Report:

MX-2272 (Fritz)

Beamtime on ID23-1 12 Sept 2020; ID30A-1 , 9-10 October 2020

In our research we aim at membrane proteins form bacterial pathogens and proteins from the innate immune system. Currently we focus on a substrate binding subunit of a membrane protein complex occurring in many multidrug resistant bacterial pathogens. We have crystallized the subunit NqrF from the pathogens *Vibrio cholerae*, *Klebsiella pneumoniae* and *Pseudomonas aeruginosa*. The crystals are used in a fragment-based screening approach to discover new inhibitor lead structures.

Moreover, we screen S100A9 – a key protein in the human innate immune response- for new high affinity inhibitors. S100A9 is a key factor in the aberrant activation of leukocytes during the so-called cytokine storm in fatal COVID-19 infections.

We have collected in total data from ca. 110 crystals at beamlines ID23-1 and ID30A-1. In particular we have profited from automated data collection at ID30A-1. We obtained a number of excellent datasets for NqrF with resolution beyond 1.5 A and good and clear difference density for a series of fragments. Moreover, we obtained a couple of good datasets for S100A9 with partial occupancy for a new inhibitor.

In summary, the experiments were very successful and the obtained data of high quality and of great value for us. For NqrF the data enable us to go ahead and start to combine first identified fragments yielding higher affinity inhibitors. For S100A9 we have to improve our soaking and co-crystallization conditions but we are very optimistic to obtain better data and more data on further inhibitors for this protein.