MS02-P04 | A Case Study of Fragment Screening: Protein Kinase A and PIM1-Kinase

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Fragment screening may be used as an alternative to high-throughput screening of large compound libraries in the drug discovery process. Here, small molecules (<300 Da) contained in small libraries of a few hundred compounds are used in the screening process. An in-house developed fragment library was used to screen protein kinase A (PKA) and PIM1-kinase. As an initial screen we applied a thermal shift assay (TSA) to identify suitable fragments for follow-up crystallographic screening. High hit rates were obtained for both kinases in the TSA assay. These fragments were then selected for further crystallographic analysis to obtain detailed binding modes for the achieved protein-fragment complexes. Also here, high hit rates were obtained. Low fragment overlap was observed for both kinases, indicating that fragments might be selective binders. TSA screening results and observed fragment binding motifs will be discussed.