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Aminergic GPCRs from a site-directed mutagenesis perspective – analysis and prediction

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Background: Aminergic subfamily of class A G protein-coupled receptors (GPCRs) is one of the main targets of drug discovery campaigns, comprising proteins participating in the staggering range of interrelated physiological processes in human organism. The determination of structural drivers for ligand affinity within aminergic proteins has long been supported by extensive mutagenesis studies.
Materials and methods: All mutagenesis data referring to ligand affinities to aminergic GPCRs were collected and analyzed from various perspectives – the distribution of the mutated amino acid residues, the reference compounds, and the effect of the mutations on ligand binding were examined. Moreover, on the basis of the docking and interaction fingerprints coupling, an *in silico* protocol for mutational effect prediction was developed.
Results: The comprehensive evaluation of mutational data studies provided deeper insight into the structural requirements for ligand activity for aminergic GPCRs and enabled to look at the data from broader perspective. The developed methodology for mutational data prediction enabled not only the correct evaluation of the effect of mutation for particular proteins, but also allowed for predicting the consequence of mutation in the other receptor subtypes.
Conclusions: The extensive mutational study carried out allows for determination of comprehensive interaction patterns which are characteristic for the particular aminergic targets. This will be of great help in the further research on development of ligands modulating the activity of these receptors in the desired way.
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