

*Validation of a 96-fragment library for crystallographic screening*

Andreas Heine<sup>1</sup>, Christof Siefker<sup>1</sup>, Namir Abazi<sup>1</sup>, Steffen Glöckner<sup>1</sup>, Nicole Bertoletti<sup>1</sup>, Engi Hassaan<sup>1</sup>, Francesca Magari<sup>1</sup>, Alexander Metz<sup>1</sup>, Manfred S. Weiss<sup>2</sup>, Gerhard Klebe<sup>1</sup>

<sup>1</sup>Institute Of Pharmaceutical Chemistry, Philipps-University Marburg, Marburg, Germany, <sup>2</sup>Macromolecular Crystallography, Helmholtz-Zentrum Berlin für Materialien und Energie, Berlin, Germany  
E-mail: heinea@mail.uni-marburg.de

In addition to high throughput screening (HTS), fragment screening is an established method by now. It is routinely used to identify small compounds (< 300 Da) that can be further developed into lead compounds in a pharmaceutical drug research project. While HTS requires huge compound libraries, typical fragment libraries are composed of only a few hundred to thousand compounds. We initially developed a fragment library composed of 361 compounds and tested it on the aspartyl protease endothiapepsin (EP).[1,2] This library is currently being extended to 1000 compounds and will be made available at the beamlines of the Helmholtz Zentrum in Berlin (HZB) for crystallographic screening.

Meanwhile, together with the HZB, we compiled a much smaller compound collection that consists of 96 fragments. These compounds are provided in a 96 well plate intended for an initial screening. Members of this library were selected based on our initial library and a library developed at HZB [3] with the prerequisite that the selected fragments showed up as hits in previous screening with EP. Finally, this selection was complemented with a small number of natural product-like compounds. In order to evaluate if this collection serves as an all purpose fragment library, we are currently testing it on a large variety of target proteins. These proteins include the kinases PIM1 and protein kinase A, the serine protease thrombin, carbonic anhydrase II, thermolysin, tRNA guanine-transglycosylase and 17 $\beta$ -hydroxysteroid dehydrogenase 14 among others. First screening results on these proteins will be presented.

[1] Köster, H. et al. (2011) J. Med. Chem. 54, 7784-7796.

[2] Schiebel, J. et al. (2016) ACS Chem. Biol. 11, 1693-1701.

[3] Huschmann, F.U. et al. (2016) Acta Cryst. F72, 346-355.

**Keywords:** [fragment library validation](#), [structure-based drug design](#), [crystallographic fragment screening](#)