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Regeneration of the thymus is a critical function that allows for renewal of immune competence following stress, infection or immunodepletion caused by cytoreductive chemo- or radiation therapy. The mechanisms governing this regeneration remain poorly understood. However, thymic renewal in all (but particularly in adult) patients can be a prolonged process that significantly impairs the recovery of adaptive immunity following cytoreductive therapy and subsequently leads to an increase in opportunistic infections and higher treatment-associated morbidity and mortality. Hence one of the most significant clinical challenges is the need for rapid regeneration of thymopoiesis following induced immunodepletion and transplantation. Understanding the processes involved in endogenous thymic repair will allow for the clinical exploitation of strategies for therapeutic thymic regeneration.

We have recently identified an endogenous network of thymic regeneration whereby 1) injury to the thymus, and in particular the depletion of CD4+CD8+ double positive (DP) thymocytes triggers 2) upregulation of Interleukin-23 (IL-23) by a subset of thymic dendritic cells (tDCs), which induces 3) the production of IL-22 by a type of innate lymphoid cells called lymphoid tissue-inducer cells (LTi). This cascade of events leads to IL-22-mediated regeneration of the supporting thymic epithelial cell (TEC) microenvironment and, ultimately, to rejuvenation of thymopoiesis.

Several interesting areas of future study have arisen from this initial discovery including 1) exploring the mechanisms of thymic damage that trigger this regenerative network, 2) the clinical translation of IL-22 as a potential regenerative therapy to boost immune function and 3) the role of IL-22 in age-related thymic involution.

Awards

2013: American Society for Hematology (ASH) Scholar Award

2013: Memorial Sloan-Kettering Cancer Center (MSKCC) Postdoctoral Research Award

2013: NIH (NCI) K99/R00 Pathway to Independence Award

Publications

Selected Publications

Chidgey AP, Dudakov JA, Seach N and Boyd RL. (2007) Impact of niche aging on thymic regeneration and immune reconstitution. *Seminars in Immunology*. 19: 331-40

Hince M, Sakkal S, Vlahos K, Dudakov J, Boyd, R and Chidgey A. (2008) The role of sex steroids and gonadectomy in the control of thymic involution. *Cellular Immunology*. 252:122-138

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Cell Select: Regenerative medicine: A cytokine for immune recovery. *Cell* 149:727-729

F1000 evaluation: Perruche S, Saas P: 2012. F1000.com/14218962#eval15732067

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