FARA Funds Four New Research Grants

Because of your generous support, FARA was able to fund an additional four grants in mid-December 2014. Three of these grants went to new investigators in the Friedreich's ataxia (FA) research community. We are excited to have well-respected and accomplished researchers from related areas bring their expertise to the effort for treatments and cure. Please find summaries of each new project below:

Zhen Yan, University of Virginia, Charlottesville, VA
Exercise impacts on mitochondria and muscle function in Friedreich's ataxia
The effect of exercise on mitochondria in FA is unknown. Dr. Yan recently developed a novel reporter gene to measure the health of millions of mitochondria in live animals under both disease and physiological exercise training conditions. Dr. Yan proposes to conduct the first exercise study using this state-of-the-art technology to assess the impact of exercise on mitochondrial health in a mouse model of FA. The findings will not only improve our understanding of the disease, but also improve the management and treatment of FA.

Massimo Pandolfo, Université Libre de Bruxelles, Brussels, Belgium
Investigation of the role of mTOR in Friedreich's ataxia and identification of new possible pathways for therapeutic intervention.
Dr. Pandolfo proposes to investigate the role of a protein called mTOR in FA. The proteins targeted by mTOR are involved in key metabolic processes known to be affected in FA. By modulating the expression of frataxin (FXN) and mTOR, Dr. Pandolfo will study how they interconnect and affect each other, and how the cellular context is important in modulating the disease. He believes these investigations will shed new light on the still unclear mechanisms that regulate frataxin physiology and may identify new targets for FA treatment and cure.

David Corey, UT Southwestern, Dallas, Texas
Activation of Frataxin Expression by Duplex RNA
Dr. Corey designed duplex RNAs to recognize the repeat region in FA and potentially interfere with chromatin contacts that might contribute to decreased transcription. He has discovered that introduction of these duplex RNAs into FA-patient derived cells caused an increase of FXN mRNA and protein to levels similar to those in normal cells. These data suggest that duplex RNAs can be used to up-regulate FXN expression and may provide a new strategy for therapy.

Hugo Bellen, Baylor College of Medicine, Houston, Texas
The role of iron accumulation and increased lipid synthesis in the pathogenesis of Friedreich's ataxia
Dr. Bellen identified a fly mutant of frataxin that exhibits an age dependent neurodegenerative phenotype that can be rescued with the human frataxin gene, suggesting that the human and fly frataxin play a conserved role to maintain neuronal function. The fly frataxin mutants exhibit a dramatic increase of iron deposits in multiple tissues. Reducing iron levels in food and neuronal activity suppresses the neurodegeneration, suggesting that iron accumulation and an impaired energy state contribute to the neurodegenerative phenotype. Furthermore, a drug that inhibits sphingolipid synthesis called myriocin significantly delayed the demise of neurons. Dr. Bellen proposes that aberrant iron deposits lead to an abnormal lipid homeostasis that causes toxicity. This project aims to investigate the mechanism of neurodegeneration in the fly frataxin mutant, which may identify new therapeutic strategies.