Iron Transport into *C. elegans* Ferritins

Guy N. L. Jameson, Sanjeeeda S. M. Mubarak, Tess R. Malcolm, Megan J. Maher, Gawain McColl
School of Chemistry and Bio21, The University of Melbourne, Parkville, Victoria, 3051, Australia; Department of Biochemistry and Genetics, La Trobe Institute for Molecular Science, La Trobe University, Melbourne, Victoria, 3086, Australia; Melbourne Dementia Research Centre, Florey Institute of Neuroscience and Mental Health, The University of Melbourne, Parkville, Victoria, 3052, Australia.

GNLJ: guy.jameson@unimelb.edu.au, SSMM: smohamedmuba@student.unimelb.edu.au, TRM: tess.malcolm@unimelb.edu.au; MJM: megan.maher@unimelb.edu.au; GM: gawain.mccoll@florey.edu.au

Iron is the 6\textsuperscript{th} most abundant element in the earth’s crust and vital to practically all forms of life, where it catalyses the most important and often most difficult chemical transformations. We are trying to understand iron metabolism using the model organism *C. elegans*, a nematode which shares many of the same fundamental processes as more complex forms of life but allows genetic modification and easy manipulation.

Iron is stored by the ubiquitous iron-storage protein ferritin which in humans has two types, H and L. H ferritin catalyses the oxidation of iron(II) to iron(III) at a di-iron site called the ferroxidase site, while L ferritin slowly nucleates iron(III).

We have expressed and purified recombinantly the two ferritins that *C. elegans* naturally expresses, FTN-1 and FTN-2. In parallel we have natively purified the same proteins from nematodes. We have compared activity and other biophysical measurements between recombinant and native protein and shown that they are similar. This validates further analysis of recombinant ferritins. Through kinetic, spectroscopic and crystallographic studies we have investigated how iron enters each of the ferritins and how they compare to each other. We find that FTN-2 stores iron even faster than human H ferritin and approximately 10 times faster than FTN-1. However, we also show that both ferritins have human L ferritin like character over longer time periods. Altogether, we have gained new insight into the ferroxidase reaction ready for further study in *C. elegans*. 