OMB No. 3145-0279 (Expiration Date 10/31/2026)

NIH BIOGRAPHICAL SKETCH COMMON FORM

Name: Krummel, Matthew Frederick

Persistent Identifier (PID) of the Senior/Key Person: https://orcid.org/0000-0001-7915-3533

Position Title: Professor

Organization and Location: University of California, San Francisco, San Francisco, California, United States

PROFESSIONAL PREPARATION

INSTITUTION AND LOCATION	DEGREE	Start Date	Completion Date	FIELD OF STUDY
University of California, Berkeley, Department of Molecular and Cellular Biology, Berkeley, California, United States	Doctor of Philosophy (PHD)	09/1989	06/1995	Immunology
University College, London, England, London, Not Applicable, N/A, United Kingdom	Other (OTH)	10/1987	04/1988	Exchange Student, Department of Chemistry
University of Illinois, School of Liberal Arts and Sciences, Urbana, Illinois, United States	Bachelor of Science (BS)	08/1985	06/1989	Honors Biology and Chemistry
University of Illinois High School, Urbana, Illinois, United States	High School (or GED Equivalent) (HS)	08/1980	05/1985	General

Appointments and Positions

2012 - present	Professor, University of California, San Francisco, San Francisco, California, United States
2018 - present	Co-Founder and Inaugural Chair, University of California, San Francisco/ ImmunoX Initiative, San Francisco, California, United States
2015 - 2016	Visiting Sabbatical Scholar, Mediterranean Institute for Advanced Studies, Aix-Marseille Univeristy, Marseille, Not Applicable, N/A, France
2008 - 2009	Visiting Sabbatical Scholar, Institut Curie, Paris, Not Applicable, N/A, France
2006 - present	Faculty Director, University of California, San Francisco/Biological Imaging Development Center, San Francisco, California, United States
2006 - 2011	Associate Professor, Department of Pathology, University of California, San Francisco, San Francisco, California, United States
2001 - 2006	Assistant Professor, Department of Pathology, University of California, San Francisco, San Francisco, California, United States
1997 - 2001	Postdoctoral Fellow, HHMI, Beckman Institute, Stanford University. Advisor: Dr. Mark M. Davis, Stanford, California, United States
1996 - 1997	Postdoctoral Fellow, Dendritic Cell Biology, Walter and Eliza Hall Institute. Advisors: Dr. Bill Heath and Dr. Ken Shortman , Melbourne, Not Applicable, N/A, Australia
1995 - 1996	Postdoctoral Fellow, MCB, UC Berkeley. Advisor: Dr. James P. Allison, MCB, Berkeley, California, United States
1989 - 1995	Graduate Research Assistant, MCB, UC Berkeley. Advisor: Dr. James Allison, Berkeley, California, United States
1988 - 1988	Stagiare (Technician), UGM, UGM, Institut Pasteur. Advisors: Dr. Julian Davies and Dr. Tom Holt, Paris, Not Applicable, N/A, France
1987 - 1987	HHMI Summer Fellow, Neurobiology, UTHSC Dallas. Advisor: Dr. Flora Katz, Dallas, Texas, United States

Products

Products Closely Related to the Proposed Project

1. Combes AJ, Samad B, Tsui J, Chew NW, Yan P, Reeder GC, Kushnoor D, Shen A, Davidson B, Barczak AJ, Adkisson M, Edwards A, Naser M, Barry KC, Courau T, Hammoudi T, Argüello RJ, Rao AA, Olshen AB, Cai C, Zhan J, Davis KC, Kelley

RK, Chapman JS, Atreya CE, Patel A, Daud AI, Ha P, Diaz AA, Kratz JR, Collisson EA, Fragiadakis GK, Erle DJ, Boissonnas A, Asthana S, Chan V, Krummel MF. Discovering dominant tumor immune archetypes in a pan-cancer census. Cell. 2022 Jan 6;185(1):184-203.e19. PubMed Central PMCID: PMC8862608.

2. Hu KH, Kuhn NF, Courau T, Tsui J, Samad B, Ha P, Kratz JR, Combes AJ, Krummel MF. Transcriptional space-time mapping identifies concerted immune and stromal cell patterns and gene programs in wound healing and cancer. Cell Stem Cell. 2023 Jun 1;30(6):885-903.e10. PubMed Central PMCID: PMC10843988.
3. Kersten K, Hu KH, Combes AJ, Samad B, Harwin T, Ray A, Rao AA, Cai E, Marchuk K, Artichoker J, Courau T, Shi Q, Belk J, Satpathy AT, Krummel MF. Spatiotemporal co-dependency between macrophages and exhausted CD8(+) T cells in cancer. Cancer Cell. 2022 Jun 13;40(6):624-638.e9. PubMed Central PMCID: PMC9197962.
4. Courau T, Desai A, Wagner A, Combes AJ, Krummel MF. The coming era of nudge drugs for cancer. Cancer Cell. 2025 Nov 10;43(11):1973-1979. PubMed PMID: 40939589.
5. Mujal AM, Combes AJ, Rao AA, Binnewies M, Samad B, Tsui J, Boissonnas A, Pollack JL, Argüello RJ, Meng MV, Porten SP, Ruhland MK, Barry KC, Chan V, Krummel MF. Holistic Characterization of Tumor Monocyte-to-Macrophage Differentiation Integrates Distinct Immune Phenotypes in Kidney Cancer. Cancer Immunol Res. 2022 Apr 1;10(4):403-419. PubMed Central PMCID: PMC8982148.

Other Significant Products Highlighting Contributions to Science

1. Cai E, Marchuk K, Beemiller P, Beppler C, Rubashkin MG, Weaver VM, Gérard A, Liu TL, Chen BC, Betzig E, Bartumeus F, Krummel MF. Visualizing dynamic microvillar search and stabilization during ligand detection by T cells. Science. 2017 May 12;356(6338) PubMed Central PMCID: PMC6364556.
2. Krummel MF, Allison JP. CD28 and CTLA-4 have opposing effects on the response of T cells to stimulation. J Exp Med. 1995 Aug 1;182(2):459-65. PubMed Central PMCID: PMC2192127.
3. Broz ML, Binnewies M, Boldajipour B, Nelson AE, Pollack JL, Erle DJ, Barczak A, Rosenblum MD, Daud A, Barber DL, Amigorena S, Van't Veer LJ, Sperling AI, Wolf DM, Krummel MF. Dissecting the tumor myeloid compartment reveals rare activating antigen-presenting cells critical for T cell immunity. Cancer Cell. 2014 Nov 10;26(5):638-52. PubMed Central PMCID: PMC4254577.
4. Mujal AM, Krummel MF. Immunity as a continuum of archetypes. Science. 2019 Apr 5;364(6435):28-29. PubMed PMID: 30948539.
5. Headley MB, Bins A, Nip A, Roberts EW, Looney MR, Gerard A, Krummel MF. Visualization of immediate immune responses to pioneer metastatic cells in the lung. Nature. 2016 Mar 24;531(7595):513-7. PubMed Central PMCID: PMC4892380.

Certification:

I certify that the information provided is current, accurate, and complete. This includes, but is not limited to, information related to current, pending, and other support (both foreign and domestic) as defined in 42 U.S.C. § 6605.

In accordance with Section 10632 of the CHIPS and Science Act of 2022 (42 U.S.C. § 19232), each individual identified as a senior/key person must certify that they are not a party to a malign foreign talent recruitment program.

Research Security Training Requirement for Federal Award Personnel: In accordance with Section 10634 of the CHIPS and Science Act of 2022 (42 U.S.C. § 19234), each individual identified as a senior/key person must certify that they have completed the requisite research security training that meets the requirements specified in Item 2 of Important Notice No. 149 within 12 months prior to proposal submission.

Misrepresentations and/or omissions may be subject to prosecution and liability pursuant to, but not limited to, 18 U.S.C. §§287, 1001, 1031 and 31 U.S.C. §§3729-3733 and 3802.

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NIH BIOGRAPHICAL SKETCH SUPPLEMENT

Name: Krummel, Matthew Frederick

Persistent Identifier (PID) of the Senior/Key Person: https://orcid.org/0000-0001-7915-3533

Position Title: Professor

Organization and Location: University of California, San Francisco, San Francisco, California, United States

Personal Statement

My lab specializes in the discovery and targeting of archetypal collections of immune systems, notably those involving networks of cells built around T cell-myeloid interaction. Our work spans scales from membrane organization, to cell biology, to entire immune systems. We focus on figuring out how immune systems, collections of cells in complex tissues, work. At the subcellular scale, we utilize high-resolution imaging, in order to understand how immune cell interact so efficiently. We often capitalize on combinations of in-house and externally generation innovations in spatial imaging and systems biology. At larger scales, my lab explores how information is exchanged in the dense cellular milieu of organs and this utilizes modalities as diverse as microscopy, genomics, and cytometry. This led, for example, to the first isolation and characterization of intratumoral Dendritic cells in cancers, demonstrating existing pathways for stimulating T cells in tumor and their draining lymph nodes.

Related to this Program Project, our lab built the UCSF Immunoprofiler.org platform to understand the shared and unique biology of tissue immunity. Our lab also co-founded the ImmunoX initiative, a radical collaboration platform focused on methods and data sharing as a means to accelerate discovery and cures, and built a series of linked cores called ‘CoLabs’, which play an integral role in the success of this project. My science has led to numerous clinical advances that started with my co-invention of anti-CTLA-4 ‘checkpoint blockade’ drugs (over 100,000 patients treated) as a graduate student and has extended to myeloid-tuning and other immune-engineering approaches, largely in cancer. The aim of all of my research is to understand and apply the immune system to improve human health.

Honors

2020	Dial Fellowship, Emerson Collective
2016	Robert E. Smith Endowed Chair in Experimental Pathology, University of California, San Francisco
2013	Pediatrics FLAG Mentorship Award, University of California, San Francisco
2009	Fellow , American Asthma Foundation
2005	Career Award, Leukemia and Lymphoma Foundation
2004	Investigator Award, Cancer Research Institute
1997	NRSA Postdoctoral Fellowship, National Institutes of Health
1996	Postdoctoral Fellowship, Juvenile Diabetes Foundation International
1989	Luce Scholars Competition Finalist, Henry Luce Foundation
1986	James Scholar, University of Illinois
1985	Illinois State Scholar, National Merit Scholar, Westinghouse Science Award

Contributions to Science

1. Invention of Two Major Classes of Immunotherapy: Checkpoint Blockade and Myeloid Tuning. My PhD. demonstrated that T cells express the CD28-homolog, CTLA-4, after activation. I generated mouse antibodies to these and demonstrated that engagement of CTLA-4 by antibodies or by its ligand resulted in dampening of T cell responses. I also demonstrated that this same antibody upregulated T cell responses in vivo serving as the method that we applied across multiple mouse models including augmenting anti-tumor immunity. Together with Jim Allison and Dana Leach, we patented CTLA-4 blockade, now ‘Checkpoint Blockade’ Therapy. The FDA approved anti-CTLA-4, as the first FDA approved ‘checkpoint blockade’ drug in cancer, in 2011 and this work formed the basis for the 2018 Nobel Prize in Medicine (awarded to Jim). In 2015 my lab moved myeloid targets from the TME into a UCSF-associated startup and in 2020 we filed INDs and initiated Phase I trials in cancer patients using anti-TREM1 and anti-TREM2 antibodies we developed. This work and related immune modulation continues in the lab today.

2. Identification of Reactive Immunity, centered on DC, in Tumors. Because of item 1 (specifically checkpoint blockade), the field had known that the immune system could be augmented to achieve tumor reactivity, but we didn't know the degree to which tumors might harbor vestiges of stimulatory immune systems. My laboratory developed mouse models through which to image the T cell-APC dynamics within spontaneous tumors in living animals. This allowed us to track antigen-presentation pathways and to identify sites and APC subsets involved in immune subversion. This was notable in Broz et al. 2014 (reference in main biosketch) that first isolated and fully characterized (IRF8, Flt3L, BATF3 dependency, ability to cross-present, ability to stimulate CD8 T cells, formation of clusters with CD8 cells) what are now termed tumor cDC1. Follow on work refined that NK cells are part of these (now sometimes termed 'hubs') and that regulatory cells limited tumor DC function. Ours was the first that also tied the frequencies of cDC1 to responder status for anti-PD1 therapies.

3. An Archetype Theory of Immunobiology, from Cancer to COVID. While item 2 showed that tumor immune systems harbored vestiges of stimulatory capacity, we wondered what the immune system was doing in tumors, if not rejecting them. We set up to study this by assembling a large dataset from 15 tumor types, all-comers. We hypothesize in a Science article (Muhal et al 2019) that a complete view of the immune system might have to include its now-apparent roles in many physiological functions beyond defense-against-pathogens. We suggested also that tumor would exploit these other functions (these 'archetypes' of immunity). In the past ten years, my lab has invested heavily to test the hypothesis of and define the nature of archetypal immunobiology—collections of cell types, linked gene expression and spatial co-localization that define normal and diseased tissues. In Combes et al, Cell 2022, we showed that tumors neatly fit into a dozen or so immunological archetypes and other works from our lab and others appear to corroborate this. This idea includes our hypothesis in this grant, that each archetype may be subject to a series of perturbations that will move it toward remission, an idea that our PPG team formalized in a theory paper in 2025.

4. T cell sensitivity and discrimination. Stemming from our success in understanding the regulation of T cells by checkpoint molecules and in order to move 'beyond' checkpoint blockade as I built a career, I focused a portion of my energies on understanding the fundamentals of T cell reactivity. We did this by building high-resolution microscopes, first that could capture full 3D scans of the T cell densities of TCR and costimulatory receptors at 2 second collection speeds, which allowed us to watch TCR synapse assembly concomitant with calcium signaling. As our microscopy got better and better, we were able to understand also how TCRs assemble on microvillar spikes (Cai et al Science reference above) and most recently to uncover how this surface topology is helping to allow the same antigens to present in tolerizing and activating formats. This also led to related studies of how molecules like MyosinIIA, Myo1g and Septin molecules could all control how efficiently T cells migrate through tissues to scan them. In Cai et al for example, we were able to show that TCR half-lives, microvillar-dwell times and T cell crawling rates are all optimized to make T cells the most efficient at scouring for antigens. These imaging studies, incidentally, also first highlighted T-T signaling since we observed T cells forming junctions with one another and showed how these led to increased T cell activation. That work also influenced and continues to influence our and the fields understanding of the importance of multi-cellular aggregates (see items 2 and 3 above).

5. Spatial and Real-Time Dynamics of Immune Responses in Tissue. and Lung Using Combinations of Custom-Built Multiphoton Microscopes and Matched Stabilization Methods. We have made substantial advances (and many of my ex-postdocs built academic labs and careers) on the unveiling of how immunity works in real time in a variety of settings. As per item 2 above, it was this work that motivated the Broz 2014 work that first identified stimulatory cDC1 and what are now termed 'hubs' of immune reactivity in tumors. Headley et al (see main biosketch) was also able to show how metastatic tumor cells initially begin to program distant organs using these tools. Various other lab members focused on lymph nodes and pancreas to understand how immune responses develop and expand in these settings. This has been formative in setting the stage for our (and often their) subsequent mechanistic studies. The work is also very influential in designing experiments for spatial sequencing approaches, some of which we've developed in-house in the past few years.

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