MS07-1-1 Obligate respiratory chain complex III2IV2 supercomplexes of Actinobacteria
#MS07-1-1

T. Kovalova [1], A. Moe [1], S. Król [1], D. Sjöstrand [1], P. Brzezinski [1], M. Högbom [1]
[1]Department of Biochemistry and Biophysics, The Arrhenius Laboratories for Natural Sciences, Stockholm University, 106 91 Stockholm - Stockholm (Sweden)

Abstract
Many pathogens including *Mycobacterium tuberculosis* and *Mycobacterium leprae* belong to the phylum *Actinobacteria*. With rising antibiotic resistance among bacteria, research of new drug targets is necessary. While respiratory chain proteins usually share significant structural and functional similarities across the different domains of life, in the *Mycobacteria* genus, there are structural differences that provide an interesting research target. Their most significant structural distinction is the requirement for respiratory chain protein complexes to form an obligate supercomplex (assembled from two copies of complex III and IV) in order to maintain standard function. To this day, there are two cryo-EM determined wild type structures of obligate respiratory chain supercomplexes, from *M. smegmatis* (3.3 Å; Wiseman et al. 2018) and *Corynebacterium glutamicum* (3.0 Å; Moe; Kovalova et al. 2021). Comparison of the structures of these sequence homologue reveals multiple differences, including the binding site of periplasmic superoxide dismutase of the M. smegmatis being occupied by a new unknown subunit in *C. glutamicum* structure. Two possible menaquinone binding positions were observed in the QP site of *C. glutamicum.* Furthermore, occurrence of two different additional menaquinone binding sites in both structures was observed. In our work we focused on gaining insight into supercomplex formation and the role of individual subunits on its functionality and stability which will include a structure-function study of various mutants.

References
Moe, A., Kovalova, T., Król, S. Yanofsky, D.J., Bott, M., Sjöstrand, D., Rubinstein, J.L., Brzezinski, P., Högbom, M. The respiratory supercomplex from C. glutamicum. Structure 30(3), 338-349.e3. (2022).

Wiseman, B., Nitharwal, R.G., Fedotovskaya, O., Schäfer, J., Guo, H., Kuang, Q., Benlekbir, S., Sjöstrand, D., Ädelroth, P., Rubinstein, J.L., Brzezinski, P., Högbom, M. Structure of a functional obligate complex III2IV2 respiratory supercomplex from Mycobacterium smegmatis. Nat Struct Mol Biol 25, 1128–1136 (2018).