Letter by Li and Hong Regarding Article, “Cross Talk of Combined Gene and Cell Therapy in Ischemic Heart Disease: Role of Exosomal MicroRNA Transfer”

To the Editor:

We read with great interest the article by Ong et al., who demonstrated that codelivery of cardiac progenitor cells (CPCs) with a minicircle plasmid carrying hypoxia-inducible factor-1 into the ischemic myocardium can improve the survival of transplanted CPCs. Their data revealed that hypoxia-inducible factor-1 was able to modulate the local niche and transform it from a hostile ischemic milieu into a hospitable environment for transplanted stem cells. Specifically, they showed that minicircle plasmid carrying hypoxia-inducible factor-1 was taken up by cardiac endothelial cells, which secreted exosomes that were internalized by the CPCs. The exosomes were enriched for miR-126 and miR-210, which induced a glycolytic switch in CPCs. The switch to the glycolytic state allows the CPCs to adapt to hypoxic stress. This study revealed a critical role for exosomes as a communicator in cardiovascular regeneration.

A recent study by Bang et al. demonstrated that cardiac fibroblast-derived exosomes induce cardiomyocyte hypertrophy via a paracrine mechanism, and exosomes are the cell communicator between fibroblasts and cardiomyocytes. Moreover, it has been shown that exosomes released from local tissue may enter the circulation and alter the function of cells at a distant site as the tissue communicator. It would be interesting to know whether hypoxia-inducible factor-induced exosomes from cardiac endothelial cells could activate cells from bone marrow to enhance cardiac regeneration.

In summary, the work of Ong et al. established the role of exosomes in altering the local niche as the cell–cell communicator. Additional studies on whether exosomes could alter distant niches, such as bone marrow, would be of great importance. The authors raised the possibility of enriching CPC-released exosomes with miRNAs that could improve cardiac regeneration. These studies will pave the way to the development of a novel exosome-based diagnosis and therapies for cardiovascular diseases.

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Disclosures

None.

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