A combined structural and biophysical approach for fragment screening with the DSI poised library

M.U.D. Ahmad, A. Perrakis

Netherlands Cancer Institute, Plesmanlaan 121, 1066CX, Amsterdam, Netherlands, **m.ud.ahmad@nki.nl**

We are aiming to validate the DSI Poised fragment library to contribute to the establishment of robust FBDD protocols for facility users. iNEXT agreed to focus on three targets: the interaction of the mitotic checkpoint proteins Mps1 and Hec1; PLA2G16, a lipid modifying enzyme that acts as a host factor for picanovirus entry; and, EPHA2, a receptor tyrosine kinase. We will follow in parallel three approaches, to be able to correlate and validate their usefulness in FBDD campaigns:

1. Biophysical characterization - monitoring changes in thermostability and aggregation properties in Prometheus (NanoTemper) and affinity of fragments to the target proteins by Surface Plasmon Resonance (Biacore).
2. Crystallographic screening at the iNEXT user facilities and
3. Screening and validation by NMR at the iNEXT user facilities.

Ultimately, we want to suggest a work-flow for future fragment screening projects.