BAG report_Hons (10/03/2021-22/09/2021)

Michael HONS in collaboration with Yarden Opatowsky used the session MX2260 on 10/03/21 - 12/03/21 for a study on hSARM1 with the addition of toxic and oxidizing agents to understand the structure-function of SARM1 in context of inhibition. This would allow the development of new classes of drugs that not only inhibit SARM1 NADase activity, but such that also modulate its involvement in innate immunity and in inflammation.

5952 images were collected in counting mode on K2 camera and resulted in a cryo-EM structure of below 3 Å.

After our previous publication on the first structure on hSARM1[1], this work on small-molecule inhibited hSARM1 is now part of a publication which is currently in submission[2].

Structural basis for SARM1 inhibition and activation under energetic stress.
Sporny M, Guez-Haddad J, Khazma T, Yaron A, Dessau M, Shkolnisky Y, Mim C, Isupov MN, Zalk R, Hons M, Opatowsky Y. https://doi.org/10.7554/eLife.62021, eLife;9:e62021, 2020.

A Duplex Structure of SARM1 Octamers Induced by a New Inhibitor.
T. Khazma, Y. Golan, J. Guez-Haddad, A. Grossman, R. Sain, R. Geries, A. Plotnikov, R. Zalk, A. Yaron, M. Hons*, Y. Opatowsky* In submission *Corresponding authors