

BIOGRAPHICAL SKETCH

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NAME: Utz, Paul J.

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POSITION TITLE: Professor of Medicine

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

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
King's College, Wilkes-Barre, PA	BS	06/1986	Biology
Stanford University School of Medicine	MD	06/1991	Medicine
Brigham and Women's Hospital, Boston, MA	Intern	06/1991- 06/1992	Internal Medicine
Brigham and Women's Hospital, Boston, MA	Resident	06/1992- 06/1993	Internal Medicine
Brigham and Women's Hospital, Boston, MA	Clinical Fellow	07/1993- 02/1996	Immunology and Rheumatology

A. Personal Statement: I am a physician scientist who has dedicated my career to understanding and curing human rheumatic diseases; to building a physician scientist pipeline that extends from high school students all the way to scientists in academia, industry, and government; and to promoting team science and interdisciplinary research. I direct a research lab in the Department of Medicine, Division of Immunology at Stanford University School of Medicine. My lab actively collaborates with many investigators on the Stanford campus, and across the world, with a goal to disseminate and implement newly-invented technologies. We study vaccines and autoimmune diseases, including systemic lupus erythematosus (SLE), scleroderma, rheumatoid arthritis (RA), myositis, primary biliary cirrhosis (PBC), Sjögren's disease, type I diabetes (T1D), vasculitis, multiple sclerosis (MS), immunodeficiency disorders, COVID-19 related autoimmunity, mixed connective tissue disease (MCTD), and autoimmunity induced by infections. In addition to trying to better understand the pathogenic mechanisms involved in autoimmunity, we are interested in developing bench-to-bedside technologies, including multiplexed diagnostics and therapeutics, for human immune diseases. Our group made several breakthrough inventions, such as protein arrays, peptide arrays, HIT, lysate arrays, Intel arrays, and more recently EpiTOF. In terms of leadership, I have extensive expertise in coordinating close to 15 different program project grants over the last 15 years, including PI of our Autoimmunity Center of Excellence, and Leadership Center PI for the \$41M Accelerating Medicines Partnership in RA/SLE initiative, Co-PI of Stanford's RECOVER program, and PI on biomarker studies for Pfizer's STOP-PASC Paxlovid trial. I was selected as Vice Chair of RECOVER's Immunology and Hematology Pathobiology Task Force Committee and currently serve on the RECOVER OCSC Steering Committee. In 2018, I was appointed Associate Dean of Medical Student Research, and I am the Director Emeritus of the Stanford MSTP. I have been a member of the MSTP Admissions Committee for over 20 years, served as Associate Director and Co-Director from 2009-2013, and directed the MSTP until 2018. I am a leader in educational initiatives. I was the first Chair of Education for the Federation of Clinical Immunology Societies. I founded and direct the Stanford Institutes of Medicine Research (SIMR) Program for high school students, which has hosted over 1,000 students in labs over 25 years. SIMR has been funded by educational grants from NIH, HHMI, CIRM, DDCF, Amgen Foundation, industry, and philanthropy. It serves as an important pipeline program for MSTP. I have served on the Immunology Program Predoctoral Committee and have won teaching and mentoring awards from the Immunology PhD Program and the Department of Medicine. In the last 25 years I have trained almost 70 scientists; served on 64 PhD thesis committees in 3 Schools on

06/2007-12/2008: Director, Center for Clinical Immunology at Stanford, Stanford University
 05/2007-present: Associate Director of Education, Institute for Immunity, Transplantation and Infection
 04/2007-10/2007: Acting Division Chief, Div. of Immunology/Rheumatology, Dept. of Medicine
 2007-present: Founder and Director, Stanford EXPLORE Summer Student Program
 08/2005-08/2012: Associate Professor of Medicine, Stanford University School of Medicine
 2000-present: Founder and Director, Stanford Institutes of Medicine Research (SIMR)
 09/1999-07/2005: Assistant Professor of Medicine, Stanford University School of Medicine
 03/1996-08/1999: Instructor of Medicine, Brigham & Women's Hospital and Harvard Medical School
 02/1996-03/1996: Research Fellow, Lab of Dr. Paul Anderson, Dana Farber Cancer Institute

Honors

2023 Guest Speaker, Distinguished Seminar Immunology Series, University of Buffalo
 2021 Alumnus of the Year, King's College
 2018 Speaker, Immunology Seminar Series and Grand Rounds, University of Pittsburgh
 2016 Rheumatology Visiting Professor and Grand Rounds Speaker, UC Denver
 2012 Immunology and Rheumatology Division Teaching Award, Stanford University
 2009 Mayo Clinic, Distinguished Visiting Professor, Department of Medicine
 2007 American Society for Clinical Investigation, Elected
 2007 The Mary Jane Kugel Award, Juvenile Diabetes Research Foundation
 2006 The Kunkel Society, Elected
 2002 Stanford University Immunology Graduate Program Teaching/Mentoring Award
 2002,2009,2012 Stanford University, Department of Medicine Divisional Teaching Award
 2000-2002 Baxter Career Development Award

C. Contributions to Science

Contributions to Science #1. Development of Protein and Peptide Arrays for Characterizing Immune Responses. The three major goals of these studies are: (1) To understand the mechanisms by which highly-conserved, diverse molecules and complexes such as histones and splicing particles are targeted by T and B lymphocytes, and to determine how an immune response directed against ubiquitous antigens leads to organ-specific autoimmune disease; (2) To use autoimmune sera as molecular probes to study basic cellular processes, particularly apoptosis signaling pathways, alternative RNA splicing, and endoplasmic reticulum protein transport; (3) To invent and validate novel technologies for high-throughput, multiplex proteomics studies. My lab is currently focusing on proteomic analysis of signaling pathways; and proteins secreted by immune cells, including cytokines and autoantibodies. My lab is particularly well-known for its expertise in the areas of protein and peptide arrays, including the invention and/or application of antigen arrays, lysate arrays, HIT, cytokine/chemokine arrays, viral protein arrays, and Intel arrays.

- a. Robinson WH, DiGennaro C, Hueber W, Haab BB, Kamachi M, Dean EJ, Fournel S, Fong D, Genovese MC, Neuman de Vegvar HE, Steiner G, Hirschberg DL, Morris RI, Muller S, Pruijn GJ, van Venrooij WJ, Smolen JS, Brown PO, Steinman L & **Utz P.J.** Autoantigen microarrays for multiplex characterization of autoantibody responses. 2002. **Nat. Med.** 8:295-301.
- b. Price JV, Haddon DJ, Kemmer D, Delepine G, Mandelbaum G, Jarrell JA, Gupta R, Balboni I, Chakravarty EF, Sokolove J, Shum AK, Anderson MS, Cheng MH, Robinson W, Browne SK, Holland SM, Baechler, **Utz PJ.** Protein microarray analysis reveals BAFF-binding autoantibodies in system lupus erythematosus. 2013. **J Clin Invest.** 123:5135-5145. PMID:PMC3859403
- c. Chang SE, Feng A, Meng W, Apostolidis SA, Ahuja N, Chung H-R, Jagannathan P, James J, Kim PS, Meyer NJ, Nadeau K, Radic M, Robinson WH, Singh U, Wang TT, Mack E, Artandi M, Barman L, Bennett K, Chakraborty S, Chang I, Cheung P, Chinthrajah S, Dhingra S, Do E, Finck A, Gaano A, Gebner R, Giannini HM, Gonzalez J, Greib S, Gundisch M, Hsu AR, Kuo A, Manohar M, Mao R, Neeli I, Neuauer A, Oniyide O, Powell AE, Puri R, Renz H, Schapiro JM, Weidenbacher PA, Witman R, Skevaki C, Prak ET & **Utz PJ.** New-onset IgG autoantibodies in hospitalized patients with COVID-19. 2021. **Nature Communications** 12:5417. PMID:PMC8440763
- d. Knight JS, Caricchio R, Casanova J-L, Combes AJ, Diamond B, Fox SE, Hanauer DA, James JA, Kanthi Y, Ladd V, Mehta P, Ring AM, Sanz I, Selmi C, Tracy RP, **Utz PJ,** Wagner, CA, Wang JY, McCune WJ. The intersection of COVID-19 and autoimmunity. 2021. **JCI.** 131(24):e154886. PMID:PMC8670833

Contributions to Science #2. Characterization of Epigenetic Modifying Enzymes in Immunology. A major new area of my lab's efforts is to apply bioinformatics (together with Purvesh Khatri's lab), CyTOF (with Garry Nolan's lab), and peptide arrays to (1) characterize epigenetic marks in blood cells; (2) identify epigenetic enzymes such as lysine methyltransferases, acetyltransferases, deacetylases, demethylases, and peptidyl arginine deiminases that are associated with immune responses; and (3) to take advantage of this information to design new diagnostics and therapeutics such as vaccines and small molecule signaling pathway inhibitors. My lab and the Khatri lab recently developed EpiTOF by leveraging the multiplexing capacity and single-cell resolution of mass cytometry. EpiTOF enables quantitative measurements of the cellular levels of histone post-translational modifications in individual immune cells, and such identification of differential histone marks and alterations in the epigenome can then guide locus-specific analyses (e.g. CITE-seq, ChIP-seq and ATAC-seq). Using EpiTOF, we successfully identified epigenetic alterations associated with aging in the human immune system, monocyte differentiation, and vaccine responses.

- a. Matthews AG, Kuo AJ, Ramón-Maiques S, Han S, Champagne KS, Ivanov D, Gallardo M, Carney, D, Cheung P, Ciccone DN, Walter KL, **Utz PJ**, Shi Y, Kutateladze TG, Yang W, Gozani O & Oettinger MA. RAG2 PHD finger couples histone H3 lysine4 trimethylation with V(D)J recombination. 2007. **Nature** 450:1106-1110. PMID: PMC2988437
- b. Cheung P, Vallania F, Warsinske HC, Donato M, Schaffert S, Chang SE, Dvorak M, Dekker CL, Davis MM **Utz PJ**, Khatri P & Kuo AJ. Single-cell chromatin modification profiling reveals increased epigenetic variations with aging. 2018. **Cell**, 173:1385-1397. PMID: PMC5984186
- c. Cheung P, Schaffert S, Chang SE, Dvorak M, Donato M, Macaubas C, Foecke MH, Li T-M, Zhang L, Coan JP, Schulert GS, Grom AA, Henderson LA, Nigrovic PA, Elias JE, Gozani O, Mellins ED, Khatri P, **Utz PJ** & Kuo AJ. Repression of CTSG, ELANE, and PRTN3-mediated histoneH3 proteolysis promotes monocyte-to-macrophage differentiation. 2021. **Nat Immunol.** 196:40-48. PMID: PMC6422338
- d. Wimmers F, Donato, M, Kuo A, Ashuach T, Gupta S, Li C, Dvorak M, Foecke MH, Chang SE, De Jong SE, Haecker HT, van der Most R, Cheung P, Cortese M, Hagan TL, Bosinger S, Davis MM, Rouphael N, Subramaniam S, Yosef N, **Utz PJ**, Khatri P & Pulendran B. Single-cell analysis of the epigenomic and transcriptional landscape of innate immunity to seasonal and adjuvanted pandemic influenza vaccination in humans. 2021. **Cell**, (6):932-940. PMID: PMC7303014

Contributions to Science #3. Development of Novel Vaccines, and Characterization of Influenza and COVID-19 Vaccine Responses. A major goal of my work is to take advantage of the information provided by proteomics technologies to develop antigen-specific tolerizing therapies for common autoimmune diseases, and to characterize immune responses in vaccinated subjects. Protein and peptide arrays were used by the Utz, Robinson and Steinman labs in animal models of multiple sclerosis to identify autoantigens which were then encoded in DNA vaccines that successfully prevented and treated animal models. After founding Bayhill Therapeutics in 2002, preclinical studies led to testing of DNA vaccines, with array-based monitoring, in 3 successful clinical trials of almost 400 subjects in multiple sclerosis and juvenile diabetes. I have been actively involved in NIAID's HIPC Consortium.

- a. Robinson WH, Fontoura P, Lee BJ, Neuman de Vegvar HE, Tom J, Pedotti R, DiGennaro CD, Mitchell DJ, Fong D, Ho PPK, Ruiz P, Maverakis E, Stevens DB, Bernard CCA, Martin R, Kuchroo VK, van Noort JM, Genain CP, Amor S, Olsson T, **Utz PJ**, Garren H & Steinman L. Protein microarrays guide tolerizing DNA vaccine treatment of autoimmune encephalomyelitis. 2003. **Nature Biotechnology** 21:1033-1039.
- b. Price JV, Jarrell JA, Furman D, Kattah NH, Newell E, Dekker CL, Davis MM & **Utz PJ**. Characterization of in a vaccine immunogenicity using whole-protein and peptide influenza microarrays. 2013. **PLoS One**, 8(5):e64555. PMID: PMC3667171
- c. Roep B, Solvason N, Gottlieb P, Abreu J, Harrison L, Eisenbarth G, Yu L, Levitan M, Hagopian W, Buse J, von Herrath M, Quan J, King R, Robinson WR, **Utz PJ**, Garren H, The BHT 3021 Investigators & Steinman L. Plasmid encoded proinsulin preserves C-peptide while specifically reducing proinsulin specific CD8 cells in Type 1 diabetes. 2013. **Science Translational Medicine**, 5(191):191ra82. PMID: PMC4516024
- d. Arunachalam PS, Scott MKD, Hagan T, Li C, Chunfeng Li, Feng Y, Wimmers F, Grigoryan L, Trisal M, Edara VV, Lai L, Chang SE, Feng A, Dhingra S, Shah M, Lee AS, Chinthrajah S, Sindher T,

MallajosyulaGao F, Sigal N, Kowli S, Gupta S, Pellegrini K, Tharp G, Maysel-Auslender S, Hamilton S, Aoued H, Hrusovsky K, Roskey M, Bosinger S, Maecker HT, Boyd SD, Davis MM, **Utz PJ**, Suthar MS, Khatri P, Nadeau KC, Pulendran B. Systems vaccinology of the BNT162b2 mRNA vaccine in humans. 2021. **Nature**, 596:410-416. PMID:PMC7665312.

Contributions to Science #4. Characterization of Signaling Pathways in Blood Cells. I co-discovered (and incorrectly named) the NFAT transcription factor as a medical student in Jerry Crabtree's lab. I studied apoptosis signaling pathways and autoantigens at Harvard following residency and fellowship. Upon arriving at Stanford as a new assistant professor, I changed direction, taking advantage of Stanford's rich technology development environment. The Utz lab has been at the forefront of inventing multiplexed assays for studying protein-protein and protein-peptide interactions for over a decade, and his lab has undergone renewed focus in recent years in studying blood cell signaling pathways. Methods used to characterize signaling pathways include lysate arrays (invented by Steven Chan and published in **Nature Medicine** in 2004, see above), multiparameter FACS, tetramers (invented by Mark Davis), and CyTOF (driven by Garry Nolan's lab).

- a. Shaw JP, **Utz PJ**, Durand DB, Toole JJ, Emmel EA, Crabtree GR. Identification of a putative regulator of early T-cell activation genes. 1988. **Science** 241:202-205.
- b. Chan SM, Weng AP, Tibshirani R, Aster JC, **Utz PJ**. Notch signals positively regulate activity of the mTOR pathway in T cell acute lymphoblastic leukemia. 2007. **Blood** 110:278-286. PMID:PMC1896117
- c. Holst J, Wang H, Eder KD, Workman CJ, Boyd KL, Baquet Z, Singh H, Forbes K, Chruscinski A, Smeyne R, van Oers NS, **Utz PJ**, Vignali DA. Scalable signaling mediated by T cell antigen receptor-CD3 ITAMs ensures effective negative selection and prevents autoimmunity. 2008. **Nature Immunology** 9:658-666.
- d. Kattah NH, Newell EW, Jarrell J, Chu AD, Xie J, Kattah MG, Goldberger O, Ye J, Chakravarty E, Davis MM, Utz PJ. Tetramers reveal IL-17 secreting CD4⁺ T cells that are specific for U1-70 in lupus and mixed connective tissue disease. 2015. **PNAS**, 112:3044-3049. PMID:PMC4364210

Contributions to Science #5. Development of Non-Fluorescence Based Methods of Detection. Most array studies to date have focused on fluorescence-based detection. More sensitive and nimble methods need to be invented and validated in order for biomarker discovery to advance. The Utz lab has optimized nearly every aspect of existing methodology, including array surfaces, methods of detection (e.g. gold-coated surfaces, carbon nanotubes), two color approaches, and data analysis. The lab has used arrays to study animal models of autoimmunity and has designed custom arrays for the study of human patients. Dr. Utz and Dr Shan Wang have been collaborating for several years on use of GMR sensors for measuring analytes in immunology, and this collaboration led to development of a rapid detection system for hepatitis B infection. This won second prize in the 2014-2015 Nokia X-Challenge Sensor Competition. Additional examples of collaborative work between the Utz lab and other Stanford investigators is provided below.

- a. Kattah MG, Alemi GR, Thibault DL & **Utz PJ**. A novel two-color fab labeling method for autoantigen protein microarrays. 2006. **Nat. Methods**. 9:745-751.
- b. Pennathur S, Baldessari F, Kattah MG, Steinman J, **Utz PJ** & Santiago J.G. Free-solution oligonucleotide separation in nanoscale channels. 2007. **Analy. Chem.** 79:8316-8322.
- c. Chen Z, Tabakman SM, Goodwin AP, Kattah MG, Daranciang D, Wang X, Zhang G, Li X, **Utz PJ**, Jiang K, Fan S & Dai H. Protein microarrays with carbon nanotubes as multi-color raman labels. 2008. **Nat. Biotech.** 26:1285-1292.
- d. Tabakman SM, Lau L, Robinson JT, Price J, Sherlock SP, Wang H, Chen Z, Tangsombatvisit S, Jarrell JA, **Utz PJ** & Dai H. Plasmonic substrates for multiplexed protein arrays with femtomolar sensitivity and broad dynamic range. 2011. **Nat. Commun.** 2:466. PMID: PMC3402035.

Complete List of Published Work in MyBibliography:

<https://www.ncbi.nlm.nih.gov/sites/myncbi/paul.utz.1/bibliography/44908500/public/?sort=date&direction=descending>