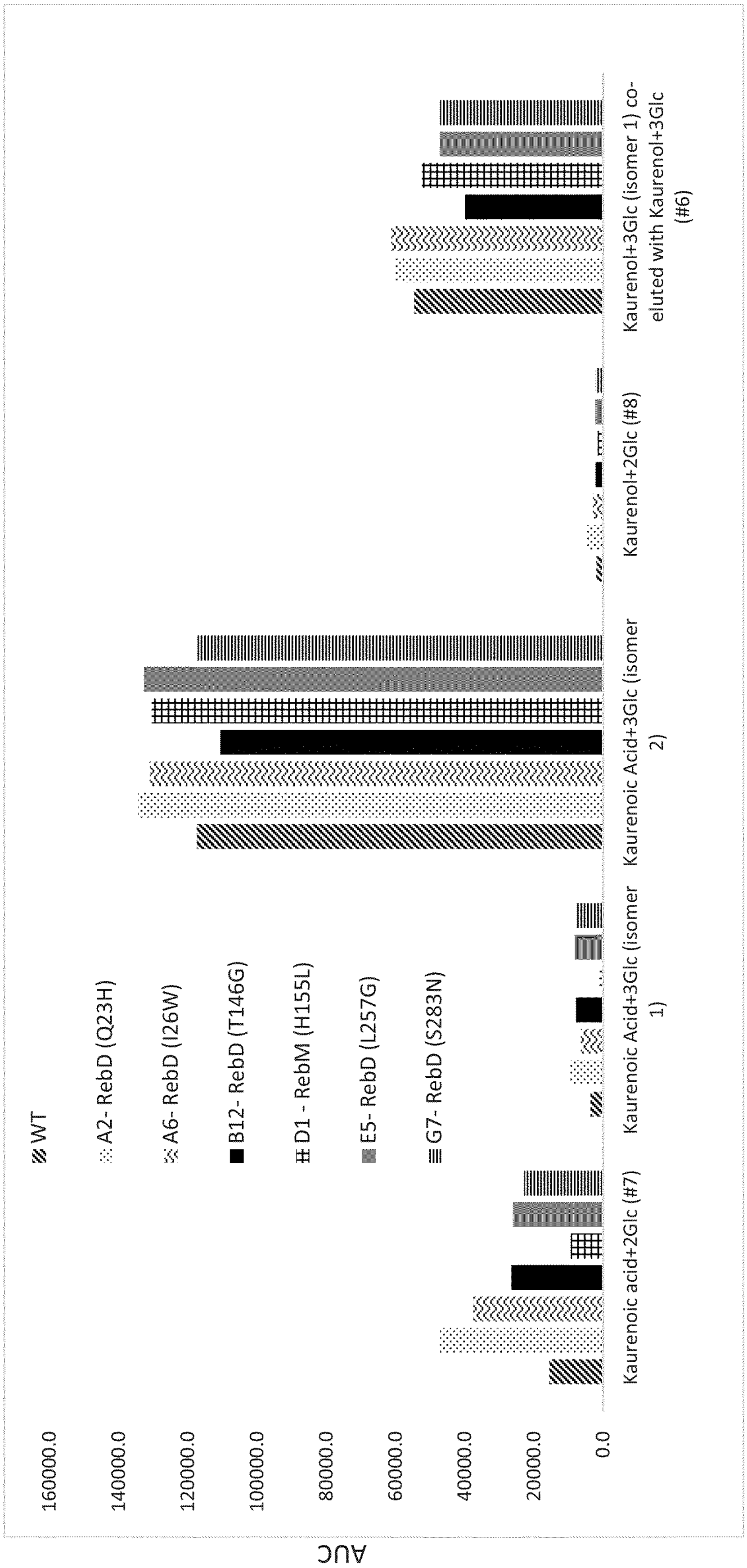

AUC
160000.0
140000.0
120000.0
100000.0
80000.0
60000.0
40000.0
20000.0
0.0
WT
A2- RebD (Q23H)
A6- RebD (I26W)
B12- RebD (T146G)
D1 - RebM (H155L)
E5- RebD (L257G)
G7- RebD (S283N)
Kaurenoic acid+2Glc (#7)
Kaurenoic Acid+3Glc (isomer 1)
Kaurenoic Acid+3Glc (isomer 2)
Kaurenol+2Glc (#8)
Kaurenol+3Glc (isomer 1) co-eluted with Kaurenol+3Glc (#6)

Figure 11B

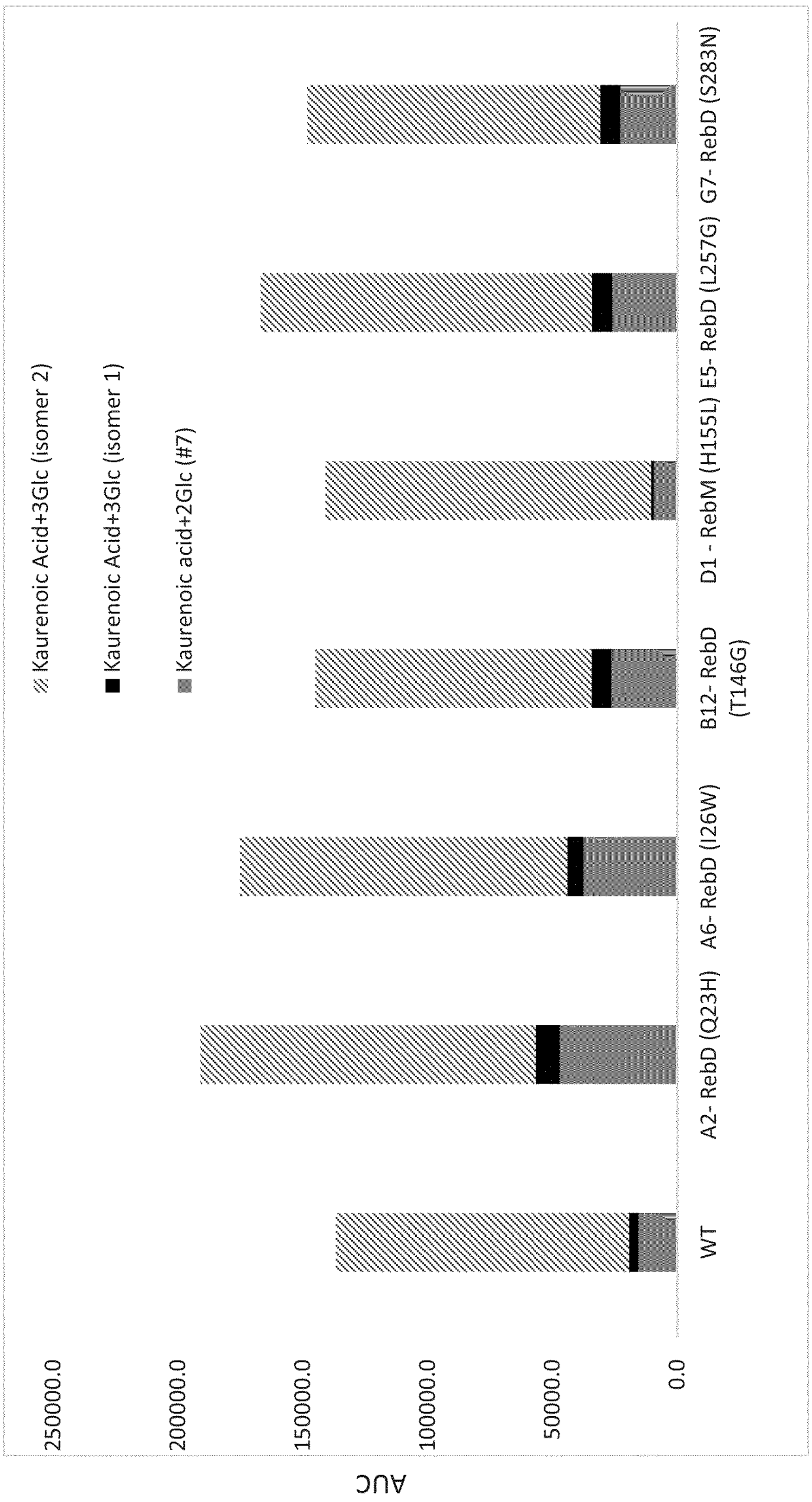

Kaurenoic Acid+3Glc (isomer 2)
Kaurenoic Acid+3Glc (isomer 1)
Kaurenoic acid+2Glc (#7)
AUC
250000.0
200000.0
150000.0
100000.0
50000.0
0.0
WT
A2- RebD (Q23H)
A6- RebD (I26W)
B12- RebD (T146G)
D1 - RebM (H155L)
E5- RebD (L257G)
G7- RebD (S283N)

Figure 11C

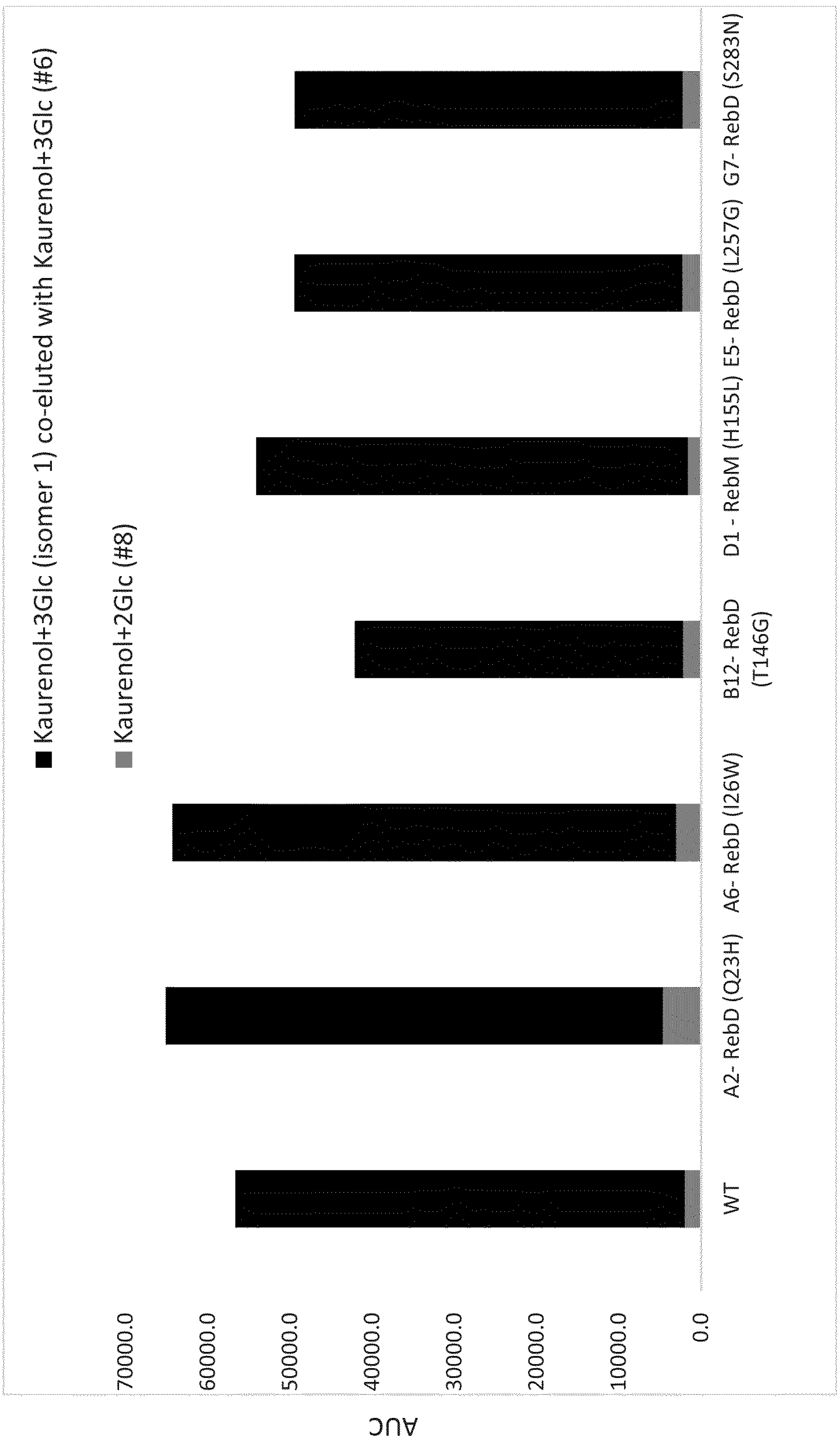

Kaurenol+3Glc (isomer 1) co-eluted with Kaurenol+3Glc (#6)
Kaurenol+2Glc (#8)
AUC
70000.0
60000.0
50000.0
40000.0
30000.0
20000.0
10000.0
0.0
WT
A2- RebD (Q23H)
A6- RebD (I26W)
B12- RebD (T146G)
D1 - RebM (H155L)
E5- RebD (L257G)
G7- RebD (S283N)

Figure 11D

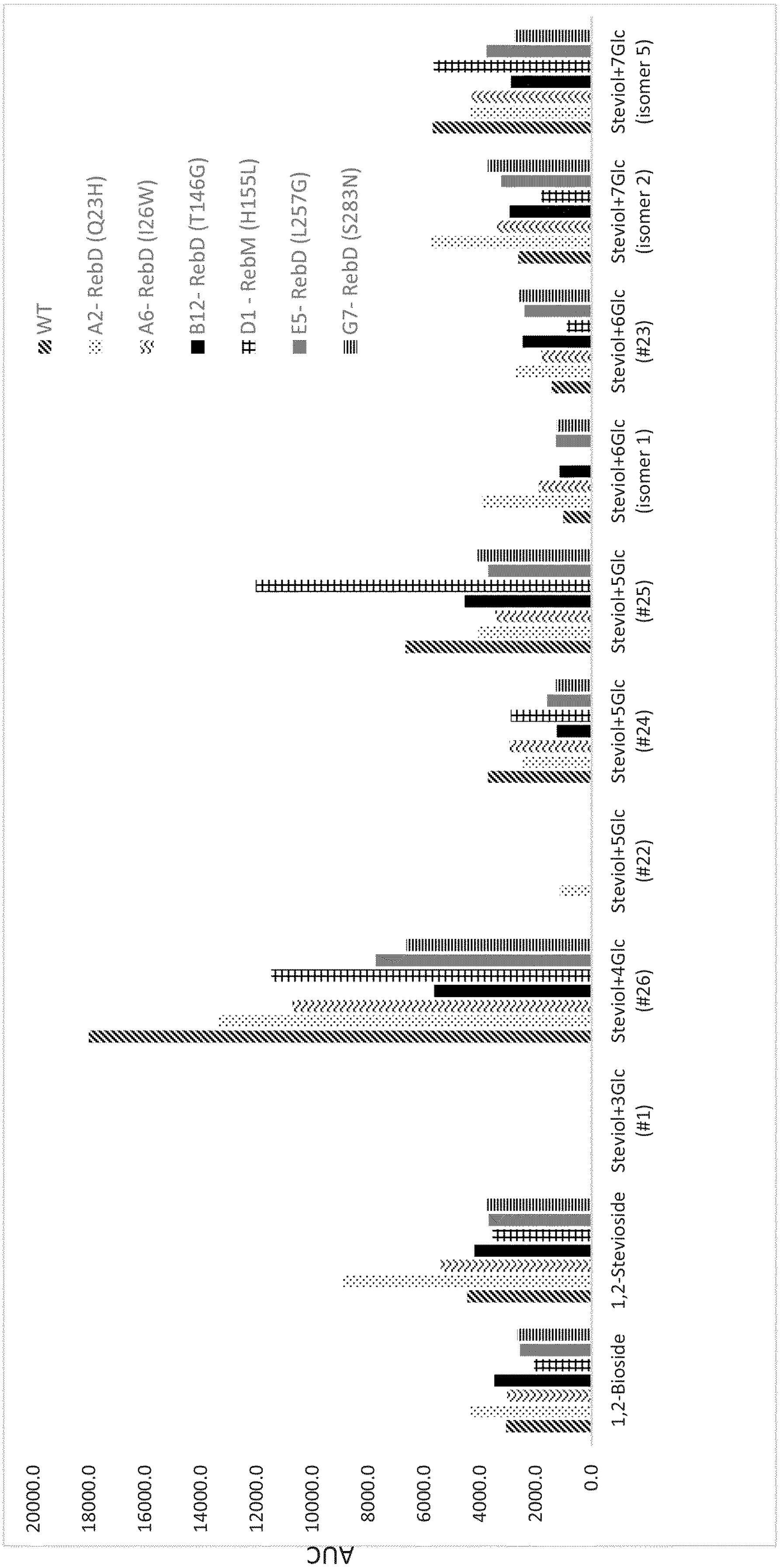
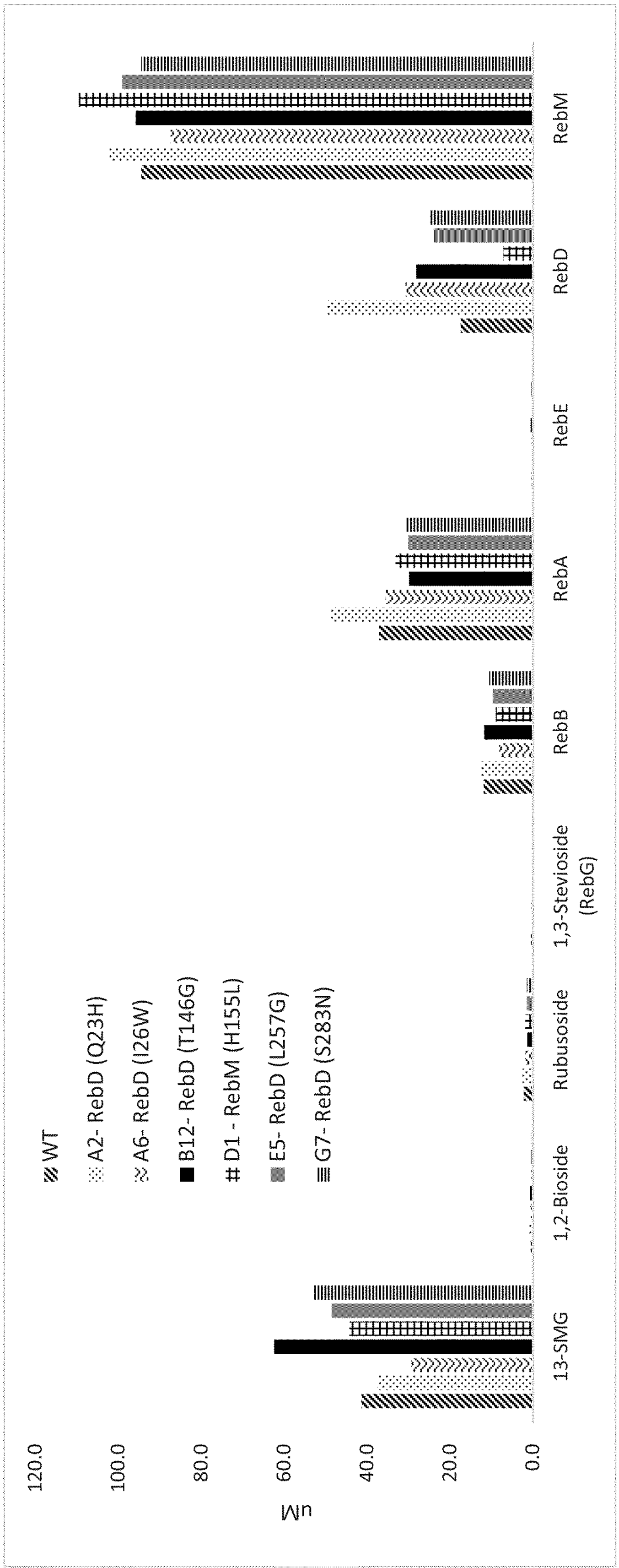

WT
A2- RebD (Q23H)
A6- RebD (I26W)
B12- RebD (T146G)
D1 - RebM (H155L)
E5- RebD (L257G)
G7- RebD (S283N)
AUC
20000.0
18000.0
16000.0
14000.0
12000.0
10000.0
8000.0
6000.0
4000.0
2000.0
0.0
1,2-Bioside
1,2-Stevioside
Steviol+3Glc (#1)
Steviol+4Glc (#26)
Steviol+5Glc (#22)
Steviol+5Glc (#24)
Steviol+5Glc (#25)
Steviol+6Glc (isomer 1)
Steviol+6Glc (#23)
Steviol+7Glc (isomer 2)
Steviol+7Glc (isomer 5)

Figure 11E


uM
120.0
100.0
80.0
60.0
40.0
20.0
0.0
13-SMG
1,2-Bioside
Rubusoside
1,3-Stevioside (RebG)
RebB
RebA
RebE
RebD
RebM
WT
A2- RebD (Q23H)
A6- RebD (I26W)
B12- RebD (T146G)
D1 - RebM (H155L)
E5- RebD (L257G)
G7- RebD (S283N)

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2016/052007

A. CLASSIFICATION OF SUBJECT MATTER
INV. C12N9/10 C12P15/00 C12P19/56 C12N1/18
ADD.

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
C12P C12N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2014/122227 A2 (EVOLVA SA [CH]) 14 August 2014 (2014-08-14) the whole document -----	1-41
X	WO 2013/022989 A2 (EVOLVA SA [CH]; HOUGHTON-LARSEN JENS [DK]; HICKS PAULA M [US]; NAESBY) 14 February 2013 (2013-02-14) the whole document -----	1-5,8-41
X	WO 2014/086890 A1 (EVOLVA SA [CH]) 12 June 2014 (2014-06-12) the whole document -----	1,2,5, 8-41
X	WO 2014/122328 A1 (EVOLVA SA [CH]) 14 August 2014 (2014-08-14) the whole document -----	1-3,5,6, 8-21, 23-41

☐ Further documents are listed in the continuation of Box C.

☒ See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
22 June 2016	04/07/2016

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Sonnerat, Isabelle

4

International application No.
PCT/EP2016/052007

INTERNATIONAL SEARCH REPORT

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.

3. ☒ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

1-41

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

☒ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 2, 5(completely); 1, 8-41(partially)

Recombinant host cell comprising a gene encoding a UGT91D2e polypeptide having at least 90% sequence identity to the amino acid sequence set forth in SEQ ID No. 11, wherein the host cell is capable of producing a steviol glycoside, glycosylated ent-kaurenol compound and/or a glycosylated ent-kaurenoic acid compound in a cell culture broth; subject-matter related thereto.

---

2. claims: 1, 8-41(all partially)

Recombinant host cell comprising a gene encoding a chimeric polypeptide having at least 70% sequence identity to the amino acid sequence set forth in SEQ ID No. 17 or SEQ ID No. 18, wherein the host cell is capable of producing a steviol glycoside, glycosylated ent-kaurenol compound and/or a glycosylated ent-kaurenoic acid compound in a cell culture broth; subject-matter related thereto.

---

3. claims: 3, 6(completely); 1, 8-41(partially)

Recombinant host cell comprising a gene encoding a UGT85C2 polypeptide having at least 55% sequence identity to the amino acid sequence set forth in SEQ ID No. 7, wherein the host cell is capable of producing a steviol glycoside, glycosylated ent-kaurenol compound and/or a glycosylated ent-kaurenoic acid compound in a cell culture broth; subject-matter related thereto.

---

4. claims: 4, 7(completely); 1, 8-41(partially)

Recombinant host cell comprising a gene encoding a UGT76G1 polypeptide having at least 50% sequence identity to the amino acid sequence set forth in SEQ ID No. 9, wherein the host cell is capable of producing a steviol glycoside, glycosylated ent-kaurenol compound and/or a glycosylated ent-kaurenoic acid compound in a cell culture broth; subject-matter related thereto.

---

5. claim: 42

Reaction mixture comprising (a) a steviol glycoside, glycosylated ent-kaurenol compound and/or a glycosylated ent-kaurenoic acid compound, (b) a UGT polypeptide, (c) glucose, fructose, sucrose, xylose, ethanol, glycerol, UDP-glucose, UDP-rhamnose, UDP-xylose and/or GlcNAc and/or (d) reaction buffer and/or salts.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/EP2016/052007

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2014122227 A2	14-08-2014	AU 2014214004 A1	30-07-2015
		CA 2899276 A1	14-08-2014
		CN 105051195 A	11-11-2015
		EP 2954058 A2	16-12-2015
		JP 2016506739 A	07-03-2016
		KR 20150115002 A	13-10-2015
		SG 11201505597S A	28-08-2015
		WO 2014122227 A2	14-08-2014
WO 2013022989 A2	14-02-2013	AU 2012294452 A1	06-02-2014
		CA 2843606 A1	14-02-2013
		CN 103732753 A	16-04-2014
		EP 2742142 A2	18-06-2014
		EP 3009508 A1	20-04-2016
		JP 2014524247 A	22-09-2014
		KR 20140057322 A	12-05-2014
		US 2014329281 A1	06-11-2014
		WO 2013022989 A2	14-02-2013
WO 2014086890 A1	12-06-2014	EP 2928321 A1	14-10-2015
		US 2015342234 A1	03-12-2015
		WO 2014086890 A1	12-06-2014
WO 2014122328 A1	14-08-2014	AU 2014213918 A1	20-08-2015
		CA 2900882 A1	14-08-2014
		CN 105189771 A	23-12-2015
		EP 2954061 A1	16-12-2015
		JP 2016506743 A	07-03-2016
		KR 20150128705 A	18-11-2015
		SG 11201506127W A	29-09-2015
		US 2015361476 A1	17-12-2015
		WO 2014122328 A1	14-08-2014