

Supplementary Information

Structural bioinformatic study of six human olfactory receptors and their AlphaFold3 predicted water-soluble QTY variants and OR1A2 with an odorant

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Table S1. SwissParam scores of octanoic acid - receptor complexes.

Receptor	SwissParam Score ¹
OR52cs	-6.1091
OR1A1	-6.0243
OR1A2	-6.1848
OR51E1	-6.0030
OR51E2	-5.7291

¹SwissParam scores were computed by SwissDock web server. Best scores for each complex were listed.

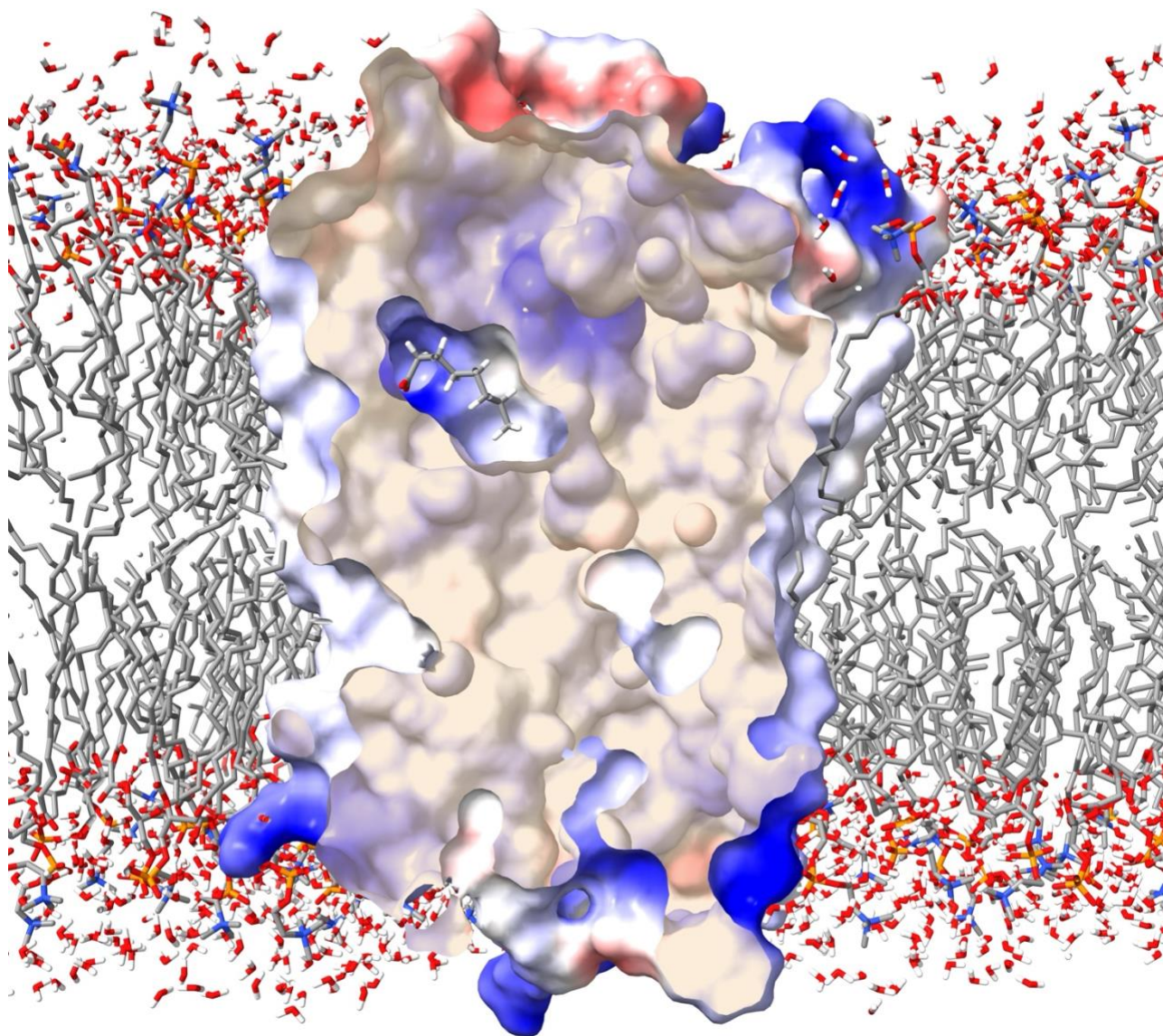
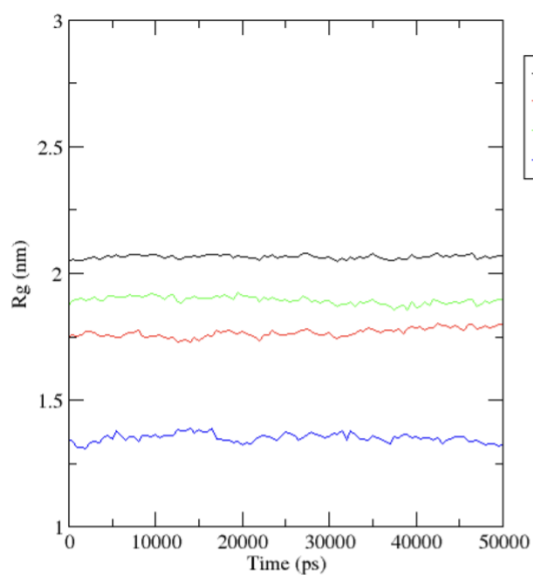


Figure S1. OR1A2-octanoic acid complex in the membrane environment. Octanoic acid (OCA) is positioned within a hydrophobic cleft. The electrostatic potential surface highlights the compatibility of the binding pocket for the hydrophobic tail and polar head group of OCA.

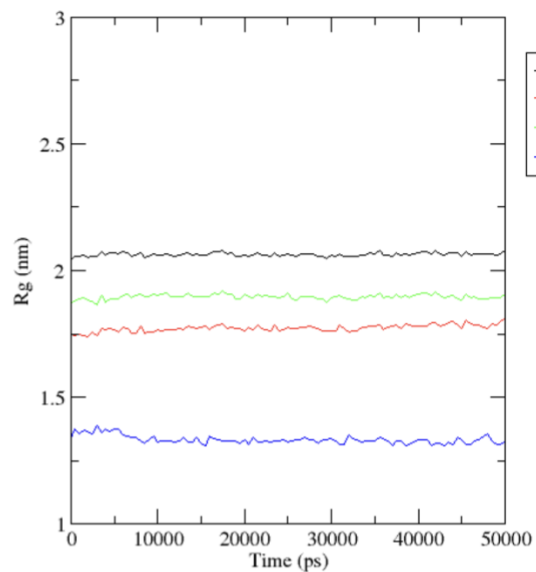
OR1A2

Radius of gyration (total and around axes)



OR1A2 - octanoic acid complex

Radius of gyration (total and around axes)



OR1A2 - octanoate complex

Radius of gyration (total and around axes)

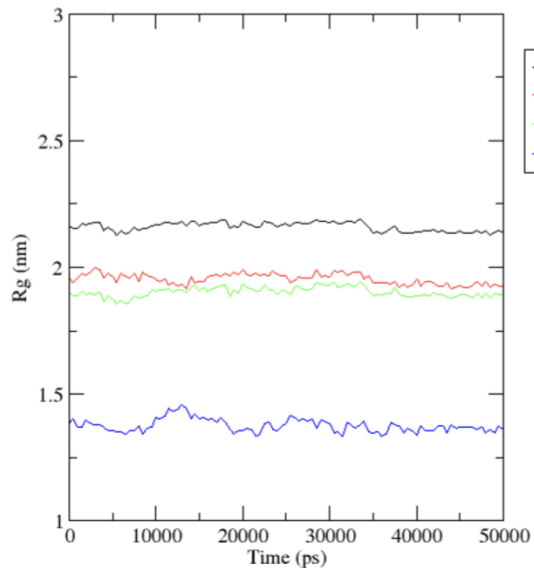
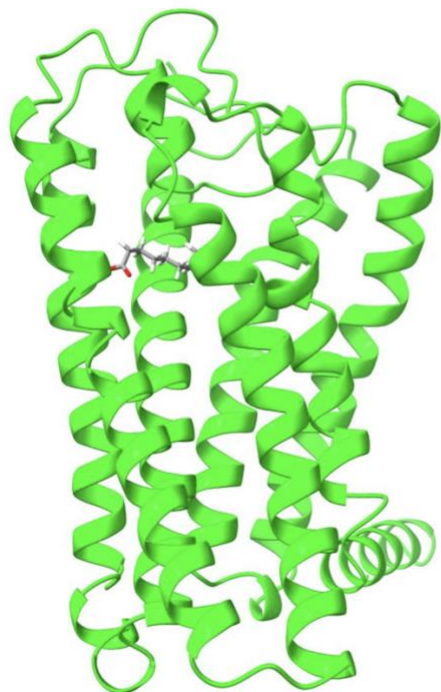


Figure S2. Radius of gyration during the 50ns MD simulation.

OR1A2-octanoic acid



OR1A2-octanoate

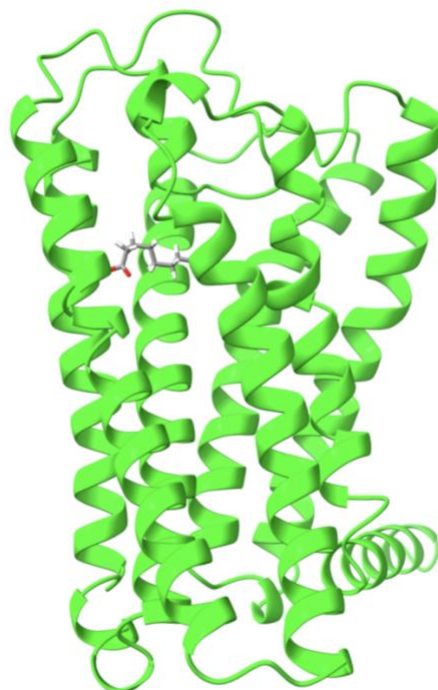


Figure S3. OR1A2 in complex with octanoic acid (left) and octanoate (right). Structural representation of the OR1A2 complex bound with octanoic acid (left) and octanoate (right). The AlphaFold predicted protein structure in green cartoon representation, with the ligand octanoic acid shown as a stick model.

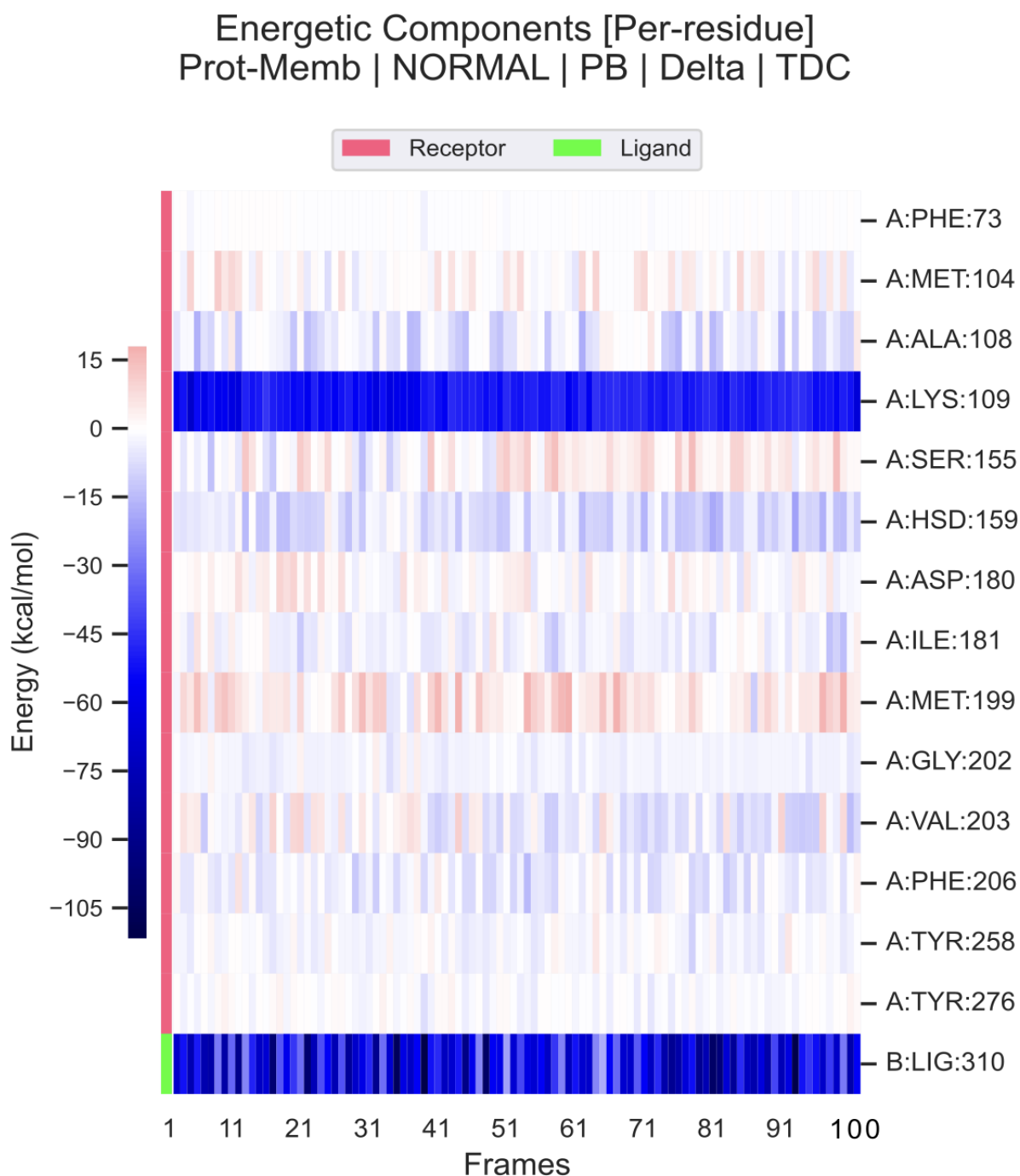


Figure S4. Residue decomposition analysis of OR1A2-octanoate complex during 50ns MD simulation. Heatmap of per-residue energetic contributions to octanoate binding (B:LIG) across 100 simulation frames (50ns). The heatmap shows the contributions of individual residues (on the y-axis) to the binding energy (indicated by the color scale, red to blue).

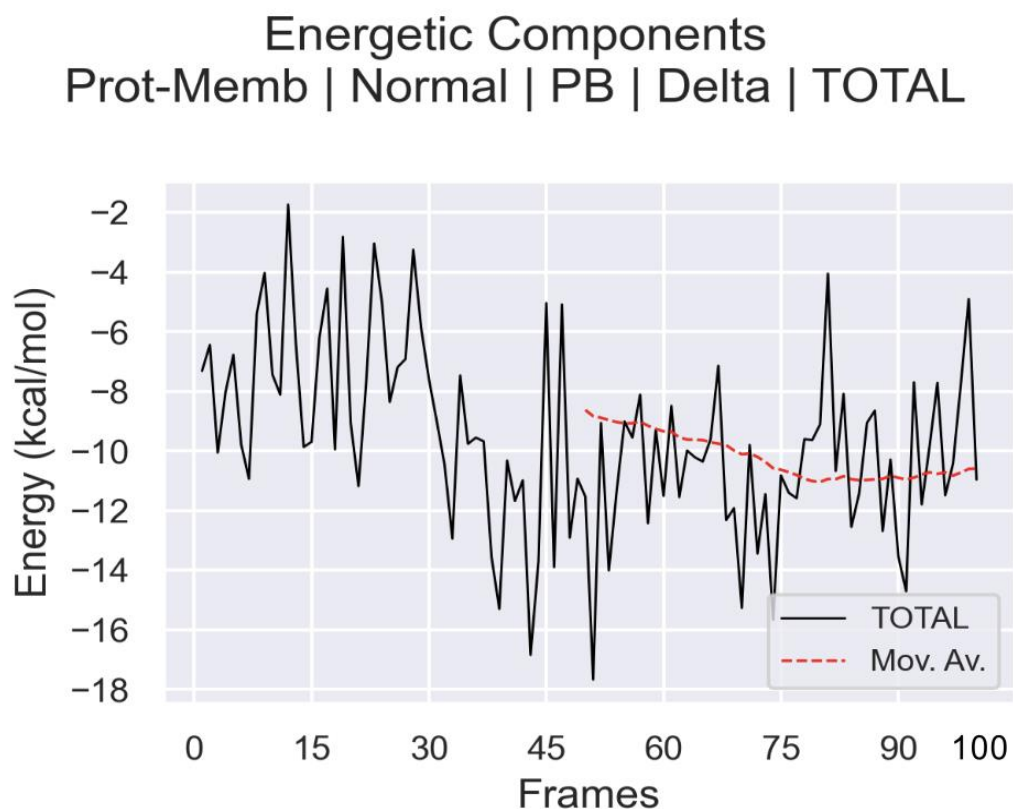
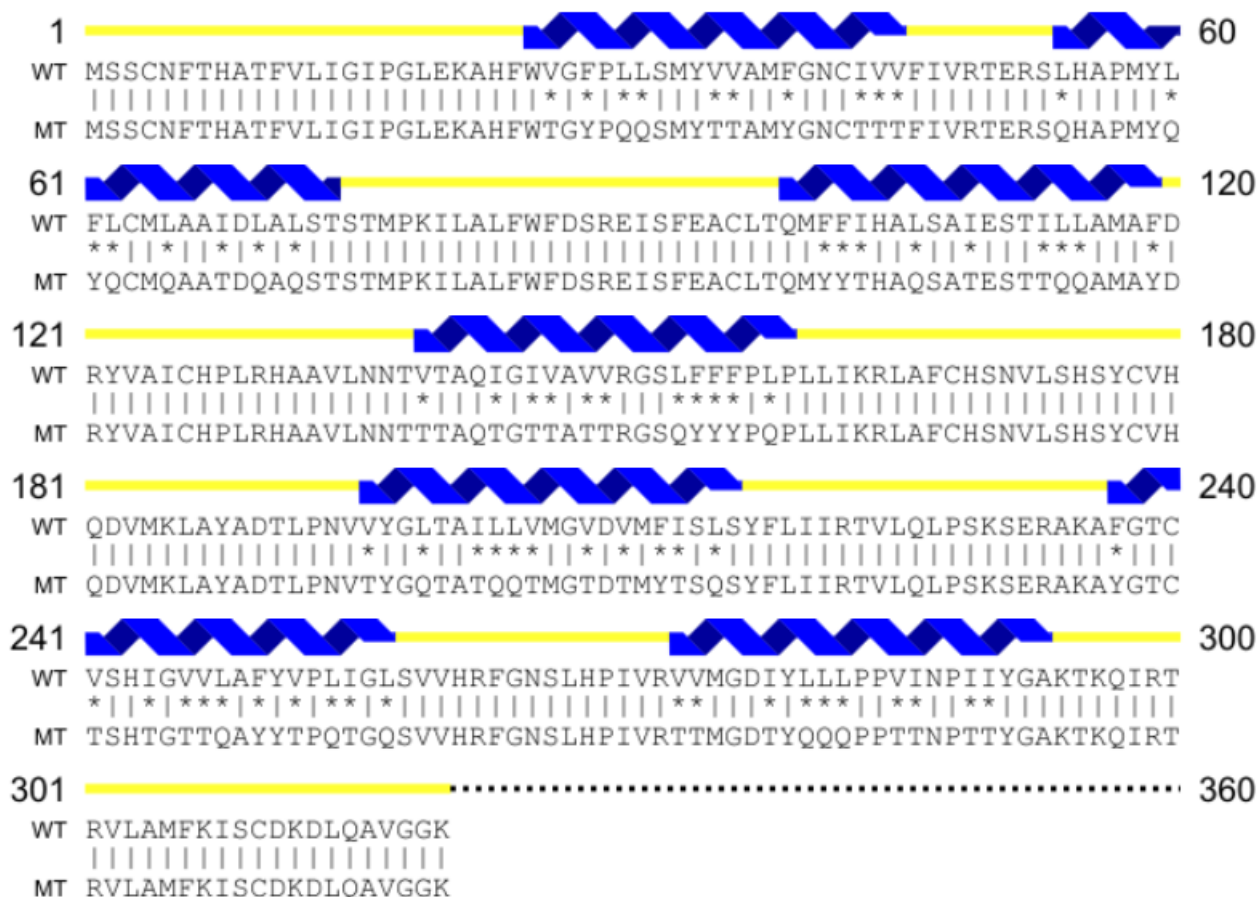


Figure S5. MMPSA calculated binding free energy of OR1A2-octanoate complex during 50ns MD simulation. MMPBSA calculated total binding energy of octanoate to the OR1A2 over 100 simulation frames (50ns). The black line represents the binding energy, while the red dashed line indicates the moving average trend across the frames.

Figure S6a-f. For clarity and easy visualization, the enlarged protein sequence alignments of six native olfactory receptor proteins with their water-soluble QTY variants. The symbols | and * indicate whether amino acids are identical or different, respectively. Note the Q, T, and Y amino acids replacing L, V and I, and F, respectively. The alpha helices (blue) are shown above the protein sequences. The characteristics of natural and QTY variants listed are isoelectric focusing (pI), molecular weight (MW), total variation %, and transmembrane variation %. The alignments are: a) OR51E2 *vs* OR51E2^{QTY}, b) OR52cs *vs* OR52cs^{QTY}, c) TAAR9 *vs* TAAR9^{QTY}, d) OR51E1 *vs* OR51E1^{QTY}, e) OR1A1 *vs* OR1A1^{QTY}, and f) OR1A2 *vs* OR1A2^{QTY}.



b) OR52cs vs OR52cs^{QTY},

1 60

WT MPTSNHTSFHPSSFLLVGIPGLESVHIWISIPFCAMYLIALLGNSTLLFVIKTERSLHEP
| | | | | | | | | | | | | | | | | | * * * | | | * * * | | | * * * | | | | | | | | | | | |

MT MPTSNHTSFHPSSFLLVGIPGLESVHIWTSTPYCAMYQTAQQGNSTQQYTTKTERSLHEP

61 120

WT MYYFLAMLAATDLVLSTSTIPKMLAIFWFNLKEISFDACLTQMFFIHSFTGMESGVLLAM
| | | * * | * * * | | | * * | | | * * | | | * * * | | | * * * | | | * * * | | |

MT MYYYQAMQAATDQTQSTSTTPKMQAIFWFNLKEISFDACQTQMYTHSYTGMESGTQQAM

121 180

WT AFDRYVAICYPLRYTTILTNTKVGIGMAVVLRAVLLVIPFPFLLKRLPFCGTNIIPHTY
| * | | | | | | | | | | | | | | * * | * | | * * * | * * * * * | * * | | | | | | | | | |

MT AYDRYVAICYPLRYTTILTNTKTTGKTGMATTQRATQQTTPYPYQLKRLPFCGTNIIPHTY

181 240

WT CEHMGVAKLACADIKVNI IYGLFVALLIVGLDVILIALSYVLILRAVFRLPSQDARLKAL
| | | | | | | | | | | | | | | * * * | * * * * * | * | * * * * * | * * * | | | | | | | * | * |

MT CEHMGVAKLACADIKVNI IYGYTAQQTGTGQDTTQTAQSYTQTQRAVFRLPSQDARQKAQ

241 300

WT STCGSHICVILAFYTPAFFSFLTHRFGHHIPPYIHILLANLYLLVPPMLNP IYGVKTKQ
| | | | | * | * * * * | | | | | * * * | | | | | | * * * * * | * | * * * | | | * * | | |

MT STCGSHTCTTQAYYTPAYYSFLTHRFGHHIPPYHTTQQANQYQQTPPMQNPTTYGKTKQ

301 360

WT IRERVLKIFFKKK
| | | | | | | | | |

MT IRERVLKIFFKKK

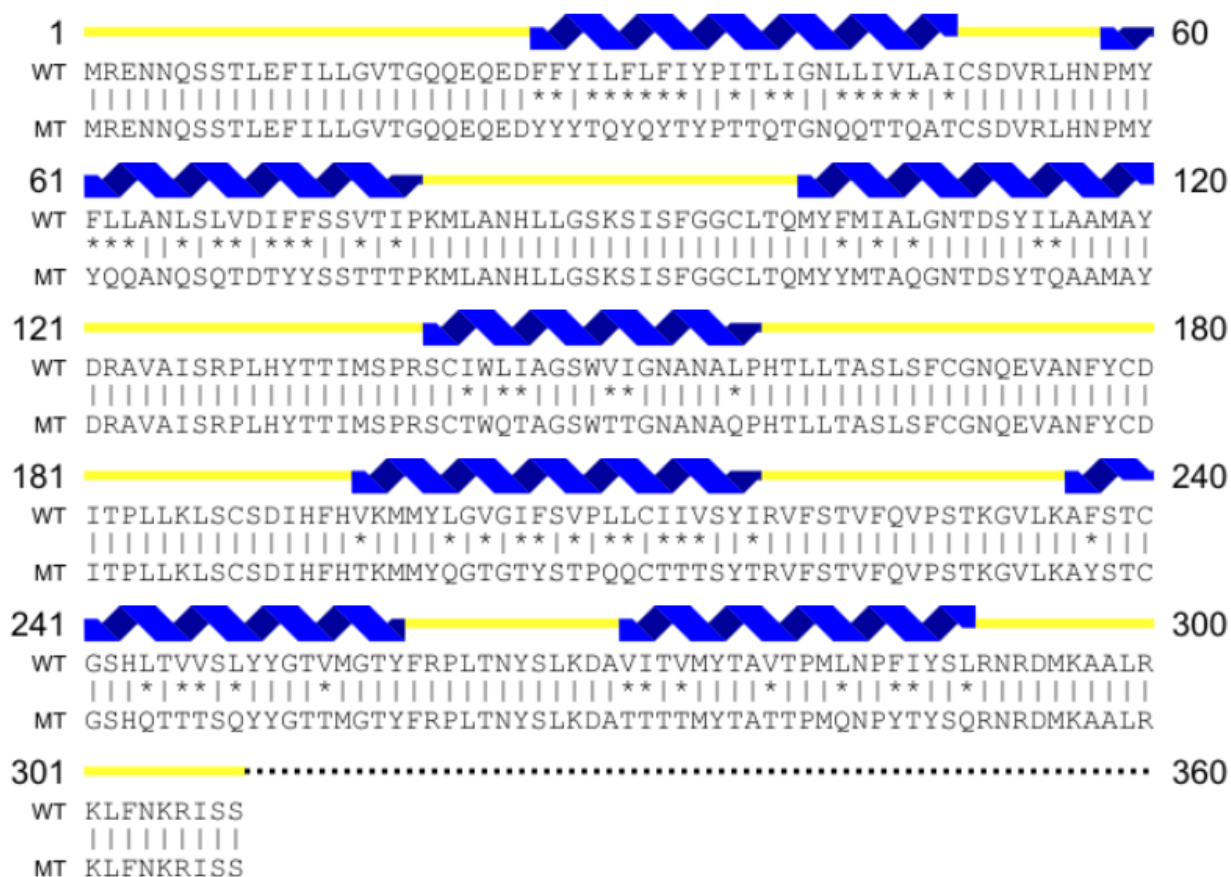
c) TAAR9 vs TAAR9^{QTY}

[illegible]

d) OR51E1 vs OR51E1^{QTY}

[illegible]

e) OR1A1 *vs* OR1A1^{QTY}



f) OR1A2 vs OR1A2^{QTY}

