

GPCR automodel: A web server for the molecular study of olfactory and other G protein-coupled receptor

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Olfactory receptors (ORs) belong to the superfamily of G protein-coupled receptors (GPCRs). ORs are present in all multicellular organisms and represent more than half the GPCRs in mammalian species. ORs are mainly expressed in the olfactory epithelium where they detect odorant molecules, but they are also expressed in a number of other cells, such as sperm cells, although their functions in these cells remain mostly unknown. It has recently been reported that ORs are present in tumoral tissues where they are expressed at different levels than in healthy tissues. A specific OR is over-expressed in prostate cancer cells, and activation of this OR has been shown to inhibit the proliferation of these cells. Odorant stimulation of some of these receptors results in inhibition of cell proliferation. Even though their biological role has not yet been elucidated, these receptors might constitute new targets for diagnosis and therapeutics. It is therefore important to understand their activation mechanism at the molecular level, in particular to be able to predict which ligands are likely to activate a particular receptor ('deorphanization') or to design antagonists for a given receptor. We present a procedure (<http://genome.jouy.inra.fr/GPCRautomodel>) that (i) automates the homology modeling of ORs based on the three-dimensional structures of available GPCRs and (ii) performs the docking of odorants on these models. ORs exhibit low sequence similarities with other GPCR and current alignment methods often fail to provide a reliable alignment. We use a fold recognition technique to obtain a robust initial alignment.

Biography

J-F Gibrat is a senior scientist at the French National Institute for Agriculture Research. He received a PhD in chemical physics from Paris 6 university. He has been postdoctoral fellow at Kyoto University in Japan and the National Center for Biotechnology Information, NIH, USA. He has published 70 papers in reputed journals (>3700 citations). He is serving as associate editor of BMC Structural Biology.

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