12] Distinct immunmodulatory effects of human embryonic stem cells (hESC) and hESC-derived cardiomyocytes on human dendritic cells and natural killer cells.

Gloria HW Tso[1,2], Ada Yim[3], Kelly Lau[1,2], Ronald A. Li[1,3,4], Camie WY Chan[1,2,3]
[1]Stem Cell & Regenerative Medicine Consortium, [2]Department of Anatomy, [3]Department of Medicine, [4]Department of Physiology, University of Hong Kong, Hong Kong.

Transplantation of human embryonic stem cells (hESCs)–derived cardiomyocytes (CM) to damaged heart provides a therapeutic strategy for cardiac tissue regeneration. However, immunologic acceptance of the transplanted CM remains a challenging aspect. Recent findings suggest that iPSC and their derivates are not immunoprivileged and can be rejected upon transplantation. Dendritic cells (DCs) are the major antigen presenting cells to T cells and are key in triggering both the innate and adaptive immune responses. In addition to killing tumor and virus-infected cells, natural killer (NK) cells distinguish allogeneic major histocompatibility complex (MHC) and are participate in transplant rejection. Here we examined the immunomodulatory properties of hESCs and hESCs-derived cardiomyocytes (hESCs-CM) in modulating human DC and NK function.
Our finding showed that HES2 inhibited TLR4-induced DC maturation. DCs co-cultured with HES2 exhibited lower surface expression of CD40, CD80, CD86 and MHC class II with a decreased production of TNF-α and increased level of TGF-β. However, HES2-CM did not inhibit TLR4-induced DC maturation. HESCs underwent minimal killing by NK cells. By contrast, hESC-CM activated DC to undergo maturation and were susceptible to NK cytotoxicity.
In summary, hESCs and hESC-CM posses distinct immunomodulatory property in modulating DC and NK functions. We conclude that HES2-CM activated DCs to acquire a maturation phenotype. Our data lay the ground work for immune cell-specific modulation for prolonging hESC-CM graft survival and efficacy.
1. Na+/Ca2+ exchanger is a determinant of excitation-contraction coupling in human embryonic stem cell-derived ventricular cardiomyocytes. Fu JD, Jiang P, Rushing S, Liu J, Chiamvimonvat N, Li RA. Stem Cells Dev. 2010; 19(6): 773-82.
2. Human cardiovascular progenitor cells develop from a KDR+ embryonic-stem-cell-derived population. Yang L, Soonpaa MH, Adler ED, Roepke TK, Kattman SJ, Kennedy M, Henckaerts E, Bonham K, Abbott GW, Linden RM, Field LJ, Keller GM. Nature. 2008; 22(453): 524-8.