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Utilizing mesenchymal stem cell (MSC) secretome elements as an alternative to whole cells in regulating neutrophilic airway inflammation in asthma

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Introduction

Immunosuppressive mesenchymal stem cells (MSCs) have been recognized as an interesting approach to treating incurable inflammatory airway diseases, including asthma. Unfortunately, years of efforts showing the effectiveness of MSC transfer in preclinical studies did not result in therapy registration. Therefore, we developed an alternative approach utilizing the extracellular vesicles (EVs) while minimizing safety issues concerning the use of whole cells.

Aim

We aimed to investigate the effects of MSC-derived EVs administration compared to originating cells in a house dust mite (HDM) extract-induced experimental asthma model.

Material, methods and results

C57BL/6J mice were challenged with 100μg HDM extract for consecutive 5 days in each of the 2 weeks to induce neutrophilic inflammation, while EVs or MSCs were administrated on the 13th day of the experiment. The lungs were collected for H&E staining to assess immune cell infiltration. Moreover, lung lobes were subjected to total RNA isolation followed by next-generation sequencing (NGS). Finally, the levels of cytokines and chemokines in bronchoalveolar lavage (BAL) were analyzed using multiplexing.

Firstly, we confirmed that both MSCs and EVs administration limit neutrophilic airway inflammation in the experimental asthma model. Moreover, analysis of canonical and noncanonical pathways revealed the downregulation in arachidonic acid metabolism and lipid metabolism while using both MSCs and EVs. However surprisingly, in contrast to MSCs only EVs administration caused the decrease in the levels of Th2-driven cytokines and some CXCL and CCL chemokines in BAL.

Conclusions

In summary, we confirmed that the administration of EVs reflects the beneficial effects of MSCs in the regulation of neutrophil airway inflammation.

Conflict of interest:

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Paper has not been ever presented during the International PTA Congress.