Supplementary Tables and Figures

# Machine learning assisted approach for finding novel high activity agonists of human ectopic olfactory receptors

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**Table S1: Experimentally tested odorants for OR1A1**

| Pubchem_CID | Odorant name | Class | Chemical nature |
|---|---|---|---|
| 443157 | (S)-(-)-citronellal[1] | Agonist | Aldehyde |
| 61875 | 4-decenal[1] | Agonist | Aldehyde |
| 7793 | (S)-(-)-citronellol[1] | Agonist | Terpene |
| 75427 | (R)-(+)-citronellol[1] | Agonist | Terpene |
| 439250 | (S)-(-)-limonene[1] | Agonist | Terpene |
| 5362695 | Z-7-decanal[1] | Agonist | Aldehyde |
| 5284507 | Nerolidol[1] | Agonist | Alcohol |
| 5702654 | E-4-decanal[1] | Agonist | Aldehyde |
| 643820 | Nerol[1] | Agonist | Alcohol |
| 64805 | Helional[1] | Agonist | Aldehyde |
| 11084068 | (-)-Carveol[1] | Agonist | Alcohol |
| 8878 | Allyl heptanoate[2] | Agonist | Ester |
| 31265 | Ethyl hexanoate[3] | Agonist | Ester |
| 439570 | (-)-Carvone[3] | Agonist | Ketone |
| 22227 | (+)-Dihydrocarvone[3] | Agonist | Ketone |
| 8174 | 1-decanol[2] | Agonist | Alcohol |
| 8093 | 2-octanone[2] | Agonist | Ketone |
| 7802 | 3-heptanone[2] | Agonist | Ketone |
| 246728 | 3-octanone[2] | Agonist | Ketone |
| 68110 | 4-chromanone[2] | Agonist | Ketone |
| 15717 | Allyl phenylacetate[2] | Agonist | Ester |
| 3102 | Benzophenone[2] | Agonist | Ketone |
| 8785 | Benzyl acetate[2] | Agonist | Ester |
| 62378 | Dihydrojasmone[2],[4] | Agonist | Ketone |
| 15077 | Nonanethiol[2] | Agonist | Sulphur compound |
| 16724 | (+)-Carvone[2] | Agonist | Ketone |
| 61052 | 3-phenyl propyl propionate[5] | Agonist | Ester |
| 92979 | Androstadienone[5] | Agonist | Ketone |
| 24433 | Butyl anthranilate[5] | Agonist | Ester |
| 637511 | Cinnamaldehyde[5] | Agonist | Aldehyde |
| 7047 | Quinoline[5] | Agonist | Cyclic compound |
| 440917 | R-limonene[5] | Agonist | Terpene |
| 6992244 | (R/S)-octen-3-ol[3] | Agonist | Alcohol |
| 16800 | 2-pentylpyridine[3] | Agonist | Cyclic compound |
| 78126 | 2-phenylethanethiol[3] | Agonist | Sulphur compound |
| 7654 | 2-Phenylethyl acetate[3] | Agonist | Ester |
| 518810 | 3-Mercaptohexyl acetate[3] | Agonist | Ester |
| 8815 | Estragole[3] | Agonist | Cyclic compound |
| 18686 | Ethyl cyclohexanecarboxylate[3] | Agonist | Ester |
| 637563 | *Trans*-anethole[3] | Agonist | Cyclic compound |

| Pubchem_CID | Odorant name | Class | Chemical nature |
|---|---|---|---|
| 529481 | 3-Methyl-2,4-nonanedione[3] | Agonist | Ketone |
| 7590 | Ethylphenyl acetate[3] | Agonist | Ester |
| 7710 | 5-Pentyloxolan-2-one[3] | Agonist | Ketone |
| 443159 | (+)-Menthone[3] | Agonist | Ketone |
| 62329 | Musk xylol[6] | Agonist | Cyclic compound |
| 66823518 | Cosmone[6] | Agonist | Ketone |
| 61585 | Celestolide[6] | Agonist | Ketone |
| 6997 | 2-ethylphenol[7] | Agonist | Cyclic compound |
| 7128 | Methyl isoeugenol[7] | Agonist | Cyclic compound |
| 7685 | P-Tolyl isobutyrate[7] | Agonist | Ester |
| 7148 | Propiophenone[7] | Agonist | Ketone |
| 7888 | Hydroxy-citronellal[1],[2] | Conflicting info. | Aldehyde |
| 638011 | Citral[1],[2] | Conflicting info. | Aldehyde |
| 5283349 | E,E-2,4-decadienal[1],[3] | Conflicting info. | Aldehyde |
| 10947 | Muscone[1],[6] | Conflicting info. | Ketone |
| 8129 | Heptanol[1],[2] | Conflicting info. | Alcohol |
| 6276 | Pentanol[1],[2],[8] | Conflicting info. | Alcohol |
| 264 | Butyric acid[1],[3],[8] | Conflicting info. | Acid |
| 5374527 | Beta-damascone[1],[3], [8],[5] | Conflicting info. | Ketone |
| 6549 | Linalool[1],[3], [8],[5], [2] | Conflicting info. | Alcohol |
| 27458 | 2,3-diethyl pyrazine [1],[5] | Conflicting info. | Pyrazine |
| 64832 | Bourgeonal [1],[9] | Conflicting info. | Aldehyde |
| 26447 | Menthone[1],[3], [2] | Conflicting info. | Ketone |
| 8051 | 2-heptanone[8] ,[1], [2] | Conflicting info. | Ketone |
| 8158 | Nonanoic acid[8],[1],[2] | Conflicting info. | Acid |
| 957 | Octanol[8],[1],[2] | Conflicting info. | Alcohol |
| 637566 | Geraniol [1],[2],[3],[9] | Conflicting info. | Alcohol |
| 5362620 | Z-4-decenal[1],[3] | Conflicting info. | Aldehyde |
| 61346 | 1-octen-3-one[1],[3] | Conflicting info. | Ketone |
| 8175 | Decanal[8],[1],[3],[2],[5] | Conflicting info. | Aldehyde |
| 8130 | Heptanal[1],[2] | Conflicting info. | Aldehyde |
| 454 | Octanal[1],[3],[2] | Conflicting info. | Aldehyde |
| 1032 | Propionic acid[8],[3],[2] | Conflicting info. | Acid |
| 10886 | Amyl hexanoate[8],[2] | Conflicting info. | Ester |
| 241 | Benzene[8],[5],[2] | Conflicting info. | Cyclic compound |
| 91604 | Lyral [8],[5],[2] | Conflicting info. | Aldehyde |
| 10890 | Amyl butyrate[2],[7] | Conflicting info. | Ester |
| 31289 | Nonanal[8],[3],[2],[1] | Conflicting info. | Aldehyde |
| 13187 | 2-nonanone[3],[5],[2] | Conflicting info. | Ketone |
| 8144 | Octanethiol[8],[5],[2] | Conflicting info. | Sulphur compound |
| 11614 | Butyl formate[8],[5],[2] | Conflicting info. | Ester |

| **Pubchem_CID** | Odorant name | **Class** | **Chemical nature** |
|---|---|---|---|
| 8461 | 2,4-dinitrotoluene[8],[5] | Conflicting info. | Cyclic compound |
| 106997 | 2-ethylfenchol[8],[5] | Conflicting info. | Alcohol |
| 6852393 | Androstenone[8],[5] | Conflicting info. | Ketone |
| 5281167 | Cis-3-hexen-1-ol[8],[3],[5] | Conflicting info. | Alcohol |
| 20499 | Coffee difuran[8],[5] | Conflicting info. | Cyclic compound |
| 61014 | Ethylene brassylate[5],[6] | Conflicting info. | Ester |
| 3314 | Eugenol[8],[9],[3],[5] | Conflicting info. | Cyclic compound |
| 7127 | Eugenol methyl ether[8],[3],[5],[7] | Conflicting info. | Cyclic compound |
| 8467 | Ethyl vanillin[8],[3],[5] | Conflicting info. | Cyclic compound |
| 1549026 | Geranyl acetate[8],[5] | Conflicting info. | Ester |
| 6558 | Isobutyl amine[8],[5] | Conflicting info. | Alkane |
| 5460291 | Laevo-arabinose[8],[5] | Conflicting info. | Aldehyde |
| 62131 | Methyl furfuryl disulfide[8],[5] | Conflicting info. | Sulphur compound |
| 61294 | Octyl octanoate[8],[5] | Conflicting info. | Ester |
| 9261 | Pyrazine[8],[5] | Conflicting info. | Pyrazine |
| 17100 | Terpineol[3],[5] | Conflicting info. | Alcohol |
| 111037 | Terpinyl acetate[8],[5] | Conflicting info. | Ester |
| 527 | Propanal[8],[3] | Conflicting info. | Aldehyde |
| 12232 | Dimethyl disulfide[8],[3] | Conflicting info. | Sulphur compound |
| 6989 | Thymol[9],[7] | Conflicting info. | Cyclic compound |
| 4133 | Methyl salicylate[8],[9] | Conflicting info. | Ester |
| 5367530 | E,E-2,4- dodecadienal[1] | Non-agonist | Aldehyde |
| 1551246 | Citralva[1] | Non-agonist | Nitrile compound |
| 7410 | Acetophenone[1] | Non-agonist | Ketone |
| 196 | Adipic acid[1] | Non-agonist | Acid |
| 1110 | Succinic acid[1] | Non-agonist | Acid |
| 21648 | Raspberry ketone[1] | Non-agonist | Ketone |
| 8012 | Butane thiol[1] | Non-agonist | Sulphur compound |
| 8103 | Hexanol[1] | Non-agonist | Alcohol |
| 552003 | 2-bromo octanoic acid[1] | Non-agonist | Acid |
| 8094 | Heptanoic acid[1] | Non-agonist | Acid |
| 12013 | 2-bromohexanoic acid[1] | Non-agonist | Acid |
| 6184 | Hexanal[1] | Non-agonist | Aldehyde |
| 31229 | Phenyl acetate[1] | Non-agonist | Ester |
| 10106 | 1,4- cineole[1] | Non-agonist | Alkane |
| 8892 | Hexanoic acid[1] | Non-agonist | Acid |
| 31245 | Methyl pentanal[1] | Non-agonist | Aldehyde |
| 11446 | 2-bromovaleric acid[1] | Non-agonist | Acid |
| 10402 | Citronellic acid[1] | Non-agonist | Acid |
| 7519 | Anisole[1] | Non-agonist | Cyclic compound |
| 31276 | Isoamyl acetate[1] | Non-agonist | Ester |

| **Pubchem_CID** | Odorant name | **Class** | **Chemical nature** |
|---|---|---|---|
| 10430 | Isovaleric acid[1] | Non-agonist | Acid |
| 2758 | 1,8- cineole[1] | Non-agonist | Alkane |
| 31268 | Pyrrolidine[1] | Non-agonist | Cyclic compound |
| 6655 | Bromobutyric acid[1] | Non-agonist | Acid |
| 7991 | Valeric acid[1] | Non-agonist | Acid |
| 8314 | 2-methylbutyric acid[1] | Non-agonist | Acid |
| 5366074 | Damascenone[1] | Non-agonist | Ketone |
| 643731 | E,Z-2,6- nonadienal[1] | Non-agonist | Aldehyde |
| 5282108 | A-ionone[1] | Non-agonist | Ketone |
| 636687 | E,E-26-nonadienal[1] | Non-agonist | Aldehyde |
| 1201529 | (R)-(-)-myrtenal[1] | Non-agonist | Aldehyde |
| 638014 | B-ionone[1] | Non-agonist | Ketone |
| 1549025 | Nerylacetate[1] | Non-agonist | Ester |
| 5283339 | E,E-2,4-nonadienal[1] | Non-agonist | Aldehyde |
| 5281516 | Farnesene[1] | Non-agonist | Terpene |
| 32594 | 2-isobutyl-3-methoxypyrazine[1] | Non-agonist | Pyrazine |
| 33166 | 2-isopropyl-3-methoxypyrazine[1] | Non-agonist | Pyrazine |
| 5283335 | 2-enonenal[1] | Non-agonist | Aldehyde |
| 15394 | Ethyl vinyl ketone[1], [3] | Non-agonist | Ketone |
| 28905 | 2,3-dietyl-5-methylpyrazine[1] | Non-agonist | Pyrazine |
| 19309 | Furaneol[1] | Non-agonist | Ketone |
| 18635 | Methional[1] | Non-agonist | Aldehyde |
| 6561 | Isobutylraldehyde[1] | Non-agonist | Aldehyde |
| 1146 | Trimethylamine[1] | Non-agonist | Methylamine |
| 7976 | 2-methylpyrazine[1] | Non-agonist | Pyrazine |
| 26331 | 2-ethylpyrazine[1] | Non-agonist | Pyrazine |
| 26808 | Trimethyl pyrazine[1] | Non-agonist | Pyrazine |
| 520098 | 3-secbutyl-2-methoxypyrazine[1] | Non-agonist | Pyrazine |
| 7363 | Furfurylthiol[1] | Non-agonist | Sulphur compound |
| 445070 | Farnesol[1] | Non-agonist | Alcohol |
| 22201 | 2,3-dimethylpyrazine[1] | Non-agonist | Pyrazine |
| 8914 | Nonanol[1] | Non-agonist | Alcohol |
| 7335 | (-)Carvyl acetate mix[1] | Non-agonist | Ester |
| 379 | Octanoic acid[1] | Non-agonist | Acid |
| 18827 | 1-octen-3-ol[1] | Non-agonist | Alcohol |
| 10448 | Methionol[1] | Non-agonist | Alcohol |
| 650 | Diacetyl[1] | Non-agonist | Ketone |
| 10900 | 1,2-dichlorethylene[1] | Non-agonist | Alkene |
| 444294 | (-)-Camphor[2] | Non-agonist | Ketone |
| 785329 | (+)-2-Phenylbutyric acid[2] | Non-agonist | Acid |
| 159055 | (+)-Camphor[2] | Non-agonist | Ketone |

| **Pubchem_CID** | Odorant name | **Class** | **Chemical nature** |
|---|---|---|---|
| 785330 | (-)-2-Phenylbutyric acid[2] | Non-agonist | Acid |
| 82229 | (-)-Fenchone[2] | Non-agonist | Ketone |
| 1201521 | (+)-Fenchone[2] | Non-agonist | Ketone |
| 68382 | 2-coumaranone[2] | Non-agonist | Ketone |
| 7895 | 2-pentanone[2] | Non-agonist | Ketone |
| 54682930 | 4-hydroxycoumarin[2] | Non-agonist | Ketone |
| 9309 | Allyl benzene[2] | Non-agonist | Cyclic compound |
| 7967 | Cyclohexanone[2] | Non-agonist | Cyclic compound |
| 24114 | Butyl butyryl lactate[2] | Non-agonist | Ester |
| 8468 | Vanillic acid[2] | Non-agonist | Acid |
| 12756 | Γ-caprolactone[2] | Non-agonist | Ketone |
| 2266 | Nonanedioic acid[2] | Non-agonist | Acid |
| 261 | Butanal[2] | Non-agonist | Aldehyde |
| 8063 | Pentanal[2] | Non-agonist | Aldehyde |
| 1031 | 1-propanol[2] | Non-agonist | Alcohol |
| 2724897 | (+)-2-heptanol[2] | Non-agonist | Alcohol |
| 80080 | (R)-(-)-2-octanol[2] | Non-agonist | Alcohol |
| 2723888 | (S)-(+)-2-octanol[2] | Non-agonist | Alcohol |
| 8184 | 1-undecanol[2] | Non-agonist | Alcohol |
| 12041 | Ethyl pyruvate[2] | Non-agonist | Ester |
| 61304 | Heptyl isobutyrate[2] | Non-agonist | Ester |
| 21596 | Butyl heptanoate[2] | Non-agonist | Ester |
| 7770 | Propyl butyrate[2] | Non-agonist | Ester |
| 88561 | Tert-Butyl propionate[2] | Non-agonist | Ester |
| 6569 | 2-butanone[2] | Non-agonist | Ketone |
| 442495 | (+)-Pulegone[2] | Non-agonist | Ketone |
| 14505 | 2-Furyl methyl ketone[2] | Non-agonist | Ketone |
| 31358 | Dimedone[2] | Non-agonist | Ketone |
| 263 | 1-butanol[2] | Non-agonist | Alcohol |
| 7765 | Acetal[2] | Non-agonist | Aldehyde |
| 19707 | 2,3-hexanedione[2] | Non-agonist | Ketone |
| 11583 | 2-hexanone[2] | Non-agonist | Ketone |
| 62539 | 3,4-hexanedione[2] | Non-agonist | Ketone |
| 8908 | Hexyl acetate[2] | Non-agonist | Ester |
| 1133 | Thioglycolic acid[2] | Non-agonist | Acid |
| 12348 | N-amyl acetate[5] | Non-agonist | Ester |
| 14489 | Prenyl acetate[2] | Non-agonist | Ester |
| 12180 | Methyl butyrate[2] | Non-agonist | Ester |
| 2969 | Decanoic acid / capric acid[2] | Non-agonist | Acid |
| 323 | Coumarin[2] | Non-agonist | Cyclic compound |
| 61809 | 2-ethoxythiazole[5] | Non-agonist | Sulphur compound |

| **Pubchem_CID** | Odorant name | **Class** | **Chemical nature** |
|---|---|---|---|
| 18467 | 2-methoxypyrazine[5] | Non-agonist | Pyrazine |
| 165675 | (+)-Menthol[5] | Non-agonist | Alcohol |
| 31244 | Anisaldehyde[5] | Non-agonist | Cyclic compound |
| 520119 | 1,3-butane dithiol[5] | Non-agonist | Sulphur compound |
| 61431 | 1,1-dimethoxy-octane[5] | Non-agonist | Alkane |
| 62835 | Caramel furanone[5] | Non-agonist | Ketone |
| 1068 | Dimethyl sulfide[5] | Non-agonist | Sulphur compound |
| 460 | Guaiacol[5] | Non-agonist | Cyclic compound |
| 10558 | Isobutyl mercaptan[5] | Non-agonist | Sulphur compound |
| 16255 | Isoamyl octanoate[5] | Non-agonist | Ester |
| 11124 | Methyl propionate[5] | Non-agonist | Ester |
| 5365991 | Neryl isobutyrate[5] | Non-agonist | Ester |
| 998 | Phenyl acetaldehyde[5] | Non-agonist | Aldehyde |
| 444212 | Trans-Aconitic acid[5] | Non-agonist | Acid |
| 181287 | 2,4,5-trimethyl-2,5-dihydro-1,3-thiazole[5] | Non-agonist | Cyclic compound |
| 8186 | Undecanal[5] | Non-agonist | Aldehyde |
| 1183 | Vanillin[5] | Non-agonist | Aldehyde |
| 7704 | (R/S)-γ-Octalactone[3] | Non-agonist | Ketone |
| 10976 | 2-heptanol[3] | Non-agonist | Alcohol |
| 8500 | 4-Methyl acetophenone[3] | Non-agonist | Ketone |
| 5282110 | Cinnamyl acetate[3] | Non-agonist | Ester |
| 637520 | Methyl cinnamate[3] | Non-agonist | Ester |
| 62385 | P,α-Dimethylstyrene[3] | Non-agonist | Cyclic compound |
| 5283316 | (E)-2-heptenal[3] | Non-agonist | Aldehyde |
| 7342 | Ethyl isobutyrate[3] | Non-agonist | Ester |
| 11747 | 2,3-pentanedione[3] | Non-agonist | Ketone |
| 5362588 | Filbertone[3] | Non-agonist | Ketone |
| 11086 | 2'-aminoacetophenone[3] | Non-agonist | Ketone |
| 27470 | 3-Methylheptan-4-one[3] | Non-agonist | Ketone |
| 179 | Acetoin[3] | Non-agonist | Ketone |
| 8369 | Maltol[3] | Non-agonist | Ketone |
| 10748 | 7-methoxycoumarin[3] | Non-agonist | Ketone |
| 6736 | 3-Methyl-1H-indole[3] | Non-agonist | Cyclic compound |
| 169110 | 2-Acetyl-2-thiazoline[3] | Non-agonist | Ketone |
| 529251 | 2-propionylpyrroline[3] | Non-agonist | Ketone |
| 33931 | Homofuraneol[3] | Non-agonist | Ketone |
| 61325 | 4-Methoxy-2,5-dimethyl-3(2H)-furanone[3] | Non-agonist | Ketone |
| 62089 | 4-Methyloctanoic acid[3] | Non-agonist | Acid |
| 61840 | 4-Ethyloctanoic acid[3] | Non-agonist | Acid |
| 176 | Acetic acid[3] | Non-agonist | Acid |
| 6590 | Isobutyric acid[3] | Non-agonist | Acid |

| **Pubchem_CID** | Odorant name | **Class** | **Chemical nature** |
|---|---|---|---|
| 61199 | 5-Ethyl-3-hydroxy-4-methylfuran-2(5H)-one[3] | Non-agonist | Ketone |
| 637542 | P-Coumaric acid[3] | Non-agonist | Acid |
| 999 | 2-Phenylacetic acid[3] | Non-agonist | Acid |
| 107 | 3-Phenyl propionic acid[3] | Non-agonist | Acid |
| 702 | Ethanol[3] | Non-agonist | Alcohol |
| 5315892 | Cinnamyl alcohol[3] | Non-agonist | Alcohol |
| 6054 | 2-phenylethanol[3] | Non-agonist | Alcohol |
| 5362833 | (2E,6Z)-Nona-2,6-dien-1-ol[3] | Non-agonist | Alcohol |
| 31260 | 3-Methyl-1-butanol[3] | Non-agonist | Alcohol |
| 8723 | 2-methyl-1-butanol[3] | Non-agonist | Alcohol |
| 6560 | Isobutyl alcohol[3] | Non-agonist | Alcohol |
| 853433 | Isoeugenol[3] | Non-agonist | Cyclic compound |
| 326 | Cuminaldehyde[3] | Non-agonist | Aldehyde |
| 12777 | 6-Propyloxan-2-one[3] | Non-agonist | Ketone |
| 12813 | 5-Hexyloxolan-2-one[3] | Non-agonist | Ketone |
| 12810 | Delta-decalactone[3] | Non-agonist | Ketone |
| 7714 | Gamma-undecalactone[3] | Non-agonist | Ketone |
| 12844 | Delta-dodecalactone[3] | Non-agonist | Ketone |
| 16821 | 5-Octyloxolan-2-one[3] | Non-agonist | Ketone |
| 62900 | 5-Butyl-4-methyloxolan-2-one[3] | Non-agonist | Ketone |
| 31253 | Myrcene[3] | Non-agonist | Terpene |
| 7460 | Alpha-phellandrene[3] | Non-agonist | Terpene |
| 443162 | (-)-alpha-Terpineol[3] | Non-agonist | Alcohol |
| 440968 | (-)-alpha-Pinene[3] | Non-agonist | Terpene |
| 82227 | (+)-alpha-Pinene[3] | Non-agonist | Terpene |
| 440967 | (-)-beta-Pinene[3] | Non-agonist | Terpene |
| 10290825 | (+)-beta-Pinene[3] | Non-agonist | Terpene |
| 10887971 | (+)-Sabinene[3] | Non-agonist | Terpene |
| 27866 | Rose oxide[3] | Non-agonist | Cyclic compound |
| 12101 | 3-ethylphenol[3] | Non-agonist | Cyclic compound |
| 31242 | 4-ethylphenol[3] | Non-agonist | Cyclic compound |
| 335 | 2-methylphenol[3] | Non-agonist | Cyclic compound |
| 342 | 3-methylphenol[3] | Non-agonist | Cyclic compound |
| 2879 | 4-methylphenol[3] | Non-agonist | Cyclic compound |
| 7771 | 2,4-dimethylphenol[3] | Non-agonist | Cyclic compound |
| 11335 | 2,6-dimethylphenol[3] | Non-agonist | Cyclic compound |
| 62453 | 4-ethenylphenol[3] | Non-agonist | Cyclic compound |
| 332 | 4-vinylguaiacol[3] | Non-agonist | Cyclic compound |
| 7041 | 2,6-dimethoxyphenol[3] | Non-agonist | Cyclic compound |
| 7144 | 2-methoxy-4-methylphenol[3] | Non-agonist | Cyclic compound |
| 14519 | 2-Methoxy-5-methylphenol[3] | Non-agonist | Cyclic compound |

| **Pubchem_CID** | Odorant name | **Class** | **Chemical nature** |
|---|---|---|---|
| 62465 | 2-Methoxy-4-ethylphenol[3] | Non-agonist | Cyclic compound |
| 17739 | 2-methoxy-4-propylphenol[3] | Non-agonist | Cyclic compound |
| 30914 | 2-acetylpyrazine[3] | Non-agonist | Pyrazine |
| 6430888 | 2-Methyl-3-sulfanylpentan-1-ol[3] | Non-agonist | Alcohol |
| 62237 | 3-Mercapto-2-pentanone[3] | Non-agonist | Ketone |
| 529635 | 2-Sulfanylpentan-3-one[3] | Non-agonist | Ketone |
| 61592 | Ethyl 3-methylthiopropionate[3] | Non-agonist | Ester |
| 34286 | 2-Methyl-3-furanthiol[3] | Non-agonist | Sulphur compound |
| 47649 | Methyl 2-methyl-3-furyl disulfide[3] | Non-agonist | Sulphur compound |
| 15380 | Bis(methylthio)methane[3] | Non-agonist | Sulphur compound |
| 80408 | Thenyl mercaptan[3] | Non-agonist | Sulphur compound |
| 6427135 | 1-p-Menthene-8-thiol[3] | Non-agonist | Sulphur compound |
| 521348 | 3-Sulfanylhexan-1-ol[3] | Non-agonist | Alcohol |
| 526487 | 3-Mercapto-3-methylbutyl formate[3] | Non-agonist | Ester |
| 88290 | 4-Mercapto-4-methyl-2-pentanone[3] | Non-agonist | Ketone |
| 526195 | 4-Methoxy-2-methyl-2-butanethiol[3] | Non-agonist | Sulphur compound |
| 19310 | Dimethyl trisulfide[3] | Non-agonist | Sulphur compound |
| 5319765 | Methyl propyl trisulfide[3] | Non-agonist | Sulphur compound |
| 12377 | Propyl disulfide[3] | Non-agonist | Sulphur compound |
| 22383 | Dipropyl trisulfide[3] | Non-agonist | Sulphur compound |
| 66282 | Allyl methyl sulfide[3] | Non-agonist | Sulphur compound |
| 16590 | Allyl disulfide[3] | Non-agonist | Sulphur compound |
| 7284 | 2-methylbutyraldehyde[3] | Non-agonist | Aldehyde |
| 11552 | Isovaleraldehyde[3] | Non-agonist | Aldehyde |
| 5281168 | 2-hexenal, (2e)- [3] | Non-agonist | Aldehyde |
| 643941 | 3-hexenal, (3z)- [3] | Non-agonist | Aldehyde |
| 5362814 | 4-heptenal, (4z)- [3] | Non-agonist | Aldehyde |
| 6427080 | 2-octenal, (2z)- [3] | Non-agonist | Aldehyde |
| 5354833 | 2-nonenal, (2z)- [3] | Non-agonist | Aldehyde |
| 6429282 | 2,4-nonadienal, (2e,4z)- [3] | Non-agonist | Aldehyde |
| 5283345 | 2-decenal, (2e)- [3] | Non-agonist | Aldehyde |
| 3018619 | 12-methyltridecanal[3] | Non-agonist | Aldehyde |
| 5283356 | 2-undecenal[3] | Non-agonist | Aldehyde |
| 7799 | Ethyl octanoate[3] | Non-agonist | Ester |
| 8048 | Ethyl decanoate[3] | Non-agonist | Ester |
| 7165 | Ethyl benzoate[3] | Non-agonist | Ester |
| 177 | Acetaldehyde[3] | Non-agonist | Aldehyde |
| 7150 | Methyl benzoate[3] | Non-agonist | Ester |
| 7762 | Ethyl butyrate[3] | Non-agonist | Ester |
| 10882 | Ethyl pentanoate[3] | Non-agonist | Ester |
| 637758 | Ethyl cinnamate[3] | Non-agonist | Ester |

| **Pubchem_CID** | Odorant name | **Class** | **Chemical nature** |
|---|---|---|---|
| 24020 | Ethyl 2-methylbutyrate[3] | Non-agonist | Ester |
| 7945 | Ethyl isovalerate[3] | Non-agonist | Ester |
| 117477 | Ethyl 4-methylvalerate[3] | Non-agonist | Ester |
| 61293 | Ethyl 3-hydroxyhexanoate[3] | Non-agonist | Ester |
| 13357 | Methyl 2-methylbutyrate[3] | Non-agonist | Ester |
| 11039 | Methyl isobutyrate[3] | Non-agonist | Ester |
| 12209 | 2-Methylbutyl acetate[3] | Non-agonist | Ester |
| 8857 | Ethyl acetate[3] | Non-agonist | Ester |
| 31272 | Butyl acetate [3] | Non-agonist | Ester |
| 5363388 | 3-Hexenyl acetate, (3Z)-[3] | Non-agonist | Ester |
| 10409 | Cyclopentadecanone[6] | Non-agonist | Ketone |
| 5362739 | Globanone[6] | Non-agonist | Ketone |
| 5317881 | Ambrettolide[6] | Non-agonist | Ketone |
| 235414 | Exaltolide[6] | Non-agonist | Ketone |
| 11107424 | Habanolide[6] | Non-agonist | Ketone |
| 6669 | Musk ketone[6] | Non-agonist | Ketone |
| 91497 | Galaxolide[6] | Non-agonist | Cyclic compound |
| 89440 | Tonalide[6] | Non-agonist | Ketone |
| 92292 | Cashmeran[6] | Non-agonist | Ketone |
| 16063567 | Helvetolide[6] | Non-agonist | Ester |
| 67525 | Cyclopentadecane[6] | Non-agonist | Cyclic compound |
| 107327 | Cyclopentadecanol[6] | Non-agonist | Alcohol |
| 73918 | Cyclodecanone[6] | Non-agonist | Ketone |
| 13420 | Cycloundecanone[6] | Non-agonist | Ketone |
| 61303 | 2-pentadecanone[6] | Non-agonist | Ketone |
| 13162 | 8-pentadecanone[6] | Non-agonist | Ketone |
| 996 | Phenol[9] | Non-agonist | Cyclic compound |
| 7136 | Eugenyl acetate[8] | Non-agonist | Ester |
| 8635 | Methyl anthranilate[7] | Non-agonist | Ester |
| 19835 | 1,9 nonanediol[7] | Non-agonist | Alcohol |
| 31252 | 2,5 dimethyl pyrazine[7] | Non-agonist | Pyrazine |
| 5281517 | Trans-beta-farnesene[7] | Non-agonist | Terpene |
| 62375 | Benzaldehyde dimethyl acetal[7] | Non-agonist | Aldehyde |
| 798 | Indole[7] | Non-agonist | Cyclic compound |
| 7731 | 4-methylanisole[7] | Non-agonist | Cyclic compound |
| 229888 | Phenethyl octanoate[7] | Non-agonist | Ester |
| 8091 | Methyl octanoate[7] | Non-agonist | Ester |

**Table S2: Experimentally tested odorants for OR2W1**

| Pubchem_CID | Odorant name | Class | Chemical nature |
|---|---|---|---|
| 8106 | Hexane-1- thiol[10] | Agonist | Sulphur compound |
| 15422 | Heptane-1- thiol [10] | Agonist | Sulphur compound |
| 8067 | Pentane-1- thiol [10] | Agonist | Sulphur compound |
| 439570 | (-)-Carvone[2], [3] | Agonist | Ketone |
| 16724 | (+)-Carvone[5],[8] | Agonist | Ketone |
| 22227 | (+)-Dihydrocarvone[2] | Agonist | Ketone |
| 440917 | (R)-(+)-limonene[3],[5], [8] | Agonist | Terpene |
| 6992244 | (R)-1-octen-3-ol ((R/S)-1-Octen-3-ol)[3] | Agonist | Alcohol |
| 7704 | (R/S)-γ-Octalactone[3] | Agonist | Ketone |
| 7793 | (S)-(-)-citronellol[2] | Agonist | Alcohol |
| 439250 | (S)-(−)-limonene[3] | Agonist | Terpene |
| 8174 | 1-decanol[2] | Agonist | Alcohol |
| 8129 | 1-heptanol[2] | Agonist | Alcohol |
| 8914 | 1-nonanol[2], [3] | Agonist | Alcohol |
| 957 | 1-octanol[2], [8] | Agonist | Alcohol |
| 19707 | 2,3-hexanedione[2] | Agonist | Ketone |
| 10976 | 2-heptanol[3] | Agonist | Alcohol |
| 11583 | 2-hexanone[2] | Agonist | Ketone |
| 13187 | 2-nonanone[3], [2] | Agonist | Ketone |
| 8093 | 2-octanone[2] | Agonist | Ketone |
| 16800 | 2-pentylpyridine[3] | Agonist | Cyclic compound |
| 78126 | 2-phenylethane thiol [3] | Agonist | Sulphur compound |
| 7654 | 2-Phenylethyl acetate[3] | Agonist | Ester |
| 62539 | 3,4-hexanedione[2] | Agonist | Ketone |
| 7802 | 3-heptanone[2] | Agonist | Ketone |
| 518810 | 3-Mercaptohexyl acetate[3] | Agonist | Ester |
| 31276 | 3-Methylbutyl acetate/ isoamyl acetate[3] | Agonist | Ester |
| 246728 | 3-octanone[2] | Agonist | Ketone |
| 68110 | 4-chromanone[2] | Agonist | Ketone |
| 8500 | 4-Methyl acetophenone[3] | Agonist | Ketone |
| 76354 | 6-Methyl-2,4-heptanedione[3] | Agonist | Ketone |
| 7410 | Acetophenone[2] | Agonist | Ketone |
| 15717 | Allyl phenylacetate[2], [3],[5],[8] | Agonist | Ester |
| 3102 | Benzophenone[2] | Agonist | Cyclic compound |
| 8785 | Benzyl acetate[2],[11] | Agonist | Ester |
| 5282110 | Cinnamyl acetate[3] | Agonist | Ester |
| 62378 | Dihydrojasmone[2] | Agonist | Ketone |
| 8815 | Estragole[3] | Agonist | Cyclic compound |
| 18686 | Ethyl cyclohexanecarboxylate[3] | Agonist | Ester |
| 8130 | Heptanal[2] | Agonist | Aldehyde |
| 637520 | Methyl cinnamate[3] | Agonist | Ester |
| 8908 | Hexyl acetate[2], [3] | Agonist | Ester |
| 31289 | Decanoic acid[2], [3],[8] | Agonist | Acid |

| **Pubchem_CID** | Odorant name | **Class** | **Chemical nature** |
|---|---|---|---|
| 15077 | Nonane thiol[2] | Agonist | Sulphur compound |
| 8158 | Nonanoic acid[2], [8] | Agonist | Acid |
| 454 | Octanal[2], [3] | Agonist | Aldehyde |
| 8144 | Octane thiol[2] , [5], [8] | Agonist | Sulphur compound |
| 62385 | P,α-Dimethylstyrene[3] | Agonist | Cyclic compound |
| 14489 | Prenyl acetate[2] | Agonist | Ester |
| 637563 | Trans-anethole[3] | Agonist | Cyclic compound |
| 64805 | Helional[8] | Agonist | Aldehyde |
| 20499 | Coffee difuran[5] ,[8] | Agonist | Cyclic compound |
| 7136 | Eugenyl acetate[8] | Agonist | Ester |
| 4133 | Methyl salicylate[8] | Agonist | Ester |
| 5283316 | (E)-2-heptenal[3] | Agonist | Aldehyde |
| 61431 | 1,1-dimethoxy-octane[5] | Agonist | Alkane |
| 80314 | 2,4-nonanedione[3] | Agonist | Ketone |
| 84192 | 2,4-octanedione[3] | Agonist | Ketone |
| 61809 | 2-ethoxythiazole[5] | Agonist | Thiazole |
| 61052 | 3-phenyl propyl propionate[5] | Agonist | Ester |
| 8635 | Methyl anthranilate[7] | Agonist | Ester |
| 24433 | Butyl anthranilate[5] | Agonist | Ester |
| 7794 | Citronellal[11] | Agonist | Aldehyde |
| 12348 | N- amyl acetate[5] | Agonist | Ester |
| 1549026 | Geranyl acetate[5] ,[8] | Conflicting info. | Ester |
| 8103 | 1-hexanol[2] ,[3] | Conflicting info. | Alcohol |
| 165675 | (+)-Menthol[8],[5] | Conflicting info. | Alcohol |
| 323 | Coumarin[2],[3], [5, 11] | Conflicting info. | Ketone |
| 379 | Octanoic acid[2] ,[3] | Conflicting info. | Acid |
| 2969 | Capric acid[2] ,[3] | Conflicting info. | Acid |
| 6184 | Hexanal[2] ,[3] | Conflicting info. | Aldehyde |
| 106997 | 2-ethyl fenchol [5] ,[8] | Conflicting info. | Alcohol |
| 637566 | Geraniol[2] ,[3] | Conflicting info. | Alcohol |
| 8467 | Ethyl vanillin[3], [5],[8] | Conflicting info. | Aldehyde |
| 1183 | Vanillin[3], [5] | Conflicting info. | Aldehyde |
| 6276 | 1-pentanol[2], [8] | Conflicting info. | Alcohol |
| 264 | Butyric acid[8] | Conflicting info. | Acid |
| 3314 | Eugenol[3], [5],[8] | Conflicting info. | Cyclic compounds |
| 8051 | 2-heptanone[2], [8] | Conflicting info. | Ketone |
| 5281167 | Cis-3-hexenol[3], [5],[8], [12] | Conflicting info. | Alcohol |
| 111037 | Terpinyl acetate[8], [5] | Conflicting info. | Ester |
| 638011 | Citral[8], [11] | Conflicting info. | Aldehyde |
| 71309167 | Propanal[3], [8] | Conflicting info. | Aldehyde |
| 11614 | Butyl formate[2], [8] | Conflicting info. | Ester |
| 17100 | Alpha-terpineol[3], [5] | Conflicting info. | Alcohol |
| 785330 | (-)-2-Phenylbutyric acid[2] | Non-agonist | Acid |
| 444294 | (-)-Camphor[2] | Non-agonist | Ketone |

| **Pubchem_CID** | Odorant name | **Class** | **Chemical nature** |
|---|---|---|---|
| 62131 | Methyl furfuryl disulphide[8] | Non-agonist | Cyclic compound |
| 82229 | (-)-Fenchone[2], [3] | Non-agonist | Ketone |
| 785329 | (+)-2-Phenylbutyric acid[2] | Non-agonist | Acid |
| 159055 | (+)-Camphor[2] | Non-agonist | Ketone |
| 637511 | Cinnamaldehyde[5] | Non-agonist | Aldehyde |
| 1201521 | (+)-Fenchone[2] | Non-agonist | Ketone |
| 68382 | 2-coumaranone[2] | Non-agonist | Ketone |
| 7895 | 2-pentanone[2] | Non-agonist | Ketone |
| 529481 | 3-Methyl-2,4-nonanedione[3] | Non-agonist | Ketone |
| 54682930 | 4-hydroxycoumarin[2] | Non-agonist | Ketone |
| 9309 | Allyl benzene[2] | Non-agonist | Cyclic compound |
| 8878 | Allyl heptanoate[2] | Non-agonist | Ester |
| 10886 | Amyl hexanoate [2], [8] | Non-agonist | Ester |
| 241 | Benzene[2], [5] ,[8] | Non-agonist | Cyclic compound |
| 7967 | Cyclohexanone[2] | Non-agonist | Ketone |
| 31265 | Ethyl hexanoate[3] | Non-agonist | Ester |
| 7342 | Ethyl isobutyrate[2], [3] | Non-agonist | Ester |
| 7590 | Ethylphenyl acetate[3] | Non-agonist | Ester |
| 24114 | Butyl butyryl lactate[2] | Non-agonist | Ester |
| 8094 | Heptanoic acid[2] | Non-agonist | Acid |
| 8892 | Hexanoic acid[2], [3] | Non-agonist | Acid |
| 91604 | Lyral[2], [5] ,[8] | Non-agonist | Aldehyde |
| 7991 | Pentanoic acid[2], [3] | Non-agonist | Acid |
| 31229 | Phenyl acetate[2] | Non-agonist | Ester |
| 1032 | Propionic acid[2], [3],[8] | Non-agonist | Acid |
| 8468 | Vanillic acid[2] | Non-agonist | Acid |
| 8175 | Decanal[2], [3], [5],[8] | Non-agonist | Aldehyde |
| 520119 | 1,3-butane di thiol [5] | Non-agonist | Sulphur compound |
| 8461 | 2,4-DNT[5] ,[8] | Non-agonist | Cyclic compound |
| 12756 | Gamma-Caprolactone[2] | Non-agonist | Ketone |
| 1133 | Thioglycolic acid[5] | Non-agonist | Acid |
| 2266 | Nonanedioic acid[2] | Non-agonist | Acid |
| 261 | Butanal[2] | Non-agonist | Aldehyde |
| 8063 | Pentanal[2] | Non-agonist | Aldehyde |
| 7765 | Acetal[3] | Non-agonist | Aldehyde |
| 7888 | Hydroxycitronellal[2] | Non-agonist | Aldehyde |
| 263 | 1-butanol[3] | Non-agonist | Alcohol |
| 1031 | 1-propanol[2] | Non-agonist | Alcohol |
| 2724897 | (+)-2-heptanol[2] | Non-agonist | Alcohol |
| 80080 | (R)-(-)-2-octanol[2] | Non-agonist | Alcohol |
| 2723888 | (S)-(+)-2-octanol[2] | Non-agonist | Alcohol |
| 6549 | Linalool[3], [5], [8] | Non-agonist | Terpene |
| 8184 | 1-undecanol[2] | Non-agonist | Alcohol |
| 12041 | Ethyl pyruvate[2] | Non-agonist | Ester |

| **Pubchem_CID** | Odorant name | **Class** | **Chemical nature** |
|---|---|---|---|
| 61304 | Heptyl isobutyrate[2] | Non-agonist | Ester |
| 21596 | Butyl heptanoate[2] | Non-agonist | Ester |
| 10890 | Amyl butyrate[2] | Non-agonist | Ester |
| 7770 | Propyl butyrate[2] | Non-agonist | Ester |
| 12180 | Methyl butyrate[3] | Non-agonist | Ester |
| 88561 | Tert-Butyl propionate[2] | Non-agonist | Ester |
| 6569 | 2-butanone[2] | Non-agonist | Ketone |
| 442495 | (+)-Pulegone[2] | Non-agonist | Ketone |
| 14505 | 2-Furyl methyl ketone[2] | Non-agonist | Ketone |
| 31358 | Dimedone[2] | Non-agonist | Ketone |
| 26447 | (-)-Menthone[2] | Non-agonist | Ketone |
| 650 | 2,3-butanedione[3] | Non-agonist | Ketone |
| 11747 | 2,3-pentanedione[3] | Non-agonist | Ketone |
| 5362588 | Filbertone[3] | Non-agonist | Ketone |
| 11086 | 2'-aminoacetophenone[3] | Non-agonist | Ketone |
| 61346 | 1-octen-3-one[3] | Non-agonist | Ketone |
| 15394 | Ethyl vinyl ketone[3] | Non-agonist | Ketone |
| 27470 | 3-Methylheptan-4-one[3] | Non-agonist | Ketone |
| 179 | Acetoin[3] | Non-agonist | Ketone |
| 8369 | Maltol[3] | Non-agonist | Alcohol |
| 10748 | 7-methoxycoumarin[3] | Non-agonist | Ketone |
| 6736 | 3-Methyl-1H-indole[3] | Non-agonist | Cyclic compound |
| 169110 | 2-Acetyl-2-thiazoline[3] | Non-agonist | Thiazole |
| 529251 | 2-propionylpyrroline[3] | Non-agonist | Cyclic compound |
| 19309 | Furaneol[3] | Non-agonist | Cyclic compound |
| 33931 | Homofuraneol[3] | Non-agonist | Cyclic compound |
| 61325 | 4-Methoxy-2,5-dimethyl-3(2H)-furanone[3] | Non-agonist | Cyclic compound |
| 62835 | Sotolon[3], [5] | Non-agonist | Cyclic compound |
| 61199 | 5-Ethyl-3-hydroxy-4-methylfuran-2(5H)-one[3] | Non-agonist | Ketone |
| 6590 | Isobutyric acid[3] | Non-agonist | Acid |
| 8314 | 2-Methylbutanoic acid[3] | Non-agonist | Acid |
| 62089 | 4-Methyloctanoic acid[3] | Non-agonist | Acid |
| 61840 | 4-Ethyloctanoic acid[3] | Non-agonist | Acid |
| 176 | Acetic acid[3] | Non-agonist | Acid |
| 637542 | P-Coumaric acid[3] | Non-agonist | Acid |
| 999 | 2-Phenylacetic acid[3] | Non-agonist | Acid |
| 107 | 3-Phenyl propionic acid[3] | Non-agonist | Acid |
| 702 | Ethanol[3] | Non-agonist | Alcohol |
| 5315892 | Cinnamyl alcohol[3] | Non-agonist | Alcohol |
| 6054 | 2-phenylethanol[3] | Non-agonist | Alcohol |
| 5362833 | (2E,6Z)-Nona-2,6-dien-1-ol[3] | Non-agonist | Alcohol |
| 31260 | 3-Methyl-1-butanol[3] | Non-agonist | Alcohol |
| 8723 | 2-methyl-1-butanol[3] | Non-agonist | Alcohol |
| 6560 | Isobutyl alcohol[3] | Non-agonist | Alcohol |

| **Pubchem_CID** | Odorant name | **Class** | **Chemical nature** |
|---|---|---|---|
| 853433 | Isoeugenol[3] | Non-agonist | Cyclic compound |
| 7127 | Methyl eugenol[3], [5] ,[8] | Non-agonist | Cyclic compound |
| 31244 | P-anisaldehyde[3], [5] | Non-agonist | Aldehyde |
| 326 | Cuminaldehyde[3] | Non-agonist | Aldehyde |
| 12777 | 6-Propyloxan-2-one[3] | Non-agonist | Ketone |
| 7710 | 5-Pentyloxolan-2-one[3] | Non-agonist | Ketone |
| 12813 | 5-Hexyloxolan-2-one[3] | Non-agonist | Ketone |
| 12810 | Delta-decalactone[3] | Non-agonist | Ketone |
| 7714 | Gamma-undecalactone[3] | Non-agonist | Ketone |
| 12844 | Delta-Dodecalactone[3] | Non-agonist | Ketone |
| 16821 | 5-Octyloxolan-2-one[3] | Non-agonist | Ketone |
| 62900 | 5-Butyl-4-methyloxolan-2-one[3] | Non-agonist | Ketone |
| 31253 | Myrcene[3] | Non-agonist | Terpene |
| 2758 | 1,8-cineol[3] | Non-agonist | Alcohol |
| 7460 | Alpha-Phellandrene[3] | Non-agonist | Terpene |
| 443162 | (-)-alpha-Terpineol[3] | Non-agonist | Alcohol |
| 440968 | (-)-alpha-Pinene[3] | Non-agonist | Terpene |
| 82227 | (+)-alpha-Pinene[3] | Non-agonist | Terpene |
| 440967 | (-)-beta-Pinene[3] | Non-agonist | Terpene |
| 10290825 | (+)-beta-Pinene[3] | Non-agonist | Terpene |
| 10887971 | (+)-sabinene[3] | Non-agonist | Terpene |
| 5374527 | (E)-beta-damascone[3], [8] | Non-agonist | Ketone |
| 5366074 | Beta-damascenone[3] | Non-agonist | Ketone |
| 638014 | Beta-Ionone[3] | Non-agonist | Ketone |
| 27866 | Rose oxide[3] | Non-agonist | Terpene |
| 12101 | 3-ethylphenol[3] | Non-agonist | Cyclic compound |
| 31242 | 4-ethylphenol[3] | Non-agonist | Cyclic compound |
| 335 | 2-methylphenol[3] | Non-agonist | Cyclic compound |
| 342 | 3-methylphenol[3] | Non-agonist | Cyclic compound |
| 2879 | 4-methylphenol[3] | Non-agonist | Cyclic compound |
| 7771 | 2,4-dimethylphenol[3] | Non-agonist | Cyclic compound |
| 11335 | 2,6-dimethylphenol[3] | Non-agonist | Cyclic compound |
| 460 | Guaiacol[3], [5] | Non-agonist | Alcohol |
| 7144 | 2-methoxy-4-methylphenol[3] | Non-agonist | Cyclic compound |
| 14519 | 2-Methoxy-5-methylphenol[3] | Non-agonist | Cyclic compound |
| 62465 | 2-Methoxy-4-ethylphenol[3] | Non-agonist | Cyclic compound |
| 17739 | 2-methoxy-4-propylphenol[3] | Non-agonist | Cyclic compound |
| 62453 | 4-ethenylphenol[3] | Non-agonist | Alcohol |
| 332 | 4-vinylguaiacol[3] | Non-agonist | Alcohol |
| 7041 | 2,6-dimethoxyphenol[3] | Non-agonist | Cyclic compound |
| 28905 | 2,3-Diethyl-5-methylpyrazine[3] | Non-agonist | Pyrazine |
| 26808 | 2,3,5-trimethylpyrazine[3] | Non-agonist | Pyrazine |
| 62237 | 3-Mercapto-2-pentanone[3] | Non-agonist | Ketone |
| 529635 | 2-Sulfanylpentan-3-one[3] | Non-agonist | Ketone |

| **Pubchem_CID** | Odorant name | **Class** | **Chemical nature** |
|---|---|---|---|
| 32594 | 2-Isobutyl-3-methoxypyrazine[3] | Non-agonist | Pyrazine |
| 33166 | 2-Isopropyl-3-methoxypyrazine[3] | Non-agonist | Pyrazine |
| 520098 | 2-Sec-Butyl-3-methoxypyrazine[3] | Non-agonist | Pyrazine |
| 30914 | 2-acetylpyrazine[3] | Non-agonist | Pyrazine |
| 61592 | Ethyl 3-methylthiopropionate[3] | Non-agonist | Ester |
| 7363 | Furfuryl mercaptan[3] | Non-agonist | Sulphur compound |
| 34286 | 2-Methyl-3-furan thiol [3] | Non-agonist | Sulphur compound |
| 6430888 | 2-Methyl-3-sulfanylpentan-1-ol[3] | Non-agonist | Alcohol |
| 47649 | Methyl 2-methyl-3-furyl disulfide[3] | Non-agonist | Sulphur compound |
| 18635 | 3-methylthiopropionaldehyde[3] | Non-agonist | Aldehyde |
| 10448 | 3-(Methylthio)-1-propanol[3] | Non-agonist | Alcohol |
| 15380 | Bis(methylthio)methane[3] | Non-agonist | Alkane |
| 80408 | Thenyl mercaptan[3] | Non-agonist | Sulphur compound |
| 6427135 | 1-p-Menthene-8- thiol [3] | Non-agonist | Sulphur compound |
| 521348 | 3-Sulfanylhexan-1-ol[3] | Non-agonist | Alcohol |
| 526487 | 3-Mercapto-3-methylbutyl formate[3] | Non-agonist | Ester |
| 88290 | 4-Mercapto-4-methyl-2-pentanone[3] | Non-agonist | Ketone |
| 526195 | 4-Methoxy-2-methyl-2-butane thiol [3] | Non-agonist | Sulphur compound |
| 1068 | Methyl sulfide[3] | Non-agonist | Sulphur compound |
| 12232 | Dimethyl disulfide[3], [8] | Non-agonist | Sulphur compound |
| 19310 | Dimethyl trisulfide[3] | Non-agonist | Sulphur compound |
| 5319765 | Methyl propyl trisulfide[3] | Non-agonist | Sulphur compound |
| 12377 | Propyl disulfide[3] | Non-agonist | Sulphur compound |
| 22383 | Dipropyl trisulfide[3] | Non-agonist | Sulphur compound |
| 66282 | Allyl methyl sulfide[3] | Non-agonist | Sulphur compound |
| 16590 | Allyl disulfide[3] | Non-agonist | Sulphur compound |
| 6561 | Isobutyraldehyde[3] | Non-agonist | Aldehyde |
| 7284 | 2-methylbutyraldehyde[3] | Non-agonist | Aldehyde |
| 11552 | Isovaleraldehyde[3] | Non-agonist | Aldehyde |
| 5281168 | 2-hexenal, (2e)- [3] | Non-agonist | Aldehyde |
| 643941 | 3-hexenal, (3z)- [3] | Non-agonist | Aldehyde |
| 5362814 | 4-heptenal, (4z)- [3] | Non-agonist | Aldehyde |
| 6427080 | 2-octenal, (2z)- [3] | Non-agonist | Aldehyde |
| 5283335 | 2-nonenal, (2e)- [3] | Non-agonist | Aldehyde |
| 5354833 | 2-nonenal, (2z)- [3] | Non-agonist | Aldehyde |
| 5283339 | 2,4-nonadienal, (2e,4e)- [3] | Non-agonist | Aldehyde |
| 6429282 | 2,4-nonadienal, (2e,4z)- [3] | Non-agonist | Aldehyde |
| 643731 | 2,6-nonadienal, (2e,6z)- [3] | Non-agonist | Aldehyde |
| 5283345 | 2-decenal, (2e)- [3] | Non-agonist | Aldehyde |
| 5362620 | 4-decenal, (4z)- [3] | Non-agonist | Aldehyde |
| 5283349 | 2,4-decadienal, (2e,4e)- [3] | Non-agonist | Aldehyde |
| 3018619 | 12-methyltridecanal[3] | Non-agonist | Aldehyde |
| 5283356 | 2-undecenal[3] | Non-agonist | Aldehyde |
| 177 | Acetaldehyde[3] | Non-agonist | Aldehyde |

| **Pubchem_CID** | Odorant name | **Class** | **Chemical nature** |
|---|---|---|---|
| 998 | Phenylacetaldehyde[3], [5] | Non-agonist | Aldehyde |
| 7150 | Methyl benzoate[3] | Non-agonist | Ester |
| 7762 | Ethyl butyrate[3] | Non-agonist | Ester |
| 10882 | Ethyl pentanoate[3] | Non-agonist | Ester |
| 7799 | Ethyl octanoate[3] | Non-agonist | Ester |
| 8048 | Ethyl decanoate[3] | Non-agonist | Ester |
| 7165 | Ethyl benzoate[3] | Non-agonist | Ester |
| 637758 | Ethyl cinnamate[3] | Non-agonist | Ester |
| 24020 | Ethyl 2-methylbutyrate[3] | Non-agonist | Ester |
| 7945 | Ethyl isovalerate[3] | Non-agonist | Ester |
| 117477 | Ethyl 4-methylvalerate[3] | Non-agonist | Ester |
| 61293 | Ethyl 3-hydroxyhexanoate[3] | Non-agonist | Ester |
| 13357 | Methyl 2-methylbutyrate[3] | Non-agonist | Ester |
| 11039 | Methyl isobutyrate[3] | Non-agonist | Ester |
| 12209 | 2-Methylbutyl acetate[3] | Non-agonist | Ester |
| 8857 | Ethyl acetate[3] | Non-agonist | Ester |
| 31272 | Butyl acetate[3] | Non-agonist | Ester |
| 5363388 | 3-Hexenyl acetate, (3Z)- [3] | Non-agonist | Ester |
| 5460291 | Arabinose, L-[8] | Non-agonist | Aldehyde |
| 7047 | Quinoline[5] ,[8] | Non-agonist | Cyclic compound |
| 61294 | Octyl octanoate[8] | Antagonist | Ester |
| 6558 | Isobutyl amine[8] | Antagonist | Alkane |
| 6852393 | Androstenone [5] ,[8] | Antagonist | Ketone |
| 181287 | 2,4,5-trimethyl-3-thiazoline[5] | Antagonist | Thiazole |
| 61014 | Ethylene brassylate[5] | Antagonist | Ester |
| 92979 | Androstadienone[5] | Antagonist | Ketone |
| 10430 | Isovaleric acid[5] | Antagonist | Acid |

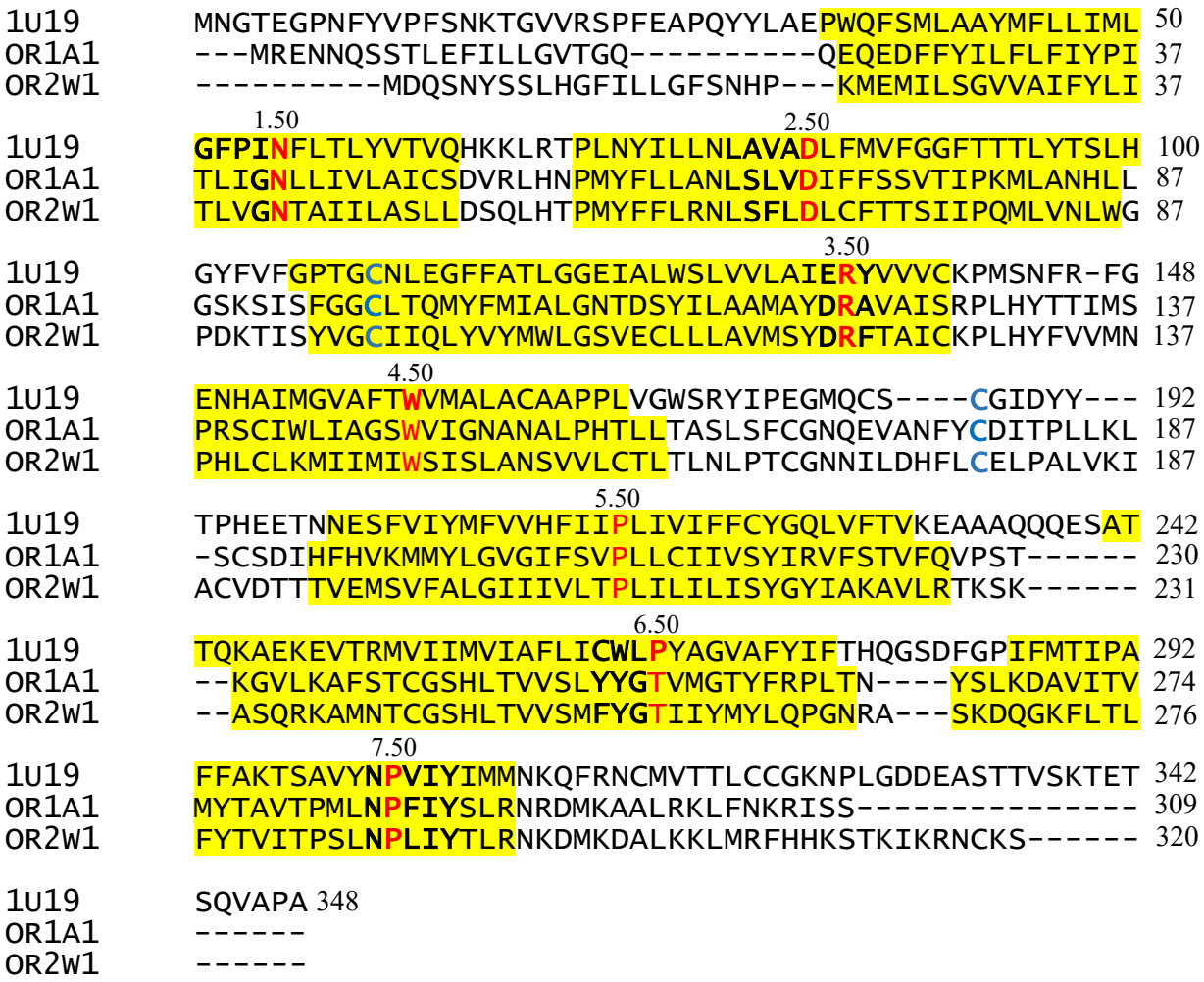



**Figure S1: Alignment of OR1A1, OR2W1 and 1U19 used for model building.** GPCR conserved motifs are bold and central helix residues are shown in red colour while cysteine residues forming disulphide bond are in blue colour. Transmembrane regions are highlighted in yellow colour. Centre residues are numbered according to Ballesteros-Weinstein residue numbering scheme.

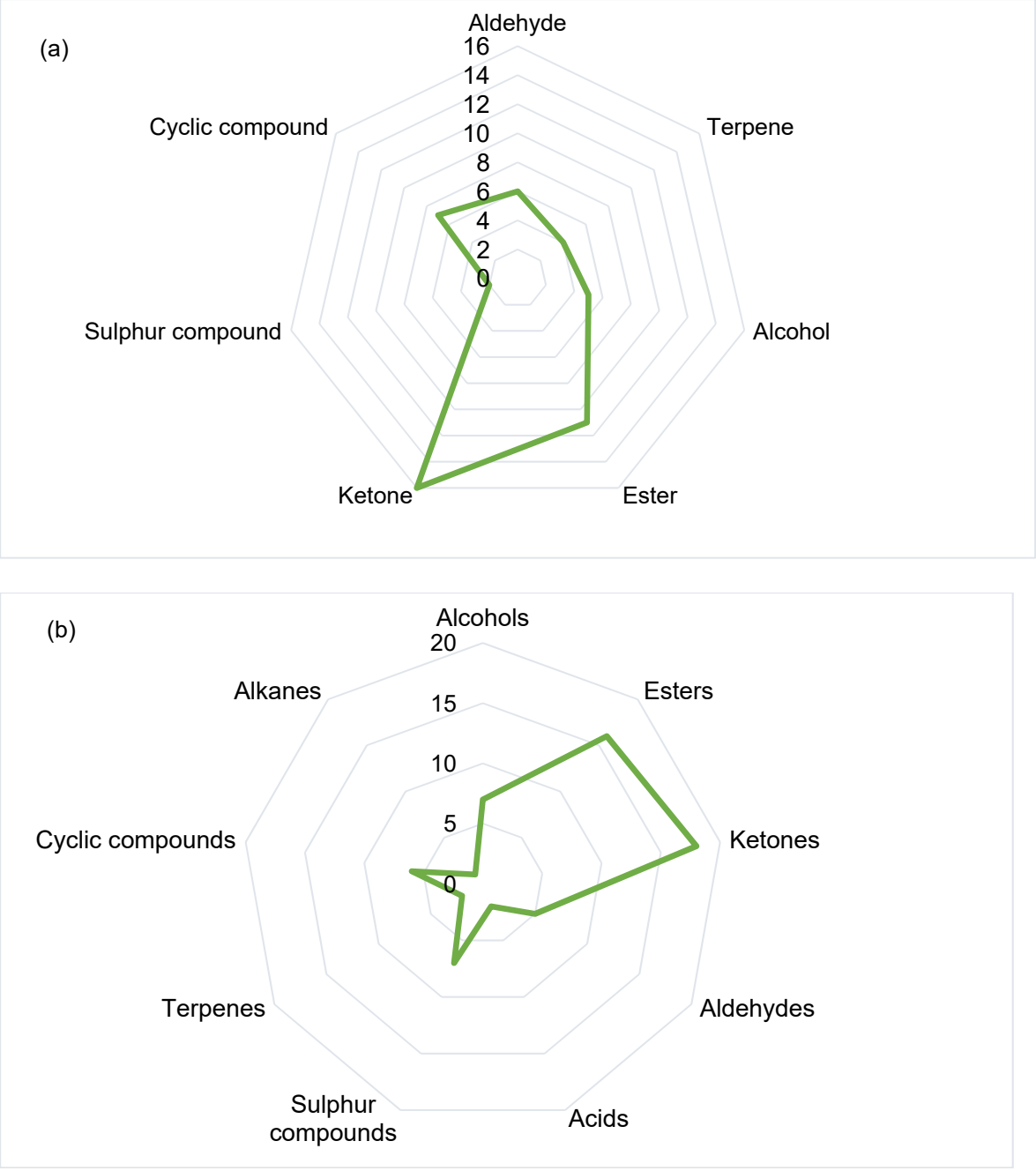



**Figure S2: Diverse chemical nature of known agonists for (a) OR1A1 and (b) OR2W1**

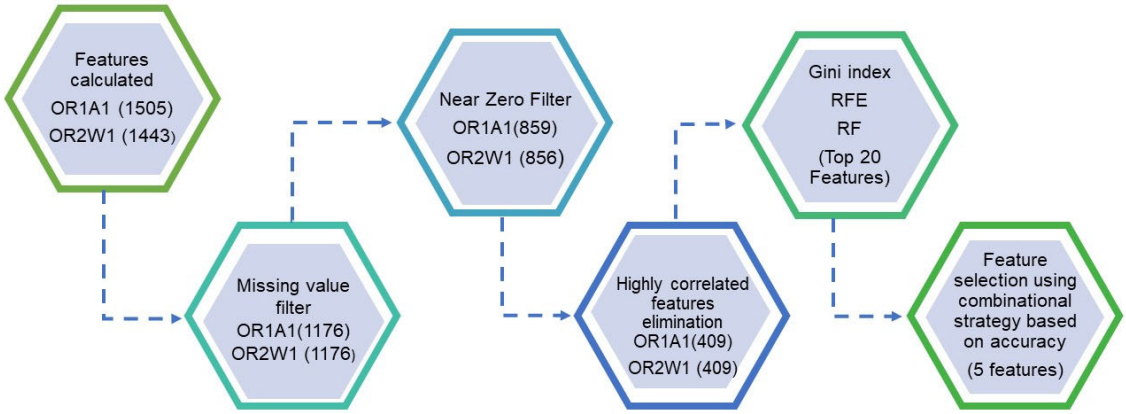
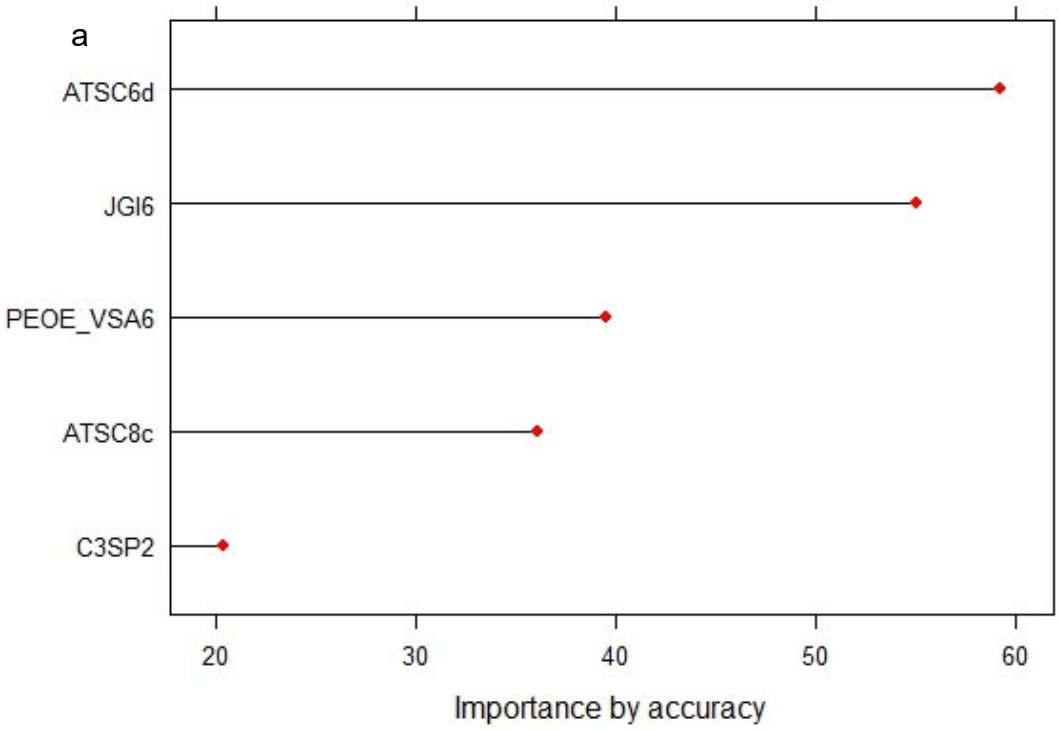



**Figure S3: Workflow for feature selection for OR1A1 and OR2W1.** Gini index is an example for filter feature selection method, RFE, recursive feature selection method is an example for the wrapper method, and RF, random forest is an example for embedded feature selection method.



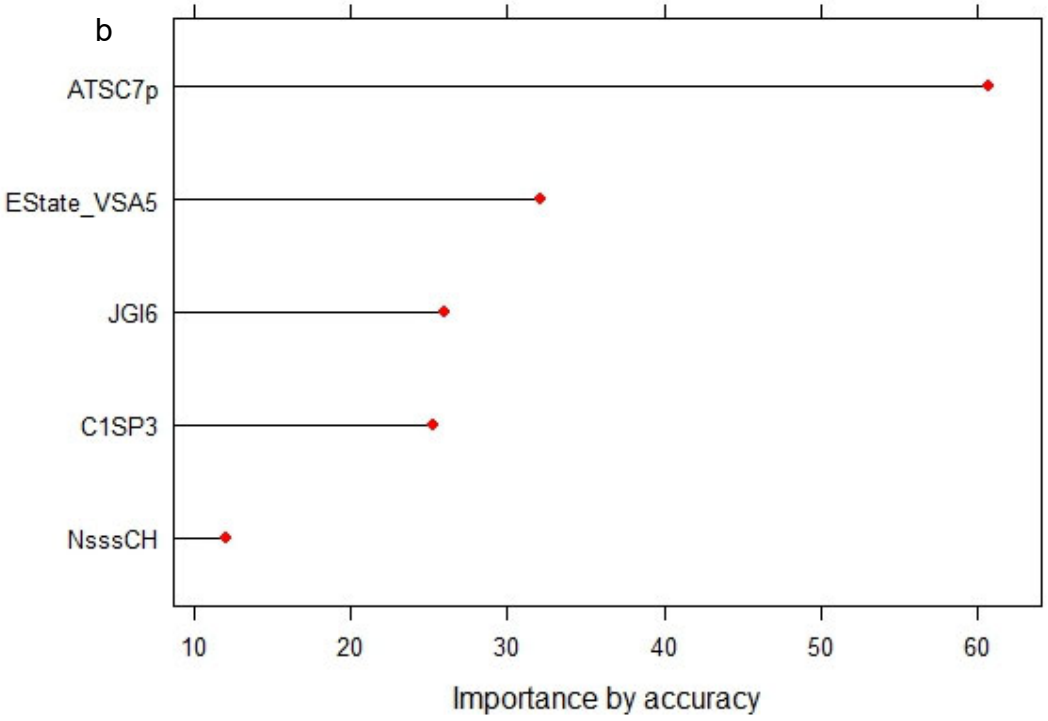




**Figure S4: Importance of selected features based on accuracy for (a) OR1A1 and (b) OR2W1**

**Table S3: Description and significance of selected features (molecular descriptors)**

| Receptor | Feature | Description | Feature class | Significance |
|---|---|---|---|---|
| OR1A1 | ATSC6d | Centered moreau-broto autocorrelation of lag 6 weighted by sigma electrons | 2D-autocorrelation | Estimates log P-values |
| OR1A1 | ATSC8c | Broto autocorrelation of lag 8 weighted by gasteiger charge | | |
| OR2W1 | ATSC7p | Centered moreau-broto autocorrelation of lag 7 weighted by polarizability | | |
| OR1A1 OR2W1 | JGI6 | 6-ordered mean topological charge | Topological | Contains structural information: size, symmetry, etc. |
| OR1A1 | PEOE_VSA6 | MOE charge VSA descriptor 6 (-0.10 <= x< -0.05 | Surface area partial charge | Depicts surface electrostatistics characteristics |
| OR2W1 | Estate_VSA5 | Estate VSA descriptor 5 (1.17 <= x< 1.54 | | |
| OR1A1 | C3SP2 | SP2 carbon bound to 3 other carbons | Carbon types | Carbon connectivity characterization in terms of hybridization |
| OR2W1 | C1SP3 | SP3 carbon bound to1 other carbon | | |
| OR2W1 | Nsssch | Number of sssch | Electro-topological state indices | Hybridization states characteristics |

**Table S4: Statistical tests for the performance of classifiers.** Best values are in bold with next best values in italics.

| | RF | | SVM | | NB | |
|---|---|---|---|---|---|---|
| Dataset | p-value | kappa | p-value | kappa | p-value | kappa |
| OR1A1-training | <2e-16 | 0.99 | <2e-16 | 0.78 | <2e-16 | 0.55 |
| OR1A1-testing | 0.57 | 0.47 | 0.22 | 0.51 | 0.95 | 0.25 |
| OR2W1-training | <2e-16 | 1 | <2e-16 | 0.70 | <2e-16 | 0.48 |
| OR2W1-testing | 0.04 | 0.56 | 0.77 | 0.25 | 0.77 | 0.27 |

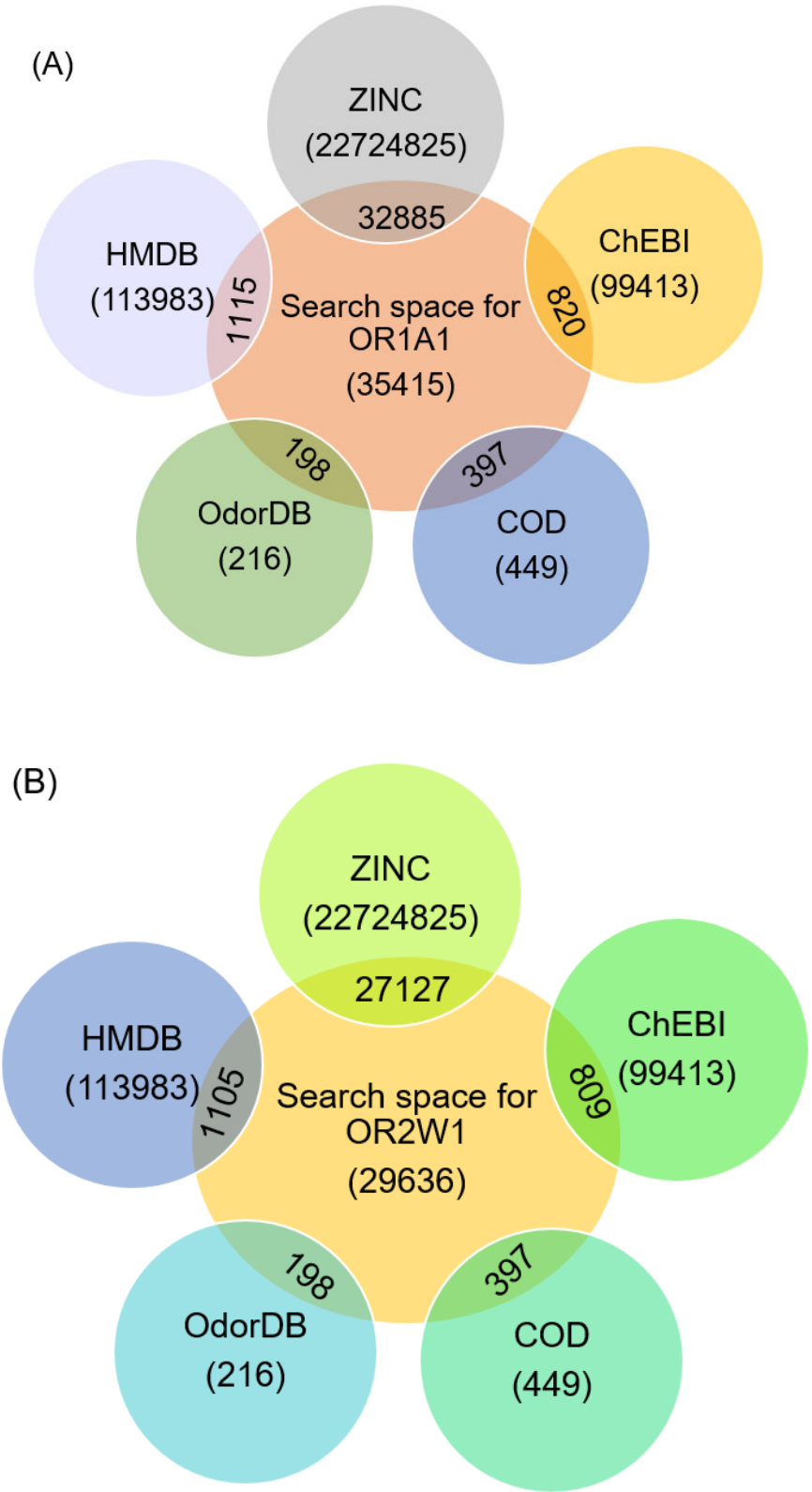



Figure S5: Search space statistics for (a) OR1A1 and (b) OR2W1

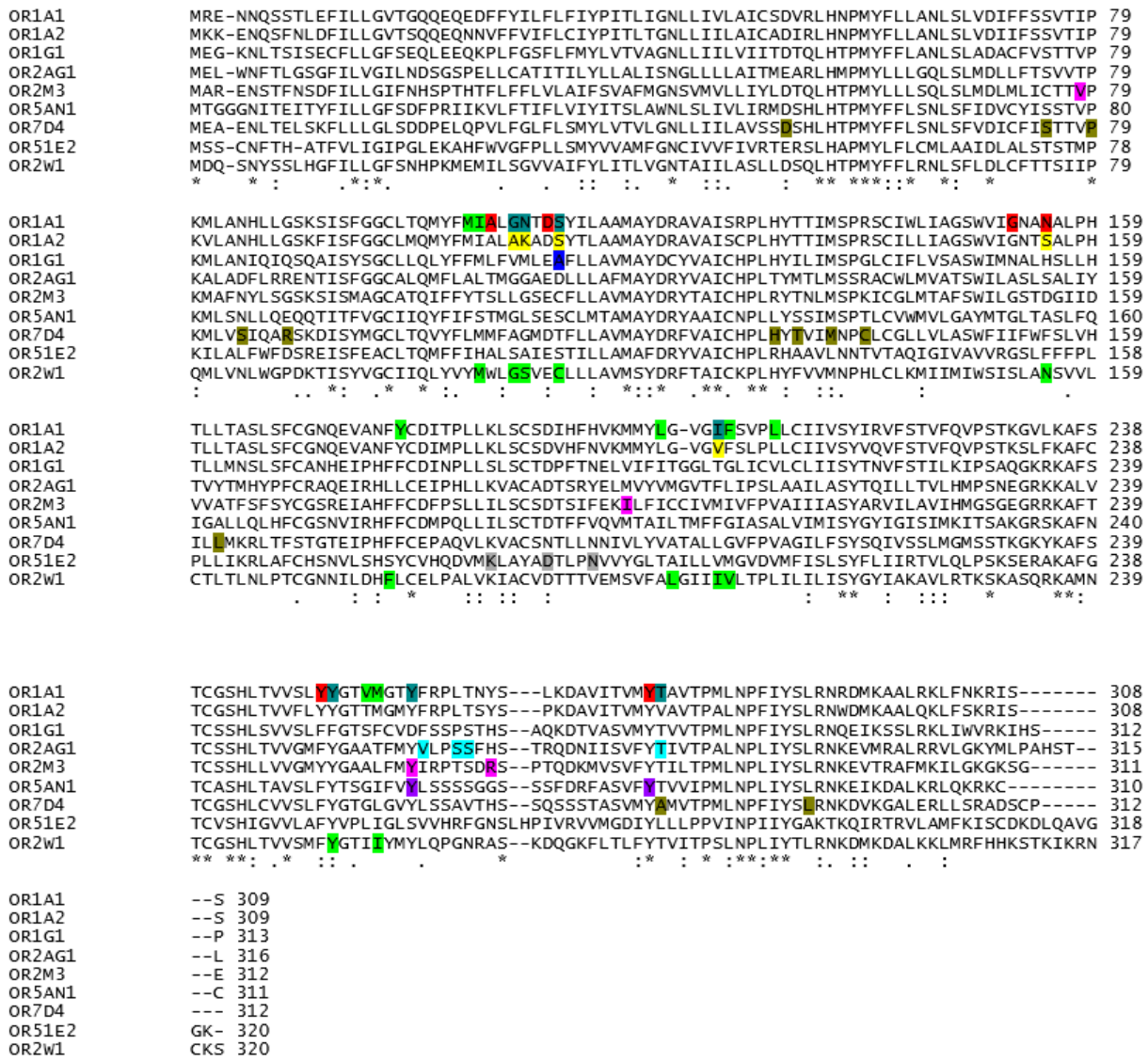
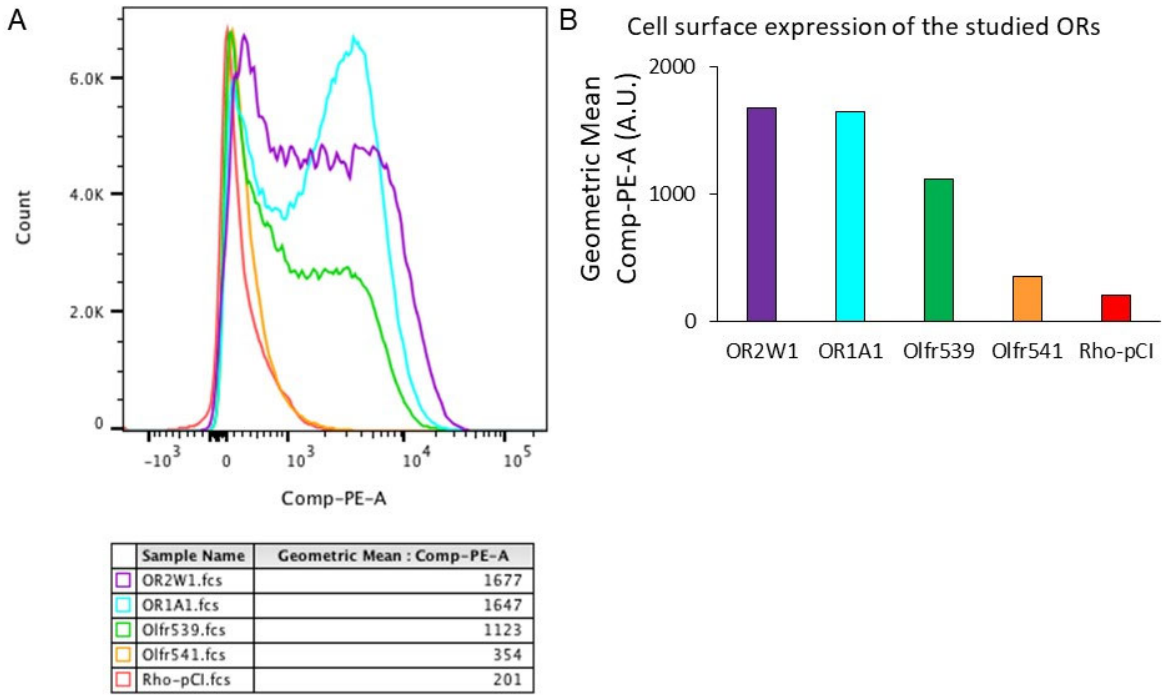



**Figure S6: Alignment of olfactory receptor sequences with mutagenesis data and OR2W1.** The predicted binding residues for OR2W1 and OR1A1 are highlighted in green, the mutagenesis data for OR1A1 in red, the consensus sites for OR1A1 i.e. sites that are predicted as well as experimentally known are highlighted in teal, OR1A2 in yellow, OR1G1 in blue, OR2AG1 in aqua, OR2M3 in pink, OR5AN1 in purple, OR7D4 in olive green, and OR51E2 in grey.




| Sample Name | Geometric Mean : Comp-PE-A |
|---|---|
| OR2W1.fcs | 1677 |
| OR1A1.fcs | 1647 |
| Olfr539.fcs | 1123 |
| Olfr541.fcs | 354 |
| Rho-pCI.fcs | 201 |

**Figure S7: Cell surface expression of the studied ORs.** A. Flow cytometry histogram showing the frequency of PE positive cells among the GFP positive, 7AAD negative, single and spheric cells. B. Geometric mean of the PE frequency for each ORs. Olfr539 and Olfr541 are positive and negative controls, respectively, of OR cell surface expression. Rho-pCI is the empty vector negative control. *In vitro* data is available from the Supplementary Data file (in Excel format).

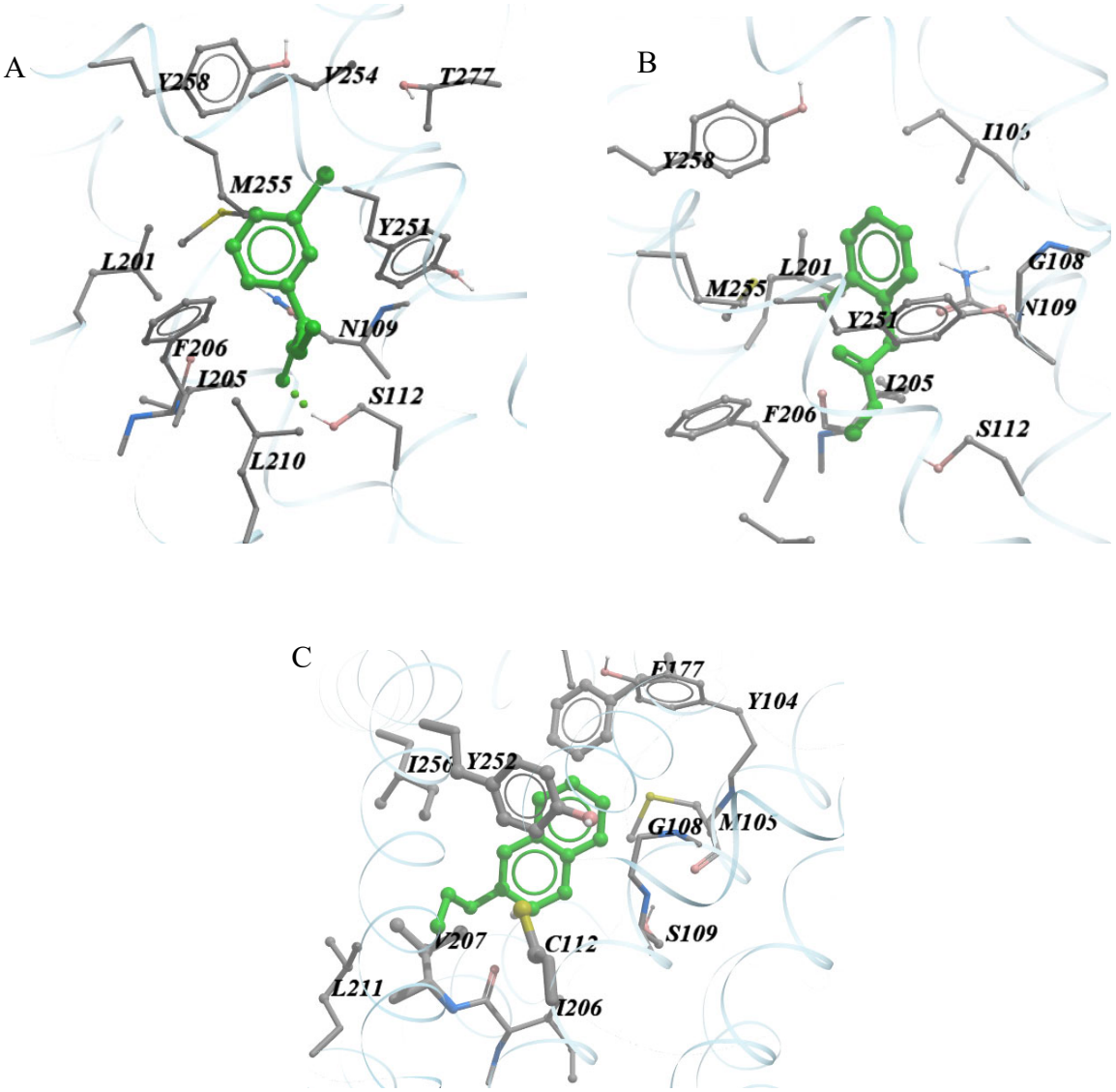



**Figure S8: Binding mode of agonists and their cognate receptors.** (A) Ethyl 2-(3-bromophenyl)acetate, (B) Methyl 2-(2-methylphenyl)acetate within OR1A1 binding pocket and (C) 2-ethoxynaphthalene within OR2W1 binding pocket. The agonists are shown in green colour.

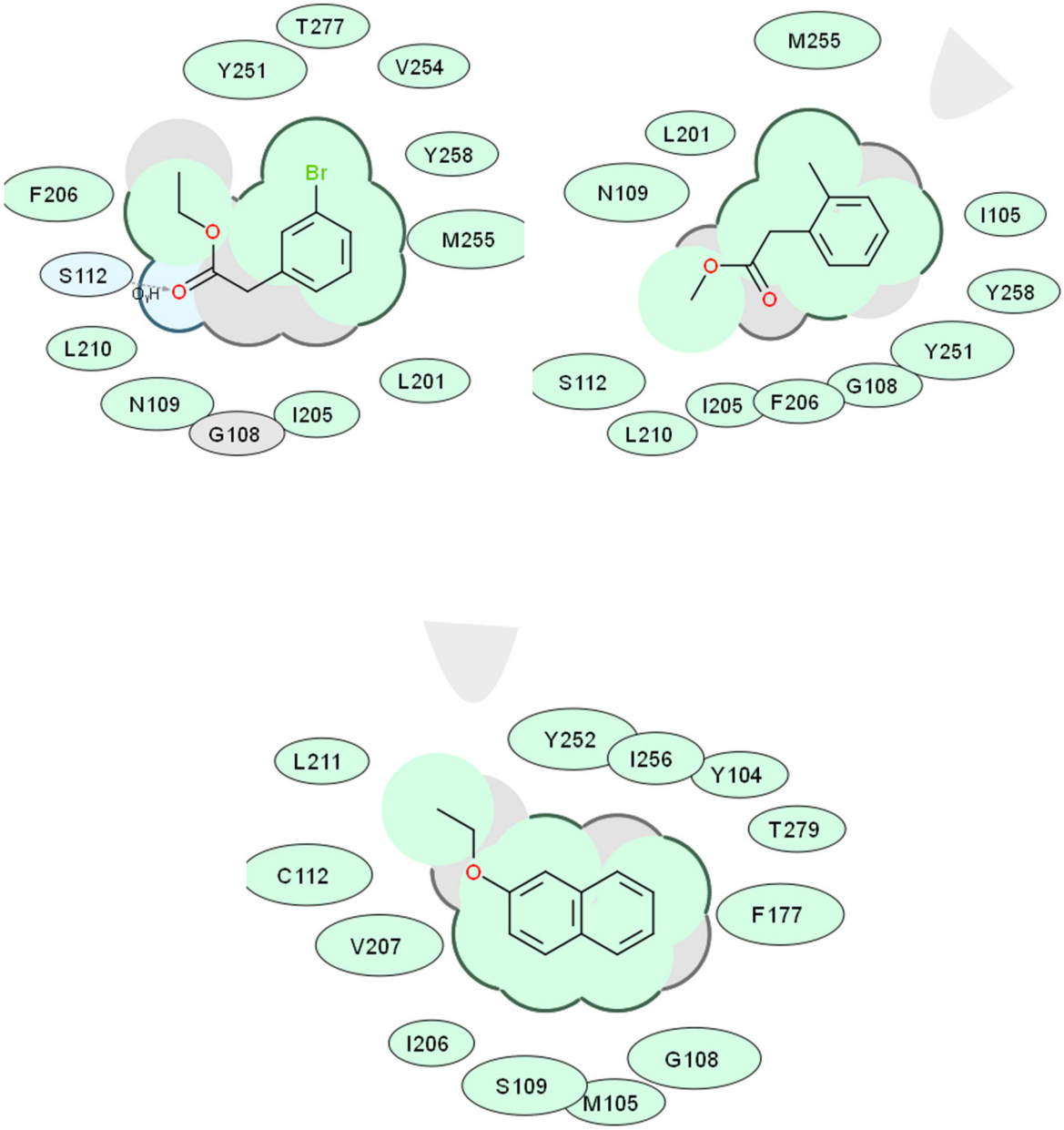



**Figure S9: Interactions of agonists and their cognate receptors.** (A) Ethyl 2-(3-bromophenyl) acetate, (B) Methyl 2-(2-methylphenyl)acetate with OR1A1 and (C) 2-ethoxynaphthalene with OR2W1: Green shading representing hydrophobic regions, gray shading represents wander waal interactions and gray parabolas represents surface accessible regions while blue shading represents hydrogen bond acceptor.

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