Stepwise chemically induced cardiomyocyte specification of human embryonic stem cells.

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Public Summary:

Because human embryonic stem cells (hESCs) can differentiate into all cardiac lineages, including atrial, ventricular and pacemaker cells, [1a-c] they are a potential source of cardiomyocytes for cell-based therapy, as well as a useful tool for studies of early embryonic cardiac development. Previous studies generated cardiomyocytes from hESCs by first forming three-dimensional embryoid bodies which were then treated with a combinantion of Wnt, Activin, and BMP proteins in an attempt to recaptitulate the key events that regulate cardiogensis.[1a,c,2a-c] However, the efficiency of these methods is poor and the signaling pathway(s) involved in the specification of cardiomyocytes from hESCs is not well defined. Cell permeable small molecules that modulate signal transduction pathways or gene expression have been used to selectively modulate ESC self-renewal or differentiation under defined monolayer cell culture conditions.[3] We therefore attempted to identify molecules that selectively and efficiently induce the differentiation of hESCs to cardiomyocytes in a stepwise process by first generating primitive streak.

Scientific Abstract: