Induced Pluripotent Stem Cell-Derived Cardiomyocytes as a Model for Ischemia Reperfusion Injury

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Animals are currently used in most models for research. Although they have been a significant part of research it often takes many years for them to translate into clinical studies. Models using animals also provide complications due to inequivalent biochemical mechanisms or physiological responses. There is a need to research models that would lead to quicker, more efficient discovery of therapeutic targets. This project was developed to determine whether induced pluripotent stem cell derived cardiomyocytes are a sufficient model for ischemia reperfusion injury. 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 a-actinin then incubated with a secondary antibody to prevent non-specific binding. IPSC derived cardiomyocytes were stressed with doses of hydrogen peroxide ranging between 250uM and 1mM. Lactate dehydrogenase (LDH) release was measured to assess cell viability after stress. By comparing this iPSC-cardiomyocyte data to established rat heart data of a 6hr clinically relevant dosage done by the Xiao lab, it has been confirmed that iPSC derived cardiomyocytes provide a similar ischemia reperfusion model to rats with less variability from the human heart.

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