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Structure based drug discovery on membrane protein targets: New developments and advancements

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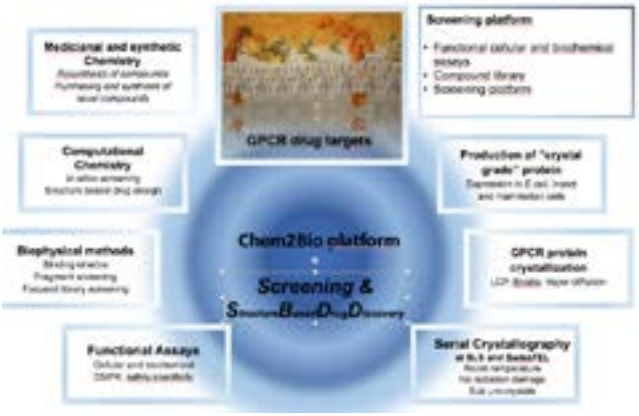
Today, structure based drug discovery is well implemented in the drug discovery engine of many pharmaceutical companies. Whereas soluble proteins are managed well within the project timelines and portfolio changes in pharmaceutical industry, transmembrane proteins still represent a significant challenge. LeadXpro combines expertise of drug discovery, excellence in high quality solubilized and purified membrane protein science and use of cutting edge biophysical methods like X-ray data collection at synchrotron and FEL sources, single particle cryo-electron microscopy, SPR and others. Strong relationship between leadXpro and Swiss large research facilities like PSI-SLS and SwissFEL as well as C-CINA will enable advances in structure determination of challenging membrane protein drug targets that have not been feasible before. Knowledge of the drug candidate and protein target 3d-structure, together with the full characterization of its interaction by biophysical binding and functional assays will enable to generate novel and better lead molecules for future medicines. Examples of recent developments include the successful fragment screening for the GPCR neutrotensin receptor 1, a fragment screening with 6369 compounds was performed with SPR and 44 hits identified. Finally, 4 selected hits were validated in NMR experiments and computational analysis gave insight into the potential fragment-binding location and interactions to inspire further chemistry efforts. Furthermore, serial crystallography was performed at synchrotron and free electron laser enables structure determination on challenging drug targets. Advantages are (1) analysis at physiologically more relevant room temperature (no freezing of crystals required), (2) low or no radiation damage and (3) the use of very small crystals.



Biography

Michael Hennig is a drug discovery Research Manager with 22 years of experience in pharmaceutical industry. He co-founded and is CEO and Chairman of the board of LeadXpro AG, an emerging biotech company and spin-out of the Paul Scherrer Institute (ETH, Switzerland) that is dedicated to structure based drug discovery of membrane protein targets. Formerly he worked 20 years at Roche research Basel as Global Head and Principle Leader of discovery technologies with responsibility for structure based drug discovery, protein science, assay development and HTS, corporate compound library, stem cell platform. In addition, he is guest Professor at the University of Basel in Structural Biology, gives lecture series in pharmacy, is author of more than 75 paper and lecturer at conferences, inventor of 8 patents in areas of technology, discovery and formulation of drug substances.

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