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SERIAL CRYSTALLOGRAPHY: OPPORTUNITY FOR STRUCTURE-BASED DRUG DISCOVERY ON MEMBRANE PROTEINS

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Application of biophysical and structure-based methods in membrane protein drug discovery projects still represents a significant challenge. leadXpro combines expertise in membrane protein expression, purification, structure determination and application of biophysical methods to facilitate structure-based design of novel medicines. The company has premium access to the synchrotron (Swiss Light Source, SLS), the free electron laser (SwissFEL) and single particle cryo-electron microscopy (University of Basel). Serial femtosecond crystallography (SFX) using X-ray free electron laser (XFEL) significantly increases possibilities of obtaining structural information on membrane proteins. SFX shows a number of advantages for structure-based drug discovery: 1. the ability to determine structures from poor quality crystals shortens the timelines for structure determination and makes some drug targets, such as challenging membrane proteins accessible; 2. higher resolution improves the accuracy of structure determination and interpretation of electron density (more reliable placement of ligand atoms); 3. structural information at room temperature (alone or in addition to cryo structures) gives better insight into protein and ligand conformational dynamics; 4. structures of proteins or ligands with radiation-sensitive groups benefit from minimal radiation damage; 5. the most exciting opportunity of FELs lies with time-resolved analysis of ligand binding and associated protein conformational change. All the benefits will have an impact on the discovery of lead compounds for G-protein coupled receptors, ion channels and transporters.

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