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STRUCTURE BASED DRUG DISCOVERY ON Membrane Protein Targets

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oday, soluble proteins are managed routinely within the project timelines and scope with the rapid portfolio changes in pharmaceutical industry. Establishment of biophysical and structure-based methods for transmembrane proteins still represents a significant challenge to have an impact on drug discovery. leadXpro combines membrane protein expression, purification and structure determination coupled to premium access to the synchrotron Swiss Light Source (SLS), the Free Electron Laser (SwissFEL) and single particle cryoelectron microscopy (cryo-EM) at the University of Basel. LeadXpro also confronts structural data to different biophysical measurements like thermal shift assays, radiobinding assay and wave guide interferometry in order to generate better lead molecules with appropriate features. The talk will show advancements in projects and technologies with examples for serial crystallography performed at synchrotron and free electron laser enabling structure determination of challenging drug targets. Moreover, recent efforts and implementation of waveguide interferometry method for analysis of small (fragment-like molecules)/large ligand binding kinetics on membrane proteins will be discussed in the context of i) lead discovery and optimization ii) biologics targeting membrane proteins. Finally, recent progress in cryo-EM will also be discussed.

Area of Interest:

- X-ray Crystallography
- Cryo-Electron Microscopy
- Biophysical methods & characterization (TSA & SPR)
- Membrane Proteins & Hot Structures

Biography

Nicolas studied at the University of Compiegne (France) and completed his Engineer in Biotechnology degree. For his master and PhD in Neuroscience from the University Pierre et Marie Curie, he moved to the Pasteur Institute in Paris, where he worked in the group of Dr. Pierre-Jean Corringer and Prof. Jean-Pierre Changeux (Channel receptors group) on the elucidation of the crystal structure of a pentameric ligand gated ion channel in an open conformation. From 2009 to 2013. Nicolas moved to FMI (Friedrich Miescher Institute for Biomedical research) as a post-doctoral fellow in the group of Dr. Nicolas Thomae, where he worked on the mechanisms of Holliday junction dissolution by solving the structure of the human Topoisomerase III in complex with a modulatory protein called RMI1. From 2013 to 2017, he worked at Roche, first as a Roche post doctoral fellow and after as a scientist in the Chemical biology department developing biophysical methods for membrane proteins as well as producing, purifying, stabilizing and characterizing GPCRs, transporters and membrane enzymes. Starting February 2017, Nicolas will work on biophysical and structural biology programs within LeadXpro AG as a senior scientist.

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