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The Emerging role of interleukin-21 in transplantation

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Since its discovery in 2000, IL-21 has been shown to play critical roles in the regulation of both innate and adaptive immune responses. IL-21 is produced predominantly by multiple effector $CD4^+$ T-cell types [T helper 17 (Th17), follicular helper T (T_{FH}), and other activated $CD4^+$ cells] and NKT cells. In addition to T cell receptor (TCR) signals, the production of IL-21 by activated $CD4^+$ T cells is intricately regulated by various extrinsic factors and intrinsic molecules, such as IL-6, IL-21, ICOS, Stat3, IRF4, and Batf. Because IL-21 receptor (IL-21R) is broadly expressed on T, B, NK, and dentritic cells (DCs), IL-21 signaling via Jak-Stat and other pathways has direct pleiotropic effects on their proliferation, differentiation, and effector function. For instance, while Th17 and T_{FH} cells produce IL-21, IL-21 also facilitates the development of these cells. IL-21–producing T_{FH} cells are important for the generation and maintenance of germinal centers, and control the differentiation of germinal center B cells and immunoglobulin production. Thus, IL-21R deficiency or IL-21 neutralization with IL-21R-Fc fusion protein prevents B cell-mediated autoimmunity in lupus-prone BXSB.B6-*Yaa*$^+$ or MRL-Fas^{lpr} mouse models, respectively. IL-21 also enhances expansion and cytotoxicity of $CD8^+$ effector T cells. During chronic lymphocytic choriomeningitis viral infection, chronic IL-21 production by antigen-specific $CD4^+$ T cells is needed to sustain $CD8^+$ T cell function for viral control. IL-21 is also required for the development of T cell-mediated type 1 diabetes in NOD mice, possibly through sustaining effector T cell function in a similar manner. Recently, two papers have shown that IL-21R-Fc prevents both auto- and allo-immune responses after islet transplantation. A timely discussion is thus needed to address the immune actions of IL-21 as well as the therapeutic potential of targeting IL-21 in transplantation.

Biography

Wenhao Chen is an Assistant Professor of Medicine at Baylor College of Medicine, Houston, Texas. He received the Ph.D. in 2006 from University of Toronto, Toronto, Ontario, Canada. His research interests are to define the molecular mechanisms of T-cell response and tolerance as well as to design immune intervention therapies for type 1 diabetes and transplantation. He has published a total of over 40 peer-reviewed papers in the field of immunology.

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