P.5-17
Homology modeling of serotonin receptor 5A

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Background: Serotonin receptors belong to Class A of the G Protein-Coupled Receptors (GPCRs), a superfamily of membrane receptors sharing common topology of seven helices penetrating the cell membrane. Serotonin receptor 5A (5-HT_{5A}) is the least known member of the 5-HTRs and its localization within brain structures is speculative. 5-HT_{5A}R is postulated to be involved in mood control and cognitive functions, and its malfunctioning can be linked to many diseases, such as schizophrenia or Huntington's disease. There is only a handful of known 5-HT_{5A}R ligands (~80) and the development of new ones is needed.
Materials and methods: As the crystal structure of 5-HT_{5A} remains unknown, homology modeling is the method of choice for the structural investigation of the receptor. Following previously published research, a series of homology models was generated for a number of available crystal templates of aminergic GPCRs. A set of 5-HT_{5A}R conformations suitable for virtual screening were selected based on docking of selected known ligands of the receptor.
Results: The homology modeling protocol resulted with a set of ten conformations used for structure-based virtual screening. Meticulous visual inspection of the best scored ligand-receptor complexes obtained via docking of commercial libraries allowed selection of compounds for *in vitro* testing.
Conclusions: The applied methodology allowed selection and evaluation of the VS-capable homology models of 5-HT_{5A}R, and in the long run, provided structural information essential for effective rational design of novel compounds active towards this challenging pharmacological target.
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P.5-18
Selected ADMETox parameters of new histamine H_4 receptor ligands

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Background: It is assumed, that the histamine H_4 receptor (H_4R), discovered in 2000/2001, is involved in inflammatory processes and immune responses, because of its mainly expression in various cells of the immune system. Potential therapeutic effects of H_4R antagonists/inverse agonists in animal models of acute inflammations, allergic rhinitis, asthma or pruritus were confirmed. As physiological role of H_4R is not yet clear - new, potent and selective ligands are