

## **Effect of Frataxin Knockout on Mouse Cardiomyocytes**

### **Using DsRed.T3 as a Quantifying Marker**

Eric Galante<sup>1</sup>, P Melanie Pride<sup>1,2</sup>, Frances Chen MD<sup>1</sup>, R Mark Payne MD<sup>1,2</sup>

<sup>1</sup>Indiana University School of Medicine,  
<sup>2</sup>Herman B Wells Center for Pediatric Research

#### **Background and Hypothesis:**

DiscoSoma Red (DsRed) is a strong fluorescent marker that has many practical uses for scientific studies. We engineered a transgenic mouse expressing DsRed.T3 only in cardiomyocyte nuclei, and then crossed this with a conditional knockout mouse with loss of Frataxin (FXN) in heart. It is known that dysfunction of the Frataxin (FXN) gene can cause Friedrich's Ataxia (FRDA), a disease associated with ataxia, weakness and dilated cardiomyopathy in humans. The current study aimed to: 1) Determine if DsRed overexpression in cardiomyocyte nuclei would negatively affect cardiac tissue, and 2) Use the DsRed.T3 mouse to determine whether FXN knockout (KO) would cause a loss of cardiomyocytes.

#### **Experimental Design or Project Methods:**

The study was done by examining three different strains of mice: wild-type, DsRed.T.3 overexpressing Tg mice, and FXN KO mice with loss of FXN in cardiomyocytes. Mice were analyzed using genotyping, frozen immunofluorescent stains,  $\alpha$ -actinin and Hoechst, TPLSM, confocal microscopy, western blotting, H&E, echocardiography, and heart:body weight ratios.

#### **Results:**

Results showed that DsRed.T3 localized to the nucleus of cardiomyocytes and that after 6.5 months there were some significant effects on cardiac function, although not on cardiac tissue. Further analysis is ongoing to determine if there is a loss of cardiomyocytes within the FXN KO group.

#### **Conclusion and Potential Impact:**

This study shows promise for how researchers can study the heart, and more specifically, Friedrich's Ataxia, while also shedding light on how FXN may ultimately affect the heart in FRDA patients.