May 20th, 12:30 PM

Detection of CD8+ T cell Responses in Individuals with Long-term Type 1 Diabetes and Generation of Human CD8+ T Cell Lines Specific to Islet-associated Autoantigens

Jenny Aurielle B. Babon  
*University of Massachusetts Medical School*

David M. Harlan  
*University of Massachusetts Medical School*

Sally C. Kent  
*University of Massachusetts Medical School*

Follow this and additional works at: [http://escholarship.umassmed.edu/cts_retreat](http://escholarship.umassmed.edu/cts_retreat)

Part of the Endocrine System Diseases Commons, Endocrinology, Diabetes, and Metabolism Commons, Immunity Commons, Immunoprophylaxis and Therapy Commons, and the Translational Medical Research Commons

This work is licensed under a [Creative Commons Attribution-Noncommercial-Share Alike 3.0 License](http://creativecommons.org/licenses/by-nc-sa/3.0/).

Babon, Jenny Auigelle B.; Harlan, David M.; and Kent, Sally C., "Detection of CD8+ T cell Responses in Individuals with Long-term Type 1 Diabetes and Generation of Human CD8+ T Cell Lines Specific to Islet-associated Autoantigens" (2014). *UMass Center for Clinical and Translational Science Research Retreat*. 11.

[http://escholarship.umassmed.edu/cts_retreat/2014/posters/11](http://escholarship.umassmed.edu/cts_retreat/2014/posters/11)

This material is brought to you by eScholarship@UMMS. It has been accepted for inclusion in UMass Center for Clinical and Translational Science Research Retreat by an authorized administrator of eScholarship@UMMS. For more information, please contact Lisa.Palmer@umassmed.edu.
Detection of CD8+ T cell responses in individuals with long-term type 1 diabetes and generation of human CD8+ T cell lines specific to islet-associated autoantigens

Jenny Aurielle B. Babon, David M. Harlan and Sally C. Kent

Diabetes Center of Excellence, University of Massachusetts Medical School, Worcester, MA

Abstract:
Type 1 diabetes (T1D) is an autoimmune disease characterized by the activation of lymphocytes against insulin-producing β-cells in the pancreas. In humans, CD8+ T cells are predominantly found in sites of insulitis and are considered to be one of the main drivers of β-cell destruction, thus indicating the need to analyze the frequency and function of these autoreactive CD8+ T cells. Peripheral blood mononuclear cells (PBMC) from individuals with long-term T1D were stained ex vivo for T cell surface markers and HLA-A2 pentamers containing known islet-associated epitopes to determine if there are autoreactive CD8+ T cells circulating in the periphery. All T1D donors tested had at least one detectable autoreactive CD8 T cell population and the frequencies of these autoantigen-specific T cells were comparable to previously published data from T1D individuals. We then developed a method of establishing CD8 T cell lines by co-culturing negatively isolated CD8 T cells and peptide-pulsed monocyte-derived dendritic cells from the PBMC of one T1D donor (A*02:01, A*33:01, B*14:02, B*40:01, DRB1*01:02, DRB1*04:04). We expanded a CD8 T cell line specific to the preproinsulin peptide PPI15-24. This cell line produced IFN-γ and expressed CD107a in the presence of PPI15-24-pulsed target cells, but not to an unrelated peptide or media alone. Using a similar approach, we were able to generate CD8 T cell lines from the same T1D donor that were cytotoxic to target cells pulsed with the autoantigens glutamic acid decarboxylase peptide (GAD65114-123) and islet-specific glucose-6-phosphatase catalytic subunit-related protein peptide (IGRP265-273). These autoreactive T cell lines can be utilized in in vivo assays using humanized mouse models to further understand the mechanism of β-cell destruction and disease progression. Studying the functionalities of these autoreactive T cells will also provide insights into identifying immune correlates to better assess both novel and existing immunotherapeutic strategies for T1D.

Contact info: Jenny Aurielle B. Babon
Jenny.Babon@umassmed.edu
508-856-1307