

**METHOD OF IDENTIFYING LAUNDRY MALODOR, MOLDY MALODOR
AND/OR SWEAT MALODOR MODULATING COMPOUNDS**

CROSS REFERENCE TO RELATED APPLICATIONS

5 The present application claims priority to U.S. Provisional Patent Application Serial No. 62/589,947, filed on November 22, 2017, European Patent Application Serial No. 18157790.9, filed on February 21, 2018, and U.S. Provisional Patent Application Serial No. 62/754,899, filed on November 2, 2018, the entire contents of which are hereby incorporated by reference in their entirety.

FIELD

10 The technical field is directed to odorant and aroma receptors and assays that can be used to identify odorant and/or aroma compounds, and more specifically inhibitors, modulators, or counteractants of malodor compounds of laundry malodour, moldy malodour, and/or sweat malodour, such as dimethyl trisulfide (DMTS), geonol, 1-octen-3-ol, butyric acid, 3-methyl-2-hexenoic acid, 3-hydroxy-3-methyl-hexanoic acid and 3-methyl-3-sulphanylhexanol (transpirol).

BACKGROUND

20 Olfaction is one of the most complex and poorly understood of human sensory systems. From olfactory receptor (OR) activation to perception, there are many steps that still require further investigation. If we can understand how the OR code for individual odorants and mixtures translates into perception then we can exploit this knowledge to bring significant benefit in several areas. These areas include odor modulators like malodor counteractants that block the perception of unpleasant odors, new flavor and fragrance ingredients that replace non-biodegradable or toxic compounds, and odor enhancers that would limit our reliance on difficult to source compounds from natural sources. The 'olfactory code' combinatorial paradigm is centered on the observation that any single OR may be activated by multiple odorants, and conversely most odorants are capable of activating several ORs. In the mouse genome there are approximately 1,200 distinct intact ORs. Humans, by contrast, have approximately 400. In both cases, the repertoire of ORs is activated by many thousands of

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odorants in the world, and it is this combinatorial complexity that allows for the breadth of olfactory sensations we can perceive. However, odorants or ligands for only 82 mouse (approximately 8%) and 17 human ORs (approximately 10%) have been identified as of 2014 using traditional deorphanization methods. In addition, the physiological relevance of most ligands for the human ORs, essentially identified *in vitro*, has not been tested.

A method that can rapidly and reliably identify a relatively small subset of ORs, within the entire repertoire of ORs that exist in an organism that are specifically activated or inhibited by one or more odorants is described in WO2014/210585. However, using this method, there remains a need to identify odorant receptors and more particularly malodor receptors that are activated by particular malodor-causing substances.

Malodor-causing compounds such as dimethyl trisulfide (DMTS), geonol, 1-octen-3-ol, butyric acid, 3-methyl-2-hexenoic acid, 3-hydroxy-3-methyl-hexanoic acid and transpirol can generate unpleasant odors that arise, for example, from laundry or body odor caused by sweat or sebum, or moldy malodor

Hence, the problem to be solved by the present invention is the provision of methods of identifying of moldy malodor, laundry malodor and/or sweat malodor modulators or counteractants that bind, suppress, block, inhibit, and/or modulate the activity of one or more olfactory receptor that is activated by a particular malodor-causing substance (MCS) characteristic for such type of malodor. Assays that rely on new malodor receptors or on malodor receptors newly identified as associated with particular malodors-causing substances to identify new compounds or compounds mixtures that bind to these receptors are further desired.

SUMMARY

The above-mentioned problem was surprisingly solved by identifying panels of MCSs which are characteristic for laundry malodor, moldy malodor or sweat malodor and panels of olfactory receptors that are activated by such MCS, and which may be used as targets to identify modulator substances to counteract activation of these olfactory receptors by such MCS.

As laundry MCS geonol, DMTS and 1-octen-3-ol have been identified. As olfactory receptor polypeptides activated by at least one of said compounds the human receptors OR2W1, OR1A1, OR2J3, OR4Q3, OR5K1, OR11A1, OR2M3, OR4S2, the mouse orthologues Olfr263, Olfr403, Olfr137, Olfr173, Olfr164, Olfr735, Olfr1193, Olfr96, and the mouse receptors Olfr1487, Olfr339, Olfr93, Olfr398, Olfr120, Olfr1364 and Olfr937 could be identified.

As sweat MCS butyric acid, 3-methyl-2-hexenoic acid, 3-hydroxy-3-methyl-hexanoic acid and transpirol have been identified. As olfactory receptor polypeptides activated by at least one of said compounds the human receptors OR2W1, OR1A1, OR2J3, OR5K1, OR51E1, OR51I2, the mouse orthologues Olfr263, Olfr403, Olfr558 Olfr641, Olfr137, Olfr164, and the mouse receptors Olfr1126 and Olfr46 could be identified.

As moldy MCS geonol, DMTS and 1-octen-3-ol have been identified. As olfactory receptor polypeptides activated by at least one of said compounds the human receptors OR2W1, OR1A1, OR2J3, OR4Q3, OR5K1, OR11A1, OR2M3, OR4S2, the mouse orthologues Olfr263, Olfr403, Olfr735, Olfr1193, Olfr96, Olfr137, Olfr173, Olfr164, and the mouse receptors Olfr1487, Olfr339, Olfr93, Olfr398, Olfr120, Olfr1364 and Olfr937 could be identified.

Further provided by the present invention are methods to assay whether a compound binds, suppresses, blocks, inhibits, and/or modulates the activity of an olfactory receptor that is activated by a laundry malodor, moldy malodor, and/or sweat malodor-causing substance, and in particular methods of identifying such compounds.

Further provided are isolated olfactory receptor polypeptides, corresponding encoding nucleic acid sequences, recombinant nucleic acids comprising such encoding sequences and corresponding expression vectors.

Further provided are non-human host organism or a host cell that has been modified to express such olfactory receptor polypeptides which are activated by MCSs which a characteristic for laundry malodor, moldy malodor or sweat malodor.

Further provided is the use of such olfactory receptor polypeptides which are activated by MCSs and which are characteristic for laundry malodor, moldy malodor or sweat malodor for identifying a malodor modulating compound.

DESCRIPTION OF THE DRAWINGS

Figure 1 shows certain MCS and olfactory receptors according to some aspects presented herein.

Figure 2 shows the potency of the antagonist 1-[(1S,7S)-2,3,4-trimethyltricyclo[5.2.1.0~1.5~]dec-4-yl) ethanone oxime as an inhibitor of the butyric acid olfactory receptor OR51E1 under highly stringent screening conditions. The black line denotes the % inhibition of the butyric acid olfactory receptor activity observed from cells treated with 81 μ M butyric acid (EC_{87}) and the antagonist at the concentrations [μ M] indicated.

Figure 3 shows a summary of the % inhibition of the butyric acid olfactory receptor OR51E1 under highly stringent screening conditions observed from cells treated with compounds according to some aspects presented herein. The structures of the compounds tested are shown to the sides of the figure.

Figure 4 shows the ability of compounds according to some aspects of the present disclosure to reduce the perceived intensity of geonol in human sensory panel tests. Many of these compounds are shown to inhibit the activity of a geonol olfactory receptor. NS, the % geonol perception remaining is not statistically different compared to geonol alone at isointense concentrations; Asterisk (*), the % geonol perception remaining is statistically different compared to geonol alone at isointense concentrations.

Figure 5 shows geonol concentration-dependent and specific activation of OR11A1, Olfr96, Olfr339, Olfr1487 and Olfr1322 in a cell-based assay, according to assays and methods disclosed in WO2014/210585 and further in the Methods of Monitoring OR Activity section. The detection method pertains to OR-dependent accumulation of cAMP in said cells, as a result of OR activation by geonol.

Figure 6 shows 1-octen-3-ol concentration-dependent and specific activation of Olfr93, Olfr398, Olfr120 and Olfr1364 in a cell-based assay, according to assays and methods disclosed in WO2014/210585 and further in the Methods of Monitoring OR Activity section. The detection method pertains to OR-dependent accumulation of cAMP in said cells, as a result of OR activation by 1-octen-3-ol.

Figure 7 shows transpirol concentration-dependent and specific activation of OR2W1, Olfr263 and Olfr46 in a cell-based assay, according to assays and methods disclosed in WO2014/210585 and further in the Methods of Monitoring OR Activity section. The detection method pertains to OR-dependent accumulation of cAMP in said cells, as a result of OR activation by transpirol.

Figure 8 shows 3-methyl-2-hexenoic acid concentration-dependent and specific activation of OR51I2, Olfr641, OR2W1 and Olfr263 in a cell-based assay according to assays and methods disclosed in WO2014/210585 and further in the Methods of Monitoring OR Activity section. The detection method pertains to OR-dependent accumulation of cAMP in said cells, as a result of OR activation by 3-methyl-2-hexenoic acid.

Figure 9 shows 3-hydroxy-3-methyl-hexanoic acid concentration-dependent and specific activation of Olfr1126 in a cell-based assay, according to assays and methods disclosed in WO2014/210585 and further in the Methods of Monitoring OR Activity section. The detection method pertains to OR-dependent accumulation of cAMP in said cells, as a result of OR activation by 3-hydroxy-3-methyl-hexanoic acid.

Figure 10 shows the NGS data from a single OSN responding to geonol, according to the method described in WO2014/210585, and further in the Methods of OR activity part. Left panel shows the relative transcriptional abundance of ORs, with Olfr96 being significantly higher than the rest. Right panel shows the presence and relative abundance of key marker housekeeping genes for OSN (omp, actb, cnga2, rtp1, gnal, adcy3), in the same NGS sample.

Figure 11 shows the NGS data from a single OSN responding to 1-octen-3-ol, according to the method described in WO2014/210585, and further in the Methods of OR activity part. Left panel shows the relative transcriptional abundance of ORs, with Olfr93 being significantly higher than the rest. Right panel shows the presence and relative abundance of key marker housekeeping genes for OSN (omp, actb, cnga2, rtp1, gnal, adcy3), in the same NGS sample.

Figure 12 shows the NGS data from a single OSN responding to 1-octen-3-ol, according to the method described in WO2014/210585, and further in the Methods of OR activity part. Left panel shows the relative transcriptional abundance of ORs, with Olfr120 being significantly higher than the rest. Right panel shows the presence and relative abundance of key marker housekeeping genes for OSN (omp, actb, cnga2, rtp1, gnal, adcy3), in the same NGS sample.

Figure 13 shows the NGS data from a single OSN responding to 1-octen-3-ol, according to the method described in WO2014/210585, and further in the Methods of OR activity part. Left panel shows the relative transcriptional abundance of ORs, with Olfr1364 being significantly higher than the rest. Right panel shows the presence and relative abundance of key marker housekeeping genes for OSN (omp, actb, cnga2, rtp1, gnai, adcy3), in the same NGS sample.

Figure 14 shows the NGS data from a single OSN responding to 1-octen-3-ol, according to the method described in WO2014/210585, and further in the Methods of OR activity part. Left panel shows the relative transcriptional abundance of ORs, with Olfr937 being significantly higher than the rest. Right panel shows the presence and relative abundance of key marker housekeeping genes for OSN (omp, actb, cnga2, rtp1, gnai, adcy3) in the same NGS sample.

Figure 15 shows the NGS data from a single OSN responding to transpirol, according to the method described in WO2014/210585, and further in the Methods of OR activity part. Left panel shows the relative transcriptional abundance of ORs, with Olfr263 being significantly higher than the rest. Right panel shows the presence and relative abundance of key marker housekeeping genes for OSNs in the same NGS sample.

Figure 16 shows the NGS data from a single OSN responding to 3-hydroxy-3-methyl-hexanoic acid, according to the method described in WO2014/210585, and further in the Methods of OR activity part. Left panel shows the relative transcriptional abundance of ORs, with Olfr1126 being significantly higher than the rest. Right panel shows the presence and relative abundance of key marker housekeeping genes for OSNs in the same NGS sample.

DETAILED DESCRIPTION

Definitions

For the descriptions herein and the appended claims, the use of "or" means "and/or" unless stated otherwise.

5 Similarly, "comprise," "comprises," "comprising," "include," "includes," and "including" are interchangeable and not intended to be limiting.

It is to be further understood that where descriptions of various embodiments use the term "comprising," those skilled in the art would understand that in some specific instances, an embodiment can be alternatively described using language "consisting essentially of" or
10 "consisting of."

The following terms have the meanings ascribed to them unless specified otherwise.

"OR" refers to one or more members of a family of G protein-coupled receptors (GPCRs) that are expressed in olfactory cells. Olfactory receptor cells can also be identified on the basis of morphology or by the expression of proteins specifically expressed in olfactory
15 cells. OR family members may have the ability to act as receptors for olfactory signal transduction.

"DMTS OR" refers to a member of the family of G protein-coupled receptors that is expressed in an olfactory cell, which receptors bind and/or are activated by DMTS in a binding or activity assay for identifying ligands that bind and/or activate GPCRs. Such assays
20 are described below. DMTS receptors herein will include fragments, variants, including synthetic and naturally occurring, and chimeras or recombinant nucleic acids or proteins that respond to or bind DMTS. The same definition applies in analogy to the following receptors:

"Geonol OR", "1-Octen-3-ol OR", "Butyric acid OR", "3-Methyl-2-hexenoic acid OR", "3-Hydroxy-3-methyl-hexanoic acid OR" and "Transpirol OR",

25 "OR" polypeptides are considered as such if they pertain to the 7-transmembrane-domain G protein-coupled receptor superfamily encoded by a single ~1kb long exon and exhibit characteristic olfactory receptor-specific amino acid motifs. The seven domains are called "transmembrane" or "TM" domains TM I to TM VII connected by three "internal cellular loop" or "IC" domains IC I to IC III, and three "external cellular loop" or "EC"
30 domains EC I to EC III. The motifs and the variants thereof are defined as, but not restricted to, the MAYDRYVAIC motif (SEQ ID NO: 53) overlapping TM III and IC II, the FSTCSSH

motif (SEQ ID NO: 54) overlapping IC III and TM VI, the PMLNPFIY motif (SEQ ID NO: 55) in TM VII as well as three conserved C residues in EC II, and the presence of highly conserved GN residues in TM I [Zhang, X. & Firestein, S. Nat. Neurosci. 5, 124–133 (2002); Malnic, B., et al. Proc. Natl. Acad. Sci. U. S. A. 101, 2584–2589 (2004)].

5 "OR" nucleic acids encode a family of GPCRs with seven transmembrane regions that have "G protein-coupled receptor activity," e.g., they may bind to G proteins in response to extracellular stimuli and promote production of second messengers such as IP₃, cAMP, cGMP, and Ca²⁺ via stimulation of enzymes such as phospholipase C and adenylate cyclase.

"Paralogous" OR genes or "paralogs" are the result of gene duplications and refer to
10 closely related homologous genes within the same species.

"Orthologous" OR genes or "orthologs" are defined as phylogenetically linked by a gene present in a common ancestor and refer to closely related homologous genes in other species.

The "N terminal domain" region starts at the N-terminus and extends to a region close
15 to the start of the first transmembrane region.

"Transmembrane regions" comprise the seven "transmembrane domains," which refers to the domain of OR polypeptides that lies within the plasma membrane, and may also include the corresponding cytoplasmic (intracellular) and extracellular loops. The seven transmembrane regions and extracellular and cytoplasmic loops can be identified using
20 standard methods such as hydrophobicity profiles, or as described in Kyte & Doolittle, J. Mol. Biol., 157:105-32 (1982), or in Stryer. The general secondary and tertiary structure of transmembrane domains, in particular the seven transmembrane domains of G protein-coupled receptors such as olfactory receptors, are known in the art. Thus, primary structure sequence can be predicted based on known transmembrane domain sequences, as described in detail
25 below. These transmembrane domains are useful for *in vitro* ligand-binding assays.

The phrase "functional effects" in the context of assays for testing compounds that modulate OR family member mediated olfactory transduction includes the determination of any parameter that is indirectly or directly under the influence of the receptor, e.g., functional, physical and chemical effects. It includes ligand binding, changes in ion flux, membrane
30 potential, current flow, transcription, G protein binding, GPCR phosphorylation or dephosphorylation, signal transduction receptor-ligand interactions, second messenger

concentrations (e.g., cAMP, cGMP, IP₃, or intracellular Ca.²⁺), *in vitro*, *in vivo*, and *ex vivo* and also includes other physiologic effects such as increases or decreases of neurotransmitter or hormone release.

By "determining the functional effect" or "confirming the activity" in the context of assays is meant assays for a compound that increases or decreases a parameter that is indirectly or directly under the influence of an OR family member, e.g., functional, physical and chemical effects. Such functional effects can be measured by any means known to those skilled in the art, e.g., changes in spectroscopic characteristics (e.g., fluorescence, absorbance, refractive index), hydrodynamic (e.g., shape), chromatographic, or solubility properties, patch clamping, voltage-sensitive dyes, whole cell currents, radioisotope efflux, inducible markers, oocyte OR gene expression; tissue culture cell OR expression; transcriptional activation of OR genes or activity induced genes such as *egr-1* or *c-fos*; ligand-binding assays; voltage, membrane potential and conductance changes; ion flux assays; changes in intracellular second messengers such as cAMP, cGMP, and inositol triphosphate (IP₃); changes in intracellular calcium levels; neurotransmitter release, and the like.

"Binder," "suppressors," "blockers," "inhibitors," and/or "modulators" of OR genes or proteins are used interchangeably to refer to binding, suppressing, blocking, inhibitory, or modulating molecules identified using *in vivo*, *in vitro* and *ex vivo* assays for olfactory transduction, e.g., ligands, agonists, antagonists, enhancers, and their homologs and mimetics.

Inhibitors are compounds that, e.g., bind to, partially or totally block stimulation, decrease, suppress, prevent, delay activation, inactivate, desensitize, or down regulate olfactory transduction, e.g., antagonists. On the other hand activators are compounds that, e.g., bind to, stimulate, increase, open activate, facilitate, enhance activation, sensitize, or up regulate olfactory transduction, e.g., agonists.

Modulators include compounds that, e.g., alter the interaction of a receptor with: extracellular proteins that bind activators or inhibitor (e.g., odorant-binding proteins, ebnerin and other members of the hydrophobic carrier family, or a member of the lipocalin family); G proteins; kinases (e.g., homologs of rhodopsin kinase and beta adrenergic receptor kinases that are involved in deactivation and desensitization of a receptor); and arrestins, which also deactivate and desensitize receptors.

Modulators also include compounds that alter the affinity or the transduction efficacy of an OR altering the effect of an activator on the OR. Modulators can include genetically modified versions of OR family members, e.g., with altered activity, as well as naturally occurring and synthetic ligands, antagonists, agonists, small chemical molecules and the like.

5 Such assays for inhibitors and activators include, e.g., expressing OR family members in cells or cell membranes, applying putative modulator compounds, in the presence or absence of flavour, fragrance or malodour molecules, e.g. a malodour-causing substance such as herein defined, and then determining the functional effects on olfactory transduction, as described above. Samples or assays comprising OR family members that are treated with a potential
10 activator, inhibitor, or modulator are compared to control samples without the inhibitor, activator, or modulator to examine the extent of modulation. Control samples (untreated with modulators) are assigned a relative maximal OR activity value of 100%. Inhibition of an OR is achieved when the OR activity value relative to the control is about 80% or less, 70% or less, 60% or less, 50% or less, 40% or less, 30% or less, or 25-0%, like 1, 2, 3, 4 ,5 ,6 7, 8, 9
15 or 10%.

The terms "purified," "substantially purified," and "isolated" as used herein refer to the state of being free of other, dissimilar compounds with which the compound of the invention is normally associated in its natural state, so that the "purified," "substantially purified," and "isolated" subject comprises at least 0.5%, 1%, 5%, 10%, or 20%, or at least 50% or 75% of
20 the mass, by weight, of a given sample. In one particular embodiment, these terms refer to the compound of the invention comprising at least 95, 96, 97, 98, 99 or 100% of the mass, by weight, of a given sample. As used herein, the terms "purified," "substantially purified," and "isolated," when referring to a nucleic acid or protein, of nucleic acids or proteins, also refers to a state of purification or concentration different than that which occurs naturally in the
25 mammalian, especially human body. Any degree of purification or concentration greater than that which occurs naturally in the mammalian, especially human body, including (1) the purification from other associated structures or compounds or (2) the association with structures or compounds to which it is not normally associated in the mammalian, especially human, body, are within the meaning of "isolated." The nucleic acid or protein or classes of
30 nucleic acids or proteins, described herein, may be isolated, or otherwise associated with structures or compounds to which they are not normally associated in nature, according to a variety of methods and processes known to those of skill in the art.

As used herein, the terms "amplifying" and "amplification" refer to the use of any suitable amplification methodology for generating or detecting recombinant of naturally expressed nucleic acid, as described in detail, below. For example, the invention provides methods and reagents (e.g., specific degenerate oligonucleotide primer pairs, oligo dT primer) for amplifying (e.g., by polymerase chain reaction, PCR) naturally expressed (e.g., genomic DNA or mRNA) or recombinant (e.g., cDNA) nucleic acids of the invention *in vivo*, *ex vivo* or *in vitro*.

The term "7-transmembrane receptor" means a polypeptide belonging to a superfamily of transmembrane proteins that have seven domains that span the plasma membrane seven times (thus, the seven domains are called "transmembrane" or "TM" domains TM I to TM VII). The families of olfactory and certain taste receptors each belong to this super-family. 7-transmembrane receptor polypeptides have similar and characteristic primary, secondary and tertiary structures, as discussed in further detail below.

The term "nucleic acid" or "nucleic acid sequence" refers to a deoxy-ribonucleotide or ribonucleotide oligonucleotide in either single- or double-stranded form. The term encompasses nucleic acids, i.e., oligonucleotides, containing known analogs of natural nucleotides. The term also encompasses nucleic-acid-like structures with synthetic backbones. Unless otherwise indicated, a particular nucleic acid sequence also implicitly encompasses conservatively modified variants thereof (e.g., degenerate codon substitutions) and complementary sequences, as well as the sequence explicitly indicated. Specifically, degenerate codon substitutions may be achieved by generating, e.g., sequences in which the third position of one or more selected codons is substituted with mixed-base and/or deoxyinosine residues.

In addition to the gene sequences shown in the sequences disclosed herein, it will be apparent for the person skilled in the art that variants also include DNA sequence polymorphisms that may exist within a given population, which may lead to changes in the amino acid sequence of the polypeptides disclosed herein. Such genetic polymorphisms may exist in cells from different populations or within a population due to natural allelic variation. Allelic variants may also include functional equivalents.

Further embodiments also relate to the molecules derived by such sequence polymorphisms from the concretely disclosed nucleic acids. These natural variations usually bring about a variance of about 1 to 5% in the nucleotide sequence of a gene or in the amino acid sequence of the polypeptides disclosed herein. As mentioned above, the nucleic acid encoding the polypeptide of an embodiment herein is a useful tool to modify non-human host organisms or host cells intended to be used in the methods described herein.

The terms "polypeptide," "peptide" and "protein" are used interchangeably herein to refer to a polymer of amino acid residues, whether comprising naturally occurring amino acids or polymers and non-naturally occurring amino acids or polymers. The term "heterologous" when used with reference to portions of a nucleic acid indicates that the nucleic acid comprises two or more subsequences that are not found in the same relationship to each other in nature. For instance, the nucleic acid is typically recombinantly produced, having two or more sequences from unrelated genes arranged to make a new functional nucleic acid, e.g., a promoter from one source and a coding region from another source. Similarly, a heterologous protein indicates that the protein comprises two or more subsequences that are not found in the same relationship to each other in nature (e.g., a fusion protein).

A "promoter" is defined as an array of nucleic acid sequences that direct transcription of a nucleic acid. As used herein, a promoter includes necessary nucleic acid sequences near the start site of transcription, such as, in the case of a polymerase II type promoter, a TATA element. A promoter also optionally includes distal enhancer or repressor elements, which can be located as much as several thousand base pairs from the start site of transcription. A "constitutive" promoter is a promoter that is active under most environmental and developmental conditions. An "inducible" promoter is a promoter that is active under environmental or developmental regulation. The term "operably linked" refers to a functional linkage between a nucleic acid expression control sequence (such as a promoter, or array of transcription factor binding sites) and a second nucleic acid sequence, wherein the expression control sequence directs transcription of the nucleic acid corresponding to the second sequence.

As used herein, "recombinant" refers to a polynucleotide synthesized or otherwise manipulated *in vitro* (e.g., "recombinant polynucleotide"), to methods of using recombinant polynucleotides to produce gene products in cells or other biological systems, or to a polypeptide ("recombinant protein") encoded by a recombinant polynucleotide.

"Recombinant" means also the ligation of nucleic acids having various coding regions or domains or promoter sequences from different sources into an expression cassette or vector for expression of, e.g., inducible or constitutive expression of a fusion protein comprising a translocation domain of the invention and a nucleic acid sequence potentially amplified using a primer. "Recombinant" means also modifications obtained by genome editing techniques, such as CRISPR/Cas9, of a cell that leads to stable or transient expression of endogenous genes such as the receptor gene referred to herein.

The term "expression vector" refers to any recombinant expression system for the purpose of expressing a nucleic acid sequence of the invention *in vitro*, *ex vivo*, or *in vivo*, constitutively or inducibly, in any cell, including prokaryotic, yeast, fungal, plant, insect or mammalian cell. The term includes any linear or circular expression systems including but not limited to viral vectors, bacteriophages and plasmids. The skilled person is capable of selecting a suitable vector according to the expression system. The term includes expression systems that remain episomal or integrate into the host cell genome. The expression systems can have the ability to self-replicate or not, i.e., drive transient expression in a cell. The term includes recombinant "expression cassettes" which can contain the minimum elements needed for transcription of the recombinant nucleic acid. The term also covers cassettes or vectors for expression of endogenous genes through, for example, genome editing methods such as CRISPR/Cas9.

By "a non-human organism or a host cell" is meant a non-human organism or a cell that contains a nucleic acid as described herein or an expression vector and supports the replication or expression of the expression vector. Host cells may be prokaryotic cells such as *E. coli*, or eukaryotic cells such as yeast, insect, amphibian, or mammalian cells such as CHO, HeLa, HEK-293, and the like, e.g., cultured cells, explants, and cells *in vivo*.

By "tag" or "tag combination" is meant a short polypeptide sequence that can be added to the odorant receptor protein. Typically, the DNA encoding a "tag" or a "tag combination" is added to the DNA encoding the receptor, eventually resulting in a fusion protein where the "tag" or a "tag combination" is fused to the N-terminus or C-terminus of the receptor. Lucy, FLAG[®] and/or Rho tags can enhance the receptor trafficking to the cell membrane, hence they can assist in expression of a functional odorant receptor for *in vitro* cell based assay [Shepard, B. et al. PLoS One 8, e68758–e68758 (2013), and Zhuang, H. & Matsunami, H. J. Biol. Chem. 282, 15284–15293 (2007)].

"Geonol" and/ or "Geosmin" refers to (4S,4aS,8aR)-4,8a-Dimethyl-1,2,3,4,5,6,7,8-octahydronaphthalen-4a-ol.

Particular Embodiments

- 5 In particular the present invention makes use of the human olfactory receptors (ORs) OR2W1, OR1A1, OR2J3, OR4Q3, OR5K1, OR11A1, OR2M3, OR51E1, OR4S2, OR51I2, OR2H1, OR2W3, OR8G1, and corresponding mouse orthologs Olfr263, Olfr403, Olfr735, Olfr96, Olfr1193, Olfr641, Olfr137, Olfr173, Olfr164, and Olfr558, as well as mouse ORs
- 10 Olfr1487, Olfr339, Olfr1126, Olfr93, Olfr398, Olfr120, Olfr1364, Olfr937, Olfr1322, and Olfr46 as receptors for the malodour-causing substances geonol, dimethyl trisulfide (DMTS), 1-octen-3-ol, butyric acid, 3-methyl-2-hexenoic acid, 3-hydroxy-3-methyl-hexanoic acid, and transpirol (3-methyl-3-sulfanylhexanol), as shown in Table 1a.

Table 1a: Human odorant receptors and pairs with orthologous mouse receptors and their corresponding identity at the amino acid level as well as further mouse ORs; together with their respective agonists.

Mouse Ortholog	Agonists	Human Ortholog	Agonists	Mouse-Human Amino Acid Identity
Olfr263	1-octen-3-ol, DMTS, 3-hydroxy-3-methylhexanoic acid, transpirol, 3-methyl-2-hexenoic acid	OR2W1	1-octen-3-ol, DMTS, 3-hydroxy-3-methylhexanoic acid, transpirol, 3-methyl-2-hexenoic acid	86%
Olfr403	1-octen-3-ol, geonol, DMTS, transpirol	OR1A1	1-octen-3-ol, geonol, DMTS, transpirol	84%
Olfr137	1-octen-3-ol, transpirol	OR2J3	1-octen-3-ol, transpirol	82%
Olfr735	1-octen-3-ol	OR4Q3	1-octen-3-ol	82%
Olfr173	1-octen-3-ol, DMTS, transpirol	OR5K1	1-octen-3-ol, DMTS, transpirol	85%
Olfr96	geonol	OR11A1	geonol	75%
Olfr164	geonol	OR2M3	geonol	75%
Olfr558	butyric acid	OR51E1	butyric acid	94%
Olfr1193	DMTS	OR4S2	DMTS	88%
Olfr641	3-methyl-2-hexenoic acid	OR51I2	3-methyl-2-hexenoic acid	89.10%
Olfr1487	geonol	None	NA	NA
Olfr339	geonol	None	NA	NA
Olfr1126	3-hydroxy-3-methylhexanoic acid	None	NA	NA
Olfr93	1-octen-3-ol	OR2H1	NA	81%
Olfr398	1-octen-3-ol	None	NA	NA
Olfr120	1-octen-3-ol	None	NA	NA
Olfr1364	1-octen-3-ol	OR2W3	NA	74%
Olfr937	1-octen-3-ol	OR8G1	NA	79%
Olfr1322	geonol	None	NA	NA
Olfr46	transpirol	None	NA	NA

Table 1b states the corresponding SEQ ID NOs of ORs as applied according to the present invention:

5 Table 1b: SEQ ID NOs of human and mouse odorant receptors

Mouse Ortholog	SEQ ID NO:	Human Ortholog	SEQ ID NO:
Olfr263	21 (NA)	OR2W1	1 (NA)
	22 (AA)		2 (AA)
Olfr403	23 (NA)	OR1A1	3 (NA)
	24 (AA)		4 (AA)
Olfr137	35 (NA)	OR2J3	5 (NA)
	36 (AA)		6 (AA)
Olfr735	25 (NA)	OR4Q3	7 (NA)
	26 (AA)		8 (AA)
Olfr173	37 (NA)	OR5K1	9 (NA)
	38 (AA)		10 (AA)
Olfr96	27 (NA)	OR11A1	11 (NA)
	28 (AA)		12 (AA)
Olfr164	39 (NA)	OR2M3	13 (NA)
	40 (AA)		14 (AA)
Olfr558	29 (NA)	OR51E1	15 (NA)
	30 (AA)		16 (AA)
Olfr1193	31 (NA)	OR4S2	17 (NA)
	32 (AA)		18 (AA)
Olfr641	33 (NA)	OR51I2	19 (NA)
	34 (AA)		20 (AA)
Olfr1487	41 (NA)	None	
	42 (AA)		
Olfr339	43 (NA)	None	
	44 (AA)		
Olfr1126	45 (NA)	None	
	46 (AA)		
Olfr93	62 (NA)	OR2H1	56 (NA)
	63 (AA)		57 (AA)
Olfr398	64 (NA)	None	
	65 (AA)		
Olfr120	66 (NA)	None	
	67 (AA)		
Olfr1364	68 (NA)	OR2W3	58 (NA)
	69 (AA)		59 (AA)
Olfr937	70 (NA)	OR8G1	60 (NA)
	71 (AA)		61 (AA)
Olfr1322	72 (NA)	None	
	73 (AA)		
Olfr46	74 (NA)	None	
	75 (AA)		

NA = nucleic acid sequence; AA = amino acid sequence

These receptors had not been previously associated with the malodor-causing substances selected from geonol, dimethyl trisulfide (DMTS), 1-octen-3-ol, butyric acid, 3-methyl-2-hexenoic acid, 3-hydroxy-3-methyl-hexanoic acid, and transpirol.

In one embodiment provided herein is an isolated nucleic acid molecule comprising a
5 nucleic acid sequence having at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to SEQ ID NO: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, or the reverse complement thereof.

In one embodiment provided herein is an isolated nucleic acid sequence as described
10 above which encodes a polypeptide comprising an amino acid sequence having at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 57, 59, 61, 63, 65, 67, 69, 71, 73, or 75.

In a further embodiment provided herein is an isolated polypeptide comprising an
15 amino acid sequence having at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 57, 59, 61, 63, 65, 67, 69, 71, 73, or 75.

In one embodiment, a non-human organism or a host cell is transformed to express a polypeptide comprising an amino acid sequence having at least 70%, 75%, 80%, 85%, 90%,
20 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 57, 59, 61, 63, 65, 67, 69, 71, 73, or 75.

In one embodiment, a non-human organism or a host cell is transformed to express a polypeptide comprising an amino acid sequence that is identical to SEQ ID NO: 2, 4, 6, 8, 10,
25 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 57, 59, 61, 63, 65, 67, 69, 71, 73, or 75.

Further provided herein is an expression vector comprising a nucleic acid that encodes a polypeptide comprising an amino acid sequence having at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to SEQ ID NO: 2, 4, 6, 8, 10, 12, 14,
30 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 57, 59, 61, 63, 65, 67, 69, 71, 73, or 75.

Also provided herein is an expression vector comprising a nucleic acid that comprises a nucleic acid sequence having at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity SEQ ID NO: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, or the reverse complement thereof.

Also provided herein is an expression vector having a nucleic acid wherein the nucleic acid comprises a nucleotide sequence that is identical to SEQ ID NO: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, or the reverse complement thereof.

More particularly, the present invention relates to the following specific embodiments:

1. A method for identifying a compound that binds, suppresses, blocks, inhibits, and/or modulates the activity of an olfactory receptor (OR) that is activated by a laundry malodour, a moldy malodour, and/or a sweat malodor-causing substance comprising:

- a. contacting a test substance and said laundry malodour, moldy malodour and/or sweat malodor-causing substance to at least one, in particular one single, olfactory receptor polypeptide selected from the group consisting of OR2W1, OR1A1, OR2J3, OR4Q3, OR5K1, OR11A1, OR2M3, OR51E1, OR4S2, OR51I2, OR2H1, OR2W3, OR8G1, Olfr263, Olfr403, Olfr735, Olfr96, Olfr1193, Olfr641, Olfr137, Olfr173, Olfr164, Olfr1487, Olfr339, Olfr1126, Olfr558, Olfr93, Olfr398, Olfr120, Olfr1364, Olfr937, Olfr1322 and Olfr46 and chimera or functional fragments thereof; or to at least one olfactory receptor polypeptide having at least 70%, as for example 75%, 80%, 85%, 90%, and particularly 95%, 96%, 97%, 98%, 99%, or 100% amino acid sequence identity to at least one, in particular one single of the aforementioned olfactory receptor polypeptides; and
- b. measuring the response of said at least one, in particular one single, olfactory receptor to the malodor-causing substance by measuring the response of said olfactory receptor in the presence and absence of the test substance.

A particular subgroup of ORs comprises human ORs OR2W1, OR1A1, OR2J3, OR4Q3, OR5K1, OR11A1, OR2M3, OR51E1, OR4S2, OR51I2, OR2H1, OR2W3, and OR8G1.

Another particular subgroup of ORs comprises the mouse ORs Olfr263, Olfr403,
5 Olfr735, Olfr96, Olfr1193, Olfr641, Olfr137, Olfr173, Olfr164, Olfr1487, Olfr339, Olfr1126, Olfr558, Olfr93, Olfr398, Olfr120, Olfr1364, Olfr937, Olfr1322, and Olfr46.

2. The method of embodiment 1, further comprising

- 10 c. identifying a test substance that modulates the response of said at least one, in particular one single, olfactory receptor on the basis of the response that was measured in the presence and absence of the test substance; and
- d. selecting the identified test substance as a compound that modulates the response of said at least one, in particular one single, olfactory receptor to the malodor-causing substance.

15 3. The method of embodiment 1 or 2, wherein said malodor-causing substance is selected from the group consisting of geonol, dimethyl trisulfide (DMTS), 1-octen-3-ol, butyric acid, 3-methyl-2-hexenoic acid, 3-hydroxy-3-methyl-hexanoic acid, transpirol, and mixtures of at least two, like two or three, of said substances.

20 4. The method of anyone of the preceding embodiments, wherein said at least one olfactory receptor polypeptide

- 25 a. comprises an amino acid sequence having at least 70%, as for example 75%, 80%, 85%, 90%, and particularly 95%, 96%, 97%, 98%, 99%, or 100%, sequence identity to SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 57, 59, 61, 63, 65, 67, 69, 71, 73, or 75; and/or
- b. is encoded by a nucleic acid molecule comprising a nucleotide sequence having at least 70%, as for example 75%, 80%, 85%, 90%, and particularly 95%, 96%, 97%,
30 98%, 99%, or 100%, sequence identity to SEQ ID NO: 1, 3, 5, 7, 9, 11, 13, 15, 17,

19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, or the reverse complement thereof.

A particular subgroup of ORs of this embodiment is or is derived from SEQ ID NO: 2,
5 4, 6, 8, 10, 12, 14, 16, 18, 20, 57, 59, or 61.

Another particular subgroup of ORs of this embodiment is encoded by a nucleic acid molecule comprising a nucleotide sequence of SEQ ID NO: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 56, 58, 60 or a nucleotide sequence derived therefrom.

- 10 5. The method of embodiment 4, wherein the polypeptide
- a. comprises an amino acid sequence having at least 90%, 95%, 98%, 99% or 100% sequence identity to SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 57, 59, 61, 63, 65, 67, 69, 71, 73, or 75; and/or
 - b. is encoded by a nucleic acid molecule comprising a nucleotide sequence having at
15 least 90%, 95%, 98%, 99% or 100% sequence identity to SEQ ID NO: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, or the reverse complement thereof.

A particular subgroup of ORs of this embodiment is or is derived from SEQ ID NO: 2,
20 4, 6, 8, 10, 12, 14, 16, 18, 20, 57, 59, or 61.

Another particular subgroup of ORs of this embodiment is encoded by a nucleic acid molecule comprising a nucleotide sequence of SEQ ID NO: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 56, 58, 60 or a nucleotide sequence derived therefrom.

- 25 6. The method of any one of the embodiments 1 to 5, wherein said malodor-causing substance is a laundry malodor causing substance selected from the group consisting of geonol, DMTS, 1-octen-3-ol, and mixtures of at least two of said substances.

7. The method of any one of the embodiments 1 to 5, wherein said malodor-causing substance is a moldy malodor causing substance selected from the group consisting of geonol, DMTS, 1-octen-3-ol, and mixtures of at least two of said substances.

8. The method of anyone of the embodiments 1 to 5, wherein said malodor-causing substance is a sweat malodor causing substance selected from the group consisting of butyric acid, 3-methyl-2-hexenoic acid, 3-hydroxy-3-methyl-hexanoic acid, transpirol, and mixtures of at least two of said substances.

9. The method of embodiment 6 or 7, wherein the olfactory receptor polypeptide is selected from the group consisting of OR2W1, OR1A1, OR2J3, OR4Q3, OR5K1, OR11A1, OR2M3, OR4S2, Olfr263, Olfr403, Olfr735, Olfr1193, Olfr137, Olfr173, Olfr164, Olfr1487, Olfr339, Olfr96, Olfr1322, Olfr93, Olfr398, Olfr120, Olfr1364 and Olfr937; chimera and functional fragments thereof; and olfactory receptor polypeptides having at least 70%, as for example 75%, 80%, 85%, 90%, and particularly 95%, 96%, 97%, 98%, 99%, or 100%, amino acid sequence identity to at least one of the aforementioned olfactory receptor polypeptides. A particular subgroup of ORs of this embodiment is selected from OR2W1, OR1A1, OR2J3, OR4Q3, OR5K1, OR11A1, OR2M3 and OR4S2.

10. The method of embodiment 9, wherein the malodour causing substance comprises 1-octen-3-ol and the olfactory receptor is selected from the group consisting of OR2W1, OR1A1, OR2J3, OR5K1, OR4Q3, Olfr263, Olfr403, Olfr137, Olfr173, Olfr735, Olfr93, Olfr398, Olfr120, Olfr1364 and Olfr937; chimera and functional fragments thereof; and olfactory receptor polypeptides having at least 70%, as for example 75%, 80%, 85%, 90%, and particularly 95%, 96%, 97%, 98%, 99%, or 100% , amino acid sequence identity to at least one of the aforementioned olfactory receptor polypeptides. A particular subgroup of ORs of this embodiment is selected from OR2W1, OR1A1, OR2J3, OR5K1, and OR4Q3.

11. The method of embodiment 9, wherein the malodour causing substance comprises geonol and the olfactory receptor is selected from the group consisting of OR1A1, OR11A1, OR2M3, Olfr403, Olfr164, Olfr1487, Olfr339, Olfr96 and Olfr1322; chimera and functional fragments thereof; and olfactory receptor polypeptides having at least 70%, as for example
5 75%, 80%, 85%, 90%, and particularly 95%, 96%, 97%, 98%, 99%, or 100%, amino acid sequence identity to at least one of the aforementioned olfactory receptor polypeptides. A particular subgroup of ORs of this embodiment is selected from OR11A1, OR2M3 and OR1A1.

10 12. The method of embodiment 9, wherein the malodour causing substance comprises DMTS and the olfactory receptor is selected from the group consisting of OR2W1, OR1A1, OR5K1, OR4S2, Olfr263, Olfr1193, Olfr173 and Olfr403; chimera and functional fragments thereof; and olfactory receptor polypeptides having at least 70%, as for example 75%, 80%, 85%, 90%, and particularly 95%, 96%, 97%, 98%, 99%, or 100%, amino acid sequence
15 identity to at least one of the aforementioned olfactory receptor polypeptides. A particular subgroup of ORs of this embodiment is selected from OR2W1, OR1A1, OR5K1 and OR4S2.

13. The method of embodiment 8, wherein the olfactory receptor polypeptide is selected from the group consisting of OR2W1, OR1A1, OR2J3, OR5K1, OR51E1, OR51I2, Olfr263,
20 Olfr403, Olfr641, Olfr137, Olfr173, Olfr1126, Olfr558 and Olfr46; chimera and functional fragments thereof; and olfactory receptor polypeptides having at least 70%, as for example 75%, 80%, 85%, 90%, and particularly 95%, 96%, 97%, 98%, 99%, or 100%, amino acid sequence identity to at least one of the aforementioned olfactory receptor polypeptides. A particular subgroup of ORs of this embodiment is selected from OR2W1, OR1A1, OR2J3,
25 OR5K1, OR51E1 and OR51I2.

14. The method of embodiment 13, wherein the malodour causing substance comprises butyric acid and the olfactory receptor is selected from the group consisting of OR51E1, and Olfr558; chimera and functional fragments thereof; and olfactory receptor polypeptides having at least 70%, as for example 75%, 80%, 85%, 90%, and particularly 95%, 96%, 97%, 98%, 99%, or 100%, amino acid sequence identity to at least one of the aforementioned olfactory receptor polypeptides. A particular subgroup of ORs of this embodiment is OR51E1.

15. The method of embodiment 13, wherein the malodour causing substance comprises 3-methyl-2-hexenoic acid, and the olfactory receptor is selected from the group consisting of OR51I2, OR2W1, Olfr641 and Olfr263; chimera and functional fragments thereof; and olfactory receptor polypeptides having at least 70%, as for example 75%, 80%, 85%, 90%, and particularly 95%, 96%, 97%, 98%, 99%, or 100%, amino acid sequence identity to at least one of the aforementioned olfactory receptor polypeptides.

16. The method of embodiment 13, wherein the malodour causing substance comprises 3-hydroxy-3-methyl-hexanoic acid, and the olfactory receptor is selected from the group consisting of OR2W1, Olfr1126 and Olfr263; chimera and functional fragments thereof; and olfactory receptor polypeptides having at least 70, as for example 75%, 80%, 85%, 90%, and particularly 95%, 96%, 97%, 98%, 99%, or 100%, amino acid sequence identity to at least one of the aforementioned olfactory receptor polypeptides.

17. The method of embodiment 13, wherein the malodour causing substance comprises transpirol and the olfactory receptor is selected from the group consisting of OR2W1, OR1A1, OR2J3, OR5K1, Olfr263, Olfr137, Olfr173, Olfr403 and Olfr46; chimera and functional fragments thereof; and olfactory receptor polypeptides having at least 70%, as for example 75%, 80%, 85%, 90%, and particularly 95%, 96%, 97%, 98%, 99%, or 100%, amino acid sequence identity to at least one of the aforementioned olfactory receptor polypeptides. A particular subgroup of ORs of this embodiment is selected from OR2W1, OR1A1, OR2J3 and OR5K1.

18. A method for identifying a compound that binds, suppresses, blocks, inhibits, and/or modulates the activity of at least one olfactory receptor that is activated by a malodor-causing substance, wherein the receptor is a polypeptide

a. that comprises an amino acid sequence having at least 70%, as for example 75%, 80%, 85%, 90%, and particularly 95%, 96%, 97%, 98%, 99%, or 100%, sequence identity to SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 57, 59, 61, 63, 65, 67, 69, 71, 73, or 75; and/or

b. is encoded by a nucleic acid molecule comprising a nucleotide sequence having at least 70%, as for example 75%, 80%, 85%, 90%, and particularly 95%, 96%, 97%, 98%, 99%, or 100%, sequence identity to SEQ ID NO: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, or the reverse complement thereof,

wherein the method comprises:

1. contacting the receptor, or a chimera or fragment thereof with a compound;

2. determining whether the compound has an effect on the activity of the receptor; and

wherein said malodor-causing substance is selected from the group consisting of geonol, DMTS, 1-octen-3-ol, butyric acid, 3-methyl-2-hexenoic acid, 3-hydroxy-3-methyl-hexanoic acid, transpirol, and mixtures of at least two of said substances.

A particular subgroup of ORs of this embodiment is or is derived from SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 57, 59, or 61.

Another particular subgroup of ORs of this embodiment is encoded by a nucleic acid molecule comprising a nucleotide sequence of SEQ ID NO: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 56, 58, 60 or a nucleotide sequence derived therefrom.

19. A method for identifying a compound that binds, suppresses, blocks, inhibits, and/or modulates the activity of an olfactory receptor that is activated by a laundry malodour, a moldy malodour and/or sweat malodor-causing substance, selected from the group consisting of geonol, DMTS, 1-octen-3-ol, butyric acid, 3-methyl-2-hexenoic acid, 3-hydroxy-3-methyl-
5 hexanoic acid, transpirol, and mixtures of at least two of said substances comprising:

- (i) contacting a cell line that expresses at least one olfactory receptor polypeptide selected from the group consisting of OR2W1, OR1A1, OR2J3, OR4Q3, OR5K1, OR11A1, OR2M3, OR51E1, OR4S2, OR51I2, OR2H1, OR2W3, OR8G1, Olfr263, Olfr403, Olfr735, Olfr96, Olfr1193, Olfr641, Olfr137, Olfr173, Olfr164, Olfr1487, Olfr339, Olfr1126, Olfr558, Olfr93, Olfr398, Olfr120, Olfr1364, Olfr937, Olfr1322 and Olfr46 and chimera or functional fragments thereof; or to at least one olfactory receptor polypeptide having at least 70% amino acid sequence identity to at least one of the aforementioned olfactory receptor polypeptides; with at least one compound;
- 15 (ii) screening for compounds that bind, suppress, block, inhibit, and/or modulate the activity of said olfactory receptor polypeptide; and
- (iii) identifying a compound that putatively modulates laundry malodor, moldy malodor and/or sweat malodor if it binds, suppresses, blocks, inhibits, and/or modulates the activity of said receptor polypeptide.

20 A particular subgroup of ORs comprises OR2W1, OR1A1, OR2J3, OR4Q3, OR5K1, OR11A1, OR2M3, OR51E1, OR4S2, OR51I2, OR2H1, OR2W3, and OR8G1.

Another particular subgroup of ORs are Olfr263, Olfr403, Olfr735, Olfr96, Olfr1193, Olfr641, Olfr137, Olfr173, Olfr164, Olfr1487, Olfr339, Olfr1126, Olfr558, Olfr93, Olfr398, Olfr120, Olfr1364, Olfr937, Olfr1322, and Olfr46.

20. An isolated polypeptide comprising an amino acid sequence having at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 57, 59, 61, 63, 65, 67, 69, 71, 73, or 75.

21. An isolated nucleic acid molecule comprising a nucleic acid sequence encoding the polypeptide of embodiment 20.

22. The isolated nucleic acid molecule of embodiment 20, comprising a nucleic acid sequence having at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to SEQ ID NO: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, or the reverse complement thereof.

23. A recombinant nucleic acid molecule comprising

- 10 a. a nucleic acid comprising a tag combination that comprises at least one of a Lucy tag, a FLAG[®] tag, and/or a Rho tag; and
- b. a nucleic acid encoding a receptor selected from the group consisting of OR2W1, OR1A1, OR2J3, OR4Q3, OR5K1, OR11A1, OR2M3, OR51E1, OR4S2, OR51I2, OR2H1, OR2W3, OR8G1, Olfr263, Olfr403, Olfr735, Olfr96, Olfr1193, Olfr641, Olfr137, Olfr173, Olfr164, Olfr1487, Olfr339, Olfr1126, Olfr558, Olfr93, Olfr398, Olfr120, Olfr1364, Olfr937, Olfr1322 and Olfr46, or the complement thereof.
- 15

A particular subgroup of ORs are OR2W1, OR1A1, OR2J3, OR4Q3, OR5K1, OR11A1, OR2M3, OR51E1, OR4S2, OR51I2, OR2H1, OR2W3, and OR8G1.

20 Another particular subgroup of ORs are Olfr263, Olfr403, Olfr735, Olfr96, Olfr1193, Olfr641, Olfr137, Olfr173, Olfr164, Olfr1487, Olfr339, Olfr1126, Olfr558, Olfr93, Olfr398, Olfr120, Olfr1364, Olfr937, Olfr1322, and Olfr46.

24. The recombinant nucleic acid molecule of embodiment 12, wherein the Lucy tag comprises SEQ ID NO: 51, the FLAG[®] tag comprises SEQ ID NO: 47, and the Rho tag comprises SEQ ID NO: 49.

25

25. An expression vector comprising the nucleic acid of any one of embodiments 21 to 24.

26. A non-human host organism or a host cell that has been modified to express a receptor that is selected from the group consisting of OR2W1, OR1A1, OR2J3, OR4Q3, OR5K1, OR11A1, OR2M3, OR51E1, OR4S2, OR51I2, OR2H1, OR2W3, OR8G1, Olfr263, Olfr403, Olfr735, Olfr96, Olfr1193, Olfr641, Olfr137, Olfr173, Olfr164, Olfr1487, Olfr339, Olfr1126, Olfr558, Olfr93, Olfr398, Olfr120, Olfr1364, Olfr937, Olfr1322 and Olfr46.

A particular subgroup of ORs are OR2W1, OR1A1, OR2J3, OR4Q3, OR5K1, OR11A1, OR2M3, OR51E1, OR4S2, OR51I2, OR2H1, OR2W3, and OR8G1.

Another particular subgroup of ORs Olfr263, Olfr403, Olfr735, Olfr96, Olfr1193, Olfr641, Olfr137, Olfr173, Olfr164, Olfr1487, Olfr339, Olfr1126, Olfr558, Olfr93, Olfr398, Olfr120, Olfr1364, Olfr937, Olfr1322, and Olfr46.

27. The non-human host organism or host cell of embodiment 26, wherein the receptor comprises the polypeptide of embodiment 19 or a polypeptide encoded by the nucleic acid of any one of embodiments 21 to 24.

28. A non-human host organism or a host cell comprising

- the nucleic acid of any one of embodiments 21 to 24; or
- the expression vector of embodiment 25.

29. The non-human host organism or host cell of any one of embodiments 26 to 28, wherein the cell is a eukaryotic cell.

30. The non-human host organism or host cell of any one of embodiments 26 to 28, wherein the cell is a prokaryotic cell.

31. The non-human host organism or host cell of any one of embodiments 26 to 29, wherein the non-human host organism or host cell is selected from the group consisting of HEK293, CHO, *Xenopus oocytes*, COS, yeast and cells derived from the olfactory placode.

32. Use of a polypeptide that can be activated by a substance, selected from the group consisting of geonol, DMTS, 1-octen-3-ol, butyric acid, 3-methyl-2-hexenoic acid, 3-hydroxy-3-methyl-hexanoic acid, transpirol, and mixtures of at least two of said substances, comprising
5 an amino acid sequence having at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 57, 59, 61, 63, 65, 67, 69, 71, 73, or 75 for identifying a malodor modulating compound.

10 A particular subgroup of ORs of this embodiment is or is derived from SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18 or 20.

As illustrated herein, the ORs as identified according to the present invention are either specific for one single MCS or they may be activated by a panel of structurally different MCS. Therefore, the present invention allows different strategies for identifying a suitable
15 modulating substance.

For example, if an inhibitor just for Geonol is of interest making use the OR11A1 or OR2M3 in the assay method of the invention may be advisable.

For example, if an inhibitor for DTMS, and 1-octen-3ol and optionally for Geonol is of interest making use the OR2W3, OR5K1 or optionally OR1A1 in the assay method of the
20 invention may be advisable. Other assay strategies for identifying modulators antagonizing laundry malodor, moldy malodor or sweat malodor causing substances or even for identifying modulators which antagonize laundry malodor, moldy malodor and sweat malodor causing substances become evident from the experimental results disclosed herein.

Further provided is any one of a number of malodor modulating compounds that binds,
25 suppresses, blocks, inhibits, and/or modulates the activity of an olfactory receptor that is activated by a malodor-causing substance selected from the group consisting of geonol, DMTS, 1-octen-3-ol, butyric acid, 3-methyl-2-hexenoic acid, 3-hydroxy-3-methyl-hexanoic acid, transpirol, and mixtures of at least two of said substances, and that is identified by the methods disclosed herein.

According to one embodiment a malodor modulating compound is provided that binds, suppresses, blocks, inhibits, and/or modulates the activity of at least one olfactory receptor selected from the group consisting of OR2W1, OR1A1, OR2J3, OR4Q3, OR5K1, OR11A1, OR2M3, OR51E1, OR4S2, OR51I2, OR2H1, OR2W3, OR8G1, Olfr263, Olfr403, Olfr735, Olfr96, Olfr1193, Olfr641, Olfr137, Olfr173, Olfr164, Olfr1487, Olfr339, Olfr1126, Olfr558, Olfr93, Olfr398, Olfr120, Olfr1364, Olfr937, Olfr1322 and Olfr46, and that is identified by the methods disclosed herein. A particular subgroup of ORs of this embodiment is or is derived from OR2W1, OR1A1, OR2J3, OR4Q3, OR5K1, OR11A1, OR2M3, OR51E1, OR4S2, OR51I2, OR2H1, OR2W3, and OR8G1. Another particular subgroup of ORs are Olfr263, Olfr403, Olfr735, Olfr96, Olfr1193, Olfr641, Olfr137, Olfr173, Olfr164, Olfr1487, Olfr339, Olfr1126, Olfr558, Olfr93, Olfr398, Olfr120, Olfr1364, Olfr937, Olfr1322 and Olfr46.

The test substances to be tested in the method of the present invention are not particularly limited. The test substance may be a naturally occurring substance or a chemically or biologically synthesized artificial substance. The test substance may be a compound or a mixture of compounds.

In order to identify unknown receptors specific for the MCS geonol, DMTS, 1-octen-3-ol, butyric acid, 3-methyl-2-hexenoic acid, 3-hydroxy-3-methyl-hexanoic acid, or transpirol, said MCS compounds can be used to screen dissociated olfactory sensory neurons (OSNs). Said MCS compounds can be further used for cell-based dose-response experiments performed on specific receptors for said MCS to assess both specificity and sensitivity of the receptors.

In one aspect, provided herein are methods to identify mammalian odorant receptors for malodour modulating compounds and the use of the receptors for screening, particularly for high throughput screening (HTS) of malodor modulators (e.g. that bind, suppress, block, inhibit and/or modulate the activity of an OR).

Methods of Monitoring OR Activity

As long as the function of the OR is not impaired, it may be used in any form in a method of the present invention. For example, the OR may be use as follows: tissues or cells which intrinsically express an OR such as olfactory sensory neurons isolated from living
5 bodies and cultured products thereof; olfactory cell membrane bearing the OR; recombinant cells genetically modified so as to express the OR and cultured products thereof; membrane of the recombinant cells; and artificial lipid bilayer membrane carrying the OR.

In a further embodiment, indicators for monitoring the activity of olfactory receptors are selected from a fluorescent calcium indicator dye, a calcium indicator protein (e.g.
10 GcaMP, a genetically encoded calcium indicator), a fluorescent cAMP indicator, a cell mobilization assay, a cellular dynamic mass redistribution assay, a label-free cell based assay, a cAMP response element (CRE) mediated reporter protein, a biochemical cAMP HTRF assay, a beta-arrestin assay, or an electrophysiological recording. Particularly, a calcium indicator dye is selected that can be used to monitor the activity of olfactory receptors
15 expressed on the membrane of the olfactory neurons (e.g., Fura-2 AM).

In a particular embodiment, compounds are screened sequentially and the odorant-dependent changes in calcium dye fluorescence are measured using a fluorescent microscope or fluorescent-activated cell sorter (FACS).

In a further embodiment, molecular 3D receptor modeling of olfactory receptors is
20 used to assess the binding potential *in silico* and to identify compounds that may activate, mimic, block, inhibit, modulate, and/or enhance the activity of an olfactory receptor.

As an example, olfactory neurons activated by geonol, DMTS, 1-octen-3-ol, butyric acid, 3-methyl-2-hexenoic acid, 3-hydroxy-3-methyl-hexanoic acid or transpirol are isolated using either a glass capillary attached to a micromanipulator or a FACS machine. Mouse
25 olfactory sensory neurons are screened by Ca^{2+} imaging similar to procedures previously described [Malnic, B., et al. Cell 96, 713–723 (1999); Araneda, R. C. et al. J. Physiol. 555, 743–756 (2004); and WO2014/210585 hereby incorporated by reference in its entirety]. Particularly, a motorized movable microscope stage is used to increase the number of cells that can be screened to at least 1,500 per experiment. Since there are approximately 1,200
30 different olfactory receptors in the mouse and each olfactory sensory neurons expresses only 1 of 1,200 olfactory receptor genes, this screening capacity will cover virtually the entire mouse odorant receptor repertoire. In other words, the combination of calcium imaging for high-

throughput olfactory sensory neuron screening leads to the identification of nearly all of the odorant receptors that respond to a particular profile of odorants. In a particular aspect, odorant receptors that respond to geonol, DMTS, 1-octen-3-ol, butyric acid, 3-methyl-2-hexenoic acid, 3-hydroxy-3-methyl-hexanoic acid or transpirol can be isolated. For example, at least one neuron is isolated.

For calcium imaging of olfactory neurons, the main olfactory epithelium may be dissected from a mouse before neuronal dissociation. Dissected olfactory epithelium may then be transferred to a dissociation buffer for mechanical and enzymatic dissociation. Dissociated neurons may then be seeded onto a coverslip allowing the screening of thousands of cells by fluorescence microscopy and the cells may be loaded with a calcium sensitive dye (Fura-2 AM) for example for about 30 minutes at 31 °C and transferred onto the microscope ready for screening. Cells are stimulated by perfusing diluted solutions of odorants (in physiological saline) over the dissociated olfactory neurons. The rare cells that respond to the malodor compound are identified by for example stimulating the receptors with 50 µM of the malodor compounds and then by monitoring the intracellular Ca^{2+} flux indicated by changes in Fura-2 fluorescence. After analysis, responding cells may be retrieved from a glass coverslip with a suction micropipette. Isolated cells are then pooled into one sample or treated individually for subsequent identification of the odorant receptor genes expressed as mRNA in the responding cells.

In a particular embodiment, the mRNAs of olfactory neurons are purified and amplified according to the method generally described in Marko, N. F., *et al.*, (2005) A robust method for the amplification of RNA in the sense orientation. *BMC genomics*, 6, 27; doi:10.1186/1471-2164-6-27 (Eberwine method). At least a portion of the transcriptome (up to including the entire transcriptome) is sequenced using Next-Generation Sequencing (NGS) technologies or hybridized to known genes using Microarray technologies. NGS is generally discussed and described in Metzker, M. L. *Nat. Rev. Genet.* 11, 31–46 (2010). In a particular embodiment, a minimum of 5 neurons presenting the same response profile are pooled. The mRNAs are released by cell lysis immediately after picking; no DNase and no purification steps are carried out. The mRNA are amplified by two consecutive rounds of *in vitro* transcription (IVT). The amplification may be done according to MessageAmpII aRNA kit (Ambion, AMA1751) with the following parameters: two rounds of consecutive 14 hour long IVT.

In a further embodiment, the mRNA of a single olfactory neuron is purified and amplified with LD-PCR (Long Distance Polymerase Chain Reaction) based methods such as the one described in NGS-ready kits (e.g., Clontech/Takara, SMARTer® Ultra® Low Input RNA Kit for Sequencing - v3, cat. 634848). Single cell mRNA is first reverse transcribed into the corresponding cDNA, which subsequently is amplified with 18 PCR cycles and serves as NGS sample for transcriptome sequencing.

In yet another embodiment, the identity of a group or gene family of olfactory receptors for geonol, DMTS, 1-octen-3-ol, butyric acid, 3-methyl-2-hexenoic acid, 3-hydroxy-3-methyl-hexanoic acid or transpirol is determined (e.g., up to as many as the number of neurons picked) by comparing the results of the NGS reads obtained from the isolated activated olfactory sensory neurons to a reference genome sequence of the same species. Particularly, the putative receptors for geonol, DMTS, 1-octen-3-ol, butyric acid, 3-methyl-2-hexenoic acid, 3-hydroxy-3-methyl-hexanoic acid or transpirol will be the most highly abundant olfactory receptor mRNA in the olfactory neuron-derived NGS sample or present in more than one independent biological replicate. Because of the combinatorial nature of the olfactory code (one compound activates many ORs and one OR can be activated by many compounds), pooling several neurons activated by given compounds allows the retrieval of virtually all of the receptors responsible for the perception of these molecules in a single NGS experiment. Pooling functionally similar neurons thus greatly improves the deorphanization throughput and speed.

Standard bioinformatics tools are then used to identify the most closely related human odorant receptor(s) to other putative mammalian (non-human) receptor(s) for geonol, DMTS, 1-octen-3-ol, butyric acid, 3-methyl-2-hexenoic acid, 3-hydroxy-3-methyl-hexanoic acid or transpirol under the assumption that homologous sequence receptors retain similar function. Several methods successfully identify human OR-ligand pairs based on this assumption [Armelin-Correa and Malnic (2017)] and up to 80% of mouse-human orthologs appear to maintain similar functional response profiles [Adipietro, K. A, et al. PLoS Genet. 8, e1002821–e1002821 (2012)]. Default parameters of BLASTP and/or BLASTN algorithm, or other ortholog pair identification algorithms such as InParanoid may be used.

The human or non-human mammalian receptors for geonol, DMTS, 1-octen-3-ol, butyric acid, 3-methyl-2-hexenoic acid, 3-hydroxy-3-methyl-hexanoic acid or transpirol may be adapted to a functional assay that can be used to identify compounds that bind, suppress,

block, inhibit, and/or modulate the activity of the olfactory receptors. In particular, the assay may be a cell-based assay or a binding assay and the method for identifying compounds may be a high-throughput screening assay. More particularly, provided herein are receptor-based assays adaptable for high-throughput screening of receptors with compound libraries for the discovery of modulating compounds (e.g., binding, blocking, inhibiting, suppressing and masking).

In a particular embodiment, geonol, DMTS, 1-octen-3-ol, butyric acid, 3-methyl-2-hexenoic acid, 3-hydroxy-3-methyl-hexanoic acid or transpirol receptor gene sequences are identified from geonol, DMTS, 1-octen-3-ol, butyric acid, 3-methyl-2-hexenoic acid, 3-hydroxy-3-methyl-hexanoic acid or transpirol -sensitive cells as follows: Pooled neurons are heated to 75°C for 10 minutes to break the cell membrane and render their mRNA available for amplification. This amplification step is important when applying NGS technologies with limited amount of starting material, typically between 1 to 15 cells. A linear amplification according to the Eberwine method (IVT) ensures the maintenance of the relative transcription levels of expressed genes. Two consecutive overnight (14h) rounds of *in vitro* transcription are used to yield sufficient amounts of cRNA; Amplified cRNA is then used to generate an Illumina HiSeq cDNA library. The resulting short sequences of typically 75 to 150 base pairs (commonly referred to as "reads") are aligned against the reference genome of the mouse (such as UCSC version mm9 or mm10) in order to build the full transcriptome of these cells. Quantitative analysis of the transcriptome data yields a list of transcribed odorant receptor genes and their respective expression levels. Odorant receptor genes that show the most abundant levels of mRNA (most abundant "reads") or are present in more than one replicate experiment are considered putative geonol, DMTS, 1-octen-3-ol, butyric acid, 3-methyl-2-hexenoic acid, 3-hydroxy-3-methyl-hexanoic acid or transpirol receptors.

The predicted mouse OR genes are then used to mine the latest versions of both the mouse and human genome databases in order to identify the most closely related receptors (i.e. highest sequence similarity) in mouse (paralogous genes) and in human (orthologous genes). This process may be performed using the BLAST search algorithm (publically available at the NCBI website), a sequence similarity search tool, where every putative gene sequence previously obtained from the initial transcriptome analysis is used as a query sequence. The newly identified genes identified from this data mining process are considered to be potential geonol, DMTS, 1-octen-3-ol, butyric acid, 3-methyl-2-hexenoic acid, 3-hydroxy-3-methyl-hexanoic acid or transpirol receptors under the assumption that paralogous

and orthologous genes are highly likely to possess similar activities. In a particular embodiment, pairwise comparison of sequence homology is carried out to identify closely related receptors in mouse and humans and the receptors are identified as described in WO2014/210585. Other approaches may also be used such as RT-PCR and microarray approaches.

In a further embodiment, to complete the deorphanization process, the candidate OR genes are further expressed *in vitro* for confirmation of activity against the compounds used to isolate the olfactory sensory neurons and other structurally-related compounds of interest. The mouse receptors identified from isolated olfactory neurons that respond to geonol, DMTS, 1-octen-3-ol, butyric acid, 3-methyl-2-hexenoic acid, 3-hydroxy-3-methyl-hexanoic acid or transpirol are modified at their N-terminus with short polypeptide sequences (e.g., FLAG[®] (SEQ ID NO: 48), Rho (SEQ ID NO: 50; 20 first amino acids of the bovine rhodopsin receptor), and/or Lucy (SEQ ID NO: 52; cleavable leucine-rich signal peptide sequence) tags), transiently expressed in HEK 293T cells, and stimulated separately with geonol, DMTS, 1-octen-3-ol, butyric acid, 3-methyl-2-hexenoic acid, 3-hydroxy-3-methyl-hexanoic acid or transpirol to confirm their identity as bona fide geonol, dimethyl trisulfide (DMTS), 1-octen-3-ol, butyric acid, 3-methyl-2-hexenoic acid, 3-hydroxy-3-methyl-hexanoic acid or transpirol receptors. In a further embodiment, an RTP1 gene can also be expressed in the cell lines whether through activation of the endogenous RTP1 gene or through transformation. Co-expression of the human G alpha subunit G α_{olf} in this cell-based assay activates the Gs transduction pathway that leads to an internal cAMP increase upon binding to the appropriate ligand. Alternatively, co-expression of the human G alpha subunit G α_{15} in the cell based assay activates the Gq transduction pathway that leads to an internal Ca²⁺ increase upon binding to the appropriate ligand. The above process and the results obtained so far serve to validate the process for rapid and reliable identification of mammalian odorant receptors for geonol, DMTS, 1-octen-3-ol, butyric acid, 3-methyl-2-hexenoic acid, 3-hydroxy-3-methyl-hexanoic acid or transpirol.

Further provided are assays for identifying compounds that bind to geonol, DMTS, 1-octen-3-ol, butyric acid, 3-methyl-2-hexenoic acid, 3-hydroxy-3-methyl-hexanoic acid or transpirol odorant receptors. In a further embodiment provided herein is a malodor modulating compound that binds, suppresses, blocks, inhibits, and/or modulates the activity of at least one olfactory receptor selected from the group consisting of OR2W1, OR1A1, OR2J3, OR4Q3, OR5K1, OR11A1, OR2M3, OR51E1, OR4S2, OR51I2, OR2H1, OR2W3, OR8G1, Olfr263, Olfr403, Olfr735, Olfr96, Olfr1193, Olfr641, Olfr137, Olfr173, Olfr164, Olfr1487, Olfr339, Olfr1126, Olfr558, Olfr93, Olfr398, Olfr120, Olfr1364, Olfr937, Olfr1322 and Olfr46 and that is identified by the methods described herein, for example, the compounds described herein below.

In one embodiment the activity of the compound is determined by comparing its binding to that of geonol, DMTS, 1-octen-3-ol, butyric acid, 3-methyl-2-hexenoic acid, 3-hydroxy-3-methyl-hexanoic acid or transpirol. In another embodiment, the receptor or a chimera or fragment thereof is contacted with a compound in the presence of geonol, DMTS, 1-octen-3-ol, butyric acid, 3-methyl-2-hexenoic acid, 3-hydroxy-3-methyl-hexanoic acid or transpirol under conditions that allow for the binding of the compound along with geonol, DMTS, 1-octen-3-ol, butyric acid, 3-methyl-2-hexenoic acid, 3-hydroxy-3-methyl-hexanoic acid or transpirol to the receptor.

In a further embodiment, a compound is contacted to a receptor, or a chimera or fragment thereof that is activated by geonol, DMTS, 1-octen-3-ol, butyric acid, 3-methyl-2-hexenoic acid, 3-hydroxy-3-methyl-hexanoic acid or transpirol, wherein the receptor, or a chimera or fragment thereof is expressed in a cell that is recombinantly modified to express the receptor polypeptide.

The activity of the compound can be determined using *in vivo*, *ex vivo*, *in vitro* and synthetic screening systems.

In another embodiment, the contacting is performed with liposomes or virus-induced budding membranes containing the polypeptides described herein.

In another embodiment, the methods for identifying compounds that bind, suppress, block, inhibit, and/or modulate the activity of an olfactory receptor that can be activated by geonol, DMTS, 1-octen-3-ol, butyric acid, 3-methyl-2-hexenoic acid, 3-hydroxy-3-methyl-hexanoic acid or transpirol, may be performed on intact cells or a membrane fraction from cells expressing the polypeptides described here.

The ORs described herein are therefore involved in the perception of malodor elicited by geonol, DMTS, 1-octen-3-ol, butyric acid, 3-methyl-2-hexenoic acid, 3-hydroxy-3-methyl-hexanoic acid or transpirol and constitute valuable candidate receptors for the identification of modulators, antagonists and/or blockers that would modulate, reduce, suppress, inhibit and/or
5 block the perception of laundry malodor, moldy malodor and/or sweat malodor.

Polypeptides applicable according to the invention

The present invention relates to "functional equivalents" or "analogs" or "functional mutations" of the polypeptides specifically described herein.

10 For example, "functional equivalents" refer to polypeptides which, in a test used for OR activity, display at least a 1 to 10 %, or at least 20 %, or at least 50 %, or at least 75 %, or at least 90 % higher or lower OR activity, as defined herein.

"Functional equivalents", according to the invention, also cover particular mutants, which, in at least one sequence position of the amino acid sequences stated herein, have an
15 amino acid that is different from that concretely stated, but nevertheless possess one of the aforementioned biological activities. "Functional equivalents" thus comprise the mutants obtainable by one or more, like 1 to 20, 1 to 15 or 5 to 10 amino acid additions, substitutions, in particular conservative substitutions, deletions and/or inversions, where the stated changes can occur in any sequence position, provided they lead to a mutant with the profile of
20 properties according to the invention. Functional equivalence is in particular also provided if the activity patterns coincide qualitatively between the mutant and the unchanged polypeptide, i.e. if, for example, interaction with the same agonist or antagonist, however at a different rate, (i.e. expressed by an EC_{50} or IC_{50} value or any other parameter suitable in the present technical field) is observed. Examples of suitable (conservative) amino acid substitutions are shown in
25 the following table:

Original residue	Examples of substitution
Ala	Ser
Arg	Lys
Asn	Gln; His
Asp	Glu
Cys	Ser
Gln	Asn
Glu	Asp
Gly	Pro
His	Asn; Gln
Ile	Leu; Val
Leu	Ile; Val
Lys	Arg; Gln; Glu
Met	Leu; Ile
Phe	Met; Leu; Tyr
Ser	Thr
Thr	Ser
Trp	Tyr
Tyr	Trp; Phe
Val	Ile; Leu

"Functional equivalents" in the above sense are also "precursors" of the polypeptides described, as well as "functional derivatives" and "salts" of the polypeptides.

- 5 "Precursors" are in that case natural or synthetic precursors of the polypeptides with or without the desired biological activity.

The expression "salts" means salts of carboxyl groups as well as salts of acid addition of amino groups of the protein molecules according to the invention. Salts of carboxyl groups can be produced in a known way and comprise inorganic salts, for example sodium, calcium, ammonium, iron and zinc salts, and salts with organic bases, for example amines, such as triethanolamine, arginine, lysine, piperidine and the like. Salts of acid addition, for example salts with inorganic acids, such as hydrochloric acid or sulfuric acid and salts with organic acids, such as acetic acid and oxalic acid, are also covered by the invention.

"Functional derivatives" of polypeptides according to the invention can also be produced on functional amino acid side groups or at their N-terminal or C-terminal end using known techniques. Such derivatives comprise for example aliphatic esters of carboxylic acid groups, amides of carboxylic acid groups, obtainable by reaction with ammonia or with a primary or secondary amine; N-acyl derivatives of free amino groups, produced by reaction with acyl groups; or O-acyl derivatives of free hydroxyl groups, produced by reaction with acyl groups.

"Functional equivalents" naturally also comprise polypeptides that can be obtained from other organisms, as well as naturally occurring variants. For example, areas of homologous sequence regions can be established by sequence comparison, and equivalent polypeptides can be determined on the basis of the concrete parameters of the invention.

"Functional equivalents" also comprise fragments, preferably individual domains or sequence motifs, of the polypeptides according to the invention, which for example display the desired biological function.

"Functional equivalents" are, moreover, fusion proteins, which have one of the polypeptide sequences stated herein or functional equivalents derived there from and at least one further, functionally different, heterologous sequence in functional N-terminal or C-terminal association (i.e. without substantial mutual functional impairment of the fusion protein parts). Non-limiting examples of these heterologous sequences are e.g. signal peptides, histidine anchors or enzymes.

"Functional equivalents" which are also comprised in accordance with the invention are homologs to the specifically disclosed polypeptides. These have at least 60%, preferably at least 75%, in particular at least 80 or 85%, such as, for example, 90, 91, 92, 93, 94, 95, 96, 97, 98 or 99%, homology (or identity) to one of the specifically disclosed amino acid sequences, calculated by the algorithm of Pearson and Lipman, Proc. Natl. Acad. Sci. (USA) 85(8), 1988, 2444-2448. A homology or identity, expressed as a percentage, of a homologous polypeptide according to the invention means in particular an identity, expressed as a percentage, of the amino acid residues based on the total length of one of the amino acid sequences described specifically herein.

The identity data, expressed as a percentage, may also be determined with the aid of BLAST alignments, algorithm blastp (protein-protein BLAST), or by applying the Clustal settings specified herein below.

In the case of a possible protein glycosylation, "functional equivalents" according to the invention comprise polypeptides as described herein in deglycosylated or glycosylated form as well as modified forms that can be obtained by altering the glycosylation pattern.

Such functional equivalents or homologues of the polypeptides according to the invention can be produced by mutagenesis, e.g. by point mutation, lengthening or shortening of the protein or as described in more detail below.

Such functional equivalents or homologues of the polypeptides according to the invention can be identified by screening combinatorial databases of mutants, for example shortening mutants. For example, a variegated database of protein variants can be produced by combinatorial mutagenesis at the nucleic acid level, e.g. by enzymatic ligation of a mixture of synthetic oligonucleotides. There are a great many methods that can be used for the production of databases of potential homologues from a degenerated oligonucleotide sequence. Chemical synthesis of a degenerated gene sequence can be carried out in an automatic DNA synthesizer, and the synthetic gene can then be ligated in a suitable expression vector. The use of a degenerated genome makes it possible to supply all sequences in a mixture, which code for the desired set of potential protein sequences. Methods of synthesis of degenerated oligonucleotides are known to a person skilled in the art (e.g. Narang, S.A. (1983); Itakura et al. (1984) (a); Itakura et al., (1984) (b); Ike et al. (1983)).

In the prior art, several techniques are known for the screening of gene products of combinatorial databases, which were produced by point mutations or shortening, and for the screening of cDNA libraries for gene products with a selected property. These techniques can be adapted for the rapid screening of the gene banks that were produced by combinatorial mutagenesis of homologues according to the invention. The techniques most frequently used for the screening of large gene banks, which are based on a high-throughput analysis, comprise cloning of the gene bank in expression vectors that can be replicated, transformation of the suitable cells with the resultant vector database and expression of the combinatorial genes in conditions in which detection of the desired activity facilitates isolation of the vector that codes for the gene whose product was detected. Recursive Ensemble Mutagenesis (REM), a technique that increases the frequency of functional mutants in the databases, can be used in combination with the screening tests, in order to identify homologues (Arkin and Yourvan (1992); Delgrave et al. (1993)).

Coding nucleic acid sequences applicable according to the invention

The invention also relates to nucleic acid sequences that code for polypeptides as defined herein.

The present invention also relates to nucleic acids with a certain degree of "identity" to the sequences specifically disclosed herein. "Identity" between two nucleic acids means identity of the nucleotides, in each case over the entire length of the nucleic acid.

For example the identity may be calculated by means of the Vector NTI Suite 7.1 program of the company Informax (USA) employing the Clustal Method (Higgins DG, Sharp PM. ((1989))) with the following settings:

	Multiple alignment parameter:	
	Gap opening penalty	10
	Gap extension penalty	10
5	Gap separation penalty range	8
	Gap separation penalty	off
	% identity for alignment delay	40
	Residue specific gaps	off
	Hydrophilic residue gap	off
10	Transition weighing	0
Pairwise alignment parameter:		
	FAST algorithm	on
	K-tuple size	1
15	Gap penalty	3
	Window size	5
	Number of best diagonals	5

Alternatively the identity may be determined according to Chenna, et al. (2003), the
 20 web page: <http://www.ebi.ac.uk/Tools/clustalw/index.html#> and the following settings:

	DNA Gap Open Penalty	15.0
	DNA Gap Extension Penalty	6.66
	DNA Matrix	Identity
25	Protein Gap Open Penalty	10.0
	Protein Gap Extension Penalty	0.2
	Protein matrix	Gonnet
	Protein/DNA ENDGAP	-1
30	Protein/DNA GAPDIST	4

All the nucleic acid sequences mentioned herein (single-stranded and double-stranded DNA and RNA sequences, for example cDNA and mRNA) can be produced in a known way by chemical synthesis from the nucleotide building blocks, e.g. by fragment condensation of individual overlapping, complementary nucleic acid building blocks of the double helix.
 35 Chemical synthesis of oligonucleotides can, for example, be performed in a known way, by the phosphoramidite method (Voet, Voet, 2nd edition, Wiley Press, New York, pages 896-897). The accumulation of synthetic oligonucleotides and filling of gaps by means of the Klenow fragment of DNA polymerase and ligation reactions as well as general cloning techniques are described in Sambrook et al. (1989), see below.

The invention also relates to nucleic acid sequences (single-stranded and double-stranded DNA and RNA sequences, e.g. cDNA and mRNA), coding for one of the above polypeptides and their functional equivalents, which can be obtained for example using artificial nucleotide analogs.

5 The invention relates both to isolated nucleic acid molecules, which code for polypeptides according to the invention or biologically active segments thereof, and to nucleic acid fragments, which can be used for example as hybridization probes or primers for identifying or amplifying coding nucleic acids according to the invention.

10 The nucleic acid molecules according to the invention can in addition contain non-translated sequences from the 3' and/or 5' end of the coding genetic region.

The invention further relates to the nucleic acid molecules that are complementary to the concretely described nucleotide sequences or a segment thereof.

15 The nucleotide sequences according to the invention make possible the production of probes and primers that can be used for the identification and/or cloning of homologous sequences in other cellular types and organisms. Such probes or primers generally comprise a nucleotide sequence region which hybridizes under "stringent" conditions (see below) on at least about 12, preferably at least about 25, for example about 40, 50 or 75 successive nucleotides of a sense strand of a nucleic acid sequence according to the invention or of a corresponding antisense strand.

20 An "isolated" nucleic acid molecule is separated from other nucleic acid molecules that are present in the natural source of the nucleic acid and can moreover be substantially free from other cellular material or culture medium, if it is being produced by recombinant techniques, or can be free from chemical precursors or other chemicals, if it is being synthesized chemically.

25 A nucleic acid molecule according to the invention can be isolated by means of standard techniques of molecular biology and the sequence information supplied according to the invention. For example, cDNA can be isolated from a suitable cDNA library, using one of the concretely disclosed complete sequences or a segment thereof as hybridization probe and standard hybridization techniques (as described for example in Sambrook, (1989)). In
30 addition, a nucleic acid molecule comprising one of the disclosed sequences or a segment thereof, can be isolated by the polymerase chain reaction, using the oligonucleotide primers

that were constructed on the basis of this sequence. The nucleic acid amplified in this way can be cloned in a suitable vector and can be characterized by DNA sequencing. The oligonucleotides according to the invention can also be produced by standard methods of synthesis, e.g. using an automatic DNA synthesizer.

5 Nucleic acid sequences according to the invention or derivatives thereof, homologues or parts of these sequences, can for example be isolated by usual hybridization techniques or the PCR technique from other bacteria, e.g. via genomic or cDNA libraries. These DNA sequences hybridize in standard conditions with the sequences according to the invention.

10 "Hybridize" means the ability of a polynucleotide or oligonucleotide to bind to an almost complementary sequence in standard conditions, whereas nonspecific binding does not occur between non-complementary partners in these conditions. For this, the sequences can be 90-100 % complementary. The property of complementary sequences of being able to bind specifically to one another is utilized for example in Northern Blotting or Southern Blotting or in primer binding in PCR or RT-PCR.

15 Short oligonucleotides of the conserved regions are used advantageously for hybridization. However, it is also possible to use longer fragments of the nucleic acids according to the invention or the complete sequences for the hybridization. These standard conditions vary depending on the nucleic acid used (oligonucleotide, longer fragment or complete sequence) or depending on which type of nucleic acid – DNA or RNA – is used for
20 hybridization. For example, the melting temperatures for DNA:DNA hybrids are approx. 10 °C lower than those of DNA:RNA hybrids of the same length.

For example, depending on the particular nucleic acid, standard conditions mean temperatures between 42 and 58 °C in an aqueous buffer solution with a concentration between 0.1 to 5 x SSC (1 X SSC = 0.15 M NaCl, 15 mM sodium citrate, pH 7.2) or
25 additionally in the presence of 50 % formamide, for example 42 °C in 5 x SSC, 50 % formamide. Advantageously, the hybridization conditions for DNA:DNA hybrids are 0.1 x SSC and temperatures between about 20 °C to 45 °C, preferably between about 30 °C to 45 °C. For DNA:RNA hybrids the hybridization conditions are advantageously 0.1 x SSC and temperatures between about 30 °C to 55 °C, preferably between about 45 °C to 55 °C. These
30 stated temperatures for hybridization are examples of calculated melting temperature values for a nucleic acid with a length of approx. 100 nucleotides and a G + C content of 50 % in the absence of formamide. The experimental conditions for DNA hybridization are described in

relevant genetics textbooks, for example Sambrook et al., 1989, and can be calculated using formulae that are known by a person skilled in the art, for example depending on the length of the nucleic acids, the type of hybrids or the G + C content. A person skilled in the art can obtain further information on hybridization from the following textbooks: Ausubel et al. (eds),
5 (1985), Brown (ed) (1991).

"Hybridization" can in particular be carried out under stringent conditions. Such hybridization conditions are for example described in Sambrook (1989), or in Current Protocols in Molecular Biology, John Wiley & Sons, N.Y. (1989), 6.3.1-6.3.6.

As used herein, the term hybridization or hybridizes under certain conditions is
10 intended to describe conditions for hybridization and washes under which nucleotide sequences that are significantly identical or homologous to each other remain bound to each other. The conditions may be such that sequences, which are at least about 70%, such as at least about 80%, and such as at least about 85%, 90%, or 95% identical, remain bound to each other. Definitions of low stringency, moderate, and high stringency hybridization conditions
15 are provided herein.

Appropriate hybridization conditions can be selected by those skilled in the art with minimal experimentation as exemplified in Ausubel et al. (1995, *Current Protocols in Molecular Biology*, John Wiley & Sons, sections 2, 4, and 6). Additionally, stringency conditions are described in Sambrook et al. (1989, *Molecular Cloning: A Laboratory Manual*,
20 2nd ed., Cold Spring Harbor Press, chapters 7, 9, and 11).

As used herein, defined conditions of low stringency are as follows. Filters containing DNA are pretreated for 6 h at 40°C in a solution containing 35% formamide, 5x SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.1% PVP, 0.1% Ficoll, 1% BSA, and 500 µg/ml denatured salmon sperm DNA. Hybridizations are carried out in the same solution with the following
25 modifications: 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 µg/ml salmon sperm DNA, 10% (wt/vol) dextran sulfate, and 5-20x10⁶ 32P-labeled probe is used. Filters are incubated in hybridization mixture for 18-20 h at 40°C, and then washed for 1.5 h at 55°C. In a solution containing 2x SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS. The wash solution is replaced with fresh solution and incubated an additional 1.5 h at 60°C. Filters are
30 blotted dry and exposed for autoradiography.

As used herein, defined conditions of moderate stringency are as follows. Filters containing DNA are pretreated for 7 h at 50°C. in a solution containing 35% formamide, 5x SSC, 50 mM Tris-HCl (pH 7.5), 5 mM EDTA, 0.1% PVP, 0.1% Ficoll, 1% BSA, and 500 µg/ml denatured salmon sperm DNA. Hybridizations are carried out in the same solution with the following modifications: 0.02% PVP, 0.02% Ficoll, 0.2% BSA, 100 µg/ml salmon sperm DNA, 10% (wt/vol) dextran sulfate, and 5-20x10⁶ 32P-labeled probe is used. Filters are incubated in hybridization mixture for 30 h at 50°C, and then washed for 1.5 h at 55°C. In a solution containing 2x SSC, 25 mM Tris-HCl (pH 7.4), 5 mM EDTA, and 0.1% SDS. The wash solution is replaced with fresh solution and incubated an additional 1.5 h at 60°C. Filters are blotted dry and exposed for autoradiography.

As used herein, defined conditions of high stringency are as follows. Prehybridization of filters containing DNA is carried out for 8 h to overnight at 65°C in buffer composed of 6x SSC, 50 mM Tris-HCl (pH 7.5), 1 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.02% BSA, and 500 µg/ml denatured salmon sperm DNA. Filters are hybridized for 48 h at 65°C in the prehybridization mixture containing 100 µg /ml denatured salmon sperm DNA and 5-20x10⁶ cpm of 32P-labeled probe. Washing of filters is done at 37°C for 1 h in a solution containing 2x SSC, 0.01% PVP, 0.01% Ficoll, and 0.01% BSA. This is followed by a wash in 0.1x SSC at 50°C for 45 minutes.

Other conditions of low, moderate, and high stringency well known in the art (e.g., as employed for cross-species hybridizations) may be used if the above conditions are inappropriate (e.g., as employed for cross-species hybridizations).

The invention also relates to derivatives of the concretely disclosed or derivable nucleic acid sequences.

Thus, further nucleic acid sequences according to the invention can be derived from the sequences specifically disclosed herein and can differ from it by addition, substitution, insertion or deletion of individual or several nucleotides, and furthermore code for polypeptides with the desired profile of properties.

The invention also encompasses nucleic acid sequences that comprise so-called silent mutations or have been altered, in comparison with a concretely stated sequence, according to the codon usage of a special original or host organism, as well as naturally occurring variants, e.g. splicing variants or allelic variants, thereof.

It also relates to sequences that can be obtained by conservative nucleotide substitutions (i.e. the amino acid in question is replaced by an amino acid of the same charge, size, polarity and/or solubility).

5 The invention also relates to the molecules derived from the concretely disclosed nucleic acids by sequence polymorphisms. These genetic polymorphisms can exist between individuals within a population owing to natural variation. These natural variations usually produce a variance of 1 to 5 % in the nucleotide sequence of a gene.

10 Derivatives of nucleic acid sequences according to the invention mean for example allelic variants, having at least 60 % homology at the level of the derived amino acid, preferably at least 80 % homology, quite especially preferably at least 90 % homology over the entire sequence range (regarding homology at the amino acid level, reference should be made to the details given above for the polypeptides). Advantageously, the homologies can be higher over partial regions of the sequences.

15 Furthermore, derivatives are also to be understood to be homologues of the nucleic acid sequences according to the invention, for example animal, plant, fungal or bacterial homologues, shortened sequences, single-stranded DNA or RNA of the coding and noncoding DNA sequence. For example, homologues have, at the DNA level, a homology of at least 40 %, preferably of at least 60 %, especially preferably of at least 70 %, quite especially preferably of at least 80 % over the entire DNA region given in a sequence specifically
20 disclosed herein.

Moreover, derivatives are to be understood to be, for example, fusions with promoters. The promoters that are added to the stated nucleotide sequences can be modified by at least one nucleotide exchange, at least one insertion, inversion and/or deletion, though without impairing the functionality or efficacy of the promoters. Moreover, the efficacy of the
25 promoters can be increased by altering their sequence or can be exchanged completely with more effective promoters even of organisms of a different genus.

Generation of functional polypeptide mutants

Moreover, a person skilled in the art is familiar with methods for generating functional mutants, that is to say nucleotide sequences which code for a polypeptide with at least 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% sequence identity to anyone of SEQ ID NO. 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 57, 59, 61, 63, 65, 67, 69, 71, 73, or 75; and/or encoded by a nucleic acid molecule comprising a nucleotide sequence having at least 70% sequence identity to SEQ ID NO: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, or the reverse complement thereof.

Depending on the technique used, a person skilled in the art can introduce entirely random or else more directed mutations into genes or else noncoding nucleic acid regions (which are for example important for regulating expression) and subsequently generate genetic libraries. The methods of molecular biology required for this purpose are known to the skilled worker and for example described in Sambrook and Russell, *Molecular Cloning*. 3rd Edition, Cold Spring Harbor Laboratory Press 2001.

Methods for modifying genes and thus for modifying the polypeptide encoded by them have been known to the skilled worker for a long time, such as, for example

- site-specific mutagenesis, where individual or several nucleotides of a gene are replaced in a directed fashion (Trower MK (Ed.) 1996; *In vitro* mutagenesis protocols. Humana Press, New Jersey),

- saturation mutagenesis, in which a codon for any amino acid can be exchanged or added at any point of a gene (Kegler-Ebo DM, Docktor CM, DiMaio D (1994) *Nucleic Acids Res* 22:1593; Barettino D, Feigenbutz M, Valcárel R, Stunnenberg HG (1994) *Nucleic Acids Res* 22:541; Barik S (1995) *Mol Biotechnol* 3:1),

- error-prone polymerase chain reaction, where nucleotide sequences are mutated by error-prone DNA polymerases (Eckert KA, Kunkel TA (1990) *Nucleic Acids Res* 18:3739);

- the SeSaM method (sequence saturation method), in which preferred exchanges are prevented by the polymerase. Schenk et al., *Biospektrum*, Vol. 3, 2006, 277-279

- the passaging of genes in mutator strains, in which, for example owing to defective DNA repair mechanisms, there is an increased mutation rate of nucleotide sequences (Greener A, Callahan M, Jerpseth B (1996) An efficient random mutagenesis technique using an E.coli mutator strain. In: Trower MK (Ed.) In vitro mutagenesis protocols. Humana Press, New Jersey), or

- DNA shuffling, in which a pool of closely related genes is formed and digested and the fragments are used as templates for a polymerase chain reaction in which, by repeated strand separation and reassociation, full-length mosaic genes are ultimately generated (Stemmer WPC (1994) Nature 370:389; Stemmer WPC (1994) Proc Natl Acad Sci USA 91:10747).

Using so-called directed evolution (described, inter alia, in Reetz MT and Jaeger K-E (1999), Topics Curr Chem 200:31; Zhao H, Moore JC, Volkov AA, Arnold FH (1999), Methods for optimizing industrial polypeptides by directed evolution, In: Demain AL, Davies JE (Ed.) Manual of industrial microbiology and biotechnology. American Society for Microbiology), a skilled worker can produce functional mutants in a directed manner and on a large scale. To this end, in a first step, gene libraries of the respective polypeptides are first produced, for example using the methods given above. The gene libraries are expressed in a suitable way, for example by bacteria or by phage display systems.

The relevant genes of host organisms which express functional mutants with properties that largely correspond to the desired properties can be submitted to another mutation cycle. The steps of the mutation and selection or screening can be repeated iteratively until the present functional mutants have the desired properties to a sufficient extent. Using this iterative procedure, a limited number of mutations, for example 1, 2, 3, 4 or 5 mutations, can be performed in stages and assessed and selected for their influence on the activity in question. The selected mutant can then be submitted to a further mutation step in the same way. In this way, the number of individual mutants to be investigated can be reduced significantly.

The results according to the invention also provide important information relating to structure and sequence of the relevant polypeptides, which is required for generating, in a targeted fashion, further polypeptides with desired modified properties. In particular, it is possible to define so-called "hot spots", i.e. sequence segments that are potentially suitable for modifying a property by introducing targeted mutations.

Information can also be deduced regarding amino acid sequence positions, in the region of which mutations can be effected that should probably have little effect on the activity, and can be designated as potential "silent mutations".

Constructs for preparing polypeptides of the invention

The nucleotide sequence as described above may be part of an expression cassette. The terms expression cassette and expression construct are used synonymously. The preferably recombinant expression construct contains a nucleotide sequence which encodes a polypeptide according to the invention and which is under genetic control of regulatory nucleic acid sequences.

In a process applied according to the invention, the expression cassette may be part of an expression vector, in particular of a recombinant expression vector.

An "expression unit" is understood as meaning, in accordance with the invention, a nucleic acid with expression activity which comprises a promoter as defined herein and, after functional linkage with a nucleic acid to be expressed or a gene, regulates the expression, i.e. the transcription and the translation of said nucleic acid or said gene. It is therefore in this connection also referred to as a "regulatory nucleic acid sequence". In addition to the promoter, other regulatory elements, for example enhancers, can also be present.

An "expression cassette" or "expression construct" is understood as meaning, in accordance with the invention, an expression unit which is functionally linked to the nucleic acid to be expressed or the gene to be expressed. In contrast to an expression unit, an expression cassette therefore comprises not only nucleic acid sequences which regulate transcription and translation, but also the nucleic acid sequences that are to be expressed as protein as a result of transcription and translation.

The terms "expression" or "overexpression" describe, in the context of the invention, the production or increase in intracellular activity of one or more polypeptides in a microorganism, which are encoded by the corresponding DNA. To this end, it is possible for example to introduce a gene into an organism, replace an existing gene with another gene, increase the copy number of the gene(s), use a strong promoter or use a gene which encodes for a corresponding polypeptide with a high activity; optionally, these measures can be combined.

Preferably such constructs according to the invention comprise a promoter 5'-upstream of the respective coding sequence and a terminator sequence 3'-downstream and optionally other usual regulatory elements, in each case in operative linkage with the coding sequence.

A "promoter", a "nucleic acid with promoter activity" or a "promoter sequence" is understood as meaning, in accordance with the invention, a nucleic acid which, when functionally linked to a nucleic acid to be transcribed, regulates the transcription of said nucleic acid.

In this context, a "functional" or "operative" linkage is understood as meaning for example the sequential arrangement of one of the nucleic acids with promoter activity and of a nucleic acid sequence to be transcribed and optionally further regulatory elements, for example nucleic acid sequences which ensure the transcription of nucleic acids, and for example a terminator, in such a way that each of the regulatory elements can perform its function upon transcription of the nucleic acid sequence. This does not necessarily require a direct linkage in the chemical sense. Genetic control sequences, for example enhancer sequences, can even exert their function on the target sequence from more remote positions or even from other DNA molecules. Preferred arrangements are those in which the nucleic acid sequence to be transcribed is positioned behind (i.e. at the 3'-end of) the promoter sequence so that the two sequences are joined together covalently. The distance between the promoter sequence and the nucleic acid sequence to be expressed recombinantly can be smaller than 200 base pairs, or smaller than 100 base pairs or smaller than 50 base pairs.

In addition to promoters and terminator, the following may be mentioned as examples of other regulatory elements: targeting sequences, enhancers, polyadenylation signals, selectable markers, amplification signals, replication origins and the like. Suitable regulatory sequences are described, for example, in Goeddel, Gene Expression Technology: Methods in Enzymology 185, Academic Press, San Diego, CA (1990).

Nucleic acid constructs according to the invention comprise in particular a sequence coding for a polypeptide for example derived from SEQ ID No. 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, or the reverse complement thereof, or derivatives and homologs thereof, and the nucleic acid sequences which can be derived therefrom and which have been linked operatively or functionally with one or more regulatory signals, advantageously for controlling, for example increasing, gene expression.

In addition to these regulatory sequences, the natural regulation of these sequences may still be present before the actual structural genes and optionally may have been genetically modified so that the natural regulation has been switched off and expression of the genes has been enhanced. The nucleic acid construct may, however, also be of simpler construction, i.e. no additional regulatory signals have been inserted before the coding sequence and the natural promoter, with its regulation, has not been removed. Instead, the natural regulatory sequence is mutated such that regulation no longer takes place and the gene expression is increased.

A preferred nucleic acid construct advantageously also comprises one or more of the already mentioned "enhancer" sequences in functional linkage with the promoter, which sequences make possible an enhanced expression of the nucleic acid sequence. Additional advantageous sequences may also be inserted at the 3'-end of the DNA sequences, such as further regulatory elements or terminators. One or more copies of the nucleic acids according to the invention may be present in a construct. In the construct, other markers, such as genes which complement auxotrophisms or antibiotic resistances, may also optionally be present so as to select for the construct.

Examples of suitable regulatory sequences are present in promoters such as cos, tac, trp, tet, trp-tet, lpp, lac, lpp-lac, lacI^q, T7, T5, T3, gal, trc, ara, rhaP (rhaP_{BAD})SP6, lambda-P_R or in the lambda-P_L promoter, and these are advantageously employed in Gram-negative bacteria. Further advantageous regulatory sequences are present for example in the Gram-positive promoters amy and SPO2, in the yeast or fungal promoters ADC1, MFalpha, AC, P-60, CYC1, GAPDH, TEF, rp28, ADH. Artificial promoters may also be used for regulation.

For expression in a host organism, the nucleic acid construct is inserted advantageously into a vector such as, for example, a plasmid or a phage, which makes possible optimal expression of the genes in the host. Vectors are also understood as meaning, in addition to plasmids and phages, all the other vectors which are known to the skilled worker, that is to say for example viruses such as SV40, CMV, baculovirus and adenovirus, transposons, IS elements, phasmids, cosmids and linear or circular DNA. These vectors are capable of replicating autonomously in the host organism or else chromosomally. These vectors are a further development of the invention.

Suitable plasmids are, for example, in *E. coli* pLG338, pACYC184, pBR322, pUC18, pUC19, pKC30, pRep4, pHS1, pKK223-3, pDHE19.2, pHS2, pPLc236, pMBL24, pLG200, pUR290, pIN-III¹¹³-B1, λ gt11 or pBdCI, in *Streptomyces* pIJ101, pIJ364, pIJ702 or pIJ361, in *Bacillus* pUB110, pC194 or pBD214, in *Corynebacterium* pSA77 or pAJ667, in fungi pALS1, pIL2 or pBB116, in yeasts 2alphaM, pAG-1, YEp6, YEp13 or pEMBLYe23 or in plants pLGV23, pGHlac⁺, pBIN19, pAK2004 or pDH51. The abovementioned plasmids are a small selection of the plasmids which are possible. Further plasmids are well known to the skilled worker and can be found for example in the book *Cloning Vectors* (Eds. Pouwels P. H. et al. Elsevier, Amsterdam-New York-Oxford, 1985, ISBN 0 444 904018).

In a further development of the vector, the vector which comprises the nucleic acid construct according to the invention or the nucleic acid according to the invention can advantageously also be introduced into the microorganisms in the form of a linear DNA and integrated into the host organism's genome via heterologous or homologous recombination. This linear DNA can consist of a linearized vector such as a plasmid or only of the nucleic acid construct or the nucleic acid according to the invention.

For optimal expression of heterologous genes in organisms, it is advantageous to modify the nucleic acid sequences to match the specific "codon usage" used in the organism. The "codon usage" can be determined readily by computer evaluations of other, known genes of the organism in question.

An expression cassette according to the invention is generated by fusing a suitable promoter to a suitable coding nucleotide sequence and a terminator or polyadenylation signal. Customary recombination and cloning techniques are used for this purpose, as are described, for example, in T. Maniatis, E.F. Fritsch and J. Sambrook, *Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor Laboratory, Cold Spring Harbor, NY (1989) and in T.J. Silhavy,

M.L. Berman and L.W. Enquist, Experiments with Gene Fusions, Cold Spring Harbor Laboratory, Cold Spring Harbor, NY (1984) and in Ausubel, F.M. et al., Current Protocols in Molecular Biology, Greene Publishing Assoc. and Wiley Interscience (1987).

5 For expression in a suitable host organism, the recombinant nucleic acid construct or gene construct is advantageously inserted into a host-specific vector which makes possible optimal expression of the genes in the host. Vectors are well known to the skilled worker and can be found for example in "cloning vectors" (Pouwels P. H. et al., Ed., Elsevier, Amsterdam-New York-Oxford, 1985).

The content of the documents cross-referenced is incorporated by reference.

Nucleic acid and amino acid sequences identified and/or used herein are listed below:

OR2W1

*Homo sapiens*_OR2W1_1-octen-3-ol, transpirol, 3-hydroxy-3-methylhexanoic acid, 3-methyl-2-hexenoic acid and DMTS olfactory receptor (GI: 26692)

DNA: SEQ ID NO: 1

atggaccaaagcaattatagttctttacatggttttattctgcttggtctcttaaccatccaaaaatggagatgatcctgtcaggagt
gtcgccatcttacttaattacattgggtgggtaacacagccatcattcttgcatctctcctggattcccagttcataccaatgtact
10 tttcctcagaaattatctttcctagatctatgtttcacaaccagcatcatccctcaggtgctgggtcaacttgggggacctgataagac
catcagctatgtgggttgatcatccaactctatgtttacatgtggttgggctcagttgagtgcccttctcctggctgttatgtcctatgatc
gtttacagctatatgtaagcccttgcatatttttagtcatgaaccacatctatgtctaaagatgattatcatgatctggagtattag
ttggccaattctgtagtattatgtacactcactctgaatttcccacatgtggaaacaacattctggatcatttctgtgtgagttgcca
gctctgggtcaagatagcttgtgtagacaccacaacagttgaaatgtctgttttcgcttaggcattataattgtcctcacacctctcatcc
15 ttattcttatatcctatggctacattgcaaagctgtgctgagaacgaagtcaaaagcaagccagcgaaaagcaatgaatacctgtg
gatctcatcttactgtagtgtctatgttctatggaactattatctacatgtacctgcaaccaggtaacagggctccaaagaccagggc
aagttcctcacctcttttacactgtcatcactccaagttcaaccgctcatttacacctaagaaataaggacatgaaggatgccct
gaagaaactgatgagatttcaccacaaatctacaaaaataaaggaggaattgcaagtcatag

PROT: SEQ ID NO: 2

MDQSNYSSLHGFILLGFSNHPKMEMILSGVVAIFYLITLVGNTAILASLLDSQLHTPMYFFLRNLSFLDLCFT
TSIIPQVLVNLWGPDKTISYVGCIIQLYVYMWLGSVECLLLAVMSYDRFTAICKPLHYFVVMNPHLCLKMII
MIWSISLANSVVLCTLTNLPTCGNNILDHFLCELPALVKIACVDTTTVEMSVFALGIIIVLTPLILILISYGYIAK
AVLRTKSKASQRKAMNTCGSHLTVVSMFYGTIIYMYLQPGNRASKDQGKFLTLFYTVITPSLNPLIYTLRNK
25 DMKDALKKLMRFHHKSTKIKRNCKS

OR1A1

*Homo sapiens*_OR1A1_1-octen-3-ol, transpirol, DMTS, and geonol olfactory receptor (GI:8383)

DNA: SEQ ID NO: 3

atgagggaaaataaccagtcctctacactggaattcatcctcctgggagtactggtcagcaggaacaggaagatttcttctacatcc
tcttctgttcatttaccatcacattgattggaaacctgtcatcgtcctagccatttgctctgatgttcgcttcacaacccatgtat
35 tttctccttgccaacctctccttggttgacatcttctctcatcggttaaccatccctaagatgctggccaacctctcttgggcagcaaat
ccatctcttttgggggatgcctaacgcagatgtatttcatgatagccttgggtaacacagacagctatatttggctgcaatggcatatg
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cccacctcacggttgctctttgtattatggtacggtcatgggcagctatttccgccctttgaccaattatagcctaaaagacgcagtgat
tactgtaatgtacacggcagtgacccaatgttaaattctttcatctacagtctgagaaatcgggacatgaaggctgccctgcggaa
actcttcaacaagagaatctcctcgtaa

PROT: SEQ ID NO: 4

MRENNQSSTLEFILLGVTGQQEQEDFFYILFLIYPITLIGNLLIVLAICSDVRLHNPMYFLLANLSLVDIFFSSV
TIPKMLANHLLGSKSISFGGCLTQMYFMIALGNNTDSYILAAMAYDRAVAISRPLHYTTIMSPRSCIWLIAGS
WVIGNANALPHTLLTASLSFCGNQEVANFYCDITPLLKLSCDIHFHVKMMYLGVGIFSVPLLCIIVSYIRVFS
5 TVFQVPSTKGVLKAFSTCGSHLTVVSLLYYGTVMGTYFRPLTNYSLKDAVITVMYTAVTPMLNSFIYSLRNR
DMKAALRKLFNKRIS

OR2J3

10 *Homo sapiens*_OR2J3_1-octen-3-ol, and transpirol olfactory receptor (GI: 442186)

DNA: SEQ ID NO: 5

atgaatgatgatggaaaagtcaatgctagctctgaggggtactttattttagttggattttctaattggcctcatctggaagtagttatct
ttgtggttcttctgattcttctacttgatgacactgataggaaacctgttcatcatcctgtcatacctggactcccatctgcacacacc
15 aatgtacttcttcttcaaacctctcatttctggatctctgctacaccaccagctctatccctcagttgctgggtcaatctctggggcccg
aaaagaccatctcttatgctggttgcattgattcaactttactttgtctcgactgggaaccgcagagtgtgtcctactggtggtgatgt
cctatgaccgttatgcagctgtgtgtagaccttgcattacactgtcctcatgcaccctcgtttctgccacctgctggctgtggcttcttgg
gtaagtggttttaccaactcagcacttcattcctccttcaccttctgggtacctctgtgtggacaccgccaagtagatcacttttctgtg
aagttccagcacttctgcgattatcgtgtgttgatacccatgtcaatgagctgaccctcatgatcacaagctccatatttgttctcatacc
20 tctcatcctcattctcattcttcttatggtgccatcgctccgagctgtactgaggatgcagtcacccactgggcttcagaaagtgttggaa
atgtggagctcatcttatggctgtatctctcttttctccggccatgtgcataatctccagccaccatcaggaaattctcaagatcaa
ggcaagttcattgccctctttatactgttgcacacctagtcttaaccctctaattacacccctcagaaacaaagttgtaagaggggca
gtgaagagactaatggggtgggaatga

25 PROT: SEQ ID NO: 6

MNDDGKVNASSEGYFILVGFSNWPHELVVIFVVVLIFYLMTLIGNLFIIILSYLDSHLHTPMYFFLSNLSFLDL
CYTTSSIPQLLVNLWGPEKTISYAGCMIQLYFVLALGTAECVLLVMSYDRYAACRPLHYTVLMHPRFCH
LLAVASWVSGFTNSALHSSFTFWVPLCGHRQVDHFFCEVPALLRLSCVDTHVNELTLMITSSIFVLIPLILIT
SYGAIVRAVLRMQSTTGLQKVFGTCGAHLMAVSLFFIPAMCIYLQPPSGNSQDQGFIALFYTVVTPSLNP
30 LIYTLRNKVVVRGAVKRLMGWE

OR4Q3

*Homo sapiens*_OR4Q3_1-octen-3-ol olfactory receptor (GI:441669)

35

DNA: SEQ ID NO: 7

atgaaaaaagaacaagattctaattgtgacagaatttgttcttctgggcctatcatcttctgggagctgcagctatttcttcttactat
tttgttttttacattgctattgtcctgggaaacctctgatagtggttaacagtgaagcccatgctcacctgctcaatctcctatgtat
tatttttaggtcatctctcttcttattgacctatgcctgagctgtgttactgtgccaagatgttaggggatttctacagcagggaaga
40 gcatctcttttcaggatgcctggccagatctacttctccactttctaggagccagtgcagatgttttctgacagctatggcctatga
caggtatgttgccatctgtaacccttgcgctaccttacagtcataacccccagctatgccttgggttggttcttgcctgctggtgtggg
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45 tcacctgacagtggctcagctgatcttctgcatgcgtattcatctatttgaggccttctgcagcttctctgtggataagatattcct
tgttttacagtgattacacctatgttgaacccctcatctacacactcagaaatactgatatgaagacagctatgaagaagctgag
gataaaaccatgtggcattccattgcctgttaa

PROT: SEQ ID NO: 8

MKKEQDSNVTEFVLLGLSSSWELQLFLFLFFYIAIVLGNLLIVTVQAHALLQSPMYFLGHLSFIDLCL
SCVTVPKMLGDFLQQGKSISFSGCLAQIYFLHFLGASEMFLLTVMAYDRYVAICNPLRYLTMNPQLCLWL
5 VLACWCGGFIHSMQ
VILVIQLPFCGPNELDNFYCDVPQVIKLACMDTYVVEVLVIANSGLLSLVCFLVLLFSYAILITLRTHFCQQQ
NKVLSTCASHLTVVSLIFVPCVFIYLRPFCSFSVDKIFSLFYTVITPMLNPLIYTLRNTDMKTAMKKLRKPCGI
PLPC

OR5K1

*Homo sapiens*_OR5K1_1-octen-3-ol, transpirol, and DMTS olfactory receptor (GI:26339)

DNA: SEQ ID NO: 9

15 atggctgaagaaaatcataccatgaaaaatgagtttatcctcacaggatttacagatcacctgagctgaagactctgctgtttgtggt
gttctttgccatctatctgatcaccgtgggtgggaatattagtttggtggcactgatattacacaccgtcggttcacaccaaata
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20 accgctatgtggccatgatgaaccactgcagtagcacatcatgatgtccaagaactctgcattcagatgaccacaggggccttcat
agctggaaacctgcattccatgattcatgtagggctgtatttaggttagtttctgtggatcgaatcacatcaaccactttactgtgat
attcttccctgtatagactcttctgtgtgatccttatcaatgaactggttctattcatcttctcaggttcagttcaagtctttaccata
ggtagtgtcttaatatcttatctctatattcttctactattttcaaaatgaaatccaaagaggggaagggccaaagctttttctacctgtg
catcccaactttttgtcagtttcattattctatggatctctttcttcatgtacgtagaccaaatgtgctgaagaaggggataaagatata
ccagctgcaattttattacaatagtagttcccttactaaatcctttcatttatagcctgagaaataggggaagtaataagtgtcttaaga
25 aaaattctgatgaagaaataa

PROT: SEQ ID NO: 10

MAEENHTMKNEFILTGFTHPELKTLLFVFFAIYLITVGNISLVALIFTHRRLLHTPMYIFLGNLALVDSCCA
CAITPKMLENFFSENKRISLYECAVQFYFLCTVETADCFLAAMAYDRYVAICNPLQYHIMMSKKLCIQMT
30 TGAFIAGNLHSMIHV
GLVFRLVFCGSNHINHFYCDILPLYRLSCVDPYINELVLFI FSGSVQVFTIGSVLISYLYILLTIFKMKSKEGRAK
AFSTCASHFLSVSLFYGSLFFMYVRPNLLEEGDKDIPAAILFTIVVPLLNPFIYSLRNREVISVLRKILMKK

OR11A1*Homo sapiens*_OR11A1_geonol olfactory receptor (GI:26531)

DNA: SEQ ID NO: 11

5 atggaaattgtctccacaggaaacgaaactattactgaatttgcctccttggttctatgacatccctgaactgcatttctgtttttat
tgtattcactgctgtctatgtcttcatcatcatagggaaatagctgattattgtacagtggttagctcccagaggctccacaaacccat
gtatattttcttggcgaatctgtccttctggatatttctacacctccgcagtgatgccaaaaatgctggagggttctctgcaagaagc
aactatctctgtggctggttgcttgcctcagttctttatcttgcgctctctagccacagctgaatgcttactgctggctgtcatggcatatg
accgctacctggcaatttctacccactccactacccactcctgatggggcccagacggtacatggggctggtggtcacaacctggct
10 ctctggatttggtagatggactggttggtggccctggtggcccagctgaggttctgtggcccaaccacattgaccagttttactgtga
ctttatgctttcgtgggcctggcttgcctcgatcccagatgggtcaggtgacaactctcatttctgtctgttctgcctcactattccttt
tggactgattctgacatcttatgccagaatttggtggcagtgctgagagttcctgtggggcaagcaggagaagggttctccaca
tgctcctccacctagctgtagtaccacattctatggaacgctcatgatctttatgttgaccctctgctgtccattcccagctcctctc
caaggctcttccctgctctacactgttggtcaccctctcttcaatcctgtgatctataccatgaggaacaaggaggtgcatcaggcac
15 ttcggaagattctctgtatcaaacaactgaaacacttgattga

PROT: SEQ ID NO: 12

MEIVSTGNETITEFVLLGFYDIPELHFLFFIVFTAVYVFIIGNMLIIVAVVSSQRLHKPMYIFLANLSFLDILYTS
AVMPKMLEGFLQEATISVAGCLLQFFIFGSLATAECLLLAVMAYDRYLAICYPLHYPLLMGPRRYMGLVVT
20 TWLSGFVVDGLVVALVAQLRFCGPNHIDQFYCDFMLFVGLACSDPRVAQVTTLILSVFCLTIPFGLILTSYA
RIVVAVLRVPAGASRRRAFSTCSSHLAVVTFYGTLMIFYVAPSAVHSQLLSKVFSLLYTVVTPLFNPVIYTM
RNKEVHQALRKILCIKQTETLD

OR2M3*Homo sapiens*_OR2M3_geonol olfactory receptor (GI:127062)

DNA: SEQ ID NO: 13

atggcaaggaggagaattcgaccttcaactccgacttcatcctcctgggaatcttcaatcacagccccacccacaccttcttctttctg
30 gtctggccatcttttcagtggttcatgggaaactctgtcatggttctcctcatctacctggacacccagctccacacccccatgtac
ctctcctcagccaactgtccctcatggacctcatgctcatctgcaccaccgtaccaagatggccttcaactacctgtctggcagcaa
gtcattttctatggctggttggtgccacacaaatcttctatacatcactgcttggctctgaatgctttcttttggctgttatggcttatga
ccgctacactgccatttgcaccctctaagatacaccaatctcatgagccctaaaatttggacttatgactgccttttctggatcct
gggctctacggatggaattattgatgtttagcaacatttcttctcctactgtgggtctcgggaaatagcccacttcttctgtgacttc
35 cctccctactaatcctctcatgcagtgcacatcaatattgaaaagattctttcatctgctgtatagtaatgattgtttccctgttgc
aatcatcattgcttctatgctcgagttatcctggctgtcattcacatgggactctggagagggctcgtcgaaagcttttactactgttcc
tctcacctcttggtgggtgggaatgtactatggagcagcttggatcatgtacatacgccacatctgatcgtccccaacacaggacaa
gatggtgtctgtattctacacatcctcactcccatgttgaaatcccctcatctacagcctccgcaacaaggaggtgaccagagcattca
tgaagatcttaggaaagggaagtctggagagtga
40

PROT: SEQ ID NO: 14

MARENSTFNSDFILLGIFNHSPHTFLFFLVLAIFSVAFMGNSVMVLLIYLDLTLHTPMYLLLSQLSLMDLM
LICTTVPKMAFNLYSGSKSISMAGCATQIFFYTSLLGSECFLLAVMAYDRYTAICHPLRYTNLMSPKICGLMT
AFSWILGSTDGIIDVVATFSFSYCGSREIAHFFCDFPSLLILSCSDTSIFEKILFICCIVMIVFPVAIIIASYARVILA
45 VIHMGSGEGRRKAFTTCSSHLLVVGMYGAAALFMYIRPTSDRSPTQDKMVSFVYITLTPMLNPLIYSLRNK
EVTRAFMKILGKGKSGE

OR51E1*Homo sapiens*_OR51E1_butyric olfactory receptor (GI: 14503)

5 DNA: SEQ ID NO: 15

atggtggatcccaatggcaatgaatccagtgtacatacttcacctaataaggcctccctggtttagaagaggctcagttctggttggc
cttccattgtgtccctctaccttattgctgtgtaggtaacttgacaatcatctacattgtgcggactgagcacagcctgcatgagcc
catgtatatatttcttggcatgctttcaggcattgacatcctcatctccacctcatccatgccccaaatgctggccatcttctggttcaatt
ccactaccatccagtttgatgctgtgtgctacagatgtttgccatccactccttatctggcatggaatccacagtgtgctggtggccatgg
10 cttttgaccgctatgtggccatctgtcaccactgcgccatgccacagtacttacgttgccctgtgtcaccaaaattggtgtggctgtgt
tggtgcgggggctgactgatggcacccttctgtcttcatcaagcagctgcccttctgccgtccaatatcctttccattcctactg
cctacaccaagatgtcatgaagctggcctgtgatgatatccgggtcaatgtcgtctatggccttatcgtcatcatctccgccattggcct
ggactcacttctcatctccttctcatatctgcttattcttaagactgtgttgggcttgacacgtgaagcccaggccaaggcatttggcact
tgctgtctcatgtgtgtgtgtgttcatattctatgtacctttcattggattgtccatggtgcatcgcttttagcaagcggcgtagctctcc
15 actgccgtcatcttggccaatatctatctgtgttctcctgtgtcacaaccaattgtctatggagtgaagacaaggagattcgac
agcgcatccttcgacttttccatgtggccacacacgcttcagagccctag

PROT: SEQ ID NO: 16

MVDPNGNESSATYFILIGLPGLEEAQFWLAFPLCSLYLIAVLGNLTIIYIVRTEHSLHEPMPYIFLCMLSGIDILIS
20 TSSMPKMLAIFWFNSTTIQFDACLLQMFHLSLGMESTVLLAMAFDRYVAICHPLRHATVLTLPRTKIG
VAAVVRGAALMAPLPVFIKQLPFCRSNILSHSYCLHQDVMKLACDDIRVNVVYGLIVIIISAIGLDSLLISFSYL
LILKTVLGLTREAAKAFGTCVSHVCAVFIFYVPFGLSMVHRFSKRDSPLPVILANIYLLVPPVLNPIVYGV
KTREIRQRILRLFHVATHASEP

25

OR4S2*Homo sapiens*_OR4S2_DMTS olfactory receptor (GI: 219431)

DNA: SEQ ID NO: 17

30 atggaaaaataaacaacgtaactgaattcattttctggggctctttctcagagcccagagattgagaaagtttgtttgtggtgtttct
ttcttctacataatcatttcttgggaaatctcctcatcatgtgacagtttgctgagcaacctgttaagtcacccatgtatttcttctc
agcttcttgtcttttggacatttgttacttctcagtcacagctccaagatgattgttgacctgttagcaaaggacaaaacctctcct
atgtgggggtgcatgttgcaactgtttggagtacatttcttgggtgactgagatcttcatccttactgtaatggcctatgatcgttatgtg
gctatctgtaaaccctacattatagaccatcatgaaccgggagacatgcaataaaatgttattaggagcgtgggtaggtgggttct
35 tactctcattatccaagtggtctgttagtccaactacccttttggacccaatgagatagatcactacttttgtgatgttcacctgt
gttgaaacttgctgcacagaaacatacattgttgggtgttgggtgacagccaacagtgggtaccattgctctggggagttttgttatctt
gctaactcctacagcatcatcctagtttccctgagaaaagcagtcagcagaaggcaggcgcaaagccctctccacctgtggctcccac
attgccatggtcggtatcttttgcggccctgtactttatgtacatgcgccctgatacgacctttcagaggataagatggtggctgtatt
ttacaccattatcactcccatgttaaatcctctgatttatacactgagaaatgcagaagtaagaatgcaatgaagaaactgtggggc
40 agaaatgttttcttgaggctaaagggaatag

PROT: SEQ ID NO: 18

MEKINNVTETIFWGLSQSPEIEKVCVVFVFFYIIILLGNLLIMLTVCLSNLFKSPMYFFLSFLSFVDICYSSVTA
PKMIVDLLAKDKTISYVGCMLQLFGVHFFGCTEIFILTVMAYDRYVAICKPLHYMTIMNRETCNKMLLGT
45 WVGGLHSHIIQVALVVQLPFCGPNEIDHYFCDVHPVLKLACTETYIVGVVVTANSGTIALGSFVILLISYSIILV
SLRKQSAEGRRKALSTCGSHIAMVVIFGPTCFMYMRPDTTFSEDKMVAVFYTIITPMLNPLIYTLRNAEV
KNAMKKLWGRNVFLEAKGK

OR51I2*Homo sapiens_OR51I2_3-methyl-2-hexenoic acid olfactory receptor (GI: 507078)*

5

DNA: SEQ ID NO: 19

atgggggtgttcaatgtcactcaccctgcattcttctcctgactggatccctggcttgagagctctcactcctggctgtcagggcccc
tctgcgtgatgtatgtctggtggccttgggggaaatacagtgatcctgcaggctgtgcgagtgaggcccagcctccatgagcccatgta
ctacttctgtccatgttgccttcagtgtgtggccatatccatggccacactgccactgtactccgaaccttctgcctcaatgccgc
10 aacatcacttttgatgcctgtctaattcagatgttttcttattcacttcttccatgatggaatcaggtattctgtggccatgagtttga
ccgctatgtggccatttgtgacccttgcgctatgcaactgtgtcaccactgaagtcattgtgcaatgggttaggtgcagctgtcg
aagcttcatcaccttttccctcttcccttcttattaagaggctgcctatctgcagatccaatgttcttctcactcctactgcctgcaccc
agacatgatgaggcttgctgtgtgatatcagatcaacagcatctatggactcttgttctgtatccaccttggcatggacctgtt
ttatcttctctcctatgtgtcattctgcgttctgtcatggccactgcttccgtgaggaacgcctcaaagcttcaacacatgtgtgtc
15 acatatcctggctgtactgtcattttatgtgcaatgattggggctccacagtgcaccgcttgggaagcatgtcccatgtctacataca
tgtcctcatgtcaaatgtgtacctatttgcctcctgtgtcaaccctctcatttatagcgccaagacaaaggaaatccgccgagccat
ttccgcatgtttcaccacatcaaaatatga

PROT: SEQ ID NO: 20

20 MGLFNVTHPAFFLLTGIPGLESSHWSLGPLCVMYAVALGGNTVILQAVRVEPSLHEPMYYFLSMLSFS
VAISMATLPTVLRFTCLNARNITFDACLIQMFLIHFFSMMESGILLAMSFDRYVAICDPLRYATVLTTEVIAA
MGLGAAARSFITLPLPFLIKRLPICRSNVLSHSYCLHPDMMRLACADISINSIYGLFVLVSTFGMDLFFILSY
VLILRSMATASREERLKALNTCVSHILAVLAFYVPMIGVSTVHRFGKHVPCYIHVLMNSNVYLFVPPVLNPLI
YSAKTKEIRRAIFRMFHHIKI

25

Olf263*Mus musculus_Olf263_1-octen-3-ol, DMTS, 3-hydroxy-3-methylhexanoic acid, transpirol, and 3-methyl-2-hexenoic acid olfactory receptor (GI:18341)*

30

DNA: SEQ ID NO: 21

atggaccaagcaattacagtactttgcatgtttttatcctgcttgattctctgaccaccctcacctggaaatgatcctctctggagttg
tcaccttctttacattattacactgggtgggaacactgtctataattcttgatccctcctggatccccatctccataccaatgtacttt
ttcctcaggaatctatcttctcctggatttgtgttcacaacaagcattgtccctcagatgctggtaactgtggggacccgaaaagacc
35 attagctctgtgggctgtattgttcagctctatgtgtatatgtggctgggctccattgagtgtctgctcctagctgtcatgtcctatgatcg
ttcacagctatttgaagcccttgattactttgtaatcatgaatccacgtctatgcgtcaagatgatagtcattgtgctgtgggtattagt
ttggccaactctgtaatattatgcacactcactgtgaatttgcctcgtatgtggacacaacatcctggaccacttctgtgtgagttgcca
gccatggctcaggatagcttgtgtagacacgacaacagttgaattgtctgttttgccttaggcattgtcattgtccttacacctctatcc
ttattcttatttcctatggctacatagccaaaactgtgtcaacatgaagtcaaaggcagggaacaaaaagcaatgaatacctgtgg
40 atcccatctcactgtgtgtctccatattctatggaactatcatctacatgtatctacaaccggtaacagggcctctaaggaccaggga
agttcctcacctcttttacacatcatcactccaagtctcaaccctcatttacaccctaaggaacagagacatgaaagatgcactg
aaaaaactcatgaggttttaccacagatttgccgaagtaaggagaaaactag

PROT: SEQ ID NO: 22

MDPSNYSTLHVIFILLGFSDDPHLEMLSGVVTFYIITLVGNTAILASLLDPHLHTPMYFFLRNLSFLDLCFTT
SIVPQMLVNLWGPEKTISSVGCIVQLYVYMWLGSI ECLLLAVMSYDRFTAICKPLHYFVIMNPRLCVKMIV
MVWGISLANSVILCTLTVNLP RCGHNILDHFLCELPAMVRIACVDTTTVELSVFALGIVIVLTP LILILISYGYIA
5 KTVLNMKSKAGQKAMNTCGSHLT VVSIFYGTIIMYLQPGNRASKDQGKFLT FYTIITPSLNPLIYTLRN
RDMKDALKKL MRFYHRFAEVRN

Olf403

10 *Mus musculus*_Olf403_1-octen-3-ol, DMTS, transpirol, and geonol olfactory receptor
(GI:404316)

DNA: SEQ ID NO: 23

atgagagaagaaaatgagcttctacatagatttcactctcctgggagttacaaggcagcgggagcaggaatatttcttctcatcct
15 cttcctgttcattaccccatcacagtgttgggaacatgctcatcatcctagccattcactctgacactcgctccataaccctatgtac
ttttcctggccaacctctccctgttgacatcttctctcctgttaactattccaagatgctggccaacctctcctaggttagcaaggc
catctccttgggggatgtatggcacagatgtacttcatgatattcattgggaaacacagacagttatatactagctgaatggcatatg
accgagctgtggctatcagtcgcccgttcattatgcaacaattatgagtcacaaactttgtgtcctgctgggtgctgggtcctgggtga
ttgcaaatgctaatactgctgccccacaccctactcacagctagattgtccttctgtggcaataaggatgtggccaacttctactgtgac
20 attacaccttctgctcagctgtcctgttctgacatccgttcaatgtgaagatgatgtaccttgggggtgggggtcttctctgtgacctgc
tgtgcatcatcatctcctatgtccgggtctttccacagtcttgcgggttccatctaccaagggttctgaaggccttgcacctgtg
ctctcacctgacagtggtgtcctgtattatgggacagtcattgggcatgtatttccggcccctgaccagttacagctgaagcatgcatt
gataactgtgatgtacacggcagtgacccaatgctgaacctttcatctacagcctgaggaaccgggacatgaaggctgctctgaa
gaaactcttcactgccactcttctcttctccctcatgtga
25

PROT: SEQ ID NO: 24

MREENESSTIDFTLLGVTRQREQEYFFILFLFIYPITVFGNMLIILAIHSDTRLHNPMYFFLANLSLVDIFFSSV
TIPKMLANHLLGSKAISFGGCMAMQMYFMISLGNTDSYILAAMAYDRAVAISRPLHYATIMSPQLCVLLVA
GSWVIANANALPHTLLTARLSFCGNKDVANFYCDITPLLQLSCSDIRFNVKMMYLGVGVSVP LLLCIISYV
30 RVFSTVLRVPSTKGFLKALSTCGSHLT VVSLYYGTVMGMYFRPLTSYSLKHALITVMYTA VTPMLNPFYSL
RNRDMKAALKKLFHCHSSSSSLM

Olf735*Mus musculus*_Olf735_1-octen-3-ol olfactory receptor (GI:257909)

DNA: SEQ ID NO: 25

5 atggtacacgcagacaagcaagaagtacttttcataattttcatTTTTgtttaatttaacctacttagtccagtttaatttttctccact
aggctgcttgatactcttggttgagaaaaacaaaacagctctgatgtgtcacgatttggctctgggctgtcgtcttctggga
gctccagttgtttctcttctcacatTTTTgttgatttacctgggtattgtcctgggaaaccttttgatagtgatggctgtccaagctgatgc
tcacctgttccagtcacccatgtactattttctaagccatctgtctttcattgacctttgctgagctgtgtggctgtacccaaaatgctag
gagatttctacagaaggagaagacaatatcttttcaggatgcctggcccaggatattctttctcactttctggagccagtgagatgt
10 tctgttgactgttatggcctatgataggtatgttgccatagcaaccctttgactacctgacggcatgaataaccacctgcgacttc
ggttgggtgtttggctgctggtgtggaggtttcattcactctatcacacaggtcatgattgtcattcagctgcctttttgtgtccaatga
actggacaacttctactgtgatgtccccaggtgtcaagctggcctgcatggacacttacttggttgaggctgtatgggtctctaaca
gtggcatactgtctctgtctgtcttggctgtcttctctatgtctctatcttgattactctgagaactcacctccaccggggccag
agcaaggcactgtccacctgtgcttctcacttgacgggtggcagcctgatctttgtaccctgtgtattcattactgaggcctttctgtac
15 ctctctgtggataaagtagtctctgtgttttacacagtatcacacctatgctgaacccctcatctatacactcagaaatgcagacat
gaagcaagccatagaaaagctgagaaagaagcaagtggcatcccactgctttgctaaaggatga

PROT: SEQ ID NO: 26

MVHADKQEVLSHNFSFLFNLTYLQFNFSSTRSLDTLGLEKNKNSSDVSRLFVLLGLSSSWELQLFLFFFLLI
20 YLVIVLGNLLIVMVVQADALFQSPMYFLSHLSFIDLCLSCVAVPKMLGDFLQKEKTISFSGCLAQVFFLHF
LGASEMFLTVMAY
DRYVAICNPLHYLTVMNNHLRLRLVFGCWCGGFIHSITQVMIVIQLPFCGPNELDNFYCDVPQVVKLACM
DTYLVEVLMVNSGILSLVCFVLVLLFSYALILITLRTHLHRGQSKALSTCASHLTVVSLIFVPCVFIYLRPFCTFS
VDKVVSVFYTVITPMLNPLIYTLRNADMKQAIEKLRKKQVASHCFAKG

Olf96*Mus musculus*_Olf96_ geonol olfactory receptor (GI:258507)

DNA: SEQ ID NO: 27

30 atgggaatcctttccacaggaaatcaaactgtcactgagtttgacttcttggtttccatgaagtcctgggctgcacctcctgttttttc
tgtgttcccatcctctatgcctccatcatcacagggaacatgtcattgcagtggtggtgagctcccagaggcttcacacacca
tgtatttctttctggtgaatctgtcctcatagagattgtctatacctccacagtgggtgccccaaatgtctggaaggcttcttacaggagg
ccaccatatctgtggctggctgcttgcctcagttctttgttttggtctctggccacagatgagtgttttctgctggctgtgatggcatat
gatcgatatctcgcaatttgcacctctacgataccacacctcatggggcctcaatgggtgcctgggggttggtgctcacagtctggct
35 gtctggcttcatggtagatggactagttgttgctctgatggccagttgagattctgtggcccaacttagttgatcattttactgtgat
ttttcacctttgatggctctggcttgctcagatacccaagtgggccagggtgactacatttgttctctgttggtcttctgactgtcccctt
gggctggttctgatctcctatgtcagattgtagtgactgtgctgagagttccttctgggaccagaagaaccaaggccttctccacatg
ctcctctcacctggctgtggtgtccacgttctatggaacactcatggtattgtacattgtgccctctgctgttcattctcagctcctctcca
aggtcattgccctgctctacacagtggctactcccattcaaccctgtcatctacaccttgaggaaccaggaggtgcagcaggcact
40 aagaaggcttctctactgcaaaccaactgaaatgtga

PROT: SEQ ID NO: 28

MGILSTGNQTVTEFVLLGFHEVPGLHLLFFSVFTILYASIITGNMLIAVVVVSSQRLHTPMYFFLVNLSFIEIV
YTSTVVPKMLEGFLQEATISVAGCLLQFFVFGSLATDECFLAVMAYDRYLAICHPLRYPHLMGPQWCLGL
45 VLTWVLSGFMVDGLVVALMAQLRFCGPNLVDFHYCDFSPMLVLACSDTQVAQVTTFVLSVVFLTVPFGL
VLISYAQIVTVLRVPSGTRRTKAFSTCSSHLAVVSTFYGTLMVLIVPSAVHSQLLSKVIALLYTVVTPIFNPV
IYTLRNQEVQQALRRLLYCKPTM

Olf558*Mus musculus*_Olf558_ butyric olfactory receptor (GI: 259097)

5

DNA: SEQ ID NO: 29

atgggtgggcttcaatagcaatgaatccagtgccacatattcatcttaataggccttccaggattggaagagggttcagtttggctggc
ttccctttgtgttccctctaccttattgctgtgtaggtaacttgacaatcatctacattgtgaggacagagcacagcctgcatgagccc
atgtatatctttcttgcagctttctggcctagacatcctcatttccacctcatccatgccaaaaatgatggccatctttggttcaattc
10 cactaccatccagtttgatgctgtctggtagatgtttgcatccattccttgtctggcatggagtccacagtgtgctggccatggcc
tttgaccgctatgtggccatttgccatcctctacggcatgccactgtgctgacattgcctcgtgttgccaagattggcatggctgtgtg
gtcaggggtgcagtactaatggcacccttacctgtcttcatcaaaagggtgcctttctgtcgttccaacatcctttctattcctactgcct
acaccaagatgtcatgaagctggcctgtgctgacatccgtgtcaatatcatttatggactcattgtcatcatctcagccattggtttgga
15 ctacttctcatttctctcatatttgcctcctcaagactgtgttgggcttgacacgtgaagcccaggcaaaagcgttggcacttgt
gtttcacatgtgtgtgctgttttcatcttctatgtgcctttcattggattgtgatggtgcaccgttcagcaagaggcgtgactctctct
gcctgtcattatggctaacaatctatctgtagttcctcctgtgtcgaacccattgtctatggagtaaagacaaaggagatccggcagc
gcattcttctgtcttttctcgtgaccacacacacttcagatcactag

PROT: SEQ ID NO: 30

20 MVGFNSNESSATYFILIGLPGLEEVQFWLAFPLCSLYLIAVLGNLTIIYIVRTEHSLHEPMYIFLCMLSGLDILIS
TSSMPKMMMAIFWFNSTTIQFDACLQMFIAHSLSGMESTVLLAMAFDRYVAICHPLRHATVLTLPRAKI
GMAAVVRGAVLMAPLPVFIKRLPFCRSNILSHSYCLHQDVMKLACADIRVNIYGLIIVISAIGLDSLLISFSYL
LILKTVLGLTREAAKAFGTCVSHVCAVFIFYVPFIGLSMVHRFSKRDSLLPVIMANIYLLVPPVLNPIVYGV
KTKEIRQRILRLFLVTTHTSDH

25

Olf1193*Mus musculus*_Olf1193_DMTS_olfactory receptor (GI: 329460)

30 DNA: SEQ ID NO: 31

atggcctcaaggacttattccatggaagaagtaaataatgtcactgaattcatttcttgggtctttctcagaaccctgaggttga
agtgtgctttgtggtgttctccttcttttacatggctcattctgctaggaaacctcctcatcatgttgacagtttgacgtggcaatctttca
agtttcccatgtatttttctcaactttctgtctttgtggacatttgctactcctcagtcacagcacccaagatgattattgacctgttag
tgaagaaaaagactatatcctatgtgggggtgcatgttacaactcttgggttcatttcttgggttgactgagatcttcattcttactgtc
35 atggcctatgatagatatgtggccatttgtaaacctctccactatatgactatgatggaccgggaaagatgcaataagatgttgctcg
gaacatggatcgggtggcttcttacattctattatccaagtggctcttgggtccagctcccctttgtggaccgaatgagattgatcacta
tttctgtgatgtacatcctgtactgaaacttgctgcactgacacttacattgttggtatttttgacagcaaacagtggcaccattgca
ttgggaagtttgcattctgctgatctcatcacagtcattctcatgtctctgagaaagcagtcattctgaaggcagacgcaaagctctc
tccacttgggatccacattgctgttgcatttttttggccctgtacttttatgtatatgcggcctgacactaccttctctgaggac
40 aagatggtagctatatttacaccattatcactccatgtgtaactccttaattacactctaagaaatgcagaagtaaagaatgcaat
gagaaaactgtgggctagaaaagtttcttgggaaactactgggaaatag

PROT: SEQ ID NO: 32

MASRTYSMEEVNNVTEFIFLGLSQNPEVEKVCVVFSFFYMVILLGNLLIMLTVCSGNLFKFPMYFFLNFLS
FVDICYSSVTAPKMIIDLLVKKKTISYVGCMLQLFVVHFFGCTEIFILTVMAYDRYVAICKPLHYMTMMDRE
RCNKMLLGTWIGGFLHSIIQVALVVQLPFCGPNEIDHYFCDVHPVLKLACTDTYIVGIFVTANS GTIALGSF
5 VILLISYTVILMSLRKQSSSEGRRKALSTCGSHIAVVIIFFGPCTFMYMRPD TTFSEDKMVAIFYITIITPMLNPLI
YTLRNAEVKNAMRKLWARKFSWETGK

Olfr641

10 *Mus musculus*_Olfr641_3-methyl-2-hexenoic acid olfactory receptor (GI: 25075)

DNA: SEQ ID NO: 33

atggcgctgttcaatgtcactcacctgcctcctttctcctgactggatccctggctctggagagcctccaccctggctggcaggaccc
ctttgtgtgatgatgccgtggccctcgaggcaatactgtgattctgcaggctgtgagagtgaggccatcctccatgctcccatgta
15 ctatttctgtccatgttcttctcagtgatgtggccatgtcaatggccacactgccaccgtgctgagaaccttctgctttgatgccgc
agcattgcttttgacgcctgtctagtccagatgttctcattcattctttctcgtatgatggagtcagggattctgctggctatgagtttga
ccgctatgtggccatgtcaatcccttgcatatgccactgtcctcaccaatgaattcattgctgggatgggcttagctgtgactgctcg
aagcttcacacccctttccctctgcccttctcatcaaaaggctacatatctgcaaatccaatgttcttccactcctactgcctgcacc
20 cagacatgatgaagcttgctgtgctgacatcacatcaacagtatattatggactctttgttctgtgtctacctttggcatggacctgct
tttattttcctctcctatgtgctcattctgcgttctgttatggccattgcttctcatgaggacgccttaaagctctcaacacatgtgtatc
acatatcttgctgtgcttgcatttatgtgccaatgataggggtctctacagttcaccgttttgggaagcatgcccacgatacataca
tgtcctcatgtccaatgtctacctctttgtgcctcctgttctcaacctctcatttacagtccaagacaaaggagatccgccgtgccata
ttccgatgtttcgccgtatcaaactgtga

25 PROT: SEQ ID NO: 34

MALFNVTHPASFLTGPGLSLHPWLAGPLCVMYAVALGANTVILQAVRVEPILHAPMYFSLMSLSFSDV
AMSMATLPTVLRTFCFDARSIAFDACLVMFLIHSFSMMESGILLAMSFDYVAICNPLHYATVLTNEFIA
GMGLAVTARSFITLPLPFLIKRLPICKSNVLSHSYCLHPDMMKLACADITINSIYGLFVLVSTFGMDLLFIFLS
YVLILRSVMAIASHEERLKALNTCVSHILAVLAFYVPMIGVSTVHRFGKHAPRYIHVLMNSNVYLFVPPVLNP
30 LIYSAKTKAIRRAIFRMFRRIKL

Olfr137

*Mus musculus*_Olfr137_1-octen-3-ol, and transpirol olfactory receptor (GI: 258481)

35

DNA: SEQ ID NO: 35

Atgggtggaaaatttcaatgcaagttgggaagggtactttatttttctgggtttttctaaatggcctcatctggaagttgttctttgtggtgata
ttgatattctacatgatgacactgatgggcaatctctcatcataattttgtcacacctagattccacctgcatacccctatgtacttcttctct
caaactctctgctttggatctctgtataccactagctctgtccccagctgctatttaacctctggggcccaaaagaaaacaatatcttatgc
40 tgggtgcatgcttcagctctattttgtccttgctctgggtaccacagagtgtgttctgttgggtgatgtcctatgaccgctatgtagctgtgt
gtaaaccttgcattactctgtacttatgaatcctcgtttttgccaaactgctggctgcagcatcctgggtatgtggctttaccacttcagccct
cactcttctttaccttctgggtaccctgtgtggccatcgcaagtagaccacttcttctgtgaagtgcctgcactgttgagttgtcctgtg
ttgatatccatgcaaatgagatgactctcatggtcatgagtgtattttgtgtcataccactattctcactctgagctcctatgctgccattg
catggactgtcctggaaatgcaatcaaccactgcacttcagaaagttttcgggacctgtggagcccatcttactgttgtttctctttttcatt
45 ccaatcatgtgcattatctcagcctcaacaaaaagtctcaagatcatgcaagttcattgctcttctacaccgttgcacacctagcct
caacctctcatttatactctaagaaacaaagatgtgagagggggcaataaggaggctgagtaggtatgagagggagaaatga

PROT: SEQ ID NO: 36

MVENFNASWEGYFIFLGFSKWPHLEVVLVVFILIFYMMTLMGNLFIIILSHLDSHLHTPMYFFLSNLSALDL
CYTTSSVPQLLFNLWGPKKTISYAGCMLQLYFVLALGTTECVLLVMSYDRYVAVCKPLHYSVLMNPRFC
QLLAAASWVCGFTTSALHSSFTFWVPLCGHRKVDHFFCEVPALLQLSCVDIHANEMTLMVMSAIFVVIPLI
5 LILSSYAAIAWTVLEMQSTTRLQKVFGTCGAHLTVVSLFFIPIMCIYLPSTKSSQDHAKFIALFYTVVTPSLN
PLIYTLRNKDVIRGAIIRRLSRYEREK

Olf173

10 *Mus musculus*_Olf173_1-octen-3-ol, transpirol, and DMTS olfactory receptor (GI: 259002)

DNA: SEQ ID NO: 37

atggttgaagaaaaccacaccatgaaacgtgagttgtcctcacaggatttacagaccacctgaaatgaaggccttctgtttgcag
tattcttttcatctatctgattaccatgataggaatatgggtctggtgattctgatttccaaagaacgttctctcacaccccaatgtac
15 atctttctgggcaacctggctttatagattctgtgtgcctgtgctattaccctaaaaatgttgagaaacttttctctgaggacagaat
aatctctctgtatgaatgtatggcacagttttatttctgtgactgttgaaactgcagactgcttcttctgtcagcaatggcctatgacc
gctatgtggccatgatgaacccactgcagtaccacaccacgatgtccaagaagctgccttcagatgacgacgggagctttcatagc
tggaacactgcattctatgggtcatgtgggctattatttagactagcattctgtgggtctaatcaatcaaccacttttattgtgatatt
cttctttgtacagactctctgtgttgacctatatcaacgagctgtattatttgcctttcaggctcaatccaagtcttcacaatagg
20 ttgtgtcctcatatcttaccttttattgtttatacaattttccaaatgaaatccaaagagggaaggatcaaagccttctccacctgtgca
tccacttttctgtctgtttcactattctatggatctctttgtttatgtacattagaccaaatttgctagaagaaggatgataaggacatgcc
agctgctattttgtttacaatagtggtcccttactaaaccattatttatagcttgagaaataaagaagtaaagaatgtcttgcagaa
aattctgcagaaaaaataatttcaaaaaattttaacaagcatctattattgtgtaa

25 PROT: SEQ ID NO: 38

MVEENHTMKREFVLGTGFDHPKMKLLFAVFFFIYLLITMIGNMGLVILISKERSLHTPMYIFLGNLAFIDSC
CACAITPKMLENFFSEDRIISLYECMAQFYFLCTVETADCFLLSAMAYDRYVAICNPLQYHTTMSKKLCLQ
MTTGAFIAGNLHSMVHVHGLLFRFAFCGSNQINHFCYCDILPLYRLSCVDPYINELVLFVSGSIQVFTIGCVLIS
YLFIVYTIFQMKSKGRIKAFSTCASHFLSVSLFYGSLFFMYIRPNLLEEGDKDMPAAILFTIVVPLLNPFIYSLR
30 NKEVKNVLQKILQKKIISKNFQASIV

Olf164

*Mus musculus*_Olf164_geonol olfactory receptor (GI: 258443)

35

DNA: SEQ ID NO: 39

atgatacaatggaacaactggaccaggaactctgatttcactcctactaggattatttgatcacagtcctcttcatactttttctttccct
aattctgggtatcttctcatggccttcataaggaaattctatcatgggtattctcatctacttgatgctcatctccacacccccatgtac
atccttctcagccaactttctctcatggatctcatgctcatctgtactacagtaccccaaatggccttcaacttcttctggaaacaagt
40 ccatctccatgggtggctgtggaatccagatattcttctatgtatcttacttgagctgagtggttttggccgcaatggcttatgac
cgttatgtagctatttgctacccattaaggtacctattctcatgagtgacaaaatatgtggcctcatggctgcctcctctgggttcttg
gctctcttgatggtataatagaagttgcagctgattgtcttttcatattgtggtgccagagaaataacctatttttctgtgatgttctt
gccttactcacactttcatgtagtaataccttgatattgaaagaattatattttctgtgtgtaattatgcttactttacctgtagcaatc
attattgcttctatactcgtgtgattctgaccgttctcatatgagctcagctgagagtcgccacaaagctttgccacctgttctctca
45 cctcatgggtggggaatgtactatggggcagccatgttcatatacatgccccttcttctggtcgttctccaccaggacaaaaatag
tgtcagctttctacactatccttacccaatgttgaacccccctatttatagctctccggaacaaagaagtagccagagcattcatgaaa
gtgttagggattgataaggcagcagcatga

PROT: SEQ ID NO: 40

MIQWNNWTRNSDFILLGLFDHSPLHTFFFSLILGIFFMFIGNSIMVILIYLD AHLHTPMYILLSQLSLMDL
MLICTTVPQMAFNFLSGNKSISMVGCIGI QIFFYV SLLGAECFLAAMAYDRYVAICYPLRYPILMSDKICGL
5 MAASSWVLGSLDGIIEVAAALSFSYCGAREIPHFFCDVPALLTLSCSNTLIFERIIFFCCVIMLTLPVAVIIASYT
RVILTVLHMSSAESRHKAFATCSSHLMVVGMMYGAAMFIYMRPSSGRSPTQDKIVSAFYTILTPMLNPLIY
SLRNKEVARAFMKVLGIDKAAA

10 **Olf1487**

*Mus Musculus*_Olf1487_geonol olfactory receptor (GI: 258629)

DNA: SEQ ID NO: 41

Atgattcagaatatttcagaattgtctgaattattcttgttgggttaacagatgcaccattcctgcaaattcctttatttatcatctttact
15 ctcatattttgacaacattgtttgggaatcttgggatgattttgctgattctgctggactccagactccacactcccatgtacttttctt
cagtaacctctctctggtggactgtgttatgcctcagctgtcactcccaaggtgatggaagggtttctcacaggaaataagatcatat
cctacaatgcatgtgctgccagatgttcttcttgcagcctttgctactgttgaaagttcatgctggcctcaatggcctatgaccgtca
tgcagcagtggtgcaaacccttgcaattactccactactatgacaactacgatatgtgtcctgcttcttgcctggatcttatgtcagtggactc
ttacaatcttcattcatgtttccttcacatttcaactctccttctgccatttcaatgtagtcaatcacttttctgtgatatccaccactat
20 tagccctttcttgcctcagattcacacaaatgaaattatactctttatgttggcagcattcaatgttgcttttactctattagttatattgt
cctcttacttactaattttgttgcaattctgagaatgcgctctgctgagagcaggaagaaggccatttccacctgtgcatccacctta
ccactgtttccatcttctatggcacaattatcttcatgtacttacagcccagctccaatcactccatggatactgacaagatggcatctg
tttctacaccatggtcattcccatgctgaaccctctgtatatagcctgagaaataaagaagtcaagaatgcattcaagaaggttgct
ggaaaagcagtgctttcactgggattagcaattaa

25

PROT: SEQ ID NO: 42

MIQNISELSEFILVGLTDAPFLQIPLFIIFTLIYLTTLFGNLGMILLILLDSRLHTPMYFFLSNLSLVDCVYASAVT
PKVMEGFLTGNKIISYNACAAQMFFFAAFATVESFMLASMAYDRHAAVCKPLHYSTTMTTTCVLLLAGS
YVSGLLQSSIHVSFTFQLSFCHSNVNVNHFCDIPPLLALSCSSIHTNEILFMLAAFNVAFTLLVILSSYLLIFVAI
30 LRMRSAESRKKAI STCASHLT TVSIFYGTIIFMYLQPSSNHSM DTDKMASVFYTMVIPMLNPLVYSLRNKE
VKNAFKKVAGKAVLSLGLVN

Olf339*Mus musculus*_Olf339_geonol olfactory receptor (GI:258951)

DNA: SEQ ID NO: 43

5 atgaggatggataatgacagcgctctgtctgagttcatcctcctggggctccccattcgagcagaagaccaagctttgtactctgtcct
gatcctggccatgtacctgacaactgtgctggggaacctgctcatcctactcatcaggctggactctcacctccacacccccatgt
acttcttctcagccacttggccttcacagacatctcttttcatcagtcacagctcctaagatgctcgtgaatatgtgacacacagta
agtccatcccatatacaggggtgtgttccaggtgtatttttactgttttgcaagcattgatagctttcttcaacatccatggcatat
10 gacaggtatgtggccatctgccatcctctgcattataacatcatcatgaatctgaggctctgtgttcttagtagtaatatcatgggcc
ttatctttaaccaatgctcttgcgcacaccttctcttggtcgcctatctcactttagaacaataccatccccactatttctgtgacct
ctctaccttgctgaagctgtctagctcagacaccacatcaatgagctggctatctttgttttaggtaatgtggctcattaccctgccattc
atatgcattctggtttcttatggctacattgggtgcaccattctgaaaactccctccatcaagggaatccacaaagccttgccacgtgt
ggctctcacctctgtgtggtatccttgactatggggccatcattggactatatttgtccctcatctaataacactaatgacaaagatg
15 tcatgtggctgtgatgtacactgtggtcataccatgctgaatccctttatttatagtctgaggaatcgggatatgaaaagaacactg
agaaatatcctcagcagaacaaatga

PROT: SEQ ID NO: 44

MRMDNDSALSEFILLGLPIRAEDQALYSVLILAMYLTTLVGNLLIILLIRLDSHLHTPMYFFLSHLAFTDISFSS
VTAPKMLVNMLTHSKSIPYTGCVSQVYFFTVFASIDSFLLTSMAYDRYVAICHPLHYNIIMNLRCLVLLVVIS
20 WALSLTNALAHLLLLARLSHFRNNTIPHYFCDLSTLLKSSSDTTINELVIFVLGNVVITLPFICILVSYGYIGVTI
LKTPSIKGIHKALSTCGSHLCVVSLYYGAIIGLYFVPSSNNTNDKDVIVAVMYTVVIPMLNPFYISLRNRDMK
RTLRLNLSRTK

Olf1126*Mus musculus*_Olf1126_ 3-hydroxy-3-methylhexanoic acid olfactory receptor (GI:258834)

DNA: SEQ ID NO: 45

atgaaattcacagaaatcagggcagaggacaatgcttcactgtgacagagtttctcctcctgggattttctgaccttcttaacttaca
30 agggattttgtttgggtgttctccataatttacttgatcatattgattggaaatagtttcataattgtgataactagaattgatcctgcac
tacagaagcccatgtatttttctggaatttttcttctctggaaatctgttatgtatcagtcactctccctaggattctgtttaacattg
ctactcaagacagaagcatttctgtggtgagctgtgccacacaaatgtgtttcttcttatgtctgggagctactgagtggttctgtctgg
ctgtgatgtcctatgatcgctatgtggccatctgcaatcctctgcactatcctctggctatgaaccaacaaagtgcactcagctggca
gcagcctcctggcttgaggcatccctgtccagataggacaaacgtgcagatatttctctacatttctgcaattctaaccaaatagat
35 cacttctttgtgacttacctccattctcaagctggcctgtggagatacttcaatacacgagttgtctgtctacttagtagctatgctgtt
tgttgattcccttcttgttgatacttgccctttataccaaaatcattgccaccattctgaagttgccaacagccacaggacgggcaaa
agccttctcaacatgttcttccatttgctgtggtgtttttgtttttggatcagctactattacctacttgaggccaaagtccaccattc
tccaggaactgataaactactcttctgttttacaccattgtgactcccatgttcaatcctctgatatacagctcttagaaataaggaggt
gattgtgcactgagaaaactgttacatatcaagtag
40

PROT: SEQ ID NO: 46

MKFTEIRAEDNASTVTEFLLGFSDLPNLQGLFGLFSIIYLIILIGNSFIIVITRIDPALQKPMYFFLANFSSLEIC
YVSVTLPRILFNIATQDRSISVVSCATQMCFFLMLGATECFLLAVMSYDRYVAICNPLHYPLVMNPTKCTQL
45 AAASWLGGIPVQIQGTCQIFSLHFCNSNQIDHFFCDLPPIKLACGDTSIHELVSYYLVAMLFVAFPFLLILASY
TKIIATILKLPTATGRAKAFSTCSSHLLVFLFFGSATITYLRPKSTHSPGTDKLLSLFYTIVTPMFNPLIYSLRNK
EVIAALRKLLHIK

FLAG[®] tag

DNA - SEQ ID NO: 47

5 gattacaaggacgacgacgataag

Protein - SEQ ID NO: 48

DYKDDDDK

10

Rho tag

DNA - SEQ ID NO: 49

atgaacgggaccgagggcccaacttctacgtgcctttctccaacaagacgggcgtggtg

15 Protein - SEQ ID NO: 50

MNGTEGPNFYVPFSNKTGVV

Lucy tag

20 DNA - SEQ ID NO: 51

atgagaccccagatcctgctgctcctggccctgctgaccctaggcctggct

Protein - SEQ ID NO: 52

MRPQILLLLALLTLGLA

25

SEQ ID NO: 53

Motif

MAYDRYVAIC

30

SEQ ID NO: 54

Motif

FSTCSSH

35

SEQ ID NO: 55

Motif

PMLNPFYIY

40

OR2H1*Homo sapiens*_OR2H1_1-octen-3-ol olfactory receptor (GI: 937628050)

DNA: SEQ ID NO: 56

5 ATGGTTAACCAAAGCTCCCCATGGGCTTCCTCCTTCTGGGCTTCTCTGAACACCCAGCACTGGAAAG
GACTCTCTTTGTGGTTGTCTTCACTTCCTACCTCTTGACCCTGGTGGGCAACACACTCATCATCCTGCT
GTCTGTACTGTACCCAGGCTCCACTCTCCAATGTACTTTTTCTCTCTGACCTCTCCTTCTTGGACCTC
TGCTTTACCACAAGTTGTGTCCCCAGATGCTGGTCAACCTCTGGGGCCCAAGAAGACCATCAGCTT
CCTGGGATGCTCTGTCCAGCTCTTCATCTTCTGTCCCTGGGGACCACTGAGTGCATCCTCCTGACAGT
10 GATGGCCTTTGACCGATACGTGGCTGTCTGCCAGCCCCTCCACTATGCCACCATCATCCACCCCCGCCT
GTGCTGGCAGCTGGCATCTGTGGCCTGGGTTATGAGTCTGGTTCAATCGATAGTCCAGACACCATCC
ACCCTCCACTTGCCCTTCTGTCCCCACCAGCAGATAGATGACTTTTTATGTGAGGTCCCATCTCTGATT
CGACTCTCCTGTGGAGATACCTCCTACAATGAAATCCAGTTGGCTGTGTCCAGTGCATCTTCGTGGT
TGTGCCTCTCAGCCTCATCCTTGCCTCTTATGGAGCCACTGCCCAGGCAGTGTGAGGATTAACCTCTG
15 CCACAGCATGGAGAAAGGCCTTTGGGACCTGCTCCTCCCATCTCACTGTGGTCACCCTCTTCTACAGC
TCAGTCATTGCTGTCTACCTCCAGCCCAAAAATCCGTATGCCCAAGGGAGGGGCAAGTTCTTTGGTCT
CTTCTATGCAGTGGGCACTCCTTCACTTAACCCTCTCGTATACACCCTGAGGAACAAGGAGATAAAGC
GAGCACTCAGGAGGTTACTAGGGAAGGAAAGAGACTCCAGGGAAAGCTGGAGAGCTGCTTAA
20 PROT: SEQ ID NO: 57
MVNQSSPMGFLLLGFSEHPALERTLFVVVFTSYLLTLVGNTLIILLSVLYPRLHSPMYFFLSDL SFLDLCFTTSC
VPQMLVNLWGPCKTISFLGCSVQLFIFLSLGTTECILLTVMAFD RYVAVCQPLHYATIIHPRLCWQLASVA
WVMSLVQSIVQTPSTLHL PFCPHQQIDDFLCEVPSLIRLSCGDTSYNEIQLAVSSVIFVVPLSLILASYGATA
QAVLRINSATAWRKAFGTCSSHLTVVTLFYSSVIAVYLQPKNPYAQGRGKFFGLFYAVGTPSLNPLVYTLRN
25 KEIKRALRRLLGKERDSRESWRRAA

OR2W3*Homo sapiens*_OR2W3_1-octen-3-ol olfactory receptor (GI: 937628231)

30 DNA: SEQ ID NO: 58
ATGGATGGAACCAATGGCAGCACCCAAACCCATTTATCCTACTGGGATTCTCTGACCGACCCCATCT
GGAGAGGATCCTCTTTGTGGTCATCCTGATCGCGTACCTCCTGACCCTCGTAGGCAACACCACCATCA
TCCTGGTGTCCCGGCTGGACCCCACTCCACACCCCATGTACTTCTTCTCGCCACCTTTCTTCTCT
35 GGACCTCAGTTTACCACCAGCTCCATCCCCAGCTGCTCTACAACCTTAATGGATGTGACAAGACCA
TCAGCTACATGGGCTGTGCCATCCAGCTCTTCTGTTCTGCGGTCTGGGTGGTGTGGAGTGCCTGCTT
CTGGCTGTGATGGCCTATGACCGGTGTGTGGCTATCTGCAAGCCCCTGCACTACATGGTGATCATGAA
CCCCAGGCTCTGCCGGGGCTTGGTGTGAGTGACCTGGGGCTGTGGGGTGGCCAACTCCTTGGCCATG
TCTCCTGTGACCCTGCGCTTACCCCGCTGTGGGCACCACGAGGTGGACCACTTCTGCGTGAGATGCC
40 CGCCCTGATCCGGATGGCCTGCGTCAGCACTGTGGCCATCGACGGCACCGTCTTTGTCTGGCGGTG
GGTGTGCTGTGCTGTCCCCCTTGGTGTGTTATCCTGCTCTCTTACAGCTACATTGTGAGGGCTGTGTTACAA
ATTCGGTCAGCATCAGGAAGGCAGAAGGCCTTCGGCACCTGCGGCTCCCATCTCACTGTGGTCTCCCT
TTTCTATGGAAACATCATCTACATGTACATGCAGCCAGGAGCCAGTTCTTCCCAGGACCAGGGCATGT
TCCTCATGCTCTTCTACAACATTGTACCCCCCTCCTCAATCCTCTCATCTACACCCTCAGAAACAGAGA
45 GGTGAAAGGGGGCACTGGGAAGGTTGCTTCTGGGGAAGAGAGAGCTAGGAAAGGAGTA

PROT: SEQ ID NO: 59

MDGTNGSTQTHFILLGFSDRPHLERILFVVILAIYLLTLVGNTTILVSRLDPHLHTPMYFFLAHLSFLDLSFTT
SSIPQLLYNLNGCDKTISYMGCAIQLFLFLGLGGVECLLLAVMAYDRCVAICKPLHYMVIMNPRLCRGLVSV
TWGCGVANSLAMSPVTLRLPRCGHHEVDHFLREMPALIRMACVSTVAIEGTVFVLAVGVVLSPLVFILLSY
5 SYIVRAVLQIRSASGRQKAFGTGSHLTVVSLFYGNIIYMYMQPGASSSQDQGMFLMLFYNIVTPLLNPLIY
TLRNREVKGALGRLLLKGRELKGE

OR8G1

10 *Homo sapiens*_OR8G1_1-octen-3-ol olfactory receptor (GI:937628054)

DNA: SEQ ID NO: 60

ATGTCAGGAGAAAATAATTCCTCAGTGACTGAGTTCATTCTGGCTGGGCTCTCAGAACAGCCAGAGC
TCCAGCTGCCCCCTCTCCTCCTGTTCTTAGGAATCTATGTGGTCACAGTGGTGGGCAACCTGGGCATG
15 ACCACACTGATTTGGCTCAGTTCACCTGCACACCCCTATGTACTATTCCTCAGCAGTCTGTCCTTCA
TTGACTTCTGCCATTCCACTGTCATTACCCCTAAGATGCTGGTGAACCTTTGTGACAGAGAAGAACATC
ATCTCCTACCCTGAATGCATGACTCAGCTCTACTTCTCCTCGTTTTTGCTATTGCAGAGTGTCACATGT
TGGCTGCAATGGCGTATGACCGTTACATGGCCATCTGTAGCCCCTTGCTGTACAGTGTCATCATATCC
AATAAGGCTTGCTTTTCTCTGATTTTAGGGGTGTATATAATAGGCCTGGTTTGTGCATCAGTTCATACA
20 GGCTGTATGTTTAGGGTTCAATTCTGCAAATTTGATTTGATTAACCATTATTTCTGTGATCTTCTTCCCC
TCCTAAAGCTCTCTTGCTCTAGTATCTATGTCAACAACTACTTATTCTATGTGTTGGTGCATTTAACAT
CCTTGTCCCCAGCCTGACCATCCTTTGCTCTTACATCTTTATTATTGCCAGCATCCTCCACATTCGCTCC
ACTGAGGGCAGGTCCAAAGCCTTCAGCACTTGTAGCTCCCACATGTTGGCGGTTGTAATCTTTTTTGG
ATCTGCAGCATTGATGACTTGCAGCCATCTTCAATCAGCTCCATGGACCAGGGGAAAGTATCCTCTG
25 TGTTTTATACTATTATTGTGCCCATGTTGAACCCTCTGATTTATAGCCTGAGGAATAAAGATGTCCATG
TTTCCCTGAAGAAAATGCTACAGAGAAGAACATTATTGTAA

PROT: SEQ ID NO: 61

MSGENNSSVTEFILAGLSEQPELQLPLFLLFLGIYVVTVVGNLGMTTLIWLSSHLHTPMYYFLSSLSFIDFCH
30 STVITPKMLVNFVTEKNIIISYPECMTQLYFFLVFAIAECHMLAAMAYDRYMAICSPLLYSVIISNKACFSLILG
VYIIGLVCAVHTGCMFRVQFCKFDLINHYFCDLLPLLKLSCSSIYVNKLLILCVGAFNILVPSLTILCSYIFIIASI
LHIRSTEGRSKAFSTCSSHMLAVVIFFGSAAFMYLQPSISSMDQGVSSVFYTIIVPMLNPLIYSLRNKDVH
VSLKKMLQRRTLL

35

Olf93*Mus musculus*_Olf93_1-octen-3-ol olfactory receptor (GI: 32060027)

DNA: SEQ ID NO: 62

5 ATGGTCAACCAGAGCACCCCCGTGGGCTTCCTCCTCCTGGGCTTCTCTGAACACCCACAACCTGGAAAA
GGTTCTCTTCGTGCTTGTCTTGTGCTCCTACCTCCTCACCTCCTAGGAAACACACTCATCCTCCTGCTG
TCCACCCTGGACCCCAGGCTCCACTCTCCAATGTACTTCTTCTCTTAACCTCTCCTTCTTGGACCTCT
GCTTCACCACAACCTGTGTTCCCCAGATGTTGTTCAACCTCTGGGGCCCCACAAAGACCATCAGCTTCC
10 TGGGATGCTCTGTCCAGCTCTTCATCTTCATGCTCCTGGGGACAACAGAGTGCATCCTGTTGACAGTA
ATGGCCTTTGACCGCTATGTGGCTGTCTGTCAGCCCCTGCACTATGCCACCATAATCCACCCCCGCCTA
TGTCGCCAGTTGGCAGGTGTGGCCTGGGCTATAGGTTTGGTCCAATCCATAGTTCAAATACCACCCAC
CCTCACACTGCCCTTCTGTTCCCATAGGCAAATAGATGACTTTCTGTGTGAAGTCCCATCTCTAATCCG
ACTCTCTTGTGGGGACACCACTTTTAATGAGATTGAGTTGTCAGTTGCAGGTGTCATCTCCTGCTTGT
15 ACCTCTGAGCCTCATCATTGTCTCTTATGGTGTGATTGCCAGGGCTGTACTAAAACTAACTCTTCAA
AGGGCGCAGAAAAGCTTTTGGGACCTGTTTCATCCACCTCATTGTGGTTACCCTCTTTTACAGCTCAG
TCATTGCTGTCTATCTGCAGCCCCAAAATCCCTATGCCCAAGAGAGGAGCAAGTTCTTTGGTCTCTTTT
ATGCAGTGGGCACCCCCACACTCAACCCTCTGTATATACCCTGAGGAACAAGGAGGTAAAGAGGGC
ATTCTGGAGGCTGCTGGGGAAGGATGCGGCTTCTGGAGGAACTAA

20 PROT: SEQ ID NO: 63
MVNQSTPVGFLLLGFSEHPQLEKVLVVLCSYLLTLLGNTLILLSTLDPRLHSPMYFFLSNLSFLDLCFTTT
CVPQMLFNLWGPTKTISFLGCSVQLFIFMLLGTTECILLTVMAFDRYVAVCQPLHYATIIHPRLCRQLAGVA
WAIGLVQSIVQIPPTLTLPFCSHRQIDDFLCEVPSLIRLSCGDTTFNEIQLSVAGVIFLLVPLSLIIVSYGVIARA
VLKTNSSKGRRKAFGTCSHLIVVTLYSSVIAVYLQPKNPYAQERSKFFGLFYAVGTPTLNPLVYTLRNKEV
25 KRAFWRLLGKDAASGGN

Olf398*Mus musculus*_Olf398_1-octen-3-ol olfactory receptor (GI: 32049056)

30 DNA: SEQ ID NO: 64
ATGGCTGTGACCAACCTCACATACAAACCACAGTTCCAGCTCCTCGGCTTGATGGATGGCACAGATCC
CCACCCGCTGCTGTTTCTTCTTTCTTAGCATTTACCTACTCAATGCCCTGGGCAATCTGAGCATGGT
GGTGCTGGTGAGGTCTGATGGGGCTCTGTGCTCCCCATGTATTATTTCTGGGTACCTGAGCCTCG
35 TGGATGTCTGCTTTACCACAGTCACTGTCCCAGACTGCTGGCCACCTGCTCCATCCTGGCCAGGCC
ATATCCTTCCAGGCTTGTTCGCCCAGATGTACTTCTTTGTAGCTCTGGGTATCACCGAGAGCTACCTT
CTGGCAGCCATGTCTTATGACCGTGCGGTGGCTGTGTGTAGACCGCTGCACTATGGTGCAGTCATGA
CACCTGGCGCTGCTTTTGTGGTGGCTGCATCCTGGGCTGTGGCCCATCTGCACTCTCTTCTACATA
CACTGCTCATCTCTGCTCTCACCTACCCTCCCTCTGCCCCAGTGCGCCACTTCTTTGTGACATGACTGT
40 AATGCTGAGCTTGGCAACCTCTGACACATCAGCTGCAGAGACTGCCATCTTCTCAGAGGGGCTAACA
GTGGTGTGACCCCTCTGCTCCTCGTGTCCCTTTCTATGCACGCATCCTGTGGCAGTGCTTGGGAATT
CGGACCACAGGAGGCCGGCACCCTGTCTTCTCCACCTGTGGGGCCACCTGGTGGTAGTGTCACTTT
TCTTTGGCTCAGTCCTCTCCGTCTACTTCCGTCCATCATCTGCCTACTCAGCTCGTTATGACCGCATGGC
CAGTGTGGTCTATGCGGTAGTCACACCGACCTTGAACCCTTTTATCTACAGTCTTCGTAACAAAGAGG
45 TCAAGAGTGCCCTAAAAAGGGGTTTCAGATGGAGAGCAGCACCCCAAGATGAGTAA

PROT: SEQ ID NO: 65

MAVTNLTYKPFQQLGLMDGTDPHPLLFLFLSIYLLNALGNLSMVVLVRS DGALCSPMYFLGHLSLVDV
CFTTVTVPRLLATLLHPGQAISFQACFAQMYFFVALGITESYLLAAMS YDRAVAVCRPLHYGAVMTPWRC
FLLVAASWAVAHLSLLHTLLISALTYPPSAPVRHFFCDMTVMLSLATS DTSAAETAIFSEGLTVVLTPLLV
5 SLSYARILVAVLGIRTTGGRHRVFSTCGAHLVVVSLFFGSVLSVYFRPSSAYSARYDRMASVVYAVVTPTLN
PFIYSLRNKEVKSALKRGFRWRAAPQDE

Olf120

10 *Mus musculus*_Olf120_1-octen-3-ol olfactory receptor (GI: 32060790)

DNA: SEQ ID NO: 66

ATGAGTGTCAACTGCTCTCTGTGGCAGGAAAATAAGTTGTCTGTCAAACACTTTGCATTTGCCAAGTT
CTCTGAGGTTCTGAAGAATGCTTCCTCCTGTTTACCCTGATTCTCCTCATGTTCTTAGTATCACTGACA
15 GGAAATGCACTTATAACCTTGCCATATGCACCAGTCCAGCCCTACACACCCCCATGTACTTCTTTCTG
GCCAACTTGTCTCTCCTGGAAATTGGCTACACTTGTTCTGTGCATACCGAAGATGTTGAAGAACCTTGTA
ACTGAGGCCCGAGGGATCTCTCGGGAAGGGTGTGCCACACAGATGTTTTCTTTATATTCTTTGGTAT
AACTGAGTGTTCCTACTGGCAGCTATGGCCTTTGACCGCTACATGGCCATATGCTCCCCACTCCACT
ATGCAACCCGAATGAGTCGTGAGGTATGTGCCATTTGGCAATAGTTTCATGGGGAATGGGATGCAT
20 AGTAGGGTTGGGACAGACCAATTTTATTTCTCCTTAACTTCTGTGGACCCTGTGAGATAGACCCT
TCTTCTGTGACCTTCCACCTGTCCTGGCACTTGCTGTGGAGATACATCCCAAATGAGGCTGCAATCT
TCGTGACAGTAGTTCTCTGCATATCTAGCCCATTTTGTGATCATTTATTCCTATGTCAGAATTTTGT
TGCAGTGCTGGTGATGCCTTCACCTGAGGGGCGCCATAAAGCTCTCTCCACCTGTTCTCCCATCTACT
TGTAATCACATTGTTCTATGGCTCAGCATCTATTACCTACTTGAGGCCCAAGTCTAGCCACTCACCAGG
25 AATAGATAAACTCTTGGCCCTTTCTACACCGCGGTGACTTCCATGCTGAACCCCATCATCTATAGCTT
AAGGAACAAGGAAGTGAAGGCAGCACTGAGAAGAACTCTGAGTCTGAAGAAACCTCTGGCAATAAA
TAGGTAA

PROT: SEQ ID NO: 67

30 MSVNCSLWQENKLSVKHFAFAKFSEVPEECFLFTLILLMFLVSLTGNALITLAICTSPALHTPMYFFLANLSL
LEIGYTCVIPKMLKNLVTEARGISREGCATQMFFFIFFGITECCLLAAMAFDRYMAICSPLHYATRMSREV
CAHLAIVSWGMCIVGLGQTNFIFSLNFCGPCEIDHFFCDLPPVLALACGDTSQNEAAIFVTVVL CISSPFL
IIYSYVRILFAVLVMPSPTEGRHKALSTCSSHLLVVTIFYGSASITYLRPKSSHSPGIDKLLALFYTAVTSM LNPII
YSLRNKEVKAALRRTL SLKKPLAINR

35

Olf1364*Mus musculus*_Olf1364_1-octen-3-ol olfactory receptor (GI: 32078800)

DNA: SEQ ID NO: 68

5 ATGATCAACCAGAGCTGCCAGGAACAGTTCATCCTGCTGGGCTTCTCAGACAGACCGAGGCTAGAAT
CCATCCTCTTTGTGTTTGTCTCATCTTCTACCTGGTGACTTTAGTGGGCAACATCATCATTATCTTAGT
TTCCTATCTGGACCCCTGTCTTCACACCCCATGTACTTCTCCTCACCAACTTGTCCTTTCTTGACCTCT
GTTTCACTACCAGTTCATCCCTCAATTGCTCTTCAACTTAGGAGGCCAGGACAAGAGCATCAGTTAC
ATTGGCTGTGCAGTCCAGCTGTTTCTTGGCCTAGGAGGTACTGAGTGTGTTTTGCTGGCTGT
10 CATGGCTTACGACCGTTTCACTGCAATCTGCAAGCCCCTTCACTACTCGGTCATTATGCATTCTCAGCT
CTGCTGGACATTGGTGTCTGTAGCCTGGAGTGTGGGACTCCTCAACTCCCTGGTCATGTCTCCTGTGA
CCATGAAGCTGCCTCGATGTGGCAGATGTCAGGTGAGGCACTTCTGTGTGAGATGCCAGCTCTGAT
AAAAATTGCCTGTGTGGACACTGTGGCTGTGGAAAGCACTGTTTTATTTTATCGGTGATAATCGTGC
TGGTGCCTTTGACTCTCATCCTCATTTCTTACAGCTATATTGCTCTAGCAGTGATGAGGATCAAGTCGG
15 CCTCAGGAAGGAGGAAGGCTTCAACACGTGTGGGTCTCACCTACCGTAGTCTCCTGTTTTACGGG
AATATCATCTATATGTATATGCAGCCTGGACACAAGGCTTCCAGGACCAAGGGAAATTTCTTACCCT
CTTCTACAACCTGGTAACCCCATGTAAACCCTGTCATCTATACACTGAGAAACAAGGATGTAAAGG
GCGCACTGAAGAGGCTTGACTACGAAATAA

20 PROT: SEQ ID NO: 69

MINQSCQEQFILLGFSRPRLESILFVFLIFLVTLVGNIIIIIVSYLDPCLHTPMYFFLTNLSFLDLCFTTSSIP
QLLFNLGGQDKSISYIGCAVQLFMFLGLGGTECVLLAVMAYDRFTAICKPLHYSVIMHSQLCWTLVSVAV
SVGLLNSLVMSPVTMKLPRCGRCQVRHFLCEMPALIKIACVDTVAVESTVFILSVIIIVLPLTILISYSYIALA
VMRIKSASGRRKAFNTCGSHLTVVSLFYGNIIYMYMQPGHKASQDQGKFLTLFYNLVTPMLNPVIYTLRN
25 KDVKGALKRLVTTK

Olf937*Mus musculus*_Olf937_1-octen-3-ol olfactory receptor (GI: 32064616)

30

DNA: SEQ ID NO: 70

ATGGCAACAGGAACTATTGCATGTTACCTGAGTTCATTCTGACTGGGCTCTCAAAGAAGCCACAAC
CCAGATGCCTCTCTCCTCCTCTCCTAGGAATCTATGTGGTCACTGTAGTGGGGAATTTGGGCATGA
TTACACTGATTAAGCTCAGTTCACCTGCATACCCCATGTACTATTTCTCAGTAGTTTGTCTTTAT
35 TGATCTCTGCCATTCCACTGTCATTACCCCAAATGTTGGTGAACCTTGTGATAGAGAAAAACATCAT
TTCCTACACTGGATGCATGGCTCAGCTCTATTTCTTCTAATTTTGTCTATTGCAGAGTGTCATATGTTA
GCTGCAATGGCATATGATCGCTATGTTGCCATCTGTAACCCCTTGCTTTACAATGTAACCATGTCCTAT
CAGATTTACACTTCCCTGATCTTTGGAGTCTATATTATTGGTGTGGTTTGTGCATCAGCTCACACAGGC
TTCATGATCAGAATACAGTTTTGTAACCTAGAGGTGATCAACCACTATTTCTGTGATCTTCTTCCCCTG
40 CTGGAGCTTGCTCACTCTAGTACTTATGTTAATGAATTGTTAGTTTTATGTTTTGGTACATTTAACATTG
TTGTTCCAACCATGACTATTCTTACTTCTTACATCTTCATCATTGCCAACATCTTACGCATTCTGTTCTACT
GGAGGCAGGTCCAAAGCCTTCAGTACCTGCAGCTCCACATCTTAGCTGTTGCTGTGTTCTTTGGGTC
TGCTGCATTCATGTACCTTCAACCATCATCAGTCAGCTCCATGGACCAAGGGAAAGTGTCTCTGTGT
TTTATACCATTGTTGTTCCCATGCTGAACCCCTTGATCTATAGTCTGAGGAATAAGGATGTCAGTGTTG
45 CCCTGAAGAAATACTAGAAAGAAATTATTCATGTAA

PROT: SEQ ID NO: 71

MATGNYCMLPEFILTGLSKKPQLQMPLFLLFLGIYVTVVGNLGMITLIKLSHLHTPMYYFLSSLSFIDLCH
STVITPKMLVNFVIEKNIISYTGCMALYFFLIFAIAECHMLAAMAYDRYVAICNPLLYNVTMSYQIYTSLIF
GVYIIGVVCASAHTGFMIRIQFCNLEVINHYFCDLLPILLELAHSSTYVNELLVLCFGTFNIVVPTMTILTSYIFII
5 ANILRIRSTGGRSKAFSTCSSHILAVAVFFGSAAFMYLQPSSVSSMDQGKVSSVFYTIVVPMNLNPLIYSLRNK
DVSVALKKILERKLFM

Olf1322

10 *Mus musculus*_Olf1322_geonol olfactory receptor (GI: 46404727)

DNA: SEQ ID NO: 72

ATGACTCAAATTCAGAAATTATTCTTTTGGGTTTTGGAGATCTCCATGGCCTTCAGTTTCTTCTTTTG
GGCTATTTCTAGCCATTTATGTTATGACTCTCCTGGGTAACATTGTAATTCTCACCGTAGTATCCACTG
15 ATTGCTCCCTTCACACACCCATGTATTTCTTCTTGGCCACTTCTCCTCCTAGAGATCAGCTACACCAC
AACAATTGAGCCTGTAATGCTGTGGACATTGTTATCGGCTCATGTGCCTATCTCCTTGCCAGCCTGTG
CTTGTCAGTTTTACTTTTTTGCATCTTTGGTGGCAACAGAATGCTTCCTCCTTGCTGTAATGTCTTATGA
TAGATACATAGCCATTTGTAACCCACTACACTATTCCAGTATCATGGACTCCTGGGGTTGTTCCAGCT
AGCATTGGCCTCTTGGTTGGCTGGATTCTGGCACCTATCTTACTCATGATCTTGATTTTTCGCTTAAC
20 ATTTTGTCTGCCAATGAGATTGACCACTTCTTCTGTGATTTGAAGCCCATCATGAACTGGCCTGCAC
TAATACTCAAGTAGCTGAAATGACTTCTTTTATATGTACCTCATTATTCGCTCTTGGTCCCTTCATACTG
ACCTTGGCTTCTTATATTACATCATTTGCACCATTCTGAGGATCCCTTCGACCACAGGGAAGCAGAG
GGCTTTCTCCACCTGTTTCATCTCACCTTATAGTGGTCAGTCTTTATTATGGGACTCTGGGCATTGTCTAT
GGCTTCCCATCAATGCCTCAATATGAAAGTATATTGAAGTTGCTTTCTTCTGTATACAGTGTTTACC
25 CCTGCTGCCAATCCTATCATTTACACCCTAAGGAACAAGGATGTGAAGGTAGCTCTGAGAAAATTGAC
ACAATGGCATAACATACCTGGTCAAAGAAGGCTAA

PROT: SEQ ID NO: 73

MTQISEIILLGFGDLHGLQFLLFGLFLAIYVMTLLGNIVILTVVSTDCSLHTPMYFFLGHFSEISYTTTIEPV
30 MLWTLLSAHVPISLPACACQFYFFASLVATECFLLAVMSYDRYIAICNPLHYSSIMDSWGCFLALASWLA
GFLAPILLMILIFRLTFCSANEIDHFFCDLKPIMKLACTNTQVAEMTSFICTSLFALGPFILTASYIHIICTILRIP
STTGKQRAFSTCSSHLIVVSLYYGTGIVYGFPSMPQYESILKLLSLLYTVFTPAANPIIYTLRNKDVKVALRKL
TQWHTYLVKEG

35

Olf46*Mus musculus*_Olf46_transpirol olfactory receptor (GI: 32054916)

DNA: SEQ ID NO: 74

- 5 ATGGTCAGTCCCAACCAGACAGTAGTGACAGAGTTTGTGCTGCAAGGGTTCTCAGAGCACCCAAGTC
TAAGACTGTTCTGATGGGCTGTTTCCTGTCCCTGTACACAGTGGCTTTAATGGGCAACATGGTGATC
ATTGCTTTGATCACCTCAAGCACTGGGCTCCACAGTCCCATGTACTTTTTCTGTGCAACTTAGCGACC
ATGGATATTATCTGCACCTCCTCTGTACTGCCCAAGGCGCTGGTTGGTCTACTGTCTGAGGAAAACAC
CATCTCCTTCAAAGGGTGCATGACTCAGCTCTTCTTTCTGTGTGGTCTGGATCCTCTGAGCTGCTGCT
10 GCTCACAGTCATGGCCTATGACCGCTATGTGGCCATCTGTTTGCCCCTGCATTACAGCTCTAGGATGA
GTCCACAGCTCTGTGGGACCTTTGCCGTGGGTGTATGGTCCATCTGCGCACTAAATGCATCTATCAAC
ACTGGTCTGATGACACGGCTGTCATTCTGTGGCCCCAAGGTCATCACCCACTTCTTCTGTGAGATTCCC
CCACTCCTCCTGCTCTCCTGTAGTCCTACATATATAAATAGCGTTATGACTCTTGTGGCAGATGCCTTTT
ATGGAGGCATCAATTTTTTACTTACCTTGCTATCCTATGGCTGCATCATTGCCAGCATCCTGCGCATGC
15 GTTCTGCTGAGGGCAAGAGGAAGGCCTTTTCTACCTGCTCATCCACCTCATCGTGGTCTCTGTGTAC
TACTCATCTGTGTTCTGTGCCTATATCAGTCCTGGTTCAGCTACAGCCCAGAAAGAAGCAAATTTACC
TCGGTTTTGTACTCAGTCCTCAGCCCAACCCTCAACCCCCTCATCTATACACTGAGGAACAAGGATGTC
AAGCTTGCCCTGAGAAGACTCTTCCCCTCTTCTCAAATTAA
- 20 PROT: 75
MVSPNQTVVTEFVLQGFSEHPSLRLFLMGCFLSLYTVAlMGNMVIIAlTSSTGLHSPMYFFLCNLATMDII
CTSSVLPKALVGLLSEENTISFKGCMTQLFFLVWSGSSELLLLTVMAYDRYVAICLPLHYSSRMSPQLCGTF
AVGVWSICALNASINTGLMTRL SFCGPKVITHFFCEIPLLLLSCSPTYINSVMTLVADAFYGGINFLTLLSY
GCIASILRMRS AEGKRKAFSTCSSHLIVVSVYYSSVFCAYISPGSSYSPERSKFTSVLYSVLSPTLNPLIYTLRNK
25 DVKLALRRLFPSFSN

The following examples are illustrative only and are not meant to limit the scope of invention as set forth in the Summary, Description or in the Claims.

5 The numerous possible variations that will become immediately evident to a person skilled in the art after having considered the disclosure provided herein also fall within the scope of the invention.

All materials and microorganisms or cells employed are commercially available products.

10 Unless otherwise specified, recombinant proteins are cloned and expressed by standard methods, such as, for example, as described by Sambrook, J., Fritsch, E.F. and Maniatis, T., Molecular cloning: A Laboratory Manual, 2nd Edition, Cold Spring Harbor Laboratory, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, 1989.

EXAMPLES

Example 1: Identification and Functional Characterization of Mouse and Human Odorant Receptors Activated by Geonol, DMTS, 1-octen-3-ol, Butyric Acid, 3-methyl-2-hexenoic acid, 3-hydroxy-3-methyl-hexanoic acid and Transpirol

5 The identification of new odorant receptors was performed according to the method disclosed in WO2014/210585. Briefly, murine olfactory sensory neurons were exposed to the following MCS's: geonol, DMTS, 1-octen-3-ol, butyric acid, 3-methyl-2-hexenoic acid, 3-hydroxy-3-methyl-hexanoic acid, or transpirol and screened using a Ca^{2+} imaging technique. Neurons that were activated by DMTS were further isolated for full transcriptome analysis to
10 identify the responsive odorant receptor. The cDNA corresponding to the isolated cell mRNA was generated and amplified by PCR based method (Clontech/Takara, SMARTer® Ultra® Low Input RNA Kit for Sequencing - v3, cat. 634848). Amplified cDNA was then used to generate an Illumina cDNA library for Next-Generation-Sequencing and the generation of 100 base pair single read sequences. Sequences were aligned to a mouse reference genome (such
15 as UCSC version mm10) in order to generate the full transcriptome. Because only a single odorant receptor (OR) is strongly transcribed per olfactory sensory neuron, the subsequent identification of the MCS responsive OR can be achieved. Phylogenetic relationship evaluation using sequence similarity searches were then used to identify the corresponding human OR. The following ORs were identified Olfr263, Olfr96, Olfr1487, Olfr339, Olfr641,
20 Olfr1126, Olfr46, Olfr1322, Olfr93, Olfr398, Olfr120, Olfr1364 and Olfr937.

 In the second method, a panel of odorant receptors comprising the 400 putatively functional human receptor repertoire were transfected into a cultured human HEK293T cell line described in WO2014/210585 expressing Human olfactory G-protein alpha subunit (Golf - SEQ. ID No. 49) and coupled to a cyclicAMP reporter. Said panel of *in vitro* odorant
25 receptors were exposed to MCSs and the level of cAMP signal was measured for each receptor. Receptors showing a signal significantly different from baseline were subsequently tested in functional dose-response experiments. Referring to Figure 1, the following human odorant receptors were identified: OR11A1, OR2M3, OR4S2, OR2J3, OR4Q3, OR51E1, OR2W1, OR1A1, OR5K1, and OR51I2.

Functional dose-response experiments were performed to evaluate the level of MCS-induced activity of the modified cell line expressing individual putative odorant receptors, according to the assays and methods disclosed in WO2014/210585, using either geonol, DMTS, 1-octen-3-ol, butyric acid, 3-methyl-2-hexenoic acid, 3-hydroxy-3-methyl-hexanoic acid, or transpirol.

Example 2: Identification of Butyric Acid Olfactory Receptor Inhibitors

A cell line expressing the OR51E1 olfactory receptor was used as an antagonist screening platform to identify compounds that have the property to decrease the butyric acid induced receptor activity. The cell line was screened with a volatile compound library for their inhibitory properties and potential butyric acid smell inhibition. First, individual binary mixtures of butyric acid with each one of the test compounds were presented to the cells.

Single concentration monitoring of the butyric acid induced cell activity in the presence or absence of a test compound allowed for the identification of compounds with a putative suppression or inhibitory effect. These hits were further confirmed in an inhibitory dose-response assay to evaluate the % inhibition normalized to the baseline agonist activity.

A dose-dependent decrease of receptor activity was recorded with increasing concentrations of test compounds in the presence of a single activating concentration of butyric acid (EC_{87}) and corresponding dose-response inhibition curves were obtained. A summary of the maximum % inhibition for the compounds tested is shown in Figure 2.

The assay system was designed to select for highly selective antagonists, in that the data were obtained using a high butyric acid concentrations (EC_{87}). These data demonstrate that the compounds of Formula (I) are butyric acid olfactory receptor antagonists. However, some compounds performed better than others, as suggested by the relative magnitudes of the inhibition of the butyric acid olfactory receptor.

Example 3: Identification of Geonol Olfactory Receptor Inhibitors

Cell-Based Screening: Cell lines expressing either the OR11A1, or the OR2M3 olfactory receptor were used as antagonist screening platforms to identify compounds that have the property to decrease the geonol induced receptor activity. Each cell line was
5 screened with a volatile compound library for their inhibitory properties and potential geonol smell inhibition. First, individual binary mixtures of geonol with each one of the test compounds were presented to the cells.

Single point monitoring of the geonol induced cell activity in the presence or absence of a test compound allowed for the identification of compounds with a putative suppression or
10 inhibitory effect. These hits were further confirmed in an inhibitory dose-response curve assay to evaluate the potency of activity inhibition as a measure of the IC_{50} (the inhibitor concentration at which the receptor activity is inhibited by the half-maximal inhibition efficacy level of a given test compound).

A dose-dependent decrease of receptor activity was recorded with increasing
15 concentrations of test compounds in the presence of a single activating concentration of geonol (EC_{80}) and corresponding dose-response inhibition curves were obtained. The compounds listed in Table 2 are examples of compounds that decreased the geonol induced activity of at least one olfactory receptor.

Sensory Evaluation: Five 16oz glass jars containing either REF (geonol only), geonol
20 only control, antagonist only, mixture of geonol and isointense antagonist, or mixture of geonol and low intensity antagonist were presented to the panelists (last four samples were randomized across panelists). The panelists were asked to familiarize themselves with the earthy/moss odor quality from the REF jar first, then rate the pleasantness, earthy/moss odor intensity and overall odor intensity of the next four samples on a 0-10 linear scale. The inter-
25 stimulus interval between the samples was two minutes to avoid adaptation. The results are superimposed in Figure 4, wherein the figure shows the percentage of geonol malodor (earthy/moss odor) remaining in binary iso-intense mixtures of geonol and 25 different antagonists to REF sample.

A one-way Analysis of Variance (ANOVA) with Duncan mean comparison at 95% confidence level was done to compare the average earthy/moss odor intensity among geonol only sample, antagonist only sample, and mixtures of Geonol reference/antagonist at two different ratios. The results from the cell-based screening and the sensory evaluation are shown in Table 2 and Figure 4.

* means that no significant difference of earthy/moss odor intensity was found between the iso-intense mixture and antagonist, and it was significantly lower than geonol only sample at 95% confidence level.

* means that the earthy/moss odor intensity was significantly higher in iso-intense mixture than in antagonist only sample, and it was significantly lower than geonol only sample at 95% confidence level.

NS means that no significant difference of earthy/moss odor intensity was found between the iso-intense mixture and antagonist, and no significant difference was found between the iso-intense mixture and geonol only sample at 95% confidence level.

NS means that the earthy/moss odor intensity was significantly higher in iso-intense mixture than in antagonist only sample, and no significant difference was found between the iso-intense mixture and in geonol only sample at 95% confidence level.

Table 2: Geonol Olfactory Receptor Antagonists

Compound	IC ₅₀	%Inhibition	% Remaining in human sensory tests
2-tertbutyl phenol	88	100	46*
thymol	107	100	53
nona-2,6-dienal	156	80	67
1,1-diethoxy-3,7-dimethylocta-2,6-diene	371	55	51*
[1R-(1R*,4R*,6R*,10S*)]-4,12,12-trimethyl-9-methylene-5-oxatricyclo[8.2.0.0 ^{4,6}]dodecane	1233	50	NT
3-(4-hydroxy-4-methylpentyl)cyclohex-3-ene-1-carbaldehyde;4-(4-hydroxy-4-methylpentyl)cyclohex-3-ene-1-carbaldehyde	217	60	NT
1,4,8-trimethyl-13-oxabicyclo[10.1.0]trideca-4,8-diene;1,5,8-trimethyl-13-oxabicyclo[10.1.0]trideca-4,8-diene	81	50	85
3-(4-tert-butylphenyl)propanal	316	50	NT
(4R,4aS,6R)-4,4a-dimethyl-6-prop-1-en-2-yl-3,4,5,6,7,8-hexahydronaphthalen-2-one	486	50	NT
6,10-dimethylundeca-5,9-dien-2-one	133	50	45*
1-(3,3-dimethylcyclohexen-1-yl)pent-4-en-1-one;1-(5,5-dimethylcyclohexen-1-yl)pent-4-en-1-one	111	45	58*
1-(3,3-dimethylcyclohexen-1-yl)pent-4-en-1-one;1-(5,5-dimethylcyclohexen-1-yl)pent-4-en-1-one	148	45	NT

Compound	IC ₅₀	%Inhibition	% Remaining in human sensory tests
2-ethoxy-5-prop-1-enylphenol	111	33	34*
1-(2,6,6-trimethyl-1-cyclohex-3-enyl)but-2-en-1-one	301	10	66*
2-ethoxy-5-prop-1-enylphenol, 8,9-epoxy-2,6,6,8-tetramethyl-tricyclo[5.3.1.0(1,5)]undecane	301	30	NT
1-(4,8-dimethyl-12-methylidenecyclododeca-4,8-dien-1-yl)ethanone; 1-(2,6,10-trimethylcyclododeca-1,5,9-trien-1-yl)ethanone; 1-(2,6,10-trimethylcyclododeca-2,5,9-trien-1-yl)ethanone	301	20	NT
nonylenic aldehyde	151	30	NT
isobutylquinoline	109	45	52*
cyclopentadec-4-en-1-one	61	45	47
(-)-(R)-3,7-dimethyl-6-octenenitrile	300	10	NT
2-methyl-5-propan-2-ylphenol	215		27**
isopropyl quinoline	400		110
5-hexyl-2-methylpyridine 10% Citr	555		37
(2,5-dimethyl-1,3-dihydroinden-2-yl)methanol			37*
2-pentylcyclopentan-1-one			78
4-(2,6,6-trimethylcyclohexen-1-yl)but-3-en-2-one; 4-(2,6,6-trimethylcyclohex-2-en-1-yl)but-3-en-2-one			59*

Compound	IC ₅₀	%Inhibition	% Remaining in human sensory tests
3-methyl-4-(2,6,6-trimethylcyclohex-2-en-1-yl)but-3-en-2-one; 1-(2,6,6-trimethylcyclohex-2-en-1-yl)pent-1-en-3-one			38*
2,4-dimethylcyclohex-3-enecarbaldehyde			45*
phenylethylol			58
3,7-dimethylocta-2,6-dienal			42*
(2,2,2-trichloro-1-phenylethyl) acetate crist			61
4-(2,6,6-trimethylcyclohexen-1-yl)but-3-en-2-one			43*
phenyl ethyl acetate			47*
7-hydroxy-3,7-dimethyloctanal			39*

Example 4: Identification of 1-octen-3-ol Olfactory Receptor Inhibitors

Cell lines expressing either the OR2W1 or the OR1A1 olfactory receptor were used as antagonist screening platforms to identify compounds that have the property to decrease the 1-octen-3-ol induced receptor activity. Each cell line was screened with a volatile compound library for their inhibitory properties and potential 1-octen-3-ol smell inhibition. First, individual binary mixtures of 1-octen-3-ol with each one of the test compounds were presented to the cells.

Single concentration monitoring of the 1-octen-3-ol induced cell activity in the presence or absence of a test compound allowed for the identification of compounds with a putative suppression or inhibitory effect. These hits were further confirmed in an inhibitory dose-response assay to evaluate the potency of activity inhibition and efficacy as a measure of the IC_{50} (the inhibitor concentration at which the receptor activity is inhibited by the half-maximal inhibition efficacy level of a given test compound) and % inhibition (normalized to baseline agonist activity) accordingly.

A dose-dependent decrease of receptor activity was recorded with increasing concentrations of test compounds in the presence of a single activating concentration of 1-octen-3-ol (EC_{80}) and corresponding dose-response inhibition curves were obtained. The compounds listed in Table 3 are examples of compounds that decreased the 1-octen-3-ol induced activity of at least one receptor.

Table 3: 1-octen-3-ol Olfactory Receptor Antagonists

Compound	IC ₅₀ (μM)	% Inhibition
Cyclododecanone	8.79	118.47
2,4-dimethylcyclohex-3-enecarbaldehyde	18.76	107.99
1,4-dioxacyclohexadecane-5,16-dione	24.25	116.54
[1R-(1R*,4R*,6R*,10S*)]-4,12,12-trimethyl-9-methylene-5-oxatricyclo[8.2.0.0 ^{4,6}]dodecane	25.11	123.63
Pentanol, 1-	28.32	94.31
OXACYCLOHEXADECAN-2-ONE	32.15	111.31
tert-butylphenol, 2-	36.95	100.34
(+)-3-methylcyclopentadecanone	43.96342	113.50
1,1,2,3,3-pentamethyl-2,5,6,7-tetrahydroinden-4-one	51.185156	118.44
(4-methyl-4-phenylpentan-2-yl) acetate	61.70	98.90
(+)-perhydro-5,5,8A-trimethyl-2-trans-naphthalenone	63.22	102.97
2,3,3-trimethyl-2H-inden-1-one	75.60	128.39
1-(4,8-dimethyl-12-methylidenecyclododeca-4,8-dien-1-yl)ethanone; 1-(2,6,10-trimethylcyclododeca-1,5,9-trien-1-yl)ethanone; 1-(2,6,10-trimethylcyclododeca-2,5,9-trien-1-yl)ethanone	82.36	113.23
4-(4,8-dimethylnona-3,7-dienyl)pyridine	134.31	111.87
Cyclopentadec-4-en-1-one	155.72	90.98
4-[(1~{R},3~{R},6~{R})-2,2,3,6-tetramethylcyclohexyl]but-3-en-2-one; 4-[(1~{S},3~{S},6~{R})-2,2,3,6-tetramethylcyclohexyl]but-3-en-2-one	186.12	90.82
(+)-(1R,7R)-10,10-dimethyl-tricyclo[7.1.1.0(2,7)]undec-2-en-4-one 90 DIPG	193.99	128.51
(9<I>E</I>)-cycloheptadec-9-en-1-one	210.10	97.22
1,4,8-trimethyl-13-oxabicyclo[10.1.0]trideca-4,8-diene; 1,5,8-trimethyl-13-oxabicyclo[10.1.0]trideca-4,8-diene	266.47	70.92

Compound	IC ₅₀ (μM)	% Inhibition
8,8-dimethyl-2,3,4,6,7,8~{a}-hexahydro-1~{H}-naphthalene-2-carbaldehyde;8,8-dimethyl-2,3,5,6,7,8~{a}-hexahydro-1~{H}-naphthalene-2-carbaldehyde;8,8-dimethyl-2,3,4,5,6,7-hexahydro-1~{H}-naphthalene-2-carbaldehyde;2,2-dimethyloctahydro-1~{H}-2,4~{a}-methanonaphthalen-8-one	1641.48	83.15
2,4~{a},8,8-tetramethyl-1~{a},2,4,5,6,7-hexahydro-1~{H}-cyclopropa[j]naphthalen-3-one;2,6,6,8-tetramethyltricyclo[5.3.1.0 ^{1,5}]undecan-9-one	2362.92	109.43
Isobutylquinoline	> 600	30.14

Example 5: Identification of Butyric Acid Olfactory Receptor Inhibitors

A cell line expressing the OR51E1 olfactory receptor was used as an antagonist screening platform to identify compounds that have the property to decrease the butyric acid induced receptor activity. The stable cell line was screened with a volatile compound library for their inhibitory properties and potential butyric acid smell inhibition. First, individual binary mixtures of butyric acid with each one of the test compounds were presented to the cells.

Single concentration monitoring of the butyric acid induced cell activity in the presence or absence of a test compound allowed for the identification of compounds with a putative suppression or inhibitory effect. These hits were further confirmed in an inhibitory dose-response assay to evaluate the potency of activity inhibition as a measure of the IC_{50} (the inhibitor concentration at which the receptor activity is inhibited by the half-maximal inhibition efficacy level of a given test compound).

A dose-dependent decrease of receptor activity was recorded with increasing concentrations of test compounds in the presence of a single activating concentration of butyric acid (EC_{94}) and corresponding dose-response inhibition curves were obtained. The compounds listed in Table 4 are examples of compounds that decreased the butyric acid induced activity of at least one receptor.

Table 4: Butyric Acid Olfactory Receptor Antagonists

IUPAC Name	IC ₅₀	Inhibition (%)	Sensory Performance (%)
(2,3,9,9-tetramethylspiro[4.5]dec-2-en-10-yl) acetate	>600	116	40%
(1,5,10,10-tetramethylspiro[5.5]undec-3-en-11-yl) acetate	72.33	72	43%
(2,3,9,9-tetramethylspiro[4.5]decan-10-yl) acetate	51.40	62	50%
(5,10,10-trimethylspiro[5.5]undec-2-en-11-yl) formate	44.37	129	
(3,5,10,10-tetramethylspiro[5.5]undec-2-en-11-yl) acetate	71.39	104	
(9,9-dimethylspiro[4.5]dec-2-en-10-yl) acetate	90.30	32	
10-methoxy-9,9-dimethylspiro[4.5]dec-2-ene	119.54	33	
4,10,10,11-tetramethylspiro[5.5]undec-2-en-11-ol, 5,10,10,11-tetramethylspiro[5.5]undec-3-en-11-ol, or mixtures thereof	47.23	94	
2,4,8-trimethylspiro[5.5]undec-3-en-11-ol, 2,9,11-trimethylspiro[5.5]undec-9-en-5-ol, or mixtures thereof	117.03	70	
3-methyl-5-propan-2-ylspiro[5.5]undec-2-en-11-ol	366.37	144	
11-methylspiro[5.5]undecan-5-ol	68.82	52	
3,10,10-trimethylspiro[5.5]undec-3-en-11-ol, 4,10,10-trimethylspiro[5.5]undec-3-en-11-ol, or mixtures thereof	>600	121	
[2,2-dimethyl-1-(2,4,6-trimethylcyclohex-3-en-1-yl)propyl] acetate	52.56	89	
[2,2-dimethyl-1-(2,4,6-trimethylcyclohexyl)propyl] acetate	241.99	101	

IUPAC Name	IC50	Inhibition (%)	Sensory Performance (%)
[(1~{R})-2,2-dimethyl-1-[(1~{S},2~{S})-2-methylcyclohexyl]propyl] acetate	169.82	86	
2,3,9,9-tetramethylspiro[4.5]dec-2-en-10-ol	78.69	16	60%
2,3,9,9-tetramethylspiro[4.5]dec-2-en-10-one			56%
2,2-dimethyl-6,6-bis(2-methylprop-2-enyl)cyclohexan-1-one	46.59	103	50%
(2,3,9,9-tetramethylspiro[4.5]dec-2-en-10-yl) formate	25.90	69	
(2,4,9,9-tetramethylspiro[4.5]dec-2-en-10-yl) acetate	34.79	131	
2,2-dimethyl-5,5-bis(2-methylprop-2-enyl)cyclopentan-1-ol	35.11	119	
9,9-dimethylspiro[4.5]dec-2-en-10-ol	44.06	91	
(4,9,9-trimethylspiro[4.5]dec-2-en-10-yl) acetate	48.52	106	
2,2-dimethyl-5,5-bis(2-methylprop-2-enyl)cyclopentan-1-one	51.71	82	
1,1',1',5-tetramethyl-2'-methylidenespiro[6-oxabicyclo[3.1.0]hexane-3,3'-cyclohexane]	75.67	37	
2-but-3-en-2-yl-6,6-dimethyl-2-prop-2-enylcyclohexan-1-one	76.42	115	
(4~{S},5~{R},6~{S},11~{S})-4,11-dimethylspiro[5.5]undecan-5-ol	76.93	54	
2,4,9,9-tetramethylspiro[4.5]dec-2-en-10-ol	81.58	22	
2,2-dimethyl-1-(2-methylcyclohexyl)propan-1-ol, 2,2-dimethyl-1-(3-methylcyclohexyl)propan-1-ol, or mixtures thereof	83.27	17	

IUPAC Name	IC50	Inhibition (%)	Sensory Performance (%)
1-methoxy-2,6-dimethyl-1-prop-2-enylcyclohexane	100.21	61	
2,4,9,9-tetramethylspiro[4.5]dec-2-en-10-one	109.82	63	
2,3,9,9-tetramethylspiro[4.5]decan-10-ol	119.78	12	
2,2-dimethyl-6,6-bis(2-methylprop-2-enyl)cyclohexan-1-ol	124.71	110	
9,9-dimethylspiro[4.5]dec-2-en-10-one	135.02	23	
2,3,8,8-tetramethylspiro[4.4]non-2-en-9-one	198.38	10	
9-methoxy-8,8-dimethylspiro[4.4]non-2-ene	237.96	100	
4,9,9-trimethylspiro[4.5]dec-2-en-10-one	267.67	102	
1-(2,6-dimethylcyclohex-3-en-1-yl)-2,2-dimethylpropan-1-ol	321.14	31	
4-methoxy-3,3-dimethylspiro[4.4]nonane	337.13	105	
(2,2,3,3,9,9-hexamethylspiro[4.5]decan-10-yl) acetate	424.91	39	
(8,8-dimethylspiro[4.4]non-2-en-9-yl) acetate	488.31	107	
methyl 1-(3-methylbut-2-enyl)cyclohex-2-ene-1-carboxylate, methyl 1-(3-methylbut-2-enyl)cyclohex-3-ene-1-carboxylate, or mixtures thereof	576.63	38	

Table 5: Butyric Acid Olfactory Receptor Antagonists

IUPAC Name	IC50	Inhibition (%)
1-(2-methyl-4-tricyclo[5.2.1.0 ^{1,5}]decanyl)ethyl acetate	97.01	23
1-(2,4-dimethyl-4-tricyclo[5.2.1.0 ^{1,5}]decanyl)ethyl acetate	54.79	34
1-[(1~{S},2~{S},4~{S},7~{R})-2,3,4-trimethyl-4-tricyclo[5.2.1.0 ^{1,5}]decanyl]ethanone	32.58	27
1-(2,4-dimethyl-4-tricyclo[5.2.1.0 ^{1,5}]decanyl)ethanone	60.53	26
2,3,4-trimethyltricyclo[5.2.1.0 ^{1,5}]decane-4-carbaldehyde	269.71	28
(2,3,4-trimethyl-4-tricyclo[5.2.1.0 ^{1,5}]decanyl)methyl acetate	60.80	27
~{N}-[[(1~{S},7~{R})-2,4-dimethyl-4-tricyclo[5.2.1.0 ^{1,5}]decanyl]methylidene]hydroxylamine	88.55	38
~{N}-[1-[(1~{R},7~{R})-2,3,4-trimethyl-4-tricyclo[5.2.1.0 ^{1,5}]decanyl]ethylidene]hydroxylamine	79.71	81
~{N}-[1-[(1~{S},7~{R})-2,3-dimethyl-4-tricyclo[5.2.1.0 ^{1,5}]decanyl]ethylidene]hydroxylamine	76.58	19

Example 6: Identification of DMTS Olfactory Receptor Inhibitors

Cell lines expressing either the OR52N5, OR2L13, OR2AJ1, OR4C15, OR5AC2, OR8H3, OR11G2, OR52N2, or OR5T1 odorant receptors were used as an antagonist screening platform to identify compounds that have the property to decrease the DMTS induced receptor activity, according to the assays and methods disclosed in WO2014/210585. Each cell line expressing a human odorant receptor was screened with a volatile compound library for their inhibitory properties and potential DMTS smell inhibition. First, individual binary mixtures of DMTS with each one of the test compounds were presented to the cells. Single point monitoring of the DMTS induced cell activity in the presence or absence of a test compound allowed for the identification of compounds with a putative suppression or inhibitory effect. These hits were further confirmed in an inhibitory dose-response curve assay to evaluate the potency of activity inhibition as a measure of the IC_{50} (the inhibitor concentration at which the receptor activity is inhibited by the half-maximal inhibition efficacy level of a given test compound). A dose-dependent decrease of receptor activity was recorded with increasing concentrations of test compounds in the presence of a single activating concentration of DMTS (EC_{80}) and corresponding dose-response inhibition curves were obtained. The compounds recited in Table 5 are examples of compounds that decreased the DMTS induced activity of at least one receptor.

Table 6: DMTS Olfactory Receptor Antagonists

1,2,3,4,5,6,7,8-octahydro-8,8-dimethyl-2-naphthalenecarbaldehyde (A) + (B,C,D) + octahydro-5,5-dimethyl-2-naphthalenecarbaldehyde
(+)-perhydro-4alpha,8abeta-dimethyl-4a-naphthalenol
3-(3,3-dimethyl-2,3-dihydro-1H-inden-5-yl)propanal (A) + 3-(1,1-dimethyl-2,3-dihydro-1H-inden-4-yl)propanal (B) + 3-(1,1-dimethyl-2,3-dihydro-1H-inden-5-yl)propanal (C)
(+)-2,5-dimethyl-2-indanmethanol
(-)-(3R,6S,8S)-2,2,6,8-tetramethyltricyclo[5.3.1.0~3,8~]undecan-3-ol
patchouli oil
(+)-2,2,2-trichloro-1-phenylethyl acetate
5RS,6RS)-2,6,10,10-tetramethyl-1-oxaspiro[4.5]decan-6-ol
2,2,7,7-tetramethyltricyclo[6.2.1.0~1,6~]undecan-6-ol
(+)-(1S,2S,3S,5R)-2,6,6-trimethylspiro[bicyclo[3.1.1]heptane-3,1'-cyclohexane]-2'-en-4'-one

CLAIMS

1. A method for identifying a compound that binds, suppresses, blocks, inhibits, and/or modulates the activity of an olfactory receptor polypeptide that is activated by a laundry malodor causing substance and/or a moldy malodour causing substance comprising:

a. contacting a test substance and said laundry malodor and/or moldy malodour causing substance to at least one olfactory receptor polypeptide selected from the group consisting of OR1A1, OR2M3, Olfr403, Olfr164, Olfr1487, Olfr339, Olfr96 and Olfr1322; or to at least one olfactory receptor polypeptide having at least 95% amino acid sequence identity to at least one of the aforementioned olfactory receptor polypeptides; wherein said malodor-causing substance is (4S,4aS,8aR)-4,8a-Dimethyl-1,2,3,4,5,6,7,8-octahydronaphthalen-4a-ol, and

b. measuring the response of said at least one olfactory receptor polypeptide to the malodor-causing substance by measuring the dose-dependent response of said olfactory receptor polypeptide in the presence of increasing concentrations of the test substance in the presence of a single activating concentration of (4S,4aS,8aR)-4,8a-dimethyl-1,2,3,4,5,6,7,8-octahydronaphthalen-4a-ol (EC₈₀) and absence of the test substance.

2. The method of claim 1, further comprising

c. identifying a test substance that modulates the response of said at least one olfactory receptor on the basis of the response that was measured in the presence and absence of the test substance; and

d. selecting the identified test substance as a compound that binds, suppresses, blocks, inhibits, and/or modulates the response of said at least one olfactory receptor to the malodor-causing substance.

3. The method of claim 1, wherein the polypeptide

a. comprises an amino acid sequence having at least 95%, 98%, 99% or 100% sequence identity to SEQ ID NO: 4, 14, 24, 28, 40, 42, 44, or 75; and/or

b. is encoded by a nucleic acid molecule comprising a nucleotide sequence having at least 95%, 98%, 99% or 100% sequence identity to SEQ ID NO: 3, 13, 23, 27, 39, 41, 43, 72, or the reverse complement thereof.