## Natural and synthetic regulators of embryonic stem cell cardiogenesis.

**Journal:** Pediatr Cardiol

**Publication Year:** 2009

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**PubMed link:** 19319460

**Funding Grants:** Chemical Genetic Approach to Production of hESC-derived Cardiomyocytes , Burnham Institute
CIRM Stem Cell Training Grant (Type II)

**Public Summary:**

**Scientific Abstract:**
Debilitating cardiomyocyte loss underlies the progression to heart failure. Although there have been significant advances in treatment, current therapies are intended to improve or preserve heart function rather than regenerate lost myocardium. A major hurdle in implementing a cell-based regenerative therapy is the inefficient differentiation of cardiomyocytes from either endogenous or exogenous stem cell sources. Moreover, cardiomyocytes that develop in human embryonic stem cell (hESC) or human-induced pluripotent stem cell (hIPSC) cultures are comparatively immature, even after prolonged culture, and differences in their calcium handling, ion channel, and force generation properties relative to adult cardiomyocytes raise concerns of improper integration and function after transplantation. Thus, the discovery of natural and novel small molecule synthetic regulators of differentiation and maturation would accelerate the development of stem-cell-based myocardial therapies. Here, we document recent advances in defining natural signaling pathways that direct the multistep cardiomyogenic differentiation program and the development of small molecules that might be used to enhance differentiation as well as the potential characteristics of lead candidates for pharmaceutical stimulation of endogenous myocardial replacement.