Towards the Crystal Structure of *Saccharomyces Cerevisiae* Frataxin

Tobias Karlberg[a], Oleksandr Gakh[b], Isaya Grazia[b], Salam Al-Karadaghi[a], [a]*Department of Molecular Biophysics, Centre for Chemistry and Chemical Engineering, Lund University, Sweden.* [b]*Department of Pediatric and Adolescent Medicine, Mayo Clinic, College of Medicine, Rochester, Minnesota, USA.* E-mail: Tobias.Karlberg@mbfys.lu.se

Due to the toxicity and insolubility of ferrous iron a conserved mitochondrial protein, frataxin has been suggested to be involved in iron delivery to the biosynthesis of iron-sulfur cluster and heme. Moreover, frataxin shows iron chaperone properties and iron-dependent oligomerisation. Insufficient production of frataxin results in Friedreich ataxia, an autosomal neuro-degenerative disease.

Frataxin from *Saccharomyces cerevisiae* is activated by Fe(II) in the presence of O_2 and assembles stepwise into a 48-subunit multimer that sequesters more than 2000 atoms of iron. In the first reaction monomeric frataxin is assembled into a trimeric form. Ferrochelatase catalyses the last step in the heme biosynthetic pathway, the insertion of ferrous iron into protoporphyrin IX to form heme *b*. Studies of a direct interaction between ferrochelatase and frataxin show interaction between dimeric ferrochelatase and trimeric frataxin.

Crystallisation of the trimeric form of yeast frataxin has given well defined three dimensional crystals in two different crystal forms. X-ray data has been collected at the synchrotron beamline at MAX-lab, Lund, Sweden. The crystal structure of the frataxin trimer will be presented. The structural basis of frataxin oligomerization and metal binding will be discussed.

Keywords: iron storage, heme synthesis, x-ray crystal structure