

Structural Biology Platform at Nuvisan ICB

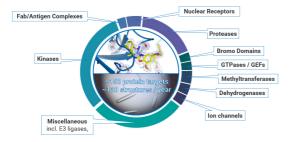
Protein Structure Determination, Cryo-electron Microscopy, HT X-ray, NMR Spectroscopy

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Protein Structure Determination

The NUVISAN structural biology team supports industrial drug discovery programs, identifying and implementing the optimal strategy to deliver timely and high-quality 3D-structural data

 >20 years experience enabling the entire gene-to-structure process for a broad range of target classes:



Tailored structural biology services enable structure-based drug discovery:

- De-novo structure determination, optimization of literature targets for industrial crystallography and our own proprietary Xrays2Go
- Close interaction with design teams to maximize learning from the structural data and to guide the rational molecule design of improved molecules





Our state-of-the-art crystallization platform includes:

- Liquid-handling systems for crystallization screen preparation of broad panel of proprietary and vendor screens
- Nanoliter liquid-handling machines (including humidity control box) for accurate drop setting for protein samples including specialized membrane protein liquid cubic phase (LCP) platform
- Automated imaging systems (visible and UV) at 4°C and 20°C for plate inspection.
- Bi-weekly access to third-generation high-brilliance synchrotron sources, complemented with our in-house automated crystal screening sample changer and two X-ray sources.

NMR Spectroscopy

NMR is a highly versatile technique that can support a range of drugdiscovery activities. We offer:

- Protein-observed NMR, as a robust and information-rich NMR method to validate and characterize compound binding.
- Ligand-observed NMR, as a method of choice for target engagement studies with larger targets and/or targets for which no labeling scheme is available.
- NMR-based fragment-screening as a powerful method in the field of fragment-based drug discovery, for hit identification or characterization of more advanced fragment analogs.

Cryo-Electron Microscopy

We offer a range of cryo-EM solutions tailored to fit your needs, including:

- stand-alone EM packages, such as negative-staining EM, to confirm sample quality.
- adaption of literature-described cryo-EM structure-determination methods to deliver target-ligand complex structures.
- complete gene-to-high-resolution-structure determination for new targets.
- Typical cryo-EM targets include membrane proteins, proteinprotein & nucleic-acid protein complexes, Fab-antigen complexes.

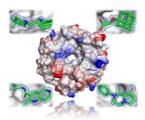




HT X-ray Platform

HTX fragment screening is a powerful technique for detecting and elucidating the binding mode of very weak binders. Our HTX workflow is fully integrated into our internal structural biology platform and allows for fast and efficient screening of up to 1,000 fragments.





- Echo Acoustic Liquid Handler for soaking large number of HTX fragments into crystals
- Crystal Shifter used for freezing crystals for data collection.
- Visual Basic scripts allow for reliable data tracking throughout the complete workflow.
- Fast and reliable crystallographic data collection through continuous access to high-brilliance synchrotron sources.
- In-house proprietary data analysis pipeline, including PanDDA, enables quick identification of datasets with a high likelihood of fragment binding.

Selected literature

Roehrig, S. et al. Design and Preclinical Characterization Program toward Asundexian (BAY 2433334), an Oral Factor XIa Inhibitor for the Prevention and Treatment of Thromboembolic Disorders. J. Med. Chem. 66, 12203–12224 (2023).

Günther, J. et al. BAY-069, a Novel (Trifluoromethyl)pyrimidinedione-Based BCAT1/2 Inhibitor and Chemical Probe. J. Med. Chem. 65, 14366–14390 (2022).

Orsi, D. L. et al. Discovery and Structure-Based Design of Potent Covalent PPARy Inverse-Agonists BAY-4931 and BAY-0069. Journal of Medicinal Chemistry 65, 14843–14863 (2022).

Hillig, RC., et al., Discovery of potent SOS1 inhibitors that block RAS activation via disruption of the RAS-SOS1 interaction. PNAS (2019).

Schaefer, M., et al., Allosteric Inhibition as a New Mode of Action for BAY 1213790, a Neutralizing Antibody Targeting the Activated Form of Coagulation Factor XI. JMB (2019).