Interaction of prohibitins with *m*-AAA proteases at the inner mitochondrial membrane

(PhD studentship held jointly between Keele University and the Institut Laue-Langevin)

In plants, yeast and mammalian systems, a multi-protein complex consisting of *m*-AAA protease and prohibitins (Phb) is responsible for ensuring proper formation [1], functionality [2] and morphology [3] of mitochondria. Prohibitins are ubiquitous, evolutionarily conserved proteins that are mainly localized in the inner mitochondrial membrane, where they regulate membrane protein degradation by the mitochondrial *m*-AAA protease [4, 5]. This PhD studentship will be part of a larger project that aims to elucidate prohibitins' role in premature cellular ageing and apoptosis by investigating how prohibitins interact with *m*-AAA proteases at a molecular level, and thus help to maintain healthy mitochondrial morphology and cellular metabolic capacity. Interactions between the proteins as well as their assembly in the membrane will be investigated using in-solution and soft matter techniques such as Small Angle Neutron and X-ray Scattering, lipid monolayer techniques, as well as biochemical assays. Data analysis with different pieces of software will be an important part of the PhD work.

The position will be based in Dr. Anja Winter's lab at the Department for Life Sciences, Keele University for year 1. For years 2 and 3 the student will be based full-time in the Life Science group of the Institut Laue-Langevin (ILL) in Grenoble, France, with strong links to the Large Scale Structure group through the main ILL supervisor, Dr. Sylvain Prévost. Recombinant protein production and preparation will be carried out in Dr. Anja Winter's lab and in the laboratories of the Life Sciences group at the ILL. SANS measurements will be carried out at the ILL under supervision of Dr. Sylvain Prévost. SAXS and X-ray crystallography will be carried out at ESRF, Grenoble, France and Diamond Light Source, Oxford, UK.

An interest in protein production and analysis using biophysical techniques such as Small Angle Neutron (or X-ray) Scattering, lipid monolayer techniques, and X-ray crystallography is essential, as well as a good degree of computer literacy. The candidate should demonstrate self-motivation and resilience to undertake advanced research study at PhD level, possess excellent communication, interpersonal and organizational skills, as well as the ability to work both independently and as part of a team. Natural inquisitiveness, a flair for problem solving and willingness to learn new practical skills are essential. Flexibility to travel on a regular basis.

For more information, please contact Dr. A. Winter (a.winter@keele.ac.uk) or Dr. S. Prévost (prevost@ill.fr)

1. Ahn, C.S., et al., *Prohibitin is involved in mitochondrial biogenesis in plants.* Plant J, 2006. **46**(4): p. 658-67.

2. Arnold, I. and T. Langer, *Membrane protein degradation by AAA proteases in mitochondria.* Biochim Biophys Acta, 2002. **1592**(1): p. 89-96.
3. Merkwirth, C. and T. Langer, *Prohibitin function within mitochondria: essential roles for cell proliferation and cristae morphogenesis.* Biochim Biophys Acta, 2009. **1793**(1): p. 27-32.
4. Steglich, G., W. Neupert, and T. Langer, *Prohibitins regulate membrane protein degradation by the m-AAA protease in mitochondria.* Mol Cell Biol, 1999. **19**(5): p. 3435-42.
5. Korbel, D., et al., *Membrane protein turnover by the m-AAA protease in mitochondria depends on the transmembrane domains of its subunits.* EMBO Rep, 2004. **5**(7): p. 698-703.