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The role of IL-23 in autoimmunity:
The tissue matters

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Abstract:

Both multiple sclerosis (MS) and psoriasis are widely held to be autoimmune diseases mediated by auto-reactive helper T cells. Even though IL-23 is among the most critical cytokines involved in the development of autoimmune diseases, its cellular targets and mechanism of action remains largely elusive. IL-23 has sparked the research into the biology of \( \text{TH17} \) cells, but a firm link between IL-23 and the development of TH17 cells cannot be established. In the context of autoimmune neuro-inflammation, IL-23 endows auto-reactive TH cells with the capacity to cause tissue damage. However, none of the signature cytokines of TH17 cells (IL-17, IL17F, IL22, IL21 etc.) is crucial for CNS autoimmunity in EAE (the animal model of MS). Analysis of the molecular signature of encephalitogenic T cells showed that GM-CSF, among the TH17 cytokines, was induced by IL-23. In contrast to IL-17 or IFN-g, neutralization of GM-CSF renders mice completely resistant to the induction of EAE. We found that GM-CSF not only marks the population of highly pathogenic helper T cells but also, in contrast to any other known helper T cell cytokine, it exerts a non-redundant function in neuro-autoimmune pathogenicity in vivo regardless of the polarization pattern of the helper T cells. Inflammation of the skin as seen in psoriasis is highly dependent of the activity of IL-23 and neutralization of IL-23 (or IL17) has made a tremendous clinical impact in patients suffering from moderate/severe psoriasis. Using an animal model of psoriasis, we could confirm the importance of IL-23, and in contrast to EAE, IL-17 was the main factor triggered by IL-23 and critical for skin-inflammation. However, the cellular target of IL-23 in the skin are skin-invading gd T cells and innate lymphocytes, whereas TH17 cells were not involved. We propose that, whereas the precise role of IL-23 in health and disease remains largely undefined, IL-17 cytokines are primarily produced by innate lymphocytes and gd T cells and that dysregulation of IL-17 leads to epithelial inflammation.

Wednesday, 17 April 2013  11am to 12pm  SBS Meeting Room 1 (SBS-01n-36)

Host: Associate Professor Ruedl Christiane