Conclusions: Macrophage migration inhibitory factor and interleukin-8 are highly produced in acute gout. Monosodium urate crystals induced macrophage migration inhibitory factor production in monocytes and interleukin-8 production in neutrophils with a reciprocal interaction between the two cytokines.

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AB0064 HIGH-EFFICIENCY TRANSDUCTION OF MESENCHYMAL STEM CELLS BY AAV2/DJ VECTOR FOR THEIR POTENTIAL USE IN AUTOIMMUNE DISEASES

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Background: Mesenchymal stem cells (MSC), multipotent non-hematopoietic progenitors, can be isolated from various tissues and can modulate allogeneic immune cell responses. These properties make MSC as a promising potential treatment of autoimmune diseases.1 Our previous studies have found that bone marrow-derived (BM)-MSC from systemic lupus erythematosus (SLE) patients are structurally and functionally,2 treatment with modified and optimised MSC may bring a better effect on patients with autoimmune diseases. Most efforts have relied on adeno- and lentiviral vectors for delivering genes to MSC. Effective as these vectors may be, concerns regarding their immunogenicity and, in the case of lentivirus, the risk of insertional mutagenesis, have led to the pursuit of safer alternatives. Among these, adeno-associated virus (AAV) holds several advantages as a vector for human gene therapy. There are many serotypes of AAV available, and certain serotypes have been found to transduce specific cell types more efficiently than others.

Objectives: To determine the efficiency of different serotypes of AAV vectors for their ability to mediate transduction of different sources of MSC and assess whether AAV transduction affects MSC multipotentiality.

Methods: Serotypes 1, 2, 5, 6, 8, 9, PHP and DJ of AAV vectors were constructed in Viral Core, Boston Children’s Hospital. The enhanced green fluorescent protein (eGFP) gene under transcriptional control of a CAG promoter was cloned into the AAV vector backbone. MSC derived from umbilical cord (UC), BM and amniotic fluid (AF) were isolated and approximately 1 × 10⁵ MSC were used for transduction with the same AAV vector serotype. In our result, AAV2/DJ transduced MSC retained the same multipotential activity to UC-MSC and AF-MSC, AAV2/DJ transduced MSC with the same AAV vector serotype. In our result, AAV2/DJ transduced MSC retained the same multipotential activity to UC-MSC and AF-MSC.

Results: AAV serotype DJ vector was the most efficient in transducing MSC. AAV vector backbone. MSC derived from umbilical cord (UC), BM and amniotic fluid (AF) were isolated and approximately 1 × 10⁵ MSC were used for transduction with the same AAV vector serotype. In our result, AAV2/DJ transduced MSC was the most efficient in transducing UC-MSC and AF-MSC. AAV2/DJ transduced MSC retained the same multipotential activity to UC-MSC and AF-MSC.

Conclusions: AAV2/DJ vector can be used as a highly efficient tool to modify MSC ex vivo for therapeutic transplantation for autoimmune diseases.

REFERENCES:

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AB0065 ROLE OF IL-35 IN THE REGULATION OF IMMUNE RESPONSE IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Interleukin 35 (IL-35) is a recently identified member of the IL-12 family of cytokines and represents a novel target for therapies of autoimmune, inflammatory, and infectious diseases, including rheumatoid arthritis (RA). Choi et al. 2013. IL-35 is a heterodimer consisting of EBV-induced gene 3 (EBI3) and IL-12 chain (p40) and binds to a receptor that lacks a transmembrane and cytoplasmic domain. It is expressed by regulatory T cells and in dampening the differentiation of Th17 cells (Niedbala et al. 2007).

Methods: PBMCs of 10 RA patients and 10 controls as well as CD14+ cells isolated from PBMCs using magnetic separation were cultured for 24 hours, and subjected to three conditions: no stimulation, stimulation with LPS (PBMC and CD14+) or stimulation with anti-CD3/anti-CD28 antibodies (PBMC and CD4+), and stimulation with added IL-35 (100 ng/ml). A panel of nine cytokines (IL-1β, IL-6, IL-8, IL-10, IL-12 (p70), IL-17a, IFN-γ, MIP-1β and TNF) was measured in the cell culture supernatants.

Results: RA patients had higher serum levels of IL-35 compared to healthy controls. A decreased secretion of IL-8 and increased secretion of TNF in the presence of IL-35 was observed in vitro in stimulated PBMCs of RA patients. In the control group, we observed an increased secretion of IL-6 by PBMCs and decreased secretion of IL-10 by T lymphocytes as a result of IL-35 addition to stimulated cells.

Conclusions: In this study, we found elevated serum levels of IL-35 in RA patients suggesting a possible involvement of IL-35 in the pathogenesis of RA. However, in vitro, the effect of IL-35 on stimulated immune cells was partially anti-inflammatory and partially pro-inflammatory, suggesting that the effect of IL-35 is pleiotropic and depends on the type and the state of the affected immune cell.

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