

Preface

G protein-coupled receptors (GPCR) represent to the best of our knowledge more at least 60% of all receptors. This vast majority keeps them still alive as the most interesting group of targets in drug finding and development. Some 18.000 reviews are listed in Pubmed, many of them dealing with structural features and peculiarities of G protein-coupled receptors. Especially their functional categorization, association with other membrane-integral proteins and dimerization/oligomerization behaviour is still a hot topic in research.

Nevertheless, the existing body of knowledge at atomic resolution, enables us to propose interaction mechanism and activation models for this type of receptor. Here it is the merit of Didier Rognan, himself being on of the leading figures in the field of molecular modelling of GPCRs, that he started to collect a number of reputed researches sharing a history in the topic of GPCRs and edited a 12 chapter volume on the state-of-the-art in ligand design for those targets.

The volume starts with a genomic overview on GPCRs, which is followed by an appropriate review of the available data and their appearance and utilisation in databases. In more specialized chapters the question is raised how to de-orphanize receptors. Strategies in these fields are urgently needed since by HTS strategies, array technologies, etc., the number of orphan receptors has grown exponentially.

Ligand interaction does not mean at all that a drug will emerge from this knowledge. So, druggability analysis, which has overcome its infant years of rule-based estimates, has become a sophisticated methodology on its own. One chapter is devoted to druggability of human GPCRs. It's the molecular mechanism which is illuminated in depth within the subsequent three chapters. Oligomerization or just dimerization, activation/inactivation processes and allosteric regulation are still complex puzzles to solve, last but not least because of the difficulties of understanding the entropy contribution.

Further chapters are dedicated to computational procedures. Chemical genomics approaches are going to be presented, the development detection of targeted libraries and privileged structures for GPCR interaction and leddhopping and virtual screening approaches to ligand design.

The final three chapters deal with the 3D-structures of GPCRs and the usefulness as a basis for rational design of ligands. Both, modelling approaches as well as virtual screening will be discussed in extenso.

Thus, we expect this new volume in the series to be of fundamental interest to a large community of scientists and researchers devoted to GPCRs. The editors are deeply convinced that the contents of this book will help to fathom the potential of GPCRs and will generate new ideas and visions for their role in drug discovery.

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Raimund Mannhold, Düsseldorf
Hugo Kubinyi, Weisenheim am Sand
Gerd Folkers, Zürich