May 16th, 1:45 PM

Broad Repertoire of T Cell Autoreactivity Directly from Islets of Donors with Type 1 Diabetes (T1D)

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

Megan E. DeNicola  
*University of Massachusetts Medical School*

David M. Blodgett  
*University of Massachusetts Medical School*

See next page for additional authors

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

Part of the [Cell Biology Commons](https://escholarship.umassmed.edu/cellbiology), [Immune System Diseases Commons](https://escholarship.umassmed.edu/immunologysystemdiseases), [Immunology and Infectious Disease Commons](https://escholarship.umassmed.edu/immunologyinfectiousdisease), and the [Translational Medical Research Commons](https://escholarship.umassmed.edu/translationalmedicalresearch)

Babon, Jenny Aurielle B.; DeNicola, Megan E.; Blodgett, David M.; Crevecoeur, Inne; Buttrick, Thomas S.; Maehr, Rene; Bottino, Rita; Naji, Ali; Kadis, John; Elyaman, Wassim; James, Eddie A.; Haliyur, Rachana; Brissova, Marcela; Overburgh, Lut; Mathieu, Chantal; Delong, Thomas; Haskins, Kathryn; Pugliese, Alberto; Campbell-Thompson, Martha; Mathews, Clayton; Clayton; Atkinson, Mark A.; Powers, Alvin C.; Harlan, David; and Kent, Sally C., "Broad Repertoire of T Cell Autoreactivity Directly from Islets of Donors with Type 1 Diabetes (T1D)" (2017). *UMass Center for Clinical and Translational Science Research Retreat*. 12.
[https://escholarship.umassmed.edu/cts_retreat/2017/posters/12](https://escholarship.umassmed.edu/cts_retreat/2017/posters/12)

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.
Presenter Information
Jenny Aurielle B. Babon, Megan E. DeNicola, David M. Blodgett, Inne Crevecoeur, Thomas S. Buttrick, Rene Maehr, Rita Bottino, Ali Naji, John Kaddis, Wassim Elyaman, Eddie A. James, Rachana Haliyur, Marcela Brissova, Lut Overburgh, Chantal Mathieu, Thomas Delong, Kathryn Haskins, Alberto Pugliese, Martha Campbell-Thompson, Clayton Mathews, Mark A. Atkinson, Alvin C. Powers, David Harlan, and Sally C. Kent

Keywords
type 1 diabetes, T1D, T cells, autoreactivity

Creative Commons License
This work is licensed under a Creative Commons Attribution-Noncommercial-Share Alike 3.0 License.

This poster abstract is available at eScholarship@UMMS: https://escholarship.umassmed.edu/cts_retreat/2017/posters/12
BROAD REPERTOIRE OF T CELL AUTOREACTIVITY DIRECTLY FROM ISLETS OF DONORS WITH TYPE 1 DIABETES (T1D)

Jenny Aurielle B. Babon¹, Megan E. DeNicola¹, David M. Blodgett¹, Thomas S. Buttrick³, René Maehr⁴, Rita Bottino⁵,⁶, Ali Najj⁷, John Kaddis⁸, Wassim Elyaman⁹, Eddie A. James⁹, Rachana Haliyur¹⁰, Marcela Brissova¹⁰, Lut Overbergh⁸, Chantal Mathieu², Thomas Delong¹¹, Kathryn Haskins¹¹, Alberto Pugliese¹², Martha Campbell-Thompson¹³, Clayton Mathews¹³, Mark A. Atkinson¹³, Alvin C. Powers¹⁰,¹⁴,¹⁵, David M. Harlan¹, Sally C. Kent¹

¹Division of Diabetes, Diabetes Center of Excellence, Department of Medicine, University of Massachusetts Medical School; ²Laboratory for Clinical and Experimental Endocrinology, Department of Clinical and Experimental Medicine, KU Leuven, Leuven, Belgium; ³Ann Romney Center for Neurologic Diseases, Brigham and Women’s Hospital and Harvard Medical School, Boston, MA; ⁴Program in Molecular Medicine, Diabetes Center of Excellence, University of Massachusetts Medical School; ⁵Institute of Cellular Therapeutics, Allegheny-Singer Research Institute, Pittsburgh, PA; ⁶Department of Biological Sciences, Carnegie Mellon University, Pittsburgh, PA; ⁷Institute for Diabetes, Obesity, and Metabolism, University of Pennsylvania School of Medicine, Philadelphia, PA; ⁸Department of Information Sciences, Beckman Research Institute, City of Hope, Duarte, CA; ⁹Benaroya Research Institute at Virginia Mason, Seattle, WA; ¹⁰Division of Diabetes, Endocrinology and Metabolism, Department of Medicine, Vanderbilt University Medical Center, Nashville, TN; ¹¹Department of Immunology and Microbiology, University of Colorado School of Medicine, Denver, Anschutz Medical Campus, Aurora, CO; ¹²Diabetes Research Institute, University of Miami, Miami, FL; ¹³Departments of Pathology, Immunology, and Laboratory Medicine, University of Florida, Gainesville, FL; ¹⁴Department of Molecular Physiology and Biophysics, Vanderbilt University, Nashville, TN; ¹⁵VA Tennessee Valley Healthcare System, Nashville, TN

Type 1 diabetes (T1D) is an autoimmune disease characterized by the infiltration of lymphocytes into the insulin-producing β-cells in the pancreas. We have isolated live T cells sorted or grown directly from the isolated, handpicked islets of human donors with T1D. We received ~500 islet equivalent EQ of variable purity (10-90%) from 12 donors with T1D (disease duration 0.42-20 years) and from seven control donors and two donors with type 2 diabetes (T2D). A total of 321 T cell lines and clones were derived from the islets of donors with T1D (3 lines from the 9 control donors). These are 131 CD4+ lines and clones, 47 CD8+ lines and 143 lines that contain both CD4+ and CD8+ T cells. From 50 lines and clones examined to date, we have determined the autoreactivity of 19 and have seen a broad repertoire of T cell autoreactivity in the islets, including characterized targets and post-translationally modified targets. Autoreactivity of CD4+ T cell lines was to three different peptides from glutamic acid decarboxylase 65 (GAD; GAD₁₁₅₋₁₂₇, GAD₂₇₄₋₂₈₆, GAD₅₅₅₋₅₆₇), proinsulin₁₇₆₋₉₀, and to chromogranin A or proinsulin expressed by DR4+DQ8+ B cells transduced with lentivirus containing constructs with the open reading frames corresponding to whole autoantigens. Reactivity to modified peptides included the glucose-regulated protein 78 and islet amyloid polypeptide with arginine to citrulline modifications (GRP78²₂₉₋₃₀₅/Arg-Cit²₉⁷) and IAPP₆₅₋₈₄(Arg-Cit ₇₃, ₸₁), deaminations (IA-₂₅₄₅₋₅₆₂(Glu-Glu ₄₈₇, ₅₅₁, ₅₅₅), and to several insulin hybrid peptides. These autoreactive CD4+ T cell lines and clones secreted only pro-inflammatory cytokines (IFN-γ, TNFα) upon peptide stimulation. For CD8+ T cells from islets, from one donor with T1D, we saw binding of a pool of HLA-A2 pentamers loaded with insulin B₁₀₋₁₈, IA-₂₇₉₇₋₈₀₅ and insulin specific glucose-6-phosphatase catalytic subunit related protein, IGRP₂₆₅₋₂₇₃. These results have implications for the development of successful prevention and reversal therapeutic strategies in T1D.

Contact:
Jenny Aurielle B. Babon, Ph.D.
University of Massachusetts Medical School
Jenny.babon@umassmed.edu