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2.3 Exosomes Derived From Endothelial Progenitor Cells Modulate Flow-Induced Remodeling and Increase Vasculogeneis in Mesenteric Arteries of Mice

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ABSTRACT

Exosomes are key regulators of cell-to-cell communication, becoming valuable tool as disease biomarker and in the development of new therapeutic strategies. We aimed to determine the role of endothelial progenitor cell (EPC)-derived exosomes (EXO) in vascular remodelling induced by flow. C57BL/6 mice underwent chronic changes in flow by mesenteric resistance arteries ligation. Arteries were thus submitted to high flow (HF), low flow (LF), or normal flow (NF). The day before surgery mice received I.P. injection with saline or exosomes (3×10^9 particle/kg), following the treatment every 3 days until sacrifice. After 14 days, arteries were studied in vitro in a pressure arteriograph. Increase in diameter and compliance by pressure found in HF arteries were not seen in EXO treated mice (Figure 1A). Decrease in diameter observed in saline treated LF arteries, was also abolished by EXO treatment. Network analysis of miRNA content in exosomes and arterial mRNA expression revealed an increased expression of components involved in angiogenesis/arteriogenesis (Figure 1B), which could contribute to flow maintenance in the tissue. Mesenteric arteries submitted to LF, HF and NF were isolated and placed in Matrigel matrix for angiogenesis analysis. We observed that change in flow is a trigger for vasculogenesis, which is enhanced by EXO treatment (Figure 1C). This study establishes the potential role of EPC-derived exosomes to regulate vascular remodelling during changes in flow. The mechanisms for these effects involve exosome-derived miRNA regulation of a network of mRNAs implicated in collateral angiogenesis/arteriogenesis, which in turn, may contribute to maintenance of tissue homeostasis.

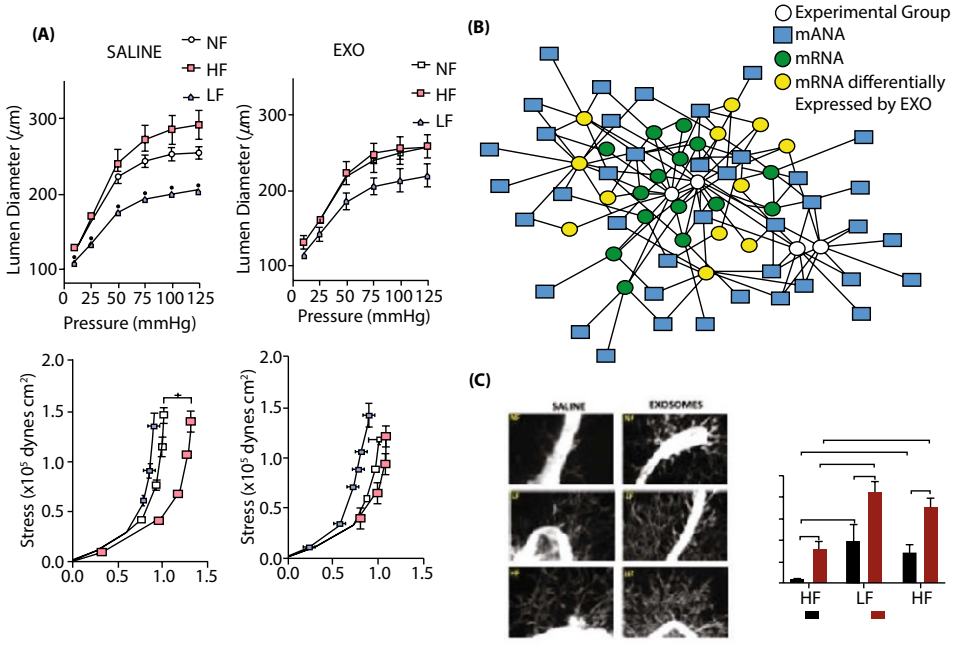

Figure 1

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