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INTRODUCTION*

Emerging Impact of Extracellular Vesicles on Tissue Engineering and Regeneration

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The importance of extracellular vesicles (EVs)—especially exosomes—in tissue engineering continues to increase because of their pivotal roles in intercellular signaling in a plethora of biological contexts, which informs both regenerative medicine approaches and modeling of disease.[1,2] In this Special Issue of Tissue Engineering Part A, entitled ''Emerging Impact of Extracellular Vesicles on Tissue Engineering and Regeneration,'' we present novel research contributions from eight different laboratories from around the world that accentuate the diverse nature of the impact of EVs on the field. This diversity is derived not only from the variety of therapeutic applications but also from the multitude of cell sources of EVs.

In the first article, Lu *et al.* report that preconditioning of adipose-derived mesenchymal stem cells with tumor necrosis factor-alpha enhances the ability of exosomes secreted by these cells to induce proliferation and osteogenic differentiation of human osteoblasts (page 1212). Next, Tian and colleagues describe the utility of EVs isolated from whole fat pads for regeneration of adipose tissue (page 1221), whereas the group of Mark Hamrick shows that EVs from the bone marrow of aged mice inhibit the osteogenic differentiation of young bone marrow stromal cells (page 1231). These three studies clearly highlight that the microenvironment of EV-producing cells is critical in defining EV activity.

Other contributions describe unique EV-based approaches to tissue regeneration that further reveal the importance of cellular context and identity to the therapeutic utility of EVs. Raj Kishore's group reports that exosomes isolated from endothelial progenitor cells deficient in interleukin-10 (mimicking systemic inflammation) have impaired potential to induce provascularization responses (page 1241). Aaron Baker's group demonstrates that glioblastoma-derived exosomes can be retasked to promote therapeutic angiogenesis in peripheral ischemia (page 1251). Furthermore, Camussi and colleagues show that EVs from bone marrow mesenchymal stromal cells induced an improvement in renal function and morphology in animal models of acute kidney injury (page 1262). Importantly, the beneficial effects of the heterogeneous EV population in this study were attributed to exosome-like vesicles, showcasing the potential of isolating and characterizing different subpopulations of EVs.

This issue also includes fundamental studies that may have wide-ranging implications for tissue engineering. Joshua Leonard's team conducted a systematic evaluation of factors affecting EV uptake. Among a number of interesting findings, this group reports that culturing cells on soft substrates (as compared with tissue culture polystyrene) enhanced their ability to uptake EVs (page 1274). In addition, Stephen Badylak's group provides evidence that matrix-bound EVs play a significant role in the regulation of macrophage phenotype that is associated with beneficial effects of extracellular matrix bioscaffolds (page 1283). These studies suggest that tissue engineers could exploit the regulatory roles of EVs in cell–material interactions.

Overall, the research reports comprising this Special Issue reinforce the growing prominence of EVs within the field of tissue engineering and highlight the versatile nature of EVs for use in regenerative medicine. We hope that this set of articles will provide the reader with a glimpse of exciting areas of EV research and demonstrate the intriguing potential of harnessing EV biology in the context of tissue engineering.

Disclosure Statement

No competing financial interests exist.

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