

## **INTESTINAL MICROBIOTA, AUTOIMMUNITY AND ALLERGY**

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The frequency of autoimmune and allergic diseases has increased significantly over the last 30 years in developed countries. At the same time, the incidence of infectious diseases has decreased. The question arose as to whether there was a causal relationship between these two observations. Many epidemiological arguments plead in this direction. Similarly, observations in animal models of these diseases show that one may completely prevent their occurrence following various bacterial, viral or parasitic infections. It recently emerged that the composition of the gut microbiome could play a role in the susceptibility to autoimmunity and allergy, and also to inflammatory bowel diseases. Thus, a correlation was observed between the occurrence of these diseases and a reduction in the diversity of the intestinal microbiota. An increase in the severity of asthma induced following immunization with ovalbumin and of the onset of insulin-dependent diabetes in NOD mice was observed after treatment of pregnant mothers and newborns by certain antibiotics which destroy all or part of the intestinal flora. Finally, the administration of probiotics can protect against both autoimmune and allergic diseases.

As a whole, these elements could, although indirectly, suggest that the reduction in the diversity of the intestinal flora, that is also influenced by surrounding sanitary conditions, constitutes a major mechanism of the effect of "hygiene", broadly conceived based on the initial hypothesis.

However, very strong arguments, both in humans and in animal models show that pathogens including bacteria, viruses or parasites, also play a very important role. One major issue, still ill-defined is that of the cellular and molecular mechanisms underlying the protective effect of infections on autoimmune and allergic diseases. A common denominator between commensals and pathogens is the presence of ligands of Toll-like receptors (TLR). The fact that systemic administration of TLR agonists prevent the onset of autoimmune diabetes or of allergic asthma is in support of the possible role of these ligands in the protective effect of infections on immune diseases. Other mechanisms may also be considered, including homeostatic regulation.

This novel line of research is important to get a better understanding on the pathophysiology of autoimmune and allergic diseases at the same time it paves the way to innovative strategies for disease prevention.