

However, the chapter on MSCs, page 4, is a bit weak. It would have been interesting to develop the immunomodulatory activities of MSCs such as their ability to inhibit T cell responses, antigen presentation, and to amplify T reg functions.

In chapter 3, we have better described the immunomodulatory properties of MSCs on the different subset of T cells, namely effector T cells and regulatory T cells.

It would also have been interesting to add a chapter on the risks of collecting MSC-derived exosomes from obese and/or type 2 diabetic patients because these pro-inflammatory MSCs could contribute to the propagation of inflammation, and/or the occurrence of T2DM by inducing insulin resistance.

*Following the reviewer's interesting observation, we have added a chapter on the possible complications arising from employing MSCs-derived EVs isolated within pathological contexts, particularly metabolic disorders. Although EVs represent a promising therapeutic tool for the management of several diseases, coexistence of pathological conditions such as T2DM and obesity may alter the MSCs-derived EVs mRNA, miRNA and protein cargo, which in turn might negatively compromise their anti-inflammatory and immunomodulatory potential.*