

7th Annual Conference on

Stem Cell and Regenerative Medicine

August 04-05, 2016 Manchester, Uk

Immunosuppressive effect of mesenchymal stem cells in combination with Cyclosporine A in a model of skin transplantation

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The immunosuppressive effects of systemically administered mesenchymal stem cells (MSCs) and immunosuppressive drugs have been well documented. In several studies it has been shown that the administration of MSCs in combination with different types of immunosuppressive drugs prolongs allograft survival for a longer period of time than the use of MSCs or the drug alone. In our study mechanism of therapeutic effect of MSCs applied locally in combination with cyclosporine A (CsA) in a mouse model of allogeneic skin transplantation was analyzed. We have shown that MSCs seeded on a CsA loaded nanofiber scaffolds applied on skin grafts migrated to the graft bed and draining lymph nodes and altered individual parameters of the local immune response. Among the most significant effects decreasing amount of graft-infiltrating macrophages and their production of nitric oxide was detected. These changes were accompanied with considerable lower production of interferon-gamma cytokine that primes classically activated macrophages. Switch from the proinflammatory, NO producing, M1 phenotype into alternatively activated M2 population of macrophages was further confirmed by the up-regulation of CD206, a marker of M2 population and by significant increase of production of IL-10 by CD206 positive macrophages. In this study we found that application of MSCs in combination with CsA direct macrophage polarization towards development of “healing” alternatively activated macrophage population that might represent important mechanism of MSC-induced suppression of the local inflammatory reaction.

Biography

Michaela Hajkova is currently a PhD candidate at Charles University in Prague, Faculty of Science. She has completed her Master's degree in Biology with thesis entitled “The role of selected cell populations and molecules in inflammatory reaction and rejection of skin allograft”. She is working in the Laboratory of Immunoregulation where she is participating in research of therapeutic potential of MSCs and their ability to contribute to tissue repair.

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