Development of Thymus Derived Mesenchymal Stem Cells for Tissue Engineering in Pediatric Cardiac Surgery

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Introduction and Objective

Congenital heart disease is the most common type of birth defect. Surgical procedures have effectively addressed many of these defects, although repair of complex defects require additional tissue in the form of patches, conduits or valves. These tissues provide a short term solution, but require replacement because of nongrowth or failure. Stem cell derived tissues are a potential solution because they can regenerate and grow. The objective of this ongoing study is to isolate mesenchymal stem cells (MSC's) from thymus glands discarded during pediatric cardiac surgery operations and to utilize them in tissue-engineered conduits, valves and pumps. Initially, MSC's will be evaluated in their utility in creating bioengineered heart muscle (BEHM).

Methods

Thymus glands from infants undergoing heart surgery were subjected to mechanical and enzymatic dissociation and MSC's have been isolated by plastic adherence. Multipotent differentiation capabilities will be determined. BEHM will be initially formed by culturing neonatal rat cardiomyocytes on fibrinogen coated plates and allowed to delaminate and form a 3D contractile tissue construct. Addition of MSC's with cardiogenic growth factors to the BEHM before and during its delamination process will be performed. Performance of the BEHM will be assessed by measuring the stimulated active force with a transducer. Immunohistological studies will be performed to determine cardiac markers in MSC's.

Results

Plastic adherent cells have been isolated successfully from infant thymuses and multipotent differentiation is being established. The primary question to be answered is if MSC's improve function of BEHM. Important secondary issues are the optimal temporal effects of adding MSC's to forming BEHM, effects of cardiogenic growth factors on MSC-BEHM size and function, optimal ratio of MSC's to cardiomyocytes and kinetics of MSC incorporation in BEHM.

Conclusions

This novel study utilizes in vitro self organization of BEHM to provide the key microniche for incorporation and transdifferentiation of thymus MSC's into cardiac tissue. The BEHM will also allow the manipulation of key growth factors and measurement of quantitative outcomes. The information provided in this study will establish the utility of thymus MSC's in tissue engineering as well as provide fundamental insight into MSC biology.