

Effect of microbes on immune regulation and development of immune-mediated diseases

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Type 1 diabetes is the most common autoimmune disease in childhood, while allergic disorders, such as asthma and allergic rhinoconjunctivitis, represent the most frequent chronic diseases in that age group. Natural contacts with microbes in our environment are thought to be important for the maturation of the immune system and for the balance and regulation of humoral and cell-mediated immune responses. It is known that several bacteria and viruses can activate regulatory T-cells and control proinflammatory immune responses. Certain microbial infections are associated with decreased risk of allergy, and the rising incidence of type 1 diabetes could reflect reduced contacts with microbes due to increased general hygiene. However, the effects of microbial exposure on immune responses in autoimmune and allergic diseases and in immune regulation are yet incompletely understood.

We are addressing the question how microbes and/or the lack of exposure to common microbes affects immune responses in autoimmune diabetes and allergies. To this end, we study certain microbes including commensal gut microbes, microbes with proposed probiotic effects and enteroviruses as modifiers of gut immunity and the induction of regulatory vs. inflammatory T cells in the gut. Our current aims are to investigate in animal models of diabetes and airway hypersensitivity the effects of orally ingested microbes on antigen-specific regulatory T cells and on dendritic cell traffic and antigen presentation in gut-associated lymphoid tissues. To develop potent but safe immunomodulatory therapies for prevention of diabetes and allergies, we test protocols where autoantigen or model allergen is given with a response-modifying microbe to desensitize the immune system and alleviate disease progression. We are also studying T cell trafficking and the role of memory T cells in protective immunity in a tumor model. Our aim is that the results can be directly applied in the design of clinical trials where such protocols would be tested among subjects with increased genetic risk for these diseases.

