Extracellular Vesicle of Adipose-derived Stem Cells: A Role in Allergic Airway Inflammation

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ABSTRACT

Outcome objectives: To evaluated the effects of extracellular vesicle (EV) of adipose-derived stem cells (ASCs) supernatant on allergic airway disease in ovalbumin (OVA) induced asthmatic mouse model.

Materials and Methods: C57BL/6 mice were sensitized to OVA by intraperitoneal injection and challenged intranasally with OVA. To evaluate the effect of EVs of ASCs supernatant on allergic airway disease, 10 μg/50 μl of control supernatant, ASCs supernatant with or without EV were administrated intranasally by OVA challenge. We evaluated airway hyperresponsiveness (AHR), the proportion of eosinophils in bronchoalveolar lavage fluid (BALF), lung histology, serum total and OVA-specific antibody, cytokine profile of BALF and lung draining lymph nodes (LLN), and T cell population of LLN.

Methods and Materials

INTRODUCTION

Extracellular vesicles (EVs) are nanosized membranous vesicles, secreted from a variety of cell types into their surrounding extracellular space. Various EVs containing proteins, nucleic acids and lipid are transferred to recipient cells and affect their function and activity. Several studies have showed that EVs released from inflammatory and epithelial cells implicated allergic disease. However, the role for EVs of adipose-derived stem cells (ASCs) in allergic airway diseases remains unclear. Our research group is interested in the possibility of using ASCs as therapeutic agents for allergic airway diseases. Although our group has found strong immune suppression effects of ASCs, the cell therapy itself has some drawbacks including tumorigenesis, immune reaction, long term safety, low level of engraftment after transplantation and storage problems. In this study, we evaluated the effects of EVs of ASCs supernatant on allergic airway inflammation in ovalbumin (OVA) induced asthmatic mouse model which can overcome the problems of cell therapy of ASCs.

RESULTS

PenH in asthmatic mice (OVA group) increased with the methacholine concentration, and ASCs supernatant with EV significantly decreased airway hyperresponsiveness (AHR) in asthmatic mice. ASCs supernatant without EV group also showed decrease in the AHR but without statistical significance compared to OVA group. The numbers of total inflammatory cells and eosinophils were significantly increased in the bronchoalveolar lavage fluid (BALF) of the OVA group compared to the PBS group. However, ASCs supernatant with EV treatment significantly decreased the numbers of total inflammatory cells and eosinophils (Fig. 2). ASCs supernatant without EV group showed decrease in the numbers of total inflammatory cells and eosinophils but without statistical significance compared to OVA group. No obvious infiltration of inflammatory cells was found in the PBS group on the histological examination in the lung, but a greater number of eosinophils in the peribronchial and perivascular areas were seen in asthmatic mice. However, no obvious infiltration of inflammatory cells and goblet cell hyperplasia were found in asthmatic mice treated with ASCs supernatant with EV treatment (Fig. 3A).

CONCLUSIONS

ASCs supernatant with EV significantly inhibited allergic inflammatory response in the lung. AHR, total immune cell and eosinophils in the BALF were significantly reduced after ASCs supernatant with EV administration. EVs of ASCs supernatant significantly decreased the serum total and allergen-specific IgE and total IgG1 level. EV of ASCs supernatant significantly inhibited Th2 cytokines (IL-4 and IL-13) in the LLN and IL-4 in BALF. EV of ASCs supernatant significantly enhanced regulatory cytokines IFN-γ in the BALF. In addition, CD25+Foxp3+ and IL-10+ T cells in LLN were significantly increased after ASCs supernatant with EV administration.

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REFERENCES
