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Extracellular vesicles from basic science observations to therapeutic application

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Exosomes are nano-sized lipid bilayer vesicles 30-~150nm that are released as part of a highly conserved cell signaling mechanism. Cardiosphere-Derived Cells (CDCs) are heart-derived stem cells that have been shown to regenerate the injured heart in animal models and in patients with permanently scarred hearts. Recently, we demonstrated that exosomes secreted from human CDCs (hCDCs) recapitulate the regenerative benefits of the cells themselves in mice with chronic myocardial infarction (Ibrahim et al, Stem Cell Reports 2014). The benefits appear to be mediated at least in part by the transfer of micro RNAs (miRs) delivered by exosomes to target cells. Among the biological pathways affected are cell survival, angiogenesis, fibrosis and inflammation. Our working hypotheses, supported by ample evidence, are as follows: i) CDC-exosomes contain a unique complement of miRs that, collectively, mediate many of the therapeutic effects of CDCs; ii) CDC-exosomes and their constituent miRs favorably modulate apoptosis, inflammation and fibrosis in the injured heart and possibly in other tissues; iii) CDC-exosomes improve functional recovery and increase tissue viability. Thus, CDC–exosomes represent a novel cell-free therapeutic candidate for tissue repair. Exosomes have the following potential advantages over living cells: 1) prolonged shelf life; 2) reductionist identity and release criteria; 3) the potential for lack of immunogenicity; and 4) the likelihood of being able to administer repeat doses safely. Thus, CDC-exosomes (as cell-free derivatives of CDC s) are of potentially significant translational value. I will present preclinical proof-of-concept data supporting efficacy in acute and chronic animal models of myocardial infarction.

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