

Fragment-Screening by Crystallography at the Helmholtz-Zentrum Berlin – workflow, tools and procedures

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Fragment screening is a technique that helps to identify promising starting points for ligand design. Given that suitable crystals of the protein of interest are available and exhibit reproducibly good X-ray diffraction properties, X-ray crystallography is nowadays probably the preferred method for fragment screening, because - in addition to a simple yes/no answer with respect to binding - it provides detailed 3D information of the binding mode. In the presentation, the complete practical workflow and the included tools on how to conduct a crystallographic fragment screening campaign at the BESSY II synchrotron radiation facility at the Helmholtz-Zentrum Berlin (HZB) are presented. This includes the use of a suitable library, the use of special tools for the handling of many crystals with ease and reliably, automated facilities for diffraction data collection and processing as well as automated structure refinement and ligand identification. Also, glimpses will be provided in how to evolve the initial fragment hits into more tightly binding compounds.