BIOGRAPHICAL SKETCH

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NAME: MALTZMAN, JONATHAN S

eRA COMMONS USER NAME (agency login): MALTZMAN

POSITION TITLE: Associate 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
MIT	BS	05/1989	Biology
University of Pennsylvania	MD	05/1997	Medicine
University of Pennsylvania	PHD	06/1997	Immunology
Post-doctoral fellowship; Gary Koretzky, University of Pennsylvania	OTH	06/2006	Immunology

A. Personal Statement

My laboratory has a longstanding interest in understanding fundamental aspects of immunological memory and regulation and their relationship to solid organ transplantation and cancer. I have been an independent investigator for a period of 9 years since completing his clinical training in Nephrology and post-doctoral training in Immunology and as an Instructor of Medicine at the University of Pennsylvania. The laboratory has developed unique mouse models that employ tissue specific and/or temporal gene deletion of T cell receptor signaling proteins and transcription factors. We were the first to use tamoxifen-mediated temporal deletion to study SLP-76 in mature T lymphocytes. We have experience in cellular and molecular immunology and have a long track record of productive collaboration to leverage these strengths. In addition to laboratory based studies, I also have maintain a limited clinical practice as a transplant nephrologist.

1. Liu X, Karnell JL, Yin B, Zhang R, Zhang J, Li P, Choi Y, Maltzman JS, Pear WS, Bassing CH, Turka LA. Distinct roles for PTEN in prevention of T cell lymphoma and autoimmunity in mice. J Clin Invest. 2010 Jul;120(7):2497-507. PubMed PMID: 20516645; PubMed Central PMCID: PMC2898609.
2. Wiehagen KR, Corbo E, Schmidt M, Shin H, Wherry EJ, Maltzman JS. Loss of tonic T-cell receptor signals alters the generation but not the persistence of CD8+ memory T cells. Blood. 2010 Dec 16;116(25):5560-70. PubMed PMID: 20884806; PubMed Central PMCID: PMC3031404.
3. Wu GF, Corbo E, Schmidt M, Smith-Garvin JE, Riese MJ, Jordan MS, Laufer TM, Brown EJ, Maltzman JS. Conditional deletion of SLP-76 in mature T cells abrogates peripheral immune responses. Eur J Immunol. 2011 Jul;41(7):2064-73. PubMed PMID: 21469089; PubMed Central PMCID: PMC3124603.
4. Corbo-Rodgers E, Wiehagen KR, Staub ES, Maltzman JS. Homeostatic division is not necessary for antigen-specific CD4+ memory T cell persistence. J Immunol. 2012 Oct 1;189(7):3378-85. PubMed PMID: 22956580; PubMed Central PMCID: PMC3448874.

B. Positions and Honors

Positions and Employment

1997 - 1998	Internship, Department of Internal Medicine, University of Chicago Hospitals
1998 - 2000	Residency, Department of Internal Medicine, University of Chicago Hospitals
2000 - 2003	Fellowship, Nephrology, Hospital of the University of Pennsylvania
2001 - 2006	Post-doctoral fellowship, Immunology, Gary Koretzky, PI, University of Pennsylvania
2001 - 2008	Attending Physician, Penn Presbyterian Medical Center
2001 - 2009	Attending Physician, Philadelphia VAMC
2001 - 2015	Attending Physician, Hospital of the University of Pennsylvania
2003 - 2004	Research Associate in Medicine, Department of Medicine, Renal Electrolyte and Hypertension Division, University of Pennsylvania School of Medicine
2004 - 2006	Instructor A in Medicine, Department of Medicine, Renal-Electrolyte and Hypertension Division, University of Pennsylvania School of Medicine
2006 - 2015	Assistant Professor in Medicine, University of Pennsylvania
2015 -	Associate Professor, Stanford University
2015 -	Staff Physician, Palo Alto VA

Other Experience and Professional Memberships

2001 -	Member, American Society of Nephrology
2001 -	Member, American Society of Transplantation
2005 -	Member, American Association of Immunologists
2010 - 2012	Member, Basic Science Advisory Council, American Society of Transplantation
2011 -	Member, Federation of Clinical Immunological Societies (FOCIS)
2011 -	Member, American Heart Association
2011 - 2011	Reviewer - Human autoimmunity memory program, Juvenile Diabetes Research Foundation
2011 - 2011	Ad Hoc reviewer, University of Kansas COBRE Pilot grants
2011 - 2012	Co-Chair, Basic Science Advisory Council, American Society of Transplantation
2012 - 2013	Member, Awards and Nominations Committee, American Society of Transplantation
2012 - 2014	Chair, Community of Basic Scientists, American Society of Transplantation
2013 -	Pilot & Feasibility Grant Reviewer, University of Michigan Kidney Translational Core Center
2013 - 2013	Reviewer - Innovative Research Grant in Basic Science, American Heart Association
2013 - 2015	Chair, FOCIS Education Committee, Federation of Clinical Immunological Societies
2013 - 2015	Co-organizer (chair 2015), Cutting Edge in Transplantation meeting/AST
2014 -	Past-chair, Community of Basic Scientists, American Society of Transplantation
2014 -	Member, Board of Directors, Federation of Clinical Immunological Societies
2014 - 2014	ZRG1 IMM-K (81) study section, NIH
2014 - 2014	ZRG1 F07-K (20) study section, NIH
2014 - 2014	Ad hoc grant reviewer, Israeli Science Foundation
2015 - 2015	Reviewer - Innovative Research Grant in Basic Science, American Heart Association

Honors

1988	New England Company Award for Undergraduate Research, MIT
1989	Medical Scientist Training Grant, NIH
1989	Elected Membership, Sigma Xi
1989	Elected Membership, Phi Beta Kappa
1996	Morton McCutcheon Memorial Prize for Meritorious Research in Experimental Pathology, University of Pennsylvania

1999	Vignette Competition Prize winner, American Colllege of Physicians Illinois Associates
2002	Renal Fellow Teaching Award, Hospital of the University of Pennsylvania
2002	AST-Novartis Fellowship in Transplantation, American Society of Transplantation
2007	Austrian Award for Junior Faculty (bench science), University of Pennsylvania
2007	John Merrill Grant in Transplantation, American Society of Nephrology/American Society of Transplantation
2009	Barra New Research Initiative Award, University of Pennsylvania
2012	Elected Member, American Society of Clinical Investigation
2012	Basic Science Career Development Award, American Society of Transplantation

C. Contribution to Science

1. I have a long-standing interest in understanding the requirements molecular mechanisms of signaling molecules in primary T lymphocytes. During my time in Gary Koretzky's laboratory, I generated conditional mice for the adaptor protein SLP-76. I was the first to show that SLP-76 expression is required for efficient positive and negative selection during development of T lymphocytes in the thymus. As an independent investigator, I significantly extended this model and was among the first to combine temporally controlled conditional deletion approaches with immune responses. Initially, using Cre-recombinase protein transduction we showed that continued SLP-76 expression is required for CD4+ memory T cell generation and turnover using an in vitro model. We then developed and an in vivo approach and showed that SLP-76 expression is critical for activation of normally developed naïve T cells and loss of the molecule was protective in an autoimmune model of disease. To rigorously address T cell memory, we were the combined temporal deletion with in vivo infection and diffinitively showed that generation but not persistence of immune memory depends on continuous antigenc and tonic T cell receptor signals. Importantly, these studies also uncoupled homeostatic division from persistence of CD4 memory T cells. In addition to work on SLP-76 we have investigated dependence of in vivo T cell responses on the adaptor MyD88 and the lipid phosphatase PTEN.

    a. Maltzman JS, Kovoor L, Clements JL, Koretzky GA. Conditional deletion reveals a cell-autonomous requirement of SLP-76 for thymocyte selection. J Exp Med. 2005 Oct 3;202(7):893-900. PubMed PMID: 16186188; PubMed Central PMCID: PMC2213170.
    b. Wiehagen KR, Corbo E, Schmidt M, Shin H, Wherry EJ, Maltzman JS. Loss of tonic T-cell receptor signals alters the generation but not the persistence of CD8+ memory T cells. Blood. 2010 Dec 16;116(25):5560-70. PubMed PMID: 20884806; PubMed Central PMCID: PMC3031404.
    c. Wu GF, Corbo E, Schmidt M, Smith-Garvin JE, Riese MJ, Jordan MS, Laufer TM, Brown EJ, Maltzman JS. Conditional deletion of SLP-76 in mature T cells abrogates peripheral immune responses. Eur J Immunol. 2011 Jul;41(7):2064-73. PubMed PMID: 21469089; PubMed Central PMCID: PMC3124603.
    d. Corbo-Rodgers E, Wiehagen KR, Staub ES, Maltzman JS. Homeostatic division is not necessary for antigen-specific CD4+ memory T cell persistence. J Immunol. 2012 Oct 1;189(7):3378-85. PubMed PMID: 22956580; PubMed Central PMCID: PMC3448874.

2. My laboratory has been active in using novel approaches to generate and understand reagents used to investigate the immune response. During my time as an independent investigator, the laboratory helped to pioneer temporal deletion during immune responses (in part described in contribution #1). The hurdle we faced was that germline or tissue specific (T cell specific) deletion strategies often altered thymocyte development leading to abnormal peripheral T cells. To rigorously investigate dependence of peripheral naive or memory T cells we began using drug inducible -- tamoxifen regulated -- cre recombinases. The laboratory

further found that medicated chow could unexpectedly activate this Cre recombinase in the absence of tamoxifen and reported this finding to the research community as a warning to other investigators. Lastly, the laboratory generated the construct used for a nur77 reporter mouse that is commonly used as an indicator of TCR signal strength.

a. Maltzman JS, Turka LA. Conditional gene expression: a new tool for the transplantologist. Am J Transplant. 2007 Apr;7(4):733-40. PubMed PMID: 17391118.
b. Moran AE, Holzapfel KL, Xing Y, Cunningham NR, Maltzman JS, Punt J, Hogquist KA. T cell receptor signal strength in Treg and iNKT cell development demonstrated by a novel fluorescent reporter mouse. J Exp Med. 2011 Jun 6;208(6):1279-89. PubMed PMID: 21606508; PubMed Central PMCID: PMC3173240.

3. Understanding of T regulatory cell homeostasis. The laboratory has a longstanding interest in fundamental aspects of immune cell biology relating to solid organ transplantation. Regulatory T cells are critical in acceptance of solid organ allografts. We have used in vivo mouse approaches both in the lab and collaboratively with others to definitively show that SLP-76 dependent T cell receptor signals are critical both as a cell intrinsic pathway and for production of IL2 by conventional T cells that acts as an extrinsic growth factor. We also collaborated to show that CD28 costimulatory signals are critical for Treg homeostasis and function.

a. Lieberman SM, Kim JS, Corbo-Rodgers E, Kambayashi T, Maltzman JS, Behrens EM, Turka LA. Site-specific accumulation of recently activated CD4+ Foxp3+ regulatory T cells following adoptive transfer. Eur J Immunol. 2012 Jun;42(6):1429-35. PubMed PMID: 22678899; PubMed Central PMCID: PMC3664195.
b. Zou T, Satake A, Corbo-Rodgers E, Schmidt AM, Farrar MA, Maltzman JS, Kambayashi T. Cutting edge: IL-2 signals determine the degree of TCR signaling necessary to support regulatory T cell proliferation in vivo. J Immunol. 2012 Jul 1;189(1):28-32. PubMed PMID: 22623329; PubMed Central PMCID: PMC3381992.
c. Zhang R, Huynh A, Whitcher G, Chang J, Maltzman JS, Turka LA. An obligate cell-intrinsic function for CD28 in Tregs. J Clin Invest. 2013 Feb;123(2):580-93. PubMed PMID: 23281398; PubMed Central PMCID: PMC3561819.
d. Schmidt AM, Lu W, Sindhava VJ, Huang Y, Burkhardt JK, Yang E, Riese MJ, Maltzman JS, Jordan MS, Kambayashi T. Regulatory T cells require TCR signaling for their suppressive function. J Immunol. 2015 May 1;194(9):4362-70. PubMed PMID: 25821220; PubMed Central PMCID: PMC4402269.

Complete List of Published Work in My Bibliography:
http://www.ncbi.nlm.nih.gov/myncbi/jonathan.maltzman.1/bibliography/41159398/public/?sort=date&direction=ascending

D. Research Support

Ongoing Research Support

R01 AI085160-05 MALTZMAN, JONATHAN S (PI) 06/01/10-05/31/16
Signals Affecting Homestasis and Tolerance in Memory T Cells
Role: PI

R56 AI108786-01 MALTZMAN, JONATHAN S (PI) 09/01/14-08/31/16
Foxp transcription factors in regulatory T cell development and homeostasis
Role: PI

Completed Research Support

K08 AI055806-01 MALTZMAN, JONATHAN S (PI) 09/01/03-05/31/07
Role of SLP-76 in Naive and Memory T Cell Function
Role: PI

T32 DK007006-28 MADAIO, MICHAEL P (PI) 07/01/75-06/30/05
RENAL RESEARCH TRAINING PROGRAM
Role: TA

13IRG13640024, American Heart Association MALTZMAN, JONATHAN S (PI) 01/01/13-06/30/15
Immunity to cytomegalovirus as a biomarker
The goals of this proposal is to determine the specificity and polyfunctionality of CMV-specific memory T cells prior to and following transplantation and correlate with CMV disease post-transplant in cardiac and renal transplant recipients not undergoing regimens involving lymphodepletion as well as to determine CMV specificity and polyfunctionality of CMV-specific memory T cells post recovery from lymphodepleting induction regimens and correlate with pre-existing repertoire and CMV disease post-transplant.
Role: PI

R01-HL111501, NHI/NIAID Kambayashi (PI) 06/08/11-05/30/15
The role of the T cell receptor in regulatory T cell homeostasis and expansion
The major goals of this project are to determine the role of T cell receptor signaling in regulatory T cell homeostasis and expansion. These findings will be translated to a clinically applicable model of graft-versus-host disease (GVHD) to increase the effectiveness of conventional GVHD therapies.
Role: Co-Investigator

R01DK055852, NIH/NIDDK Gasser (PI) 04/01/09-03/31/13
Spontaneous tubulointerstitial nephritis in kd/kd mice
Mice homozygous for the kd/kd mutation have defects in Pdss2 gene and develop spontaneous interstitial nephritis and significant proteinuria. The overall goal of this project is to determine the mechanisms underlying the kidney disease and inflammation.
Role: Co-Investigator

R01AI058019, NIH/NIAID Koretzky (PI) 07/01/10-01/31/11
Regulation of T cell and mast cell function by DGKz
Role: Co-Investigator

John Merrill Grant, American Society of Nephrology/American Society of Transplantation Maltzman (PI) 07/01/07-12/31/10
Role of adaptor proteins in Regulatory T cell proximal signaling
Role: PI

AST-Novartis Fellowship, American Society of Transplantation Maltzman (PI) 07/01/02-08/31/03
ADAP Isoforms in T lymphocytes
Role: PI