

## Comparison of Homology Models of 5-HT<sub>6</sub>R Created with Different Crystal Templates.

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Structures of proteins with transmembrane domains cannot be easily determined, since proper conformation is acquired only in the presence of lipid bilayer, and thus it is almost impossible to construct its 3D structure using common physical methods. This is why homology modeling is extremely helpful in determining structures of such proteins.

5-HT<sub>6</sub>R (5-hydroxytryptamine receptor 6) is a protein containing 7TM (7 transmembrane helices) domain and is a member of class A GPCR (G-protein coupled receptor) family. It is widely expressed in neural tissue and is considered to be involved in learning and memorizing processes. Blocking the receptor leads to increase in neurotransmission and improves cognition abilities of rodents. The receptor itself is a target for anti-depression drug research.

In the present study a vast number of 5-HT<sub>6</sub>R homology models was generated on different templates available: adenosine 2 receptor (PDB ID: 3QAK), beta1 (PDB ID: 2Y00) and beta2 (PDB ID: 3P0G) adrenergic receptors, C-X-C chemokine receptor type 4 (PDB ID: 3OE0) and dopamine 3 receptor (PDB ID: 3PBL). Next, a set of representative ligands, from chemically diversified clusters, was used for selecting the best models. They were further used for docking of a complete set of 5-HT<sub>6</sub>R ligands (over 4000 compounds from ChEMBL database) to determine the best models for further research.

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