Analysis of the Therapeutic Effect of Bifidobacterium Administration on Experimental Autoimmune Myasthenia Gravis in Lewis Rats.

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Beneficial effects of probiotics on gut microbiota homeostasis and inflammatory immune responses suggested the investigation of their potential clinical efficacy in experimental models of autoimmune diseases. Indeed, we previously described that administration of two bifidobacteria and lactobacilli probiotic strains prevented disease manifestations in the Lewis rat model of Myasthenia Gravis (EAMG). Here, we demonstrate the clinical efficacy of therapeutic administration of vital bifidobacterial, and we dissect the mechanisms involved in immunomodulation with ex vivo and in vitro experiments.

Improvement of EAMG symptoms was associated to decreased anti-rat AChR antibody levels, and differential expression of TGFβ and FoxP3 immunoregulatory transcripts in draining lymph nodes and spleen of treated-EAMG rats.

Exposure of rat bone marrow-derived dendritic cells to bifidobacteria strains upregulated toll-like receptor 2 mRNA expression, a key molecule involved in bacterium recognition via lipotheicoic acid. The effect of probiotic/BMDCs interaction demonstrated TLR2 redistribution in cell membrane after engagement with LTA. In addition, BMDC membrane reorganization could interfere with the formation of the MHC-Ag-TCR complex, a preliminary step to effector T cell activation. Live imaging experiments of AChR-specific effector T cells, co-cultured with BMDCs pre-exposed to bifidobacteria, demonstrated increased percentages of motile effector T cells, suggesting a hindered formation of TCR-peptide-MHC complex.

Composition of gut microbiota was studied by 16S rRNA gene sequencing, and α and β diversity were determined in probiotic treated EAMG rats, with altered ratios between Tenericutes and Verrucomicrobia (phylum level), and Ruminococcaceae and Lachnospiraceae (family level). Moreover, the relative abundance of Akkermansia genus was found increased compared to healthy and probiotic treated EAMG rats.

In conclusion, our findings confirm that the administration of vital bifidobacteria at EAMG onset has beneficial effects on disease progression; this study further supports preclinical research in human MG to evaluate probiotic efficacy as supplementary therapy in MG.