Contribution ID : **123** Type : **Oral**

Structural insights into the ferroxidase and iron sequestration mechanisms of ferritin from Caenorhabditis elegans

Wednesday, 24 November 2021 12:05 (15)

Iron is an essential trace element that, when in excess, becomes highly toxic [1]. Intracellular iron concentration must be strictly regulated by a network of interacting mechanisms [2]. Ferritin is a ubiquitous iron-storage protein that forms a highly conserved 24-subunit spherical cage-like structure. Ferritin catalyses the oxidation of iron (II) to iron (III) and sequesters the newly oxidised iron (III) as a mineral core to prevent cellular damage [3]. In this study, we use the model organism, Caenorhabditis elegans, to investigate iron uptake, oxidation, storage and release by ferritin.

C. elegans expresses two ferritin proteins, FTN-1 and FTN-2, which both exhibit ferroxidase activity [4]. FTN-2 functions at a rate significantly faster than FTN-1 despite conservation of all catalytic residues, suggesting that structural differences at a location distinct to the ferroxidase centre may influence catalytic activity. We solved the X-ray crystal structures of FTN-1 (1.84 Å) and FTN-2 (1.47 Å), and the cryo-EM structure of FTN-2 (1.88 Å). FTN-1 and FTN-2 both adopt the conserved 24-subunit cage-like structure and bind one iron (II) in the ferroxidase centre of each chain. We postulate that iron (II) accesses the ferroxidase centre through a three-fold symmetrical pore. This pore is notably larger and more negatively charged in the FTN-2 structure and may facilitate easier access of iron (II) to the ferroxidase centre, resulting in a faster catalysis rate.

These structural insights further our understanding of the mechanisms used by ferritin to regulate iron storage and the overall role of ferritin in iron homeostasis.

Level of Expertise

Early Career <5 Years

Presenter Gender

Woman

Pronouns

She/Her

Which facility did you use for your research

Australian Synchrotron

Students Only - Are you interested in AINSE student funding

Do you wish to take part in the Student Poster Slam

Condition of submission

Yes

Primary author(s) : MALCOLM, Tess (Bio21 Molecular Science and Biotechnology Institute)

Co-author(s) : Mrs MOHAMED MURBARAK, Sanjeedha (Bio21 Molecular Science and Biotechnology Institute); Dr HAMISH, Brown (Ian Holmes Imaging Centre, Bio21 Molecular Science and Biotechnology Institute); Dr ERIC, Hanssen (Ian Holmes Imaging Centre, Bio21 Molecular Science and Biotechnology Institute); Dr GAWAIN, McColl (The Florey Institute of Neuroscience and Mental Health); MAHER, Megan (La Trobe University); Dr GUY, Jameson (Bio21 Molecular Science and Biotechnology Institute)

Presenter(s) : MALCOLM, Tess (Bio21 Molecular Science and Biotechnology Institute)

Session Classification : Biomedicine, Life science & Food Science

Track Classification : Biomedicine, Life science & Food Science