Identifying Limiting Nutrient on Stem Cell Spheroid Viability for Human Cardiac Tissue Regeneration

Yao, Jenny

Objective: Stem cell-derived cardiomyocyte spheroids show enormous potential as cell delivery systems that improve cell retention and engraftment. Their survival post-transplantation in ischemic infarcted myocardium is critical to their success as regenerative therapies. This study 1) identified the limiting nutrient (oxygen/glucose) on viability, 2) analyzed energy metabolism, and 3) designed a new spheroid to improve nutrient transport. Methods: The effect of nutrient availability on human adipose-derived stem cell (hADSC) spheroid viability was determined in vitro using TUNEL assay to identify the limiting nutrient on cell survival. A computational model coupling primary energy metabolism and nutrient diffusion was developed to determine internal glucose, oxygen, and lactate concentration and ATP production profiles. The model facilitated a novel spheroid design with enhanced nutrient transport. Results: Cell viability decreased with increased spheroid diameter and positively correlated with glucose availability. The spheroids were more sensitive to glucose depletion with increased size than oxygen. Over 60% ATP in the spheroids was produced through glycolysis. A novel spheroid with a core-shell structure obtained higher glucose availability and viability. Discussion: Due to diffusion limits, nutrient availability is inversely related to spheroid size. Glucose proved the primary limiting factor in hADSC spheroid viability with respect to diameter over oxygen. While aerobic and anaerobic respiration co-exist, glycolysis proved the dominant ATP production mechanism. The core-shell model can achieve higher viability due to increased glucose supply. This study's nutrient analyses provide crucial information for the development of cardiac regenerative technologies.

Awards Won:

Florida Institute of Technology: Full Tuition Presidential Scholarship