PROPHYLACTIC ADMINISTRATION OF *PARABACTEROIDES DISTASONIS* LYSATE REDUCES THE SEVERITY OF EXPERIMENTAL AUTOIMMUNE ENCEPHALOMYELITIS

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Objectives: The gut microbiota influences the immune system and contributes to differences in host susceptibility to inflammatory diseases. Patients with multiple sclerosis have low abundance of *Parabacteroides distasonis* (Pd) in their gut microbiota and live Pd suppress the T-cell responses and prevent severe forms of experimental autoimmune encephalomyelitis (EAE) in mice. The aim of this study is to determine whether a protective effect can also be achieved by Pd lysate and whether this administration affects the gut microbiota composition.

Methods:Lysate of anaerobically cultured Pd was administered orally to C57BL/6 mice in four weekly doses. Subsequently, EAE was induced by subcutaneous administration of myelin oligodendrocyte glycoprotein emulsified in complete Freund's adjuvant and intraperitoneal injection of *Bordetella pertussis* toxin. After 3 weeks, we compared the neurological impairments with controls and measured the immune profile by flow cytometry and ELISA. Microbiota composition was analyzed by next-generation sequencing.

Results:Pd lysate significantly delayed and decreased the severity of EAE. It significantly increased the frequency of regulatory T cells in mesenteric lymph nodes, but not in axial lymph nodes. The increase in regulatory T cells was accompanied by a significant increase in IL-10. In addition, Pd-lysate significantly increased gut abundance of the genera *Ruminococcus* and *Parabacteroides* in mice with EAE, but not in control group. Administration of Pd lysate without disease induction resulted in significantly higher abundance of the genus *Lactobacillus*. Induction of EAE resulted in higher abundance of *Prevotellaceae* in both study groups.

Conclusion: Oral administration of Pd lysate delays clinical symptoms and prevents severe forms of EAE by inducing a T regulatory response. Even killed Pd can protect against severe forms of central nervous system inflammation.
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