

CLAIMS

1. A high-throughput assay system for identifying one or more compounds from a group of compounds wherein the one or more compounds positively modulates the activity of an olfactory receptor induced by an agonist odorant compound, comprising:
 - a) one or more isolated cells, each cell expressing one mammalian olfactory receptor, wherein the one or more cells comprises a target olfactory receptor that is activated by one or more odorant,
 - b) a first compound that binds to the olfactory receptor and that activates the olfactory receptor, and
 - c) at least one second compound that binds to the receptor non-competitively relative to the first compound and that enhances the activity of the receptor exposed to the first compound when compared to the activity of the receptor exposed to the first compound in the absence of the second compound,
wherein the receptor is selected from the group consisting of OR5AN1, Olfr1440, OR10J5, or Olfr16,
wherein the first compound is an agonist odorant compound of the olfactory receptor,
wherein the first compound and the second compound are different compounds,
wherein the second compound is not an agonist of the receptor,
wherein the second compound is a positive allosteric modulating compound,
and
wherein the activity of the receptor is synergistically enhanced by the combination of the first compound and the second compound.
2. The assay system of claim 1, wherein the at least one second compound is selected from a pool of compounds based on structure-activity relationship (SAR) analysis.
3. The assay system of claim 1 or 2, wherein the second compound binds to a site on the olfactory receptor distinct from the site where the first compound binds.

4. The assay system of any one of claims 1 to 3, wherein the one or more isolated cells in part (a) comprised one or more isolated cells that were transformed to express the target olfactory receptor.
- 5 5. The assay system of claim 1, wherein at least one of the olfactory receptors comprises a polypeptide
 - a) comprises an amino acid sequence having at least 90% sequence identity to SEQ ID NO: 2, 4, 6, or 8; and/or
 - b) is encoded by a nucleic acid molecule comprising a nucleotide sequence having at
10 least 90% sequence identity to SEQ ID NO: 1, 3, 5, or 7, or the reverse complement thereof.
6. The assay system of claim 5, wherein the polypeptide
 - a) comprises an amino acid sequence having at least 90%, 95%, 98%, 99% or 100%
15 sequence identity to SEQ ID NO: 2, 4, 6, or 8; and/or
 - b) is encoded by a nucleic acid molecule comprising a nucleotide sequence having at least 90%, 95%, 98%, 99% or 100% sequence identity to SEQ ID NO: 1, 3, 5, or 7, or the reverse complement thereof.
- 20 7. The assay system of claim 1, wherein the mammalian olfactory receptor is a mouse olfactory receptor or a human olfactory receptor.
8. The assay system of any one of claims 1 to 7, wherein the first compound is a musk or a floral compound.
- 25 9. The assay system of any one of claims 1 to 8, wherein the first compound comprises a musk compound and the olfactory receptor is OR5AN1 or Olfr1440; chimera and functional fragments thereof; and wherein the olfactory receptor comprises a polypeptide that
 - a) comprises an amino acid sequence having at least 90% sequence identity to SEQ ID
30 NO: 2 or 6; and/or

- b) is encoded by a nucleic acid molecule comprising a nucleotide sequence having at least 90% sequence identity to SEQ ID NO: 1 or 5, or the reverse complement thereof.

5 **10.** The assay system of claim 8 or 9, wherein the musk compound comprises a macrocyclic ketone or a nitromusk compound.

10 **11.** The assay system of any one of claims 1 to 8, wherein the first compound comprises a floral muguet compound and the olfactory receptor is OR10J5 or Olfr16; chimera and functional fragments thereof; and wherein the olfactory receptor comprises a polypeptide that

- a) comprises an amino acid sequence having at least 90% sequence identity to SEQ ID NO: 4 or 8; and/or
 - b) is encoded by a nucleic acid molecule comprising a nucleotide sequence having at least 90% sequence identity to SEQ ID NO: 3 or 7, or the reverse complement thereof.
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12. The assay system of any one of claims 1 to 11, wherein the modulated activity comprises

- a) modulating the binding affinity of the first compound to the orthosteric site,
 - b) modulating the binding activation efficacy of the first compound to the orthosteric site, and/or
 - c) modulating the G-protein binding site.
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13. A method for identifying at least one positive allosteric modulating compound that enhances the activity of an olfactory receptor in the presence of an agonist of the receptor, comprising

- a) providing one or more isolated cells, each cell expressing one mammalian olfactory receptor,
 - b) exposing the one or more cells to a first compound that activates the olfactory receptor,
 - c) exposing the one or more cells to one or more test compound, and
 - d) selecting at least one second compound from the one or more test compounds when the at least one second compound in combination with the first compound has a
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synergistic effect on the receptor activity as a positive allosteric modulating compound;

wherein the receptor is selected from the group consisting of OR5AN1, Olfr1440, OR10J5, or Olfr16,

5 wherein the first compound is an agonist odorant compound of the olfactory receptor,

wherein the first compound and the second compound are different compounds, and

wherein the second compound is not an agonist of the receptor.