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## ACCEPTED MANUSCRIPT

### Mesenchymal Stem Cell Exosomes

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- 16 Key words: Mesenchymal stem cell, exosome, homeostasis
- 17 Abstract
- 18 MSCs are an extensively used cell type in clinical trials today. The initial rationale for their clinical
- 19 testing was based on their differentiation potential. However, the lack of correlation between
- 20 functional improvement and cell engraftment or differentiation at the site of injury has led to the
- 21 proposal that MSCs exert their effects not through their differentiation potential but through their
- secreted product, more specifically, exosomes, a type of extracellular vesicle. We propose here that
- 23 MSC exosomes function as an extension of MSC's biological role as tissue stromal support cells. Like
- 24 their cell source, MSC exosomes help maintain tissue homeostasis for optimal tissue function. They
- 25 target housekeeping biological processes that operate ubiquitously in all tissues and are critical in
- 26 maintaining tissue homeostasis, enabling cells to recover critical cellular functions and begin repair
- 27 and regeneration. This hypothesis provides a rationale for the therapeutic efficacy of MSCs and their
- secreted exosomes in a wide spectrum of diseases. Here, we give a brief introduction of the
- 29 biogenesis of MSC exosomes, review their physiological functions and highlight some of their
- 30 biochemical potential to illustrate how MSC exosomes could restore tissue homeostasis leading to
- 31 tissue recovery and repair.

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