Diabetic Stem Cell Derived Cardiomyocytes in Disease Modeling and Therapeutic Discovery

Schmidt, Karina

Currently heart disease is the number one cause of death in patients with type two diabetes. Studies show that individuals with diabetes are 2 to 4 times more likely to suffer and die from heart disease than individuals without diabetes. Heart disease is a prominent problem in diabetic patients, so there is a need to determine why diabetic patients are more susceptible to heart disease than non-diabetic patients. One possible explanation is genetic differences. This project was developed to determine differences in stress responses and differentially expressed genes between diabetic iPSC cardiomyocytes and non-diabetic iPSC cardiomyocytes. Differentiation protocols were initiated when iPSCs reached 100% confluency, according to the Palecek protocol guidelines. Cells were exposed to CHIR99021 and IWP4, molecules which manipulate the Wnt signaling pathway and encourage differentiation into cardiomyocytes. The differentiation of the iPSCs into cardiomyocytes was confirmed through immunostaining. Cells were incubated with a primary antibody for either cardiac troponin T or sarcomeric α-actinin then incubated with a secondary antibody to prevent non-specific binding. Diabetic and non-diabetic iPSC cardiomyocytes were stressed with doses of hydrogen peroxide and PI stained to determine cell viability. PI staining showed the diabetic model was significantly more susceptible to stress compared to the non-diabetic model. It was determined these changes were not due to difference in morphology or differentiation, but a quantitative PCR showed nine cardiovascular disease markers which were differentially expressed in the diabetic model. Diabetic patient derived Cardiomyocytes express differences in stress response and show differential gene expression of cardiovascular disease mar