OC07 - **The role of sex in the connection between the microbiome and autoimmunity**

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Unresolved low grade systemic inflammation represents the underlying pathological mechanism driving immune and metabolic pathways involved in autoimmune diseases (AID). Mechanistic studies in animal models of AID and observational studies in patients have found alterations in gut microbiota communities and their metabolites, suggesting a microbial contribution to the onset or progression of AID. The gut microbiota and its metabolites have been shown to influence immune functions and immune homeostasis both within the gut and systematically. Microbial derived-short chain fatty acid (SCFA) and biotransformed bile acid (BA) have been shown to influence the immune system acting as ligands specific cell signaling receptors like GPRCs, TGR5 and FXR, or via epigenetic processes. Similarly, intestinal permeability (leaky gut) and bacterial translocation are important contributors to chronic systemic inflammation and, without repair of the intestinal barrier, might represent a continuous inflammatory stimulus capable of triggering autoimmune processes. Recent studies indicate gender-specific differences in immunity, with the gut microbiota shaping and being concomitantly shaped by the hormonal milieu governing differences between the sexes. A bi-directional cross-talk between microbiota and the endocrine system is emerging with bacteria being able to produce hormones (e.g. serotonin, dopamine and somatostatine), respond to host hormones (e.g. estrogens) and regulate host hormones' homeostasis (e.g by inhibiting gene prolactin transcription or converting glucocorticoids to androgens). We review herein how gut microbiota and its metabolites regulate immune function, intestinal permeability and possibly AID pathological processes. Further, we describe the dysbiosis within the gut microbiota observed in different AID and speculate how restoring gut microbiota composition and its regulatory metabolites by dietary intervention including prebiotics and probiotics could help in preventing or ameliorating AID. Finally, we suggest that, given consistent observations of microbiota dysbiosis associated with AID and the ability of SCFA and BA to regulate intestinal permeability and inflammation, further mechanistic studies, examining how dietary microbiota modulation can protect against AID, hold considerable potential to tackle increased incidence of AID at the population level.