S.12-1
Molecular mechanism of activity of non-basic ligands of 5-HT$_6$ receptors

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Background: The activity of serotonin receptors ligands has been linked to formation of charge-assisted hydrogen bond with Asp$^{3.32}$, supported by countless compounds containing protonated nitrogen in physiological conditions presumably interacting with this residue of the 5-HTRs. There is, however, a group of ligands that lack this structural feature, yet remain active towards 5-HT$_6$R, thus denying the established mechanism of interactions with serotonin receptors. Research described herein aims to explain the molecular mechanism of interactions between atypical ligands with 5-HT$_6$ receptor.
Materials and methods: The basis for the study is a series of non-basic compounds derived from indolyl-sulphonyl moiety with their affinity towards 5-HT$_6$R evaluated in radioligand binding assay. The interactions with the receptor were investigated by docking to a series of homology models of 5-HT$_6$R developed on available crystal structures of serotonin receptors 1B and 2B (PDB codes: 4IAR and 4IB4, respectively) and molecular dynamic simulations.
Results: The results prove that the mode of interactions between non-basic ligands and 5-HT$_6$R does not involve Asp$^{3.32}$ and the specific and non-specific contacts are formed with TMH5,7 and ECL2, where number of residues unique for serotonin receptor 6 were identified.
Conclusions: The designed series of tool compounds along with computational studies allowed to explain the mechanism of action of atypical ligands of 5-HT$_6$R. It emerged that interaction with Asp$^{3.32}$ is not necessary for high affinity binding and several residues from ECL2 and TMs 5 and 7 can compensate for that.
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S.12-2
Monoamine oxidase B activity of novel xanthine derivatives

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Background: Monoamine oxidase B (MAO-B) is known for its crucial role in neurodegenerative diseases. MAO-B inhibitors, such as selegiline and rasagiline are drugs registered in the treatment of Parkinson's disease. We investigated new compounds from the group of tricyclic xanthine derivatives as potential MAO-B inhibitors.
Material and methods: Compounds were investigated for inhibition of human recombinant MAO-B. The Amplex Red® Monoamine Oxidase kit was used. Inhibition activity was measured in presence of the reference substrate, p-tyramine (200µM). Data were calculated in GraphPad Prism 7 free trial. Instant JChem was used for structure database management, search and prediction.
Results: We investigated 90 new compounds for their activity towards MAO-B in one concentration (1µM). Compounds, which exhibited more than 50% of the maximum inhibition