

Resident Cardiac Stem Cells in the Left Atrial Appendage- an Untapped Source

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Background. In the past few years compelling evidence has accumulated suggesting that the heart may retain some regenerative potential, in reaction to pathologic stresses. Cardiac stem cells (CSC) were demonstrated to concentrate in specialized niches, rather than be uniformly distributed throughout the heart. Inferring from other organs, niches of stem cells are likely to be found mainly in crypt-like area. Thus, we hypothesized that the left atrial appendage (LAA) is a very likely place to find stem cells.

Methods. LAA tissue from mouse and rat was cut into 1- to 2 mm² pieces, washed and digested three times with trypsin and collagenase IV. The remaining tissue fragments were cultured as explants in complete explant medium (CEM). After three weeks, a layer of fibroblast like cells outgrew from the adherent explants. Undifferentiated cells that grew as self-adherent clusters-cardiospheres over this layer were characterized by specific stains for stem cell (c-kit) and cardiac progenitor cell (GATA4) markers. To assess clonality, single cells were seeded on matrigel and expanded in DMEM - Ham's F12(1:1) medium containing growth factors.

Results. The round undifferentiated cells grew in large numbers around the explant. These cells stained positive for c-kit and GATA4. Clones of up to 15 cells grew 4 days after separate seeding of a single cell. In one case, spontaneous differentiation occurred with spontaneous contraction.

Conclusions. We have isolated, in substantial numbers, multiplying and clonogenic cells from LAA of mice and rats. These cells exhibit a cardiac stem cell phenotype. This preliminary study suggests that the LAA may be a source of cardiac stem cells. These may be used for potential cardiac replacement therapies, and to better understand the mechanisms driving cardiomyocytes to reenter the cell cycle.