Dissecting the role of the gut microbiota in immune modulation of Multiple Sclerosis

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The intestinal microbiota composition orchestrates the physiology and pathology of different organs and systems, playing a key role in the development and modulation of the immune system. Data obtained in patients and preclinical models of extra-intestinal autoimmune diseases, such as type 1 diabetes, rheumatoid arthritis and multiple sclerosis (MS), a brain disorder mainly triggered by T helper 17 (Th17 cells), show an alteration in the gut microbiota pattern, although it is still not fully clear whether this is a cause or a consequence of the improper immune activation.
Specifically, in MS, different studies have found modifications in the gut microbiota composition in patients versus healthy controls (HC); nevertheless, these findings are still correlative and a causal link between gut microbial strains and the immune pathogenesis of MS is yet to be determined.
We recently analysed by16S rRNA sequencing the mucosa-associated microbiota in the small intestine of relapsing-remitting (RR)MS patients and HC and found that patients with high disease activity (neurological and MRI signs of MS activity in the 2 year follow-up) have specific alterations in the microbiota composition, namely high *Streptococcus* and low *Prevotella* in comparison with HC and RRMS patients with no disease activity. Interestingly, the analysis of the intestinal immunological profile by flow cytometry of the same cohort revealed that RRMS patients with high disease activity have also an increased number of effector Th17 cells in the intestinal mucosa *(Cosorich I et al., Science Advances 2017)*. Importantly, the percentage of intestinal Th17 cells inversely correlated with the relative abundance of *Prevotella* strains.
Our data suggest that a specific microbiota composition with low relative abundance of *Prevotella* promotes the differentiation of effector Th17 cells in the intestine of RRMS patients and this is linked with increased disease activity.
Our next goal is to characterize the molecular and cellular mechanisms through which the gut microbiota promotes MS immune pathogenesis and, specifically, which metabolic profiles generated by gut microbiota modulate brain autoimmunity. The results of our study will correlate mechanistically the gut microbiota with brain autoimmunity and could be ultimately applied to other extra-intestinal and systemic autoimmune/inflammatory diseases, leading to new therapeutic perspectives.