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Up-regulation of Cox 2 pathway in interferon-γ treated mesenchymal stem cells suppress interleukin-10 production by activated B cells

Barbora Hermankova^{1,2}

¹Academy of Sciences of the Czech Republic, Czech Republic ²Charles University, Czech Republic

Mesenchymal stem cells (MSCs) are a good candidate for regenerative medicine and treatment of various diseases. They are able to suppress immune response by a cell contact, production of soluble factors and by other mechanisms. In this study we analyzed the effects of mouse bone marrow-derived MSCs on IL-10 production by lipopolysaccharide (LPS) activated B cells. The production of IL 10 by B cells was significantly enhanced in the presence of IFN-γ. Untreated MSCs had no significant effect on IL-10 production by B cells. However, when B cells were co-cultured with MSCs and IFN-γ, the production of IL-10 was strongly suppressed. Moreover, a similar effect was observed when MSCs were pre-incubated with IFN-γ and then co-cultured with activated B cells. On the other hand, the production of IL 10 was unchanged after cultivation IFN-γ pre-treated B cells with MSCs. A strong up-regulation of genes for indoleamine 2,3 dioxygenase (IDO), cyclooxygenase 2 (COX-2) and programmed cell death ligand-1 (PD-L1) was detected in MSCs treated with IFN γ. To identify the molecule which is responsible for the suppression of IL-10 production, we used neutralization monoclonal antibody anti PD L1 or inhibitors of IDO and COX-2. The suppression of IL-10 production was abrogated only in cultures with inhibitor of COX-2. The suppressor effect of COX-2 involving pathway was verified by adding prostaglandin E2 (PGE2) to the cultures with activated B cells. The mechanism of MSCs and involves COX-2 pathway leading to the production of inhibitory PGE2.

Biography

Barbora Hermankova is currently a PhD student in the field of Immunology at the Faculty of Science, Charles University in Prague. She prepared her dissertation thesis at Department of Transplantation Immunology at Institute of Experimental Medicine, Academy of Sciences of the Czech Republic. Her work is focused on the study of mesenchymal stem cells (MSC) and their immunomodulatory effects. MSC are able to suppress immune response and she studies mechanisms of this suppression which can be mediated by a cell contact, production of soluble factors or by other ways.

barbora.hermankova@biomed.cas.cz

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