BIOGRAPHICAL SKETCH

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NAME: Maltzman, Jonathan S.

eRA COMMONS USER NAME (credential, e.g., agency login): MALTZMAN

POSITION TITLE: Staff Physician; Associate Professor of Medicine

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE	Completion Date MM/YYYY	FIELD OF STUDY
Massachusetts Institute of Technology, Cambridge, MA	BS	05/1989	Biology
University of Pennsylvania, Philadelphia, PA	MD	05/1997	Medicine
University of Pennsylvania, Philadelphia, PA	PhD	06/1997	Immunology
Post-Doctoral Fellowship; Gary Koretzky, University of Pennsylvania, Philadelphia, PA	OTH	06/2006	Immunology

A. Personal Statement

I have been an independent investigator for a period of approximately 20 years since completing clinical training in Nephrology and post-doctoral training in Immunology. I was recruited to Stanford University and the VA Palo Alto Health Care System (VAPAHCS) in August 2015. My laboratory has a longstanding interest in understanding fundamental aspects of immunological memory and regulation and their relationship to solid organ transplantation. 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 among the first to use tamoxifen-mediated temporal deletion to study signal transduction in mature T lymphocytes. I have experience in cellular and molecular immunology and have a long track record of productive collaboration to leverage these strengths. I have invested heavily in developing techniques to study human immunology at a fundamental level and have applied this to the study of immune response following solid organ transplantation, recently linking immune responses to accelerated immune aging in CMV seropositive transplant recipients. With the SARS-CoV-2 pandemic, the lab began studying immune responses to the virus and vaccination in transplant recipients. In addition to laboratory-based studies, I have a strong interest in the education of undergraduates, medical students, medical residents and fellows, and PhD graduate students and post-docs. This includes involvement in MSTP, physician-scientist residency programs, didactic sessions, fellowship training and importantly individualized training in my laboratory resulting in multiple first-author manuscripts in peer review journals from the trainees – some of which are listed below. In addition, I have maintained a limited clinical practice as a transplant nephrologist.

Ongoing and recently completed projects from the past three years that I would like to highlight include:

I01CX001971; Veterans Administration Clinical Science R&D
Maltzman (PI)
10/01/19-06/30/24 (NCE)
Immune control of chronic viral infection in solid organ transplantation

I01BX005142-01A1; Veterans Administration Biomedical Laboratory R&D
Maltzman (PI)
01/01/21-12/31/24
Foxp transcription factors in regulatory T cells

R21 AI171923-01A1: NIH/NIAID
Maltzman (MPI)
8/21/2023-7/31/2024
Deciphering the Molecular Mechanisms of Response to COVID Vaccine in Kidney Transplant Recipients

Citations:

1. Corbo-Rodgers E, Staub ES, Zou T, Smith A, Kambayashi T, **Maltzman JS**. Oral ivermectin as an unexpected initiator of CreT2-mediated deletion in T cells. Nat Immunol. 2012 Feb 16;13(3):197-8. PMCID: PMC4508671.
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. PMCID: PMC3031404.
3. Higdon LE, Gustafson CE, Ji X, Sahoo MK, Pinsky BA, Margulies KB, Maecker HT, Goronzy J, **Maltzman JS**. Association of Premature Immune Aging and Cytomegalovirus after Solid Organ Transplant. Front Immunol. 2021 May;12:661551. PMCID: PMC8190404.
4. Higdon LE, Schaffert S, Huang H, Montez-Rath ME, Lucia M, Jha A, Saligrama N, Margulies KB, Martinez OM, Davis MM, Khatri P, **Maltzman JS**. Evolution of Cytomegalovirus-Responsive T Cell Clonality following Solid Organ Transplantation. J Immunol. 2021 Oct 15;207(8):2077-2085. doi: 10.4049/jimmunol.2100404. Epub 2021 Sep 22. PMCID: PMC8492537.

B. Positions, Scientific Appointments, and Honors

Positions and Scientific Appointments

2023	Conferral of Tenure, Stanford University
2022 -	Investigator, Geriatric Research and Education Clinical Center, VA Palo Alto
2020 -	Scientific Advisory Board, Qihan Biotech
2018 - 2021	Board of Directors, American Society of Transplantation
2018 - 2020	Member, Kidney Week Education Committee/ASN
2017 -	Secretary / Treasurer, Federation of Immunology Societies
2017 - 2019	Chair, Transplantation and Immunology Research Network/AST
2016 - 2020	Federation of Clinical Immunological Societies, Steering Committee
2015 -	Associate Professor of Medicine, Stanford University, Stanford, CA
2015 -	Director, Basic Science Research, Division of Nephrology, Stanford University, Stanford, CA
2015 -	Staff Physician, VA Palo Alto Health Care System, Palo Alto, CA
2015 - 2018	Adjunct Associate Professor of Medicine, University of Pennsylvania, Philadelphia, PA
2015	Reviewer - Innovative Research Grant in Basic Science, American Heart Association
2014 - 2019	Steering Committee, Virtual Global Transplantation Laboratory
2014 - 2015	Board of Directors, Federation of Clinical Immunological Societies
2014	Ad hoc grant reviewer, Israeli Science Foundation
2014	ZRG1 F07-K (20) study section, NIH
2014	ZRG1 IMM-K (81) study section, NIH
2013 - 2020	Committee Member, Transplantation and Immunology Research Network/AST
2013 - 2015	Co-organizer (Chair 2015), Cutting Edge in Transplantation meeting/AST
2013 - 2015	Chair, FOCIS Education Committee, Federation of Clinical Immunological Societies
2013	Pilot & Feasibility Grant Reviewer, University of Michigan Kidney Translational Core Center
2013	Reviewer - Innovative Research Grant in Basic Science, American Heart Association
2012 - 2016	Chair/Past-Chair, Community of Basic Scientists, American Society of Transplantation
2012 - 2013	Member, Awards and Nominations Committee, American Society of Transplantation
2011 -	Member, American Heart Association
2011 -	Member, Federation of Clinical Immunological Societies (FOCIS)
2011 - 2012	Co-Chair, Basic Science Advisory Council, American Society of Transplantation
2011	Reviewer - Human Autoimmunity Memory Program, Juvenile Diabetes Research Foundation
2011	Ad Hoc reviewer, University of Kansas COBRE Pilot grants
2010 - 2015	Member, Penn Institute for Immunology, University of Pennsylvania
2010 - 2012	Member, Basic Science Advisory Council, American Society of Transplantation

2009 - 2015 Member, Abramson Cancer Center, University of Pennsylvania
2007 - 2015 Member, Penn Immunology Graduate Group
2006 - 2015 Assistant Professor in Medicine, University of Pennsylvania
2005 - Member, American Association of Immunologists
2004 - 2006 Instructor A in Medicine, Department of Medicine, Renal-Electrolyte and Hypertension Division, University of Pennsylvania School of Medicine, Philadelphia, PA
2003 - 2004 Research Associate in Medicine, Department of Medicine, Renal Electrolyte and Hypertension Division, University of Pennsylvania School of Medicine, Philadelphia, PA
2001 - Member, American Society of Transplantation
2001 - Member, American Society of Nephrology
2001 - 2015 Attending Physician, Hospital of the University of Pennsylvania, Philadelphia, PA
2001 - 2009 Attending Physician, Philadelphia VAMC
2001 - 2008 Attending Physician, Penn Presbyterian Medical Center
2001 - 2006 Post-doctoral fellowship, Immunology, Gary Koretzky, PI, University of Pennsylvania
2000 - 2003 Fellowship, Nephrology, Hospital of the University of Pennsylvania
1998 - 2000 Residency, Department of Internal Medicine, University of Chicago Hospitals
1997 - 1998 Internship, Department of Internal Medicine, University of Chicago Hospitals

Honors

2021 Basic Science Investigator Award, American Society of Transplantation
2012 Basic Science Career Development Award, American Society of Transplantation
2012 Elected Member, American Society of Clinical Investigation
2009 Barra New Research Initiative Award, University of Pennsylvania
2007 John Merrill Grant in Transplantation, American Society of Nephrology/American Society of Transplantation
2007 Austrian Award for Junior Faculty (bench science), University of Pennsylvania
2002 AST-Novartis Fellowship in Transplantation, American Society of Transplantation
2002 Renal Fellow Teaching Award, Hospital of the University of Pennsylvania
1999 Vignette Competition Prize winner, American College of Physicians Illinois Associates
1996 Morton McCutcheon Memorial Prize for Meritorious Research in Experimental Pathology, University of Pennsylvania
1989 Elected Membership, Phi Beta Kappa
1989 Elected Membership, Sigma Xi
1989 Medical Scientist Training Grant, NIH
1988 New England Company Award for Undergraduate Research, MIT

C. Contributions to Science

1. I have a long-standing interest in understanding the 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 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 combined temporal deletion with in vivo infection and definitively showed that generation but not persistence of immune memory depends on continuous antigenic 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 the 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. 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. 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. 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. 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. Corbo-Rodgers E, Staub ES, Zou T, Smith A, Kambayashi T, **Maltzman JS**. Oral ivermectin as an unexpected initiator of CreT2-mediated deletion in T cells. Nat Immunol. 2012 Feb 16;13(3):197-8. PMCID: PMC4508671.
   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. PMCID: PMC3173240.
   c. **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.

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. 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. 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. 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. PMCID: PMC4402269.

4. SARS-CoV-2 in transplant populations: SARS-CoV-2 is the etiologic agent of COVID-19. Transplant recipients are at increased risk of severe disease with infection. To best study the immune response to infection and vaccination, we have collaborated to develop and validate a multiplex assay for identification of antibodies directed against multiple SARS-CoV-2 epitopes and begun experiments to describe immune responses in humans waiting for transplant and those with solid organ cells.
   a. Gandolfini I, Zanelli P, Palmisano A, Salvetti D, Parmigiani A, **Maltzman JS**, Labate C, Fiaccadori E, Cravedi P, Maggiore U. Anti-HLA and anti-SARS-CoV-2 antibodies in kidney transplant recipients with COVID-19. Transpl Int. 2021 Jan 22; PMCID: PMC8013187

b. Bray RA, Lee JH, Brescia P, Kumar D, Nong T, Shih R, Woodle ES, **Maltzman JS**, Gebel HM. Development and Validation of a Multiplex, Bead-based Assay to Detect Antibodies Directed Against SARS-CoV-2 Proteins. Transplantation. 2021 Jan 1;105(1):79-89. PubMed PMID: 33273320.
c. Cravedi P, Ahearn P, Wang L, Yalamarti T, Hartzell S, Azzi Y, Menon M, Jain A, Billah M, Fernandez-Vina M, Gebel H, Woodle E, Haddad N, Morrison-Porter A, Lee FE, Sanz I, Akalin E, Girnita A, **Maltzman J.** Delayed Kinetics of IgG, but not IgA, Anti-spike Antibodies in Transplant Recipients following SARS-CoV-2 Infection. J Am Soc Nephrol. 2021 Oct 1:ASN.2021040573. doi: 10.1681/ASN.2021040573. Epub ahead of print. PMCID: PMC8638399.
d. Furian L, Russo FP, Zaza G, Burra P, Hartzell S, Bizzaro D, Di Bello M, Di Bella C, Nuzzolese E, Agnolon C, Florman S, Rana M, Lee JH, Kim Y, Maggiore U, **Maltzman JS**, Cravedi P. Differences in Humoral and Cellular Vaccine Responses to SARS-CoV-2 in Kidney and Liver Transplant Recipients. Front Immunol. 2022 Apr 14;13:853682. doi: 10.3389/fimmu.2022.853682. PMID: 35493446; PMCID: PMC9047689

5. Control of viral reactivation following solid organ transplantation: Solid organ transplantation requires lifelong immunosuppression which impairs immune responses that normally control latent viral infection. The laboratory has developed cutting edge techniques to examine immune responses in transplant recipients. To date, we have shown that despite a lack of detectable viremia, CD8 T cells responsive to cytomegalovirus increase rapidly following kidney and heart transplantation.
   a. Higdon LE, Trofe-Clark J, Liu S, Margulies KB, Sahoo MK, Blumberg E, Pinsky BA, **Maltzman JS** Cytomegalovirus-Responsive CD8+ T Cells Expand After Solid Organ Transplantation in the Absence of CMV Disease. Am J Transplant. 2017 Aug;17(8):2045-2054. PMCID: PMC5519416.
   b. Higdon LE, Gustafson CE, Ji X, Sahoo MK, Pinsky BA, Margulies KB, Maecker HT, Goronzy J, **Maltzman JS**. Association of Premature Immune Aging and Cytomegalovirus after Solid Organ Transplant. Front Immunol. 2021 May;12:661551. PMCID: PMC8190404.
   c. Higdon LE, Schaffert S, Cohen RH, Montez-Rath ME, Lucia M, Saligrama N, Margulies KB, Martinez OM, Tan JC, Davis MM, Khatri P, **Maltzman JS**. Functional Consequences of Memory Inflation after Solid Organ Transplantation. J Immunol. 2021 Oct 15;207(8):2086-2095. doi: 10.4049/jimmunol.2100405. Epub 2021 Sep 22. PMCID: PMC8492533.
   d. Higdon LE, AA Ahmad, S Schaffert, KB Margulies and **JS Maltzman**. CMV-responsive CD4 T cells have a stable cytotoxic phenotype over the first year post-transplant. Front. Immunol. 2022. 13:904705. Doi: 10.3389/fimmu.2022.904705

Complete List of Published Work in My Bibliography:
https://www.ncbi.nlm.nih.gov/myncbi/jonathan.maltzman.1/bibliography/public/