BIOGRAPHICAL SKETCH

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NAME: Bayer, Allison Lorayne

eRA COMMONS USER NAME (agency login):

POSITION TITLE: Research Assistant Professor

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)*

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
Eckerd College, St. Petersburg, Florida	BS	05/1993	Marine Biology
Medical University of South Carolina, Charleston	PhD	08/1998	Microbiology and Immunology

A. Personal Statement

I am interested in understanding the basic immunobiology of T_{reg} cells and applying that knowledge for future clinical translational applications. What makes this research so motivating is the fact that it may provide a basis to design novel therapies for the treatment of autoimmune diseases including type 1 diabetes (T1D). I have a broad background in immunology and expertise in T_{reg} cell immunobiology, cytokine signaling, and the NOD model, with technical capabilities in multi-color flow cytometry and cell sorting, skin and bone marrow transplantation, adoptive transfer into neonatal and adult mice, and genotyping of transgenic and knockout strains of mice. I also have expertise in cellular immunology techniques, including MLR and CTL assays. I have presented my work at numerous scientific conferences and have been invited to give short oral presentations at Keystone Symposium on T regulatory Cells in 2004 where I was awarded a travel scholarship, Keystone Symposium on Tolerance in Transplantation and Autoimmunity in 2008, and Keystone Symposium on Immunoregulatory Networks in 2011. I have numerous publications on T_{reg} cells, as well as review articles and a book chapter on the role of IL-2 in T_{reg} cell development and homeostasis in "T Regulatory cells and Clinical Application" as documented below. I was recruited to the Diabetes Research Institute (DRI) and appointed to rank of Research Assistant Professor. The mission of the DRI is to cure T1D and implement a multidisciplinary approach to research working towards a cure is closely aligned to my research goals. During part of 2012, my career was interrupted due to family responsibilities. I immediately continued my ongoing research projects and collaborations and to compete for grant support. I am motivated and passionate about my research and I do believe that my most creative and productive years still lie ahead.

a. Malek TR and **Bayer AL**. Tolerance, not Immunity, Critically Depends upon IL-2. *Nature Reviews Immunology* (2004); 4: 665 – 674. [Review].

b. Bayer, AL. and Malek, T.R. The role of IL-2 in the development and peripheral homeostasis of naturally occurring $CD4^+CD25^+Foxp3^+$ regulatory T cells. In: *Regulatory T cells and Clinical Applications*. S. Jiang, ed. Springer New York, (2009). [Book Chapter]

c. **Bayer AL**, Pugliese A, and Malek TR. The IL-2/IL-2R system: from basic science to therapeutic applications to enhance immune regulation. *Immunol Res.* (2013); 57(1-3):197-209. [Review]

d. Cabello-Kindelan C, Mackey S, and **Bayer AL**. Adoptive T Regulatory Cell Therapy for Tolerance Induction. *Current Transplantation Reports* (2015); Jun1:2(2): 191-201. [Review]

e. Fraker, C and **Bayer AL**. The Expanding Role of Natural Killer Cells in Type 1 Diabetes and Immunotherapy. *Curr Diab Rep* (2016);16:109 DOI: 10.1007/s11892-016-0806-7 [Review]

B. Positions and Honors

Positions and Employment

1998-2002 Postdoctoral Fellow, Loyola University Medical Center, The Cardiovascular Institute

2002-2006 Postdoctoral Fellow, University of Miami-School of Medicine, Department of Microbiology and Immunology

2006-Present Research Assistant Professor, Department of Microbiology and Immunology and Diabetes Research Institute, University of Miami Miller School of

Medicine, Miami, Florida.

Professional Activities

Grant Review Commitees:

2009 JDRF Autoimmunity Fall Innovative Review Panel, Invited Reviewer
2009-2012 JDRF Study Section panel for Autoimmunity
2012-2013 JDRF Medical Scientific Review Community for the Immune Therapies Training Awards
2015 NIH Ad hoc Mail Reviewer, NIH Cellular Aspects of Diabetes and Obesity [CADO] study
2016 NIH/NIAID Cooperative Study Group for Autoimmune Disease Prevention (CSGADP) U01

Editorial Responsibilities:

Blood, Invited Reviewer *(since 2006)*
BMC Immunology, Invited Reviewer *(since 2005)*
Cell Transplantation, Invited Reviewer *(since 2007)*
European Journal of Immunology, Invited Reviewer *(since 2008)*
Immunobiology, Invited Reviewer *(since 2008)*
Journal of Immunology, Invited Reviewer *(since 2008)*
PLos ONE, Invited Reviewer *(since 2009)*

Honors and Awards:

Dean's List, College of DuPage, 1989-1991

President's List, Eckerd College, 1991-1993

Travel Award, Society of Leukocyte Biology, Baltimore, MD 1997

Presidential Award Finalist, Society of Leukocyte Biology, Baltimore, MD 1997

NIH Travel Award, 11th Int Conf on Second Messengers and Phosphoproteins, Melbourne, Australia 2001

2001 Abstract Trainee Award, American Heart Association, Anaheim, California 2001.

Travel Scholarship, Keystone Symposium: Regulatory/Suppressor T cells, Banff, Canada, 2004.

American Association of Immunologists, Trainee Membership 2004-2005

American Association of Immunologists, Membership 2006-2010

Pre-Award Enhancement Program, University of Miami Miller School of Medicine, 2013

NIH/NIAID High Priority Short-term R56 Grant, 2013

University of Miami Miller School of Medicine Dean's NIH Bridge Award, 2014

Stanley J. Glaser Foundation Research Award, 2015

Goodman Prize for Outstanding Young Scientist 2017

C. Contribution to Science

1. My work focuses on T regulatory (T_{reg}) cells. These cells inhibit both self and allogeneic immune responses, and thus are attractive for novel cell-based therapy approaches for the treatment of autoimmune diseases, to prevent and treat disease at onset, and to restore insulin secretion through transplantation in the case of type 1 diabetes (T1D). My work has significantly contributed to the role of IL-2 in T_{reg} generation and homeostasis. Furthermore, these studies demonstrated that manipulation of the recipient's immune system is likely going to be necessary to realize the therapeutic potential of T_{reg} immunotherapy for autoimmune diseases and transplant rejection.

a. **Bayer AL**, Yu A, Adeegbe D, and Malek TR. Essential Role for IL-2 for $CD4^+CD25^+$ T Regulatory Cell Development during Neonatal Period. *Journal of Experimental Medicine* (2005); 201(5):769-777.

b. Adeegbe D, **Bayer AL**, Levy R and Malek TR. Allogeneic $CD4^+CD25^+$ $FoxP3^+$ T Regulatory Cells Suppress Autoimmunity while establishing Transplantation Tolerance. *Journal of Immunology* (2006); Jun 15;176(12):7149-53.

c. **Bayer AL**, Yu A, and Malek TR. Function of the IL-2R for thymic and peripheral $CD4^+CD25^+$ $Foxp3^+$ T regulatory cells. *Journal of Immunology* (2007); April 1; 178(7):4062-71.

d. **Bayer AL,** Lee JY de la Barrera A, Surh C, Malek TR. A function for IL-7R for $CD4^+CD25^+$ $Foxp3^+$ T regulatory cells. *Journal of Immunology* (2008); July 1 181(1):225-34.2.

2. This work focuses on T_{reg} cells as a novel cell-based therapy approaches to promote self and transplantation tolerance. However, the use of these cells for therapy is hindered by the inability to generate the sufficient number of cells required to inhibit the desired immune response(s) and achieve stable engraftment of the donor T_{reg} cell

inoculums. Understanding the immunobiology of T_{reg} cells and the in vivo biological environment to promote stable, long-term engraftment of adoptively transferred T_{reg} cells for the treatment of T1D was underappreciated. We have recently identified critical factors for successful adoptive T_{reg} cell therapy: 1) generation of peripheral space for engraftment/persistence of infused T_{regs}, 2) overcoming competition from endogenous T_{regs}, 3) provision of IL-2 to support survival/proliferation of adoptively transferred T_{regs} and 4) availability of relevant antigens.

a. **Bayer AL**, Jones M, Chirinos J, de Armas L, Schreiber T, Malek TR, and Levy RB. Host $CD4^+C25^+$ T cells Can Expand and Comprise a Major Component of the T_{reg} Compartment Following Experimental HCT. *Blood* (2009), 13(3): 733-43.

b. **Bayer AL**, Chirinos J, Cabello C, Yang J, Matsutani T, Malek TR, Levy RB. Expansion of a Restricted Residual Host Treg Repertoire is Dependent on IL-2 Following Experimental Autologous HSCT. *European Journal of Immunology* (2011) Dec;41(12):3467-78.

c. Cabello-Kindelan C., de la Barrera A, Malek TR, and **Bayer AL**. In Vivo Environment Necessary to Support Transplanted Donor T Regulatory Cells. *American Journal of Transplantation* (2014) May;14(5):1032-45. [Accompanying response Letter to Editor, *American Journal of Transplantation*, 13 (10): 2432-2433.]

d. Yang EY, Kronenfeld JP, Gattas KA, **Bayer AL**, and Stabler CL. Engineering an Infectious T_{reg} Biomimetic through Chemoselective Tethering of TGFβ of PER Brush Surfaces, *Biomaterials* (2015) Oct;67:20-31. [Accompanying Editor's Choice, Science Translational Medicine, 7(301):301EC143.]

3. These studies were aimed on the immunobiology of transplantation and autoimmune diabetes. Using an islet transplant model in the anterior chamber of eye allowed for noninvasive longitudinal monitoring allowing for the study of immune cell dynamics at the transplant site. This technique has been adopted by several laboratories that have continued to contribute to the field of islet autoimmunity and transplantation tolerance. A diabetes prevention study in NOD mice with hyperbaric oxygen therapy (HOT). HOT reduces autoimmune diabetes incidence in NOD mice via increased resting T-cells and reduced activation of DCs with preservation of β-cell mass resulting from decreased apoptosis and increased proliferation. The safety profile and noninvasiveness makes HOT an appealing adjuvant therapy for diabetes prevention and intervention trials.

a. Abdulreda MH, Faleo G, Molano RD, Lopez-Cabezas M, Molina J, Tan Y, Echeverria OA, Zahr-Akrawi E, Rodriguez-Diaz R, Edlund PK, Leibiger I, **Bayer AL**, Perez V, Ricordi C, Caicedo A, Pileggi A, Berggren PO. High-resolution, noninvasive longitudinal live imaging of immune responses. Proc Natl Acad Sci U S A. (2011) Aug 2;108(31):12863-8.

b. Faleo G, Fotino C, Bocca N, Molano RD, Zahr-Akrawi E, Molina J, Villate S, Umland O, Skyler JS, **Bayer AL**, Ricordi C, Pileggi A. Prevention of Autoimmune Diabetes and Induction of β-Cell Proliferation in NOD Mice by Hyperbaric Oxygen Therapy. *Diabetes*, July 2012 61:1769-1778. [with accompanying Commentary, *Diabetes* (2012) 61:1664-1666].

4. This work focused on the role of transferrin receptor (TfR) in T-cell activation. The role of TfR in T-cell responses apart from iron uptake was unknown. TfR expression appears on activated T-cells following the interaction of the antigen-major histocompatibility complex with the T-cell receptor and the resulting expression of the IL-2 receptor (IL-2R). The modulation of T-cell TfR expression is associated with altered T-cell responses to alloantigen. Using a heterotopic, nonvascularized cardiac allograft model, anti-TfR antibody was demonstrated to be an effective immunosuppressant in prolonging cardiac allograft survival and altering T-cell responses to alloantigen. In combination with anti-IL-2R antibody, TfR blockade resulted in even greater allograft prolongation. The possible mechanisms responsible for this allograft prolongation and altered cell-mediated immunity included alterations in T-cell surface receptors, altered intragraft cytokine profiles, and modulation in signaling pathways. These studies described a novel strategy that altered T-cell responses leading to prolonged allograft survival and potentially provided additional insights into the development of better immunosuppressive regimens for clinical transplantation.

a. Woodward JE, **Bayer AL**, Chavin KD, Boleza KA, and Baliga P. Anti-Transferrin Receptor Monoclonal Antibody: A Novel Immunosuppressant. *Transplantation* (1998); 65: 6-9.

b. **Bayer AL**, Baliga P, and Woodward JE. Transferrin Receptor in T Cell Activation and Transplantation. *Journal of Leukocyte Biology.* (1998); 64: 19-24.

c. **Bayer AL**, Baliga P, and JE Woodward. Differential Effects of Transferrin Receptor Blockade on the Cellular Mechanisms Involved in Graft Rejection. *Transplant Immunology* (1999); 131-139.

d. Woodward JE, **Bayer AL** and Baliga P. Enhanced Allograft Survival Via Simultaneous Blockade of Transferrin Receptor and IL-2 Receptor. *Transplantation* (1999); 1369-1376

Complete List of Published Work in MyBibliography:

http://www.ncbi.nlm.nih.gov/sites/myncbi/1fGg3MkwqDY5Z/bibliography/48117252/public/?sort=date&direction=ascending

D. Research Support

Ongoing Grant support:

1) NIH/NIDDK, 1R01 DK109929-01A1 (PI: Alice Tomei, UM) 09/01/17–08/30/22
Conformal islet encapsulation for transplantation at vascularized sites to allow physiological insulin secretion: This work will focus on the conformal coating technology for translation and application in clinical trials. If successful, this technology can significantly impact the field by promoting graft survival, the success rate of islet transplantation yet reducing the need for islets and immunosuppression. Role:Co-investigator

2) American Diabetes Innovative Basic Science Award, 1-17-IBS-264 01/01/17-12/31/20
The interplay of innate and adaptive immunity in autoimmune diabetes: This work will characterize NK subsets in NOD mice, and define the relationship with T_{regs} in experimental settings relevant to T_{reg}-based therapies. Our work could create impetus to incorporate consideration of the innate immune system in the design of novel immunotherapies for autoimmune diseases. Role: PI

3) JDRF, Discovery and Development of Immune Tolerance Delivery Systems for Antigen Specific Therapies in Type 1 Diabetes, 2-SRA-2016-316-S-B (PI: Alice Tomei, University of Miami) 09/01/16 - 08/31/18
Engineering a novel therapeutic hydrogels with CCL21 and beta cell autoantigens to induce antigen-specific tolerance: The goal of this award is to develop a novel strategy to stimulate immune regulatory pathways to inhibit autoimmune responses that destroy insulin-producing beta cells in the pancreas. We will utilize bioengineered hydrogels to delivery factors that promote antigen-specific T regulatory cells and deletion of autoreactive T cells. Role: Co-PI

4) NIH/NIDDK, 1R56DK109929-01 07/05/16 – 06/30/17
Conformal islet encapsulation for transplantation at vascularized sites to allow physiological insulin secretion: This work will focus on the conformal coating technology for translation and application in clinical trials. If successful, this technology can significantly impact the field by promoting graft survival, the success rate of islet transplantation yet reducing the need for islets and immunosuppression. *Role: Co-investigator*

5) Stanley J. Glaser Foundation Research Award, UM SJG 2016-14 6/1/15-12/31/16
Interplay of innate and adaptive immunity in autoimmune diabetes: The goal of this award is to begin to examine the role of NK subsets and their effects on T_{regs} in autoimmune diabetes. This award allows the PI to continue her work in this new line of investigation. *Role: PI*

6) NIH/NIDDK, R01DK100654 (PI: Cheri Stabler, University of Florida) 6/1/2014-5/31/2019
Engineering Ultrathin Immunomodulatory Coatings for Islet Encapsulation: his grant focuses on developing a novel encapsulation approach that serves to minimize or eliminate the need for anti-rejection therapy following an islet cell transplant. Tethering of bioactive agents capable of instructing immune responses will further enhance long-term survival of the transplanted islets in the absence of chronic, systemic immunosuppression. *Role: PI of Subcontract*

Completed Grant Support:

1) University of Miami, Dean's NIH Bridge Award, UM DBA 2015-1 8/1/14-07/31/15
Immunomodulation Requirements for T_{reg} Immunotherapy for autoimmune diabetes: The overall goal of this proposal is to elucidate mechanisms that regulate successful T_{reg} therapy. *Role: PI*

2) NIH/NIAID High Priority Short-term Grant, 1R56AI101278-01A1 8/15/13-07/31/14
Immunomodulation Requirements for T_{reg} Immunotherapy for autoimmune diabetes: The overall goals of this proposal are: 1) to elucidate the mechanisms that regulate successful T_{reg} therapy and to develop clinically translatable protocols for the treatment of T1D, using preclinical models to investigate if clinically applicable T_{reg} therapy can be achieved for the prevention or reversal of autoimmune diabetes or to suppress graft rejection of islet cell transplantation for the treatment of diabetes. *Role: PI* (1-year no-cost extension 07/01/14-06/30/2015)

3) American Diabetes Association Junior Faculty Award, 7-09-JF-06 01/1/10-12/31/12
T Regulatory Cell Therapy for Type 1 Diabetes: The overall goal of this proposal is to elucidate the mechanisms by which successful T_{reg} therapy can be achieved for the prevention or reversal of autoimmune diabetes or to suppress graft rejection of islet cell transplantation for the treatment of diabetes. *Role: PI*