Seminario CIPF

Targeting Nuclear Hormone Receptors in Inflammatory Disease

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Abstract: Inflammation is a beneficial host response to infection, but it also contributes to inflammatory disease if unregulated. CD4+ helper T (TH) lymphocytes are essential organizers of adaptive immune responses and key mediators in immune-mediated inflammatory diseases. Interleukin (IL)-17-producing T cells (TH17) have been recently identified as a subpopulation of CD4+ T cells. TH17 cells form an important fraction of pathogenic T cells in autoimmune disease patients and they orchestrate the initial steps in many autoimmune responses. We have recently described that pro-inflammatory TH17 cells are able to trans-differentiate into regulatory cells and contribute to the resolution of inflammation. Furthermore, while TH17 cell instability/plasticity has been associated with pathogenicity, this could present a therapeutic opportunity, whereby formerly pathogenic TH17 cells could adopt an anti-inflammatory fate. The trans-differentiation of TH17 cells into regulatory T cells it has been illustrated by a change in their transcriptome and the acquisition of potent regulatory capacity. Our data suggest that TH17 cell instability and plasticity could be a therapeutic opportunity for treating inflammatory diseases. Also, in new studies, we have identified different nuclear hormone receptors (NHR) as key players controlling pathogenicity of TH17 cells. Nuclear hormone receptors are ligand activated transcription factors that regulate a variety of physiological functions including development, metabolism and immune function. By using newly generated synthetic compounds targeting different NHR we were able to control inflammation mediated by proinflammatory TH17 cells. The function of TH17 cells in starting and organizing complex immune responses is just beginning to be examined. This is an emerging area that has the potential to yield novel therapeutic approaches to treat different inflammatory and autoimmune diseases.

https://medicine.yale.edu/immuno/people/enric_esplugues-2.profile