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

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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.
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