Myalgic encephalomyelitis (ME) is characterized by an assortment of physical and immunological symptoms; nevertheless, some of the most commonly reported observations by those who suffer with ME are gastrointestinal (GI) abnormalities[1] [2] [3]. This is not unexpected in that the gut-associated lymphoid tissue represents the largest immune compartment in the body. Indeed, it has been estimated that more than 60% of all T lymphocytes reside within the small intestine[4], emphasizing the ability of the gut to impact systemic immunity. Additionally, mounting evidence suggests that the gut microbiota dramatically impacts neurological function[5].

It is common for pathogenic organisms to infect the intestinal tract, and it is therefore important for the immune system to discriminate commensal microbes from pathogenic microbes as well as to discriminate self from non-self. This process is referred to as tolerance, and a loss of tolerance is associated with autoimmune disease. Previous reports of individuals with ME expressing autoantibodies[6] [7] and the efficacious treatment of ME cases with the B-cell-depleting drug Rituximab[8] [9] suggest that some components of ME pathology may also overlap with those of autoimmunity. Furthermore, neurobiology of gut-brain communication (the so called "gut-brain-axis") tells us that bidirectional signaling between the gastrointestinal tract and the brain plays a central role in neuroimmune disease. It is for these reasons that the focus of our current research program is directed toward the gut's contribution to ME and its potential involvement with the pathology that overlaps with autoimmunity and neuroimmunity.

Our investigation into the pathophysiology of ME has revealed that the duodenum of many ME subjects is often inflamed and infiltrated with lymphocytes. We have further identified a component of this cellular infiltrate as a subset of dendritic cells known as plasmacytoid dendritic cells (pDCs). These cells are the principal producers of type I interferon and are also heavily implicated in virtually every autoimmune disease. Our research suggests that these cells are dysregulated and may contribute to the gut-related pathology observed in ME. Additionally, our work has also identified a key contribution of the cytokine interleukin (IL)-7 in ME pathophysiology. IL-7 plays a putative role in autoimmunity. Our current investigations are focused on how IL-7, gut pathology, and neuroimmunity are connected.

---

[1] Chia J, Chia A, Voeller M, et al. Acute enterovirus infection followed by myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) and viral persistence. J Clin Pathol 2010;63:165-8.

[2] Lakhan SE, Kirchgessner A. Gut inflammation in chronic fatigue syndrome. Nutr Metab (Lond) 2010;7:79.

[3] Maes M, Coucke F, Leunis JC. Normalization of the increased translocation of endotoxin from gram negative enterobacteria (leaky gut) is accompanied by a remission of chronic fatigue syndrome. Neuro Endocrinol Lett 2007;28:739-44.

[4] Guy-Grand D, Vassalli P. Gut intraepithelial T lymphocytes. Curr Opin Immunol 1993;5:247-52.

[5] Camilleri M, Di Lorenzo C. Brain-gut axis: from basic understanding to treatment of IBS and related disorders. J Pediatr Gastroenterol Nutr 2012;54:446-53.

[6] Konstantinov K, von Mikecz A, Buchwald D, et al. Autoantibodies to nuclear envelope antigens in chronic fatigue syndrome. J Clin Invest 1996;98:1888-96.

[7] von Mikecz A, Konstantinov K, Buchwald DS, et al. High frequency of autoantibodies to insoluble cellular antigens in patients with chronic fatigue syndrome. Arthritis Rheum 1997;40:295-305.

[8] Fluge O, Bruland O, Risa K, et al. Benefit from B-lymphocyte depletion using the anti-CD20 antibody rituximab in chronic fatigue syndrome. A double-blind and placebo-controlled study. PLoS One 2011;6:e26358.

[9] Fluge O, Mella O. Clinical impact of B-cell depletion with the anti-CD20 antibody rituximab in chronic fatigue syndrome: a preliminary case series. BMC Neurol 2009;9:28.