Production of steviol glycosides in recombinant hosts

Douchin, Veronique; Mikkelsen, Michael Dalgaard; Møller-Hansen, Iben

Publication date:
2016

Document Version
Publisher's PDF, also known as Version of record

Link back to DTU Orbit

Citation (APA):
Abstract: The invention relates to recombinant microorganisms and methods for producing steviol glycosides and steviol glycoside precursors.
PRODUCTION OF STEVSOL GLYCOSIDES IN RECOMBINANT HOSTS

BACKGROUND OF THE INVENTION

Field of the Invention

[0001] This disclosure relates generally to the recombinant production of steviol glycosides such as rebaudioside A (RebA), rebaudioside B (RebB), rebaudioside D (RebD), and rebaudioside M (RebM) by recombinant hosts such as recombinant microorganisms and isolation methods thereof. In particular, this disclosure relates to modifications to transport systems in a recombinant host to increase production of such steviol glycosides and/or transport of such steviol glycosides into the culture medium.

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 rebaudiosides and other 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 produce high yields of desired steviol glycosides, such as RebD and RebM.
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] In particular, the invention provides a recombinant host capable of synthesizing a steviol glycoside, comprising a gene encoding a transporter polypeptide and/or a gene encoding a transcription factor polypeptide that regulates expression of at least one transporter gene; wherein expression of the gene encoding the transporter polypeptide and/or the gene encoding the transcription factor polypeptide that regulates expression of at least one transporter gene is modified and the recombinant host transports at least a portion of the synthesized steviol glycoside from the host into a culture medium.

[0007] In some aspects of the recombinant host disclosed herein, the gene encoding the transporter polypeptide is an endogenous gene.

[0008] In some aspects of the recombinant host disclosed herein, the transporter polypeptide comprises an ATP-binding cassette (ABC) transporter, a major facilitator superfamily (MFS) transporter, an amino acid/auxin permease (AAAP) family transporter, ATPase transporter, a sulfate permease (SuP) family transporter, a lysosomal cystine transporter (LCT) family transporter, a Ca2+:cation antiporter (CaCA) family transporter, an amino acid-polyamine-organocation (APC) superfamily transporter, a multidrug/oligosaccharidyl-lipid/polysaccharide (MOP) transporter, a ZRT/IRT-like protein (ZIP) metal transporter family transporter, a mitochondrial protein translocase (MPT) family transporter, a voltage-gated ion channel (VIC) family transporter, a monovalent cation:proton antiporter-2 (CPA2) family transporter, a ThrE family of putative transmembrane amino acid efflux transporter, an oligopeptide transporter (OPT) family transporter, a K+ transporter (Trk) family transporter, a bile acid:Na symporter (BASS) family transporter, a drug/metabolite transporter (DMT) superfamily transporter, a mitochondrial carrier (MC) family transporter, an auxin efflux carrier (AEC) family transporter, an ammonia channel transporter (Amt) family transporter, a metal ion (Mn2+-iron) transporter (Nramp) family transporter, a transient receptor potential Ca2+ channel (TRP-CC) family transporter, an arsenical resistance-3 (ACR3) family transporter, a nucleobase:cation symporter-1 (NCS1) family transporter, an inorganic phosphate transporter (PiT) family transporter, an arsenite-antimonite (ArsAB) efflux family transporter, an IISP family of transporter, a glycerol uptake (GUP) family transporter, a metal ion transport (MIT) family transporter, a copper transport (Ctr) family or a cation diffusion facilitator (CDF) family transporter.

[0009] In some aspects of the recombinant host disclosed herein, the modified expression comprises modified expression comprises:
(a) overexpressing the gene encoding the transporter polypeptide and/or the gene encoding the transcription factor polypeptide; or

(b) deleting the gene encoding the transporter polypeptide and/or the gene encoding the transcription factor polypeptide.

[0010] In some aspects of the recombinant host disclosed herein, the gene encoding the transporter polypeptide and/or the gene encoding the transcription factor polypeptide has an activity that is increased.

[0011] In some aspects of the recombinant host disclosed herein, one or more of the genes encoding the transporter polypeptide and/or one or more of the genes encoding the transcription factor polypeptide are overexpressed.


[0013] In some aspects of the recombinant host disclosed herein, YBR043C set forth in SEQ ID NO:88, YDL100C set forth in SEQ ID NO:95, YDL054C set forth in SEQ ID NO:94,

[0014] In some aspects, the recombinant host further comprises:

(a) one or more genes encoding a sucrose transporter and a sucrose synthase;

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

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

(d) a gene encoding a kaurene synthase (KS) polypeptide;

(e) a gene encoding a kaurene oxidase (KO) polypeptide;

(f) a gene encoding a steviol synthase (KAH) polypeptide;

(g) a gene encoding a cytochrome P450 reductase (CPR) polypeptide;

(h) a gene encoding a UGT85C2 polypeptide;

(i) a gene encoding a UGT76G1 polypeptide;

(k) a gene encoding a UGT91 D2 functional homolog; and/or

(l) a gene encoding a EUGT1 1 polypeptide;

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

wherein the host is capable of producing one or more of RebA, RebB, RebD and/or RebM.

[0015] In some aspects of the recombinant host disclosed herein, at least one of the genes is codon optimized for expression in the host.
In some aspects of the recombinant host disclosed herein, at least one of the genes is codon optimized for expression in *Saccharomyces cerevisiae*.

In some aspects of the recombinant host 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: 149;

(b) the CDPS polypeptide comprises a polypeptide having at least 70% identity to an amino acid sequence set forth in SEQ ID NO: 150;

(c) the KO polypeptide comprises a polypeptide having at least 70% identity to an amino acid sequence set forth in SEQ ID NO: 152;

(d) the KS polypeptide comprises a polypeptide having at least 40% identity to an amino acid sequence set forth in SEQ ID NO: 151;

(e) the KAH polypeptide comprises a polypeptide having at least 60% identity to an amino acid sequence set forth in SEQ ID NO: 154;

(f) the CPR polypeptide comprises a polypeptide having at least 70% identity to an amino acid sequence set forth in SEQ ID NO: 153 and/or a polypeptide having at least 65% identity to an amino acid sequence set forth in SEQ ID NO: 155;

(g) the UGT85C2 polypeptide comprises a polypeptide having at least 55% identity to an amino acid sequence set forth in SEQ ID NO: 156;

(h) the UGT76G1 polypeptide comprises a polypeptide having at least 50% identity to an amino acid sequence set forth in SEQ ID NO: 158;

(i) the UGT74G1 polypeptide comprises a polypeptide having at least 55% identity to an amino acid sequence set forth in SEQ ID NO: 157;

(j) the a UGT91D2 functional homolog comprises a UGT91D2e-b polypeptide having at least 90% identity to the amino acid sequence set forth in SEQ ID NO: 159; and

(k) the EUGT11 polypeptide comprises a polypeptide having at least 65% identity to an amino acid sequence set forth in SEQ ID NO: 148.

In some aspects, the recombinant host disclosed herein comprises a microorganism that is a plant cell, a mammalian cell, an insect cell, a fungal cell, or a bacterial cell.

In some aspects, the fungal cell is a yeast cell.

In some aspects, 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.

In some aspects, the yeast cell is a *Saccharomycete*.

In some aspects, the yeast cell is a cell from the *Saccharomyces cerevisiae* species.

The invention further provides a method of producing a steviol glycoside, comprising:

(a) growing the recombinant host disclosed herein in a culture medium, under conditions in which the genes comprising recombinant host disclosed herein are expressed,

wherein the steviol glycoside is synthesized by the host; and

(b) optionally isolating the steviol glycoside.

In some aspects of the methods disclosed herein, the steviol glycoside is RebA, RebB, RebD, and/or RebM, and wherein:

(a) RebA is capable of being synthesized in the recombinant host disclosed herein expressing UGT85C2, UGT76G1, UGT74G1, and UGT91D2;

(b) RebB is capable of being synthesized in the recombinant host disclosed herein expressing UGT85C2, UGT76G1, and UGT91D2;

(c) RebD is capable of being synthesized in the recombinant host disclosed herein expressing UGT85C2, UGT76G1, UGT74G1, and UGT91D2 and/or EUUG1; and

(d) RebM is capable of being synthesized in the recombinant host disclosed herein expressing UGT85C2, UGT76G1, UGT74G1, and UGT91D2 and/or EUUG1.

In some aspects of the methods disclosed herein the steviol glycoside is produced at a concentration of between about 500 mg/L to about 10,000 mg/L.

The invention further provides a method of increasing production or transport of a steviol glycoside into a culture medium, comprising:

(a) growing the recombinant host disclosed herein in a culture medium, under conditions in which the genes comprising the host disclosed herein are expressed,

wherein the steviol glycoside is synthesized by the host; and

(b) optionally isolating the steviol glycoside.

In some aspects of the methods disclosed herein, the steviol glycoside is RebA, RebB, RebD, and/or RebM.

The invention further provides a method increasing production of steviol or a steviol glycoside in a recombinant host, comprising modifying expression of a gene encoding a transporter polypeptide and/or a gene encoding a transcription that regulates expression of at least one transporter gene, wherein the host is capable of transporting at least a portion of the produced steviol or a steviol glycoside from the host into a culture medium.

These and other features and advantages of the present invention will be more fully understood from the following detailed description of the invention 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.
DESCRIPTION OF DRAWINGS

[0032] Figure 1 shows the chemical structures and synthesis pathways for various steviol glycosides.

[0033] Figure 2 is a bar graph of the amount (µM) of RebA, RebB, RebD, or RebM in the supernatant of a steviol glycoside-producing strain overexpressing transporter genes YGR181W (SEQ ID NO:38) or YDR061W (SEQ ID NO:26), compared to a control steviol glycoside-producing strain. See Example 4.

[0034] Figure 3A and Figure 3B are bar graphs of the amount (mg/L) of RebA, RebD, or RebM in the supernatant (Figure 3A) or total culture (Figure 3B) of a YGR181W (SEQ ID NO:38) or YDR061W (SEQ ID NO:26) overexpressing strain, compared to a control steviol glycoside-producing strain. See Example 4.

[0035] Figure 4A shows levels of 13-SMG (total levels and supernatant levels; µM/O$_{600}$). Figure 4B shows levels of RebA (total levels and supernatant levels; µM/O$_{600}$). Figure 4C shows levels of RebB (total levels and supernatant levels; µM/O$_{600}$). Figure 4D shows levels of RebD (total levels and supernatant levels; µM/O$_{600}$), and Figure 4E shows levels of RebM (total levels and supernatant levels; µM/O$_{600}$) in a steviol glycoside-producing S. cerevisiae strain with a genomically integrated transporter gene. The genomically integrated transporter genes of Figures 4A-E are YBR043C (SEQ ID NO:88), YEL027W (SEQ ID NO:102), YJL093C (SEQ ID NO:48), YJR106W (SEQ ID NO:48), YMR166C (SEQ ID NO:132), YIL166C (SEQ ID NO:121), YKL120W (SEQ ID NO:126), YDL054C (SEQ ID NO:94), YDL128W (SEQ ID NO:22), YDR536W (SEQ ID NO:30), YGL167C (SEQ ID NO:112), YKL146W (SEQ ID NO:127), YKR039W (SEQ ID NO:129), YOL122C (SEQ ID NO:68), and YPR011C (SEQ ID NO:82). See Example 6.

[0036] Figure 5A shows supernatant levels of RebA, RebB, RebD, and RebM (in µM/O$_{D600}$) of a steviol glycoside-producing strain overexpressing YMR166C (SEQ ID NO:132), YEL027W (SEQ ID NO:102), YKL120W (SEQ ID NO:126), YIL166C (SEQ ID NO:121), YJR106W (SEQ ID NO:48), YJL093C (SEQ ID NO:48), and YBR043C (SEQ ID NO:88) by the USER cloning system. Figure 5B shows total levels of RebA, RebB, RebD, and RebM (in µM/O$_{D600}$) of a steviol glycoside-producing strain overexpressing YMR166C (SEQ ID NO:132), YEL027W (SEQ ID NO:102), YKL120W (SEQ ID NO:126), YIL166C (SEQ ID NO:121), YJR106W (SEQ ID NO:48), YJL093C (SEQ ID NO:48), and YBR043C (SEQ ID NO:88) by the USER cloning system.
DETAILED DESCRIPTION

[0037] All publications, patents and patent applications cited herein are hereby expressly incorporated by reference in their entirety for all purposes.

[0038] 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.

[0039] 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.

[0040] 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.

[0001] 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 (PGR) 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 PGR Protocols: A Guide to Methods and Applications (Innis et al., 1990, Academic Press, San Diego, CA).

[0041] 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.

[0042] As used herein, the terms "microorganism," "microorganism host," "microorganism host cell," "host cell," "recombinant host," "recombinant microorganism 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 the non-recombinant 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.

[0043] 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. Said recombinant genes are particularly encoded by cDNA.

[0044] As used herein, the term "engineered biosynthetic pathway" refers to a biosynthetic pathway that occurs in a recombinant host, as described herein, and does not naturally occur in the host.

[0045] 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 transporter. In some embodiments, the transporter is endogenous to S. cerevisiae, including, but not limited to S. cerevisiae strain S288C. In some embodiments, an endogenous yeast transporter 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 transporter gene 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
interchangeably 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. In some embodiments, a deleted/knocked out gene is a transporter gene or a transcription factor gene that regulates expression of a transporter gene.

[0046] 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.

[0047] 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, PGR 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.

[0048] 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.

[0049] 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.

[0050] 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), Duicoside A (CAS # 64432-06-0), Rebaudioside I (RebI) (MassBank Record: FU000332), Rebaudioside Q (RebQ), 1,2-Steviol (CAS # 57817-89-7), 1,3-Steviol (RebG), 1,2-Bioside (MassBank Record: FU000299), 1,3-Bioside, Steviol-13-O-glucoside (13-SMG), Steviol-19-O-glucoside (19-SMG), a tri-glycosylated steviol glycoside, a tetra-glycosylated steviol glycoside, a penta-glycosylated steviol glycoside, a hexa-glycosylated steviol glycoside, a hepta-glycosylated steviol glycoside, di-glycosylated kaurenoic acid, tri-glycosylated kaurenoic acid, di-glycosylated kaurenol, tri-glycosylated kaurenol, and isomers thereof.


[0052] 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 geranylgeranyl diphosphate synthase (GGPPS) polypeptide, a gene encoding an ent-copalyl diphosphate synthase (CDPS) polypeptide, a gene encoding a kaurene synthase (KS) polypeptide, a gene encoding a kaurene oxidase polypeptide (KO), a gene encoding a steviol synthase (KAH) polypeptide, a gene encoding a cytochrome P450 reductase (CPR) polypeptide, and a gene encoding a UGT polypeptide can produce a steviol glycoside and/or steviol glycoside precursors in vivo. See Example 2.

[0053] In some embodiments, a recombinant host comprises a nucleic acid encoding a UGT85C2 polypeptide, a nucleic acid encoding a UGT76G1 polypeptide, a nucleic acid encoding a UGT74G1 polypeptide, a nucleic acid encoding a UGT91D2 polypeptide, and/or a nucleic acid encoding a EUG71 polypeptide. 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 microorganism. In a particular embodiment, a steviol-producing recombinant microorganism comprises exogenous nucleic acids encoding UGT85C2, UGT76G1, or UGT91D2 polypeptides. 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 UGT91D2 (including inter alia 91D2e, 91D2m, 91D2e-b, and functional homologs thereof), and EUGT11 polypeptides. See Example 2.

[0054] In certain embodiments, the steviol glycoside is RebA, RebB, RebD, and/or RebM. RebA can be synthesized in a steviol-producing recombinant microorganism expressing UGT85C2, UGT76G1, UGT74G1, and UGT91D2. RebB can be synthesized in a steviol-producing recombinant microorganism expressing UGT85C2, UGT76G1, and UGT91D2. RebD can be synthesized in a steviol-producing recombinant microorganism expressing UGT85C2, UGT76G1 UGT74G1, and UGT91D2 and/or EUGT11. RebM can be synthesized in a steviol-producing recombinant microorganism expressing UGT85C2, UGT76G1, UGT74G1, and UGT91D2 and/or EUGT11 (see Figure 1, Example 2).

[0055] 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.

[0056] 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.

[0057] In some embodiments, a steviol glycoside or steviol glycoside precursor composition produced in vivo, in vitro, or by whole cell bioconversion comprises less contaminants than a stevia extract from, inter alia, a stevia plant. Contaminants 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-methylloctadecane, pentacosane, octacosane, tetracosane, octadecanol, stigmasterol, β-sitosterol, α- and β-amyrin, iupeol, β-amyrin acetate, pentacyclic triterpenes, centauredin, quercitin, epi-alpha-cadinol, caraphyllenes and derivatives, beta-pinene, beta-sitosterol, and gibberellin.

[0058] As used herein, the terms "detectable amount," "detectable concentration," "measurable amount," and "measurable concentration" refer to a level of steviol glycosides measured in AUC, μM/OD∞∞, 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, 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).

[0059] 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.
Transporters and Transcription Factor Expression

[0060] This document describes reagents and methods that can be used to efficiently produce steviol glycoside compositions. Modification of transport systems in a recombinant host that are involved in transport of steviol glycosides into culture medium can allow more effective production of steviol glycosides in recombinant hosts.

[0061] As set forth herein, recombinant cells having modifications to cellular transport are capable of producing steviol. Recombinant hosts described herein can produce steviol and have altered expression of at least one endogenous transporter gene. Recombinant hosts described herein can produce steviol and have altered expression of a transcription factor that regulates expression of at least one endogenous transporter gene. Altering expression of endogenous transporter genes can be useful for increasing production of steviol and/or excretion of steviol into the culture medium.

[0062] As set forth herein, recombinant cells having modifications to cellular transport are capable of producing at least one steviol glycoside, including, but not limited to, RebA, RebB, RebD, and/or RebM. Recombinant hosts described herein can produce at least one steviol glycoside such as RebA, RebB, RebD, and/or RebM and have altered expression of at least one endogenous transporter gene. Recombinant hosts described herein can produce at least one steviol glycoside such as RebA, RebB, RebD, and/or RebM and have altered expression of a transcription factor that regulates expression of at least one endogenous transporter gene. Recombinant hosts described herein can produce at least one steviol glycoside such as RebA, RebB, RebD, and/or RebM and have altered expression of a plurality of endogenous transporter genes and/or of a plurality of transcription factor genes that regulate expression of a plurality of endogenous transporter genes. Altering expression of endogenous transporter genes and/or transcription factors regulating expression of at least one transporter gene can be useful for increasing production of steviol glycosides and/or excretion of steviol glycosides into the culture medium.

[0063] Recombinant hosts disclosed herein can include one or more biosynthesis genes, such as one or more genes encoding a sucrose transporter and a sucrose synthase; a gene encoding a geranylgeranyl diphasphate synthase (GGPPS) polypeptide; a gene encoding an ent-copalyl diphasphate synthase (CDPS) polypeptide; a gene encoding a kaurene synthase (KS) polypeptide; a gene encoding a kaurene oxidase (KO) polypeptide; a gene encoding a steviol synthase (KAH) polypeptide; a gene encoding a cytochrome P450 reductase (CPR) polypeptide; a gene encoding a UGT85C2 polypeptide; a gene encoding a
UGT76G1 polypeptide; a gene encoding a UGT74G1 polypeptide; a gene encoding a UGT91D2 functional homolog; and/or a gene encoding a EUGT11 polypeptide; wherein expression of one or more of these genes results in production of steviol steviol glycosides such as RebA, RebB, RebD, and/or RebM.

[0064] As used herein, the terms "transport of a steviol glycoside," "steviol glycoside transport," "excretion of a steviol glycoside," and "steviol glycoside excretion" can be used interchangeably.

[0065] As used herein, the term "transporter" (also referred to as a membrane transport protein) refers to a membrane protein involved in the movement of small molecules, macromolecules (such as carbohydrates), and ions across a biological membrane. Transporters span the membrane in which they are localized and across which they transport substances. Transporter proteins can assist in the movement (i.e., transport or excretion) of a substance from the intracellular space to the culture medium. Transporters are known to function as passive transport systems, carrying molecules down their concentration gradient, or as active transport systems, using energy to carry molecules uphill against their concentration gradient. Active transport is mediated by carriers which couple transport directly to the use of energy derived from hydrolysis of an ATP molecule or by carriers which make use of a pre-established electrochemical ion gradient to drive co-transport of the nutrient molecule and a co-transported ion. The latter category comprises symporters and antiporters, which carry the ion in the same or opposite direction, respectively, as the transported substrate.

[0066] Transport proteins have been classified according to various criteria at the Transporter Classification Database (on the world wide web at tcbi.org). See, Saier Jr. et al., Nucl. Acids Res., 42(1):D251-258 (2014). Non-limiting examples thereof include, among others, the family of Multiple Drug Resistance (MDR) plasma membrane transporters that is thought to be ubiquitous among living organisms. The MDR transporter superfamily can be further subdivided according to the mode of operation by which the substrate is transported from one side of the membrane to the other. Transporters can operate to move substances across membranes in response to chemiosmotic ion gradients or by active transport. ATP-binding cassette transporters (ABC transporters) are transmembrane proteins that utilize the energy of adenosine triphosphate (ATP) hydrolysis to carry out translocation of various substrates across membranes. They can transport a wide variety of substrates across the plasma membrane and intracellular membranes, including metabolic products, lipids and sterols, and drugs. Particular non-limiting examples of endogenous ABC transporter genes include PDR5, YDR061W, PDR15, SNQ2, YOR1, YOL075C, MDL2, ADP1, CAF16, VMR1
and STE6 (or a functional homolog thereof). In some aspects, ABC transporters transport steviol glycosides.


[0068] Another transporter family, the Major Facilitator Superfamily (MFS) transporters are monomeric polypeptides that can transport small solutes in response to proton gradients. The MFS transporter family is sometimes referred to as the uniporter-symporter-antiporter family. MFS transporters function in, inter alia, in sugar uptake and drug efflux systems. MFS transporters typically comprise conserved MFS-specific motifs. Non-limiting examples of endogenous MFS transporter genes include DTR1, SE01, YBR241C, VBA3, FEN2, SNF3, STL1, HXT10, AZR1, MPH3, VBA5, GEX2, SNO1, AQR1, MCH1, MCH5, ATG22, HXT15, MPH2, ITR1, SIT1, VPS73, HXT5, QDR1, QDR2, QDR3, SOA1, HXT9, YMR279C, YIL166C, HOL1, ENB1, TP04 and FLR1 (or a functional homolog thereof). In some aspects, MFS transporters transport steviol glycosides.

[0069] Other transporter families include the SMR (small multidrug resistant) family, RND (Resistance-Nodulation-Cell Division) family, and the MATE (multidrug and toxic compound extrusion) family. The SMR family members are integral membrane proteins characterized by four alpha-helical transmembrane strands that confer resistance to a broad range of antiseptics, lipophilic quaternary ammonium compounds (QAC), and aminoglycoside resistance in bacteria. See, Bay & Turner, 2009, BMC Evol Biol., 9:140. In some aspects, SMR transporters transport steviol glycosides.

[0070] The MATE family members comprise 12 transmembrane (TM) domains. Members of the MATE family have been identified in prokaryotes, yeast such as S. cerevisiae and Schizosaccharomyces pombe, and plants. See Diener et al., 2001, Plant Cell. 13(7):1625-8. The MATE family members are sodium or proton antiporters. In some aspects, MATE transporters transport steviol glycosides.

[0071] Additional transporter families include the amino acid/auxin permease (AAAP) family (for example, YKL146W/AVT3, YBL089W/AVT5, YER119C/AVT6 and YIL088C/AVT7), the ATPase family (for example, YBL099W/ATP1, YDL185W/VMA1, YLR447C/VMA6, YOL077W/ATP19, YPL078C/ATP4, YEL027W/VMA3, YKL016C/ATP7, and YOR332W7VMA4), the sulfate permease (SuP) family (for example, YBR294W/SUL1, YGR125W and YPR003C), the lysosomal cystine transporter (LCT) family (for example, YCR075C/ERS1), the Ca2+-cation antiporter (CaCA) family (for example, YDL128W/VCX1
and YJR106W/ECM27), the amino acid-polyamine-organocation (APC) superfamily (for example, YDL210W/UGA4, YOL020W/TAT2, YPL274W/SAM3, YNL268W/LYP1, YHL036W/MUP3, YKR039W/GAP1 and YOR348C/PUT4), multidrug/oligosaccharide-lipid/polysaccharide (MOP) (for example, YDR338C), the ZRT/IRT-like protein (ZIP) metal transporter family (for example, YGL225W/ZRT1 and YOR079C/ATX2), the mitochondrial protein translocase (MPT) family (for example, YGR181W/TIM13, YNL070W/TOM7, YNL121C/TOM70, the voltage-gated ion channel (VIC) family (for example, YGR217W/CCH1 and YJL093C/TOK1), the monovalent cation:proton antiporter-2 (CPA2) family (for example, YJL094C/KHA1), the ThrE family of putative transmembrane amino acid efflux transporters (for example, YJL108C/PRM10), the oligopeptide transporter (OPT) family (for example, YJL212C/OPT1 and YGL114W), the K⁺ transporter (Trk) family (for example, TKR050W/TRK2), the bile acid:Na symporter (BASS) family (for example, YMR034C), the drug/metabolite transporter (DMT) superfamily (for example, YMR253C, YML038C/YMD8, and YOR307C/SLY41), the mitochondrial carrier (MC) family (for example, YMR056C/AAC1, YNL083W/SAL1, YOR130C/ORT1, YOR222W/ODC2, YPR011C, YPR058W/YMC1, YPR128C/ANT1, YEL006W/YEA6, YER053C/PIC2, YFR045W, YGR257C/MTM1, YHR002W/LEU5, YIL006W/YIA6, YJL133W/MRS3, YKL120W/OAC1, YMR166C, YNL003C/PET8 and YOR100C/CRC1), the auxin efflux carrier (AEC) family (for example, YNL095C, YOR092W/ECM3 and YBR287W), the ammonia channel transporter (Amt) family (for example, YNL142W/MEP2), the metal ion (Mn²⁺-iron) transporter (Nramp) family (for example, YOL122C/SMF1), the transient receptor potential Ca²⁺ channel (TRP-CC) family (for example, YOR087W/YVC1), the arsenical resistance-3 (ACR3) family (for example, YPR201W/ARR3), the nucleoebasexation symporter-1 (NCS1) family (for example, YBR021W/FUR4), the inorganic phosphate transporter (PiT) family (for example, YBR296C/PH089), the arsenite-antimonite (ArsAB) efflux family (for example, YDL100C/GET3), the MSP family of transporters, the glycerol uptake (GUP) family (for example, YGL084C/GUP1), the metal ion transport (MIT) family (for example, YKL064W/MNR2, YKL050C and YOR334W/MRS2), the copper transport (Ctr) family (for example, YLR411W/CTR3) and the cation diffusion facilitator (CDF) family (for example, YOR316C/COT1). Particular members of any of these transporter families are included within the scope of the disclosed invention to the extent that altered expression in a cell capable of producing steviol glycoside increases production of said steviol glycoside from the cell; exemplary members are disclosed above and in Tables 5, 6, and 14.

[0072] As used herein, the term "transcription factor" refers to a DNA-binding protein that regulates gene expression. Preferably, the transcription factor regulates expression of at least one transporter gene.
Methods for identifying a gene affecting production or transport of steviol glycosides and steviol glycoside pathway intermediates are disclosed herein. Such methods can involve inactivating at least one endogenous transporter gene or modifying expression of at least one transporter gene. Typically, a library of mutant microorganisms is prepared, each mutant in the library having a different endogenous transporter gene inactivated. Methods of inactivating genes and determining their effect in a microorganism are known to a person having ordinary skill in the art; additional methods are disclosed in WO 2014/122328, the disclosure of which is incorporated by reference in its entirety. The mutant microorganisms comprising one or more steviol glycoside pathway genes are cultured in a medium under conditions in which steviol or a steviol glycoside is synthesized, and the amount of total, supernatant, and/or intracellular steviol glycosides produced by the microorganism is measured (e.g., using LC-MS) as described herein.

The disclosure is directed to recombinant host cells in which expression of endogenous transporter or transcription factor genes is modified. In some embodiments, the transporter or transcription factor gene is endogenous to S. cerevisiae, including, but not limited to S. cerevisiae strain S288C. In some embodiments, expression of an endogenous transporter or transcription factor can be modified by replacing the endogenous promoter with a different promoter that results in increased expression of the transporter protein (e.g., at least a 5% increase in expression, such as at least a 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, or 50%, 100%, 200% increase or more in expression). For example, an endogenous promoter can be replaced with a constitutive or inducible promoter that results in increased expression of the transporter. Homologous recombination can be used to replace the promoter of an endogenous gene with a different promoter that results in increased expression of the transporter. In other embodiments, the inducible or constitutive promoter and endogenous transporter or transcription factor can be integrated into another locus of the genome using homologous recombination. In other embodiments, the transporter or transcription factor gene can be introduced into a microorganism using exogenous plasmids with a promoter that results in overexpression of the transporter or transcription factor in the microorganism. In yet another embodiment, the exogenous plasmids may also comprise multiple copies of the transporter or transcription factor gene. In a further embodiment, the endogenous transporter or transcription factor can be induced to be overexpressed using native mechanisms to the recombinant microorganism (e.g. heat shock, stress, heavy metal, or antibiotic exposure). In yet a further embodiment, the activity of an endogenous gene product is enhanced or increased (for example, by mutation). In yet another embodiment, a homologous or orthologous gene of an endogenous yeast transporter or transcription factor gene is overexpressed.
In certain other embodiments, modified expression of a target gene in a recombinant microorganism comprises overexpressing a transporter gene and/or a transcription factor gene involved in expression of said transporter gene. In yet other embodiments, a plurality of endogenous transporter genes or transcription factor genes is overexpressed in said recombinant microorganism.

Modification of transcription factor expression can be used to increase transporter expression. For example, yeast transcriptions factor PDR1 regulates expression of the genes encoding ABC transporters PDR5, SNQ2 and YOR1. Therefore, in some embodiments, promoters for the endogenous PDR1 locus can be replaced with a different promoter that results in increased expression of the transcription factors, which can increase production of endogenous transporters.


In some embodiments, deletion in a steviol glycoside-producing strain of YDL128W (SEQ ID NO:22), YDL194W (SEQ ID NO:24), YDL210W (SEQ ID NO:25), YDL536W (SEQ ID NO:30), YFL011W (SEQ ID NO:33), YGL006W (SEQ ID NO:34),
YGL013C (SEQ ID NO:35), YGL255W (SEQ ID NO:36), YGR181W (SEQ ID NO:38), YGR217W (SEQ ID NO:39), YHL016C (SEQ ID NO:42), Y1L088C (SEQ ID NO:43), YJL094C (SEQ ID NO:45), YJR106W (SEQ ID NO:48), YKR050W (SEQ ID NO:51), YNL065W (SEQ ID NO:59), YNL083W (SEQ ID NO:61), YNL121C (SEQ ID NO:63), YNL142W (SEQ ID NO:64), YOR291W (SEQ ID NO:74), YOR306C (SEQ ID NO:75), YOR334W (SEQ ID NO:77), YPL270W (SEQ ID NO:79), YPR011C (SEQ ID NO:82), YPR128C (SEQ ID NO:84) results in a measurable decrease of RebD excreted into the culture medium, indicating that each plays a role in RebM excretion. See Example 3 and Tables 7-10.

[0079] In some embodiments, deletion in a steviol glycoside-producing strain of YBR180W (SEQ ID NO:13), YAL067C (SEQ ID NO:14), YBR241C (SEQ ID NO:17), YCL096W (SEQ ID NO:19), YCR075C (SEQ ID NO:21), YDL128W (SEQ ID NO:22), YDL194W (SEQ ID NO:24), YDR093W (SEQ ID NO:27), YDR338C (SEQ ID NO:28), YDR406W (SEQ ID NO:29), YER166W (SEQ ID NO:32), YFL01 W (SEQ ID NO:33), YGL006W (SEQ ID NO:34), YGL103C (SEQ ID NO:35), YGL255W (SEQ ID NO:36), YGR217W (SEQ ID NO:39), YHL016C (SEQ ID NO:42), YJL094C (SEQ ID NO:45), YJL212C (SEQ ID NO:47), YJR106W (SEQ ID NO:48), YJR160C (SEQ ID NO:49), YKR050W (SEQ ID NO:51), YKR106W (SEQ ID NO:53), YML116W (SEQ ID NO:55), YMR034C (SEQ ID NO:56), YMR056C (SEQ ID NO:57), YMR253C (SEQ ID NO:58), YNL070W (SEQ ID NO:60), YNL083W (SEQ ID NO:61), YNL095C (SEQ ID NO:62), YNL121C (SEQ ID NO:63), YOL075C (SEQ ID NO:66), YOL122C (SEQ ID NO:68), YOR087W (SEQ ID NO:70), YOR222W (SEQ ID NO:73), YOR291W (SEQ ID NO:74), YOR306C (SEQ ID NO:75), YPL274W (SEQ ID NO:80), YPR003C (SEQ ID NO:81), YPR011C (SEQ ID NO:82), or YPR201W (SEQ ID NO:85) results in a measurable decrease of RebM, indicating that each plays a role in RebM excretion. See Example 3 and Tables 7-10.

[0080] In some embodiments, overexpression of YGR181W (SEQ ID NO:38) or YDR061W (SEQ ID NO:26) improves RebD and RebM transport into the culture medium by approximately 2-fold (-400-500 mg/L of supernatant RebD and RebM in YGR181W (SEQ ID NO:38) and YDR061W (SEQ ID NO:26) overexpression strains versus -250 mg/L of supernatant RebD and RebM in a control steviol glycoside-producing strain). See Example 4, Figure 2, and Figure 3.

[0081] In some embodiments, overexpression of a transporter of Table 11 increases excretion of RebA, RebB, RebD, and/or RebM by at least 20%. In some embodiments, overexpression of a transporter of Table 12 increases production of RebA, RebB, RebD, and/or RebM by at least 40%. See Example 5.
In some embodiments, a transporter gene is integrated into the genome of a steviol glycoside-producing host. In some embodiments, the integrated transporter is YBR043C (SEQ ID NO:88), YEL027W (SEQ ID NO:102), YJL093C (SEQ ID NO:44), YJR106W (SEQ ID NO:48), YMR166C (SEQ ID NO:132), YIL166C (SEQ ID NO:121), YKL120W (SEQ ID NO:126), YDL054C (SEQ ID NO:94), YDL128W (SEQ ID NO:22), YDR536W (SEQ ID NO:30), YGL167C (SEQ ID NO:12), YKL146W (SEQ ID NO:127), YKR039W (SEQ ID NO:129), YOL122C (SEQ ID NO:68), or YPR011C (SEQ ID NO:82). In some embodiments, integration of YBR043C (SEQ ID NO:88), YEL027W (SEQ ID NO:102), YJL093C (SEQ ID NO:44), YJR106W (SEQ ID NO:48), YKL120W (SEQ ID NO:126), or YMR166C (SEQ ID NO:132) improves excretion and/or total production of 13-SMG. In some embodiments, integration of YBR043C (SEQ ID NO:88), YEL027W (SEQ ID NO:102), YJL093C (SEQ ID NO:44), YJR106W (SEQ ID NO:48), YKL120W (SEQ ID NO:126), or YMR166C (SEQ ID NO:132) improves excretion and/or total production of RebB. In some embodiments, integration of YBR043C of SEQ ID NO:88, YEL027W of SEQ ID NO:102, YJL093C of SEQ ID NO:44, YJR106W of SEQ ID NO:48, and YMR166C of SEQ ID NO:132 improves excretion and/or total production of RebD, and YBR043C of SEQ ID NO:88, YEL027W of SEQ ID NO:102, YIL166C (SEQ ID NO:121), YJL093C of SEQ ID NO:44, YJR106W of SEQ ID NO:48, and YMR166C of SEQ ID NO:132 improves excretion and/or total production of RebM, as measured by an increase in RebD and RebM levels in the supernatant compared to a control steviol glycoside-producing strain. See Example 6.

In some embodiments, steviol glycoside-producing S. cerevisiae strains overexpressing YJL093C (SEQ ID NO:44) or YBR043C (SEQ ID NO:88) produce higher levels of RebD + RebM, compared to a steviol glycoside-producing S. cerevisiae strain that does not overexpress YJL093C or YBR043C. See Example 7.

In some embodiments, a transporter that is knocked out can also have specificity for transport of larger molecular weight steviol glycosides (for example, RebD and the knockout of YGR181W of SEQ ID NO:38 or YOR291W of SEQ ID NO:74), and therefore, can be useful to overexpress in strains where transport of RebD into the culture medium is desired. With appropriate balancing of the rate of glycosylation activity through expression of pathway UGTs, smaller molecular weight steviol glycosides are further glycosylated before they are transported into the culture medium. For example, higher expression levels of a UGT76G1 and UGT91D2e and/or EU7T11, as compared to the UGT74G1 and UGT85C2 enzymes, can prevent accumulation of the steviol monogluosides that are transported more readily. If the UGT activity level is higher (so the glycosylation rate is
faster) than the rate of transport, then greater amounts of larger molecular weight steviol glycosides will be produced.

**Steviol and Steviol Glycoside Biosynthesis Nucleic Acids**

[0085] 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.

[0086] 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, promotor 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.

[0087] 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.

[0088] 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 comprises an origin of replication, and one or more selectable markers for maintenance of the construct in appropriate species.

[0089] 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.
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 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. As another example, expression of membrane transporters involved in transport of steviol glycosides can be activated, such that transportation of steviol glycosides is increased. Such regulation can be beneficial in that transportation of steviol glycosides can be increased for a desired period of time during culture of the microorganism, thereby increasing the yield of glycoside product(s) at harvest. 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.

**Recombinant Hosts**

Recombinant hosts can be used to express polypeptides for the producing steviol glycosides, including mammalian, insect, plant, and algal cells. A number of prokaryotes and eukaryotes are also suitable for use in constructing the recombinant microorganisms described herein, e.g., gram-negative bacteria, yeast, and fungi. 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).

Typically, the recombinant microorganism is grown in a fermenter at a defined temperature(s) for a desired period of time. 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, kaurene and kaurenoic
acid, can be determined by extracting samples from culture media for analysis according to published methods.

[0093] 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, carbon 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.

[0094] After the recombinant microorganism has been grown in culture for the desired period of time, 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.

[0095] 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 produce steviol and/or steviol glycosides.

[0096] 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.

[0097] 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, Kluveromyces, Laetiporus, Lentinus, Phaffia, Phanerochaete, Pichia, Physcomitrella, Rhodoturula, Saccharomyces, Schizosaccharomyces, Sphaceloma, Xanthophyllumyces or Yarrowia. Exemplary species from such genera include Lentinus tigrinus, Laetiporus sulphureus, Phanerochaete chrysosporium, Pichia pastoris, Cyberlindnera jadinii, Physcomitrella patens, Rhodoturula giuatinis, Rhodoturula mucilaginosa, Phaffia rhodozyma, Xanthophyllumyces dendrorhous, Fusarium fujikuroi/Gibberella fujikuroi, Candida utilis, Candida glabrata, Candida albicans, and Yarrowia lipolytica.

In some embodiments, a microorganism can be a prokaryote such as *Escherichia coli*.

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

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.

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*.

Saccharomyces *spp*.

*Saccharomyces* 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.

Aspergillus *spp*.

*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.

**E. coli**

[00104] *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.


[00106] *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 (Blastobotvs adeninivorans)**

[00107] *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**

[00108] *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 microorganism. *Yarrowia lipolytica* 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; Beopoulous *et al.*, 2009, *Biochimie* 91(6):692-6; Bankar *et al.*, 2009, *Appl Microbiol Biotechnol.* 84(5):847-65.

**Rhodotorula sp.**
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**

Rhodosporidium *toruloides* is oleaginous yeast and useful for engineering lipid-production pathways (See e.g. Zhu et al., 2013, Nature Commun. 3:112; Ageitos et al., 2011, Applied Microbiology and Biotechnology 90(4):1219-27).

*Candida boidinii*

*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* xylene 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*)

*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 *Klyveromyces 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.

*Klyveromyces lactis*

*Klyveromyces 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**

*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.*

[00115] *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**

[00116] 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) and have a consistent taste profile. 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. Hosts described herein do not produce the 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.

[00117] The amount of an individual steviol glycoside (*e.g.*, RebA, RebB, RebD, or RebM) produced can be from about 1 mg/L to about 2,800 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 1,400 mg/L, at least about 1,600 mg/L, at least about 1,800 mg/L, or at least about 2,800 mg/L. In some aspects, the amount of an individual steviol glycoside can exceed 2,800 mg/L. The amount of a combination of steviol glycosides (*e.g.*, RebA, RebB, RebD, or RebM) produced can be from about 1 mg/L to about 6,000 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, or at least about 6,000 mg/L. In some aspects, the amount of a combination of steviol glycosides can exceed 6,000 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.
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 steviosi and/or steviosi glycosides. For example, a first microorganism can comprise one or more biosynthesis genes for producing steviosi and null mutations in a first group of endogenous transporters, while a second microorganism comprises steviosi glycoside biosynthesis genes and null mutations in a second group of endogenous transporters. 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.

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., steviosi, 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. The microorganisms can have the same or a different group of mutations in endogenous transporters. 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.

Stevioi glycosides do not necessarily have equivalent performance in different food systems. It is therefore desirable to have the ability to direct the synthesis to steviosi glycoside compositions of choice. Recombinant hosts described herein can produce compositions that are selectively enriched for specific steviosi glycosides (e.g., RebD) and have a consistent taste profile. Thus, the recombinant microorganisms 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 steviosi glycoside that is consistent from batch to batch. Microorganisms described herein do not produce the undesired plant byproducts found in Stevia extracts. Thus, steviosi glycoside compositions produced by the recombinant microorganisms described herein are distinguishable from compositions derived from Stevia plants.

Stevioi 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 2013/022989, WO 2013/022989, WO 2014/122227, and WO 2014/122328, each of which has been incorporated by reference in its entirety.
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. For example, recombinant microorganisms described herein can express transporters specific for transport of a particular rebaudioside into the culture medium. When a transporter is specific for a particular rebaudioside it will enrich the concentration of that compound in the fermentation broth, preventing it from being further reacted to a different compound, and by selectively transporting the rebaudioside into the fermentation broth it will make it easier to recover from the other rebaudiosides and therefore making the process more efficient.

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. 2007/01 2831 1. In some embodiments, the steviol or steviol glycoside may be provided with a flavor (e.g., citrus) as a flavor modulator.

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 a 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.

[00125] For example, such a steviol glycoside composition can have from 90-99% 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.

[00126] Such a steviol glycoside composition can be a RebB-enriched composition having greater than 3% 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.

[00127] Such a steviol glycoside composition can be a RebD-enriched composition having greater than 3% 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.

[00128] Such a steviol glycoside composition can be a RebE-enriched composition having greater than 3% 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.

[00129] Such a steviol glycoside composition can be a RebM-enriched composition having greater than 3% 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.

[00130] 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.

[00131] The invention will be further described in the following examples, which do not limit the scope of the invention described in the claims.

EXAMPLES

[00132] 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

[00133] The LC-MS methods described here are oriented towards the separation, general detection and potential identification of chemicals of particular masses (i.e. steviol glycosides) in the presence of a mixture (i.e. culture media). LC-MS analyses were performed on: (A) an UltiMate® 3000-TSQ (Thermo Fisher Scientific); (B) a 1290 Infinity - 6130SQ (Agilent); or (C) an Acquity -XevoTQD (Waters) sytem. Specific methods used for each system are described below.

[00134] Method A: LC-MS analyses were performed using an UltiMate® 3000 UPLC system (Dionex) fitted with a waters ACQUITY UPLC® BEH shield RP18 column (2.1 x 50 mm, 1.7 µm particles, 130 A pore size) connected to a TSQ Quantum® Access (ThermoFisher Scientific) triple quadrupole mass spectrometer with a heated electrospray ion (HESI) source, unless otherwise indicated. 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 25% to 47% B from min. 0.0 to 4.0, increasing 47% to 100% B in min. 4.0 to 5.0, holding 100% B from min. 5.0 to 6.5 re-equilibration. The flow rate was 0.4 mL/min and the column temperature 35°C. The steviol glycosides were detected using SIM (Single Ion Monitoring) with the following m/z-traces.

Table 1. MS analytical information for Steviol Glycosides

<table>
<thead>
<tr>
<th>Description</th>
<th>Exact Mass</th>
<th>m/z trace</th>
<th>compound (typical $t_r$ in min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Steviol + 1 Glucose</td>
<td>[M+H]$^+$ 481.2796</td>
<td>481.2±0.5</td>
<td>19-SMG (2.29), 13-SMG (3.5)</td>
</tr>
<tr>
<td></td>
<td>[M+Na]$^+$ 503.2615</td>
<td>503.1±0.5</td>
<td></td>
</tr>
<tr>
<td>Steviol + 2 Glucose</td>
<td>[M+Na]$^+$ 665.3149</td>
<td>665±0.5</td>
<td>Rubusoside (2.52), Steviol-1,2-bioside (2.92), Steviol-1,3-bioside (2.28)</td>
</tr>
<tr>
<td>Steviol + 3 Glucose</td>
<td>[M+Na]$^+$ 827.3677</td>
<td>827.4±0.5</td>
<td>1,2-Stevioside (2.01), 1,3-Stevioside (2.39), RebB (2.88)</td>
</tr>
<tr>
<td>Steviol + 4 Glucose</td>
<td>[M+Na]$^+$ 989.4200</td>
<td>989.4±0.5</td>
<td>RebA (2.0)</td>
</tr>
<tr>
<td>Steviol + 5 Glucose</td>
<td>[M+Na]$^+$ 1151.4728</td>
<td>1151.4±0.5</td>
<td>RebD (1.1)</td>
</tr>
<tr>
<td>Steviol + 6 Glucose</td>
<td>[M+Na]$^+$ 1313.5257</td>
<td>1313.5±0.5</td>
<td>RebM (1.3)</td>
</tr>
</tbody>
</table>

[00135] The levels of steviol glycosides were quantified by comparing with calibration curves obtained with authentic standards from LGC Standards. For example, standard solutions of 0.5 to 100 µM RebA were typically utilized to construct a calibration curve.

[00136] Method B: A second analytical method was performed on the Agilent system 1290 Infinity fitted with a waters ACQUITY UPLC® BEH shield RP18 column (2.1 x 50 mm, 1.7 µm particles, 130 Å pore size, Waters) was connected to a 6130 single quadrupol mass detector (Agilent) with a APCI ion source. Elution was carried out using a mobile phase of eiuent B (MeCN with 0.1% Formic acid) and eluent A (water with 0.1% Formic acid) by increasing the gradient from 23% to 47 % B from min. 0.0 to 4.0, increasing 47% to 100% B in min. 4.0 to 5.0, holding 100% B from min. 5.0 to 6.5 re-equilibration. The flow rate was 0.6 mL/min and the column temperature 50°C. The steviol glycosides were detected using SIM (Single Ion Monitoring) with the following m/z-traces.

Table 2. MS analytical information for Steviol Glycosides

<table>
<thead>
<tr>
<th>SIM trace No</th>
<th>time window</th>
<th>m/z trace</th>
<th>Exact Mass</th>
<th>Description</th>
<th>compound (typical $t_r$ in min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.0-1.51min</td>
<td>1289.5</td>
<td>[M-H]$^-$</td>
<td>Steviol</td>
<td>RebM (0.91)</td>
</tr>
</tbody>
</table>
[00137] The levels of steviol glycosides were quantified by comparing with calibration curves obtained with authentic standards from LGC Standards. For example, standard solutions of 0.3 to 25 μM RebA were typically utilized to construct a calibration curve.

[00138] Method C: A third analytical method used was LC-MS analyses performed using a Waters ACQUITY UPLC (Waters Corporation, Milford, MA) with Waters ACQUITY UPLC® BEH C18 column (2.1 x 50 mm, 1.7 μm particles, 130 A pore size) coupled to a Waters ACQUITY TQD triple quadrupole mass spectrometer with electrospray ionization (ESI) in negative mode. Compound separation was achieved by 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-equilibrate for another 0.6 min. The flow rate was 0.6 mL/min and the column temperature 55°C. RebD (m/z 1127.5), RebM (m/z 1289.5), redaudioside A (m/z 965.4) and RebB (m/z 803.4) were monitored using SIM (Single Ion Monitoring) and quantified by comparing with authentic standards.

**Example 2. Construction of a Steviol Glycoside-Producing Yeast Strain**

[00139] Steviol glycoside-producing *S. cerevisiae* strains were constructed as described in WO 201 1/153378, WO 2013/022899, WO 2014/122227, and WO 2014/122328, each of which is incorporated by reference in its entirety. For example, a yeast strain comprising a recombinant gene encoding a *Synechococcus* sp. GGPPS polypeptide (SEQ ID NO:1, SEQ ID NO:149), a recombinant gene encoding a truncated *Zea mays* CDPS polypeptide (SEQ ID NO:2, SEQ ID NO:150), a recombinant gene encoding a truncated *Zea mays* KS polypeptide (SEQ ID NO:3, SEQ ID NO:151), a recombinant gene encoding a recombinant *S. rebaudiana* K01 polypeptide (SEQ ID NO:4, SEQ ID NO:152), a recombinant gene encoding...
an *A. thaliana* ATR2 polypeptide (SEQ ID NO:5, SEQ ID NO:153), a recombinant gene encoding an *O. sativa* EUGT11 polypeptide (SEQ ID NO:12; SEQ ID NO:148), a recombinant gene encoding an SrKAHel polypeptide (SEQ ID NO:6, SEQ ID NO:154), a recombinant gene encoding an *S. rebaudiana* CPR8 polypeptide (SEQ ID NO:7, SEQ ID NO:155), a recombinant gene encoding an *S. rebaudiana* UGT85C2 polypeptide (SEQ ID NO:8, SEQ ID NO:156), a recombinant gene encoding an *S. rebaudiana* UGT74G1 polypeptide (SEQ ID NO:9, SEQ ID NO:157), a recombinant gene encoding an *S. rebaudiana* UGT76G1 polypeptide (SEQ ID NO:10, SEQ ID NO:158), and a recombinant gene encoding an *S. rebaudiana* UGT91D2 variant (or functional homolog), UGT91D2e-b (SEQ ID NO:11, SEQ ID NO:159) polypeptide produced steviol glycosides. As analyzed by LC-MS (Method C) following DMSO-extraction of total steviol glycosides from the whole cell and broth mixture (total production), the strain produced between 18-21 µg/mL or 1-1.5 µg/mL/OD₆₀₀ RebM after growth for five days in 1 mL SC (Synthetic Complete) media at 30°C with 400 rpm shaking in deep-well plates. See Table 3.

Table 3. Steviol glycoside production in a representative *S. cerevisiae* strain comprising genes encoding GGPPS, truncated CDPS, KS, KO, ATR2, EUGT11, SrKAHel, CPR8, UGT85C2, UGT74G1, UGT76G1, and EUGT11 polypeptides.

<table>
<thead>
<tr>
<th>RebB (µg/mL/OD₆₀₀)</th>
<th>RebA (µg/mL/OD₆₀₀)</th>
<th>RebD (µg/mL/OD₆₀₀)</th>
<th>RebM (µg/mL/OD₆₀₀)</th>
<th>Normalized by OD₆₀₀</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.21</td>
<td>0.33</td>
<td>0.33</td>
<td>1.3</td>
<td>Average</td>
</tr>
<tr>
<td>0.028</td>
<td>0.054</td>
<td>0.032</td>
<td>0.14</td>
<td>Std Deviation</td>
</tr>
<tr>
<td>RebB (µg/mL)</td>
<td>RebA (µg/mL)</td>
<td>RebD (µg/mL)</td>
<td>RebM (µg/mL)</td>
<td></td>
</tr>
<tr>
<td>3.1</td>
<td>4.9</td>
<td>5.0</td>
<td>19.0</td>
<td>Average</td>
</tr>
<tr>
<td>0.42</td>
<td>0.81</td>
<td>0.48</td>
<td>2.1</td>
<td>Std Deviation</td>
</tr>
</tbody>
</table>

[00140] A second strain, which comprised additional copies of the genes of the first strain, was analyzed for steviol glycoside production. The second strain produced RebD and RebM as primary steviol glycosides, although at higher levels than the first strain.

[00141] As analyzed by LC-MS (Method C) following DMSO-extraction of total steviol glycosides from the whole cell and broth mixture (total production), the second strain produced between 60-80 pg/mL or 4-6 µg/mL/OD₆₀₀ RebM, after growth for five days in 1 mL SC media at 30°C with 400 rpm shaking in deep-well plates. Production of RebA, RebB, RebD and RebM by the second strain is shown in Table 4.
Table 4. Steviol glycoside production in a S. cerevisiae strain comprising additional copies of genes encoding GGPPS, truncated CDPS, KS, KO, ATR2, EUGT11, SrKAHe-I, CPR8, UGT85C2, UGT74G1, UGT76G1, and EUGT11 polypeptides.

<table>
<thead>
<tr>
<th>RebA</th>
<th>RebB</th>
<th>RebD</th>
<th>RebM</th>
<th>Normalized by OD600</th>
</tr>
</thead>
<tbody>
<tr>
<td>(µg/mL/OD600)</td>
<td>(µg/mL/OD600)</td>
<td>(µg/mL/OD600)</td>
<td>(µg/mL/OD600)</td>
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</tr>
<tr>
<td>2.1</td>
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<td>1.6</td>
<td>4.8</td>
<td>Average</td>
</tr>
<tr>
<td>0.66</td>
<td>0.21</td>
<td>0.75</td>
<td>2.3</td>
<td>Std Deviation</td>
</tr>
<tr>
<td>31.0</td>
<td>10.1</td>
<td>23.7</td>
<td>72.5</td>
<td>Average</td>
</tr>
<tr>
<td>9.9</td>
<td>3.1</td>
<td>11.3</td>
<td>34.4</td>
<td>Std Deviation</td>
</tr>
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</table>

Example 3. Knockout of Yeast Endogenous Transport Genes and Transport-Related Genes

[00142] Observations from deep-well studies of Example 2 and similar strains indicated that the fraction of RebA, RebB, RebD or RebM in the supernatant changes with time, and the effect was determined not to be the result of cell lysis. To determine the effect of various transporters on steviol glycoside excretion in S. cerevisiae, deletion cassettes for homologous recombination were obtained by designing primers annealing approximately 200 bp upstream and downstream of the open reading frame (ORF) and then amplifying the ORF-specific deletion cassette from the S. cerevisiae deletion collection. The candidate genes selected include identified ORFs with relation to transport or comprising membrane spanning domains, regardless of subcellular localization. In the resulting colonies, the presence of the deletion cassette at the correct locus was verified by colony PGR. A maximum of 6 clones of each deletion was frozen down as freezer stock. All samples for analysis were initiated from the freezer stock and grown in SC medium for 5 days (30°C, shaking 400 rpm) prior to harvest and extraction of samples for LC-MS. Samples were analyzed for the presence of RebA, RebB, RebD and RebM in the culture broth lacking cells (Supernatant) as well as in the whole cell and broth mixture (Total production).

[00143] Concentrations of total and supernatant RebA, RebB, RebD and RebM were compared to the levels in a control steviol glycoside-producing strain. The amounts of RebA, RebB, RebD and RebM in each sample were normalized to the control strain by dividing the value of a particular steviol glycoside with the corresponding value for the control strain, thereby calculating a percentage to the control strain, where 1 equals 100 percent. The "ideal candidate" would exhibit a decrease in RebA, RebB, RebD and/or RebM levels in the supernatant, as compared to the control steviol glycoside-producing strain, without decreasing RebA, RebB, RebD, and/or RebM total production.
The effect of yeast gene knockouts on transport of higher molecular weight steviol glycosides into the culture medium was tested in a strain that produces steviol glycosides, such as the strains described in Example 2. Disruption of each specific transporter gene was performed by homologous recombination. After 5 days of growth in 1 mL SC medium at 30°C and 400 rpm, cells were harvested. A 50 µL aliquot of the culture was mixed with an equal volume of 100% DMSO, vortexed, and heated to 80°C for 10 min. The suspension was then centrifuged to remove cell debris. 60 µL of the mixture were analyzed by LC-MS as the "Total" sample. The remaining culture was then centrifuged to pellet cells. An aliquot of 50 µL was removed from the supernatant (i.e., the culture medium) and mixed with an equal volume of 100% DMSO. The suspension was heated to 80°C for 10 min and centrifuged. 60 µL of the mixture were analysed by LC-MS as the "Supernatant" sample. The amounts of higher molecular weight steviol glycosides (including RebA, RebB, RebD, RebM) were measured by LC-MS (Method C), as described in Example 1.

The data demonstrate that disruption of a single endogenous yeast transporter gene in a steviol glycoside-producing strain resulted in a decrease in the level of various steviol glycosides in the supernatant of the culture media, as evaluated by the normalized amount transported into the supernatant (see Tables 5-10). Tables 5-10 comprise lists of transport related genes that were knocked out in a steviol glycoside-producing strain. More specifically, Table 5 comprises a compiled list of genes by ordered locus name found to affect steviol glycoside excretion in steviol glycoside-producing strains and are therefore identified as having a role in steviol glycoside excretion. When the specified genes were knocked out, a more than 40% decrease in either the supernatant alone or in the ratio of supernatant/total production of RebA, RebB, RebD, and/or RebM was observed. This corresponded approximately to more than 2 standard deviations removed from the mean of a control steviol glycoside-producing strain (a value of 1 equals 100 percent of the control strain, whereas a value of 0.5 indicates a 50% decrease).

Table 6 comprises a compiled list of genes by ordered locus name found to affect steviol glycoside excretion in steviol glycoside-producing strains and are therefore identified as having a role in steviol glycoside excretion. When knocked out, these genes caused a mean of between 20-40% decrease in either the supernatant alone or in the ratio of supernatant/total production. This corresponded to approximately between 1 and 2 standard deviations removed from the mean of the control strain (a value of 1 equals 100 percent of the control strain, whereas a value of 0.5 indicates a 50% decrease).
Table 5A. Transport related genes with over a 40% decrease in Reb A, RebB, RebD or RebM levels compared to a control steviol glycoside-producing strain.

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<tr>
<th>SEQ ID No.</th>
<th>Ordered Locus Name</th>
<th>Family</th>
<th>Description</th>
<th>Gene name</th>
<th>Uniprot Accession No.</th>
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Table 5B. Continued list of Transport related genes with over a 40% decrease in Reb A, RebB, RebD or RebM levels compared to a control steviol glycoside-producing strain.

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<th>No.</th>
<th>Ordered Locus Name</th>
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Table 6A. Transport related genes with a 20-40% decrease in Reb A, RebB, RebD or RebM levels compared to a control steviol glycoside-producing strain.

<table>
<thead>
<tr>
<th>SEQ ID No.</th>
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<th>Family</th>
<th>Description</th>
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<th>Uniprot Accession No.</th>
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Table 6B. Continued list of Transport related genes with a 20-40% decrease in Reb A, RebB, RebD or RebM levels compared to a control steviol glycoside-producing strain.

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<th>No.</th>
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<th>Description</th>
<th>Gene name</th>
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<td>P15380</td>
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<td>ATP-Dependent</td>
<td>PMA2</td>
<td>P19657</td>
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</tbody>
</table>

[00147] Steviol glycoside exporter candidates were selected from the data based on two selection criteria for each steviol glycoside measured (i.e., two methods of normalizing expression).

[00148] Transporter selection criterion 1 corresponded to selection based on the level of high molecular weight steviol glycosides (RebA, RebB, RebD, or RebM) available in the supernatant, as well as the total production of the said steviol glycoside. Both values were normalized to the value of the corresponding steviol glycoside-producing control strain. The control level was set to 1, and the corresponding steviol glycoside level was calculated as a
percentage of the control. For Ordered Locus Names (i.e., genes) of interest, the steviol glycoside available in the supernatant should be below 0.6 (below 60% of the control) or between 0.8-0.6 (80-60% of the control). To avoid false positives or a bias towards transporters that decrease the production in general, the calculation had an additional requirement that the total production had to be similar to the control. In the current calculation, production was set to be between 0.85 and 1.15 of the control, when the control is set to 1. In this regard, steviol glycoside production levels did not affect results. Table 7 shows the supernatant/total ratio for each candidate that fulfills the selection criteria.

[00149] Transporter selection criterion 2 corresponded to selection based on the ratio of high molecular weight steviol glycosides (RebA, RebB, RebD, or RebM) in the supernatant relative to total production of the said steviol glycoside. The supernatant-to-total production ratio was normalized to the ratio of the corresponding steviol glycoside-producing strain control. The control level was set to 1, and the corresponding steviol glycoside ratio was calculated as a percentage of the control. For Ordered Locus Names (i.e., genes) of interest, the supernatant-to-total production ratio for a given steviol glycoside should be below 0.6 (below 60% of the control) or between 0.8-0.6 (80-60% of the control). To avoid false positives or a bias towards transporters that decrease the production in general, the calculation had an additional requirement that the total production had to be similar to the control. In the current calculation, production was set to be between 0.85 and 1.15 of the control, when the control is set to 1. In this regard, steviol glycoside production levels did not affect results. Table 8 shows the supernatant/total ratio for each candidate that fulfills the selection criteria.

[00150] The data demonstrate that disruption of a single endogenous yeast transporter gene in a steviol glycoside-producing strain resulted in a decrease in the level of various steviol glycosides in the supernatant of the culture media, as evaluated by the normalized amount transported into the supernatant (see Tables 5-10), and are therefore identified as having a role in steviol glycoside excretion.

[00151] For example, deletion in a steviol glycoside-producing strain of YDL128W (SEQ ID NO:22), YDL194W (SEQ ID NO:24), YDL210W (SEQ ID NO:25), YFL01 1W (SEQ ID NO:33), YGL006W (SEQ ID NO:34), YGL013C (SEQ ID NO:35), YGL255W (SEQ ID NO:36), YGR181W (SEQ ID NO:38), YGR217W (SEQ ID NO:39), YIL088C (SEQ ID NO:43), YJL094C (SEQ ID NO:45), YJR106W (SEQ ID NO:48), YNL065W (SEQ ID NO:59), YNL083W (SEQ ID NO:61), YNL121C (SEQ ID NO:63), YNL142W (SEQ ID NO:64), YOR306C (SEQ ID NO:75), or YPR01 1C (SEQ ID NO:82) led to a measurable decrease of RebD excreted into the culture medium, indicating that each plays a role in RebD excretion.
This was confirmed by transporter selection criteria 1 and 2 (see Tables 7 and 8, RebD column).

[00152] Furthermore, for example, deletion in a steviol glycoside-producing strain of YBR180W (SEQ ID NO:13), YBR241C (SEQ ID NO:17), YCL069W (SEQ ID NO:19), YCR075C (SEQ ID NO:21), YDL128W (SEQ ID NO:22), YDL194W (SEQ ID NO:24), YDR093W (SEQ ID NO:27), YDR338C (SEQ ID NO:28), YER166W (SEQ ID NO:32), YFL011W (SEQ ID NO:33), YGL006W (SEQ ID NO:34), YGL013C (SEQ ID NO:35), YGL255W (SEQ ID NO:36), YGR217W (SEQ ID NO:39), YJL094C (SEQ ID NO:45), YJR106W (SEQ ID NO:48), YJR160C (SEQ ID NO:49), YKR106W (SEQ ID NO:53), YML116W (SEQ ID NO:55), YMR056C (SEQ ID NO:57), YNL070W (SEQ ID NO:60), YNL083W (SEQ ID NO:61), YNL095C (SEQ ID NO:62), YNL121C (SEQ ID NO:63), YOR087W (SEQ ID NO:70), YOR291W (SEQ ID NO:74), YOR306C (SEQ ID NO:75), YPL274W (SEQ ID NO:80), or YPR011C (SEQ ID NO:82) led to a measurable decrease of RebM, indicating that each plays a role in RebM excretion. This was confirmed by transporter selection criteria 1 and 2 (see Tables 7 and 8, RebM column).

[00153] Table 7 represents the calculated ratio, normalized to a steviol glycoside-producing strain comprising genes encoding GGPPS, truncated CDPS, KS, KO, ATR2, EUGT1 1, SrKAHel, CPR8, UGT85C2, UGT74G1 , UGT76G1 , and EUGT1 1 polypeptides, of supernatant/total production for each gene (by ordered locus name) deleted in the steviol glycoside-producing strain. The supernatant or supernatant/total ratio of less than 0.6 represented a more than 40% decrease in either the supernatant alone or in the ratio of supernatant/total production of RebA, RebB, RebD, or RebM, which corresponded approximately to more than 2 standard deviations removed from the mean of the control steviol glycoside-producing strain and indicates the gene as having a role in steviol glycoside transportation (Table 7). The supernatant or ratio supernatant/total of between 0.6 and 0.8 represents a 40-20% decrease in either the supernatant alone or in the ratio of supernatant/total production of RebA, RebB, RebD, or RebM, which corresponds to approximately between 1 and 2 standard deviations removed from the mean of the control steviol glycoside-producing strain, and indicates the gene as having a role in steviol glycoside transportation and/or production (Table 8). Total production of each steviol glycoside was between 0.85 and 1.15 compared to the steviol glycoside-producing strain. Table 8 shows the supernatant/total ratio for each candidate that fulfills the selection criteria.

| Table 7. Transport related genes with over a 40% decrease in RebA, RebB, RebD or RebM compared to a control steviol glycoside-producing strain comprising genes |

<table>
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<tr>
<th>Transporter selection criterion 1</th>
<th>Transporter selection criterion 2</th>
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<td>Total vs. Supernatant</td>
<td>Ratio Sup/Total vs. Total</td>
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<tr>
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<tr>
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<tr>
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<tr>
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Table 8. Transport related genes with a 20-40% decrease in Reb A, RebB, RebD or RebM compared to a control steviol glycoside-producing strain comprising genes
encoding GGPPS, truncated CDPS, KS, KO, ATR2, EUGT11, SrKAHel, CPR8, UGT85C2, UGT74G1, UGT76G1, and EUGT11 polypeptides.

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[00154] The effect of yeast gene knockouts on transport of higher molecular weight steviol glycosides into the culture medium (i.e., supernatant) also was tested in a steviol glycoside-producing strain comprising additional copies of genes encoding GGPPS, truncated CDPS, KS, KO, ATR2, EUGT11, SrKAHel, CPR8, UGT85C2, UGT74G1, UGT76G1, and EUGT11 polypeptides, which was described in Example 2. The data demonstrated that disruption of a single endogenous yeast transporter gene in the steviol glycoside-producing strain resulted in a decrease in the level of various steviol glycosides in the supernatant of the culture media, as evaluated by the normalized amount transported or by the supernatant-to-total-production ratio (see Tables 9 and 10, RebD column). For example, deletion in the steviol glycoside-producing strain of YDR536W (SEQ ID NO:30), YHL016C (SEQ ID NO:42), YKR050W (SEQ ID NO:51), YOR291W (SEQ ID NO:74), YOR334W (SEQ ID NO:77), YPL270W (SEQ ID NO:79), YPR058W (SEQ ID NO:83), or YPR128C (SEQ ID NO:84) led to a measurable decrease of RebD transported into the supernatant, indicating that they play a role in RebD excretion. This was confirmed by transporter selection criteria 1 and 2 (see Tables 9 and 10, RebD column).

[00155] Furthermore, for example, deletion of YAL067C (SEQ ID NO:14), YDR406W (SEQ ID NO:29), YHL016C (SEQ ID NO:42), YJL212C (SEQ ID NO:47), YKR050W (SEQ ID NO:51), YMR034C (SEQ ID NO:56), YMR253C (SEQ ID NO:58), YOL075C (SEQ ID NO:66), YOL122C (SEQ ID NO:68), YOR222W (SEQ ID NO:73), YPR003C (SEQ ID NO:81), or YPR201W (SEQ ID NO:85) led to a measurable decrease of RebM transported into the supernatant, indicating that they play a role in RebM excretion. This was confirmed by transporter selection criteria 1 and 2 (see Tables 9 and 10, RebM column).

[00156] Table 9 represents the calculated ratio, normalized to a steviol glycoside-producing strain comprising additional copies of genes encoding GGPPS, truncated CDPS, KS, KO, ATR2, EUGT11, SrKAHel, CPR8, UGT85C2, UGT74G1, UGT76G1, and EUGT11 polypeptides, of supernatant/total production for each gene (by ordered locus name) deleted in the steviol glycoside-producing strain. The supernatant or ratio supernatant/total of less than 0.6 represents a more than 40% decrease in either the supernatant alone or in the ratio of supernatant/total production of RebA, RebB, RebD, or RebM, which corresponds approximately to more than 2 standard deviations removed from the mean of a control steviol glycoside-producing strain, and indicates the gene as having a role in steviol glycoside transportation or production (Table 9). The supernatant or ratio supernatant/total of between 0.6 and 0.8 represents a 40-20% decrease in either the supernatant alone or in the ratio of supernatant/total production of RebA, RebB, RebD, or RebM, which corresponds to approximately between 1 and 2 standard deviations removed from the mean of the control strain, and indicates the gene as having a role in steviol
glycoside transportation and/or production, and indicates the gene as having a role in steviol glycoside transportation and/or production (Table 10). Total production of each steviol glycoside was between 0.85 and 1.15 compared to the control steviol glycoside-producing strain. Table 10 shows the supernatant/total ratio for each candidate that fulfills the selection criteria.

### Table 9. Transport related genes with over a 40% decrease in Reb A, RebB, RebD or RebM compared to a control steviol glycoside-producing strain comprising additional copies of genes encoding GGPPS, truncated CDPS, KS, KO, ATR2, EUGT11, SrKAHel, CPR8, UGT85C2, UGT74G1, UGT76G1, and EUGT11 polypeptides.

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Table 10. Transport related genes with a 20-40% decrease in Reb A, RebB, RebD or RebM compared to a control steviol glycoside-producing strain comprising additional copies of genes encoding GGPPS, truncated CDPS, KS, KO, ATR2, EUGT11, SrKAHel, CPR8, UGT85C2, UGT74G1, UGT76G1, and EUGT11 polypeptides.

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[00157] Knockouts of YDL210W (SEQ ID NO:25) and YPL270W (SEQ ID NO:79) resulted in decreased RebD excretion in the steviol glycoside-producing strain comprising genes encoding GGPPS, truncated CDPS, KS, KO, ATR2, EUGT11, SrKAHel, CPR8, UGT85C2, UGT74G1, UGT76G1, and EUGT11 polypeptides and the steviol glycoside-producing strain comprising additional copies of genes encoding GGPPS, truncated CDPS, KS, KO, ATR2, EUGT11, SrKAHel, CPR8, UGT85C2, UGT74G1, UGT76G1, and EUGT11 polypeptides. As well, knockouts of YJL212C (SEQ ID NO:47) and YOL122C (SEQ ID NO:68) resulted in decreased RebM transport in both strains.

Example 4. Confirmation of Knockout of Yeast Endogenous Transport Genes by overexpression in a RebD/M-producing strain
Overexpression of a subset of the initial candidate transporters from Example 3 was performed using both plasmid-based expression and an integration cassette. First, deep-well microtiter plate culture experiments were carried out. Two transport genes were overexpressed using a plasmid in a RebD/M-producing strain in order to confirm the results from the knockout experiments. YGR181W (SEQ ID NO:38), a TIM complex, helper protein for insertion of mitochondrial inner membrane proteins, and YDR061W (SEQ ID NO:26) an ABC-like transporter were overexpressed. The data shown in Figure 2 demonstrate that the phenotype based on the knockout studies was confirmed with a plasmid based overexpression phenotype for YGR181W (SEQ ID NO:38) and YDR061W (SEQ ID NO:26) in deep-well plates.

Next, confirmation of the phenotype in fermenters was performed in additional steviol glycoside-producing strains, which were characterized by integration of YGR181W (SEQ ID NO:38) or YDR061W (SEQ ID NO:26) on chromosome XII. The steviol glycoside-producing strains were grown on defined media at 30°C in a fed-batch fermentation for about 5 days under glucose-limited conditions, and the levels of RebA, RebB, RebD, and RebM were measured using LC-MS (Method B, Example 1). The graphs shown in Figure 3 illustrate an approximate 2-fold increase in RebD and RebM transported in the culture medium for the new integration constructs, and little change in RebA and RebB transport. Overexpression of YGR181W (SEQ ID NO:38) or YDR061W (SEQ ID NO:26) resulted in improved (~2-fold) RebD and RebM transport into the culture medium (~400-500 mg/L of supernatant RebD and RebM in YGR181W (SEQ ID NO:38) and YDR061W (SEQ ID NO:26) overexpression strains versus ~250 mg/L of supernatant RebD and RebM in a control steviol glycoside-producing strain). See Figure 3A. The ratio of transported RebD as compared to the total RebD increased from 0.158 in the control strain to 0.21-0.25 with the candidate genes overexpressed. RebM transport into the culture medium was also simultaneously improved. See Figure 3.

Example 5. Overexpression of Selected Yeast Endogenous Transport Genes

Overexpression in a steviol glycoside-producing strain (as described in Example 2) using a plasmid with a constitutive promoter of the transporter genes shown in Table 11 resulted in greater than a 20% increase in excretion of RebA, RebB, RebD, and/or RebM. Results were analyzed using criterion 2 described in Example 3. Additionally, overexpression of the transporter genes shown in Table 12 resulted in greater than a 40% improvement in production of RebA, RebB, RebD, and/or RebM. Table 11 shows the supernatant/total ratio for each candidate that fulfills the selection criteria.
Table 11. Transport related genes with over a 20% increase in RebA, RebB, RebD or RebM excretion, compared to a control stevitol glycoside-producing strain.

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<th>Ratio Supernatant/Total</th>
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### Table 12. Transport related genes with over a 40% increase in RebA, RebB, RebD or RebM production, compared to a control stevioside-producing strain.

<table>
<thead>
<tr>
<th>Gene</th>
<th>RebB</th>
<th>RebA</th>
<th>RebD</th>
<th>RebM</th>
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<tbody>
<tr>
<td>YJR106W</td>
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<td></td>
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<tr>
<td>YBR043C</td>
<td>1.20</td>
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<tr>
<td>YPR011C</td>
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<td></td>
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</tbody>
</table>

### Increases in Production

<table>
<thead>
<tr>
<th>Gene</th>
<th>RebB</th>
<th>RebA</th>
<th>RebD</th>
<th>RebM</th>
</tr>
</thead>
<tbody>
<tr>
<td>YMR166C</td>
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<td></td>
<td></td>
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<tr>
<td>YIL166C</td>
<td>1.41</td>
<td>1.50</td>
<td>1.55</td>
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<tr>
<td>YKR039W</td>
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<tr>
<td>YKL146W</td>
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<td></td>
</tr>
<tr>
<td>YJL093C</td>
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<td>1.43</td>
<td></td>
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<tr>
<td>YOR306C</td>
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<td>YHR096C</td>
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</table>
Example 6. Genomic Integration of Transporter Genes

DNA of the transporter genes selected for integration into the genome of a RebD/M-producing S. cerevisiae strain (see Example 2) was amplified from an S288C background by PGR and cloned into a plasmid with homology regions for the integration site and a PGK1 promoter for overexpression, using the USER cloning system. See, e.g., Nour-Eidin et al., 2010, Methods Mol Biol. 643:185-200. The USER cloning construct including the homology regions and the transporter was cut out from the plasmid using restriction enzymes, and the linear piece of DNA was integrated into the genome of the receiving RebD/M-producing strain by standard LiAc method. The genomically integrated transporters were tested in plates that release glucose from a polymer after addition of a growth medium. A polymer that releases 20 g/L glucose over 3 days was used to mimic the feed profile during fermentation. Steviol glycoside levels were measured by LC-MS (see Example 1), and OD$_{600}$ was measured on a Perkin Elmer 2104 Multilabel reader. YBR043C (SEQ ID NO:88), YEL027W (SEQ ID NO:102), YJL093C (SEQ ID NO:44), YJR106W (SEQ ID NO:48), YKL120W (SEQ ID NO:126), and YMR166C (SEQ ID NO:132) showed improved excretion of 13-SMG. (Figure 4A). YBR043C (SEQ ID NO:88), YEL027W (SEQ ID NO:102), and YMR166C (SEQ ID NO:132) showed improved excretion of RebA (Figure 4B). YBR043C (SEQ ID NO:88), YEL027W (SEQ ID NO:102), and YMR166C (SEQ ID NO:132) showed improved excretion of RebB (Figure 4C). YBR043C of SEQ ID NO:88, YEL027W of SEQ ID NO:102, YJL093C of SEQ ID NO:44, YJR106W of SEQ ID NO:48, and YMR166C of SEQ ID NO:132 showed improved production of RebD, and YBR043C of SEQ ID NO:88, YEL027W of SEQ ID NO:102, YIL166C (SEQ ID NO:121), YJL093C of SEQ ID NO:44, YJR106W of SEQ ID NO:48, and YMR166C of SEQ ID NO:132 showed improved production of RebM, as measured by an increase in RebD and RebM levels in the

<table>
<thead>
<tr>
<th>Genes</th>
<th>RebB</th>
<th>RebA</th>
<th>RebD</th>
<th>RebM</th>
</tr>
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<tr>
<td>YDR338C</td>
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<td>1.44</td>
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<tr>
<td>YBR043C</td>
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<tr>
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supernatant compared to a control steviol glycoside-producing strain. See Figures 4D and 4E. Controls with a URA marker are also shown in Figure 4.

[00162] Figure 5A shows supernatant levels of RebA, RebB, RebD, and RebM of an additional steviol glycoside-producing strain overexpressing YMR166C (SEQ ID NO:132), YEL027W (SEQ ID NO:102), YKL120W (SEQ ID NO:126), YJR106W (SEQ ID NO:48), YJL093C (SEQ ID NO:44), and YBR043C (SEQ ID NO:88) by the USER cloning system. The strain of Figure 5 comprised a recombinant gene encoding a *Synechococcus sp.* GGPPS polypeptide (SEQ ID NO:1, SEQ ID NO:149), a recombinant gene encoding a truncated *Zea mays* CDPS polypeptide (SEQ ID NO:2, SEQ ID NO:150), a recombinant gene encoding an *A. thaliana* KS polypeptide (SEQ ID NO:3, SEQ ID NO:151), a recombinant gene encoding a recombinant *S. rebaudiana* K01 polypeptide (SEQ ID NO:4, SEQ ID NO:152), a recombinant gene encoding a KO polypeptide (SEQ ID NO:XX, SEQ ID NO:XX), a recombinant gene encoding an *A. thaliana* ATR2 polypeptide (SEQ ID NO:5, SEQ ID NO:153), a recombinant gene encoding an O. sativa EUGT11 polypeptide (SEQ ID NO:12; SEQ ID NO:148), a recombinant gene encoding an SrKAHel polypeptide (SEQ ID NO:6, SEQ ID NO:154), a recombinant gene encoding an *S. rebaudiana* CPR8 polypeptide (SEQ ID NO:7, SEQ ID NO:155), a recombinant gene encoding an *S. rebaudiana* UGT85C2 polypeptide (SEQ ID NO:8, SEQ ID NO:156), a recombinant gene encoding an *S. rebaudiana* UGT74G1 polypeptide (SEQ ID NO:9, SEQ ID NO:157), a recombinant gene encoding an *S. rebaudiana* UGT76G1 polypeptide (SEQ ID NO:10, SEQ ID NO:158), and a recombinant gene encoding an *S. rebaudiana* UGT91D2 variant (or functional homolog), UGT91D2-e-b (SEQ ID NO:1 1, SEQ ID NO:159) polypeptide. Figure 5B shows total levels of RebA, RebB, RebD, and RebM of the above described steviol glycoside-producing strain overexpressing YMR166C (SEQ ID NO:132), YEL027W (SEQ ID NO:102), YKL120W (SEQ ID NO:126), YIL166C (SEQ ID NO:132), YJR106W (SEQ ID NO:48), YJL093C (SEQ ID NO:44), and YBR043C (SEQ ID NO:88) by the USER cloning system.

Example 7. Production of RebD and RebM by Fermentation of Steviol Glycoside-Producing *S. cerevisiae* strains overexpressing YJL093C or YBR043C

[00163] YJL093C (SEQ ID NO:44) and YBR043C (SEQ ID NO:88) were individually overexpressed in the steviol glycoside-producing strain described in Example 3. The strains were cultivated by fermentation (fed-batch, minimum medium, glucose-limiting) for approximately 130 h. Production of RebD and RebM was measured by LC-MS. As shown in Table 13, the strains overexpressing YJL093C or YBR043C produced higher levels of RebD and RebD + RebM, as compared to a control steviol glycoside-producing strain.
Table 13. Production of RebD and RebM in *S. cerevisiae* strains overexpressing YJL093C and YBR043C.

<table>
<thead>
<tr>
<th>Strain</th>
<th>Ferm. Length (h)</th>
<th>Final Cell Dry Weight</th>
<th>RebD Titer (g/L)</th>
<th>RebM Titer (g/L)</th>
<th>RebD + RebM</th>
<th>RebD/Reb M Ratio (g/g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>126.83</td>
<td>104.53</td>
<td>1.38</td>
<td>4.47</td>
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<td>YJL093C</td>
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<td>2.72</td>
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</table>
Table 14. Sequences disclosed herein.

SEQ ID NO: 1
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</thead>
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<td></td>
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SEQ ID NO: 2
Zea mays truncated CDPS

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</tbody>
</table>

The sequences are provided in the context of the table, with start and stop positions indicated. The sequences are compared with those from Zea mays (truncated CDPS), and the alignment is shown with specific nucleotide positions highlighted.
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agaagagagtc  taacttga 2358

SEQ ID NO: 3
Arabidopsis thaliana KS (similar to GenBank AEE36246.1)
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S. rebaudiana KOI (codon optimized)

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taatcataa aacatcattc acagcaccctt tgggccctta tcgcagaaac 480
aagcaataaa ttcacagaga tatacatgta gataacatat tataacttaa tcatgaattc 540
gtgcctaacc aacacaagctt gccgcaagct aataacttttta atccgagtta 600
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SEQ ID NO: 8
Stevia rebaudiana UGT85C2 (codon optimized)

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120

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180

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CCGTGACGTTTGGTAA
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SEQ ID NO: 9
S, reubadiaena UGT74G1 (GenBank AAR06920.1)

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CGTAAGGAAA AAAAACTTCG TTGGTTTTAT CTGCTTTCAT 660
GTCTTCTTCA AACTTATGCT TTTATACACG 1140
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SEQ ID NO: 10
S, reubadiaena UGT76G1 (codon optimized)

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GCTGTGCTT TCTTCTTCTT GATATCAGTG 1140
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rebaudiana UGT91D2e-b (codon optimized)

Oryza sativa sequence encoding EUGT11 (codon optimized)

YBR180W

>sp|P38125|DTR1_YEAST Dityrosine transporter 1 OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=DTR1 PE=1 SV=1 MGSEPFQQKKNGLQINSQESGTTSTRFSLEDLDVINESWDQVNQKRANIDHDFVHEH PSSPSLSAQKAKTKEEEVAVKSSNSQSRDPSDTPQAHIPYFSKDQRLI IFGII IFIG FLGPMGNIYIPALPLLQREYDVSDATTINAVSFVMASVGFPLHMGALADFFGRKFLYM VSLSLMILVAAVPVNLIAL FLRIFQAFASSSVISLGAHTPGVPPKRGKAIAY FMGMGMGPI IAPIVAKLMLMKYWRNLFQTSMTIGIALILVTALLPETLRCIVNGD PKWGDKKRERENESEPFQGDIHRPFQVYDQFQENFPFPPKLGLLYW KMKCPI IITSVSTALFSYYAAYVTFSSYYHEHDFMLTEIGAAYVCPGMMLLSGQ SGGHLSFWRKSHPKKFFAEPRLLNLGIGILITIGTGYGWAIFHYFVVLV FSALTAGMTWCSNTMLYELFPRKAAAGTVAVSSFFRNVAIIAISIL ILQLCNAMIG WCFTGLGCISISLIGILYLLI FQRKYTAKE F

YAL067C

>sp|P39709|SE01_YEAST Probable transporter SE01 OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=SE01 PE=1 SV=1 MYSIVKEIIVDPYKRLKWGFIPVKRQVEDLPDDLNSTEIVTISNSIQSHETAENFITTS EKDQLHFETSYSSEHDKNVSVRTSSEYRDEADRFPWRRFFDEQEPYRINEKERSHKNKWSWF KQGTSFPEKKRKLKLDVALLFASYCIAYWKYLYTDVNINAYVMKEDLGFQGNDLVHTQ VMYTVGNI YNLKLPLNYVPSLDCWSSLTVAVAYGNYPVLKAIRFICAG EAISYALAYQLFSGYFKHDMVRASSAIFAYQIGILSAAGIQASYSSLNVNGVLEGWR WNF1 IDAIVSVVVVLIGFYSLPGFDPYCNISIFLTDEIRLARKLENQGTKSDETFKVF DIKLWKTIFSDKLYILTLLNIFCNDSNVSSGAYLLWKLKRYSIPKLQNLSTLTPGMVYLMILGTV IADKLHSRWFAII FTOVFNIIGNSILAADWDAEGAKWAFMLQCGFWAMA PVLYSWQNDICRRDAQTRAITLVTMNIMAQSSTAWISVVLKTEEPARYLGKFTFTACSA FCLSIWTFVVLVFYKRDERRNAKNGIVYNKSHGVEKPTSKDVE LTSVSD

YBL089W

>sp|P38176|AVT5_YEAST Vacuolar amino acid transporter 5 OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=AVT5 PE=3 SV=2 MPSNVRSGVLLTHTACAGCAGLVAMFPFKPFLMPGLTTLTFCGICSCLGALLQTRIAKY VPKSENAFKAKLQNLPSISVVFDFAIAYCFGVGVSYLLIVGDLYQPI VQSFYRNDD NMSGSQEHMIHFLDRLRYTILI IFVVISPLCFKRSLNLSRYASMIAIVSVAYLSGLIYHF VNRHQLERQGQVFYMPHGDQSHPSPLTLPI FVFAYTCHongFVSEINAQVDKSFKVIIRI PEGIAVLYLQFYI IIGRTGMTFGENIVGNLILYPSNISITITGRALMLILVMAFLQLC HPRCSSVKNII IFIENFRKGKYDNRSFPIPLDFNSEDQEPATQQNEENPLRSELSR
HINITLCLILLFSYLLAIISITSLAKVLAIVGATGSTSISFlPGFLGYKLGSEFTGNE
RVPSIKFKYLSLSIFWGIAMAVMSLAIIFVLGTSSH

SEQ ID NO: 16
YBR099W
>sp| P07251|ATPA__YEAST ATP synthase subunit alpha, mitochondrial
OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=ATP1
PE=1 SV=5
MLARTAARLSRRTLINSTKAAPAAAALASTRRLASTKAQPTEVSSILEERIKGVSDEA
NLMETGRVLAVGDIGARVFGLNQAEELVE FSSGKGMALNLE PQQVGIWLFGS DRLVK
EGELVKRTGNIIVDPVGGLGRLVDAALGNPIDKGP IDAGRSRQAQVAKPGLRPRSVH
EPVQQTGLKAVALVP IGRGQRELIGDQGTKAVALDT ILSNKNWNS DESKLCYCVY
VAVQGKRVSTVAVQLTEQHDAMYSIIVAATAASEAPLQYLAPFTASAIGEWFRDNKHH
ALIVYDLSQKVAYQVRQPPGGTPPRPPPPPPPPPPPPPPPPPPPPPPPPPPPPPPPPPPPPPP
PVWSTQGGDVSAYIPNVIISITDDQGFLAEFYYGKIRPAINFVGLSVSRVGSAAQVKAL
KQVAGSLKFLAQYREVAAFAFQGSLDDLASTQTLVGERLTQQLKQONYSPATEEQVP
L1YAGVNYHGDIEGIESRIGEFESSFLYLSKSNHELLEIREKGELKELASLKATES
FVATF

SEQ ID NO: 18
YBR241C
>sp| P38142|YBR91__YEAST Probable metabolite transport protein YBR241C
OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=YBR241C
PE=1 SV=1
MAETERLMPNGGSRETKPLITGHILGTIVACLSIQYGHIAELNAPQFLSCRSREAP
DENISYDDTWWQGHGLQKCIATDSQYGAITSIFSISGLLGYSYAGANRNAYRKYVSMG
ASACMVLSSLFFLSNQLLLGFRVGLMSCGTAIVITPLFNEIFAVPEWREGAMSMNQ
VSINLGLILLTLALSYDNAWRLWLFSGSVIAVANILAWLKDPSRLWVSHGFSVEASA
ETAFLKLRPTGQYAKQIEPDQHSGNSSHSGPSGLYQTQSSATQHWEAFAIGLGPFPFLI
IGELSYPQDA
ATAQSFSTVCNWLAFLTIVYGFLPIHGMGGYVFAFAIAAMFATYYVKVRPETKGKT
YSEWAGY

SEQ ID NO: 18
YBR2 94W
>sp| P38359|SUL1__YEAST Sulfate permease 1 OS=Saccharomyces cerevisiae
(strain ATCC 204508 / S288c) GN=SUL1 PE=1 SV=2
MSRKSSTEYVHNEQEDAEIEFESEYRESEAENRDGLHNGDEENWVKVNSSQKFGV
T KNELSVLVDS IPAYEESTVTLEKEYYDS IKNNLTAKSAGS YLVSLFPI IKWFPHYNFTW
GYADLVAGITVVCVPLQPPMMSYAIQASLSPEYGLYSFIGAFYISLFSATKDGCVGDVV
MSLQATKAVIEVLKYPDEPTQVIIATLCLLGIVATGGLRLGLFVMLISNAV
AGFMHGSASFNI IWQGIPALMGYNSLNTRENTYKVINTLKHLPNTLDAVFGLII PLVIL
YVVKWCGTFGILLDYRNPQPKVANRLKSFYQAQAMNAVIVVVFIAWSISWTIRNKRS
SKDRPISILGTVPSSNLNVQGVMKIPDGLLSNMSSEIPASI ILMVLEHIAISKFGRINDY
KVPFDQELIAIGVNTLIGGTFSYATGGSFAKCAKNVRTFFSGVFTGCVLALICY
LTDAAFFIPKATLSLAVIHSNLLTSYKTTFWKTNFLDCISFIVTFITVFISSENG
IFYMAMCSCAMLLKKQAFFAPFGKLGRVEAELNPTQEDIDAVISSNLEPNELNKQKKS
TVEVLFPAPEYKFS VKWVPFDHGYSRELINTTVRRPPPGVIVYRLGDFTYVNCRSRYHDI
IFDRIQLRTREQLQILTRKSSDRPNDPGKMPDSLLSFKHRSATTNDSLPSNINGS
SNGETYEKPLLLKVCDLDSQVAQDDAVSLVLDLRAVNYADROQVFHFAGIIPWIK
RSLL5VKFGTTNEEYSDSIIAGH5SFHVAKLDDYDYIEDD5RISTSYSNYETLCAAT
GTNLFFPFDIPDFSKWDV

SEQ ID NO: 19
YCL069W
>sp|P25594|YBA3_YEAST Vacuolar basic amino acid transporter 3
OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=YBA3
PE=1 SV=1
MMNLIVGRWVASGGLQTLCFVICTMVGERSRPLVISILSCAFAVAAIVGPI IGGAF
TTHTVWRWFYINLPFGLGLAI IMFLILYKAENKIGLQQIKAIGHTISSFTSFKRHQVN
FRLMGGII FKDFDGFGALCSAGLVLFLLGLFGGNKYSWNSGQQVIAYLVGLVLLFIPFLR
YDFFLDFKFNPEFDNISYRPPLLRLVAKPAI IIINMVFLLLCTGYNGQMIYSVQFFQLI
FASSAWKAGLHPIPIVITNVAAIASGVITKGLLVKDLLIFGGLVGIGALMTLMNTT
STKSTIQIVVLLPPGSLGFALQASLSAQLOLQITKDRPEAAMDFIEVTAFNTFMKSLGTTL
GGVLSTTVFSAFPHNKVSRHLEPEYGTKVDDMILYLRLQNYDSHSTIGNLSDSINKVF
WMDLGFYALGFCSFSNNKLL IPKDETPEDNLEDK

SEQ ID NO: 20
YCR028C
>sp|P25621|FEN2_YEAST Pantothenate transporter FEN2
OS=Saccharomyces cerevisiae (strain ATCC 204508 / 528c) GN=FEN2
PE=1 SV=1
MMKESKSITQHEVERESVSSKRAIKKLLFIDFLFVLSFVCQWNYVWDRGVFTNAYI
SGMKEDDKAMVNGDVTNTVMIFIGNYGMFPNNMLLLCVPPRIWLSFCTAWGLLIGMY
KVTSSFHKICRFQFALFESCSTFTSHVFVSLWEKEDELPIRSAIFTGSGLGVGMSFGF
QTSIFTHLNGLARGRLWFLPIDFCILPIAI YGFIFFGPLDQTSAVKSFSRTYIFN
EQLHYARRRLLPARDESTRLDWSTIPVRKLHRHWWMSLVWVGGENLFGASNFSTALWL
QNKQYTLAQRNYPNPSIFAVGVSTLCASVYMSKI PRARHWHSVFISLVMVIVAHLRA
DPLNPKVVSASQYLGAAQAVFVSSDWIIICAGDPRAIAVLASMNFSGAVNAWNWSI
LEFASDMVPKFPERGCVYALLATISSGIVSVIRSLQIKENLSSKQQVPYIDANDMPGEDD
DDQDNENDDGDESMEVELHNEEMAEISNPRF

SEQ ID NO: 21
YCR075C
>sp|P17261|ERS1_YEAST Cystine transporter OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=ERS1
PE=1 SV=1
MVSDLDDILGIVYTSWSISYMPPIITBRHRKASASAIMDFVLMNATAGYSLVISILQLY
CWMKMTGDDESGLRPKLQLQQDFWYCLHGLCMVNLQVVGARIRWRFGKGRKMNWPYL
RIASLAILFSSITTQVFMSNYDWDNNRTLAYCNFLKLSMISLIXIPQTVHNSTR
KSMDCFPIQGVFDTVGAIASLLQLIQWLSNDQGFSSLDTFTVNGKVLMSFLIFNIFN
IMQWFYVYRSRHDLASEYPL

SEQ ID NO: 22
YDL128W
>sp|Q99385|VCX1_YEAST Vacuolar calcium ion transporter
OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=VCX1
PE=1 SV=1
MDATTPPLTVANSHPARNPKHTAWRAAAYDLQYILKASPNMLFLLVFPLGLWHGFQLSH
TLFFLNFPLAI IPLAAILANATEEALDKAGNTIGGLNATFNAVELLVISI IALKKQVFR
IVQASMLGLSLLSNLLLVLGCLFI FGYNVQFTQFTQTAQQTMNSSLLAIACSLTI PAAFR
SEQ ID NO:23
YDL185W

>sp|P17255|YAT_A_yETAST V-type proton ATPase catalytic subunit A
OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=YMA1 PE=1 SV=3
MAGAIENARKEIRSLIDHAESEYGIAYSGFYIAENMGICAMELYKVGHDLNHVGE
VIRIDGKATIQVYEEETAGLTGDPVLRTGKPLSLVELGFLGMETI YDGQRPPLKAIEES
QSYSIPRGIPTDPALRTIKWQFTPQGHDISHGDIYGSXENLSSHKILLPPRSR
GITWIALAPAGETLDLKEILEVFDGGKSDFTLYHTWPRFRPPVTKEKLSADYPLLTQGVR
LDALFPCVQGTTCPGFCQGKTVISQGKLSDKNSDAII YVGFCAKGNVLMADGISIEC
IENIEWVNKMKGDGRPREWIKLPRGREMTSWYQKSQHRAHKDSRESSVPELLKFTCN
THELVVIRYRSLWRRSLRNGYFVFEVFTEMQKAPDRGRVELEVKSYSPISEGPE
RANELVYESYRKSANRFYWTEWIERADLSSILGHVHKATQTAPILYEHNFDDYMQKSK
FHTLIEGPKVLLAYGLLWGLDRLATFVSRDSTRLMDRTYEAKLNCAEYDNRKE
POQAYKTVNLYSKYVRGNIIRNLENFLDIAVYGGLFKDKMGKN PSFLSTDNGTRET
FLAGLDSYDGYTDHEGIKATIKTIHTSVRDLVSLARSGLLVVSNAEPAKVDMNGTKH
KISAYIMSGDGVVNLSVKSCAGSKSKFRPAAPAFAERCGRFYEQLKEDDYGTLIS
DDSDQFLQANVYHVNCQGNERGMVEMFPELYTEMGTEPIMKRTLWANTSNMP
VAAREASITYGTLAIEYFRQDGKWNMSIAADDSSSRWAELREISRGLGEQMDQGFPAYL
AKLAS FYERAGKAVLGS PRTDSGV YIAAWS PAGGDS DPYTATLGI TQVFWGLDKL
AQRKHFSINTSYSKYTNLVKAFYDSYFFPVLNDRMEILSNAEELEQVQVQLLVK
ALSDDDKITLDAVATILIKEDFLGTVIVPLQEGFQPDYRDMMRASFYIHDEAQAFAVANGA
NWSKLADSTGDVKHAWSKFFEFSERGEKVEHGEFKEKLSTIMQERFAEST

SEQ ID NO:24
YDL194W

>sp|P10870|SNF3__YEAST High-affinity glucose transporter SNF3
OS=Saccharomyces cerevisiae (strain ATCC 204508 / 5288c) GN=SNF3 PE=1 SV=3
MDPNSNSSESETLRIQEOKQFLDALKARPVKGIALRNNSNKHDTDDDTTGSIRTPTLSQQR
SRDQSNSTMSTVDIDSTTIDNLSIPQROQSMMSICVGFVAVGFLFCYDTGLINS
ITSMNYVKSHVAPNHDFTQAQMSILVSFLSLGTFGALTAPPISDYSGRKPTI IPSTIF
IFSIGNLQVAGGITYLLGVRWISGGIGAISAVPLYQAEATHKSLRGAI ISTYQWA I
TWGGLVSSAUXQGTHANDASYSRIPILQYVWSSLFAIGMFLFESPRPYWWLKDLEA
AKSLSFRLQGVDVHSGLLLEELVEIKATYDEAECSFSSNDICFISSSRPSQKTRLMFQGI
ALQAGFQSFQGFIPIFYYFENKTSGVSNYSVLFISITAYVNVFNPGVFVEFFGRRKV
LTVGVGVMITIANFIAVGCSLKVAAAKYMAIFCLIFIAFMASEATWGVVWVISAELYPL
GVRSDKCTAICAAANNLFICLPITYVIDTSGHTSSLGAKI FFIIWSLNAMGYIVVYL
ETYKFLGGLEDIGPLKSTGVSVPKFKNDIERALFKQYDPQLRLEDGKNTFVAKRRN
FDDETPRDNITSGPSHINSQNPKEVHSIPERDIPTSIELESPNKSSGMTPYPSPL
QDVPIQPTEPAIPRTKYVLQNLNLNTNRRPPSSLSSDSEDYTEDIIEGGPSSQGQDS
NRSTMINDYMYARIHISTASSNTTDKSQNOSTLYHTAHSHSDTTEEDSNLMGNG
LALNAYRNGFPSILMNSDEAANGGETSDNLNTAQLDGMERKAQAFAQSYIDKRGGLEN
ETQSNILSTLSVMADTNHEHNLSEHSSSEATNQFVPNENNDLK
SEQ ID NO: 25
YDL210W
>sp|P32837 |UGA4_YEAST GABA-specific permease OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=UAG4 PE=1 SV=1
MSMSSKNKIVSVQIRSTDGIQAYQLQGLSNLRSIRSKTGAGEVNYIDAKSVNDQL LAEIYQKQELKRFSTQLQVFGIAFSSISGMLLPSIASVMMGGGPGATLWGVFVAAPFL 
LVGTMAEHAIPAGGLYYNTYYAEGYEKI ISFI IGCNSLALAAVCGSIDIYLAE EIAAVATLKDGFNEVTSGKLYIAGAVVVMCITCVASGAIAIRLQTLSIFANFLIVL 
LFIALPKTTHRMMGGFNDGDIFGKYENLSDWNNGWFCLAGFMPAVTIGSPDSCVHS 
EEAKDAKXSVPGI ISSIAAVCWILGWI IICLMACINPDISVLDSDSKYGFALAQI YIDSL 
GKWWAIAFSLSLAFQCFLMGASITTTASRUQVAFSRDNGLPLSYIKRVDSDKYSVFFAI 
LAACGVGSLILGCLLCLIDDADALFSLAVAGNNLAWSTPTVFRLTSGRDLFPGFYYL 
GKWSPIVAVTGQVFQFII ILMVFMPSQHQHITKSTMNAYCIVGPIGWILAGI YYYKVKYK 
YHGATNLSDDDLYTEAVGADVIDTMSKQEP

SEQ ID NO: 26
YDR061W
>sp|Q12298 |YD061__YEAST Uncharacterized ABC transporter ATP-binding protein YDR061W OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=YDR061W PE=1 SV=1
MSTNKFVVRTNLFKSSLSASPPFVYYPKRIRNFIELPNEKWVIGPGKFKDLVNNKY 
ICEFPLSLRFGFLKESNINLPIERIEQVAFVKGVMPTAHLSARAYEFKDDYDQTCKQFIFDKA 
SGSNVSYKVFETNRMQLINLYLALNVLNLSLQRWVMGSLNSQMRARLRSILKEP 
DILLLIDDPFLGLDPAIAATISFQLAKDYSEISVSGCPVIPGKYQDTIPAWCHICCVDE 
KNGLIFEGPEIKLQTHKMDFSLRRALEQQLKASANSKEDISIDCIHMPYGMKKEH 
IKNMPLHIEDGLDSYKGEAVELNLMVQPGSKWHIRGDNQSKSTL4LLTAEHFPSW 
NSRVIDNGVPRTPTGTNYFDLSNKLMSSEPHELH FLKNAAGRNIESVATGHYHEASN 
NYLPINKLRKDNSEQIVNMVYKFLGFKDASDVLFQSLVSDQDKLVFSLVRLIKMPOII 
LDEAFSGEVEPMRCHFELWEFVGTLVVHAHVAAETPKCAHYRLISPEGIEGMNEN

SEQ ID NO: 27
YDR093W
>sp|Q12675 |ATC4_YEAST Phospholipid-transporting ATPase DNF2 OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=DNF2 PE=1 SV=1
MSSPSKPTSPFVVDIEHEHGESGAASNGLSSMSPFDSQFEKPSSAHGNIIVAKTGGSVLKR 
QSKFNMKDI2FSLKVTFDGDIDYSNDNDNDDDELDNGKTEIEIHENEVDDMLHFSQAP 
PMPNTGGFEDVELDNGESNNDQADHKLKRVRFGTRRNKSGRIDINRSTKWKANNFH 
NAIDESTKEDSINSALNQERLTVYSNNLPLPDEMDEGLPLAVYFRNKIRTTKY 
PLTFPPPKNLIFQPHFANIFYLILLIGLAFIQIFVPNTGAFASYPLIVIVI ITAIKGDIED 
SRRVTLDRLOPNECRFACKDQWNKVDIVRVHNNDEIPADMILLSTSDVDGACVET 
KNLNDELTKVRQSLKCSKIIKSSRDITRTKFWVESEGPANHLYSYQGNFKWQDTQNGI 
RNFENVNNLLNRLRGCLKTRNWGMW1FTDGDITKMINAGVPTP4KSKRISRELNSVIL 
NFFVLPFILCAFGTVNGVYQKPSKSRSDFYFEFGT1GSAANGFVSVAVILYQLSVPI 
SLYISVEI ITQAIQIFITDYLVLYNALKLYFCTPKSWINDLQGQRYEYIFSKRTILTIQN 
VMFKEKCTINGVNYEARLALGLKRRQGVDSEREREKIEAKDRTMEIDLSMDS 
NTQPCPEDFLTVSVEDEYDSSGHDWQKQKCEHFLLALALCHSLVEPNKDPKDLIK 
AQPDESAVLSTARQLGYSVGSGSKSLIVEIQGQKFEQFQVNLNVEFNSKRMSCI IK 
PGSTPKDEPKALLICGADSVYISLRDLRTQNDAILTEKALHLEAYEGLTRLCLAQRE 
LTWSEYERWVKTYDVAAGAVNTREEEELDQVDVIERELILLGGTAYEDRLQDGVPDSIAL
LAEAGIKLWVLTGDKVETAINIGFSCNVLNNDMELLVVKASGEDVEEFGSDPIQVVNNLV
TKYLREKFGMSGSEEELKEAKREHGLPQGNFAVI

SEQ ID NO: 28
YDR338C
>sp|Q05497|YD338__YEAST
Uncharacterized transporter
YDR338C
OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=YDR338C PE=1 SV=1
MAGILSKTLESEVPSLRTNMGIGNTHRRISLGLFLPPNKNNPLVRKFRARTRNIDQSRFR
SLTDFFGNSNHEPNYLGIINDEEELDFYHIDEDGELSKRISLPSRVESTFELSPQVDWII
LHHEERRYSVSCNDNEASQSNTPRQIEYSGRELEDFMNRLQQAQKQLTSAVTDAC
KGTSHRRPSVSTSGTVPTQIEQIDENSEALAEHSHTVFKSEARVLSYSPFLI
FFTFLLEQIFPVMCSLVTGHLKRENLAASLSMTNITLAEPIGIAITSLIDTLCQPAQYSGS
RFYSVSVHVQLCIAFSLVI YIFPAVMWYSEPLLSI IPEKELINLTSRFLVLVILGAPA
YIFFENKLQFYQGFDAGI YTVLICAPNLYSVLVWNYKGFIGGAIAYVNLFWLM
FMFLLLFLYALIDGRKCGWPSGKAGTHWNLGHLAFGIIMLEAEELSYELTLSA
YGCVYSLAAYXAMAILLYMFPIAGISTRIANFIGAKRTDFAHISSQVGLSFSIAT
GFINCCILVFRNLIANIYSKDPEVIKKLIAQVLPLVQIVNFDLSNAVAGCSLRRQGMQS
LGSIVNMLAYLFPIPLALLLSWFFDMKLYGLWIGIGSAMOLLGLVEAYVLFFPDWDKIM
TYAEILKTEDDEVDSDEYLTDSSPDENTALLGA

SEQ ID NO: 29
YDR40 6W
>sp|Q04182|PDR15__YEAST
ATP-dependent permease
PDR15 OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=PDR15 PE=1 SV=1
MSSSDIDVEERNRSSSSSSSSNAAISQHQYPGDSEAERHELARLTSQSLLYT
ANSNSSNSSNHANADSRVST MEQGNVFPNPTDGPNKLDNPSQFSTAWVQMN
MANICSTDPDYPFXYCGLVKNLSAGSDADVSYOQSTFANIVPFLKLLRLKPSKEE
DTFQILKMDGCNPPELLLVGRPSGCTTLLKSISSNHSFGKIAKDSIVSNGLSSSD
IRKHRYGEVYNAESIDHLPHTLTYQTLTFTVARMKTQPNIKGDREAYANHTVEVATAM
YGLSHTRDTKVGNDLVRGVSUGGERKRSVIAEVAICGARFQCDWNNATRGLSDALETIFRA
LKTQADIGKTAAVAYCQSOADYDLDFVKCVLDGDYQLYFGPAKAKYYQFDMGYYCPC
QRTTADFILTSPTERI ISKEFIEKTRQPFTKDMAEYLWQLSYESYNKLIDISTLEK
NTDEARNJIRIIHARKAKRPFN SPVYNNMGQVKYLL IRNFWRMKQSA SVTLWQVI GN
SVMAFILSGMFYKMKNDSTFIFYROAMFPAIFNASCCLLEI FSLYETPITEKHKRT
YSLYHPSADASFLVSEMPKLIATVFNCNIIYFLVDFRNOVVFVYYFLVINTIFTLIS
HLFRCVGLSLTAFIQAMEPAVSSLAMLLIAISMTYFAIPKTIRLKGSWIWHYINPLAYFESL
MINEFHDREDFPFCAQYI PAGPAQYNITGQTQVCSAVAYPNGYVGLDDEKSYEDYEHK
KWKRGGFICMAVYVFVVFIVLYLCENYAGKQGEMMVFLRSKIKQLKKEKLIQEKHRPDG
IENNAASPPDASTTEKEISMGNKDSNNADSSLKSEAIHPWHRLCVDVIPKKQQR
RILNNVGDWKGFTLTMGASGAAGKTTLDDLCAERTMVGVTGNI FDVGRLADESFRS
IGYCGQQDLHLKTATVEFLSAYLQPSSSIEEKNRYVEEVIKLEMQYSDAVGV
AGEGLINVQKRPRITIGELARFKLFLDEPTSLGLSQTAWDTCQLMRKLAHGQAIC
TIHQFSAILMQQFDRLFLLFQKGQTVYFYGDLGEGCKTMIDYFESGKAHKCPPDANPAEWM
LEVVGAAPGSHATQDYNEVWRNSDEYKAVQEELDWMEKNLPGRSKEPTAEEHKPFAASLY
YQFKMVTIRLFQQYWRSPDYLWSKFILTIFNQVFIGFTFFKADRSLQQLQNQMLSPMYTV
IFNPILOQYLPSFVQDRLYERARPSTSFWSLAFQLSIII IVEIPWNLITAYI CY
YAYGFYANASAAGQLHERGALFWLFSIAFYVYYIGSMGLLMISFNEVAETAAMHTLLFTM
ALSFCGVMATPKMVPFWIFMRVSPVLYMI DALALTGAVNVDKSCNYEMVKFTPPSGT
TCGDYMAYSKLAGTGYLSDPSATDICSFAVSTNAFLATFSSHYYRRWNYGIFICY
AFDYIAATFLYWLSRVPKNGKISEPKK

SEQ ID NO: 30
YDR356W
>sp|P39932|STL1_YEAST Sugar transporter STL1 OS=Saccharomyces cerevisiae (strain ATCC 204508 / S28c) GN=STL1 PE=1 SV=2
MKDLKLSNFKGFISRTSHWGLTGGKLYFTIASMTGFSFLGFYDQGLMASLITGQFYNY
EPATKENGHDRQTHVQATTSCYELYGCFSALFYVMFCGERIGRKLPMGSVITIG
AVISTCAPRGYHALGQPI IGRVTGGVGTGLNTSTI PVWQSEMKAENRGLLVLNLEGSTIA
FGMTIAWIDFGLSYNVESTQSVQWRFPSMVQIFVFLALLAMIFKLMPESFRWLSQSRTEEAR
YLVGTLDADDNEVITEVNAVSTKHFHEKSHHSLSSFGRSQRNLQARAALASTQF
FQQPCTGCAAIAYYSTVFNTKIKLQRLMIGGFAITYALSTIGSFL1EIKGKRKLF
LLGATQAVVIPFIALKENKNCARAGAVGFLFTIFFGGLSLLPLWIPYFPEEASMKV
RASTNASTCITNLWCFSAVMFMTIIQGQSWGCLFVFVAVMNYLIPFFYFQPETAGRS
LLEEID IFKAYEDETPQWPRWANILKPSLQVEVHANALGSDMEKEFDGEDVETD
YNQINGDNSSSSNIKNEDTVNDKANFEG

SEQ ID NO: 31
YEL031W
>sp|P39986|ATC6_YEAST Manganese-transporting ATPase 1 OS=Saccharomyces cerevisiae (strain ATCC 204508 / S28c) GN=SPF1 PE=1 SV=1
MTKKSFSVSSP1VRDSTLLVPSLIAKPYVLFPSSLYATFAQLYFQQDYRIKGPETFVFV
LGTLLSVNLINLVMMPANWVKIAKFNYSSTTKNVNEATHILYITTPNNSGDIVIEQVTE
AGSlQTFQFQKFLHNQEHVLPEEFPKFLDSPIKDFCKGHSDLTHKLXLYGEN
SFDPIPTMFELMWEEKAVAPLFQFQCVCLALWLLDEFYYSLFLNFMISMEAAAVFQRL
TAILKEFRTMGYPITNYVRKQWMVQALTNNELMDLVSTIRTAESAIPCIDLLDNGA
IVNEAMLSTPGLIESIKLKPSEDNQLQDGMDCKLAVHGGTAKQVTPPEHKSIDIPPDDGALAVITKFFETGQSLSVRLMI YSAERVSVDKNEALMFILLLIFAVISWVYTWVE
GTMKMRGQSKL ILDCILV ITSIVVPELPMTLMAVNSLAAYKPPYVCefEFPF PAFRG
IDVCCFDKTLTGILGSDLFEGLAGISADSENIRLYSAAEAEPESTILVIGAAHALVKLED
GLDIGNPDEKALTKAVGAWERKNSYREGTGLDIIYRFQFSSALKRSASISHNADLF
AAVKGAPETIREKLSIDPNKSYEIYKFSFRGSRVIALASKLPMKMSQSKILNDRDVE
SELIFNGFLIFHCPLDDAIETIKMLNESSHRSMITGDNPLTNATVHEAVGIVFGETIL
LDRAQKSDQNLQFLRFREVETVS IPFDKSKTDHSLKFDRYDIAVTGYALNALEGSHLR
LLRHWVTAYRSVSQKEFLLNKLDMGYQITLCCDGTVDVGKQAHYGIALNTGEE
LKKLGEQRRLEGMKKMYKTEFARMWNPQPPPFFFFAIAHLPFPFGKNPHLYKASKGT
VITPEIRKAVEAN5KIPvKPNGLSEKKPADILASLLNNSAGAQGDEAPALKLGASC
AAPFSTOLKLNVSATVNI IRQGRCALVNTIQMYKLALNCAYSLSI IYMAVGKFPDGQ
ATVSGLSSLCSLFCGLKQLEKLSQRPQSFGNYSIMLSQFAVIAHYLVIIETH
YKLEPREPQVDLEKEFAPSLNTGIFIIOLQQVOSTFAVNYQGGEPFREINSNKGMYGL
LGVTLALASATEFLFELNEAKMFVPMDTFKIKLTLDLLDFFGSWGEHFFKFMMDD
KPSDISEVQVKIAST

SEQ ID NO: 32
YER166W
>spi P32660 |A|C5_YEAST Phospholipid-transporting ATPase DNF1
OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=DNF1 PE=1 SV=2
MSGTTHGDGHPMSPFEDTFQFEDNNSNEDTHIAPTHFDDGATSNKYSRPQVSNFDETPK
NKRE DAEFFTPNDTYHNFSQPTPKLLNNGSFTDDNELDSGPHNTYDGRFMRG
TKRNKGNIFMGSTKLWARKNIPNPFPEDFKDDIDPAGAINRAQLRTYVNMNLPDKM
IDGEENPMQYPNPKRTIKTYPTLFPLKNILFQHNANVYFLVLIIGAQIFGVTNP
GLASPVLIVVI ITAIKDAILDSRTTLVDLEVNNNKTHILEGENENVDSTNSDLRERFK
KANRSLKFQYIQYCHTLEETGEKKRMQKRHRHELRVQKTVGTSGPRSSLSLSDSRYVSD
YGRPSLNDLNEQQAGEANIIVDRLLPRTDCKFANKYNGVGVKTVDRHINNDEI PADII
LLSTSDTDGACVYTNKLDGTNLVQSLKCTNTIRTSDIAARTKFIESEGPHSNLYT
YQGNNMKRNWLADGEINRPEITINN PLLRGCTLRTKXAMGVVMFTGDKTMLNSITP1
KKSRRSRELNSFVIDVNFVILFICFVSGIANVGYDKKRGRSFSYESFTGIAGSAAATNFV
SFEWAVIILYSLVPISLYISVEIITKQAFAQIYGDVVLNYAKLDPCTPKSWNISDLIQG
VEYIFSDKTGLTQNVMFPEKCTINGVSGRYTEALAGLRKQGIDVETGEERREKAIA
KDTRDMIDRALSNGTLSNKQVEEIVFTFVKSFERDLKGASEQVQQRCEHMLALCHSV
LVEANPNFKKDLKQAQSPDEAALAVTARDFGFSVPKTKGLIOEMQUQKEFEILNIL
EFNSRSSRMCSIVKI PGLNPDERALICKKGADS IIYSLRSQGSNSNEAILEKTLAHL
EQYATELGRCISLEWSEYKNEKDIAASALNEDELEVADISERELISSG
TAIERDLQGVPCIEIALLAEAGIKLVLTGKVTAINIGFSCSNLLNEMELVIIIKTGD
DVKKEFGSEISVEIDALLSKYKLYNFTSEERIEFEAKDHEFPKGNAYIVIGDALKLA
LYGEDIRKFLLLCKNCRAVLCCRVSQKAAVVKLVKDSLVDMLAIGDGSNDVAMIQ5
ADVIGAEGEERQGFMCSDIFQRYLRALLVLHVNGWSYKLAEMIBEFFYMKMIFAL
ALFWYG1YNDFDGSYLYEYTYMFMYNAFLSTLPVI FLGILDQDVNDTISLVQPQYRVGI
LRKEWNRQFKRLWMYLGDQLQSI1CFFFFFYLVHKNMIVSNGLGHDHRYFGVYVTTIAV
ISCNTRYVLLLQRYWRDFSFGSLCLVWAVTGWISSAIASREFKAAARI YGAPSFWA
VFVFVAVLFCLLSFRTYDFSQKFFYPTDVEIVREMWHGHFHDYPFGPDTPNRKPVTKA
GQHGEKI IEGIALSDNLGSNYSRSVDVATEGTPMFTMHGDSFSGQKGETWMTSPKET
QDLIDQSPQFOQATFGGRPSNSTVRSSLDRTERQMIATNQLDNRSVERARTSLDLPGVTN
AASLIGTQNN

SEQ ID No: 33
YFL011W

>sp| P43581 IHX10JYEAST Kexcse transporter HXT10 OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=HXT10 PE=1 SV=1
MVSSSVSILGTSKAKASTLSLRDKEEKLPTREASLDPYKPI1AYYWTVMGLCMLMIAFGG
FIFGWTGTSIFQGSGDFQERQRGQDQFLSDLVTRGLVGI FNIGCALGGGLTIGRL
GDIYGRKIGLMCSVLYSIVGIQIASSDWWQYFQIFRIVSGMGVGGVVALPSLISEIS
PKHHLRGTCVSFQYLMTLGIIFLGYCIONYGTKKSINQIERWQPGGLCFAIFMVIGMMV
PEPSRYLVEKQYEERRALSALSXKSVTVDPGVVFEFDVTIVANEMLERAVGNAWHLEFS
NKGAIPLPVIMGIVQSLQLTPGNCYFYGTITFNAVGMQDFTESILVGLAVNFASTFV
ALYIYDKFRGRKCLLWGSASMAICFVIATFGVTRLWQPQGSDSQASGVMIVFTCF
IFSFAITWAPIYVQVAETYPPLRVLKNRMAAIAGVANWMGWFLIGFFTPFITSISGFRSYG
VFYMGLCIFSFYFVVFVCETKGLLLEEVMNEYERIKPWKSNGWI PSSRRTPQTPSTSTPL
VIVDSDK

SEQ ID No: 34
YGL006W

>sp| P38929 |ATC2__YEAST Calcium-transporting ATPase 2 OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=PFC1 PE=1 SV=1
MSRDENSALLANNENKPSYTGNEVGNVDNFKLKSQSLSDLHNPKSIKRSFVRFLGYESN

74
SLFKYLKT DKA GISLP EISNYRKTNRYKNYGDNS LPERIK SFLQLV AANFY DKMQLL
TVAAVSVFVLGLEYLMQPPQ YDPENKNKQVD WIEGVAIAMIAVFFVLLVAAN DQYKEL 
QPALKLNKIVQRNLQGELISHHV LVLGVDVIPQGDVPADCMISGKEADES 
SITGESNITQPKF VDNSRFLFK NSIDSHNHK SLDIGDV NEDGKNIADCMILGSGRIL 
SLGQGTVITSVNHISVQGNTSLSNAPAESTPIQLHSLQNLADNISVYGVSAI 
IFLFLV TRYLFFI PEDGRHDLDPAQKSGFPMNIFITIV VVAVEGFLPLA VTLALAFATRM 
KDGNLVRVLQSETCMSATAVSCKDGTVFPGNSKFDSDKSLPVSEQRK 
LNSKKVF EENCSSLRLDLANANLSTANFEADYKRK KNDNTNKSNSMKLFSLDKCKS 
RSLKFFKRSNIGREDDEDFQLFKNKVRQEPFISGKTETALLSLARSLSLQGPQELYLRDDQP 
MEKFNIEKVQTIIPESRWAGSLVUYKKEGNNKKPFFRYFKGAAIEVSKCSYKRNNSD 
DITLEEINEDNKETDIEKLNASALRAISVAHKDFCECDSWPPEQLKDPSNIAAALDL 
LFNSQKGLLIDLGILQDPNLQG TVREVQQC ORAOGTVRMVGDNLTA KAIARCAILS 
TDISSEAYSAMEGETFRLKTKNERIIRLPLNLVLRASSPS DKEIRLVE LKGMGDVVAV T 
gtndapakla vgsmsigst evr easa diil lmtdd faireaai n vkaigcr v cs kfi 
QFQLIVNITAVILTFVSSVASSDETSVTAVQLLWNLIMDTLAALALATD KPDPMNID 
KPRGrSTL SS VSTWMLS QATILQ LIVTFILHFG PELFFK KHEDEI TISHQQQLNAMT 
FNTFVWLQF TMLVSRLEDGDSINWRGRISAANLNFQDLGRNYYFLTIMAIGSQ 
LIMFEGGAPF SIAJQTSI KSMWITAVLCGMLSLIMGVLVRICPDEVAVKFPAAFVQRFKYV 
FGELEIRKNIHTGKHDDEEALLES DES PESTA FY

SEQ ID NO: 35
YGL013C
>sp|P12383|PDR1_YEAST Transcription factor PDR1 OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=PDR1 PE=1 SV=2 MRGLTPKNGVHIETGPDTESSADSSNFSTGFSGKRSPKVKSCADNCRKRKIKCNKFGP "PCASCEIYSCCTFSTRQGARIKNLHKSLETGTVQKEEEDSSTSFNSPQRCGITDGC AVEQPFTKFPENHKLRGSGSNSGSDGNNDDVNVRNFYEDDSESQALTLSQTLTLLK EMAHGLHTVTAIESIELQISDLKLRKEWPKVRKETLATTKFYPKNIETQLMKNCYCDV VHLTYAWSENNKKDDTSQQPLIDEIFGLYSPFQFLSLOQGKGFCNQRYSKSCIEFPRT AKETIYMLRDFVCDFHINQGCVSIANPLENYQKMNLPLSPSSISAGPAINTAHKS HVALVNIHLPQPFVNRNITGNSNELLSEMNNDISMFGILKLMDHKNYSQNFMLEITSN PSVAKNTQSIDVLFQEHYQAGEALIALCYSYNTINLYVDTCIDIGHQLYFLDLL LFWSLSEIYGFEKVNLAVHFVSRLGRSEFYYGLDENFAERRRNLWKAFFYETKLSK LGYPSNDISCKKNFKRDFVQGFDLNRDFIENHVLVRSEAFNMCISLDKYGELEAV LQIVSHFSSSVLFNFEKTSIRNTSKPSVREKLLFELVEIFNETMEKYDAIKEQTGKLD IAFAKSTDEKLVREDKISAFMKTVHELPHEHCFMVNESDINVINALCVRHPSILIESILKLYHIKYSWDTMNKLILDFFDNDSYSRFSAHYISICLII VQLSAF奎EIKVINVDVNMIR VFKRFDLIKIIFENENETUVHVFNSQSKFDVTAIRSFILTVRIMLLAYEGESSSTNDLVS IKYDENDAPJLGI IELVLTDCACRYFILLELPQFGHLTVSOMKLQKRFQEPLMSENDK QMKHMNGKQNLPSLKLKGTSSCLNEGIESQPQFNFGRASAPQVRRNLSPEAQPLPSFRS LSVSDNMDPDAQPTNGNTQVNQSPKINAQQIPTSVQVFMPNTEINNNNNNNNN NNINININININNSATSFNLGTLDEFVNDGLEDLYSILWSDVFYD

SEQ ID NO: 36
YGL255W
>sp|P32804|ZRT1_YEAST Zinc-regulated transporter 1 OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=ZRT1 PE=1 SV=1 MSNVTPWVKWQDPSEVTLDKTDPPDVKTCLQGVYFGGNEYNGNLRSSVFILVF TSTFTMFPLISTKVKRLRIPLYVLYFALYFGSGIVIVATAFHLMDPAYAIGGTTCVGQT GNQGLYSLWCMAIPILFFLLDLSLVSSWIRKYLGLSHDHTDEIKDVTVRNANTAVSSE NDNENTGANSHDTKNGVEYEDSATSMDVDVQSFQAOQFAMDIEFEGVHFSSVI GNL GSVGDEEFSSLPVIFVHDFSFEGLGIGARLSAIEFPRSKRWFWALCVAYGLTTPCVAIG
LG YR TVY5G5YTALW 5GWL DAI5 AGL YTLG WELLARDFI NPQRIKDRL RELSFNW1
CTLFGAG IMALIGKWA

SEQ ID NO: 37
YGR125W
>sp|P53273|YEAST Uncharacterized vacuolar membrane protein YGR125W OS=Saccharomyces cerevisiae (strain ATCC 204508 / 5288c) GN=YGR125W PE=1 SW=1
MGRTIRRNSSSLSEASEYSLGINQDSWNYKMRASWSAMSPPLCRSYMSGGFTGGNSP MINNLSDLPSKNQHPKIYIHELPNLNHRQTAQLSNFCSSESNENTSPIKDMYDI IGN
DRKDQSMRTIEIENIEDSEYSRLLSPASNWWDDNRLGQNSSLPELEDGYAGGYQ
SLRPSHNLRFPRNWLHMCSTSFPSKFAHLYPAAYLGLLLLNDALSYGMMIIPFIPETPVS
HLGPTFIYISTI ISQAFYSGGWSSFSPSGIGSEMIEITPFYHTMALAIKEALAGNDDE
IITTITFCYYSMLTYGYFيةالكلاسيكيًا GIGGYFLI ITGIETUVT
RWAKFYEYWSPSGFLDFTYDITKWLPPPVLVTYLGITQYFKNSLWLPSFYIITLVLF
FIVA IFPI LSLDLARQAGWI FPIANS DSKWYDHYRLFNW HWSLWLQQI PTTMTAFF
GILWPNVFALASMGLMDKTDVDELIAHGSNFFSGLGSYQNYTNYNSVLFIRAGA
DSSFAGFLILLAIAG IFPIICISGWSLILFGYELLWEALVDTWKLNRFEY
LTVWYWFTMIGDFLYGIIYGILACFSLWDSTKLQTINGEYNGWARSHTYRDPYQT
KFDLGIGIE YLYKQNLLNFGTISIEEEKERLYLQISKDARKRIRYLLDLKFNNIDN
NIDYSAAGENFGRNAFNYGLNDLWDLADNLASLEW CNEFELQYQKQLRKKAKERLEEGKQNSWNYSAAYIATKKIDTIIGNLNRGNSDANRN
MSLPNTNPKNQLSQAQNFVWDEAQKYNFKKEYKDDPQLFYLPFLAKQYRPDI ISYE
QKVRKEKFIMLCPYFTQLRASQSHLHADINIFWETGMLKAYEIPQTYILEIFSG
NGTCFGKIIAPGNAMFREQKLR Trườngтся TETETDSVLW YIDSSSLNKLKEDNLALYVEA LAMWMI
KDTRFKELLGYTLYS A

SEQ ID NO: 38
YGR181W
>sp|P53299|YEAST Mitochondrial import inner membrane translocase subunit TIM13 OS=Saccharomyces cerevisiae (strain ATCC 204508 / 5288c) GN=TIM13 PE=1 SW=1
MGLSSI FGGEAPQQKEEATTAKTPNPIAKELKNQIAQELAYNATELYNKISENCFE
CLTSPYATRNACIDQCLAKYMRSNWNSKAYISRIQNASASGEI

SEQ ID NO: 39
YGR217W
>sp|P50077|YEAST Calcium-channel protein CCH1 OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=CCH1 PE=1 SW=1
MQGRKRTLITEFEPFPNTNPFGDNAAMTDKNPEWENSETDGRNLESKPAALYPVALNIVPPE
SISHTEEEKGDEYNGNDSASMIFRTRVRGSHENLSRKLKSLKTASFQGAESSRN
YSPTSKAKSSQYIDLNDERLRRFSYSSYRSRVSNSPSTDRFPPRSAKYLSSLIAA
DDMDFEDFQGKFSAIDDEGLTWPLQKLSEKSRPSDYGEDGERGEGEQEISFYHTPNYG
ASATPGSHLPIEAPQNGSVEEGLESGINNSRKKPSKFFHLSPLQKEDKQTEYIEAYE
DIILEDFTLQKLESRPFVLYGHSLGVEFSTPNLRIKIAFRFHLHHYSLLYNITLYFIAL
LAIRTYPHNLFYRSWNWTDFYDILFACTGNDIAKIAIFGFDWDSEMFAYKREY
SILQRRGIMKLYIYLREKYGRKLIDFII PFRIISPGEETYQRSSLSLSTTLPYGAKENQ
RPFFTPFRARFSSWNRDLISSLWSFSLGWGFLSISKSYDRTGIIFKPLAILRLILRW
D TGMSILRLGKYGIP GLCNVSSMLWFWFIFGILGQYQIFQFSRQCVMVFNPEDPTDIYQ
YDMQFCGGYLDP¥TKRKQNYIYEDGSEGSY5KGFLCPQY5KC¥5NANPYNGRI5FDNI¥N
SMELVFVIMSANTFTDLMYYTMDSDEMAACLFFIVCIFVLTIWLLNLLIAVLVSSFFEIAN
EYEEKKKKFYGRKTGYVARITGTWYFKFWKLANQTKFPNWQSKGLAIYSHVFEFIVILI
ICDGMRASVSTANSCTNILLTDQGTSVLFESLARLVLVLPNWKFFLTPSYVD
FIISIIITLVI SCLAEGVGLGHMYAWLS IFHISRFYVI IFSNLTKKLWKQI LSNGMVWI
LSSYYFTFTFLVAILMAVYFEGVIPPEAEGDFQGMSLPLSNFLSLFIIISGTENWTDILY
ALQKHSPNISSTFCVSVFFI IFWLLSNVILNIFIALISEMSEVEEKEERAPFQIQIKHLK
VYFQPIQYEYTHASLVARIFKKKFGHNNEQRDDFQKLMRGTAIMNIAQHMNGELADEFKE
PSPENLFLKSLKLTGIVPSPMMIFKLEVSNDFVTETINDRGTYILENEYED
EKIDLYKCKLPLFNYFSPQHRRFQCRLFVPESTGRDGTDSRFREDDSTDLYNKSYFH
HIERDFVVFIFALATIIIVCSCYTVPLYRMHHKMTWNSALDAFICAGFSIFEVFK
TVADGFYSPNAYLNPWFIDFCVLISMMWINLIAYLKNNSLRIFKGLTALRCLT
ISNTARQTFNFLVMDGFLNKFIEAGLISLSLLFFTTVWGLSIFKGRGTCDNGSLGRCADCY
NEYNSVFQWDIMSRVYYQQPHELDSFASAFSSLYQIIISLEGWVDLLENNMNSSGIGTP
ATVMSAGNALFILVFLNFLSMVFILNFLVFIVNQNARAGTTGSAYTIEEKAWSLEQKLLS
QAKPEKAI PNLIELSRVRQ FFYQALVEAFKNFYFASFLQVVLHLH IMLLJRSYN PGNLIGY
QGVYFMTFSEQLALEHMCCEGEPRLYFQWKWSIRLSII IAFIMNAVAFHVPSHWF
FHNIKGFLFLLVFLPI IFQNDTLETETEMASLPILLSTLTYWGVLFLVAYALNQIFG
LTRLGSNTDNDINFPILKSMIVCFEGWNYIMADLTSEFYCSDSSDNYTDCGS
ETAYOLLMLMSWNNISMYFVVNNMVSISI IGNFSYVYRSGGRSGGRSEIKKEYEASKFED
TDGTGTELSSYILMSHPFDFSPKWEENRTLTKSLENEMEVNPDDPYVDKVLIDIGNL
KELNTDIDKAKIQRLQVRFQPSIHYNAYNGCIRFSDLLLLQPILEYTASARELIGDQ
YVHHYLLGKVDKLENQNFVDLEMVTRWKHCRMKRITIEEPWDKDPVTHSISINN
VNLEPAPGILEREPIATPMYDVGNWFWMPRQNDQSTMEPEEPIDNNDSDANDLIDR

SEQ ID NO: 40
YGR224W
>sp|P50080|AZR1_YEAST Azole resistance protein 1 OS=Saccharomyces
 cerevisiae (strain ATCC 204508 / S288c) GN=AZR1 PE=1 SV=1
MKGEPKTYSMDSLGYGEKAQQNEKEQKQYVVRNNTQSTSKQVNVSVDENASENEL
PKGFILYALAILALSLFAALDMLIVSTIIIEEVAQFGYSEIGWLFTGYSفنLALAL
IWRGATIPGKETLMKTMVLSAALSALSNMSMLIGGRVIAVGCCGQLSFLVIG
STLVEESQRGILAVLSCSFAISAVSGPFGLGVFTSSVTWRFYVNLPPIDGEFLFF
FYNPGLTQETFMDNIRKPFQPEIEVNAYHLLKICFKSKLNWRKPFMELI FMDYII
EFVFCSAGFTCILAFETFGGNYAWNSASI IILFIIGIVLWLAGYIFDLFVPFPKINVKA
TFHYQPLSMWTEIKKGTPVTNIALFLCTAGYISQFTIVYQFYLINSWAWAAVHILVA
CIISTVQVTCAGCAITKRTIQIIPIVQISSGFVGAGILITLNNNANNASHIHLILLPG
VAFQGLQQSSMLASQILQQDKKSTFRRDFVSITTFNTFCNKQLQALGVISNTVFSAAI
KKLTKANQILPDGTVDNDVLYIYQRTNDGFSSHKLGNIIESLTDVFYMALGFIYLISFA
VFASNKKVTASLR

SEQ ID NO: 41
YGR281W
>sp|P53049:YORl__YEAST Oligomycin resistance ATP-dependent permease
YORl OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c)
GN=YORl PE=1 SV=1
MTITVGDAVSTELNKSSQNVLSPKASASSDISTDVDDKSLPSSSLTQGEYIVDR
NKPQTYLNSDDIEKVTESDIFQPKRLFSLHSHKIKEPEVDERKIKYPLFHTNI ISNMF
FWWWLPILRVRKYRTIQPNLDFMDPRNINTERNETLYDFDEKNIYFYEKRTRKXRLPHET
EVEENVENAKLPHKLVALRLLTFTKQKYQFIFMSIIVAILANCTSGFMNIMITRLFEEVEKAI
FHSNMRKSGIYAGICLMMFYGNFLTNHHFQ7LTVQAKSILTKAAMKMMNANSYA
SEQ ID NO: 42
YHL016c

>sp|P33413|DUR3_YEAST Urea active transporter OS=Saccharomyces cerevisiae (strain ATCC 204508 / 528c) GN=DUR3 PE=1 SV=2
MEGFKKPLPGAGGYAVLGLGAVFAGMMVLTTYLLKRYQKEIITAAEETTAGRSVKTLGVAAVVSWSICSTLLTSTSKKEYADGFIGNYAYAYAGACFIIIAFALAIKTPQMPNHTYLELVRTRYGKIGHGCGLYFYAIATNLINTSLTTSGASVFDLTMGNTIASCFLLLPGVVVTYTLPGGIKATFLTDMHCTVIIIILVLFVAFKYATSDVLGLSGPGCYDVLYREAOAKRHPVGDNYYQGMYMSTSKGSGLIIINLGNFVTFLDNGYWNKAISSASPAASLKAYAGIHALWFIGVPSILSLMGCLAQITNGVPSLAAAIAGKKGAVASLLIMFAVTSAMSASLAVSSTVPTYIREDTTRASGGKLITYSHVACIFFLGLAMSGFSGVLYYGGISGMYLREMIGAISAVLWLPSLCMNDNLVAAVAPSLGTLAISWLVCTKSLYKELTDVTTFMDYPMNLGNVALLSPAIFIPILTYVFKPOQNFDEWMKDIITRVDTAELVQADPFDIGYDAEANDQEEETENSTLVSDESKNVELEPNKLPGVISNAIFQEDDTQLQNELDEQEREQLARKIKAFFLCCVFAFAFLVWMPMYSKVIIFSKKFSTGWWMVIIILWLFSSAFACIVLPMLMGRHITYIITLRLGVLDSQTYREWSQNSFQDLHVTSQISAR
AHRQQSSHFGQVDIEII

SEQ ID NO: 43
YIL088c

>sp|P40501|AVT7__YEAST Vacuolar amino acid transporter 7 OS=Saccharomyces cerevisiae (strain ATCC 204508 / 528c) GN=AVT7 PE=1 SV=1
MEATSSALSTANLVKTVAGTALIPYSFKSDGVGLVGVTLLAAVTSGLGFVLSKCSKTLLNPNSRSTLFCLMTLYLPFILAMVQCFGVLGLSVLGLDLPFGLFGGNYWVIIAQAVIIIPCLCVKLKDQKYSILLGLFAALSILVSHFVFVFLGKELTFNILRDNCWWKHDIFFKGLLSSTFSIAFAFGSMLNPMLNLDKSMEITFVNNINSLSTALFLIGLSGYLTFTQGNTLGNTNLNYDPSNIVIWIGFCLGSMILSFPFLLFPLRIAVNNWIIIEITYGGANTEPVPQVETRASNLNPMEVDPAQFPSLDALTSEYNCECLELLPNNFDSNGSIESQENNNDERTMGAVAGDENHHAPVFVESFYWITALLLISMTLALSVESQSFALVLSF
VGATGSTSISFTLPGLLGYKLIGLDSLAIGKMI
PPKDRFYKRCSSLVLYGFVGLSVFMRLY
VTFVNRSEDEA

SEQ_ID NO: 44
YJL093C
>sp| P40310 ITOK1__YEAST Outward-rectifier potassium channel
OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=ITOK1
PE=1 SV=1
MTRFNMNFSAKKTLGYNMATVEQSSAQVDSHSNTPKQAKGVLAEELKDALRFRDERV
SINAEPSSTLFLFVFWVSCYPFVITACLGPGVANTISRACWKWRKNKNSVTVNPSSN
DTDVMQVKTVPFDPPGL FAVNISLVLGFTSNI IMLHFSKCTLKYLSQILNITGWTIA
GGMLLVDVCSLMDPSYISKSTIFWACISSGLYLVCTI ILTHIFIGYKLGKYPPTFN
LPLNERSIMAYTVVLLSWLWGAAMFSGSSLHITYGNALYFCTVSLTLVGLDPILPKVGA
KIVMLI FSLSGVVLMLGLVMTRIS IQKSSGPI FFFHRVEKGRSKWKMDSKKNLoser
EADFLMKCIRQATSRQKHWSLSTVIALFAWMALVFKAFENWSVFNCI YPFCFLCLL
TIGYGDYAPTRGAGRAFPWALGAVPLMGAILSTVDGGDLFDISTSLDKIESFNNKV
SIVFNRGRALSFVMNTEFILEEEDTADGDLEETTSSQSSQISEFDDNNEENDEGTVS
PPASILQESFSSLKSSPSEGI LPLEYVSSAELQDSTGCNRLNLQELLKAVKHLRCIL
ADKDYTLFSFWYSYHKLHRLNIITDIEETYRGPFWFISPDTPLKFNLPEHFAFMMLFKN
IEELVGLNVEDEEYYKISKRRKFLGHEHKTL

SEQ_ID NO: 45
YJL094C
>sp| P40309 ITHAL_YEAST K (+)/H (+) an. tipporter
OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=ITHAL
PE=1 SV=1
MANTVGILSVNPVHSNSSLTTLFLPOALILLLLNCNLHIPFMRQPKVISEVSIG
ILGPTIQQIPYNTTIFPTSS JPNLMLANLGI ILFMFGLVGEVDIAFIKHKLALVI
GIVTAVPFPGFCGLAIPLFHTYANTEGERHFKFSVFMVIASVTAPFVLPCLNLNE
LRLKDRAGTVLAAIGISINDIMGIWLLASIISSAEGSPVTorrYILLITFAFWLFLYPFP
LKYLLWRLTIRHELDRSIP PLATMC ILFIMFISAY FTDIIVGHPFPAFIALGLVPPRD
DHYVVKLTEDRRY NPVFIPI YFAVAGLVDLILLSNEGRWGNYVFATIGAIFKTI ISG
TLTAKTGLFLWREATAGDLVHMSVI I VVTLVGNAGI ISRKIFFMFVIMLAVSTFVT
TPLTQLYVPSYDGRVKLSLPATEDGADDGDSEVGKTEINTQLNISLVDSYKRYGIE
LTTTVINTEAISIFSLNNLYLSLGVSPKNNKKNETSLSRMTTADSTLKTNSFTKIKK
MVHIWSSVKDVDTNLVIDKEITFPEGVALRSTAIHLRLLTEEGLDLQSSQLYNDPDPH
TANSTDSLQIYDFIFNLSKIPFSSEVISFSTMREAANITMARKDSTDLLLPPKASAYEY
RGSPVFVDEKYNFIHYSHLLLNLNSTFIFSKISIFQSLKANFQVISNYGRNLADRFK
RKRFNLPLLKPFLPYLQSDYLGYYLLLLCYRDGYNNDASCSIFINSNIDFAXDLSTFA
EHDLNNESTIKVIDIPFETKVPVEIAEKPSFIEIVLVDGLSDTALADIEETFII IGEDLP
DESEPPSEEVRVTIFEGSNRRFDTLVHFFSSE

SEQ_ID NO: 46
YJL108C
>sp| P42946 PRM10_YEAST Pheromone-regulated membrane protein 10
OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=PRM10
PE=1 SV=1
MIVSFGDATTRTSEVQLVRCTQGLNLWKLHQVHAVYKRVVLHDLKAEGNALLQILADT
NLYPWWMCVLLEAFCSAMTVTPYGFPDNLALSIFMGLCVSLQFILSQQMYSNFVE
ISASI NSFCGARFGSIPRSHICFGAVTGQGSLALIPGY1ILCGALELQRSVLAGAVRM
FYAIYSLFLFGFIITLGLSALFGMWWNYHATNEISCQLI SWPRFPLFVPAFTISTSILNQA
HISQLPVMVFTSCTGYVVTYWAGKHFANSTEFTAALAAFVIGVLGNLYSRIWKGLAVSAM
LPAIFVQVPSGIAQSQNLSSLGQLQANTIVNANETITTSSTDPSSSMSFGMTMIQVCVGIS
VGLFASSLFVPFGKKTGLFLS

SEQ ID NO: 47
YJL212C
>sp|P40897|0PT1__YEAST Oligopeptide transporter 1 OS=Saccharomyces cerevisiae (strain ATCC 20420B / S288c) GN=OPT1 PE=1 SV=1
MSTIYRESDSESEPSTPTIIPIQINMEMEEKDAFVKNIDEDVNNLTTATDEERDPES
QKFDRHSIQEEGLVWKGDPTYLPNSPYPEVRSAVSIEDDPTIRLHWRTLFTTVVVF
AGVNQFSLRYPSLEINFLAVQVCYPGRILALLPDWKSCKVFPFDLNPQFTKKEAH
VTIAVALTSTAYAMILNAAGSFDNYMKLNLYQFLLVTSQMGNYGAAGLRRWYNPNA
SSNPWTSLPSLSDSHEYKETYANGWTMPYRYFLLYLGSIYNYWYPPGLFTGLS
YNYILWGSKTRANPFANTIFGTQSGGLAPITFDTYQVSAMSGSVATFPFYYSANTY
SVLHFVYLPCLYFTNTWYAKMPVGSIYSTGNQKNVTVKILDENYSINLEKEYS
PYYFVFPSYLSYLANPAIAAVAFYCYHCLYHGKLIVAKFKRDNGTKTDIHMRI
YSKNYKDC

SEQ ID NO: 48
YJR106W
>sp|P47144|ECM27__YEAST Protein ECM27 OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=ECM27 PE=1 SV=2
MDWAIINVAHPRLLYKDKFSYTVFSPFHLIIIAFALLGLICASSFLCPNVWISPNSL
SGNSLTKSASHTISGUALMAVISWINNSSPDLSNLWMSWATRSTSTSYSLIGEWL
GACGGTIYEGSI F1IMSRTHI1E1 SQIOQKLS IMRDLLFLSAMCYMSYSLMNOVTNL
CLLMAPFAYLYVVKTFKLNHSALTDEPDETSRENSWSPSLDSLASMGLLPPIQ
GFDSNITHI1KPSLASSDMFSLPLSENSSEEDDSDRNNAAETLTSMPQGQWSA
SATVAGETAISEPFNAFTERDSERAINSSPAPYAPRNPDDDESEQVLYLETT
THGDFQAGEMRFRPSKRLSWGI IFKPHSNSFQKSISDAISIFISITYFFFI IFKLPSCQQP
PSDILSDPTIRNLNITLIPPLILLIQS ITAPPFLLC ILSVLTVLYHLGYLYLFPFLLAM
ALILLLATFIYKWNKHFPLNSLNNQLQKRRKLLENLNITSIQIFIAGINII I
WISLANNALIEMIEYQKILGLSKIAIGLTLIFAWGNSVGLDILSNISMCRLYKQTQTHYQDR
YRLATKFFMIICASCASGGLDDSMGGIGFQGSWSMLIGFAGFNNWFLRKYKLQETSQL
DNLNYKFIYVSCVFL IQLI ILLLFFGGPNNIIRKRLTKEMKLWGISMCGLWALATLINILELFS

SEQ ID NO: 49
YJR160C
>sp|POCEO|MPH3__YEAST Alpha-glucosides permease MPH3 OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=MPH3 PE=1 SV=1
MKNLSPLNRRKENDTSSNYYPGKASHEPWSIEMDQQTKGDLDIYXHEFSPDTRAPSD
SNKVIITEFIDATEDKAEADSIDSMPLALNNTYPKAAAWLLVSWTILMEGYDTIILGA
FYALPFFQRKFGSQQNQDKTGEWEISASWQIQLTLCYMAEGIQYGLQTGSPSWLGVNRYTLI
IALFF''LAAFFILFVFCNSLGMIAV'GQALCGMPFQGCQCLTVS YASEICP1ALRYYLITYS

80
NLCWLFGQLFAAGIMKNSQKKYADSELGYKLPFALQWILPVPLALGIFFAPESPWWLVKK
GRFDEARRSLRRTSGKPEKEILVTLEVDKIKVTIDEKRLTSGKEGYSDCFEDKINRR
RTRITCLCWAGQATCSCIGILYSTYFYEKARGVTEEMSFTFSIQYCYLCIGATFLSWSAWK
YFGRYDLYAFGLAQTFIVFIIIGLGCSTTHGSMGSGSLLMAVAFYNYLGIAPVVFCLV
SEMPSSRLRTIIILARNTYNVSVICSVLILYQLDNSKKWNWAGSKGFFGWGLCFCITLIW
AVVDPETAGKTVEINELFKGVARKFSTKVDFFVVKTPKDVSHNDPKGDIASIAEE

SEQ ID NO: 50
YKL064W
>sp|P35724|MNR2_YEAST Manganese resistance protein MNR2
OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=MNR2
PE=1 SV=1
MSTDNSQKDEGVPLLPSYSSPSQLRKRRKNRRKRRDKFVGHKLSDSRPRQTQLLDNLQHN
HCGQTIDFQIDSGWLHESDSNIDIKSEPSLKGAFIDHRPMSMQPREGPSQVSSTVTQ
PQP1MKFSIYKPKAGLPLDQPRQDNLVSIDLSEPESLWKKSHFVQDENSFQQDR
QSNANNVNVDDAMHVNNNATSGVNDNKRRKGDSDNSNKSTSDSNDEED
EYNRSPPSSSLGSNSSLDDCVLVLDEGEEVPKAQSTCQVEEFTSEETERLRSQAIQDA
EAFHFQYDQFIFKPIVTINVDELPGNRRVNETINLKNGRLPRKIAWP
HLIGRMPVLSNSTDQSRQGQLQDNNLGVINIQYPPHI ISNPEHFRTFYPFVLDLS
TVHPSITGLLQPGQKFQDLFVAYISQDNSAGIKHTPNPSTPGIKAETVSQGLTAK
NFSFLSSMSWANIEDVPFWLDVSNPFEEEMKILSKAFGHPLTEDIFLDGVERKVELF
RDYLYCLFRSFQDAVEAQRDRQKETQLASLDSLSEILDSQAYGATMSNENANNNS
TSNASRSKRFLWPIARRRASSARNTTNSSSSYRKRKKMEENEEKFRKSKDRHKH
REGELEPLNYIVIFRTDGLTFHPAFTHPINVRRAALLKDYLNVTSWIAAYALIDIT
DAFAMPENIELDEYVIIEDAYAILMKMQDSDDSDSDSDGASDEDAPFDFYSKKS
YSSAKSSVSSRSMTSEASFANLIGWKRGMGLMRIGECRKRVS IRLLGSGKAVIKG
FARKRENEQWEASPSQQEIANYLGDIDQHIVTMVSSLNHYKLSRSHSNLYLAINIDTKV
NNDMDNVLGKJ RTGILTGI VLFMNVITGLWGMNVI VPQYRDSLTFVGIVLFCGMLACSAY
MYTKRRGFG

SEQ ID NO: 51
YKR050W
>sp|P28584|TRK2__YEAST Low-affinity potassium transport protein
OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=TRK2
PE=1 SV=1
MPTAKRTSSRALPFLQLRFHKSWHRLFRDFISGFLKCRPIAKYVFNPFWYI
LIITLSISILLYPCKNTAFIDVLFLAAAGASTQGGLATKSTFDNLQYIQVLYVIIISSL
PILHIGFVLRVLYFERYFDNRIDSIKQFKLLRTMLTLQRELSGSSNAARSRSKFKDN
LRFKGFVRSDPRQASDVPMSQTDALSSLISIPMVSSSEEDTQSSPPSNKPRQ
SDVPDRIYKSIMMLQKQEQSANSNATSDSETNGAFIVQERHERRAHCSLKRHSV
PSQQLNKLQATOFSKQLGLRDEGDHDYDFAGHPKYMVTKKISRTQSCNITYTAS
PSKTPSQQQVVENHNLRKASAPSSFEQDEMSFSQPQESLNLQFQAHPPKPKRREGIDGHPT
RTMSTNYLSWQDFQSGNVSFVIQGLTKQKEELGVEYRALRLLCIMVYYIGFNILAVF
IVPFWACTHHRHIEIIRNYNPSSTWGFMTAMSFNLSLIALSMDVSFTPQAPYLIFF
MFIIIGNLTFPLRFIIIMWMTSRDLSQFKEGSFLFFDHPKRCCFLLFSPMTWLELF
TLVVLNATDILWIFI ILFDNASVRQVAKYRALMGLQFSQCSCTATGFNLVSDLHPSQI
VSYLMMVYMSLVLPIARTRYNEEQSLGLYDSTOPDENITHEDJKTDHGSEEDER
TVSTKSKPKQQPSKFGVLAHRLQLSDFLWLFLGI ICICEGKIEDVYKDFNVFAG
LFEVSAYTVGLSLGLYPNTNSLSAQVFIVLKIY IAMLIGRNRGPLYTDRAIMLPS
DKLEQIDRLQDMKAAGKLAKVGEDPMTTYVKKRSHKLKIAKTFWKGH
SEQ ID NO: 52
YKR105C
>sp P36172 |VBA5_YEAST| Vacuolar basic amino acid transporter 5
OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=VBA5
PE=1 SV=1
MEETKYSSQEQIEGACGSDALNARGSNDPMLSLYLACLSTLTLVFITALDILIVGTI
IDVVAEQFQNSKGTQLWTVGYSPLNAISSLWGRFASI IGFQHSSLAILIFEAGSLIAA
LASSMMMLFGRQVAVGSGQGQTLCFVIGCTMVGERSRPLVISILSCAFAVAAIVGPIII
GGAFTTHVTWRWCFYINLPIGLAI IMFLLYTAENKGILQIQIKDAIGTISSTFTSKFRH
QVNFKRLMNG IFKPFDGFPGALCSAGLVFLGLLGTFNKSWSNGQGVITYLVGFLVLI
FSVLYDFFLFKPNFEPDNISYRPPLLRLRRVAKPAI IVNMTVFLLCTQNGQMI YSFQF
QOLI FASSAWKAGLHLIPIVITNIAAISGVIKTKLGLVKLPLLFGGVLVIGAGLMTL
MTNTSTKSTWVGLSQFLGAQLSAQLSIQITKDRAEAMDIFIEVTAFTNKLSL
GTLQGGVLSTTVFSAFPKVSRAHFEPYEAGKTVDDMLYLQNYDGHSTIGNLSDS
KNVFWMGDGFYALGFCSFSSNKKLI IFKDDTPEDNLEDK

SEQ ID NO: 53
YKR106W
>sp P36173 |GEX2__YEAST| Glutathione exchanger 2
OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=GEX2
PE=1 SV=1
MSSSVVGVASSNKKSGIRQSCIEIERHERSNDDTYSMTSTFFKLENEIMSQFDSLKYKI
LLISTAFVCQFGISLDTYLSTYGTATNSYNSEHSSLSTVQINAVVSVQGQYVYRLSD
HFGMLRSLQTVAFIGNMMFQAQOAAGSVFYNGCYVTNLLSCILDSFSSKL
WSRMYFQYASQHYPYII IPWISGNI ITAANPKWSWNIAMWAFI YPLSTLIPIFILLLYMKY
KSSKTAEWRLKQEQRKERTGGFLFENLFLFWKLDIVGILLITVSGLCIILPLLANETS
QRWHNSKRI IATLVSQGCLFFI FLYWEAKFASKPLFKKLLSDRGIWAPLGVTFNNFIFF
ISCDYLFVVLVSMKESTSAAIRVINLDFVAATASPFYSLLVAKTRKLKLSVIGGCAAW
MVCMLFYKYRRGGSSHEGVAIASVIMGSSLCSNSVIVILQAMTHSRMAVITG1YT
FSKLGAAIAVGSGSAINTQTPNQLYNKnGNDLTAIIAYASYPFISDYPGSPERADV
ESRYVQRIIMTVGLACTVPFFFTFTFMRFNRPEILDKATHEEFTEDGLVLVPNENIFSQI
KALFRHRNRSKNKGC

SEQ ID NO: 54
YLRI447C
>sp P32366 |NA0DJYEAST| V-type proton ATPase subunit d
OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=VMA6
PE=1 SV=1
MEGVYFNIDNGFIEGVVRGYNRLLSNNQYINLTQCDTLEDKLQLSSTDYIGNFLSVSS
ESLTSLIQEYASSKLYHFEFNYIRDQSGGSTRKMDYITYGYMDNVALMGTITHDRDK
GEILQRCHPLGWFDTLPFLS VATDLESLEYTVLVDTPLAPYFKNCDFTAEELDDMNIEII
RNKLYKAYLEDYFNVTEIIEPEPAKECMTLLLGEADERRSSINALSQSSSDPDQLKD
LLPINICKLYPLATFILQAQDFEGVRALANYVEYRGFLETGNLEDFHYQLEMELCRDAF
TQQFAISTVWAMKSKSEQEVRNITWIAECIAQNOERINNYISVY

SEQ ID NO: 55
YML116W
>sp P13090 |ATR1_YEAST| Aminotriazole resistance protein
OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=ATR1
PE=1 SV=2
MGNQSLVVLTESKGEYENETELPVKKSSRDNNIGESLTATAFTQSEDEMVDSNQKWQNPN
YFKYAWQEYLFIFTCMISQLLNQAGTTQTLSIMNILSDSFGSEGNSKSWLMASFPLVSGS
FILISGRFLYGKLMLLVGVLIIIWSLISGCITKYSGDSTFIFI
ISAFQGQLGIAFVLP
NVNGI INIYVVGTTFKRNIVISIFVGAMAPIAGLCLFAGLIGTEDPKQWPWAFAYYSISIA
APINFVLSIAITYPIITIINHHFSDMWSIGVLGVILILLNFNVQPISGNVQAYIIVI
LIIISVIFLVFVIEYERFAKTPLLPAV3KDREMIQ1MLAFFGWGSF1FYYFYYFQQL
NIQRYTALWAGTYPMFLWGIAALLLGVTKNVSPSVFLFMSVAIVNSIMASVTIP
HTFYFR0TQLGMTIMSFQMDLSPASS IFSDNLPMEYQQMAGSLVNTVNHSMMSLCLGM
GAVETQVNS DGGHLLKGYRAGQYLGI GLASLACMISGLYMVES P1KGRARAAAE YDCT
VA

SEQ ID NO: 56
YMR034C
>sp rQ05131 rYMS4___YEAST Uncharacteri sed membrane protein YMR034C
OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=YMR034C
PE=1 SV=1
MKTQYSIRIKIWASHVEFTEFKSQWFECILAILIVARAPFNLRDGGLIKGQSYIGYGC
AWIFQLSGCMKSLIMANMLWNRHHTILVLSFLLSITIVYFGCCAVKAAAANPDEDVW
LIGILILATCPPTTVNASVMNTNAGGNGLCCVECVFIGNLLGGATFITPALVQMTNPRAFPA
GYNPATGNMGIRKVRKMQVGSFVFLVGQIQNPCFPKTYAYLGFLKYYHIGSY
MLLMIFSSSTAFYQDAFTSSVHCVIIFLCFFNLGI YIFTFGLSYLCARFWFLKLFPH
EPIEGKSTRLYRISNIFPAFPYDWEADAICIIMFCGPAKTAALGVSLITSQYGDKHELGK
LLVPLVLIQVEQVMTANFFVSLFRLWIQDAQDGSSESCANENEEVDLEK ISIGTGEN
QSVSLNNVYPTQR

SEQ ID NO: 57
YMR056C
>sp 1P04710 |ADT1___YEAST ADP, ATP carrier protein 1 OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=AAC1
PE=1 SV=1
MSHETQ10QSHFVGDFLMGVSAAIAKTGAAP1IERVKLMQNEGMLGGGLODRYKGI
LDCF0KRTATHEGIV5FWQRTANVLVYFTQALNFAFKDKKSLSSYDRENDYKAWFAG
NFLSGGAAGGLLSLFVPVYSLDARYTALADARSGKTSQFRFQMLLDVYKTLKTDGGLGL
YRGFVPSVGLI IYYRGYLGFLYDSKFVFLLTGAEGSFSFVASFLGWVQMTGASTASYFPLD
TSKUKRMMTSQGQT1KDYDAGDLCLRIVQKEGAYSLFKGCGANI FRGVAAAGVISLYDQLQ
LINMGKKF

SEQ ID NO: 58
YMR253C
>sp| Q04835 |YM87___YEAST Oncharacterized membrane protein YMR2 53C
OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=YMR2 53C
PE=1 SV=1
MNPSVVKMRENTHLVIKSMNQELQPLSTTRSLSPKESNSNEDFDGNETTLQRI
SKDKVLPKGNVLLTYSFNSAMSVSTKVLNDEPPDIANDRQ1KPLQILLVMMITYIG
TLIYMYINKIDSTSGFPDKPE VRKSLVLRLGCTGFVFGYMYS LMVTISDAVLTIFLAP
STLITFLSV1LRERFTVEALGSLISLLGVLIVRPFLFGPCLTDSSQIVSSDPK
RPLATLVAFMGGMCCYVI IRYIGKRAHAIMSVYSFLSATDNABIAFINTPSMKQFI
PSLKKQWLFGNLGVSQFI FQLLLTMIRERAGLMSLYQLLYAVFVDVALYKHWPN
IWSWIGMI IISATLWIRIRAAMNETTAKDLTPIDDEENIPLTEFDLSDSK
SEQ ID NO: 59
YNL065W
>sp|P53943|AQR1_YEAST Probable transporter AQR1 OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN-AQR1 PE=1 SV=1
MSRNSIYTEDIEMYPTHNEQHLLRTREYKPDQGTKSEKLNFEGAYINSHGLTKTTREI
EGDLDSETHSSSDDKVDPTQIATETKAPYLLLGSYYQKWGMVAILTMCGFWSSLGSIY
YPALRQLEKQPNVDENMVNTVYVYLLFBGQISPSTVGGLADCFGRPIIAGMLIYVIAS
IGLACAPSYGVIIILRCIQSISIGSTIAISSSVGVGDFTLHERGTFVGATSFGVLLGQCF
GSLIGAVLTIARWDAWFILTIGGCSCFLIAFLILEPETKRTAGNLSIKPKFINR-API
FLLGPVRFFKYDNPDYTELDPTIPKLDSLSSGKILVLPEIILSLPSSLLFAMWTLMLS
SISSGLSVAPYNHYLIIGVCYLPGGIGGLMSSTFTGRIIDMYFGRRIKKFEQDKANGLI
PQDAEINMFVKRVLCLLPQNFLAVVAYLLFGWSIDKWRIESILITSFVCSYCAMSTLST
STTLLVDLYPTKSSTASSCFNFVRCSTSTIFMCFAMKMAAMTVGFTTFCLAVFFFFN
FLMI PMKYGKSWEDRLLKQQRQSWLNLAVKAKGKTKRDQNDNHN

SEQ ID NO: 60
YNL070W
>sp|P53507|TOM7_YEAST Mitochondrial import receptor subunit TOM7 OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=TOM7 PE=1 SV=2
MSFLPSFILSDESKERISKILTTHNVAHYGWIFPVLYGLWAHTSNRPNFLNNLSSPLSV

SEQ ID NO: 61
YNL083W
>sp|D6W196|CMC1__YEAST Truncated non-functional calcium-binding mitochondrial carrier SAL1-1 OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=SAL1 PE=1 SV=2
MLLKNCETDKQRDITYACLKELDKVNGQVTLNLISAFKNHPLKGNDEAIKMLFTA
MDVNKDSVVDLSKKYASNAEINSQIWFQRIDLDHDGKIGINEYRSLDNQISICNN
ELNHLSNEKVNKFLEFWEAFPKRKAQNALRGQASHKNTDNSRKTTSDDLYVTYDQ
WRDUFFLPPRQGSLHITAYSFFYLFNEVEDLSSQEGDVTLLINDFKQFGFIIAGISVI
STRTCAPPDRCLKVFLIARTDLSSLNSKTDLLAKPNANDKISSPLAKAVKSLYRQGG
IKAFYVNGNLNVIKVPFEISSIKPSVEFKTTKIMTKLECRDTKDLSKFSYIAGGLAGMA
AQFSVYPIDTLKLFVQCAPLDTLKVKNLLNFQTKADMEFREGGQGI ILQRCHSRSYGHSIL
CCIRFGDFCLLKMVYIQTGKDFEPFFTSRGSHQFGCTSNCGICWNRSLSNFSFKN
KTTSPRNICTSLCV

SEQ ID NO: 62
YNL095C
>sp|P53932|YNJ5_YEAST Uncharacterized transporter YNL095C OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=YNL095C PE=1 SV=1
MVHITLGGAIWSVKPI IKYLIIGVGLMAKGMILTVEATRI ISDILTVLVLPSLSFNK
IVANIEDKDVSIGICLSALLIFGGSPFFAYVVRLLFVPQWGGILAGGFPMFRSDL
PIAYLQSDQGLVSEEEEKNGVKANVIIFLTMFLICIFNLGDFRLIESDFEYNDEASVR
VSETKQFQAVATTNTDSFNNQEFANNTYARDSTLAEIGTKGNAVDFPPISR
RSTNS1APLSLPTDSSNKSITKVFQVQKARTIATCQSEQATRGSNPFLDQSASSTHS
YNTSESYESIDTMARRATASQFPRAYNTTLEENCLDEKCPNMSAALEPFISDMRA
LSQNIHILIREYSNVDQYGHQRRNSSLRGADMNDVHSISNNSTLQTIKTANLTRILTS
ATAVSKKDIETSQESLPQMRKFLSLTFLVFLKLRCRPSMAVIALTIFVAF
PWVKAFLV
TTANTPHISQAPNAPFLSRFSDFMDFTSVYGAACVPGGLIIALLGATLRKGNLYPGFWKAA
VTLVLIRQCVMPI FGVLNCDRLVKGAWNQDDRMLLFLVIAISWNLTMTTILYFTASFT
PPETTAPIQMECVSSFPLMQYPLMVVSLPFVSLYFKVQML

SEQ ID NO: 63
YNL121C
>sp|P07213|TOM70_YEAST Mitochondrial import receptor subunit TOM70
OS=Saccharomyces cerevisiae (strain ATCC 204508 / 5288c) GN=TOM70
PE=1 SV=2
MKSFITRNKTAILATVAATGAYAYYNQLQQQQQGKNTINKDEKKDTSQKETE
GAKKSTAPSNNPPIYSPSNSGPFSNKANFLAEEDKVLALDKGDNQFRRFNPDDAIIK
YYNWALKEKDVPVFYSNLACYSVGDLKKVEMSTKALELKPDSYKVLRRASANEGLG
KFADAMFLPSNLGDFN DSASIPMLERLNNQAMSLKEKFGDIDTATATPTELSTQP
AKERKDKQNFLPPVTSMASFSGFI FKPETFANYDESNADEKMLNGSLYKRKSPESDYK
ADFSFTKAARLEEFQDLKSNDEKLEKLAISELEHTGIFKFLNDPLGAHEDDIKAIELF
PRVNSYIYNALIMANDNVTYFDFKALKLDNNSVVYYHRQGMNIFLQNYDQAGDF
DKAKELEPEN IFPIQLACLAYRENKDFCTELFSAEARKFPEAEPEVNPFAEILTLDND
FDKALKQYDIAIELENKLDGI YVGIAPLGVKATLTLRNPVENTFIEATNLLEKSKL
PRSEQAKIGLAMQKLLQEDIDEAALTLEESADLARTMEKEKLAGIRTFAAAKVQRIRSDPV
LAKKIQETLAKLQEDQML

SEQ ID NO: 64
YNL142W
>sp|P41948|MEP2_YEAST Ammonium transporter MEP2
OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=MEP2
PE=1 SV=1
MSYNFTGPTPATEGGNSSLTLDLNQFDLAMNGWIGVASAVWMPGIGLGLYSLSRKK
HALSSLWASMMASACVFQFWFGWYSLASHNTRCGNGFTLLEFFGFRNVLGAPSSVSSIL
PDILFAVYQGM FAAVT GALML GGACE RARLFPMMVFLFLMTMITYPCIAQVWNQNEGWLV
KLGLSLYAGGCLHLSTGHHGLVAYLLIKRPDNPVRGKMPKHYPSVSVTLGTVFLWF
GMWFNGGSGAGNATIRAWYSIMSTNLAACCG辽TWDMYFRCRGKWTTVGLACSGIAGL
VGTIPAGPAIPWSAVSIVYGVTACGNLNAVLKSLRIDLGLCDYHVGVCIGS
VLTG IFAADYVNTAGSY1SPDGGWNHYYQVYLAGICAALAWTVTVSILILLTNAIPF
LKLRLSADEEELGTDAAQIGFETYESTAYEPEIRSKTSQMPHFNIDDKIENVN
TA EKNSTFSADSTKTNDTQHV

SEQ ID NO: 65
YLO20W
>sp|P38967|TAT2_YEAST Tryptophan permease
OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=TAT2
PE=1 SV=1
MTEDFISSVRNSEELEKRSNFVFVEYKSQKLTSSSSHSNSHDDDNQHGKRNFQR
CVDSSFKLPSGDFTSNKLRTKPRHLIMIAIGSGITGLFGSGKAIAGGPLGVW
IAAGSIG IGTIHIGGEIVTFSPVVGAFANYTFDPSISIFVSTIIYLVQFFFLPLEI
I AAMMTQVYNSSIDPVPWIVAYIVSVNLFGVRRGGEAEAFSTIKAITVCGFIIILC
VILCIGGPDFDEIGARYWHPDCPLANGFPGVLSVVLASLSWGLGIIEMTCLAGEDTPKGL
PSAIQKFVRWFLISLLTFLVGLYTPNLQMLGSSVDNFSVIAKLIHAKLPSIV
VALILSLSVGNSCNISASRTLCLSAHQLIGIPWFWYIDARGRPLYGMANSFLGGLAF
LVKSGMSMSEFVNLMAIGLACLIVWLSNLHIRFLRMAKQSGSDELFVSAVIVG
SAYSALINCILIALAQYFCSLPIGGWTSGKERAIIFFQNYQLCALILMFIFIVHKIYYKCQ
TGKWWGVKALKDI DLETDKIDIEIVKQEIAEKMYLDSRPWVYRQPHFWC

SEQ ID NO: 66
YOL075C

>sp |Q08234 |Y0075__YEAST Uncharacterized ABC transporter ATP-binding protein/permease YOL075C OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=YOL075C PE=1 SV=3
MSQENQDVATELIERLFSRIPSLHVRDLISI VASKNTTIVNTFSMDLPSGSVMAVMCGGSGGKTTLNLVASKISGGLTHNSIRYVLEDTGSEPNETEPLKHDLQDHPIQKVIMAYLPQDVLSRPTCLSTRKLFAADLKLNSERTKKLMVEQLIEELGLKCDATLVQGNHRLGSGKEKRLSITQGQMSNFSIMLDEFPTGLDAYSALVIKVTLKKLAKEDGRTFMSHIDQPRSLIDLLDLQVCSILSKGNVVVCMDKMTIPYFESIGYHVQPQLNPADYFIDLSSVDSRDREEAATQSLNLSLHDWYERTHLQLAQEYSNATETIQQNMTTRLPFWQVTVLTTRNNFLKNSFDVLSTLISTFAEPLITGTVCGWIIYKDPSSISGLRTTACASTYLSTCYLynnFDTYRLCEQDIADLYDREAEASVTPLAIVARKISLFLSDFFAMTMFIVSYTMFMGFLDAIRKFQFYQAPVVFCLQLSCGLSLMSAVSFSDKASLVMQMTFLVMSCGCAFVNAVKVMYPVRWKSYFTGFLMSTFTNSCTTNDLCEGQILEYVCFFRAPNWITPVAVVVLCSWVSFGYVFVAVITYLHKLTDITLQNEVKSQKKKSPGKPIPIELDLYVYVHOKDLKAEHNIIHITIKLEDILLRVIFSPAFSNWKEGNNFFHETKILQSVNIIFKPGMNIAIMPSSGSKSLNLISGRLKSSVFAKDTSGSIFMNDIQVSELMFKNVCSYVSQDDDHLAALTVKETKLYAALRHLLHTEARMETRNDNLIRSLHICCENIGNFVKGISGGEKRRVMTGQVLNDPPLLDEEGTSLDSFSTALIEELKLERCEQGTKIITIHEQPRSELFKRFQGNNVLLLAAGSKRTAFAFNPSDEMAIFTELGYCNPCSTFNAVDFDLLISVNTQNEQNEISSARVEKILSAWNANMDNESLPTIPESEKQYESFFTEYSEVFVTRPANLVLAYIVNVRQFQTTTRSRSDLARIAIQPGLVIFALFFAPVKHNYTISINRLGQAESTALYTFVGLMNLCAYPTERYEYYEENDNVYGAAPFILAYMTLLEPLSLASVLASYVTVFVLACGLPRANGTFFATVCSFAGCAEGALMNTFNTERPGFVNCISILSITGQMGLMSLCMSVRLKGFNLPVFYTMISIFAPFGNLKTLCEDGKNSDGTCEFAANGHDVLSYGGLVRNTQKYLIGIVCAVAYRLLAIIFFILKAKLEIKW

SEQ ID NO: 67
YOL077W-A

>sp |P81451|ATP19__YEAST ATP synthase subunit K, mitochondrial OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=ATP19 PE=1 SV=1
MGAAYHFMGKAIPPHQLAIGTGLLGLLVVPNPFKSAKPKTVDIDKDNDEEKEFIENLYKKHSEKQDA

SEQ ID NO: 68
YOL122C

>sp |P38925|SMF1__YEAST Manganese transporter SMF1 OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=SMF1 PE=1 SV=2
MVNVGPSHAAVADASEARKRRISEEEVEVLKRDSTTVVEGAEAPVRTFSSSSNHEREDTYVSKRQVFMDIFAKYLFIFGSSVQISDNYSMNFLDPNYSTAVDAGASNQFSLLCIISSLMNFIAFLQCLCILKSLVGTGLDSRRACRELPRWLNWTLYFAACVIADTIAEVGTIAALNIILKVPPLFAGIYTDVMFIMPTYKPGASSIFRIFIRIFECFVAVLVGVVCICFAIEAYPKSTTSVKQVFQVRFGVSAMFDHGMYTAISILGATVMPSHLSLFLGSAVFPLLLDYVDKHGNYTVSEEQDPSKKSTKDEEEMEYKFEQNYRTNAAIKYCKMYSMVSELSSITLFTALNVCAILVVAIGATLNSPEADGADLDHTELHSSRNLAPAAGTIFMLARRAYSAGVCTMSGQIVSEGIINFWKQFWQQLRATRICISAIAPCLVISIJCIGREALSIALNASHSQQVLSISYLFPLWALPIFFCQKSMKETEIVDTEDESHNQNNNRRSAGSVIEQDQGSSGMEIENGKDVIVYMANNWIIITVIAIIVWFLSLNLNNVAYAIQVLGMGHDGDIS
SEQ ID NO: 69
YOR079C
>sp|Q12067|ATX2_YEAST Metal homeostasis factor ATX2 OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=ATX2 PE=1 SV=1
MKFLQVILASSFITLAFGLILGIVYIDKQSSIVINQEGADSISDFTNADQTINDD
VSSYRKAVLSQFQGMMLGTSFVMLVI PEGIKACVEDHGNVNGNLIGFLGVLYLRVL
TLWVSRKQTYYTHDAVKQSWKDIINHPQIQWMNLQNNVVFALFIHGLSDGIALGTGNN
NDSLLLVVLIAVHHKAPVLSLTSLSMVQNRQMKEWIVCNVFILASSTFGYIVLSSLNL
LHSHSMTDWSGNLMMGSSLYYASTFAVGGSDDHDSLVSQEVEVLPHDQESVLYILV
CIPLVISYCEE

SEQ ID NO: 70
YOR087W
>sp|Q12324|YVC1__YEAST Calcium channel YVC1 OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=YVC1 PE=1 SV=2
MVSANGDLHLPISNEQCMPENNGSLGFAPTPRQILRVTLNKLYLKDVKVPIFYPDIV
CDHSEILSPKVKLAYEACCGNNPKDKANKRKYQSVII FSLLKCVWYSILATMEVHNAKL
YETRNLSAQQLCQRLDQFLQMLLLRRYVINEDEDQFLNLAELDMHT
TVIGSGSFORCLKWIRGWIWQNVLDQPTFIDKDSLAEVSLSHNFNPVRKAPVYQNYLQ
MIIFSLFLGLYTLVNGKDSERVEIFSELIFSIFVNTGFLDELTLKLYGIAHLSF
LFNTDYYLIIFAMGRSMVPLNAXYSEDWDKISYRLSACAFWSRLLLLSEQR
FIGIMLVLKHMKESIVFLFLIFLIMIGFTQFLGLDSADGKRDITGPILGLNTITVLG
LGSDVFVFEFAPVYAALLLYYGYFIVSFLNILLALAYSTAYKVvdNADDEYMAIMQK
TLYRIPADERVVIPNLIEVFVMTPI FRILPPKRAKDSLSTVMTIVYVPSSFLILLI
SVKTRARRIKYNRKLNDADNYTFWDLTDGLFLDSNNSMSMATQKLNRSRKLQ
QRTAEQEDVHFKVPKWKYKVNCPSFEQYNDNTDDAGEDKDEVKELTQVENLTAV
ITDLLEKDLIKDKKE

SEQ ID NO: 71
YOR092W
>sp|Q99252|ECM3_YEAST Protein ECM3 OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=ECM3 PE=1 SV=1
THITLQQAIAWSVRPIIKIYLLIIIVGFGLCMKNILTQVATRSISDIVLTILLPCFSNK
IVANIENCEDNIKDVIG1CI1S11FATGGLGFACIFVRSVLVPKRWRGGILAGMFPNISDL
PIAYLQMDQGFITEAEDEGKGVAVNI IFLAMFLICVF1NLGGFLNFLNDFQGDDDEEN
TLTNDSDAQOQNPITQPIEGNSSSSNQDILKEPNESTVFNSQSAQYSIEKNKKEKTELSVPK
PTHTAPPAIDDRSNSSAASV2SIDHSITHSRLTNHVDAGSVEILNDPTYRTRSQIAYTITES
RTSHVHNNRRNRTSTILSRIDMRLEPAEAGMSDILEYSNVQYGRRRKSSISSQAGPSVL
QADGTISPNLTRTLSTLRQVTSNLTR ISTDATVSKKDIETSGSLLPKWLQFLTKFFV
FLLLKNCILRCPSMAVILALI IAIFPFWVKALFVTTSTNTPK IKQAPDAPALTPFIMDFTSYVG
AASVFPLGILLGATLGLKIKLGYPFWKSAVVLVFLRQCMIFIGVWCDLRVKAGWIN
WENDKMMLFLVTAIWNLPTMTTITYASYTPEDETEPVQMECSTFSLMLQYPMLVSVLP
FLVSYFKVQMKL

SEQ ID NO: 72
YOR130C
>sp|Q12375|ORT1__YEAST Mitochondrial ornithine transporter 1 OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=ORT1
SEQ ID NO: 73
YOR222W

>sp|Q99297|ODC2_YEAST Mitochondrial 2-oxodicarboxylate carrier 2
OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=ODC2 PE=1 SV=1
MSSDSNAPLFPIFYGISAVAGISELTVMYPLDVVKTRFLEVTPTAAYGKQVERYN

SEQ ID NO: 74
YOR2 91W

>sp|Q12697|YPK9_YEAST Vacuolar cation-transporting ATPase YPK9
OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=YPK9 PE=1 SV=1
MDIIPSSNQIQHGQGSSGRASFSSTATTSTAALTSAMVDQNNSEPYAGATFEAV

88
SEQ ID NO: 75
YOR306C
>sp|Q08777|MCH5_YEAST Riboflavin transporter MCH5 OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=MCH5 PE=1 SV=2
MSDSSLTPKDTIPVEEPTQNLQPQLDESDSIIHYDEPADDLESLETTASYSTSVSAKVT
KEVNGKTIDIESQHPHGWENTSSTDHSDKEESENSNEEIESPPEGGFAWWFTFCFLGLLIAC
FGLNSTGVIESHLNQLSSESVSTGWFLSFLFVCNASCIS IGTYFDRNGFRTIMIV
GTVDHVAQFLATANSTKYHWFILSAICFGNGVIVLPSLVSVPAYFFRRGTLALAMAT
IGGSVGGVVFPMMLRSMKSDTDPYGFVWGIRLGLFDLLLALLLIS ILVKEKLPVHI
ENSKGDESWRYLRTYKLYFDDMLKYLFCLGTVFSELSINALSITYGSGYATSH
GISANDAYTLIMI INVCGIPGRWPVGYSQKFLKDNFLKFFNPFLGFTNL
TNMYYISALYFCSGVSFLPPCCQISKTEEFKRSTMYFVGVTLGVIGITGAI I
SIKTADYQHYI IFCGLATFVSAVYI ISRAYCVGFKWRF

SEQ ID NO: 76
YOR316C
>sp|P32798|COT1__YEAST Cobalt uptake protein COT1 OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=COT1 PE=1 SV=2
MKLSKQVKISLISLTDVFGIEITTYGYSMSLALIASMFHLNDIISLIVALWAVNVA
KNNPFDSTTYGWWKAEILGANIAFVIALCSVIEALQiAPIPVIVENPKFLVLYGV
AGLISNTVGLFILPDHNDQUEGHHGHGSHGIFADHEHMPSSTHTHHAHDGIIENFMD
STDNISEIMPNAIVDSFMNENTRLLTPEASKPSYSTSHHTIASGNYEHNNKRRSLN
MHGVFLHVQALDNGVMSLASSFIWKDSMYK¥TDPLVSLI ITGIFSSALPLSCKAS
KILLQATPSLSDLGQVEGDLLKI PGI IAIHDFHIWNLTERIFASIALHQLDIPSojiTDL
AKIVRSKHLRYGHSATLQPQFETIREVTSTERADSGQHDPLSLRPKTYGTSIGSG
TCLIDDAANCNTDLEDCH

SEQ ID NO: 77
YOR334W
>sp|Q01926|MRS2__YEAST Magnesium transporter MRS2, mitochondrial OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=MRS2 PE=1 SV=2
MNARLLLVRSISCQPLSRITFGRPNTPFLAKYADTSTAANTNSTLRLKQLLSFKIASD
SLIFISTICVFNSKGN ISMEKFFKWSFLEHSFLPPDRLKIDNSSISI IPTIMCKNCI V
INLLHIKALIERDKYVFIDTNPSSAAALSKVLMYDELSKSLSTKNNQSYEHRALESIFI
NVMSALETDFKHLHSICIQILNDLENEVRKLHRLLIKSKDLTLYQKTILLRDELLE
LENDDDLANYTVKLKSPKDFDSLEMLIETYTYQCEVQQQESLQIKDISTEIVNI I
LDARNRSLMLELLEKVTQITLTGFTVASVLPAPFYGMNLKNNFIEEEWEFHTSVAVFISVASY
ITKKNNFNSLSRTVKMTMYPNSPANSSVYTPKTSASIALTNLKLRKRKKWSTKQRGLVLYL
GSSYTNKANLSNKINKCGFVKKNMENDIKNQNDRDMIWKLIEDKKN

SEQ ID NO: 78
YPL078C
>sp|P05626|ATP_YEAST ATP synthase subunit 4, mitochondrial OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=ATP4 PE=1 SV=2
MSMSSMGVRGLALRSVSKTLFSQVRCPSMVIGARYMSSTPEKQTDPKAKANSIIAIPGN
NLIKTGVLGQSAAAVFYAI SNEVLVINDESILLTLFLGTGLVAKYALAYKDFADARM
KVKSVDLNASRKNHEAVKDRSFESQVLQNAEKTKVLFDVSKETVEASEAFKQKE
LAHEAKAVLDSVYREASLRQELQRQLAKSVISRQSELGNPKFAQKVLQOSSIEEIQEQL
SKLK
SEQ ID NO: 79
YPL270W
>sp|P33311|MDL2_YEAST ATP-dependent permease MDL2, mitochondrial
OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=MDL2
PE=1 SV=3
MLNRGLPLLRLGCRNMLRSFPLPLKSRFIRSLVPSSSQLIPLSLRCLRSFAVNGKLQQLS
LQSFRCNSSKTVETSLPSASIPOSKGASARSHAKEQSKDDYDKIIRLFLMLAKRDKWLLL
TAILLISCSNGMSPKGVILDFLTLKTSGSDEFDLKLIPFSFLPYEFLSFFTVALLI
GCAANGRFLRLRISERVRARLNVIKTHTLQDAEFDHNVGLDSLRGSDLAYVSVR
SMTQKVSDVGKALICGVVMCSLSPQLSILLSLLFTTPVPLFSASVFGKQIRNTSDKLQ
EATGQLTRVAEQLGSKGTDVTQSVFSAEGNLSRYNVAIRDI FPQGKTAATFNAKFTTTS
LQGDSLFTVLAYSLQQLSQSLIGDGLTAFLMYETGNAVFGLSTFYSEIMQGAAASR
LFEIETRKRPSFTVGHKYKPDGRVIEFKDVSFTPVSIPKKNFKIAPGSSVCIV
GSPGRKGTSTIALLRLRYNPFTGTTIDNDQDISKLNCRLRRHGIGQVEPFSMTGIRD
NITYGLTVTPTKEERSSAVKEPSFCHNFTKFPNTYDTVIPLGHGLSSQQGKQIRAIARAL
IKKPTIILIIDEATASL DVESEGA IYNYFGQKLMS KSMT IVSIAHRLST IRRSENVILGH
DGVSGVEMKFKELYANPSALSQILNEKAAAPGFSDQQQLIEKVEKEDLNEKSEHDDQK
DDDDNNDNHNDDSNQSQPETKDNSSDIEKSVHEELTKDAEKEANPKITFPQ

SEQ ID NO: 80
YPL274W
>sp|Q0896 |SAM3_YEAST S-adenosylmethionine permease SAM3
OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=SAM3
PE=1 SV=1
MDILKRGNESDKFTKIEDTITIPNDSDRSGSLLRRMKDSFKQSNLHVIPEDLESEQTE
QEKLQWKLASQETPNSDQSRGQHLMHAIAGTGLTCLGFLGGLSAPALGGFLPVLGTS
MFCVVQSAELSCQPFSQGYSATHVSRFINDESGFTAVNATYALAWLISFSPSELICALT
SYWQNTQVPFVWAVFAIFYFIFMLNLFGVRGFAETEFALSI IKVIAFFFEIIIGVLIAGG
GPNSTGIGAKYWDHCOPAFAKPVFNLCCNFVSAEFSFGGEVLVLITSTESKNNIASRA
AKGFTWRIAIFYITTVIGGCLVPYNDPRLSNGNNSEVDAASFFVIALSNNTGMGAKVSN
FMNVVLVAVSVVCNVCYASSRLQALGASQGQPVLFSVCSYMDRKGRPLVGIGISGAFGLL
GFLVASKKEDVEFTWKLFALCISISSFTTWFCICMSQIRFMLARKAQRGNSDEIAYKSLGV
YGGILGCVNALLIGAIIEIVYSAAPGVSSSAEAEYYECLSPIMIVVYFAHRFYYYYRDW
KHYIKRSEIDDLTGSVENLELFKAQEAEQLIASKPFYKYIYRFW

SEQ ID NO: 81
YPR003C
>sp|P53394|SULX_YEAST Putative sulfate transporter YPR003C
OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=YPR003C
PE=1 SV=1
MTSNSSLGRGRMSYSSTAPPFRKRVSDQDRTFSDDNFDYDKDSNQRTYIAASNITTGV
FPFFNRSSGCTSNNTSNTNSSNTNSNTNNSVENTVFETILYPYLFCSWLFPEYTNKLW
GDVIAGISVASQFQIPLASYTTSAIHPVPLCLGLYSLAIIFPVYIGLSVPQMVGPAISAI
SLVQVQAVESITLHKKVSLIDISTVFTVSSTILLFSGRFSRGGLNVLSKALLRGFIS
SVGLVMI INSLEEKLKLDKLFLPVQHPTFPEKFLILIDYAQPQYHIPTAIFSGCCLIV
LFLTRLLKLKLMKYKSAIFFPDDLVLIVTILISMKFLNKHRYGIS IGDFSMDNFDEL
KNPLRFRPKLQDLFSLAVLMALGFFESTASKLSGTYNTLTVSNRELVALGFMIN
ISLFGALPAFGGYRGRSALQGASVMGVSFGVMTITMLNLQVHYIFPVCVLSVIT
TIIGISSSLLEEPDIFKHPRLCQFSFSELPFSFVATFTCTIFYESIAAGICOVYSI INI IKH
SAKSRQILARVGTIISSDNNKRRKNSLDEGTEEGCIMIVRIEELPTNSED
LKRQSLRIFYSGKHPRSKRSKDIYKFDLGMNTIDASAQVLEEI ITSYK
NVFI YLNVSINDKVRRLRFKAGVAASVERAQNANNEENNTSNTFSDAGETYSYFDSIDA
ALYEIEEEKMKGNVPNNDSEFMSNTLFLSSLV
SEQ ID NO: 82
YPR011C
>sp|Q12251|YP011___YEAST Uncharacterized mitochondrial carrier YPR011C
OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=YPR011C
PE=1 SV=1
MAEVLTVLEQPSIKDFKQDSNIAFLAGGVAGAVSRTVVSPFERVKILLLQVQSSTTSYN
RGIFSSIRQVHEEGTQLRFGLNCRIRIFPSAVVQFVYEACKKLFHVNGNQEQQL
NTQRLFSGALCCGCSVVATPLDNLKRTLISOQTANLSSLNRRSKASKPFIGWQLLSE
TYRLEGGLRLGRGVRGVPSTGVLGVYVVALNFAYEQVLEFQGNVNSDAPWSKLSNLKTLIG
AISGQVATITYPFDLRRRFQVLANMGNLFGRFTSVDALVTIGRAEVSogyyqglaa
NLFKVVPSTAV5WLVYEVVCDSVRNW

SEQ ID NO: 83
YPR058W
>sp|P32331|YMCl___YEAST Carrier protein YMCl, mitochondrial
OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=YMCl
PE=1 SV=2
MSEEFPSPQLIDDLDEEHPPQHDDNARVVKDLLAGTAGIAQVLGVQFDTTKVRQTSSTPT
TAMEVVRKLANEIPGRYKTLTPLIGVACVSQFQVNEAMKRFFHRNADMSSTSLSS
PQYACGTTVGIINVSFLASPHEVRIRLQTQHTSTGNAEFKPLEICIKLRHNKALLRGL
TPTILREGCGTYFLVYEALIANQNMKRRLERKDPWKLPCI FGAISGTALWLMVYPL
DVKSVMQDTNLQKPKFGNSISSSVAKTLYANGGIGAFFKGFGLMLRAAPANGATFATFE
LAMRELLG

SEQ ID NO: 84
YPR128C
>sp|Q06497|ANT1___YEAST Peroxisomal adenine nucleotide transporter 1
OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=ANT1
PE=1 SV=1
MLTLESALTGAVASAMANI AVYPLDLSDKTI IQSQQSPSSSEDSEGKVLPNRXYKTVVC
MNIIFKEKKGILGLQGTMVTT VATFVQNFVFYYTFIRKSYMKHKLGLQSLKRRNIDPI
TPSTIEELVLGVAAASISQFSMTSPMATEQOTVHAESASKTNVIKDIYRENNGDTA
FWKGLRGTLPINSPSAPATQLKEVFFHDNDASLSLVSQNFILQVGSLKIMSTLV
QPLIYAKAMLQASGSKFTQFALLLYKNEGLKLWVLQVGPLQTLKGVQVQGFFFERGE
LTKSLKRLF ILYSSFLKHNGQMRKLAST

SEQ ID NO: 85
YPR201W
>sp|Q06598|ARR3___YEAST Arsenical-resistance protein 3
OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=ARR3
PE=1 SV=1
MSEDQREUNPSVNXMVNRDILTITKSLWLDLFMLPFIT ILSII IAVI TSVYVPSRH
TFDAEHPHNLGVSIPFLVGMVMIMPCKVSWSIHYFYRSYIKRLQALSFLNNVII
GPLLMTALAWMALFDYKEDQTRGTMMGVACIMVLWNIQAGGNDLCCVQLVTILNQ
MVLAPLQIGFYCYSHHDHLNSRFPVEEAVSKVQFGLIPGIGIIIRLSLTAGKS
NYEKYIFPISWMAGFHYLFLFY FISRGYQFIEHEGSAICLCFVPFLVYFFIAPWLPFA
LMRYLSI SRSRTQORECDSEQELLKRRVWGRKSCIESAFSSTTMQCTCTMASNNFESLBAIAI
SLYGNNSKQAIARATFQGPLEVILLILAIYARILKPYIYNNRN
SEQ ID NO: 86
YBR008C
>sp|P38124|FLR1_YEAST Fluconazole resistance protein 1
OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=FLR1
PE=1 SV=1
MVYTYRHTIVDLLELYLGIUVSNLTEQLSAREDETTRKFENTDKKECKPDPYDIECGPNRS
CSESSTDSSDGGQIEKNDFFRDVWNGFPSDENPQNWPLLKLSSLVFLQMLLCTVYMGSS
YIPFQGYIQEEEFHVGHVATNLNSLYLGYGLGIPIFSPLSETARYGRNLNYMVLFF
FMIFQVCGATVHIGNIGLVMFICSGILCSPLATGGGTAVDIISPEMVLVMNWASAGAV
APAVLPALGAAVDAMKNNRFIFWLMLWSAATTQFAPPFETPQHHNILYRRALLKRE
TGDDRYYTEDQDKLDREVARTFLNTLYRLPKMI IKEPAILAFDLVIAVAYGCFYLFFEA
FPFIFVGVYHPSLVEGVGLAYLFGILNMRIIVPRFNGFTTEAPLIVA
MCVCWCLPLSLFLFGWTRAVHWHVILPVIESEFVFLAVFNFQIFATFAYLATCYPYAVSF
AGMFCRASFACAFFLFGRAMYDNALTNYFVAWGLGFLTLGLAIIPFILYKGYGSLR
TRSSYTEE

SEQ ID NO: 87
YBR021W
>sp|P05316|FUR4__YEAST Uracil permease OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=FUR4
PE=3 SV=2
MPDNLSSLHSRSQRMLMNSNETFAPNNVLDLEKEYKSSQSNITTEVEASSFEKKEV
VSSEKRPQYSSFWK1IYEVWDKS1LSIGVSLDSMYQDLKPEKERRW8WNYNCYFW
LAECFNINTWQIAATQLQLDWQCWIT1YIGFGVFAGFVFLASRGVAYHLSFIPISR
ASGIFGISLPWMNVRVMIAQNYRWSVQAYIAATPVSLMLKSFQDKLQDKIPDHFGPSNAT
TYEFMCCFIFWAASLPFPFVPKIRHLFTVKAFLVPLASFGFLIWAIRRAHGRIALGSLT
DVQPHGSAFLWAFRLSLMGGCAMESTINMVAPSDRFSKNGPNNALSWLQVCIFPLFSIT
CLIGILVTAAQYEIYGINYSPLDVLFKLTTYNKTRAGFVLISFVFAVQLGTNISA
NSLSCGTDM5AIFPKFINKRGLSFLCAAMALCICPWNLMATSSKFTMLASAYAIFLISSIA
GVVCSDYFVVQVYIKITHIYSHQKGFSMYGNRFGINRHALAYLCGVAPCLFGIAE
GAPAINTVSQDAKMYLYSLJXWVYGLFSFSSYTALCFLYFPVPCPVNIIIDKGWQFWRANW
DDFEESWKDTERDDLVDNISVYHEHEKTF

SEQ ID NO: 88
YBR043C
>sp|P38227|QDR3__YEAST Quinidine resistance protein 3
OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=QDR3
PE=1 SV=2
MQAQSQS5NVGLRSRNCDSNLPPNHVMHCDSESSGSPHEHNDSYEKTNLESTASNREHDNQLSRKOEVYVPVKPLQLAIFIEPFDKARYPPMMKMIYVFILAFS5MGMF
PGMTSIFPAINSITFEKTSMIMVNSIGYVLLSLGLVPFWSSLSELEGRTTITYSFA
ALLAFPNIAGWLARDILORLMLCGASAASVQSVGATVDLYISEDRKGLNLSYYYLG
PLLAPLLSFPSGLLVNRWPRSTQFWWTVLSSCNGNFLVLIPTLPRLKDQSDKGAIQIL
ARRERIQVQNEQIDEQDRGQEDETDRDENQVATLSTEHNXYGEVRQDSDLKLESSH
PNTYDGRAGETQLQRIYTEASRSLYEYQLDDRSDGIDTATATQVRTIRSTDPKLARSIRENS
LRKLOTNLLEEQVKVLSSNGEIEAPQKVSARVVRWDTTFVFYIFPKLSSLHFLVEYPVALA
TFSAIQPSSTVETFNTVEKYSRRPPYNFKPILYGLLIPNSVYFASSIGYGRWVDMMLK
RKEKYG1LAPESI5WSNVTSISFPIALLIFGWCLDKKHWVTPLVGTALFGYAMMT
IGATLSYLVDSLFPGKATGVALNNLRQILATAAFTVFTTFMLNGMHGGAFTMLAFIVLGA
ASSVLLLKKKHGDYWRENYDQLKLYDKID
SEQ ID NO: 89
YBR287W
>sp|P38355|YB8B_YEAST Uncharacterized transporter YBR287W
OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=YBR287W PE=1 SV=1
MVTFTSFPAHLAYLVSQTVQVVIALAGFWSSGGLLPKQSQKI ISLLNVDLFTPCLIFS
KLAKLSMAKIFEIA IFIPFGGTGIFSGKIMSRLDDLDKETNFVVANSVFNGNNS
LPVLSTLSSLAYLPLNLDIQPNDRDNVASKRARGYLLII PQQIQQMRLWSGWYKLMKWS
GENTHQPFSQVSPQTNPNIDNEELVNQEEQELLEENNRMSSFLSSSSGIDKW
QSCTVFERIRANLNPPLYSMFAVAVGQPQREFMEDGFQINTFAEAVTTGGSVSI
PLILVIGSNLYPSAEEFPTVHSHKLLIGSI IGRMLPSCLPPIIAIAVKNVSLD
DPIFLVGGFLLTSPPAIQTLTQTLQNEFFEAMIDILFYGWYAVLSLPVSI IVVSGAIVYQ
LQWANPT

SEQ ID NO: 90
YBR295W
>sp|P38360|IATU1_YEAST P-type cation-transporting ATPase
OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=PCA1 PE=1 SV=2
MKPEKLFSLGTSDGEYGVNENISIDAMQDNRECHRRSEMHEANDNLGLVSRQDDCTN
RPKTIQPQELSLETQICHGENRTKAOLVDVDAEETGDHTRNESCEDCAEVNTDETTGL
DVDSCCGDAQGTEGDNESCDVGCDCCVRSVMVEEVTGSEAVSSQELFSEVPVSKS
EGLQSIHDIRETTRCTNSNSQHTGKRCLIESSDTSLLKRSCKVSRQKIEVSSKPEECNI
SCVERIASRSCERRTFKQSNVIGSSSTDSLEKFFSEQYSRMGRYSSLKNCIC
NYLRTLGKESSCPLKVRFCSGEASKTCTYSRYNSGSLCTKKTGGDKERLSDNGHAFD
VCSSKSCCTKMKDCAVTSTISGHSSESEISRIVSMFIEHNHLNEAGSTGETHEILVSLVSAGS
CTGECESKLKSGFALCLOKHLKTLSSQAEFNLDLLAQGSKVDKVIKLSTKETFTQYEQIS
NHGSTIDDDVFYAAKDFINEWQPQVETLKlVNERNIIRI YFDPKVIGARODLNVEGWSVPV
SFAPCSTFQVRKHLRVRGCTTASIILTIPILVMAWPQLERKISTASASMVLATI
IQVFIAQPFYLNALKSI FSRLIEMDILLIVLSTSAAYIFSISGTVGVGVRLSTEQFFE
TSSLVILMIVGFYSELARHRAVKSISVRSQASSAILVDOKTGKEINIRLQLQYGDIF
KVLPLDSRPIRTDGTISGGSSEVEEALTIQGSMPPVKCQSI VVAGSVGTGLFKVLKSLP
GNNTIISTATMVEADKLTTPKIQNIADAKASYFVPFTIIITGVTFCVWAVIGIRVEKQSR
SDAOVQAIYAIATVLIVSVCPCVILAGVLPFVIAVSGAVAAKRGVIFKSAESIEVAHNTHSV
VFDTKGTLEGKTLVVHETVRGDHRHQSLLLGLTEGIKHPSMAIAISYLKEKVSAQNY
SNTKAVTGTKVGGITSYSGKLQGGNCWMLGHNNFDPVRKALEQGYSVFCSVNGSVTAVY
ALEDSLRAVSTINLLRQRG1SLHSLSGDGDGAVRSMARLQGISSNIRSHATPAEKSE
YIKDIVEGRNCDSSQSKRFVVFVKDCGDGTNAIGLTQATIGIVHINEGSEVAKLAADVVML
KPKNLNIKTVTSQKAFRVMKLNLWSTFYNLAILAAGAFVDFHI PPEYAGLHELVS
ILPVFVAILRYAKI

SEQ ID NO: 91
YBR296C
>sp|P38361|PH089_YEAST Phosphate permease
OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=PH089 PE=1 SV=1
MALH0QFYIYAIAMLFALDFNIGANDVANSFASISRSSRSKLKYWQAMVLGCLCEFGLAV
LAGARVSSTIKNNI IDSSIFTNPDAPVMLTMTSALISSGSCWLTIFATAIMPVSTTHSIVG
GTIGAGAIAAGGANGVVGGWSGSVQI IASWFIAPILAGAIAIAIVFS1RSFSVLEVSKLERS
IKNALLILVVLFVFATFS IFTMLVIWVKSPNLHLDLSETETASVILTVGAIASIYVFIFF
YPFYRKLVDQWLKLLIDIIFRPGFSSFYSTKDDDFPMMPEGHQLTIDYEGRNRONGLTGV
EDEENKAAANNSNSVKNKEDIQEVDLVRTEPETKTLSKTQYWWSLLKQGPKKWPLLFWL
VISHGWTQDVIAVQNVDRNSGLDQGKYAKFDFYDNVEYIYISVLAITAATMSIGHTAHGA 
NDVANATGPFLSAVYVIWKNTG1AKSEVPWVLAYYGVALVIGCWTYGYNI1IK1N1NGMI 
LQSPSRMGAIILAVAIIVMTAQLGIPPTSTQIAVVGIVAVGCLNLKSVNVWMVWACY 
SGSWLTLPIAGLIAI ING1 I1NAPRFVGYQMT

SEQ ID NO: 92
YCL038C

>sp|P25568|ATG22_YEAST Autophagy-related protein 22 OS=Saccharomyces 
cerevisiae (strain ATCC 204508 / 5288c) GN=ATG22 PE=1 SV=1 
MSYGTINDMNESVTNYRIKRAANNIKGWASFYSEFFVVSAYTYPILLLQQFASINGV 
KVDHHSSCP1TSGDSDKCLGFLFNSNRI1 FVDTSSFALYVFSLVSFLQITI IVISVSGIVD 
LWGGVXFGRRILLVWGFIVGALSTVIAKSLNDTQI YSIALGYIVANGCGYVINVGLNLPP 
IFVKDSLKCQSGQAYEPDKVSLLTTVISGGRASLGYSALIVIQISMFVASKGSKQDV 
QVAVLFLVGIWFWQVWQPLMWLIDVTFIRVDDSTLASARSPYFEGQDLGQLNKNYLS 
YGWVSLSFESKFHARWLVDMLIAISD1TINSTAVLFSKAEIMSTLNLMSIV 
LTVVNAMLQAFMI PQFLATKFWRTSSQTLMIY I1WASFPSFYGILGGFNAFLGKHKFEM 
FLLAIWYGLSLGGLSASRSRSVFSLVPPGKESTFSMSF1TDKGGSSILGFLVGLLTDKT 
HNIRYSFYFFFLLLMLSVLNPINLKDVRREAEELSQQVLPESERL

SEQ ID NO: 93
YCR011C

>sp|P25371|ADP1__YEAST Probable ATP-dependent permease 
OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=ADP1 
PE=1 SV=2

MGSHRYRLYYSILSFLLLCSVVLAKQDKTPFEGETSSKNSRLTATDQKNDTCCPFCNMC 
LPFIEFCQFSECNSTYGRCIECEIIGFGDQCSLPLCGGLPSDESGKDRPSIAQNTDCHCD 
NGWGGINCDCVQCDVFCDVFDAFMDPSIIGTYCNGMVSKFVSGCNVTNEKLQILM1KIP 
QITTACDKPNQECNFLQWIDLQLESFYGCGLSDCAFEYDEQNTSHYNKCVQDVCVDPVTL 
CFAKGSIDISFLTEDTIGKFDFSCDLETRQKFSEPSMNDLLTTLVFGDPYITLCESE 
CVHYYSE1P1GS2K2DP2TSWQGKLVL1ALTAVMVLALFTAFYISKSP1FRNGLSK 
P1R1PDVENNFLQEDDTLATLSFENITYSVPSINSDDVEETVLNIEISIG1VPQGI1A 
IMGSSGAKSHTL1ILAMKRTGHYSGGPIKNG Imm1SMDKFSKIG1FVFQDDFL1LPTLT 
FETVLSALLLLPFLAFLSEKKAKRYKYMKELIREIDIKDR1IGNEDFGRISGGFERRSV1 
ACELVTSILPPLVLDESLASDANNVIECLVLRDSSNRTLVS1IHPQRSNP1FYDFK 
LVLSKGMVYSGNNAKCVSEFLRNEIGYCI1DNSYADYL1D1FITFAGPQ1KGRIRRINSD 
LEAGTDINDT11HTTFTSSGTQREW1HAHHRAEDR1SLLREDDEVEGTDGRGRAT 
EIDLNTKLHHDC1VYSDS1EEL1SEELSDENES1NVNGLDFTQGQG1QGLSIL 
NSR5FKNMYRNP1LL1GLYNVILL1LSSFLGLTLYIYNVSDISG1QNRGMLFFFLITYFPGV 
TFTGLSFLFALRIFKERSN1NY11LLYISK1IMSEVPLRVVPP1LSSLV1YMP1TMLG1N 
MKD1NFFK1C111111F1SL1E1LEIT11111F1DFL1NN1I11LSLV1LV1111SFL1FL1F1T1 
ITNVAFK1YK1N1F1V1YAYE1SL11NE1V111ML11K111K11111111111111L1111111111111 
F1DIKLAL1FLV1F1L1M1GL11LKW11VEQK

SEQ ID NO: 94
YDL054C

>sp|Q07376|MCH1__YEAST Probable transporter MCH1 OS=Saccharomyces 
cerevisiae (strain ATCC 204508 / S288c) GN=MCH1 PE=1 SV=1 
MPLSKVEHYLSYHTRLLLPHVLSLQCGSHRVAYIFS2LSASVTSTGIF1LS1LYS1QFWKHLN 
YSWQINTASMTNLMYLGTPPLGMIADSHGPITLLAILIG1FI PSYSYALAYVFNHEP 
SLGGGDSFSLNLS111CFVF1G1STASALYF11ALL1CT1L1YPHTK11SLISLPCTYG1SSV 
GSSALL1R1KWFSWSSASSSSSNDSLGLVRQFTALV1VYY1GLI1AW1T1SS1V1L1HFN1EEQ
DNQKRLDDQTDVEQS PLLERSNHVQEKFTQIYRFS LPDERSNHVQEKFQTMRI FSDPVTYI LAVSILLSLGPLEMFI A
NMGSLNLLVQDLAPTSLKSSLSTYALSTSTFRTLAVTGVADAPPKAKKSISIKWILLTLFLSL
GVCAQLLPKMTSASAPWSGLVPTGLSGVLGFGFQYPTLVLVWLGERSFGTXYGLLLI
APAIGSMI MCMLYAKFYSRCMLQGDLRNPSCISAVYKSYSSAFVSVSAVSAVF
SRKLRLI

SEQ ID NO: 95
YDL100C
>sp|Q12154|GET3_YEAST ATPase GET3 OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=GET3 PE=1 SV=1
MLTVPEPNLHSLITTTTHKWFIVGKGGVGHTSSCSIAIQLMALSQPNKQFLLISTDPAH
NLSDAFGFQGKDARKVGMNNLSCMEIDPSAALKDMDMADVSRANNNGSDQDDILGSL
LQGGALADLGTS IPG DEALS FMEVNHK1KQREQGEGQGETFDTVI FDTAPTGLHTRFGLQLLP
NTFLKSLKLTREFEITNKLGPLMNSFGMAGNVDISGKSLNELKAN veterinQFQFDPDLTFFV
CVISEFLSLYERLIGELISYSDMDVNSITVNQLFAENQDEHACKRCQDKWMLQKYLD
QIDELYEDFHVVKMPLCAGEIRGLNMTKFSQFLNKEYNPITDGKVIYILEDK

SEQ ID NO: 96
YDL242C
>sp|P54854|HXT15__YEAST Hexose transporter HXT15 OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=HXT15 PE=1 SV=1
MASEQSSPEINADNLNSSAADVHQPGEWDSGDFYDKEVINGNTDPAPKRFGLYLIIYLCCPVFGGFLPGWDSUILTINAFGNMDNFKNMNGSYKHSTGELYNVMRGLMVAMFV
GCSIGGVAFARPLDALTLGGRLAIVIVVLYLVYMGAIQISSIONKHYYQFVGFKI
YIGLGAAGGC
SVLCPMLSEIAPTDLRGGILSLYQLNMFTGIFGFCYVGTRKSYNATQWPRFVGLCF
WALIIIVGMLLVEPSPRYLIECERHAAEVCAIKNVSEPDEVWLVKQADEINAGVLQA
RHELAWSEKLSFVKTQVLQRLTIGILQTFLQLTGENYFFYQYTMIIKSGS
FVLYQFVIQRMFSDQSHFYQYFVGLVMFLVFFFLPETIGLSLEEQLLYEEG IKPWSASWVPSS
RGGASRETEAKKSWKEVLKFPKSFN

SEQ ID NO: 97
YDL247W
>sp|POCD99|MPH2__YEAST Alpha-glucosides permease MPH2 OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=MPH2 PE=2 SV=1
MKNLSPNLINKKNTSDSNVPGAKSHFISWEMDDQTKKDGLDIVHVEFSQPDTAPSE
SNKVIETIIFDADEKASEDESERGMPLALATNALNTPKAAAWSLIEEESSLIMETYDGTDAILGA
FYALPPLIFQRKFGSGQNDKTEGWESIASWQILTLICYMAGEIVGQGTLGSPDLVNGRTLI
IALFLLAFYGALCSVHGQLACMGPWFCQCLTSVEASACIPALRYLITYTYS
NLCWFLQGFLAQAGMKNQSKYADSELGYKLFAPALQWLPILAPALIFFAPESPMWLVK
GRFDEARRSLRRTLSGKGPEEILVTEVDPKIVTDKIDEKRLTSKASEGYSISDFMFR
RTRITICLCAWQAATCGSIIILYTYFYGKAVGEVESMSTDFSII IQYCLGIGCATFLSLWAW
SKYFGRYDLYFAQLGIGTIFVII IGGLGCSSTHSKSAGGGLSMLMAVAFYNLGIAFVFCLV
SEMPSRSSRTKTI ILARNYTVNSS ICSSVLILYQLNSKKWNWAGSDKFWVGWLCFLTIIW
AVVDSLPEATGKTFVEINELFKLGVSARKFKSTKVDPPVVFVKTPLKTSLTPREISKLPLQ
RNSNVSHHL
SEQ ID NO: 8
YDR110W
>sp IP32568 | SNQ2_YEAST Protein SNQ2 OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=SNQ2 PE=1 SV=2 MSNKSTQDSSHNVAASSASASFAAESFTGIDKDEODTSPPADLTKMLTIMADTA SQISATSEMPAUDVSKESFAALRHTRGFNAFMDSDGDGFAHAIFEFDDVA DEGQIIHRKAGVIEFMVTRQAGITAPKQGSGTADADAGATAGSTKTFNPSKIIKPLAQQS YDTRPLQTFQVSTQFAKFVTLKAPIVYKRLication receptor subunit alpha homolog OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=SRP101 PE=1 SV=2 MFDOLAVFTPOQGQVLQVNLQGKSSFESIQINSFPSQITPSVTRKESVANADGDFNLT LTINSEKHPSNLPFQELVVPVTVAFQTELNLNQTPQQTLALVLKLWNLHLE SILKNQRQGNEKNKHNYNDLQGGEKLKQEVFQFRYEYSESIKQDHHINPDNTKNSVPS QSNHKNKTKKRLRDKGKQSTGNGVSQGKRGDGMLDDNHDAAKLDASSNSSHNSQ VALDSTINKDFGDRVQIEIDKEELDHSSHEITSGNEAKNSGYVTAEGFLQKHV LGKTINNDSLQKVLKPEQSLQTQNLTVQANAEADYTQVSHDLGVSKTANWTSVENTARE SLLKTLNQITLPVSVDDLRELQKSRKDEEGKCDPYYFVSIVGNGVSKSTNLKAFW LLLQDNFIVLÇADCFRSGAVELQVRHQVENLQMDSSHRGSKKNKGTGNYLVEFAE GYYGGSILVIATQAKYQSRDQNFQVLMNTADRRHNDPFLSMPLSKSFQADKPK1I MV GELAVGSTDVQQAKN FNDAPFKGRNL DFFISKCDTVGEMLGTMNVMMYATGQ PILFVGV QGTYTDLRALSVKWAVNLM

SEQ ID NO: 9
YDR2 92C
>sp IP32916 | SRPR_YEAST Signal recognition particle receptor subunit alpha homolog OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=SRP101 PE=1 SV=2 MFDPQALVFTPOQGQVLQVNLQGKSSFESIQINSFPSQITPSVTRKESVANADGDFNLT LTINSEKHPSNLPFQELVVPVTVAFQTELNLNQTPQQTLALVLKLWNLHLE SILKNQRQGNEKNKHNYNDLQGGEKLKQEVFQFRYEYSESIKQDHHINPDNTKNSVPS QSNHKNKTKKRLRDKGKQSTGNGVSQGKRGDGMLDDNHDAAKLDASSNSSHNSQ VALDSTINKDFGDRVQIEIDKEELDHSSHEITSGNEAKNSGYVTAEGFLQKHV LGKTINNDSLQKVLKPEQSLQTQNLTVQANAEADYTQVSHDLGVSKTANWTSVENTARE SLLKTLNQITLPVSVDDLRELQKSRKDEEGKCDPYYFVSIVGNGVSKSTNLKAFW LLLQDNFIVLÇADCFRSGAVELQVRHQVENLQMDSSHRGSKKNKGTGNYLVEFAE GYYGGSILVIATQAKYQSRDQNFQVLMNTADRRHNDPFLSMPLSKSFQADKPK1I MV GELAVGSTDVQQAKN FNDAPFKGRNL DFFISKCDTVGEMLGTMNVMMYATGQ PILFVGV QGTYTDLRALSVKWAVNLM

SEQ ID NO: 100
YDR497C
>sp IP30605 | ITR1__YEAST Myo-inositol transporter 1 OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=ITR1 PE=1 SV=2 MFDPQALVFTPOQGQVLQVNLQGKSSFESIQINSFPSQITPSVTRKESVANADGDFNLT LTINSEKHPSNLPFQELVVPVTVAFQTELNLNQTPQQTLALVLKLWNLHLE SILKNQRQGNEKNKHNYNDLQGGEKLKQEVFQFRYEYSESIKQDHHINPDNTKNSVPS QSNHKNKTKKRLRDKGKQSTGNGVSQGKRGDGMLDDNHDAAKLDASSNSSHNSQ VALDSTINKDFGDRVQIEIDKEELDHSSHEITSGNEAKNSGYVTAEGFLQKHV LGKTINNDSLQKVLKPEQSLQTQNLTVQANAEADYTQVSHDLGVSKTANWTSVENTARE SLLKTLNQITLPVSVDDLRELQKSRKDEEGKCDPYYFVSIVGNGVSKSTNLKAFW LLLQDNFIVLÇADCFRSGAVELQVRHQVENLQMDSSHRGSKKNKGTGNYLVEFAE GYYGGSILVIATQAKYQSRDQNFQVLMNTADRRHNDPFLSMPLSKSFQADKPK1I MV GELAVGSTDVQQAKN FNDAPFKGRNL DFFISKCDTVGEMLGTMNVMMYATGQ PILFVGV QGTYTDLRALSVKWAVNLM
MGHPIYLTQSTSNVGDAVGNADSVEFNSEHSPSKRGKITLESHEIQRAPASDDEVDR
IQIKPVEFTISVMTFTQQLSPLFI ITLTFVAVISGFMFYGTGDTYSSALISIGTDLDH
KVTLYGEKCTSALGALISIGTDLDH FGRKRCMLGSGNLMEFVGAQ LGVSAHFTW
QMAVGRGMLFGVIGISLAFISPLFISEAPMKMIRGRLTVNSLWTGGQLVAYGCAGLNY
VGNNWRILVGLSLITPAVQFTCFLPDPRTYPYVMKGDLARATEVLKRSYTDSEEIERT
KVEELVTLOQIPGKNVEKWNITKEHHTVSNLRLAIGCGCQAIQFQTGWNSLMYFS
TGFETVFGKNSASVIIISGTFNIFPTLAVFSSIDKIGRTIRILLIGFLGTMALVCSIA
FHLGIIKFGDAVAVVSVSGFSSGWIGGIVFIF YVFAFYALGTVFQPSFQPONVIRG
I GSYATATNWAGSLVIASFTLMQNIPTFFAGFSLCSTIFCYFCYPCESGLELE
EVQTLIHKDFEI KAS KALAKKRRQOVARHELKE I PTQEIIIEDI

SEQ ID NO: 102
YEL027w
>sp|P25515|VATL1_YEAST V-type proton ATPase subunit c
OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=VMA3
PE=1 SV=1
MTELCPYATGFAIGCASAIIFTSLLAGAYTGASKGICATCVLRPDLLFKNIVPVIMA
GIIAYGTVSVLVLCYSLSQKQALTYIFQILGAGLSVGLSGLAAGFAIGIVGDAGVRGSS
QQPRLFVGMILILIFAEVLGLYGLIVALLLNSRATQDVVC

SEQ ID NO: 103
YEL065w
>sp|I1P39980|ISIT1JYEAST Siderophore iron transporter 1
OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=SIT1
PE=3 SV=1
MDPGIAHNLPEEFEVPEEMEHVEGAKDVKPTLTTSPAPSYEELIDPGVHNIIEY
AEMYNRF IYRALFSSLFLIAAYAGLDGNIRTYFQAYATSSYQSHSSLSTVNCIKTVIA
VGQICIIFARLSDI FGRFSIMIVSI IFYSMTGI IESQAVNITRAFGCCFIGQLTIGAILIL
EVIAFDFSNLWALSRAFILPAPIFNITSGNVS steep ANKGGWIGMAIFLPLACIPL
GICLHMRYLARKHDRKLFPEELMNKLKWSFCIDIAFWKLDIGMLLIIFVFGCCLLV
FPFLAGGLKKEWTKAI IVPEVIGQVTVLPYLMVLEIKYSRHLPFWDLIQDRI IFALL
IAFFINFNWMQGYQDMYTVLVTVAHEKSESAITRSYSVESVIVGTLGILKIRRTK
PFIIFGISCWIVSFGLVHRYGDGSAH5GI IGSCLCLGFAGSAFYVTQASIAQASAKTHA
RMAVVYTLAYNIGAFPSVSGAVWNTLIPKESIKRISFPTLAAQAYGSFPTFTITY
TWGTPERIALVMSRYYEYKMICLIGLIGVFCPPLLGCMAFLMRNHKLDISIALEGNDHESKN
TFEIEEKEESFLNKKFFHTSSKDRKD
SEQ ID NO: 104
YER019C-A
>sp|P52871|SC6B2__YEAST Protein transport protein SBH2
OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=SBH2
PE=1 SV=1
MAASVPQGQRILKRRQASIEKKEQAKQTPTSTRQAGYGGSSSSILKLYTDEANGFRVD
SLVVLFLSVGFI6PSVIALHLLTFTII

SEQ ID NO: 105
YER053C
>sp|P40035|PIC2_YEAST Mitochondrial phosphate carrier protein 2
OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=PIC2
PE=1 SV=1
MESNKQPRKIQLYTEFKYATCTCLGGI IACGPThSSITPLDLVKCRLLQVNPKLYTSLNQGF
RPKIANEGKWKVYTFGAVYGLQAGKYGGYEFKHNLYSSWLSGPGTVTVMASATAE
FLADIMLPFGFQMKTVTTMPFCDNLAIKCGFVGVSYMIVGDLMQPQMSWTRANNWLL
NRNQVISLMLFFVAPL5FLKKNLRSYASMVAI SSAYLCLVVLILLYHAVPS DEILRLKG
RISYLLFPQSHDLNVLNPTIFPVAYTCHHNMFS INENQRSSREVMKIPLIAISLALI
LVIAICAGYLTSGDNH IGN1 IMLYPQAVSSTIGRAIVLVMALPLQCMHPARASIHQI
LQHFAENVSIDSATSADEPTVATESSPLRDSSSLDEVIEESI YQPKETPLRGSFIV
ITCSIIVASYILVAISVSLVLAIVGATGTSISIFILPGFYGKLGTEHKTAVPLTTK
IFKYTGLLLLFWGLIIMITCILTAALKLN

SEQ ID NO: 106
YER119C
>sp|P40074|JAVT6_YEAST Vacuolar amino acid transporter 6
OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=JAVT6
PE=1 SV=1
MVASIRGVLTLIIHTACGAGILAMPYAFKPFGLIGVIMVLCACAMPQSLFQARVAKY
VPQGRASFSALTLPINLGNFVCDAAIICFGVGVSYMIVGDLMQPQMSWTRANNWLL
NRNQVISLMLFFVAPL5FLKKNLRSYASMVAI SSAYLCLVVLILLYHAVPS DEILRLKG
RISYLLFPQSHDLNVLNPTIFPVAYTCHHNMFS INENQRSSREVMKIPLIAISLALI
LVIAICAGYLTSGDNH IGN1 IMLYPQAVSSTIGRAIVLVMALPLQCMHPARASIHQI
LQHFAENVSIDSATSADEPTVATESSPLRDSSSLDEVIEESI YQPKETPLRGSFIV
ITCSIIVASYILVAISVSLVLAIVGATGTSISIFILPGFYGKLGTEHKTAVPLTTK
IFKYTGLLLLFWGLIIMITCILTAALKLN

SEQ ID NO: 107
YFL028C
>sp|P43569|CAF16_YEAST CCR4-associated factor 16 OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=CAF16
PE=1 SV=1
MVQFAIEVRNLTYKBEFLPSVSVDNLQIPWTRSLVGAAGNGKSTLLKGKHL
LDQGIKNMLDFPSMLQVDDDEQVDDVSTYQTTTYLGTECHMIS INRDI7VLELLK
SIGFDFHREGERLVRILIDVRWRMRHLSQDGKRRQVI6AML6KLKPRVLLLDEVTDILD
VIARARLLEPLKFETEITRCG VVYATHIDFGGLAKWPQNYHMKSGKI VDNLQYQDVEFS
EVNAYKNGQVAFENNDNVSKVNSLHLPAELWKLRDNQIPDKEIGI

SEQ ID NO: 108
YFR045W
>sp|P43617|YFL5_YEAST Uncharacterized mitochondrial carrier YFR04 5W
OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=YFR045W
PE=1 SV=3
MANQNSLYKQITAAGSVAAVFQTMTMYFPEYLFKTLGQLQPKGTAEFIIPLQIKSYFGVCS
ALNVAYSFKTITRFVFDKLCHSLNNIDNDNDFQRLTGYNLILGATLGTGIVESLFI IPF
ENIKTTLIQSAMDHVKKLEKNQPVNASKATFHKATKSTPVARIEKLLPAVKHYMYQTRGP
AAFVQG7TATTFRQIANTSIQTAYTAFKRLQARNDKASSVITGLATSF7LVAMTQPID
VKTRMMSQNAKTEYKNTLNCYRIFVQEGMATFWKGSIFRMPKVGISGGLTFVYTEQVS
LGGFSSRS

SEQ ID NO: 109
YGL084C

>sp|P53154|GUP1__YEAST Glycerol uptake protein 1 OS=Saccharomyces
cerevisiae (strain ATCC 204508 / 5288c) GN=GUP1 PE=1 SV=1
MSLS1SILPSTSEGLSRKPSKKDDATTTRKSLLWKTTEFKFYIAFLVVP1MFYAG
LQASSPENNYARLLLQGWLFRGKVDNDSDSQYRFRRDNFALLSVMLMVTISKRIVL
YSTNITKLRFDLIQLFLVAHGVN5IRIHALMLILAYAIHVLKNFRRATISIWIYGI
STLFSINDNFRAVPFNGCIFSLPSLIDHHRGTYRGI IFRVDVFNFTLRRVSYLNFLERWENL
QKKKPSYKESK4SAIVNLNERALTAHIPQDYSLMNYIAVTVTFQLIAGPI ITFNDY
VYQSHKTLPSINFKFIYFYAARVFVAILLSSMFILHLHVVAISKTKAWNTDFQISMIG
LFLNLIWKLRLI PWRILRLWALLDGI DTPEMNRCVFDNNSYSSAFWRAWHRS YNKWVVR
YIYIPGKSNKRRLFLASVFSFAWHDIEKLWLLGWL VLFLLPEIATQIFSHTDAA
WYRHVCAGAVF9VMINANFLFGCISHGDKTLLSDMCTVSFGKVILASVFLIA
VQIMFEIREEEKRRHGLYLC

SEQ ID NO: 110
YGL104C

>sp|P53142|VPS73__YEAST Vacuolar protein sorting-associated protein
73 OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=VPS73
PE=1 SV=1
MNRILSSAIIILSNVEMPQKHIKTIFCLAI YIASISIQGFQHLSNELNAPQQLSCSE
FDIPEMGYPYDRTLWKGKRYQCYI PLNEQIGIVTSTVFCEGILGYSFATLJAI YGRKF
SSLNCTLNVGSLII FNSNYSGLGVI GRLVGISCGLIVI I1FLIKEVAPSGWEGLLG
SMTQICRLGVLTQIGIALPLTDYSRMWIFLGSFLIAVNNFFMWIVDESPWLLAHGR
VTDAKLSLCKLRGVTDFEAEQGQDQWPQIESGDPIEPTTNSIAGSNSLWYKLYRDTN
VKSRHVTVLIFQPQCGINSIVLTYGTKI ISQLYPQHARINNFISMNPMVNLTVLSSLI
HSLRPKLPLMTSTLSVTLVAFTIGIAMIMWNKMNLIIVF5SI YMGVFMTGMLNPLLPIIMRE
VSKPQDMLAQRQYTICINNWGTFI IAYTFPI IFDHVLSYVFI IFAI IACSISAFIKKVP
ETKRSG

SEQ ID NO: 111
YGL114W

>sp|P53134|YGL4__YEAST Putative oligopeptide transporter YGL114W
OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=YGL114W
PE=1 SV=1
MPQSTPSQEVQRPVDNKFPALKITLRATIAIGIAISLGILTVTSNFQFLQTGNSVMSMLS
PALLACAFFKNIFLPHPFNDRFSDEVVNYVQSMANAVGTPFLAFGIFV1PAIEKFLND
EGGGLRREQGQSFRTREALLLWSTALAFFGIAVPLKVPQVREKLPPFSGSAATALISL
NGTJEILQVESSKELRMAELCEPEVQPRNDPEEAAYLMNSSHSLGEDYATSGDS
SILSTGSEYRANI IIIIRFCVSSLTVYMSVFVPRISIFVFHYLSNNYLMNFQ5PSA
YIQGGNI1GI1PTEVSYMLICFGFLGWGLAPLARJKRWMVPADHDWEVGEQGWV4LSLS
INWADSVVAPII VTVKS1KVFLII DDKAALMNNIIIDTFQSIMLLEEREAXNASRNTYD
GRQDTVRILS1VSRDNEIEVDSKHLVYTVTISGACLVSICICIVSI YLF1G1QVIPLAYITA
L1ALLFISILQLGETDLNPVSGIKISLIQIFAI IFPRDPSVLMNVS5GIAEASA
QAGDMDDLMQKTHGILGASA PRAQFCAQLI GACWS11LSSFYLMCYYNKYS IPSEQFRI PT
AVVWIDCARLVTGKLDKALECSMIGVIFAVLSLIRNTYDHYGWILYPGVAVGV
GIFNSPSFTIARFQGGMASHFVWKNLHRGDLNATKMIVFSSGLVLEGIFSVMINMLCFL
NVPHY
SEQ ID NO: 112
YGL167C
>sp|P13586 | ATC1_YEAST Calcium-transporting ATPase 1 OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=PMR1 PE=1 SV=1 MSDNPFAASLLEDNREIREILDAEALSKPSLFYCTSLVDVEALEKLDTNKDNGRLRS SNEANNRSYGPENITVEDDESFFKLFSNFDERMILLLIGAVSAVSLFMNGI DDASVI TLAFIY VTVTFQVREYRSEKSLVPAECLMRCCQESHVLASTLVPGDVLHFRIG DRIPIADIRIEAEDLSDIESNLGEPNVKTQSEIYESNDQPNSIVPISERSCAYM GVLKVEHGHGKQPRFTSGAVFEMMNNIEKPRKPTQLMDDKLGDKLSLVSFIVIGM ICYVGI IQGRSWLEMFQISVSLAVAA VPEGLPI IVVTTLALGVLRMAKRRK VRRLPVES VLGSFNVICSĐTGLTSHMVTSLKWLCLDSMKSNNLVLSLSDKDNKKTNSNGLKYNL TEVRETLTIGNCNNSASQFHEAFILGFNPTDVALLEQLANFEMPDIINTVQKQEPFNSK RKLMAKILNPVDNKCTVVKGAFERILEYSTSYYLSKGGKTEKLEAQAKTINEACNSM ASEGLVRFVGFKALTLSSTPTLDELIKDTFTGLMNIDPDRPNNVKFAEqEQLQQGVHI IMITGDSENTSAYNIAQIGHIPVI DPKLSVLSGKDLDEMDDQQLANVI DHVNIFARPEH KLNIVRALRKRGGVVTAMTDGVN DAPALKLSDIGSMGRIQTVAKEASDMVLTDDDFST ITLAEIEEGKGGNQNIQLFQLQSTLSVAALSLVLSALSTAFKLPNLNAMLQILDWLDG DPAQSLQVEPVKQPKDVQNYRDILTHWVMKQLTTAAICIVGTVYIFVKEAMAEDKV TARDTMFTCFCVVFDDMFNAALACRHNKSGFEIGGFTNKMNYAVGLSSLGQMACIYIFP FQSIKTEKLGISDILLILLISSSVFIVDELRKLWTRKKNEEDSTYSFNSV

SEQ ID NO: 113
YGR257C
>sp|P53320 | MTM1___YEAST Mitochondrial carrier protein MTM1 OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=MTM1 PE=1 SV=1 MSDRNTSNSTLTLKERMALSAGSVLTSLILTPMDVVRIRLQQQQMPDCSDGAAEVPNA VSSGSKMKKTFTFVQPGQNLNMIKAKIIFWESACFQELHCKNSLKFGNEAFTKISVESGITS LWRGSLSTLMAIPANVYIFSQGYEYIRDVPIASTYPILNPFCGAIARVFAAIESLAPIE LVKTLQSI PRSSKSTKTMWDVMDLNETRMKEMMVPSRIFLKGEINTLWRDVPFSAI Y WSSYELCRLERLSTRFASKANWIFHVINSFASCGISCISMIAICHTFDFVKTQWRQISM MNNSDPKGNRSSNRMMFFLQETIWRTEGLAALYGLAIYVKKIRFSCAIMISSYEIIKVF GNLHQQ

SEQ ID NO: 114
YHL035C
>sp|P38735 | VMR1___YEAST ABC transporter ATP-binding protein/permease VMR1 OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=VMR1 PE=2 SV=1 MGDTPLI IARNGSWEVDDFTRLGRQQLS YLPLAIASIGI FALCRSGLSRYVRSAC GDLVNEYLFQAGQEEERKSENRLLRRLNLTQANYVNKKQGRILKLRHFDITTDVQIDA KNHGGLTFRPSSTDHILRKSSEIVLMQLQI IGLSFlRVTKINELTNRDVTTLFLWIL LSSLILRVRKSYLNAWICTFAHTTHTISWI PIRSVYIGNIDDFVSQI FYEFVFEYIQST LQPK1ILPSKDNSSI YVRDHTSPSREHISSLSCITWSWITNFWEAKQNTIKLKDI WGLSMDLSDFLSFILFQTRRRKNNLNTLAFLFSEKYIIILGMWLVNSVNNLPIITLMK RPLFEIYDNPPRSSSCMNMLAWYI RGMICLRLTACNSQQQVFSDKLRCRRAILGEI Y AEGRKLRLPSKSSDSDSNANLIINILDSISKSVSELANYLYTVQAMIVIYUM GGFLPNFLCVSAAGISIILVMFPLNFLANLLKGKFOQQLKTCDQRISSKLNECLQNRI V KYFAWERNIEIKSIRQKLRSKLKLSSLVWVSFTSFLWFVTPLTVGVTAFICTFVQHED LNAPLAFLTLISLFTLQFLQDLQLSMLFQLOKLYRLISNRFMDDTEKYNLFSITSPD KNNKEFKNATLTWNENDSDMNAPKFCLGNIKQFGQIKLNNILGSTSGKSALLGLGELN
LISGSIIVPSLEPKHDLIPDCEGLTNSFAYCSQSAWLLNDTVKNNI IFDNFYNEDRYNVK IDACGLRDICLEIPLAGDLEIGEKIGTLSGGKQRQSLARAVYSSAKHVLVLDCCLAVDS HTAVWIYINCTGPMLKNRTCILVTHNVLTLRNAHAIFVLENGKVKNQGTIELTQSGK 5 FKKYQYQVLSSDRSINKEANRLRKPQNDKQIEKVPIVMTNIFDNFVNDQGLIEEEEKSN GAIASPQYKWLKFFGGFKALTALFALYITAQILFISQSWIRHWNDTVRINAPGFAM DTFPLQKGMDSKSNKHNAFYLYTLVYFLIGI IYAMLLGGFKTMNFTLSGGRASRIK FNNLLELHLAHIYFQFDFVDTPVGRMNRFSDKIEGVDQELI PYLEVTFCFICASIFIITVI TFRTVAVIFVLYFIFGKWKYLTASRELKRLSITKSPIFQHSETLVGCTAIFPGDRRF ILEMNKNQDNRFRSLYSVTKWFSPYFVMDAIFVLASGSFILLNIAINSDGLAGSIY TAITYLDGALWVLRLYSTFEMMNNSVERLKEYSSIEQENYLHDEGRILLNESPWKD GEIIEINSLLRNPVRNFSDQVSFIGTCSRQGATGKSTI ITALRRLLEPITGCIKIDQQDISKIDLTVLRRSTIL IPQDDPILFATGKTENVDPYDEYDEKII FKALSOQNLIS SHEEEVVLNSEEERFSTHKNFNLHTEAEGGLNLSSQERQOLLFIARSLLREPKI ILLDE ATSSIDYSDSHLOQII IRSEFNKSTILTIAHRRLSVDYDRIIVMDAGEVKEYDRPSELL KEDRGIFYSMCDSGGLEGLELLQIAKQSSKMMK

SEQ ID NO: 115
YHL036W
>sp|P38734|MUP3__YEAST Low-affinity methionine permease
OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=MUP3 PE=1 SV=1
MEPLLNSGKANPSQDFVDFIDVEQGDITTKYGSTNTGSFSSMDTVEAQAIAKETAFMEVPE QGRHLGVSTVYLVRSMIGMSQFHGWSPVILLNTGNNKLYFAIFVFSAAAFAGLYFL EFQSWIPKSGGRKFLERSFRPRLISI VVFSCYSLTGYALTGIVFQKGYLSAFGVTDDSWSKYVISIFIAVFLHVSVHRQFQIQLAGKLHVLIMCFLAGLYITFQKSYTGQ VAWDLVTFVQKEDSLLSVSSILAIATAFISSFFCFSGWDTVHTVSEIKNPVLTKVGSPILSL IIIFVCTCYMNMMVAYLKVLTYEIEEIVSAGPLVSLFTFLGPRVVGKFAIFASIAIAASNI LVYVISQVRNSIFEGYELPFIHMSKKNWPDNPALTVSILCGFITAWILLPKEGSSF NYLVSMQDGYNGQFLLVAIQFLFIRWFMKHEVNEPEIRASTFGVLAI ITLSLYLMAPFFA DPLSNRVGFLPYQIMSLLVLVACFFWLVKFKFHPKHYKLKITYLHDLGIVTEWV KKPCLC

SEQ ID NO: 116
YHR002W
>sp|P38702|LEU5__YEAST Mitochondrial carrier protein LEU5
OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=LEU5 PE=3 SV=1
MTRDSPDSNYKIHINNTKTQTFSRDNSFDYIVRSGLAGGISGSCAKTIAPDLRIKIFQFTSNHYKTYGSLIGVLEAAAKHINDWVFROFGQHSTSALLRRFYAATAKVFYEQIR NLTRPSKFEHSHWRVSLSLGACVSFYPLLDLVRLAYETHKRVKLGRI IKKIYK EBSATLLKNDYIPMWFCHCNFNYRGYTPVLGMIPYAGVSSFAHDLHVLKSPFAPY SVLSELEDDELPRQKQRPRLTWAELISGLGAMQTAAYPFEL IRRRLQVSAFLPK TMYDHKFSQISEIAH11FKERGVRGFGVGLSI YGIKVTPMVACSFFVYERMKWNFGI

SEQ ID NO: 117
YHR096C
>sp|P38695|HXT5__YEAST Probable glucose transporter HXT5
OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=HXT5 PE=1 SV=1
MSELENAHQPLEGSAVSTNSNSYNEKSMNSTAPTAGYNDNLAQAKPVSSYISHEGPP
KDELEELQKEVDKQLEKKSKSDLLFVSVCCLMVAFGGFVFGWDTGTISGFVRQTDFIRRF
GSTRANGTTYLSDVRTGLMVSIFNIGCAIGGIVLSKLGDMYGRKIGLMTVVVIYSIGIII...VIAGRYLN
WNYRRRLKYYQNWLGKKRSKLLEEHDNDLNLVQRIIENDPKYTFNIFKARLQPAFVTLLL

SEQ ID NO: 118
YIL006W
>sp|P40556|YIA6__YEAST
Mitochondrial nicotinamide adenine dinucleotide transporter 1 OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=YIA6 PE=1 SV=1
MTQTDNPVCNGLLPFQQYCSADHEEPLLHEEQLFLFDHSQQLSSADI IEPIKMSSTE SIIGTTLRRKKWVPLSTMQTIALSAGAFGLSAGAVCPVLAVRQLAQGLQTFRFNPYR GIMGTLSTIVDREPRGLYKVLIPVLYFPTWI YSFYEFSSKHFHGFQFDPAVQ5S CAAITAAGA ASSTLNP1VWKTMLQSNLGEHPTYKGFDAFRLKYFQEGFKA YAGL VPSLLGLFHPHIFIYELLKDVRHCYSENNNTNSNLQRLIMASSVKMIAV YPHE ILRTMRQLKS dIPS IQRRLFPLI KATAYEQGLKGFSGFTTNLVRT IPASAITLVS FEY FRNRLENSTMI

SEQ ID NO: 119
YIL120W
>sp|P40475|QDR1__YEAST
Quinidine resistance protein 1 OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=QDR1 PE=1 SV=1
MTKQQTSVMRNASIAKEEREESGDNNVDRSSSDAISDNDAE RNSHSEIDNESNFDMVY SRFSKHQRMVLLVQCAFTGFSTVAGISYYPVLTIEERKFNITEELAVVYVFIFQGV APS IMGGLADTFGRPFI VLWAILYFCAC IGLACAHNYAQL LALRCLQAAGI SPVIAINS GIMGTVTKVERGYQLVAGQVQVTFAGALIGGLSSKGWRAIFWFLAIGSICLVF STLLMPETRKRLVNGSVRTPSFNLRSILHLHGVSKTLHDDDPETLEPSVDFFLAP LKILHIREI DILLS IAQLQFSTWTQHTALTIVLSSKYNLSVAKICLFLPAGISTLSTI ISAGRYLNWSYTRKVNIRNHEQELQMEKYKGDNKVAELIHNSHYAFNLVEARLH PAFVILLLSSISGFATFQWCSVKTPLTAVALCTSAFASFSLNCILTFSTLILDLPKAS TATGCLNLFLRCLLSASPAIAALT MVKMEKRYGKVFTFLSAITSSSSLLFYLLKNGQLSF DRIRANDKSA GRSGVKNSEKVST

SEQ ID NO: 120
YIL121W
>sp|P40474|QDR2__YEAST
Quinidine resistance protein 2 OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=QDR2 PE=1 SV=1
MAGATSSII RENDFEDELAESMQSYNRETA DKLALTRTESKVPEPEITAPPHSRSFRSFK TVLIAQC AFTGFSTIAAGAIYPVLS VIERKF DIDEELWNVTVVVYVFQLAPTFMGGF ADSLRPRPVVLAIVI YPGACIGLACAQTYAQL IVRCLQQAAGI SPVIAINS1MGDVT T RAERGGYGVYVAGQVQLSAGAFGALIGGLSSKGWRAI FWFLAIGSICLFLAPLILPET KRNISGNSVTFSYLMRPAVLPVRLPTVRKSLHLNDPETYELPQNLNLAPFKILKAYE ICILMLVAGLQFAMYTTHTALSTALSKQYHTVAKVLGFPGCTLCSI VIAGRILN WNYRRRLKYYQNWLGKSKRLLEEHDNDLNLVQRIIENDPKYTFNIFKARLQPAFVTLLL

102
SSSGFCAYGWCITVKAPLAAVLCMSGFASLFSNCILTFSTTLI VDLFPTKTSTATGCLNL
FRCILSAVFIAALSVMVEKKMFVGGVFTFLGALTSSSILLSFLREKAFKKLELG
VNG

SEQ ID NO: 121
YIL166C
>sp|P40445 IYIQ6__YEAST Uncharacterized transporter YIL166C
OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=YIL166C
PE=1 SV=1
MSVQKEEYDIVEKALQSVASELTDSEESISHNPFDHFHAERWVKVESSGEGLSKFD
PEFTWTKDEEKVLKMDCLKFLWVFMFALSFLDLIRKNIARAVSNFVVLKDMNNDYNL
GQTLYLVLFLASLPNGDLLKRFQGEPRVQPIVQLWSVCITQAGKLNQRGFIATRCCLG
MVQQGFIPDNILYLSYYTGAEILFTLSFFWCAIPFLQIEGLLSLASSGI IEMRGIHNLAGW
QYLFIIIEGFILSLSVQAVSYLMRRGPTQTGESAFHKGKSLFTEVEEKMVRNIHRDPSK
GDMSNRQPVTFKEILYTLTLEFDLWPLFIQGITAFLSQTVGS YLSLLIKSLNYSTFLSNI
LAIPGQALLNLAPPLLALKKEKSLCVQIVWNVLIVPLSLALPTDNKLVYIIIL
TGILGLPYTHSAIAGWSEISNSVRSTVGTALYNMSEQVAIIASNMYNDDRKFYTRG
NKILLGFTCFCNICMAMATKYISRNKYYKDRKNSMTKEEQINYLYDTKDGKMRDLYRF
IH

SEQ ID NO: 122
YJL133W
>sp|P10566 MRS3__YEAST Mitochondrial RNA-splicing protein MRS3
OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=MRS3
PE=1 SV=4
MVENSSSNNSTRPIAPAIPDIPYEALPHTAPLYHIQLAGAFAGIMEHSVMFPIDALKTR
IQSANAKLSSNPMLQGISHLSTSEGTLALWKGVQVSILGPAHAHYFGYEFCKNLI
DSSDTQTHPFKTAISGACATASSADLMNPDTIKRQROIQLNTASVWQIIQKIQSEGIA
AFYYSYPTTNMI PFAAFNFIYIYESTKFNPSNEYNPLIHCLCGISGSTCAAITTPL
DCIKTVLQIRGSQTVSLLE1MRKDFTSKAASAITYQYVYGKFWKFRPVRANMPFATI
SWTAYECAKHFLMTY

SEQ ID NO: 123
YJL219W
>sp|P40885 HXT9__YEAST Hexose transporter HXT9 OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=HXT9 PE=1 SV=1
MSGVNNTSANDLTTSNEVSANAPSVKTEHDSKSNLNLATEPPIDLPQPKPLSAYTT
VAILCLMIAFGGFI FGWDITIISGFVNLSDFIRRFQGKNDKTYYLSKVMGGLI VQIFNI
GCAIGGGIVSLKVDGYIRGGLITVTA YVVGILIQITSINKWKYQYFIGIRISGGLWGVGI
AVLSPMLISEVAPQGIRGLTVQLYMCTMG FLYCYNTGKNHNTAQWRYGLGCLFA
WWTFMVSGMMMFVPESPRLYE VGGDEAEKRSLSKSNVSVDPALLAEYDITIKAGIELEK
LAGNMSWLLSKTTKVFQRVLMGVMIQSLOQLTGDNYFYFGITY FKSGLKDQSFTSI
IIGVNNFSSFPSIAVYITFGRGRCLLWGAAASMLCFAVFAVSVKTLWQGSSHQDITS
QAGACNMLCVFTMFFIFSFAATTWAGGYVIVSETTFPLRVSRAIAATAAANMMGFLISFF
TPFITGAIIYFYGGVLGCYVFAYFYVFFVFETKGLTLEEEVNIMNLEGVPAWKSASWVP
PERRATDYDAIDHDDPRMYPKRFESS

SEQ ID NO: 124
YKL016C
>sp|P30902 ATP7__YEAST ATP synthase subunit d, mitochondrial
OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=ATP7
PE=1  SV=2
MSLAKSAANKLDWAKVIISSLRITGSTATQLSFSSFKKRNDEARRQLLELQSOPTEVDFSHPYR
SVLNTSVIDKIESYVQKYPKIDASKQLQVIESFEKHMTNAKTESLVSKEKDLQS
TLDNQSRPFDELTVDLLTKIKEADKVEEMVKGKWDVPGYKDRFGEQVNLNVM

SEQ ID NO: 125
YKL050C
>sp|P35736|YKF0_YEAST Uncharacterized protein YKL050C
OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=YKL050C
PE=1  SV=1
MSLILASQTDVEVSQTSPEQTERKAVRSTLQESLHSEMHRAMPEPRSI  SNSVHKL
KTIYSTYQQSQGQLSKEAIFRAKQKGILNTPANYKTLGGLDSKESVDDLARLASKRT
VSDPVDCVETAIEQKARGAEFKVFSTFSLPETPDPITVNLGLKGRDFLTRLAAQKALA
FSPSLDNSMGTSDDSSVKKKRFSGAPIGNEFDANLVPQHPAGFKSSDLKSLVGLDAGER
AISVRNDRLYQFVRNFKNGLQSSDQSVSKANKVEFKGTLEKLEHSAEQFLESHAGNER
QRSILQDQQYMQAKAGV DKLDPKTEDPFAAREAQQKLYIKQVAPVVLNEAQKLNAR
KLQIDIRSRTYMLLFGNQAYNLAVNIALQHYSVKQEEXKKIKYLLGGLWMTPEEVNAVAK
KLISPVNNASRQDDVRKDIERRSVRVDQYEDGNSMERAKEQNDQCLLAMASQ
QQKEAKKAEEQDRYQDFQVMNKLQQKEKENARENERNLNLQERLSKNSLGEND
ELNDWNDACERLSIESIEHYYAVRSHDFDNLSERGTYDEELRESKRQVEIYLAVSLA
EHKTAIHGFETADDAGAPIAVPQKIQ  PTKDDLDAVNDPLVISAMAKEEAAEMATEEC
MLKELQVDEMI IRRNLMECREEETEEKATRSRGTEEEKKNSNFRSVDIMTPDN
EKVTPIGKSASPKDVKSRLSTVNTGKDDASSARSTIGSVGVLLDPKPTSNKENE
LIDDEVSYSKQHAQVDTGEDISIANKDKSSRPANSSGSIETIEQFLKNADKQGLST
ESVTRMKREPPDVQMDKSGKHDFTHCNDNRRSSFGFSQGSIENDYSENVTDQQDDQEGSE
IRVRSNDSNTSPKESFFKEV

SEQ ID NO: 126
YKL120W
>sp|P32332|OAC1_YEAST Mitochondrial oxaloacetate transport protein
OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=OAC1
PE=1  SV=1
MSSSNSKQDQKIEKAAQKISFKFGSFVAGGLAICAVTNTNIELIKIRMQLOQGEMSAASA
AKVYKNIQPMGAVIFKNEKIQGKLQNLAAIYIQGLNGSRGFLYEPicerSLLQFLFPDQ
EHPKQVSVGVNVSAGASIIIGAVIGSPLVLVRQYSEFISIKEQTHYGTVWGVLGVT
IFKTEGVGKLFQIDAILKSRTAGSSVQPLPYNTAKNILVNDKMDQGPAHLHTASIG
LGVAVMNPVDWLITRI YNQKDLYKGPDCLVKTVRIEGVTLAAGKFQAVFRIAPHTI
MCLTFMEQTMMKLVYIESRVLGHN

SEQ ID NO: 127
YKL14 6W
>sp|P36062|AVT3__YEAST Vacuolar amino acid transporter 3
OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=AVT3
PE=1  SV=1
MNQKSVSSGSRTGSNNNKNNNNGGTSIAGSPLTDGGGNGNSNRSRSRSRSKSG
TTGGFLKPKKPLLNVNEAVHASPASHTSCNNTGTVLESINNNPEHVDVAVARHLIRPNEN
SLIQQQGDLRILLYKWNHDPSSPSSQYPSQPOLSTSI  PSQPFSRKMSMFSASAII
ASSSHLNNNSEANGLPALLAGAPMPHEERAPPGFRFSFI  IQKRRKHNVDAIPNPF
TRNFIEFLTYGHFAGEDLSEEEEEEEEETEEEPDEALETESTQLVSRHGRPHKSTTV
SEQ ID NO: 128
YKR039W
>sp|P19145|GAP1__YEAST General amino-acid permease GAP1
OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=GAP1
PE=1 SV=2
MSMTSSEYKENNPDNKLKNGITIDSEFLQEPITI PSNSGSASIDTSGSKWQDFKDSF
KRVKPIEDPNLSEAEKVA ITAQTPPLKHLKRNHLQMQIAIGAIGTGLLVGSALTGGE
PASLLIGWGSTGTMI YAMVMALGELAVI FPISGGETYATRFIDESFGYANNFNYMLQWL
VVLPVEISNVEINFGDPKRYDGEFVALELAIVI INMGFKGYGEAEVF5F1KIVTVT
VVGPIILGI LINCQGGITRYGKYHWDPPAFAGDTPGAKFGVCVSVTVAASFGASE
LVGLAASESVPKSVPAQQGFWRILFYILSLMLGGLFYVNDKSLIGASSAAADAS
PVFAKTYHIGKGLPSVNVVIIAVLSVGSANAYACRSRMEALAEQREFLVPEFSTYD
KRGLPGVIAFSLFAAIAAAKEVEFVNNLALGSLSFSTWGCICIEHFRKLAAL
QGRGLEDFLKPLTGVGWSYGLFVMIIQMFIAQFYVAIVGFDPSAEGFFEAFLSFPLY
MVVYIGHKITYRNWKLFPALMEKIDTGRREVDLVLIQEIASEKAMATKPWYRINWF

Wc
SEQ ID NO: 130
YLR411W

>sp|Q06686|CTR3_YEAST Copper transport protein CTR3 OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=CTR3 PE=1 SV=1
MNMGGSSTAAKCATCKSLMWNWTIDTCFIARSWRNTDGKFAGSCICGFALVVAQW
LTRFSRQGFDEVLKRRKQIKHLASYSPEEEYVVKCGEEDAKSIDIIEEQQYFNEPSWKTTLIS
LQKSFIYSFYVWGPPLNEDDDLLKVLSCCTLITPVDLPTFDHMIRVTIFVLQWGL
SYIIMLFMMYNGYIIISCLIGAIVGRIFIFCYPGLSLGANGSAQGVTSYDKESDRKCC
L

SEQ ID NO: 131
YML038C

>sp|Q03697|YMD8_YEAST Putative nucleotide-sugar transporter YMD8 OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=YMD8 PE=1 SV=1
MNRTVFLAFVGWYFCSIALSIYNRWMDPKDLGIGYPVLVTTFHQAFLWLLSGYIYKL
RHKKPVKLRKNGNFSPFLFFLIPTAVASAGIDGLSNVSQFYVPFLYTIIIKRSSIAF
VLLFGCIFKLEFKHWWLALSVLIMFVGVMVFPSDSTSTKQNDLALVIIFGSFLVLASSC
LSSLRWWYQLMRLNPQNTNVAAAEDSGALFTENEDNVDEPNVNLANKMLNSFGE
SKPHPIHTHIQAPMGITLTLTSLVEKFPFGIIFSSISIFLRTDSNGVTETTVLISIVR
GIVLLILIPGFAVFLLTICEPSIFSLQETPFLTOSVGIVKELLTVIFGIIILSERLSGFYNW
LGMLIIMADVCCYYNYFRYQDLDLLKEYHSVSTQDNRELKGFQDFEQGLSGKIAPYSISVD
LTNQYEYELDIAQVNSRSSQQV

SEQ ID NO: 132
YMR166C

>sp|Q03829|YM39__YEAST Uncharacterized mitochondrial carrier YMR166C OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=YMR166C PE=1 SV=1
MNSWNLSISIPITHTHPDHPPTEDPQPNRRKDDKHLKKRGDSDELSPIWHCVSG
GIGKIGDSAMHSLDTVKRQGAPNVKYNMISAYRIRWLEEGVRGGLYGGYMAAMLG
SFPSSAIRFSGYETEKRTMEDWQINTDITIHLSAGFLGDIFSSVVFPSVEKLTRLQLOG
RFNNPPQFSQNSLYINSLAIVITEKEGFRSLFQFYKATLARDLPSALQFAQYFKQRL
APKIEQKQDGRDGELSPNIPENILGACGGLAGIITTMDVVKTRVQTPQFQPSQNSKSYSVT
HPHVTNGPAALSNSISLSSLTXYQSEVGLFSGVFQPRFVTSQVSISLLLYQMTLRGM
LSNAPFTD

SEQ ID NO: 133
YMR279C

>sp|Q03263|YM8M__YEAST Uncharacterized transporter YMR279C OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=YMR279C PE=1 SV=1
MFSIFKKTSVQTDSEIDEKIYTVKDDKVKVVTDEDEVTIVTSKSTQVTNDSPWQDP
TYSFSSFGKELFMFATCMALQLNNQAGQTHALCMNVLSFSEANNQAWLMASFLPAAG
SFILISGRLGIYGLKMLIVYIVIWIIISGLKYSNDAFFITSIRAFQGVGIALIP
PNIMLGLVNYVKGFFRKNIVISFICAGPTGGMFFLGFGLIVTEDPQWPVFPVFAYFGI
ATFLLSLLWYISIFNVPTRHGSLMSDWTGALSAILIILIFFNWFNNQAPIVGWDPKPIYIV
LIIISVIIFLVAFVFFYESYAVEYPPLLPRAMTKNRMIMILLAVFLGSGGIFTWFFYVSFQ
LNLRRHYSPVWTGTGYFVFVFIFVFAAFFAFAISIKLGPALLCFLSMADFAGSIMFVSLP
VEQSYWKLNFAMQIALCFQMDLSPASSIIILDGLPMQYQMGASLVLTVNYSASLCLG
MGTVHEQINKSGNDLLKKGRAYAVYLGVSSLGVVISVTYMLENLWNRHRKSEDRSLEA
SEQ ID NO: 134
YNL003C
>sp! P38 921 |PET8_YEAST Putative mitochondrial carrier protein PETS
OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=PET8
PE=1 SV=1
MNTFSLLSQAAAGTSTDLVPPFDITDITRLQAKGFFANGGYKGYRGLGSAVVASAP
GASLFFISYDYMVKVSRPFIYSLYSQGQEQLITTDMHLSIGCIALCVRPFAEVVKQ
RTQVHSTN5SWQTLQSLRNDNKEGLRKNLRYGWTSTTIMREIPFTCIQPFLYEYLKKTWA
KANGQSQVEPWFKAGCISGIAGGIAATTTPLDLFKTRLMLNKTASLGSVI IRIYREEGP
AVFFSGVGRPRMWAAGGAILGLMYETVKSLLSKSFPTAGEMRA

SEQ ID NO: 135
YNL2 68W
>sp|P32487 |LYP1__YEAST Lysine-specific permease OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=LYP1
PE=1 SV=2
MGRFNSITSNKWDKEQNNIGQMELPDQIEHEMEAIDPSNKTPFYSISDEKYNTIK
KHGSQLOGGAADVSNITNSLRLQVSHETDINEDEEEAHEDKVHRALKQRHIQMIAL
GGTIGTLGVIQTSPLSNAPVGSLIAYMFGTVYFQSLGEMATPFPITVSTFVSK
RFLSPAFGVSNGYMYWFWNIAITYAVEVSIGQVIEYWTDKVPLAAMIAIFWV ITLMNFF
PVKVGEGEFWASVKSVAICMGYIYALIVCQGSHQQPFGFRYWBNPGWGPYISSDK
SEERFLGWSLLNAAATFTQGTELQITGATEAAANPRKTPVRAINVKVFVRLYIFILFF
IGLLVYVYNSRDSLASSAVIASSFPVISQNAQTYALDPIDFINAVVLITVSAANSNVYGS
RVLISLARTNGAFQKGYTRQGVYPLGTVCTAAAGLALFLVWVNANANTFWLINISTL
AGLCWFLPSLAHHRFQALKHRGRSDLPLFKAKLMYPGAYAFFFVTIVFIQFGQAF
CPFKVSEFTSYYSLILLAVFVFGQCIYKCRFIWKLEDIDSDREIEAIWEDDEPK
NLWKEFMWAAVA

SEQ ID NO: 136
YNR055C
>sp|P53289 |HOLL1_YEAST Protein HOLL1 OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=HOLL1
PE=1 SV=1
MDKTYNRDHPDFYIPFTNYSSQNLNENGI IYESKLKKTSSVVLIPQPSYPNDPLNWSS
WKRKAEHFGMALAFIATAFATSADAGAQSISNE TYGIYDSMNTGAYVLFLGIGWSTFLFL
APFANLYGRKITY VCTTTLGFLGALWFALARSDSTDSTWQLFGVISESCEAQVQLSQSLD
IFFHQHQLGSLTVYICMTSITFTLGPLIAGYISAFTNFRWVGWAVAVI ISGGLITIIIFGC
EEYTFDRQGYMTPLTSQCGYEDGTITLQNSDNTAVRRRLALDKLSTPGAMEKGVLDS
ETAEEFEVNNNEEETP RETRELDSGKEHLKPYKPVRVAILTKAINLKGYGFKYFKLYKIN
LRMLEFPPWVSAMWFQDVFVLTFLYITQESAYEYPWPNSYDFQAVAINMVFPLIGAVIG
CICAGIVSDFYVFLWNRHNRGILEAEFRLYFSIATAI IGPAGLMLMGTARQWFWQA Y
VGLGFGVFAQWGCSQDAMAYLMDCYPDVMLEGMVCTAI INNTSCI FTFTCSDWLASSGT
ENYIAŁAVINFGITAFALMPYYKIRLRWTRLKWYLQSVNLQVLDGV

SEQ ID NO: 137
YOL158C
>sp|Q08299 |ENB1_YEAST Siderophore iron transporter ENB1 OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=ENB1
PE=1 SV=1
MLETDHRSNLDKLKSTCVYSEKTDSNVEKSTTSGLRRIDAVNVKSLSDYSSFTAFVTF
SLKTALLVALFLQGYCTGLGGQISQS IQTYAANSFGKHSQVGSINTVKS IVASVAVPYA RISDRFCRIECWFIFALVVLYTIGIEIIAATPTFSGLFAGIQVQFGYSGRFLALTALTGDL SGLRDRTFAMNIFLPIYNTWNGSIIVSSAVGNYPKRWGYYGIFCIIVIPSTILILVL PVYYAQYISWRSKLPNLLKKEQGTLQLWKFADDINLIGVLFALLVLVLLPLTTA GGTASWKREWGIAMI VVGGCLQFI FLIELWKLFAKNNPI PRYVLQDQI YVALLMEFVWR LGLQIELEYLVQSTNIVVGMLHFYHPKVFVAVAG SLLGVGMGLLYKYRRVYGDSIGLAEIAGVAGMIFFMNTLHVASHTHNEMATVG LIMSVYIQ IDGAVAGSI AGIWITQRKAKELIQRGLGSLGMAI YKSPLYLKKYPGESEVRV VMIESYKIQRLLIIVSISFAFNAVLCCFLLRGFTVNNKQSLSAEEREKLEKIKQQSIL RRVIGY

SEQ ID NO: 138
YOR100C
>sp|Q12289 |CRC1_YEAST Mitochondrial carnitine carrier
OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=CRC1 PE=1 SV=1
MSDDTSLSESSLKKEESGSLTKSRPPIKSNPVRENIKS FVAGGVGVCAVFTGHPFDLI K VRCQONQANSTVHAINTIKKEAKTVQKTLFTNSVKFYKGVIPPLGLVTPIFAVSF WGY DVGKVLTFNQKGSSNEFMTGQAAGFISAIPPTLTVTAPERTKVVLQTSSSGFIQ A KTI VKEGGIASLFKSRALDGRPGLSALYFASYEISKYNLYNRSQRPQDAGKDEP VNIL NVCLAGGIAAGSMWLAVFPIDITIKTLQASSTRQONLSATKEIYLRGEGKFPG LP LLRSSFPANAATPLGVMETFSLFKKYI

SEQ ID NO: 139
YOR153W
>sp|P33302 |PDR5_YEAST Pleiotropic ABC efflux transporter of multiple drugs
OS=Saccharomyces cerevisiae (strain ATCC 204508 / 5288c) GN=PDR5 PE=1 SV=1
MPEAKLNNNVNDVTSYSSASSSTENAAOALNHYNGDFDETEARIQKLARTLTAQSMQNSTQ SAPNKSDAQSIFVQSGEVGNPIFSDDEAPFYDFKLPDFNSENFSAAWVKMMAHFSAADFP FYKPYSGACAIWNLSSASQASADVAQSTVNIYPYKLLIKSLRKFQRSKETNFQILKPMD GCLNFGEVLLVRLPGSGCTTLLKISSTTHFGDLGADTKIYSYSGDDIKKHFREGEV YNAEDAVHPLHTFLHVTFVLARLTNPQRIKGVDRESYAHNLAEVAMLYGLSHRTNK VGNDIVRGVSGGKRVRSSIAEVSICGSKFCWDNATRGDSSATEFIRALKTQADISNT SATVAIYQCSQAYDLNFKVCLLDDGYIQYIYPADAKKKFEDMGYCPQSRPQTADEFLTS VTSPERTINLKKIGHPQITPKEMDNYYWKSNERYMKEVQDQLNDEDEAESREAIK EAAIHAKQSRRRPSPPSTYVVMQVYKULLNRWRLNNIGFTLFMLGNCMALILGSM FKFMKMKDSTSTYFYGFRSMAMFSTNAFSSSLLEIENSFLYEARPIKEHRTSLYHP DSA FAHSVLEISPKLIIIAVCFNI IFYIVLFDRNNGVGVFFYLLINIVAVFMSHLRFVC GLT KTLSEAMVPSMLLSLMSMTYGAIPKKIKILRWSKWIWINPLAYLFSLLLIENFHGIK P CAEYVPPFRPACYANISSTESVCTVGVAVPQDYVLGDDIFRGTQYYHKDRWRFGIGMA YVVEFFVYLFILCNEYNAGKQREILVFPRS I VJKRMRKGRVLEKRANDNPVEN GERSDLSD SRDKMLQESSEEEESDTYEIGLSKSEAI FHWNRNCYEVQIKAEIRRI LNNVGDVWKPGLT TALMGASAGKTTLDCALERTMVGITDILVNGIPRDKSFRSIFIGCQODHLKLTAT VRESLFLRSFIEQIEEKNRYVEYVIMEKLEYMAADVAVGAGVGLNEQFRLTI GVELTAKPKLLVLDEPSTSGLDSQATWICQIOMKMLHANHQAICLCTI HPQSAIGGLEDFR LLFMQORGGTXYFGDLDGEGCTMIDYFESHAGHKACPADAPAEWLMEVGVAGPAHANQD YEVWRRNISREYAVQSSDNLWREPLPKKGGTSTAADKHEFQSOI II YQTDLRSFLQFYQW RSPDYLWKSFIILTVETGSLQQLONQLMAMVMFTVIFNPLQYLPSFV QQRDLYARERPSRTFWSIFISI YQP1FVEFWN. LAGT YF I YYYPIGYSNASAAAGQL HERGALFVLSFCAYYYVGSMLLVLISFNQVAESANLASSLFTMSLSFCGV NTPSAMP RFWIFMYKSVPLTYFIQALLAVGAVNVDVKACDELEFTTPSSMTGQYMPE YQLARK

WO 2016/023844
PCT/EP2015/068314
SEQ ID NO: 140
YOR271C
>sp|Q12029|FSF1_YEAST Probable mitochondrial transport protein FSF1
OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN-FSF1
PE=1 SV=1
MASSVPGIDLPESRYDLSSTYGRIRHCAEISDPTMLLTTEKDLAHAREI ISAYRHGELK
ETTEFPRXKQAKLDSTVHPTGKVTPLPFMRSSNVNLNVTVTGMILPGLTGATVFWQW
ANQSLNVANSANANKSHPMTSQLLTNYAAAVTASCGVALGLNNLVRLKNISPSKLI
LGRLVFAVAVAQIINVNFLMRGNEIRKGISVFDSNGDEVGKSXAAEMAVGETALS
VRVATPTMVPIPLILVRQGVLKGLSVQTLANGLISVTMFSLPFAIFQPRQAIHL
NKLEPELHGKKDGDKGPIKEVYFNRGI

SEQ ID NO: 141
YOR273C
>sp|Q12256|ITP04_YEAST Polyamine transporter 4
OS=Saccharomyces cerevisiae (strain ATCC 204508 / 5282c) GN-ITP04
PE=1 SV=1
MPSSLTKTESNSPRTNIQQVPKALNVNSGNLDSSTSSSTSITESDEKREPNDASN
MTGEGPDPRDLDGWDPGDDPNHWNSSLKWWYMTTMTASFLCLVTMVGSSLYVSSVFELV
ERYHVSQITALFLGYLLSTVIALGPELSEVFGRKPVYLFLIPSMLFTMVGLSNGHM
RIILPLRFSQVPASPLSVGSSTILDI FDVDQSVAMTFVLSFPGVLPSEMGAF
EAHKWRSWQLIAGGLLPFAIPALMPETHKG ILRKRKKNIALKFKSREAOKEFKLT
TVITITLRLKMLVYPEIVPFVSYYVAFAILFGFEAYAYVRGIVHMSMGISLPIF
GIGVGLWIGAFFYLYDRLKFPPAGTQPLTEKERTSKRTYPARGAETGELLPEPV
FEKFLACKFGSVALPILIGF% 4QAWTARSDVHMAPAAGVPGFGLILI FSVLMYFSTC
YPPLTVASCLAANLRLYVMMSSVFPLFTIQMYTNIWASTFLALCVVMI PIPWVF
EKGSKLRHKSGQFAAAMIKAEATEGGIDDVAVDGLNTRMMTTLRMTFOPSTREKGER
LSLRRHTQTQVPASFDREDGQAQNRPNENPLSIALNDGEDGSTEMATDASRMV

SEQ ID NO: 142
YOR307C
>sp|P22215|SLY41_YEAST Uncharacterized transporter SLY41
OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN-SLY41
PE=1 SV=2
MIQ7QSTA1KRRNSVHKNLFDPDSLQIEPEPRPGGFQHQKKEYSKETFNSQVFYDITSKL
KRQLFQ9PLMNQFLEPDLRTI ICSWNYWISSNSNLSKAILRTNFIPIALTELQFLV
SAILCVFGASIVNLFRLFRKLHKTFSKALNSFPDGIPEYLDGNFRSILHKLFLVSLKLV
LMTFWPMGGFQ9FLIGHTSKHAVIMFSVPVLHVSVKALSPI ITCVYKFFEHRYNMYAT
LLLL4FVMTTWSTHGSKRSDNKSIGSSLILLFAFISMI IFVAQNI FAKNIILTIRK
GLPSSSTDDVTSTEQGFSLDKTRSFQPLVDKILFYCSCIIFSLTLPLLFTGELMHHG
SVINDLITELVALVAIHIAHHFQAMLAFQQLGLSSINYSVANIMKRVISVALFWE
TLKNNFQVFQVGILTIAGLYGDKWLSKDDGRQA

SEQ ID NO: 143
YOR332W
>sp|P22203|VATE_YEAST V-type proton ATPase subunit E
OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN-VMA4
PE=1 SV=4
MSSAITALTPQVNDELNKMQAFAKIKAEAEKAIIQKDAQYEIEKTNIVRNETNNIDG
NFKSLKKAMLSSQQTITKSITMNKRLKVLCSAREQSLDGIFETTEKKEKLGIANNRDEYKPI
LQSLIVEALLKLLEPKAIVKALERDVDLIESMKDDIMREYEGQARPELIEEIVSNLYN
KDLVSGGVVVNASDKIEINNTLEERLKLLSEEALPAIRLELYGPSKTRKFFD

SEQ ID NO: 144
YOR348C
>sp|P15380|PUT4_YEAST Proline-specific permease OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=PUT4 PE=1 SV=2
MVNILFPHKNRRHSAGVVTADYSGDGGDGTKEEVDVQTESPSGSRNNHRSNDNEK DDAIRMKEISKNASASSIREDLMVDEKLSPVDGDEPHLKLQGQLRQVQLIAL GGAIGTGLVGTSSSTLHTCGGAPFLGFLISYIIIASIAY PIMCALGEMVCFPLPGDSADSAGST ANLTRYVPDSDLATGWNFYCVILVAAECTAASGVEYWTAVPKGWTIFCVCV
ILNFSAVKEGSEWFASIKILCIVGLI ILSFILFWGPPNHDLGFRYWQHPGAPAH LTGGSGLNPTDI YTGI IKGAFAPILGPFLVCMTSAECADQQRNII AKASRRFWRLI FFYV LGTIALSIVIVYNDTFLNVALAQKGPKAGSSPFVIGIQNAGIKFLPHI INGCIILTSAWSAA NAANMFASRSLTLMAQTQAPKLGRINKGVPYAVAVSFCLCSLAYLNVSSSTADVFNWNSNFSTISISFLGWMCGCIAYLRFRKAIFYNGLYDRLPFKTWGQPYTFWFLSILIGITI ITNGAYAPIFQKRYWVARFADPIAAIYTPFILFLVWLFHKLHYTRWQRWQPVLSEIDVTGGLVE IEEKSREIEERLPLPTGFKDKFLDALL

SEQ ID NO: 145
YPLO36W
>sp|P19657|PMA2_YEAST Plasma membrane ATPase 2 OS=Saccharomyces cerevisiae (strain ATCC 204508 / S288c) GN=PMA2 PE=1 SV=3
MSSTSEAKQKKEKPSKEYLHASDGDDPANNAASSSSTSTSATSASSAAVPRKAASAAD ADDDDSDEDIQLDMELQSONYEGDESFEEVTDGGHAVQVRVPDKLSTDPAYGLTSDE VARRRKKYGLQMAEENESLVKFLFVFGFIPQFVMEAAAILAAGLSWDDVVGICALL LNASVGFQIEFQGQSIVDELKKTLYLANTATVIRDQGQLEIPANEVPVEGLQLESGT IAP ADGRVITEDCFQIDOSAIETGESSLAAEKHYGEDFSSTTVGTKGEAFMVVTATDNTFVGR AAALVQASQEGVHTEVLNIGILLVLVIATLLWVTACFTRVTGIVSILRYLGITI IGVPVLFAPVVTTMGGAVAYAKKQAIQVKLASAIESLAGVEILCSDKTGTLTNKSLHL EPYEVQGSPDLMLTACLAASRKKGLDAI DAKFLKSLLIEYPKAKDALTLYKVLLEHFPFDPVSKKVTAVVESPEGERIVCVKAPLIFVLKTEEDHPIEPDVENYNKVAELASGRFR ALGVARKRGEHWEILGVMPCMDPFRDDTAQIQINEARNLGLRKLMTGDAVIKETCRQ LGFLTNYNAERLCLGGGDMPSELEDVPENADGFAEVPQHKVRVVELIQRNGYLVAM TDGVNDPLASKDQGTAADSAARADSIVLVAPGGLSAI IDALKTQRQIFHRMYSSV YYRIALSLHLIEFLGLMLIAINLNSLDINLIVFIAI FADVATLTIAYDNAPYAEPKVWN LPRWGMSISLILGVLIAIWGTITLMIFPNGIQ IONFGAMNGVMFLQISLTENLWIFVRAAGGFWSSISWPQLAGAVFAVDIAMTFLFGWSENWTIDSVSVRVWVWISGIFCVLGFFYYIMSTQAFDRLMNGKSLKEKSTRSVEDMAAMQVRSTQHEKSS

SEQ ID NO: 146
YDL198C
MPHTDKQSG LARLLGSASA GIMEIAVFHP VDTISKRMLS NHTKITSQGE LNRFIREDHF SEPLGKRLFT LFPGGLYAS YKVLQRVYKY GQQPFANFEL NKHYKDKFDN LFGEKGTKAM RSAASGLIG IBVILLFDL VLKIKRQTNP ESFKGRGFIK ILRDEGLFLN YRGGWTAAM

SEQ ID NO: 147
YPLO54C
MSYEGSRRSS SSEPSTRPTL KEEPNGKIAW EESVKSREN NENDSTLLRR KLGETRKAIE TGGSSRNKL ALTPLKKVVD ERKDSVQPYQ PSMGFTYSLP NLKTLNSFSDE AEQARIMQDY LSRGVNQGNS NNYVPDLYRQ LNPTMSSRNR RPWLSNLQFL PHVLDRGLAA KMIRQNMDAR SRASSRGGST DISRGGSTS VDKWKRLLRG AAPGKGLGDII EAQTQRDNTV GADVXKPTKLE

110
SEQ ID NO: 148
Oryza sativa sequence encoding EUGT11

MAQHTSESAA VAKGSSTLTP VRTDAESRST RWPTDDEDAAE PLVDEIRAML TSMDSGDISV
SAYDITAQVG LVPRLDGEGP QFPAAVRMIR NNQLPDSGWI DAAALPSAYDR LINTLACVVT
LTRWNEPEMP RGRGLSFLGR NMMKLATEDE ESMPIFELA FPSSILAEKS LGVHDFPYDH
QALQGIYSSE EIKMKRIPKE VMHTVPTSTL HSLHEMGPGLD WAAMLKQLSS DGSFLFSPAA
TAYALMNTGD DRFCYSYIDRT VKFKFNGVVPN VYVDFLHFI WAVDLRLEGA ISRYFQKEIE
QCMRYWNNHR TEDGYICWYN DDVKEVDATA MAFRLRLRHG YSVPVDFKMN FEKGDGEFFA
VQGSNQAVTG MYNLNRASQI SFQFEDVHLR AGAFSEYFLR KEAEGALRD WIISKDLPG
EVVYTLDFFW YGLNLFVEAR DLYQGYGGGD DVWIGLYTLM MLPVNENDVL ELARNINGHC
QALQHEWQEG LRKWTYENRL KDFGQVQAEA LRAFLAEAS YVEPCRAER AAWARRAILA
NAVSTHILNS PSFHRLEHSS LCRPSEETD GSWNFNSSGS DAVLKVACL RLTDSEFRQ
PQHGGPDDEI LRRGSAWAW ESQECQCGAS DSCNGGGSV EOEGRMRHVHD QKQTIYRMH
1EISAGRAAG EAASEDGEDR IQQLTGSCI SLKQKMLQSV DPEKNEEMMS HVDEDELKRI
REFVQYLLRL GEKKTIGSSET QRTFSLIVKS CYYYAHPGHPV VFDDHISISVR FPVSAK

SEQ ID NO: 149
Synechococcus sp. GPPS

MAQHTSESAA VAKGSSTLTP VRTDAESRST RWPTDDEDAAE PLVDEIRAML TSMDSGDISV
SAYDITAQVG LVPRLDGEGP QFPAAVRMIR NNQLPDSGWI DAAALPSAYDR LINTLACVVT
LTRWNEPEMP RGRGLSFLGR NMMKLATEDE ESMPIFELA FPSSILAEKS LGVHDFPYDH
QALQGIYSSE EIKMKRIPKE VMHTVPTSTL HSLHEMGPGLD WAAMLKQLSS DGSFLFSPAA
TAYALMNTGD DRFCYSYIDRT VKFKFNGVVPN VYVDFLHFI WAVDLRLEGA ISRYFQKEIE
QCMRYWNNHR TEDGYICWYN DDVKEVDATA MAFRLRLRHG YSVPVDFKMN FEKGDGEFFA
VQGSNQAVTG MYNLNRASQI SFQFEDVHLR AGAFSEYFLR KEAEGALRD WIISKDLPG
EVVYTLDFFW YGLNLFVEAR DLYQGYGGGD DVWIGLYTLM MLPVNENDVL ELARNINGHC
QALQHEWQEG LRKWTYENRL KDFGQVQAEA LRAFLAEAS YVEPCRAER AAWARRAILA
NAVSTHILNS PSFHRLEHSS LCRPSEETD GSWNFNSSGS DAVLKVACL RLTDSEFRQ
PQHGGPDDEI LRRGSAWAW ESQECQCGAS DSCNGGGSV EOEGRMRHVHD QKQTIYRMH
1EISAGRAAG EAASEDGEDR IQQLTGSCI SLKQKMLQSV DPEKNEEMMS HVDEDELKRI
REFVQYLLRL GEKKTIGSSET QRTFSLIVKS CYYYAHPGHPV VFDDHISISVR FPVSAK

SEQ ID NO: 150
Zea mays truncated CDPS

MAQHTSESAA VAKGSSTLTP VRTDAESRST RWPTDDEDAAE PLVDEIRAML TSMDSGDISV
SAYDITAQVG LVPRLDGEGP QFPAAVRMIR NNQLPDSGWI DAAALPSAYDR LINTLACVVT
LTRWNEPEMP RGRGLSFLGR NMMKLATEDE ESMPIFELA FPSSILAEKS LGVHDFPYDH
QALQGIYSSE EIKMKRIPKE VMHTVPTSTL HSLHEMGPGLD WAAMLKQLSS DGSFLFSPAA
TAYALMNTGD DRFCYSYIDRT VKFKFNGVVPN VYVDFLHFI WAVDLRLEGA ISRYFQKEIE
QCMRYWNNHR TEDGYICWYN DDVKEVDATA MAFRLRLRHG YSVPVDFKMN FEKGDGEFFA
VQGSNQAVTG MYNLNRASQI SFQFEDVHLR AGAFSEYFLR KEAEGALRD WIISKDLPG
EVVYTLDFFW YGLNLFVEAR DLYQGYGGGD DVWIGLYTLM MLPVNENDVL ELARNINGHC
QALQHEWQEG LRKWTYENRL KDFGQVQAEA LRAFLAEAS YVEPCRAER AAWARRAILA
NAVSTHILNS PSFHRLEHSS LCRPSEETD GSWNFNSSGS DAVLKVACL RLTDSEFRQ
PQHGGPDDEI LRRGSAWAW ESQECQCGAS DSCNGGGSV EOEGRMRHVHD QKQTIYRMH
1EISAGRAAG EAASEDGEDR IQQLTGSCI SLKQKMLQSV DPEKNEEMMS HVDEDELKRI
REFVQYLLRL GEKKTIGSSET QRTFSLIVKS CYYYAHPGHPV VFDDHISISVR FPVSAK

SEQ ID NO: 151
Arabidopsis thaliana KS (similar to GenBank AEE36246.1)

MAQHTSESAA VAKGSSTLTP VRTDAESRST RWPTDDEDAAE PLVDEIRAML TSMDSGDISV
SAYDITAQVG LVPRLDGEGP QFPAAVRMIR NNQLPDSGWI DAAALPSAYDR LINTLACVVT
LTRWNEPEMP RGRGLSFLGR NMMKLATEDE ESMPIFELA FPSSILAEKS LGVHDFPYDH
QALQGIYSSE EIKMKRIPKE VMHTVPTSTL HSLHEMGPGLD WAAMLKQLSS DGSFLFSPAA
TAYALMNTGD DRFCYSYIDRT VKFKFNGVVPN VYVDFLHFI WAVDLRLEGA ISRYFQKEIE
QCMRYWNNHR TEDGYICWYN DDVKEVDATA MAFRLRLRHG YSVPVDFKMN FEKGDGEFFA
VQGSNQAVTG MYNLNRASQI SFQFEDVHLR AGAFSEYFLR KEAEGALRD WIISKDLPG
EVVYTLDFFW YGLNLFVEAR DLYQGYGGGD DVWIGLYTLM MLPVNENDVL ELARNINGHC
QALQHEWQEG LRKWTYENRL KDFGQVQAEA LRAFLAEAS YVEPCRAER AAWARRAILA
NAVSTHILNS PSFHRLEHSS LCRPSEETD GSWNFNSSGS DAVLKVACL RLTDSEFRQ
PQHGGPDDEI LRRGSAWAW ESQECQCGAS DSCNGGGSV EOEGRMRHVHD QKQTIYRMH
1EISAGRAAG EAASEDGEDR IQQLTGSCI SLKQKMLQSV DPEKNEEMMS HVDEDELKRI
REFVQYLLRL GEKKTIGSSET QRTFSLIVKS CYYYAHPGHPV VFDDHISISVR FPVSAK
MLELTKAAQS YPHESALKKQ CCWTQYLEM ELSSWVKSVE RDKYLKEVE DALKAFSYAS
LERSDHRKRI LNSGAVENTR VTKTYSVRLHN ICTSDILKLA VDDVNFNCQSI HREEMERLR
WIVENLRQEL KFARQKLAYC YSFGAATFIS PELSARISW AKGGVLTIVGD DDFFDVGGSK
ELELNLHV EKWDLNGVPE YSSEHEVIIF SVLRDITLLET G DakotaHYQR NVTTHIKVIN
LIDLKSLMRE AEWSSDSTKP SLEDYMENAY ISFALGPIVL PYTLYLPGL PEKTVDSHQY
NQLYKVSTM GRLLNDIQGF KRESAEGKLN AVSHMMLKHER DNRSKEVIIE SMKGLAERKR
EELEHKLVLEE KGSVPVEPRECK EAFLKMKSVL NLFRYKDDGF TSNDLMLSLVK SVIYEPVSLQ
KESET

SEQ ID NO: 152
s. rebaudiana KOI
MDAVTGGLTV PATAITIGGT AVALAVALIF WYLKSYTSAR RQSNHLPRV PEPFGVPLLG
LLLQKLKEKP YMIFTRWAAT YGPIYISIKTG ATSMVVSSEAI EIAKEALVTR FQSLSTRNLS
KALKVTALDK TMVAMSRYDD YHKTVKWHIL TAULGNPNAQK KHRHDEIIM DNSTQHLHEF
VKNPQEQQEV DLRKIQFQSEL KVDSLYVED LTMRNMDR EIYNLVDY PMN
GAIIDVDRDF FPYKLVWNPK FKEFIQ sack MIKEKHKIAS GEKSPHIDY
LLESQATLTD QOQLMLSLWEI IIISSDTIMV TTEWAMEYELA KNPKLQDRLY RDIKCVCGSE
KITEEHLQSL PYITAIHFT HPLRSHPVPII PIRHLVHDTEL LGYYHPAGT ELAVNIIYGCN
MDKNNVENPE EWNPEPMFKM NETIDFQKTM AFGGJKRVCV GSYQALLTAS IGIGRMVQEF
EWKLKDQTAQ EVNITGLTTQ MLRPRAIIK PRI

SEQ ID NO: 153
A. thaliana ATR2
MSSSSSSSTS MIDLMAAIK GEPIVVSIPDA NA5AYEVEAA ELSSLMIENR QFAMIVTTSI
AVLIGCVLML WVBRSRSGNRE KRVEPLKHPY KIPREEEDD GRKVTIFQGG TDQGTAEGFA
KALGEEAKAR YEKTRFKIVD LYYAADDDE YEELKLLKEDV AFPLVAYGQGEPTDNARQF
YKVTGEGRN GWEKLMLKYG VDGLGNNRQY HFNKVAKVVD DILVEQGAGQ LGVQVLGFDG
QCIIEDDFTAW REALMPELTD ILREEGDTR AAPTYAAVLLE YRSVIAHSED AKPNIDTILAN
GNYTVFDAQ HPYKANVVK RELHTPESDR SCIHELFDIA GSGLTMKLGD HVGLCDNLS
ETVEADLRII DMSFTVTFSL HAEKEDGTPY SSSLPPPFPP CNLRTALTRY ACLSSPIMKKS
ALVALLAHAS DFTEAEELKLK HAPSFKEQY SKWVQDGQR LSQ MMATTPS AKPPLGDFVA
GVAPRQPRPF YSISSPKIA ETHIRHTCAL VYEKMPFTIGI HKGVCTSWMK NAVPEYKESK
LFPLGPIIPFR QSIFKLPSDS VIKPIIMGGP TGLAPFRGFG QERLADELGA VELGSPVLIFF
GCRNRMDKFD YEELEQRFVEQG GALELSLVA FSREGPTKEY YQKHHMKDKAS DIWMIQSGA
YLYVCGDAKG MARDVHRSLH TIACQEQGSD STKAEGFVKN LQTSRGLRDV W

SEQ ID NO: 154
Stevia rebaudiana CAHel
MEASYLWISI LLLLLSYPFL TQLRRKSNAL PPTFVPSSIPI IGHLYLLKKP LYRTLAKTQA
KYGPILQLQG YRVVLVIII PSSAAECFTN NDVIFFANRPF TLFKGVGVT SLGSLSYGQ
WRNRLRVAS FIHIVHNLRE FDFIRTVMLN LILIRLKHSS SPVTLITPFY ALTINLMRM
ISGKRYFDSG DRELEEGKRX FREILDETL LAGASNVGYD LPILWNLGKV SLEKIVLIALQ
KKRDDDFQGL IEQVTRKSRA KVGGKRKMTI ELILLSQIESE PEYTYDAMIR SFVLGLLAAG
SDTSMTEW AMSSILVNHHP LLRKAQAEID VVGNRRNLID EDIPEKGY GCINLITLR
YAPGLPLLPH ESSADCIVIS YNIPRGMFLQ VNQWAIHHDP KVWDDPMTPK PERFQLEGRT
RDGKFKLMFG SGRGCGPPEG LAIRLLGTLG GSVIQCDFWE RGVDMEDVMT EGLGVTLPKA
VPLVAKCFPR SEMTNLLSLE

SEQ ID NO: 155
Stevia rebaudiana CPR8
MQSNVSKISP LDVLTALFGS KVLDSNASE GESAMLPTI AMIMENRELL MILTTSVAVL
IGCVDVTLVR RSSRKLKSALE PPVIVPKRPQ QBEVEVDGGK KVTYFGQQT GTAEGFAKAL
VEEAKARYEK AVFKVIDLDD YAADDDEYF ELKKEHLAFF FLATYGDGE TDNAARYFYKW
Stevia rebaudiana

SEQ ID NO: 156
S. rebaudiana UGT85C2
(MGenBank Accession No. LC069240.1)

SEQ ID NO: 157
S. rebaudiana UGT74G1

SEQ ID NO: 158
S. rebaudiana UGT76G1

SEQ ID NO: 159
S. rebaudiana UGI91D2-e-b
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.
WHAT IS CLAIMED IS:

1. A recombinant host capable of synthesizing a steviol glycoside, comprising a gene encoding a transporter polypeptide and/or a gene encoding a transcription factor polypeptide that regulates expression of at least one transporter gene;

   wherein expression of the gene encoding the transporter polypeptide and/or the gene encoding the transcription factor polypeptide that regulates expression of at least one transporter gene is modified and the recombinant host transports at least a portion of the synthesized steviol glycoside from the host into a culture medium.

2. The recombinant host of claim 1, wherein the gene encoding the transporter polypeptide is an endogenous gene.

3. The recombinant host of any one of claims 1 or 2, wherein the transporter polypeptide comprises an ATP-binding cassette (ABC) transporter, a major facilitator superfamily (MFS) transporter, an amino acid/auxin permease (AAAP) family transporter, an ATPase transporter, a sulfate permease (SulP) family transporter, a lysosomal cystine transporter (LCT) family transporter, a Ca2+:cation antiporter (CaCA) family transporter, an amino acid-polyamine-organocation (APC) superfamily transporter, a multidrug/oligosaccharidyl-lipid/polysaccharide (MOP) transporter, a ZRT/IRT-like protein (ZIP) metal transporter family transporter, a mitochondrial protein translocase (MPT) family transporter, a voltage-gated ion channel (VIC) family transporter, a monovalent cation/proton antiporter-2 (CPA2) family transporter, a ThrE family of putative transmembrane amino acid efflux transporter, an oligopeptide transporter (OPT) family transporter, a K+ transporter (Trk) family transporter, a bile acid:Na symporter (BASS) family transporter, a drug/metabolite transporter (DMT) superfamily transporter, a mitochondrial carrier (MC) family transporter, an auxin efflux carrier (AEC) family transporter, an ammonia channel transporter (Ami) family transporter, a metal ion (Mn2+-iron) transporter (Nramp) family transporter, a transient receptor potential Ca2+ channel (TRP-CC) family transporter, an arsenical resistance-3 (ACR3) family transporter, a nucleobase.cation symporter-1 (NCS1) family transporter, an inorganic phosphate transporter (PIT) family transporter, an arsenite-antimonite (ArsAB) efflux family transporter, an MSP family of transporter, a glycerol uptake (GUP) family transporter, a metal ion transport
(MIT) family transporter, a copper transport (Ctr) family transporter, or a cation diffusion facilitator (CDF) family transporter.

4. The recombinant host of any one of claims 1-3, wherein modified expression comprises:
   (a) overexpressing the gene encoding the transporter polypeptide and/or the gene encoding the transcription factor polypeptide; or
   (b) deleting the gene encoding the transporter polypeptide and/or the gene encoding the transcription factor polypeptide.

5. The recombinant host of any one of claims 1-4, wherein the gene encoding the transporter polypeptide and/or the gene encoding the transcription factor polypeptide has an activity that is increased.

6. The recombinant host of any one of claims 1-5, wherein one or more of the genes encoding the transporter polypeptide and/or one or more of the gene encoding the transcription factor polypeptide is overexpressed.

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YDR536W set forth in SEQ ID NO:30, YEL006W set forth in SEQ ID NO:101,
YEL027W set forth in SEQ ID NO:102, YEL031W set forth in SEQ ID NO:31,
YEL065W set forth in SEQ ID NO:103, YER019C-A set forth in SEQ ID NO:104,
YER053C set forth in SEQ ID NO:105, YER19C set forth in SEQ ID NO:106,
YER166W set forth in SEQ ID NO:32, YFL011W set forth in SEQ ID NO:33,
YFL028C set forth in SEQ ID NO:107, YFR045W set forth in SEQ ID NO:108,
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YGL084C set forth in SEQ ID NO:109, YGL104C set forth in SEQ ID NO:110,
YGL14W set forth in SEQ ID NO:111, YGL167C set forth in SEQ ID NO:112,
YGL255W set forth in SEQ ID NO:36, YGR125W set forth in SEQ ID NO:37,
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YGR224W set forth in SEQ ID NO:40, YGR257C set forth in SEQ ID NO:113,
YGR281W set forth in SEQ ID NO:41, YHL016C set forth in SEQ ID NO:42,
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YPR003C set forth in SEQ ID NO:81, YPR011C set forth in SEQ ID NO:82,
YPR058W set forth in SEQ ID NO:83, YPR128C set forth in SEQ ID NO:84, or
YPR201W set forth in SEQ ID NO:85.

8. The recombinant host of any one of claims 1-7, wherein YBR043C set forth in SEQ
ID NO:88, YDL100C set forth in SEQ ID NO:95, YDL054C set forth in SEQ ID
NO:94, YDL128W set forth in SEQ ID NO:22, YDL198C set forth in SEQ ID NO:146,
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set forth in SEQ ID NO:44, YJR106W set forth in SEQ ID NO:48, YKL120W set forth
in SEQ ID NO:126, YKL146W set forth in SEQ ID NO:127, YKR039W set forth in
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ID NO:132, YOL122C set forth in SEQ ID NO:68, YOR079C set forth in SEQ ID
NO:69, YPL270W set forth in SEQ ID NO:79, and/or YPR011C set forth in SEQ ID
NO:82 are overexpressed.

9. The recombinant host of any one of claims 1-8, further comprising:

(a) one or more genes encoding a sucrose transporter and a sucrose
synthase;
(b) a gene encoding a geranylgeranyl diphosphate synthase (GGPPS) polypeptide;
(c) a gene encoding an ent-copalyl diphosphate synthase (CDPS) polypeptide;
(d) a gene encoding a kaurene synthase (KS) polypeptide;
(e) a gene encoding a kaurene oxidase (KO) polypeptide;
(f) a gene encoding a steviol synthase (KAH) polypeptide;
(g) a gene encoding a cytochrome P450 reductase (CPR) polypeptide;
(h) a gene encoding a UGT85C2 polypeptide;
(i) a gene encoding a UGT76G1 polypeptide;
(j) a gene encoding a UGT74G1 polypeptide;
(k) a gene encoding a UGT91D2 functional homolog; and/or
(l) a gene encoding a EUGT1 polypeptide;

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

wherein the host is capable of producing one or more of RebA, RebB, RebD and/or RebM.

10. The recombinant host of claim 9, wherein at least one of the genes is codon optimized for expression in the host.

11. The recombinant host of claim 10, wherein at least one of the genes is codon optimized for expression in *Saccharomyces cerevisiae*.

12. The recombinant host of claim 9, wherein:

(a) the GGPPS polypeptide comprises a polypeptide having at least 70% identity to an amino acid sequence set forth in SEQ ID NO: 149;
(b) the CDPS polypeptide comprises a polypeptide having at least 70% identity to an amino acid sequence set forth in SEQ ID NO: 150;
(c) the KO polypeptide comprises a polypeptide having at least 70% identity to an amino acid sequence set forth in SEQ ID NO: 152;

(d) the KS polypeptide comprises a polypeptide having at least 40% identity to an amino acid sequence set forth in SEQ ID NO: 151;

(e) the KAH polypeptide comprises a polypeptide having at least 60% identity to an amino acid sequence set forth in SEQ ID NO: 154;

(f) the CPR polypeptide comprises a polypeptide having at least 70% identity to an amino acid sequence set forth in SEQ ID NO: 153 and/or a polypeptide having at least 65% identity to an amino acid sequence set forth in SEQ ID NO: 155;

(g) the UGT85C2 polypeptide comprises a polypeptide having at least 55% identity to an amino acid sequence set forth in SEQ ID NO: 156;

(h) the UGT76G1 polypeptide comprises a polypeptide having at least 50% identity to an amino acid sequence set forth in SEQ ID NO: 158;

(i) the UGT74G1 polypeptide comprises a polypeptide having at least 55% identity to an amino acid sequence set forth in SEQ ID NO: 157;

(j) the a UGT91D2 functional homolog comprises a UGT91D2e-b polypeptide having at least 90% identity to the amino acid sequence set forth in SEQ ID NO: 159; and

(k) the EUGT11 polypeptide comprises a polypeptide having at least 65% identity to an amino acid sequence set forth in SEQ ID NO: 148.

13. The recombinant host of any one of claims 1-12, wherein the recombinant host comprises a microorganism that is a plant cell, a mammalian cell, an insect cell, a fungal cell, or a bacterial cell.

14. The recombinant host of claim 13, wherein the bacterial cell comprises Escherichia bacteria cells, Lactobacillus bacteria cells, Lactococcus bacteria cells, Cornebacterium bacteria cells, Acetobacter bacteria cells, Acinetobacter bacteria cells, or Pseudomonas bacterial cells.

15. The recombinant host of claim 13, wherein the fungal cell is a yeast cell.
16. The recombinant host of claim 15, 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.

17. The recombinant host of claim 16, wherein the yeast cell is a *Saccharomycete*.

18. The recombinant host of claim 17, wherein the yeast cell is a cell from the *Saccharomyces cerevisiae* species.

19. A method of producing a steviol glycoside, comprising:
   
   (a) growing the recombinant host of any one of claims 1-18 in a culture medium, under conditions in which the genes discussed in any one of claims 1 to 18 are expressed, wherein the steviol glycoside is synthesized by the host; and
   
   (b) optionally isolating the steviol glycoside.

20. The method of claim 19, wherein the steviol glycoside is RebA, RebB, RebD, and/or RebM, and wherein:
   
   (a) RebA is capable of being synthesized in the recombinant host of any one of claims 1-18 expressing UGT85C2, UGT76G1, UGT74G1, and UGT91D2;
   
   (b) RebB is capable of being synthesized in the recombinant host of any one of claims 1-18 expressing UGT85C2, UGT76G1, and UGT91D2;
   
   (c) RebD is capable of being synthesized in the recombinant host of any one of claims 1-18 expressing UGT85C2, UGT76G1, UGT74G1, and UGT91D2 and/or EUGT1; and
   
   (d) RebM is capable of being synthesized in the recombinant host of any one of claims 1-18 expressing UGT85C2, UGT76G1, UGT74G1, and UGT91D2 and/or EUGT1.

22. The method of any one of claims 19-21, wherein the steviol glycoside is produced at a concentration of between about 500 mg/L to about 10,000 mg/L.

23. A method of increasing production or transport of a steviol glycoside into a culture medium, comprising:

(a) growing the recombinant host of any one of claims 1-18 in a culture medium, under conditions in which the genes discussed in any one of claims 1 to 18 are expressed, wherein the steviol glycoside is synthesized by the host; and

(b) optionally isolating the steviol glycoside.

24. The method of claim 23, wherein the steviol glycoside is RebA, RebB, RebD, and/or RebM.
INTERNATIONAL SEARCH REPORT

A. CLASSIFICATION OF SUBJECT MATTER

According to International Patent Classification (IPC) and/or national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

A23L C12N C07H

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, EMBASE, WPI Data, Sequence Search

C. DOCUMENTS CONSIDERED TO BE RELEVANT

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<th>Citation of document, with indication, where appropriate, of the relevant passages</th>
<th>Relevant to claim No.</th>
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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 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

*Z* document member of the same patent family

Date of the actual completion of the international search 15 October 2015

Name and mailing address of the ISA/
European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040
Fax: (+31-70) 340-3016

Date of mailing of the international search report 20/01/2016

Authorized officer

Spri nks, Matthew

Form PCT/ISA2/10 (second sheet) (April 2005)
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<td>8 December 2011 (2011-12-08) abstract paragraph [0014]; table 1; sequence 38</td>
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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).

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.:

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.:

   I-24(partially)

**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.
This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: l-24(partially)

   A recombinant host capable of synthesizing a steviol glycoside and transporting it into the culture medium, comprising a gene encoding a transporter polypeptide, the expression of which is modified, wherein the transporter polypeptide is an endogenous ABC transporter, and subject-matter relating thereto.

   ---

2-32. claims: l-24(partially)

   As subject 1 but wherein the transporter polypeptide is selected from the list in claim 3, starting with MFS transporter.

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