Distinct cardiogenic preferences of two human embryonic stem cell (hESC) lines are imprinted in their proteomes in the pluripotent state.

Journal: Biochem Biophys Res Commun

Publication Year: 2008

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PubMed link: 18503758

Funding Grants: Stem Cell Research Training Grant

Public Summary:

Scientific Abstract:
Although both the H1 and HES2 human embryonic stem cell lines (NIH codes: WA01 and ES02, respectively) are capable of forming all three germ layers and their derivatives, various lines of evidence including the need to use different protocols to induce cardiac differentiation hint that they have distinct preferences to become chamber-specific heart cells. However, a direct systematic comparison has not been reported. Here we electrophysiologically demonstrated that the distributions of ventricular-, atrial- and pacemaker-like derivatives were indeed different (ratios=39:61:0 and 64:33:3 for H1 and HES2, respectively). Based on these results, we hypothesized the differences in their cardiogenic potentials are imprinted in the proteomes of undifferentiated H1 and HES2. Using multiplexing, high-resolution 2-D Differential In Gel Electrophoresis (DIGE) to minimize gel-to-gel variations that are common in conventional 2-D gels, a total of 2000 individual protein spots were separated. Of which, 55 were >2-fold differentially expressed in H1 and HES2 ($p<0.05$) and identified by mass spectrometery. Bioinformatic analysis of these protein differences further revealed candidate pathways that contribute to the H1 and HES2 phenotypes. We conclude that H1 and HES2 have predetermined preferences to become ventricular, atrial, and pacemaker cells due to discrete differences in their proteomes. These results improve our basic understanding of hESCs and may lead to mechanism-based methods for their directed cardiac differentiation into chamber-specific cardiomyocytes.