PhD Program in Basic and Applied Immunology and Oncology (BAIO)

The role of diet, microbiota and gut immunity alterations in the pathogenesis of Multiple Sclerosis

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Mechanisms that regulate effector and regulatory T cell differentiation in the intestinal mucosa are instrumental to maintain immune tolerance towards self-tissues and to prevent extra-intestinal autoimmune diseases like Multiple Sclerosis (MS) (1,2). Along this line, we recently demonstrated that RR-MS patients have an increased differentiation of effector Th17 cells in the intestinal mucosa (manuscript in preparation). Intestinal mucosal immunity is strongly influenced by diet composition either directly or through modulation of the gut microbiota (3,4). Specific food components such as fermentable fibers and omega-3 fatty acids promote intestinal immune tolerance by increasing the relative abundance of bacterial species that release pro-tolerogenic metabolites such as butyrate, propionate and acetate (SCFA-producing bacteria). Those findings raised the hypothesis that dietary changes and the resulting substantial modification of the human microbiota are responsible for the dramatic increase in the incidence of autoimmune diseases like MS in western countries in the past decades (5).

The objective of this study is to establish a direct causative link between diet, microbiota composition, alteration of gut immunity and the pathogenesis of RR-MS. First, we will perform metagenomic and metabolomic analysis of the gut microbiota to correlate alteration of gut immunity and intestinal inflammation with specific microbiota profiles in RR-MS patients. Specifically, we will assess whether increased Th17 cell differentiation in RR-MS patients is linked with a high relative abundance of pro-inflammatory bacteria and under-representation of pro-tolerogenic SCFA-producing bacteria. In parallel, we will perform pre-clinical studies in EAE, the experimental model of RR-MS, to assess whether a diet enriched in fermentable fibers and omega-3 promotes a protective microbiota composition thus reducing Th17 cell differentiation in the intestine and autoimmunity in the brain.

References:

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