BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME	POSITION TITLE
Matthew F. Krummel	Professor of Pathology
eRA COMMONS USER NAME (credential, e.g., agency login)	University of California-San Francisco
Krummel	

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)*	MM/YY	FIELD OF STUDY
University of Illinois at Champaign-Urbana	B.S.+B.S.	05/89	Biology and Chemistry
University of California at Berkeley	Ph.D.	05/95	Immunology
Walter and Eliza Hall Institute, Melbourne Aus.		09/97	Immunology
Stanford University.		10/01	Immunology

A. Personal Statement

My lab and I specialize in the study of the spatio-temporal dynamics of immune responses, largely using imaging approaches. We focus upon molecular mechanisms that coordinate T cell biology as well as upon cellular dynamics that result in information-sharing amongst cells of the response in vivo. In the early 2000s we described the dynamics of cluster coalescence at the immunological synapse and have since identified key Myosin motors driving cellular motility towards synapses (mid 2000s). These remain a focus of the lab as we unravel the mechanisms that control T cell movement and establishment and movement of signaling clusters. We have also described the roles of costimulation and chemokines in modulating these behaviors. In the mid-2000s, we custom-built 2-photon microscopes and related biological tools for analyzing T cell function in situ. Concurrently, are exploiting new models of human breast cancer and human lung disease to provide insight into the 4-dimensional coordination of the immune system.

B. Positions and Honors

Positions and Employment

1987 Summer Undergraduate Research Fellow. UTHSCD.
1988 Stagiare (Technician) Institut Pasteur, Paris, Unite de Genie Micro-Biologique.
1989-1996 Graduate Student and Postdoctoral Fellow, University of California at Berkeley, Department of Molecular and Cell Biology.
1996-1997 Postdoctoral Fellow, Walter and Eliza Hall Institute, Melbourne Australia.
1997-2001 Postdoctoral Fellow, Beckman Institute, Stanford University, Stanford, CA.
2001-2006 Assistant Professor, Department of Pathology, UCSF
2006-Present Associate Professor, Department of Pathology, UCSF
2006-Present Faculty Director, Biological Imaging Development Center, UCSF
2012-Present Professor, Department of Pathology, University of California at San Francisco

Honors

1985 Illinois State Scholar, National Merit scholar, Westinghouse Science Award
1986 James scholar, University of Illinois
1987 Summer Undergraduate Research Fellowship, Howard Hughes Medical Institute
1989 Luce scholars competition finalist, Henry Luce Foundation
1996-1997 Postdoctoral Fellowship, Juvenile Diabetes Foundation International
1997-2000 NRSA Postdoctoral Fellowship, National Institutes of Health
1998 PATENT: J.P.Allison, D.R.Leach, and M.F. Krummel. *Blockade of T Lymphocyte Down-*
2004-2007 Cancer Research Institute, Investigator Award
2005-2010 Leukemia and Lymphoma Foundation, Career Award
2009-2012 Fellow of the American Asthma Foundation

C. Selected peer-reviewed publications

1. **Krummel, M.F.** and Allison, J.P. 1995. CD28 and CTLA-4 have opposing signals which regulate the response of T cells to stimulation. *J. Exp Med.* **182**, 459-465. PMCID: PMC2192127
2. **Krummel, M.F.**, Sullivan, T.J. and Allison, J.P. 1995. Superantigen responses and costimulation: CD28 and CTLA-4 have opposing effects on T cell expansion *In Vitro* and *In Vivo*. *Int.Immunol.* **8**, 101-105. PMCID: 8671638
3. **Krummel, M.F.**, Sjaastad,M.D., Wülfing,C., and Davis, M.M. 2000. Differential clustering of CD4 and CD3ζ during T cell recognition. *Science*. 289, 1349-1352. PMID: 10958781
4. Moss,W.C., Irvine,D.C, Davis,M.M., and **Krummel, M.F.** 2002. Quantifying Signaling-Induced Reorientation of Cell Membrane and TCRs During Immunological Synapse Formation. *PNAS.* **99** 15024-15029. PMCID: PMC137538
5. Jacobelli, J. Chmura, S.A., Buxton,D.B., Davis , M.M. and **Krummel, M. F.** 2004. A single class II myosin modulates T cell motility and stopping, but not synapse assembly*. Nat Immunol.* **5,** 531 – 538. PMCID: 15064761
6. Friedman, R.S. Jacobelli, J, and **Krummel, M.F.** 2006. Surface-bound Chemokines Capture and Prime T cells For Synapse Formation. *Nature Immunology* **7**, 1101-8. PMID: 16964261
7. Sabatos, C.A., Doh, J. Chakravarti, S. Friedman, R.S., Pandurangi, P.G., Tooley, A.J. **Krummel, M.F**. 2008. A Synaptic Basis for Paracrine Interleukin-2 Signaling in Activating T cells. *Immunity.* **29(3**): 238-248. PMID: 18674934
8. Tooley, A.J., Gilden, J., Jacobelli, J., Trimble, W, Kinoshita, M. and **Krummel, M.F.** 2009. Amoeboid T lymphocytes require the septin cytoskeleton for cortical integrity and persistent motility. *Nat Cell Biol.* Jan;**11(1)**:17-26. Epub 2008 Nov 30. PMID: 19043408
9. Jacobelli J., Friedman R.S., Conti M.A., Lennon-Dumenil A.-M., Piel M., Sorensen C.M., Adelstein R.S., **Krummel M.F.** Confinement-optimized three-dimensional T cell amoeboid motility is modulated via myosin IIA-regulated adhesions. *Nat Immunol.* **11**: 953-961. PMCID: PMC2943564
10. Friedman, R.S., Beemiller, P., Sorensen, C.M., Jacobelli, J., **Krummel, M.F.** 2010. Real-time analysis of T cell receptors in naive cells in vitro and in vivo reveals flexibility in synapse and signaling dynamics. *J Exp Med.* **11(10)**:953-61. PMCID: PMC2989766
11. Looney, M.R., Thornton, E.E., Sen, D., Lamm, W.J., Glenny, R.W., **Krummel, M.F.** 2011. Stabilized Imaging of immune surveillance in the mouse lung. *Nat Methods.* **8(1)**:91-6. PMCID: PMC3076005
12. Englehardt, J.E., Boldajipour, B., Beemiller, P., Werb, Z., Pandurangi, P, Sorenson, C., Egelblad, M., **Krummel M.F.** Marginating dendritic cells of the tumor microenvironment cross-present tumor antigens and stably engage tumor-specific T cells. *Cancer Cell.* 2012 Mar 20;21(3):402-17. doi: 10.1016/j.ccr.2012.01.008. PMCID: PMC3311997
13. Thornton, E.E., Looney M.R., Bose, O,. Sen, D., Sheppard, D., Locksley, R., Huang, X., **Krummel, M.F**. 2012. Spatiotemporally Separated Antigen Uptake by Alveolar Dendritic Cells and Airway Presentation to T Cells in the Lung. *J Exp Med.,* 209(6) :1183-99.
14. Beemiller, P., Jacobelli, J., **Krummel, M.F.** , 2012. Integration of Signaling Microclusters Movement with Cellular Motility in Immunological Synapses. *Nat Immunol.* Jul 1. doi: 10.1038/ni.2364.
15. Gérard, A., Khan, O., Beemiller, P., Oswald, E., Hu, J., Matloubian, M., **Krummel, M.F.** 2013. Secondary T cell-T cell synaptic interactions drive the differentiation of protective CD8+ T cells. *Nat Immunol*. 2013 Mar 10. doi: 10.1038/ni.2547. [Epub ahead of print]

D. Research Support

Ongoing Support

5R01AI052116-12 (PI: Krummel) 01/15/2008-12/31/2017
NIH/NIAID

Cytoskeletal Regulation of T cell Motility and Synaptic Signaling

The major goals of this project are to analyze MyoIIA regulation during T cell motility and synapse formation. This includes mutational analyses as well as generation and analyses of knockout animals.

5U01CA141451-05 (PI: Krummel) 09/01/2009-08/31/2014
NIH/NCI
Collaborative Innate-Adaptive Immune Regulation of Tumor Progression
The major goals of this project are;
Goal 1: Visualize the progression in crosstalk between the innate and adaptive immune response during tumor development using mouse models of luminal and basal breast cancer.
Goal 2: Define the specific attractants that regulate immune cell-cell interactions in the tumor.
Goal 3: Use mouse models to determine mechanisms of existing and putative immuno- and cytotoxic anti-cancer regimens and to design and test combinatorial therapies based upon this information.

5P01HL024136-35 (PI: Caughey) 05/01/2010-03/31/2015
NIH/NHLBI
Evolving Microenvironments in Airway Inflammation
The aims of this proposal are to identify shifts in antigen-trafficking into APC, the temporal pairing of specific APC with T cell subsets, and the effects of Mycoplasma-mediated inflammation and mast-cell-mediated regulation upon T cell-APC pairing in lung microenvironments.
Role: Co-PI

5P01HL024136-35-CoreB (PI: Caughey) 05/01/2010-03/31/2015
NIH/NHLBI
Evolving Microenvironments in Airway Inflammation
Core B: This core supports the basic activities of the PPG
Role: Co-PI

5U54CA163123-03 (Multi-PIs: Coussens, Krummel, Van't Veer) 09/01/2011-08/30/2016
NIH/NCI
Leukocyte Biomarkers for Predicting Human Breast Cancer Outcome
In this proposal, we will identify clinically significant leukocyte biomarkers in breast cancer, reveal correlation of outcomes in human breast cancer with leukocyte transcriptomes and novel leukocyte biomarkers, and drive translation of leukocyte biomarkers into clinically applicable diagnostic and therapeutic probes.

5U01HL111054-03 (Multi-PIs: Chapman, Chuang, Krummel) 12/01/2011-11/30/2016
NIH/NHLBI
Epithelial Progenitor Cells in Lung Repair and Regeneration
The major objectives are (1) to define the transcriptional program of heretofore uncharacterized distal airway and alveolar progenitors and test the hypothesis that differential expression of adhesion receptors underlies the capacity of epithelial subtypes of self-organize and promote repair, (2) to define the requirement for neuroendocrine cells (PNECS) and alveolar progenitor cells in maintenance and reconstitution of distal airway and alveolar cells following lung injury, and (3) to analyze and further develop a novel, single cell in vivo lung organoid assay in kidney capsules in order to optimize the capacity of adult epithelial progenitor cells to generate functional respiratory units de nevo.

2U19A1077439-06 (Project 3 Leader) 04/01/2008 - 03/31/2018
NIH/NIAID
Program: IL-13 and IL-17 Dynamics in the Asthmatic Airway
Project 3: Dynamic Imaging of IL13/IL17 Immune Infiltrates in Asthma
Roles: Project Leader of Project 3
In conjunction with Projects 1 and 2, this project will directly analyze the unfolding of asthmatic responses in the context of the intact airway epithelium. It develops cutting-edge imaging technologies in mouse, applies them to human samples via the *Clinical Subject and Biospecimen core* and significantly develops reagents and methods that will advance our capacity to study living human biopsies at the subcellular level.

Completed Support (past 5 years)

NIH/Mouse Models Consortium 06/01/2004-05/30/2009
Immune Enhancement and Therapy of Cancer
Role: Co-Investigator

CRI/Young Investigator (PI: Krummel) 08/01/2004-02/28/2009
Synapse and Migratory Dynamics of Lymphocytes in the Tumor Microenvironment

1-2007-170 (PI: Krummel) 03/01/2007-02/28/2010
Juvenile Diabetes Research Foundation
Visualizing Feedback Loops in Type I Diabetes
The major goal for this study is our ability, for the first time, to observe autoimmune cells in their native environment and ask questions about how that environment creates feedback events that brings the disease to the forefront after many years of apparent disease-free state.

R21 RR024895 (PI: Krummel) 04/01/2008-03/31/2010
NIH/NCRR
New Models for Molecular-Level Imaging of Cell Signaling in vivo
This proposal will create new mouse strains that will permit us to look into tissues using microscopy and observe cells being activated to divide and/or remodel the tissue of which they are a part. It is important for us to understand which cells are being activated and deactivated in the context of many diseases of humans, and our results are likely to provide great insight into the nature of many of these.
Role: PI

1169-06 (PI: Krummel) 07/01/2005-06/30/2010
Leukemia and Lymphoma Society
Tumor Supressors in T cell Synapse Formation and Signaling
Aim 1. We will determine the role of Septin9/MSF in T cell synapse development, signaling, and proliferative control.
Aim 2. We will determine the role of lgl proteins in T cell synapse development, signaling, and proliferative control

09-0052 (PI: Krummel) 07/01/2009-06/30/2012
American Asthma Foundation
Directing Antigens to Specific APC and T Cell Subsets in the Lung
The major goals of this project are to screen for conditions that bias antigens towards particular antigen presenting cell populations and then to read out, through imaging and functional assays, the resulting T cell responses with the aim of optimizing regulatory interaction pathways.

1S10RR029266-01 (PI: Krummel) 06/05/2011-06/04/2013
NIH/NCRR
Multiphoton Instrumentation for Translational Assays from Human Tissue Biopsies
This equipment grant is to purchase a state-of-the art multiphoton microscope specifically configured and situated to accommodate a portfolio of translational imaging approaches and further dedicated to extension of two-photon technology to human biopsy tissues.

5R21CA167601-02 (PI: Krummel) 04/01/2012-04/30/2014
NIH/NCI
Defining the First Hours of Lung metastasis using Intravital
This proposal will apply novel intravital imaging of the lung to define the first hours following the arrival of metastatic cells into the mouse lung. As we know very little about why metastatic tumor cells survive in this environment, this represents a major undertaking in determining how to decrease their success.