Report:

MX-2272 (Hunte/Wirth)
Beamtime on ID30B 13th of Febrary 2021

Our group aims at understanding the structure as well as the mechanism and regulation of medically relevant membrane proteins. One focus is on Na+/H+ antiporters or exchangers (NHX) which are crucial for ion homeostasis, pH regulation and control of cell volume. Defective NHX are implicated in several human diseases and they also comprise drug targets. We determined recently the high-resolution structure of STNhaA, a Na+/H+ antiporter from Salmonella Typhimurium (manuscript submitted). Thanks to antibody-mediated crystallization, we can obtain reproducibly well diffracting, but anisotropic, crystals. The structure suggest pathways and key residues for substrate uptake, we identified for instance the binding site of a competitive inhibitor. We are now systematically analyzing structure/function relationships by substitutions of selected residues by site-directed mutagenesis followed by structural and functional characterization of the variants. So far, variants could be readily purified and crystallized.

The aim of this beamtime was to collect X-ray diffraction data for two of these STNhaA variants. About 60 crystals were exposed to X-rays. The diffraction quality was variable due to heterogeneous sample quality and freezing. Best crystals of the first variant diffracted X-rays only to the limited resolution of ~ 4Å. In contrast, several better datasets from crystals of the second variant were collected. The best data set reached a resolution of about 3Å.

Overall, the experiment was successful. The beamline, besides one issue with the sample changer that could be fixed by the local contact, was very stable and allowed reliable data collection. We thank the local contact for the excellent support.