

Endogenous cardiac stem cells

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The field of cardiology is poised for a revolution in which cell-based methods will be used to regrow healthy heart muscle after myocardial infarction or in chronic heart failure. Cardiac stem cells (CSCs) show great promise for regenerative therapy. These are resident stem cells within the heart that were first discovered in 2003; until then, the heart was thought to have little or no regenerative potential. We have isolated CSCs from adult human and porcine endomyocardial biopsy specimens, differentiated them in vitro and characterized their functional properties. When minced and maintained in primary culture for 2-7 days, ventricular or atrial biopsy specimens produce small, round cells budding off from the explant. Such cells can be expanded as monolayers with a doubling time of days, or, if grown in suspension culture, form multicellular clusters dubbed cardiospheres (CSps). CSps are partially differentiated toward the cardiac lineage, expressing MHC, TnI, connexin-43, and ANP by immunostaining. CSps co-cultured with neonatal rat ventricular myocytes (NRVMs) become flattened, stellate and contractile after 6 or 7 days. Co-cultured CSp-derived cells are fully excitable: they exhibit spontaneous action potentials (APs) with a morphology akin to nodal cells. CSp-derived cells also cycle calcium and exhibit functional coupling with NRVMs in co-culture, as evidenced by Rhod-2-sensitive intracellular calcium transients synchronous with those of neighboring heart cells by confocal imaging. CSCs injected into infarcted SCID mouse hearts engraft, differentiate and improve function. Thus, CSCs and CSps can be isolated and expanded from routine biopsy specimens; they readily become excitable and contractile in synchrony with cardiomyocytes in vitro. Experiments with delivery of autologous porcine CSCs into injured pig hearts are ongoing. Taken together, these observations provide both a simple method and a solid rationale for the use of CSCs and CSps for autologous cardiac regeneration therapy.

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