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“Mismatch in Mice and Men”

Friedreich ataxia is a progressive degenerative neuromuscular disease that is caused by the expansion of a repetitive region of DNA, composed of three nucleotide repeats (GAA•TTC). Expansion of the DNA occurs throughout the lifespan of the patient and has been linked to the activity of specific DNA mismatch repair proteins. Disease onset occurs when the expansion increases in size beyond a certain threshold, silencing the gene and causing progressive ataxia, diabetes mellitus, and cardiomyopathy. These symptoms are linked to an increased repeat number observed within the heart, pancreas, and brain relative to other tissues within an individual. Friedreich ataxia is a fatal disease, most patients die of heart failure due to cardiomyopathy.

Transgenic mice are commonly used as a model to study disease. Friedreich ataxia repeat expansion has been shown to be highest in human cardiac tissue. In contrast, our lab has observed that no expansion occurs in the heart of Friedreich ataxia model mice. The purpose of this experiment was to perform a Western Blot assay on the cardiac tissue of transgenic mice to detect the presence of specific mismatch repair proteins. The goal was to compare this to the expansion positive tissue of the same mouse and normal human cardiac tissue. Primary antibodies specific to the human mismatch repair protein subunits available in the lab were used following protein extraction from the target tissues with the intention of cross-reactivity between species. Unfortunately, the human-specific primary antibodies did not cross react with the mouse mismatch repair protein subunits. Acquisition of mouse specific primary antibodies was restrained by financial and temporal limitations. Next steps in the investigation of tissue specific mismatch repair proteins present within mice include western blot analysis using mouse-specific, preferably polyclonal primary antibodies to ensure visualization of the proteins present is achieved.