# PhD position in Biochemistry: Mechanism of Fe-S cluster assembly

**Contract type:** PhD thesis 36 months
**Salary Range:** 25,000 € annual gross salary
**Start date:** 01 october 2017

**Employer/contact:** REDOX BIOLOGY team at I2BC (http://www.i2bc.paris-saclay.fr/spip.php?article108)
Contact Benoit D'Autréaux, benoit.dautreaux@i2bc.paris-saclay.fr
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**Working environment:** I2BC is a recently created institute in the South-Paris area that gathers cell biologists, biochemists and biophysicists (about 700 researchers). Our team is an internationally recognized group studying redox biological processes and their links with human pathologies such as ageing, neurodegeneration and cancer.[1-6] The PhD fellow will integrate this team to work on Friedreich's ataxia, a rare neurodegenerative and cardiac disease caused by defective expression of the Frataxin protein which controls the assembly of iron-sulfur (Fe-S) cluster. Fe-S clusters are prosthetic groups of proteins providing redox functions to a multitude of proteins. Their synthesis is a complex multistep process that is tightly controlled to prevent oxidative stress. The molecular function of Frataxin in this process is unclear which for the development of therapeutic strategies based on the replacement of Frataxin is a major hindrance. We recently made a significant advance in this field by reporting the stimulatory effect of Frataxin on the mobilization of sulfur for Fe-S cluster biogenesis but still the exact molecular function of Frataxin remained elusive.[2]

**Project:** Based on new preliminary data on the specific role of Frataxin in Fe-S cluster synthesis, the project is to provide the structural basis of the effect of Frataxin using an in vitro reconstituted machinery with purified proteins. The structural investigations will be carried out by NMR and X-ray crystallography on several intermediates we recently managed to isolate. The PhD fellow will be in charge of protein purification and reconstitution of protein complexes under anaerobiosis and will conduct preparation of samples and analysis by structural methods in collaboration with our partners. In a second part of the project, the PhD fellow will be associated with the identification of the other pathways that are controlled by frataxin using proteomics and metabolomics analysis of cellular extract.

**Collaborations:** The project will be carried out in collaboration with ICSN (Gif-Sur-Yvette) and College de France (Paris) for the structural parts and with ESPCI (Paris) and SPI at CEA Saclay for proteomics and metabolomics which should also provide opportunities for exchanges with other students and researchers.

**Candidate profile:** a good background in biochemistry and biophysics (NMR, crystallography, mass spectrometry) is necessary. Specific skills in one or more of these areas: protein purification, metallo-proteins, handling of anaerobic conditions using a glove box, biochemistry and biophysics will be appreciated.

**Funding:** The lab is funded by several agencies (CNRS, CEA, FRM, ANR). The project is specifically funded by an ANR grant (2017-2021).

**Bibliography:**

1 Bersweiler A, D'Autreaux B, Mazon H, Belli G, Delaunay-Moisan A, Toledano MB, Rahuel-Clermont S. (2017). **Nat Chem Biol.**
2 Parent A, Elduque X, Cornu D, Belot L, Le Caer JP, Grandas A, Toledano MB, D'Autreaux B. (2015). **Nat Commun.** 6, 5686.
3 Kumar C, Igbaria A, D'Autreaux B, Planson AG, Junot C, Godat E, Bachhawat AK, Delaunay-Moisan A, Toledano MB. (2011). **EMBO J.** 30, 2044-2056.
4 D'Autreaux B, Toledano MB. (2007). **Nat Rev Mol Cell Biol.** 8, 813-824.
5 D'Autreaux B, Tucker NP, Dixon R, Spiro S. (2005). **Nature**. 437, 769-772.
6 Hanzen S, Vielfort K, Yang J, Roger F, Andersson V, Zamarbide-Fores S, Andersson R, Malm L, Palais G, Biteau B, Liu B, Toledano MB, Molin M, Nystrom T. (2016). **Cell**. 166, 140-151.