Molecules and Cells

Mesenchymal Stem Cells Suppress Severe Asthma by Directly Regulating Th2 Cells and Type 2 Innate Lymphoid Cells

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Patients with severe asthma have unmet clinical needs for effective and safe therapies. One possibility may be mesenchymal stem cell (MSC) therapy, which can improve asthma in murine models. However, it remains unclear how MSCs exert their beneficial effects in asthma. Here, we examined the effect of human umbilical cord blood-derived MSCs (hUC-MSC) on two mouse models of severe asthma, namely, *Alternaria alternata*-induced and house dust mite (HDM)/diesel exhaust particle (DEP)-induced asthma. hUC-MSC treatment attenuated lung type 2 (Th2 and type 2 innate lymphoid cell) inflammation in both models. However, these effects were only observed with particular treatment routes and timings. *In vitro* co-culture showed that hUC-MSC directly downregulated the interleukin (IL)-5 and IL-13 production of differentiated mouse Th2 cells and peripheral blood mononuclear cells from asthma patients. Thus, these results showed that hUC-MSC treatment can ameliorate asthma by suppressing the asthmogenic cytokine production of effector cells. However, the successful clinical application of MSCs in the future is likely to require careful optimization of the route, dosage, and timing.

Keywords: cell therapy, innate lymphoid cells, mesenchymal stem cells, severe asthma, Th2 cells

INTRODUCTION

Asthma is a chronic inflammatory disease with symptoms of shortness of breath, dyspnea, and coughing. It is not only the most common chronic airway disease, its prevalence is still rising in many parts of the world (Lundback et al., 2016). Asthma treatment is based on bronchodilators, which provide short-term symptom relief, and corticosteroids that depress the inflammatory responses (McCracken et al., 2017). However, some patients have difficulty controlling their symptoms even if they adhere closely to such standard treatment regimens. Therefore, new treatment regimens are needed for poorly controlled asthma, and one possibility is mesenchymal stem cell (MSC) therapy.

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AUTHOR CONTRIBUTIONS

J.W.S. and S.R. designed, and performed the experiments. J.W.S., S.R., K.J., and H.Y.K. wrote the manuscript. S.L. and D.H.C. analyzed the data. J.H. and H.R.K. contributed to human sample preparation. H.Y.K. supervised the project.

CONFLICT OF INTEREST

The authors have no potential conflicts of interest to disclose.

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