Poster

High throughput fragment screening at the beamline P11 at PETRA III

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P11 is a Macromolecular Crystallography (MX) beamline at PETRA III (DESY, Hamburg) [1]. The instrument can provide variable experimental setups with multiple focus sizes (from 200 x 200 to 5 x 10 μm^2), in an energy range from 6 to 28 keV. With a maximum flux of 10^{13} ph/s at 12 keV, the beamline can be used to perform both standard and serial macromolecular crystallography.

Equipped with an EIGER2 X 16M detector (133Hz data acquisition) and an automated sample changer with a large capacity (23 unipucks i-e 368 samples capacity and 20 s mounting time), P11 is ideal for large campaigns of fragment or ligand screening with a total time per sample reduced to less than 2 minutes.

To complement these capabilities, the P11 laboratory offers the possibility to use the OLT Crystal Shifter for semi-automated crystal harvesting and soaking of crystals from 96 wells crystallization plates [2]. Another advantage of the use of Shifter is that the sample information can be easily archived and exported to ISPYB, to facilitate sample tracking during data collection. Upon request there is also the possibility of using the Echo Liquid Handler, which can precisely deliver in the nanoliter scale. Echo can be also used for soaking crystals directly in 96 wells crystallization plate, which in combination with the use of Shifter could reduce significantly the amount of time spent for the sample preparation.

Last year, the P11 team and the company CrystalsFirst (present on the DESY campus) have started a project aiming to use AI to increase the success rates of Fragment Based Drug Design campaigns. The first screening campaign, on a human nuclear protein identified as validated target for inhibition in several cancer types, was performed at the end of 2023 using the F2X-Entry library [3]. A second campaign will start during the spring, screening a larger library of more than 400 compounds.

The experiments are used as test cases to develop a full platform dedicated to fragment screening at P11, from the sample preparation to the implementation of a pipeline for automated ligand/fragment identification using Pan-Dataset Density Analysis (PanDDA)[4].

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