A System for Automated Validation of GPCRs Homology Models Against Mutational Data

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Sequence alignment between target and template sequence is the most troublesome stage of homology modeling protocol. Misplacing amino acids responsible for interactions with ligands may lead to improper binding mode of so created model and render it useless. This is the reason of wide usage of mutational data in either aligning sequences or models verification.

In this study we present a tool allowing automated comparison of mutagenesis data retrieved from tinyGRAP[1] database with corresponding residues of the model. TinyGRAP database is queried for the investigated sequence and its close homologs (i.e. group members), and substitution mutations are retrieved. Query results are then checked whether appropriate residues face inside of the receptor (with some margin), and if not, the tool produces report in PyMOL pse file pointing amino acids violating mutational "constraints".

References

1. Beukers MW, Kristiansen K, IJzerman AP, Edvardsen I, TinyGRAP database: a bioinformatics tool to mine G protein-coupled receptor mutant data., Trends Pharmacol Sci. 1999 Dec;20(12):475-7.