Contribution ID: **423** Type: **Poster**

Fragment Screening on Protein Kinase A and PIM1-Kinase

Monday, 17 September 2018 17:45 (15 minutes)

Fragment screening has been developed into a routine method in the drug discovery process. Compared to high-throughput screening, fragment libraries can be much smaller in size and are therefore amenable to crystallographic screening, either directly or after a suitable prescreening method. Particularly, synchrotron beamlines, such as MX14-2 at Helmholtz-Zentrum Berlin, dedicated to fragment screening allow data collection of numerous data sets within a short time period.[1]
We used a 361 compound library developed in our laboratory [2,3] to screen 2 protein kinases - protein kinase A (PKA) and PIM1. As a prescreening method we used a thermal shift assay (TSA). Here, 31 fragments were detected for PKA and 52 for PIM1. These subsets were then selected for crystallographic screening where we obtained 15 complex structures for PKA and an additional 13 for PIM1, revealing a high crystallographic hit rate. Observed hits in the TSA assay are deviating for both kinases and only a single fragment was crystallographically observed binding to both kinases. Results from the TSA and crystallographic screening, together with observed binding motifs for both kinases will be presented.

[1] Mueller, U. et al. (2012) J. Synchrotron Radiat. 19, 442-449.
[2] Köster, H. et al. (2011) J. Med. Chem. 54, 7784-7796.
[3] Schiebel, J. et al. (2016) ACS Chem. Biol. 11, 1693-1701.

Primary authors: Prof. HEINE, Andreas (Institute of Pharmaceutical Chemistry, Philipps-University Marburg); Mr SIEFKER, Christof (Institute of Pharmaceutical Chemistry, Philipps-University Marburg); KLEBE, Gerhard (Inst. Pharm. Chemie, Univ. Marburg)

Presenter: Prof. HEINE, Andreas (Institute of Pharmaceutical Chemistry, Philipps-University Marburg)

Session Classification: Poster session 1

Track Classification: P3 Structure and dynamics in life sciences