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The Relation Between Gut Microbial Flora and Autoimmune Diseases

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Abstract:
Autoimmune disorders are characterized by the generation of autoantibodies against self-antigens that attack the body's own tissues, resulting in damage. Genetic and environmental triggers have been long known as the major contributors to the development of autoimmunity. Increasing evidence in recent years suggests that microbial translocation and intestinal barrier dysfunction, which may be affected by gut microbiota, are another important causative element for autoimmune disorders. This reporte summarizes the role of microbial translocation and leaky gut syndrome in autoimmune diseases.

Introduction:

Autoimmune disease is a condition arising from an abnormal immune response to a normal body part.

Leaky gut syndrome: is the destruction of the integrity of the gut wall to the point of allowing particles of undigested food and toxins to enter the blood stream. It is associated with many chronic diseases, including diabetes, lupus, and MS (multiple sclerosis).

The intestinal epithelial lining, together with factors secreted from it, forms a barrier that separates the host from the environment. In pathologic conditions, the permeability of the epithelial lining may be compromised by activation of zonulin (is a protein that modulates the permeability of tight junctions between cells of the wall of the digestive tract)allowing the passage of toxins, antigens, and bacteria in the lumen to enter the blood stream creating a "leaky gut.

Growing evidence shows that the gut microbiota is important in supporting the epithelial barrier and therefore plays a key role in the regulation of environmental factors that enter the body.

Therefore, it is hypothesized that modulating the gut microbiota can serve as a potential method for regulating intestinal permeability and may help to alter the course of autoimmune diseases in susceptible individuals.[1]

- **Disscussion:**

Gut bacteria have been linked to a range of diseases, including autoimmune conditions characterized by immune system attack of healthy tissue. To shed light on this link, a Yale research team focused on Enterococcus gallinarum, a bacterium they discovered is able to spontaneously "translocate" outside of the gut to lymph nodes, the liver, and spleen.

In models of genetically susceptible mice, the researchers observed that in tissues outside the gut, E.gallinarum initiated the production of auto-antibodies and inflammation -- hallmarks of the autoimmune response. They confirmed the same mechanism of inflammation in cultured liver cells of healthy people, and the presence of this bacterium in livers of patients with autoimmune disease.

Through further experiments, the research team found that they could suppress autoimmunity in mice with an antibiotic or a vaccine aimed at *E. Gallinarum*.[2]

- Type 1 Diabetes (T1D) has the same pathogenic challenges as other autoimmune diseases . Certain HLA (Human leukocyte antigen**)** class II alleles account for 40% of the genetic susceptibility to T1D; however, the majority of individuals with these HLA alleles do not develop

T1D. This supports the concept that reaction to some environmental products triggers autoimmune destruction of beta cells and leads to T1D.
This hypothesis is supported by studies performed in an animal model that develops T1D spontaneously that showed an increased permeability of the small intestin of rats that preceded the onset of diabetes by at least a month . Further, histological evidence of pancreatic islet destruction was absent at the time of increased permeability but clearly present at a later time. Therefore, these studies provided evidence that increased permeability occurred before either histological or overt manifestation of diabetes in this animal model.[3]

- Safety and efficacy testing of zonulin inhibitor, larazotide acetate, are currently being carried out. Results from experiments using rats prove promising. Larazotide acetate administration to rats prevents disrupted intestinal barrier function, autoantibody production, pancreatic islet destruction and disease development (70% decrease in diabetes incidence).[4]

Conclusion:
The primary functions of the gastrointestinal tract have traditionally been perceived to be limited to the digestion and absorption of nutrients and electrolytes, and to water homeostasis. A more attentive analysis of the anatomic and functional arrangement of the gastrointestinal tract, however, suggests that another extremely important function of this organ is its ability to regulate the trafficking of macromolecules between the environment and the host through a barrier mechanism. Together with the gut-associated lymphoid tissue and the neuroendocrine network, the intestinal epithelial barrier, with its intercellular tight junctions, controls the equilibrium between tolerance and immunity to nonself-antigens. When the finely tuned trafficking of macromolecules is dysregulated in genetically susceptible individuals, both intestinal and extraintestinal autoimmune disorders can occur.

Recommendation:
My recommendation is to perform more detailed studies to determine the mechanism and action of gut microbiota on mucosal and systemic immunity, which may be lead to improvement of therapeutic methods agianst autoimmune disease and arresting the interplay between genes and environmental factors through intestinal barrier function re-establishment, can be used in prevention or treatment of autoimmune disorders.

References:
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