UNIVERSITY OF CALIFORNIA MERCED | School of Natural Sciences

Quantitative & Systems Biology
Ph.D. Dissertation Defense
Candidate: Kristen Valentine

Pathogenic Follicular CD8 T Cells Promote Autoimmune Disease

Abstract:

The contribution of CD8 T cells to autoimmune disease remains in debate. We show autoimmune CD8 T cells which induce antibody class switching and plasma cell differentiation act synergistically with CD4 T cells in promoting germinal center reactions. We have identified CXCR5+PD-1+ CD8 effector T (CD8 T follicular; Tfc), within the germinal center, that expand during late autoimmune disease progression. Here, we show that CD8 Tfc cells transcriptionally and phenotypically resemble CD4 T follicular helper (Tfh) cells in multiple models of spontaneous autoantibody-mediated disease including IL-2 deficient (IL-2-KO), scurfy and MRL/MpJ-FAS^{lpr} mice. CD8 Tfc cells maintain the capacity to produce significant amounts of cytotoxic proteins Granzyme B, CD107a and TNFα as well as helper-associated cytokines IL-21, IFNγ and IL-4. Functionally, CD8 Tfc cells promote cytokine-mediated antibody class switch using mechanisms independent of IFNγ or IL-21. When adoptively transferred CD8 Tfc cells in combination with CD4 Tfh cell promote autoantibody production. Our results indicate that CD8 Tfc cells contribute to autoimmune disease synergistically with CD4 Tfh cells to induce B cell class switching and autoantibodies during disease progression. Evidence of CD8 Tfc cells in autoimmune disease defines a novel immune setting during which CXCR5+ CD8 T cell develops beyond situations of chronic viral infection and cancer. Thus, pathogenic CD8 T cells expand to influence germinal center reactions and promote autoimmune responses.

Date:

Friday
May 3rd, 2019

Time:

2:00pm – 3:00pm

Location:

KL 217

Bio:

Kristen Valentine M Valentine is a fifth year Ph.D. candidate in Quantitative and Systems Biology at UC Merced. She completed her Bachelor of Science at UC Merced in 2014 and directly joined the lab of Dr. Katrina Hoyer in 2014 to study CD8 T cell responses during autoimmune disease. She expects to graduate with her Ph.D. in May of 2019, after which, she has secured a post-doctoral position with Dr. Sujan Shresta at the La Jolla institute of Immunology to study CD8 T cell responses during ZIKA and Dengue virus infections

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