The promise of Interleukin-2 Therapy

for autoimmune and inflammatory diseases, allergy, transplantation and cancer

IL-2 2024 PARIS

Centre International de Conférences Sorbonne Université
September 4-7, 2024
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International Organizing Committee

Abul Abbas, Christophe Benoist, Jeff Bluestone, Laurie Dempsey, David Klatzmann (Chair), Thomas Malek, Qizhi Tang, Shimon Sakaguchi, Georges Tsokos, Lucy Walker

Local Organizing Committee

Caroline Aheng, Encarnita Mariotti-Ferrandiz, Michelle Rosenzwajg, Nicolas Tchitchek

Current list of confirmed invited speakers

Christoph Binder, Pierre Ellul, Ron Germain, Jonathan Kipnis, David Klatzmann, Hardeep Kataria, Zhanguo Li, Adrian Liston, Jeff Lyons, Ziad Mallat, Diane Mathis, Thomas Malek, Alexander Marson, Marc Martinez-Llordella, Janie Robert, Aleksander Rudensky, Jamie Spangler, Shimon Sakaguchi, Qizhi Tang, Lucy Walker, Benjamin Youngblood, Jonathan Zalevsky

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AGENDA

Wednesday 4

18.00

Opening Session
Welcome words

Keynote lectures

Chair: Jeff Bluestone

- *Treg 2024* – Shimon Sakaguchi
- *IL-2 based therapies 2024* – David Klatzmann

20.00

Welcome reception

Thursday 5

9.00 Session I - On mechanistic aspects

Chair: Tom Malek

1. *Regulatory T cells: There and Back Again* - Alexander Rudensky
2. *Regulation of FOXP3 expression in human CD4+ T cells* - Jennifer Umhoefer

Talks from abstracts

a. *IL2R signaling and Foxp1 expression maintain Treg cell identity in the absence of Foxp3*- Louis-Marie Charbonnier

b. *The soluble IL-2 receptor α/CD25 as a modulator of IL-2 function* - Juliane Lokau

10.30 – 11.00 – Coffee break

11.00 Session II - Lessons from current clinical trials with native IL-2 and muteins

Chair: Alberto Pugliese

1. *IL-2 dosing and predictive markers in treatment of SLE* - Zhanguo Li

Talks from abstracts

c. *The TCR repertoire as an early predictor of SLE response to low-dose IL-2* - Martin Pezous

2. *IL-2 in atherosclerosis* - Ziad Mallat

Talks from abstracts

d. *The clinical development of MK-6194, an Fc-conjugated, modified IL-2 for treatment of autoimmune disorders* - Claudia Kaiser-Albers

e. *Pharmacodynamic biomarkers of BMS-986326, a novel IL-2/CD25 fusion protein that induces highly selective and durable expansion of regulatory T cells following administration in healthy volunteers - Eun Mi Hur*

13.00 – 14.00 – Lunch

14.00 Session III - On mechanistic aspects

Chair: Shimon Sakaguchi

1. *The Spatial Regulation of Immune Activity in Tissues* - Ron Germain
2. *Interplay between IL-2 and costimulatory pathways in shaping T cell immunity* - Lucy Walker
3. *TCR/CD28- and IL-2R-dependent human regulatory T cell 1 homeostasis and function is cooperatively controlled by BLIMP-1 and CEACAM1* - Thomas Malek

Talks from abstracts

f. *Centrally controlled regulatory networks enable context-specific expression of IL2RA by CD4+ T cells* - Maya Arce

g. *The plasticity of human FoxP3+ Tregs in Rheumatoid Arthritis synovial fluid* - Nainisha Shah

16.00 – 16.30 – Coffee break

16.30 Session IV – Treg and IL-2 in brain disorders

Chair: Laurie Dempsey

1. *What do T cells do in healthy and damaged brain?* - Jonathan Kipnis
2. *Meningeal Treg control of neural stem cell differentiation* - Diane Mathis
3. *The Treg/Th17 balance in neuro-psychiatric disorders* - Pierre Ellul

Talks from abstracts

h. *Schnurri 3 acts as a transcriptional checkpoint* - Makio Iwashima

i. *Decoding the TCR repertoire and antigen-specificity in ALS Patients* - Wassim Elyaman

18.30 End of the day

Friday 6

9.30 Session V – IL-2 in other settings
Chair: Alberto Pugliese
Gene delivery of IL2 and IL2 muteins as a therapeutic - Adrian Liston
Talks from abstracts

j. *Low-dose interleukin-2 in patients with bipolar depression: a phase 2 randomized double-blind placebo-controlled trial* – Nicolas Tchitchek
k. IL-2 in allergy – Michelle Rosenzwajg

10.30 – 11.00 – Coffee break

11.00 - Session VI - IL-2 and Treg cell therapies
Chair: Christophe Benoist

1. *Translating epigenetic mechanisms of T cell exhaustion into durable immunotherapy* - Benjamin Youngblood
2. *Enhancing Treg cell therapy with autocrine IL-2* Qizhi Tang
3. *Targeting eTregs to inflammatory sites* - Janie Robert
4. *Engineered CAR-Treg therapies to enhance immune regulation in transplantation and autoimmunity* Marc Martinez Llordella

13.00 - 14.00 – Lunch

14.00 - Session VII - Novel IL-2s, vectorisation and combination therapies
Chair: Lucy Walker

1. *Low-dose IL-2/CD25 remodels inflamed tissues to limit autoimmunity* – Janika Poder
2. *Engineered cytokine/antibody fusion proteins for Treg-targeted immunotherapy* - Jamie Spangler

Talks from abstracts

l. *Targeted nanoparticles containing IL-2 induce Tregs and novel tolerogenic TGF-β producing NK cells that synergize for long term therapeutic effects* - David Horwitz
m. *MDNA209, a High Affinity IL-2b Biased IL-2/IL-15 Super-antagonist, for the Treatment of Autoimmune Diseases* - Hardeep Kataria

15.30 - 16.00 – Coffee break

16.00 - Session VII - Novel IL-2s, vectorization and combination therapies
Chair: Lucy Walker

1. *Oxidation Specific epitopes for targeting IL-2 to inflammatory sites* Christoph Binder

Talks from abstracts

n. *EGL-003, a novel IL-2 mutein to selectively expand and activate regulatory T cells and improve therapeutic efficacy in autoimmune disease* - Fiorella Kotsias
o. *CUE-401: A Novel IL-2/TGF-beta fusion protein for the induction & expansion of FOXP3+ regulatory T Cells* - Steven Quayle
p. *Phagekine directed evolution: a platform for the optimization of human Interleukin-2 biological activity and developability profile* - Gertrudis Rojas
q. *A novel IL-2 and IL-33 bifunctional cytokine reverses ongoing Type-1 Diabetes and promotes repair in pancreatic islets* - Rahul Sharma

18.00 – 19.00 Drinks and posters
19.00 End of the day
20.00 speaker dinner

Saturday 7

9.00

Session VIII- IL-2 in cancer therapy

Chair: Abul Abbas

1. *Clinical safety and efficacy of TCR-specific engagers that selectively target IL-2 to tumor-specific T cells* - Matteo Levisetti

Talks from abstracts

r. *STK-012, a first-in-Class_α/β IL-2 receptor biased partial agonist in advanced solid tumors – Initial results of a Phase 1 study* – Martin Oft

s. *MDNA113, an IL-13Ra2 tumor targeting and conditionally activatable anti-PD1-IL-2^{SK} BiSKIT Shows enhanced eafety and potent therapeutic efficacy* - Aanchal Sharma

t. *Muteins of Interleukin 2 for cancer therapy: From mice to humans* - Kalet Leon

u. *In vivo gain of function CRISPRa screens uncover regulators of T cell accumulation in the tumor microenvironment with antitumor activity* - Rosmely Hernandez

11.00 – 11.30 – Coffee break

11.30

Session IX – IL-2: the pharma perspective

Chair: Abul Abbas & David Klatzmann

1. Nektar: *Update on rezpegaldesleukin revelopment as a potential treatment for autoimmune diseases including atopic dermatitis* - Jonathan Zalevsky
2. ILTOO*: low dose native IL-2: from PoC to market*
3. Round Table: What 's next? (BMS, MERCK, Cue Biopharma, biotech…)

13.30 End of the meeting

CHAIRS & INVITED SPEAKERS
(in alphabetical order)

Abul Abbas received his MBBS (MD equivalent) in India, completed training in Pathology at Harvard and was on the faculty at Harvard Medical School and the Brigham and Women's Hospital for 20 years. From 1999-2018, he was Professor and Chairman of the Department of Pathology at the University of California San Francisco. Dr. Abbas' honors include election to the Institute of Medicine of the National Academy of Sciences, and the Rous-Whipple Award and Robbins Educator Award of the American Society of Investigative Pathology. He has served as one of the founding Editors and Associate Editor of Immunity, Associate Editor and Section Editor for The Journal of Immunology, Associate Editor of Cell, Consulting Editor of The Journal of Clinical Investigation, founding Editor of the Annual Review of Pathology: Mechanisms of Disease, and Co-Chief Scientific Advisor of Science Immunology. From 2011-2013, he was the President of the Federation of Clinical Immunology Societies (FOCIS). Dr. Abbas' research interests are in Immunology, with a focus on the control of immune responses and the causes of autoimmunity. His laboratory has used experimental models to analyze the generation and maintenance of regulatory T cells. He has published over 200 peer-reviewed papers and invited reviews, and is the author of four widely read textbooks, two in Immunology and two in Pathology. He has taught Immunology at Harvard Medical School and UCSF, and has organized and conducted Immunology courses worldwide.

Christophe Benoist is a molecular immunologist, Professor at Harvard Medical School. M.D. (U. of Paris, 1980), Ph.D. (U. of Strasbourg, P. Chambon, 1981), postdoctoral study in Stanford (H. McDevitt). Has run a joint laboratory with Diane Mathis, first at the IGBMC, Strasbourg, then at HMS (associate member, Broad Inst.). The lab has made seminal contributions to understanding gene regulation in the immune system, the Aire gene, the impact of Tregulatory cells, generated key mouse models, and pioneered Systems Immunology approaches, in part within the ImmGen consortium. Elected to the French Académie des Sciences (1999), US National Academy of Sciences (2005).

Christoph J. Binder (born 1973) received his MD degree from the University of Vienna, Austria, in 1997 and his PhD degree in Molecular Pathology from the University of California San Diego (UCSD), USA, in 2002. Following postdoctoral training at the Department of Medicine of UCSD, he established his own research group at the Department of Laboratory Medicine of the Medical University of Vienna in 2005. In 2009, he was appointed Full Professor of Atherosclerosis Research at the Medical University of Vienna. He is a clinical specialist in Laboratory Medicine and currently Deputy Head of the Department of Laboratory Medicine at the Medical University of Vienna. Between 2006 until 2021 he was Principal Investigator at the Center for Molecular Medicine of the Austrian Academy of Sciences. Christoph Binder's research interests span the interface of vascular biology, lipid oxidation, and immunity. His group is investigating immune mechanisms of atherosclerosis with a special focus on the role of innate and humoral immunity and how this can be exploited for the treatment of

cardiovascular disease. Christoph Binder has won numerous prestigious fellowships and awards and has authored >200 original and review articles in important international journals, including Nature and Nature Medicine. He is Co-Editor of Atherosclerosis and Section Editor of Thrombosis & Haemostasis, and since 2017 PI of the Austrian Familial Hypercholesterolemia Registry. He is currently Vice President of the European Atherosclerosis Society. In 2024 he became Vice President of the Austrian Science Fund (FWF).

Jeffrey Bluestone is the A. W. and Mary Margaret Clausen Distinguished Professor at the University of California San Francisco and CEO/President Sonoma BioTherapeutics. He is a leading immunologist in the field of T-cell activation, co-stimulation, and immune tolerance research, which has led to the development of multiple pro-tolerogenic immunotherapies and the first checkpoint immunotherapies for cancer treatment. Dr. Bluestone's research has focused on the critical role of regulatory T cells in autoimmune diseases, organ transplantation and cancer. Dr. Bluestone was the founder and first director of the Immune Tolerance Network, an NIH-funded clinical immunology research program, former UCSF Diabetes Center Director, Executive Vice Chancellor and Provost at UCSF and CEO of the Parker Institute for Cancer Immunotherapy. Dr. Bluestone has authored more than 400 peer-reviewed publications, mentored over 60 graduate students/post-doctoral fellows, and received numerous awards for his work, including election to the American Academy of Arts and Sciences and the National Academy of Medicine.

Laurie Dempsey is Senior Editor at *Nature Immunology*. Laurie obtained her B.S. degree in Microbiology at the University of Michigan and her Ph.D. in Microbiology at New York University, where she studied extrachromosomal DNA replication and recombination with Dave Dubnau. Following post-doctoral stints with Nick Cozzarelli (University of California-Berkeley) and Saleem Khan (University of Pittsburgh), Laurie switched to the study of immunoglobulin gene recombination with Nancy Maizels at Yale University. Laurie, with her molecular biology skills, was invited to join the transplantation biology group led by Jeff Platt, then at Duke University and subsequently with group at the Mayo Clinic in Rochester, MN. Laurie joined the editorial ranks of *Nature Immunology* in 2001

Pierre Ellul is associated professor in child and adolescent psychiatry at the Center of Excellence for Autism and Neurodevelopmental Disorders (InovAND) headed by Prof. Delorme at the Robert-Debré Hospital. Alongside his medical studies, he obtained a Master 2 in immunology from Sorbonne Université/Ecole normale supérieure in 2016. Since 2019, he has been a doctoral student in immunology in Pr David Klatzmann's I3 laboratory at Hôpital Pitié-Salpêtrière. He is working on a better understanding of the neuro-immunological basis of autism spectrum disorders, with a view to developing targeted therapies. This background has enabled him to develop in-depth expertise in the links between immunology and psychiatry. His research focuses on neuro-immunological interactions and the development of new immunotherapies in the field of psychiatry.

Ronald N. Germain received his M.D. and Ph.D. from Harvard University. Since then he has investigated basic immunobiology, first on the faculty of Harvard Medical School, then in the Laboratory of Immunology, NIAID, NIH, and most recently at NIAID, NIH as Chief of the Laboratory of Immune System Biology. He has made key contributions to understanding MHC class II molecule structure–function relationships, the cell biology of antigen processing, the molecular basis of T cell recognition, and the application of systems biology to understanding immune function. More recently, his laboratory has explored the immune system using dynamic and static *in situ* microscopic methods that his laboratory helped pioneer. He has published more than 400 scholarly research papers and reviews. Among numerous honors, he was elected Associate member of EMBO (2008), elected to the National Academy of Medicine (2013), received the Meritorious Career Award from the American Association of Immunologists (2015), chosen as NIAID Outstanding Mentor (2016), elected to the National Academy of Sciences (2016), designated an NIH Distinguished Investigator and named a Distinguished Fellow of the AAI. He has trained more than 70 postdoctoral fellows, many of whom hold senior academic and administrative positions at leading universities and medical schools.

David Klatzmann, Professor of Immunology and Director of the Biotherapy Department at the Pitié-Salpêtrière hospital and Sorbonne Université medical school. His main activities have been to advance translational research in Immunology. He built-up a global organization capable of developing biotherapies from bench to bedside.

His current specific interests and research activities span from Fundamental Immunology (studying Tregs in tolerance using systems immunology approaches) to Biotherapy (development of Treg-based immunotherapies, notably low dose IL-2).

Jonathan Kipnis is BJC Investigator, Alan A. and Edith L. Wolff Distinguished Professor of Pathology and Immunology and Professor of Neurology, Neuroscience, and Neurosurgery at Washington University in St. Louis, School of Medicine. He is also the inaugural Director of Brain immunology and Glia (BIG) Center at Washington University. Jony graduated from the Weizmann Institute of Science in Israel, where he was Sir Charles Clore Scholar and a recipient of distinguished prize for scientific achievements awarded by the Israeli Parliament, The Knesset. The Kipnis lab is dedicated to unraveling the intricate interactions between the immune system and the central nervous system (CNS). It explores the cellular and molecular mechanisms that underpin these interactions across a spectrum of conditions, including neurodegenerative, neurodevelopmental, and mental disorders, as well as in physiological states like healthy aging.

Matteo Levisetti is Senior Vice President of Clinical Development at Cue Biopharma. Dr. Levisetti has extensive drug development experience in the pharmaceutical and biotech industries, where he led global clinical development and regulatory strategies for multiple programs across several therapeutic areas. Prior to joining Cue Biopharma, Matteo served as CMO at DNAtrix directing and managing clinical operations and regulatory strategy for viral-based immunotherapies to treat cancer. Matteo also served as CMO at Dauntless Pharmaceuticals where he was responsible for all aspects of clinical development of endocrinology and oncology assets. Previously, Matteo directed immuno-oncology programs at Mirati Therapeutics, served as Global Head & Vice President, Translational Medicine, Immunology and Inflammation at Roche pRED and held senior positions with Pfizer. Earlier in his career, Matteo held joint appointments as Assistant Professor in the Departments of Medicine, Pathology, and Immunology at Washington University School of Medicine. Matteo received his MD from the University of Chicago Pritzker School of Medicine, completed residency training in internal medicine at the University of Chicago Hospitals, and completed subspecialty training in endocrinology and a research fellowship in immunology at Washington University School of Medicine, St. Louis, Missouri.

Zhanguo Li is the President of Clinical Immunology Association of China, the Honorary President of Chinese Rheumatology Association (CRA), the Past President of Asian and Pacific League Against Rheumatism (APLAR). He is also the Past President of International League of Associations for Rheumatology (ILAR). He is the Chief Editor of Chinese Journal of Rheumatology, and the Chief Editor of Chinese Journal of Clinical Immunology and Rheumatology. In addition, he serves on the editorial boards of Nat Rev Rheum, Ann Rheum Dis, Lancet Rheumatology. He has published over 500 articles on peer reviewed journals, e.g. Nat Med, Nat Genet, Immunity, Cell H&M, Ann Internal Med, Nat Rev Rheum, and Ann Rheum Dis. He has contributed as Chief-Editor or author to over 30 textbooks and book chapters in Rheumatology and Immunology. His interests are immune therapy and mechanism of rheumatoid arthritis, Sjogren syndrome and systemic lupus erythematosus.

Adrian Liston is Senior Group Leader at the Babraham Institute and Senior Research Fellow at Churchill College, University of Cambridge. The Liston laboratory currently works on understanding the interaction between the immune system and the tissues, in particular the brain and lung. The laboratory has extensive experience in the fields of autoimmune genetics, diabetes, primary immunodeficiencies, systems immunology, the thymus and regulatory T cells. Dr Liston's PhD research was on T cell tolerance and diabetes with Professor Chris Goodnow at the Australian National University, followed by post-doctoral research on regulatory T cell biology with Professor Sasha Rudensky at the University of Washington. From 2009-2018, Dr Liston ran his independent laboratory and founded two core facilities, on flow cytometry and CrispR, at the VIB and the University of Leuven, in Belgium. In 2019, Liston relocated his research team to the Babraham Institute, in Cambridge, UK.

Marc Martinez-Llordella is co-founder and Vice President Biology at Quell Therapeutics. Marc has forged a deep academic research career focused on Tregs biology and immunological tolerance. His most recent research as Senior Lecturer at King's College London has combined pre-clinical models and immunomonitoring analysis of clinical trials to identify new strategies to modulate Treg homeostasis and function. Marc's group has investigated the role of microenviromental cues such as IL-2 availability and inflammation shaping the phenotypic characteristics of tissue resident T cells. His translational research has supported the implementation of new tolerogenic therapies such as low-dose IL-2 and CAR-Tregs into transplantation and autoimmunity. Prior to that he worked in Professor Jeff Bluestone's lab at University College San Francisco where he carried out post-doctoral research on the transcriptional profile of CD28 signalling in T cell activation and the analysis of Treg phenotypic plasticity in autoimmunity. Marc holds a PhD from the University of Barcelona focussed on the identification of transcriptional and phenotypic biomarkers to predict transplantation tolerance.

Ziad Mallat received his MD and qualification in Cardiovascular Diseases from University of Pierre et Marie Curie in 1996, and his Ph.D. in Vascular Biology, Thrombosis and Haemostasis from University of Paris-Diderot in 1999. He joined INSERM, Paris in 1998 as Assistant Research Professor, became Associate Professor in 2002 and Research Professor in 2007. He is currently the British Heart Foundation Professor of Cardiovascular Medicine at the University of Cambridge, UK, and has been elected fellow of the Academy of Medical Sciences, UK. He is Co-Editor of *Atherosclerosis*, Consulting Editor for *Cardiovascular Research*, and serves on the Editorial Board of *Circulation Research*, *and JCI Insight*. His work aims to understand the role of the immune system in the development and progression of cardiovascular diseases. Mallat was the first to identify a major atheroprotective role of regulatory T cells and associated anti-inflammatory cytokines, IL-10 and TGF-b. More recently, he identified selective pathogenic and protective roles for defined B cell and innate lymphoid cell subsets in atherosclerosis and cardiac remodelling following ischemic injury. His basic science research is complemented by proof-of-concept clinical trials in patients with coronary artery disease.

Thomas Malek received his Ph.D. in 1977 after training with Dr. Katherine Knight at the University of Illinois Medical School in Chicago. After postdoctoral training with Ethan Shevach at the NIH, he joined the faculty of the University of Miami in 1985, where he currently is Professor and Chair in the Department of Microbiology and Immunology. His research has a long-standing focus on the role of the IL-2R in T cell development and function. In 2002 his group provided direct evidence that IL-2R signaling is essential for regulatory T cells. More recently his group established that low IL-2R signaling effectively supported Treg, but not T effector cell function, providing a scientific underpinning for the use of low-doseIL-2 to boost Tregs in the context of autoimmunity. His group also developed a new IL-2-based biologic to improve the efficacy of this therapy. Current research from his lab investigates the cellular and molecular mechanisms by which the IL-2R contributes to Treg and T effector cell

function, with an emphasis on translating these findings in the context of autoimmunity and cancer.

Diane Mathis obtained a PhD from the University of Rochester and performed postdoctoral studies at the Laboratoire de Génétique Moléculaire des Eucaryotes in Strasbourg, France and Stanford University Medical Center. She returned to Strasbourg at the end of 1983, establishing a laboratory at the LGME [later the Institut de Genetique et de Biologie Moleculare et Cellulaire (IGBMC)] in conjunction with Dr. Christophe Benoist. The lab moved to the Joslin Diabetes Center in Boston in 1999. Through 2008, Dr. Mathis was a Professor of Medicine at Brigham and Women's Hospital and Harvard Medical School (HMS), and Associate Research Director and Head of the Section on Immunology and Immunogenetics at Joslin. She is currently a Professor in the Department of Immunology at HMS and holder of the Morton Grove-Rasmussen Chair in Immunohematology. She is also a Principal Faculty Member at the Harvard Stem Cell Institute and an Associate Faculty Member of the Broad Institute. She presently serves on the advisory boards of Rockefeller University, the Howard Hughes Medical Institute, Genentech, Pfizer, Amgen, Janssen and Goldman Sachs Life Sciences (amongst others), and of several research institutes worldwide. Dr. Mathis was elected to the US National Academy of Sciences in 2003, the German Academy in 2007, and the American Academy of Arts and Sciences in 2012. She received the FASEB Excellence in Science Award in 2016, the inaugural Excellence in Immunology Award from the International Union of Immunological Societies in 2023 and the William B Coley Award for Distinguished Research in Basic Immunology in 2024. Her lab works in the fields of T cell differentiation, immunological tolerance, autoimmunity and inflammation. She has trained over 175 students and postdoctoral fellows from all over the world.

Janie Robert is a research scientist with expertise in cell and gene therapy, particularly in the development of regulatory T cell (Treg) therapies for autoimmune and inflammatory diseases. She recently earned her PhD in Cell and Gene Therapy from Sorbonne University, Paris, where she conducted pioneering research on IL-2 self-sufficient Tregs. With over five years of experience in both academic and applied research environments, Dr. Robert has developed expertise in Treg sorting, culture, and transduction, as well as preclinical studies using autoimmune and inflammatory disease models. She is passionate about translating scientific discoveries into therapeutic solutions that can make a tangible impact on patient care.

Shimon Sakaguchi obtained an M.D. in 1976 and a Ph.D. in 1982 from Kyoto University, Japan, where he was trained as a pathologist and immunologist. After performing postdoctoral studies at Johns Hopkins University and Stanford University as a Lucille P. Markey Scholar, he served as an Assistant Professor in the Department of Immunology at the Scripps Research Institute. He returned to Japan in 1991 and continued his immunology research as the Head of the Department of Immunopathology at Tokyo Metropolitan Institute of Gerontology, Tokyo. From 1998 to 2011, he was a Professor of Institute for Frontier Medical

Sciences Kyoto University and served as the Director of the Institute for several years. He is currently a Distinguished Professor at the Immunology Frontier Research Center (IFReC) Osaka University, Japan.

Jamie Spangler is The Brody Faculty Scholar and Associate Professor of Biomedical Engineering and Chemical & Biomolecular Engineering at Johns Hopkins University. Dr. Spangler earned a Bachelor of Science degree in Biomedical Engineering at Johns Hopkins University and went on to earn a PhD in Biological Engineering at MIT. After completing a postdoctoral fellowship at Stanford University School of Medicine, Dr. Spangler launched her independent research group at Johns Hopkins University in 2017, jointly between the departments of Biomedical Engineering and Chemical & Biomolecular Engineering. Her lab, located in the Translational Tissue Engineering Center at the School of Medicine, applies structural and mechanistic insights to re-engineer existing proteins and design new proteins that therapeutically modulate the immune response. In particular, her group is interested in engineering immune molecules such as cytokines, growth factors, and antibodies for targeted treatment of diseases such as cancer and autoimmune disorders.

Jennifer Umhoefer is a postdoctoral scholar at the Gladstone-UCSF Institute of Genomic Immunology in the laboratory of Dr. Alexander Marson. Dr. Umhoefer completed her B.S. in Biology at the University of Wisconsin-Madison and her Ph.D. in Biomedical Sciences at the University of California, San Francisco in the laboratory of Dr. Alexander Marson. Dr. Umhoefer's graduate research explores the genetic circuits controlling expression and induction of FOXP3 in human CD4+ T cells. Her work leverages CRISPR genetic and epigenetic screening technologies in primary human regulatory T cells (Tregs) and conventional T cells (Tconvs) to identify gene trans- and cis-regulators in high-throughput. Cas9 deletion and CRISPRi tiling across ~123 kb of the *FOXP3* locus identified novel cis-regulators that govern Tconv FOXP3 expression, including the Treg enhancer CNS0, a Tconv-specific enhancer, TcNS+, and a repressive element, TcNS-, overlapping with the promoter of a neighboring gene. Pooled CRISPR knockout screens revealed multiple trans-factors required for proper expression of FOXP3 in Tregs and Tconvs, a subset of which bind to known and novel cis-regulatory elements. Collectively, her work adds new complexity to FOXP3 regulation by deciphering cell-type distinct and overlapping regulation and identifying novel regulators of FOXP3 in human cells.

Qizhi Tang is a professor of immunology in the Diabetes Center, the Department of Surgery, the Gladstone Institute of Genomic Immunology, and the Institute of Regenerative Medicine at the University of California, San Francisco (UCSF). One area of research focus in the Tang Lab is on investigating regulatory T cell control of autoimmune diabetes and transplant rejection and translating insights from basic mechanistic research to novel therapies. In the past 10 years, she has led translational efforts to design and implement 10 Treg-based clinical trials in autoimmune diseases and organ transplantation. Currently, pre-clinical research in her lab focuses on developing cellular

engineering strategies to enhance human Treg potency and lineage stability. Another area of research in the Tang lab is to optimize beta cell replacement therapy for type 1 diabetes by improving islet survival in ischemia and designing strategies to avoid immune rejection without systemic immunosuppression.

George C. Tsokos, MD, is a Professor of Medicine at Harvard Medical School and Chief of the Rheumatology and Clinical Immunology Division at Beth Israel Deaconess Medical Center in Boston. Dr. Tsokos' laboratory has opened and led the field of molecular abnormalities on immune cells in patients with systemic lupus erythematosus and identified previously unknown pathways which have served as the basis for novel treatments which are currently in various phases of development. He has served various leadership positions including President of the Clinical Immunology Society, the Board of Directors of the American College of Rheumatology member or chair of multiple federal study sections and editor or the editorial boards of scientific journals. He holds a MERIT Award from the National Institutes of Health and has received several prestigious awards including the Kirkland, Howley, Evelyn Hess awards and the Distinguished Basic Investigator Award from the American College of Rheumatology, the Lupus Insight Award, the Carol Nachman International Prize in Rheumatology and the Marian Ropes Physician Achievement Award.

Lucy Walker is Professor of Immune Regulation at the Institute for Immunity & Transplantation at University College London. She has a longstanding interest in immune regulation with a particular focus on how costimulatory pathways set T cell activation thresholds. Lucy received a Wellcome Trust International Prize Travelling Fellowship to train in Prof Abul Abbas's group at UCSF before returning to the UK supported by a series of Career Development and Senior Fellowships from the Medical Research Council. Her group uses both mouse models and patient samples with the aim of understanding regulatory mechanisms in autoimmunity, with particular focus on Type 1 Diabetes. Lucy's work led to the discovery that regulatory T cells (Tregs) are not anergic in vivo, but instead proliferate in response to self or foreign antigens. She went on to show that Tregs can use the inhibitory protein CTLA-4 to elicit suppressive function, *via* an unusual mechanism involving the capture and degradation of costimulatory ligands, and that Tregs from patients with CTLA-4 mutations show impaired function. Her interest in T cell / B cell collaboration led to the early demonstration that CD28 costimulation is required for the development of follicular helper T cells and subsequent work has identified a key role for CTLA-4 in regulating this population. Lucy has served as Panel Chair for several funding bodies including the MRC, the Wellcome Trust and NC3Rs. She was selected for the UK *Innovators in Diabetes* programme in 2011, received a Royal Society Wolfson Research Merit Award in 2015 and an EFIS Lecture Award in 2016.

Benjamin Youngblood, PhD, is currently a member in the Department of Immunology at St Jude Children's Research Hospital. He received a Bachelor of Science degree in Biochemistry from Oregon State University in 2001 and went on to do his graduate training in Biochemistry studying enzyme specificity of DNA methyltransferases at University of California Santa Barbara. He joined Professor Rafi Ahmed's laboratory in 2007 for postdoctoral training focused on epigenetic regulation of memory CD8 T cell differentiation. In 2014, he joined the faculty at St Jude Children's Research Hospital, and has developed a research program focused on epigenetic mechanisms involved in the development of functional and nonfunctional CD8 T cells, and translating novel discoveries into therapies that treat chronic viral infection, cancer, and autoimmunity.

Jonathan Zalevsky was appointed Nektar's Chief Research & Development Officer in October 2019 to lead all aspects of the R&D organization, including research, clinical development, regulatory affairs, and biologics process development. Dr. Zalevsky joined the Company in 2015 and has served as our Chief Scientific Officer since 2017. During his tenure at Nektar, Dr. Zalevsky's expertise in immunology, and across biological modalities and therapeutic areas, has helped fuel the growth of the company's immuno-oncology and immunology pipeline. Dr. Zalevsky led the early development for bempegaldeskleukin and NKTR-358. Prior to joining Nektar, Dr. Zalevsky was Global Vice President and Head of the Inflammation Drug Discovery Unit at Takeda Pharmaceuticals. As the leading immunologist for Takeda, he was responsible for an immunology pipeline that spanned from early target discovery to late-stage development and marketed products. Prior to his work at Takeda, Dr. Zalevsky worked in research and development at Xencor, where he oversaw the discovery and development of Xencor's first four clinical-stage assets. Dr. Zalevsky received his Ph.D. in Biochemistry from the Tetrad Program at the University of California, San Francisco. He received dual B.S. degrees in Biochemistry and Molecular, Cellular, and Developmental Biology from the University of Colorado at Boulder.