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Development and Stem Cells

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The immune system has 2 essential types of thymus-derived (T) cells: i. Conventional T cells (T-conv) promote inflammation to rid the body of pathogens and tumours, and ii. Regulatory T cells (T-reg) suppress inflammation.

Charles Darwin referred to competition between individuals and species as a “struggle for existence”. T-conv and T-reg cells also compete against each other for resources. A feature of a safe immune system is that T-reg cells outcompete T-conv cells in the steady state. A key limiting resource is antigen, to which a T cell binds via its unique T-cell receptor (TCR). Self-proteins dominate the body’s antigen landscape in the steady state. We aim to understand mechanisms that focus T-reg cells on key self-proteins. We hope that detailed insight into the T-reg/self-protein axis will improve diagnostic accuracy and therapeutic efficacy in autoimmune diseases and cancers.

Research Projects

1. Defining the B-cell-dependent T-regulatory cell repertoire

Selected significant publications:

1. Hu DY, Yap JY, Wirasinha RC, Howard DR, Goodnow CC, **Daley SR**. 2015. A timeline demarcating two waves of clonal deletion and Foxp3 up-regulation during thymocyte development. *Immunol Cell Biol*. Oct 29.
2. Altin JA, **Daley SR**, Howitt J, Rickards HJ, Batkin AK, Horikawa K, Prasad SJ, Nelms KA, Kumar S, Wu LC, Tan SS, Cook MC, Goodnow CC. 2014. Ndfip1 mediates peripheral tolerance to self and exogenous antigen by inducing cell cycle exit in responding CD4+ T cells. *Proc Natl Acad Sci USA*. 111, 2067-74.
3. **Daley SR**, Hu DY, Goodnow CC. 2013. Helios marks strongly autoreactive CD4+ T cells in two major waves of thymic deletion distinguished by induction of PD-1 or NF-κB. *J Exp Med*. 210, 269-85.
4. **Daley SR**, Coakley KM, Hu DY, Randall KL, Jenne CN, Limnander A, Myers DR, Polakos NK, Enders A, Roots C, Balakishnan B, Miosge LA, Sjollem G, Bertram EM, Field MA, Shao Y, Andrews TD, Whittle B, Barnes SW, Walker JR, Cyster JG, Goodnow CC, Roose JP. 2013. Rasgrp1 mutation increases naive T-cell CD44 expression and drives mTOR-dependent accumulation of Helios T cells and autoantibodies. *Elife*. Dec 12; 2: e01020.
5. Silva DG*, **Daley SR***, Hogan J, Lee SK, Teh CE, Hu DY, Lam KP, Goodnow CC, Vinuesa CG. 2011. Anti-islet autoantibodies trigger autoimmune diabetes in the presence of an increased frequency of islet-reactive CD4 T cells. *Diabetes*. 60, 2102-11.
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