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# Divergent immunomodulation capacity of individual myelin peptides-components of liposomal therapeutic against multiple sclerosis

Ivanova V., Khaiboullina S., Gomzikova M., Martynova E., Ferreira A., Garanina E., Sakhapov D., Lomakin Y., Khaibullin T., Granatov E., Khabirov F., Rizvanov A., Gabibov A., Belogurov A.
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## Abstract

© 2017 Ivanova, Khaiboullina, Gomzikova, Martynova, Ferreira, Garanina, Sakhapov, Lomakin, Khaibullin, Granatov, Khabirov, Rizvanov, Gabibov and Belogurov. Multiple sclerosis (MS) is an autoimmune disease characterized by demyelination and consequent neuron injury. Although the pathogenesis of MS is largely unknown, a breach in immune self-tolerance to myelin followed by development of autoreactive encephalitogenic T cells is suggested to play the central role. The myelin basic protein (MBP) is believed to be one of the main targets for autoreactive lymphocytes. Recently, immunodominant MBP peptides encapsulated into the mannosylated liposomes, referred as Xemys, were shown to suppress development of experimental autoimmune encephalomyelitis, a rodent model of MS, and furthermore passed the initial stage of clinical trials. Here, we investigated the role of individual polypeptide components [MBP peptides 46-62 (GH17), 124-139 (GK16), and 147-170 (QR24)] of this liposomal peptide therapeutic in cytokine release and activation of immune cells from MS patients and healthy donors. The overall effects were assessed using peripheral blood mononuclear cells (PBMCs), whereas alterations in antigen-presenting capacities were studied utilizing plasmacytoid dendritic cells (pDCs). Among three MBP-immunodominant peptides, QR24 and GK16 activated leukocytes, while GH17 was characterized by an immunosuppressive effect. Peptides QR24 and GK16 upregulated CD4 over CD8 T cells and induced proliferation of CD25 + cells, whereas GH17 decreased the CD4/CD8 T cell ratio and had limited effects on CD25 + T cells. Accordingly, components of liposomal peptide therapeutic differed in upregulation of cytokines upon addition to PBMCs and pDCs. Peptide QR24 was evidently more effective in upregulation of pro-inflammatory cytokines, whereas GH17 significantly increased production of IL-10 through treated cells. Altogether, these data suggest a complexity of action of the liposomal peptide therapeutic that does not seem to involve simple helper T cells (Th)-shift but rather the rebalancing of the immune system.

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## Keywords

Cytokines/chemokines, Dendritic cells, Liposomal peptide therapeutic, Multiple sclerosis, Myelin basic protein, T helper cells, T regulatory cells, Treatment

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