

## **X-RAY FREE ELECTRON LASER: OPPORTUNITIES FOR DRUG DISCOVERY**

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Past decades have shown the impact of structural information derived from complexes of drug candidates with their protein targets to facilitate the discovery of safe and effective medicines. Despite recent developments in single particle cryo-electron microscopy, x-ray crystallography has been the main method to derive high resolution structural information for drug design. Recently, x-ray free electron laser (XFEL) have become available in the US (LCLS), in Japan (SACLA) and in Europe (EUXFEL and SwissFEL). The unique properties of x-ray free electron laser (XFEL) with unmet peak brilliance and beam focus allow x-ray diffraction data recording and successful structure determination from smaller and weaker diffracting crystals. This shortens timelines in crystal optimization. To best capitalize on the XFEL advantage, innovations in crystal sample delivery for the x-ray experiment, data collection and processing methods are required. This leads to the development of serial crystallography which allows structure determination at more physiologically relevant room temperature. The ability of time resolution provided by the femtosecond x-ray pulse, enables monitoring and capturing of dynamic processes of ligand binding and associated conformational changes with great impact to the design of candidate drug compounds. In addition, structure determination at room temperature gives more realistic data on protein flexibility at the ligand binding site with new insights for computational chemistry. The talk will show the progress made in this area as well as examples for successful application of serial crystallography.

## **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, 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, 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 >75 paper and lecturer at conferences, inventor of 8 patents in areas of technology, discovery and formulation of drug substances.

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