

## **Understanding the role of frataxin in cell survival**

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### **Scientific summary**

Frataxin-deficient cells exhibit enhanced sensitivity to oxidative stress and die prematurely. We therefore plan to investigate the role of frataxin in the control of the stress response and cell death programs. In particular, based on our preliminary observations which suggest that frataxin may also reside outside the mitochondria, we will investigate the metabolic function of extramitochondrial frataxin and its possible role in cell survival. We will look for extramitochondrial frataxin-interacting proteins, by a combination of genetic and biochemical approaches, to reveal relevant molecular partners. We also generated frataxin-deficient *C.elegans* by RNAi and observed that these animals live longer and have altered sensitivity to oxidative stress. We will use frataxin RNAi nematodes, frataxin heterozygote and KO nematodes, to study the stress response elicited by frataxin deficiency and perform a detailed epistatic analysis to map the role of frataxin within the conserved cell death program. This project is expected to generate novel information about the role of frataxin in cell survival, that might be potentially useful in the development of innovative therapeutic approaches to FA.

### **Lay summary**

We know that Friedreich's ataxia (FA) is caused by the inherited deficiency of a protein called frataxin. Frataxin deficiency likely generates oxidative stress of specific set of neurons and cardiac cells, which eventually die prematurely, causing the disease. Consequently, current therapy is based on anti-oxidants. However more specific and effective therapeutic approaches are needed. To design a definitive cure for the disease we need to understand better why frataxin-defective cells die prematurely. This project will directly investigate the role of frataxin in the protection of human cells. It will also take advantage of a simple animal model of frataxin deficiency, which will allow a wide genetic analysis of the protective role of frataxin at the whole organism level and which could also be exploited for the rapid screening of effective new drugs.

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