



Inflammaging

*Mechanisms, Markers, and
Intervention Strategies*

September 22-23, 2025

Rooms 1255/1256

The Neuroscience Center
6001 Executive Blvd
Rockville, Maryland 20852

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Inflammaging: Mechanisms, Markers, and Intervention Strategies.

September 22-23, 2025
6001 Executive Blvd, Rooms 1255/1256
Rockville, MD

Agenda

Day 1, September 22, 2025

7:30 – 8:00 AM	Registration
8:00 – 8:05 AM	Welcome and Introduction of Dr. Hodes and Keynote Speaker: <i>Mulualem E. Tilahun, D.V.M., Ph.D., NIA</i>
8:05 - 8:15 AM	Opening Remarks: Richard Hodes, M.D., NIA
8:15 - 8:45 AM	Keynote Presentation: <i>Vishwa Deep Dixit, D.V.M., Ph.D., Yale School of Medicine</i> Title: Inflammaging Checkpoints.
8:45 – 10:45 AM	Session 1: Molecular Mechanisms of Inflammaging <i>Moderator: Christina Liu, Ph.D., NIMH</i> <i>Notetaker: Divi Rao, Ph.D., NCI</i>
8:45 – 9:05 AM	<i>Rugang Zhang, Ph.D., MD Anderson Cancer Center</i> Title: The innate immunity in senescent cells during tissue aging.
9:05 - 9:25 AM	<i>Bimal Desai, Ph.D., University of Virginia</i> Title: Reduced mitochondrial calcium uptake in macrophages is a major driver of inflammaging.
9:25 - 9:45 AM	<i>Emily Goldberg, Ph.D., UCSF</i> Title: Lipids as drivers of neutrophil inflammation in age-related disease.
9:45 – 10:05 AM	<i>Yuxiang Sun, M.D., Ph.D., Texas A&M University</i> Title: Nutrient-sensing GHS-R in macrophage reprogramming and inflammaging.
10:05 – 10:45 AM	Panel Discussion
10:45 – 11:05 AM	Break

11:05 – 1:05 PM	Session 2: Hallmarks of Inflammaging Moderator: Mulualet E. Tilahun, D.V.M., Ph.D, NIA Notetaker: Leela Rani Avula, Ph.D., NCI
11:05 - 11:25 AM	Daniel Winer, M.D., Buck Institute for Research on Aging Title: B cell – T cell intercellular communication contributes to T cell immunosenescence.
11:25 -11:45 AM	Gaylia Jean Harry, Ph.D., NIEHS Title: Dysregulation of tissue-resident macrophages; possible contribution to inflammaging.
11:45 AM - 12:05 PM	Jie Sun, Ph.D., University of Virginia Title: Targeting macrophage self-renewal to dampen age-associated chronic diseases after respiratory viral infection.
12:05 - 12:25 PM	Cornelia Weyand, M.D., Ph.D., Mayo Clinic Title: T cell aging and organelle failure drive autoimmune tissue inflammation.
12:25 - 1:05 PM	Panel Discussion
1:05 - 2:05 PM	Lunch Break
2:10 – 4:10 PM	Session 3: Measures of Inflammaging Moderator: Merriline Vedamony, Ph.D., NIAID Notetaker: Leela Rani Avula, PhD., NCI
2:10 - 2:30 PM	Yang Mao-Draayer, M.D., Ph.D., Oklahoma Medical Research Foundation Title: Immunosenescence and MS: inflammaging for prognosis and therapeutic consideration.
2:30 – 2:50 PM	Maxim Artyomov, Ph.D., Washington University of St. Louis Title: Comprehensive profiling of an aging immune system reveals clonal GZMK ⁺ CD8 ⁺ T Cells as conserved hallmark of inflammaging.
2:50 – 3:10 PM	Jingzhong Ding, Ph.D., Wake Forest University Title: T helper cells in development of chronic inflammation and multimorbidity.
3:10 - 3:30 PM	Corina Amor Vegas, M.D., Ph.D., Cold Spring Harbor Laboratory Title: Deconstructing aging with senolytic CAR T cells.
3:30 – 4:10 PM	Panel Discussion
4:10 – 4:15 PM	Wrap Up: Christina Liu, Ph.D., NIMH
4:15 PM	Day 1 Adjourn

Day 2

September 23, 2025

7:30 – 8:00 AM	Registration
8:00 - 8:10 AM	Opening, Day 1 Recap, and Keynote Speaker Introduction: <i>Pushpa Tandon, Ph.D., NCI</i>
8:10 - 8:40 AM	Keynote Presentation: Janko Ž. Nikolich, M.D., Ph.D., University of Arizona Title: The role and the mechanisms of stromal lymph node aging in defective T cell homeostasis and primary immune responses.
8:40 – 10:50 AM	Session 4: Technologies for detecting and monitoring Inflammaging Moderator: Divi Rao, Ph.D., NCI Notetaker: Leela Rani Avula, Ph.D., NCI
8:40 – 9:00 AM	<i>Mohammad Rashidian, Ph.D., Dana-Farber Cancer Institute</i> Title: CD45-PET is a robust, non-invasive tool for imaging inflammation.
9:00 – 9:20 AM	<i>Amanda Latham, Ph.D., Mayo Clinic</i> Title: Biological agents and the aging brain: glial inflammation and neurotoxic signaling.
9:20 – 9:40 AM	<i>Duygu Ucar, Ph.D., The Jackson Laboratory</i> Title: The Role of Aging- and Infection-Induced Inflammation in Shaping Human Immune Responses
9:40 – 10:00 AM	<i>Qiuyang (Lisa) Zhang, Ph.D., Tulane University</i> Title: A Novel Strategy to Model Age-Related Cancer for Elucidation of the Role of Th17 Inflammaging in Cancer Progression.
10:10-10:50 AM	Panel Discussion
10:50-11:10 AM	Break

11:10 – 1:10 PM	Session 5: Role of Inflammaging in Age-Related Diseases Moderator: Mercy Prabhudas, Ph.D, M.B.A., NIAID Notetaker: Johanna Dwyer, D.Sc., RD. ICF, Contractor to NIH OD-ODS and Tufts Medical Center
11:10- 11:30 AM	Danica Chen, Ph.D., UC Berkeley Title: Inflammation and Aging-Associated Diseases.
11:30- 11:50 AM	Mohamed Abdel-Mohsen, Ph.D., Northwestern University Title: Glycomic Modulation of Inflammaging and Immune Functions during HIV Infection.
11:50 AM- 12:10 PM	Curtis J. Henry Ph.D., University of Colorado Anschutz Medical Campus Title: Delineating the Impact of Inflammaging on B-ALL Development and the Efficacy of Chimeric Antigen Receptor T-cell Therapy.
12:10 – 12:30 PM	Marta Rodriguez-Garcia, M.D., Ph.D., Wayne State University Title: Impact of Aging and Inflammaging on Mucosal Immune Protection.
12:30 – 1:10 PM	Panel Discussion
1:10 – 2:10 PM	Lunch Break
2:10 – 4:30 PM	Session 6: Interventions Moderator: Johanna Dwyer, D.Sc., RD. ICF, Contractor to NIH OD-ODS and Tufts Medical Center Notetaker: Qian Liu, Ph.D, NHLBI
2:10 - 2:30 PM	Lisa A. Lesniewski, Ph.D., University of Utah Title: Senolytic drugs attenuate inflammation and ameliorate physiologic function in old age.
2:30 – 2:50 PM	Elizabeth J. Kovacs, Ph.D., University of Colorado Title: Targeting the gut to reduce excessive inflammation after burn injury in aged mice.
2:50 – 3:10 PM	Christina D. Camell, Ph.D., University of Minnesota Title: Reversal of immune ageing in inflammatory macrophages.
3:10 – 3:30 PM	Payal Ganguly, Ph.D., University of Leeds (UK) Title: Cellular Senescence and Inflammaging in the Bone: Pathways, Genetics, Anti-Aging Strategies, and Intervention.
3:30 – 4:10 PM	Panel Discussion
4:10 - 4:30 PM	Closing Remarks and End of Workshop

Workshop Webpage:

<https://www.nia.nih.gov/research/dab/workshops/inflammaging-mechanisms-markers-and-intervention-strategies>.

Speaker Biographies and Contact Information



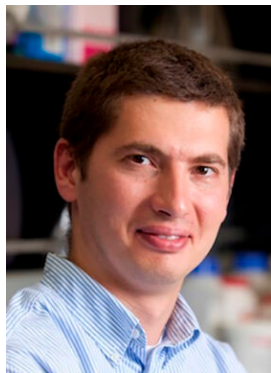
Mohamed Abdel-Mohsen, Ph.D.

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Dr. Mohamed Abdel-Mohsen is an Associate Professor of Medicine at Northwestern University's Feinberg School of Medicine, a member of the Potocsnak Longevity Institute and the Center for Human Immunobiology, and Director of the Virology, Immunology, and Technology Core at the Third Coast Center for AIDS Research. He received his training at the University of California, San Francisco, and the Vitalant Research Institute. He established his independent laboratory at The Wistar Institute in 2017 and joined Northwestern in 2024 to expand his research in aging science and human immunobiology. Dr. Abdel-Mohsen leads a research program at the intersection of glycoscience, immunology, and aging. His team investigates how the body's "sugar code," glycosylation, shapes immune function, inflammation, and mechanisms of premature biological aging, particularly in people living with chronic diseases. His laboratory has identified biomarkers that predict biological age and disease risk and developed glyco-immunotherapeutic strategies that harness the body's innate defenses to combat chronic conditions and extend healthspan. At Northwestern, Dr. Abdel-Mohsen collaborates across disciplines to translate glycoscience discoveries into interventions that can prevent age-related illnesses and improve long-term health. His work continues to advance translational research, revealing how glycosylation can be harnessed to protect against disease and promote healthy aging.



Maxim Artyomov, Ph.D.

Alumni Endowed Professor, Pathology & Immunology

Washington University of St. Louis

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Maxim Artyomov, Ph.D., is the Alumni Endowed Professor of Pathology and Immunology, at the Washington University of St. Louis. The Artyomov lab works on understanding immune cell responses through systems level approaches. They are focused on linking high-throughput data generation, hypothesis-centered data analysis and experimental validation of the system in question. Major interest is in the integrating epigenetic, transcriptional and metabolic regulation of the immune system on the cellular level. Specifically, Dr. Artyomov's lab developed state-of-the-art high-throughput transcriptional-metabolic profiling and analysis pipeline. Using it, they discovered and validated novel metabolic mechanisms controlling macrophage polarization as well as provided comprehensive description of the global metabo-transcriptional rewiring. They then followed up on their global

reconstruction of metabolic rewiring in macrophages and discovered novel immunoregulatory role for LPS-inducible metabolite itaconate.



Christina Camell, Ph.D.

Associate Professor, Department of Biochemistry, Molecular Biology, and Biophysics

Masonic Institute on the Biology of Aging and Metabolism

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Christina Camell is an Associate Professor at the Masonic Institute on the Biology of Aging and Metabolism and a faculty member of the Department of Biochemistry, Molecular Biology and Biophysics at the University of Minnesota. She is a Kavli Alumni, McKnight-Land Grant Fellow and Fesler-Lampert Chair (2021). The research in her lab focuses on fundamental questions addressing the biology of aging: how does inflammation promote age-related diseases? And, can those changes in the immune system be targeted to improve health-span? She is particularly interested in the visceral white adipose tissue, an organ that shows early signs of immune activation during aging. Her research has revealed distinct roles for immune cell subsets in the adipose tissue that become immunosenescent-like – including an inflammatory and exhausted phenotype of CD8 T cells, macrophages and B cells. These age-dependent phenotypes have a negative impact on adipose tissue function, such as lipolysis, and on the resilience of the older organism. A main emphasis of the lab optimized a mouse model of the humanized immune system – the normal microbial experience – mice that exhibits the diverse and mature immune system seen in humans. This work is published in *Science*, *Nature Aging*, *Cell Reports* and *Immunity&Ageing*.



Danica Chen, Ph.D.

Professor, Metabolic Biology, Nutritional Sciences & Toxicology

University of California at Berkeley

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Danica Chen is a Professor of Metabolic Biology, Nutritional Sciences & Toxicology at University of California at Berkeley. She is a Searle Scholar, an Ellison Scholar, a Kavli Fellow, a Hellman Fellow, and an elected member of Academy for Healthy Longevity Research. Dr. Chen received Ph.D. in molecular and cell biology from University of California at Berkeley and obtained postdoctoral training in biology of aging at Massachusetts Institute of Technology. Her research aims to understand the molecular and cellular mechanisms underlying aging-associated conditions and diseases and elucidate which aspects of aging-associated conditions are reversible.



Bimal Desai, Ph.D.

Professor of Pharmacology
University of Virginia School of Medicine
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Bimal grew up in Mumbai, India and came to the U.S. for graduate training in biomedical research. For his Ph.D. training in Immunology, he used chemical biology approaches to study cell signalling (advisor: Dr. Stuart Schreiber, HHMI & Department of Chemistry, Harvard University). During his postdoctoral training, Bimal became interested in how electrical signals govern biological processes. He focused on ion channel physiology and calcium signaling (advisor: Dr. David Clapham, HHMI & Boston Children's Hospital). In 2012, Bimal started his research lab in the Department of Pharmacology at UVASOM. The Desai Lab seeks to understand how immune cells use electrical signals to rapidly interpret the physical and chemical changes in their tissue environment, and the consequences of these processes on host defense, inflammation, and tissue homeostasis.



Jingzhong Ding, Ph.D.

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Vishwa Deep Dixit, D.V.M., Ph.D.

Waldemar Von Zedtwitz Professor of Pathology, Immunobiology, and Comparative Medicine
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Dr. Vishwa Deep Dixit is the Waldemar Von Zedtwitz Professor of Pathology, Immunobiology, Comparative Medicine and the director of the Yale's Center for Research on Aging at the Yale University. Deep studied veterinary medicine in India, did PhD research at the University of Hannover, Germany and postdoctoral research in the Laboratory of Immunology at the US-National Institute on Aging (NIA), in Baltimore. Deep started his laboratory in 2006 at the Pennington Biomedical Research Center in Baton Rouge, Louisiana and was recruited to Yale in 2013. Among notable findings, Dixit lab discovered nerve-associated macrophages as the regulators of inflammation and lipolysis in aging and that NLR family pyrin domain containing 3 (NLRP3), is a metabolic inflammasome that controls

inflammaging driven disorders. Working on the interface of metabolism and immune system, Dixit and colleagues found that ketone bodies block inflammasome and elevating tissue FGF21 protects against thymic involution, loss of T cell diversity and organismal aging. Through interdisciplinary team science, Deep's laboratory discovered that the moderate calorie restriction (CR) in humans revealed CR-mimetic targets (SPARC, PLA2G7 and cysteine metabolism) that reigns in inflammaging and enhanced metabolic healthspan. Most of his mentees have gone on to successful careers in academia and industry.

Dixit is a member of the Academy of Health Lifespan Research and Connecticut Academy of Science and Engineering. His papers (>100) are published in leading scientific journals. Dixit's service is recognized by multiple awards, including the Glenn award and NIA's 2017 Nathan Shock Award for his pioneering work on Immunometabolism of aging.



Payal Ganguly, Ph.D.

Project Manager, Faculty of Medicine and Health
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Dr. Payal Ganguly completed her PhD on 'Bone resident mesenchymal stromal cells in healthy ageing and osteoarthritis' in 2016. Since then, she has worked on bone regeneration, cellular senescence, biomaterials and biologics with anti-aging potential. Previously, she investigated the effect of pharmaceutical agents on patient derived 3D-tissue explants for inflammatory arthritis. She is currently a project manager in Faculty of Medicine and Health at University of Leeds, UK. Her current work focuses on polymyalgia rheumatica (PMR) related investigations. She was recently invited to the 1st Medical Innovation and Knowledge share (MIKS) congress in Spain (3-5th April, 2025) as a speaker. She graduated with B.Pharm from NMIMS University, Mumbai, India and Master's in Nanomedicine from Newcastle University, UK. She then worked as a project assistant at Institute of Chemical Technology (ICT), followed by a research engineer role under a Gates foundation project for novel transdermal nanoparticle system at Indian Institute of Technology (IIT), Mumbai, India. She is a co-inventor on the patent for the same. She has also given a Tedx talk on 'sustainable healthcare systems' (https://www.youtube.com/watch?v=klH3XPLmbk&ab_channel=TEDxUniversityofLeeds). Her research interests include rheumatology, bone marrow stem cells and aging, combating cellular senescence, 3D in-vitro models, tissue engineering and nanomedicine.



Emily Goldberg, Ph.D.

Assistant Professor, Physiology
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Dr. Emily Goldberg is an Assistant Professor of Physiology at UCSF. She obtained her PhD from the University of Arizona, under the mentorship of Dr. Janko Nikolich, and then continued her training as a postdoctoral fellow at Yale University in the laboratory of Dr. Vishwa Deep Dixit. The Goldberg lab combines biochemistry, immunology, and genetic approaches to uncover new molecular mechanisms that control inflammation and metabolic health.



Gaylia Jean Harry, Ph.D.

Head, Neurotoxicology Research Group
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Dr. Jean Harry received her Ph.D. from Virginia Commonwealth University with an emphasis on neuropharmacology/neurotoxicology followed by post-doctoral training at the University of North Carolina/Chapel Hill in lipid biochemistry and neuropathology. She joined the National Institute of Environmental Health Sciences as Head of the Neurotoxicology Group where she continues to lead a research group focused on examining the brain immune cells within a framework of understanding how they can be modified by environmental or genetic factors. The research focuses on understanding how the normal regulatory function of these cells and the neuroimmune system can be affected, leading to dysfunction and altered brain development, aging, and neurodegeneration. The work continues to explore the homeostatic functions of tissue resident macrophages and their contribution within the framework of adverse effects from environmental exposures.



Curtis Henry, Ph.D.

Deputy Associate Director of Faculty and Staff Relations
Associate Professor of Immunology and Microbiology
The David F. and Margaret Turley Grohne Endowed Chair in Translational Cancer Research
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Dr. Curtis J. Henry is the Deputy Associate Director of Faculty and Staff Relations at the University of Colorado Cancer Center, an Associate Professor of Immunology & Microbiology at

the University of Colorado Anschutz Medical Campus, and The David F. and Margaret Turley Grohne Endowed Chair in Translational Cancer Research.

Dr. Henry received his undergraduate degrees in Molecular Biology and Chemistry from Florida Agricultural and Mechanical University (2003), followed by his doctorate degree in Immunology from Wake Forest University School of Medicine (2008) under the tutelage of Dr. Elizabeth Hiltbold-Schwartz. Dr. Henry then completed his postdoctoral fellowship (2008-2012) and was promoted to Research Instructor (2012-2016) under the guidance of Dr. James DeGregori at the University of Colorado Anschutz Medical Campus. Dr. Henry transitioned to his first independent position as an Assistant Professor of Pediatrics at Emory University School of Medicine where he was a member of the Aflac Cancer and Blood Disorders Center and a member of the Cancer Immunology program at the NCI-designated Winship Cancer Institute (2016-2023).

During his career, Dr. Henry has received several prestigious grants including an NCI-funded K01, an American Cancer Society Junior Faculty Achievement Award, an Aflac Pilot Grant, and the Mark Foundation for Cancer Research ASPIRE Award. Dr. Henry has also been listed as the first or senior author on numerous manuscripts published in highly-cited journals including Nature Communications, Cancer Research, the Proceedings of the National Academy of Sciences of the United States of America, and the Journal of Clinical Investigation. In addition to Dr. Henry's publications, several patents have been awarded to his team and collaborators for their research endeavors. These accolades have led to Dr. Henry being recognized by Cell Press as one of 100 More Inspiring Black Scientists in America (June 2020) and 1,000 Black Scientist in America (December 2020).

Research conducted in the Henry laboratory focuses on understanding how immunological changes induced by cancer-associated comorbidities (e.g., aging and obesity) impact cancer progression and responses to immunotherapies.



Elizabeth Kovacs, Ph.D.

Professor and Vice Chair of Research, Department of Surgery

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Dr. Elizabeth J. Kovacs received her B.A. degree from Reed College in Portland, OR and her Ph.D. from the University of Vermont. Her postdoctoral training was at the National Institutes of Health, where she explored gene expression in macrophages. After 20+ years of working at Loyola University Chicago, where she served as Director of Research of the Burn and Shock Trauma Institute and Director of the Alcohol Research Program, in 2016, Dr. Kovacs relocated her laboratory to the University of Colorado Denver. In Colorado, she is a Professor and Vice Chair of Research in the Department of Surgery and Director of Burn Research. For most of her career, Dr. Kovacs investigated innate immunity in the lung after traumatic injury in patients and in murine models of injury. Over the past

decade, her research has expanded to include the gut-liver axis and its role in regulating pulmonary inflammatory responses and lung failure following remote injury. Most recently, Dr. Kovacs has incorporated neuroinflammation and cognitive impairment into her studies and is interrogating the gut-brain axis.



Amanda Latham, Ph.D.

Postdoctoral Research Fellow

Mayo Clinic

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Dr. Amanda Latham is a postdoctoral research fellow in Dr. Marissa Schafer's laboratory at the Mayo Clinic in Rochester, MN. She earned her B.S. in Microbiology, Immunology, and Pathology and her Ph.D. in Toxicology from Colorado State University. Her doctoral research explored how infectious agents, environmental neurotoxicants, and aging contribute to neurological dysfunction, bridging the fields of neuroimmunology and toxicology to reveal how diverse exposures impact the brain. At the Mayo Clinic, Dr. Latham investigates the biology of brain aging, with a particular focus on the cellular mechanisms that drive neuroinflammation and cognitive decline. She is especially interested in how aged immune cells and the accumulation of senescent cells contribute to hippocampal dysfunction and impaired cognition across the lifespan. By applying spatial transcriptomics and proteomics, her work aims to define the pathways through which cellular aging influences brain function and to uncover therapeutic strategies to preserve cognition.



Lisa Lesniewski, Ph.D.

Co-Director, Translational Vascular Physiology Laboratory and Director,
Vascular and Genetics Program

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I am the Co-Director of the Translational Vascular Physiology Laboratory at the Nora Eccles Harrison Cardiovascular Research and Training Institute, where I also serve as Director of the Vascular and Genetics Program. I received my Ph.D. in Exercise Physiology from Texas A&M University and performed post-doctoral training in metabolism in Dr. Jerrold Olefsky's laboratory at University of California at San Diego and in Vascular Aging in Dr. Douglas Seal's Laboratory at University of Colorado-Boulder. The overarching goal of my research program is to elucidate the cellular and molecular mechanisms underlying age- and obesity-associated vascular and metabolic dysfunction and disease, as well as to develop novel interventions to combat these common comorbidities. My current research projects are aimed at (1) exploring the role of hyaluronan synthase 2 and alterations in hyaluronan in age-related vascular dysfunction, as well as to explore the therapeutic potential

of targeting HA to ameliorate age-related vascular dysfunction, (2) elucidating the role of T cells, and their interaction with senescent cells, in mediating age-related metabolic dysfunction; and (3) identifying novel senolytic therapies that can be used to improve vascular and metabolic function and reduce disease risk in the settings of aging and obesity.



Yang Mao-Draayer, M.D., Ph.D.

Professor and Director of Clinical and Experimental Therapeutics
Oklahoma Medical Research Foundation
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Dr. Yang Mao-Draayer is a Professor and Director of Clinical and Experimental Therapeutics at the Oklahoma Medical Research Foundation. She has been a neurologist and physician scientist specializing in Multiple Sclerosis and Neuromyelitis Optica since 2005. She completed both MD and PhD degrees, the latter degree in Biology and Molecular Genetics from the University of Iowa. She completed neurology residency and Neuroimmunology fellowship training at the University of Vermont, where she served as chief resident. She has authored over 100 peer-reviewed research articles and >100 abstracts. She has served in many national and international study sections, including NIH, DOD, NMSS, and FDA. Dr. Yang Mao-Draayer has served on the National Healthcare Advisory Committee for the National Multiple Sclerosis Society. She was also named the chair of the Health and Economic Committee for the North American Registry for Care and Research in MS (NARCRMS). In addition, she has been an elected member of the Neuromyelitis Optica (NMO) Guthy Jackson Charitable Foundation International Clinical Consortium and Biorepository (ICCB) among a total of 80 ICCB members worldwide since 2015.



Janko Nikolich, M.D., Ph.D.

Department Head and Professor, Immunobiology
Director, Aegis Consortium for Pandemic-Free Future
Co-Director, Arizona Center on Aging
University of Arizona
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Dr. Janko Nikolich is an internationally recognized leader in immunology and gerontology. He received his M.D., MSc and Ph.D. in Immunology from Belgrade University School of Medicine. After postdoctoral training at the Scripps Clinic and Research Foundation (with Mike Bevan), he held faculty positions at the Memorial Sloan-Kettering Cancer Center/Cornell University, and at the Oregon Health & Science University. In 2008, he moved to the University of Arizona to lead the Department of Immunobiology and the Arizona Center on Aging.

His long-term interests include basic mechanisms of T-cell function, immunity to acute viral infection in older adults, persistent virus interactions over the lifespan, vaccines and biomarkers of declining immunity in the elderly, immune rejuvenation, immune monitoring in chronic conditions of aging and the impact of inflammation and nutritional intervention in aging, immunity and metabolic disorders. He has published over 230 scientific papers and reviews describing his work and has held or holds grant awards from the National Institutes of Health totaling >\$120M so far. In 2024, he was elected to the Serbian Academy of Sciences and Arts and in 2025 was named Regents Professor by the Arizona Board of Regents, the highest academic honor at the Arizona public universities.



Mohammad Rashidian, Ph.D.

Assistant Professor

Dana-Farber Cancer Institute and Harvard Medical School

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Dr. Mohammad Rashidian is an Assistant Professor at Dana-Farber Cancer Institute and Harvard Medical School, where his laboratory develops next-generation imaging tools to visualize the dynamics of the immune system in cancer, inflammation, and autoimmunity. His group engineers protein-

based PET tracers that enable real-time, whole-body tracking of immune responses, including distinct immune cell subsets such as T cells and myeloid cells. In parallel, his lab integrates imaging with protein engineering to develop novel immunotherapies, including engineered cytokine fusions and “T-cell enhancer” platforms that reprogram therapeutic T cells.

Dr. Rashidian earned his PhD in Chemical Biology and Protein Engineering from the University of Minnesota and completed postdoctoral training at the Whitehead Institute for Biomedical Research at MIT.



Marta Rodriguez-Garcia, M.D., Ph.D.

Associate Professor, Department of Biochemistry, Microbiology, and Immunology

Wayne State University

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Dr. Marta Rodriguez-Garcia obtained her M.D. from the University of Granada and Ph.D. from the University of Barcelona (Spain). She completed her medical residency in Clinical Immunology and then moved to the USA for postdoctoral training, first at the Ragon Institute of MGH, MIT and Harvard, and then at Dartmouth in Dr. Wira's laboratory to focus her research on reproductive immunology and HIV infection. She then became an Assistant Professor in the Department of Immunology at Tufts, and recently moved to Wayne State University as an Associate Professor in the Department of Biochemistry, Microbiology and Immunology and the C.S Mott Center for Human Research and Development. Her research, funded by NIH and the Burroughs Wellcome Fund (PATH awardee), focuses on

understanding the early events of mucosal HIV acquisition in the female genital tract and how innate immune protection changes with age.



Jie Sun, Ph.D.

Harrison Distinguished Teaching Professor of Medicine
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Jie Sun, Ph.D., is the Harrison Distinguished Teaching Professor of Medicine at the University of Virginia (UVA). He obtained his PhD from the University of Pennsylvania and did his postdoc training at UVA. He was faculty members at the Indiana University and the Mayo Clinic (Rochester) before coming back to UVA in 2022. His lab has been studying the immune mechanisms underlying mucosal protection, acute viral pathogenesis, lung recovery and chronic sequelae after respiratory viral infections including influenza and SARS-CoV-2. His lab also explores how chronic inflammation triggers cellular senescence and tissue aging, seeking ways to rejuvenate the older populations by targeting the immune system.



Yuxiang Sun, M.D., Ph.D.

Professor and Associate Department Head
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Dr. Yuxiang Sun is Professor and Associate Department Head in the Department of Nutrition at Texas A&M University. She earned her M.D. from Beijing Medical University in China and her Ph.D. from the University of Manitoba in Canada. Dr. Sun is a leading investigator in the field of hormone ghrelin, she generated a series of mouse models for ghrelin and its receptor, and uncovered novel roles for ghrelin signaling in nutritional regulation, diabetes, thermogenesis, inflammation, and aging immunity. Her work demonstrated that suppressing ghrelin signaling shifts metabolism from obesogenesis to thermogenesis and reprograms inflammation from pro-inflammatory to anti-inflammatory state, establishing ghrelin as a critical nutrient sensor, metabolic regulator, and immunomodulator. These discoveries have significant implications for preventing/treating chronic disease and extending healthspan.

Dr. Sun's current research focuses on ghrelin signaling in liver disease, colitis, Alzheimer's disease, and nutrition in lifespan. She has published over 145 peer-reviewed articles (10,297 citations; H-index 48; i10-index 91). She currently serves as PI on two NIH R01 grants on immunometabolism and inflammaging and two foundation grants on liver cancer, as well as Co-I on additional NIH-funded projects. She received the 2024 Osborne and Mendel Award from the American Society for Nutrition for her scientific contributions.



Duygu Ucar, Ph.D.

Professor

The Jackson Laboratory

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Dr. Duygu Ucar is a Professor at The Jackson Laboratory for Genomic Medicine, where she leads a multidisciplinary research program on immune system aging and reduced vaccine responses. Dr. Ucar earned her B.S. in Computer Science from Bilkent University and her Ph.D. from The Ohio State University, developing network biology algorithms to study gene and protein interactions. During her postdoctoral training at Stanford University's Department of Genetics and the University of Iowa, she pioneered computational methods to identify complex epigenomic patterns linked to aging and cell identity, contributing to foundational discoveries in the epigenetic regulation of cellular aging. Since establishing her laboratory at The Jackson Laboratory in 2013, Dr. Ucar has integrated functional immunology, computational biology, and single-cell genomics to uncover molecular signatures of immune system aging. Her work examines how biological sex and prior infections shape age-associated immune changes, and how these changes influence responses to vaccines. Her NIH- and foundation-funded research aims to define the genomic programs that govern immune resilience and dysfunction, guiding development of targeted strategies to promote healthy immune aging.



Corina Amor Vegas, M.D., Ph.D.

Assistant Professor and CSHL Cancer Center Program Co-Leader

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Corina received an M.D. from Universidad Complutense de Madrid in Spain and a Ph.D. from the Gerstner Sloan Kettering Graduate School at Memorial Sloan Kettering Cancer Center in NY. During her time as a graduate student, she developed the first CAR T cells able to eliminate senescent cells. This innovation was extensively highlighted in scientific journals and technology publications and led to several awards including the F99/K00 from the NCI, the Chairman's Prize award from MSKCC or the listing as Forbes 30 under 30. Following graduation she established her own research group at Cold Spring Harbor Laboratory as an Independent Fellow in January 2022 and was awarded the NIH Director's Early Independence Award (DP5). After two years, she was promoted to assistant professor in 2024 and became an HHMI Freeman Hrabowski Scholar in October 2025. The Amor laboratory studies aging biology with a focus on cellular senescence. The long-term goal of their research is to elucidate the contribution of senescent cells to the

aging process and to develop novel cell-based therapeutic strategies to treat age-related pathologies.



Cornelia Weyand, M.D., Ph.D.

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Cornelia M. Weyand, M.D., Ph.D., is a Professor of Medicine and Immunology at the Mayo Clinic College of Medicine and Science and the Mayo Alix School of Medicine. She holds joint appointments in the Departments of Immunology and Cardiology and leads the Program in Immunity and Inflammation, a translational program bridging basic immunology to disease.

Weyand earned her M.D. in Germany, followed by a fellowship at the German Cancer Research Center and a residency at Hannover Medical School, Germany. She subsequently completed a fellowship in Immunology at Stanford University. Dr. Weyand joined Mayo Clinic in 1990, became a Professor of Medicine and Immunology in 1998 and the Barbara Woodward Lips Professor of Medicine & Immunology in 2000. From 2004 to 2009, she was the David Lowance Professor of Medicine at Emory University, where she served as the Director of the Lowance Center for Human Immunology and the Division of Rheumatology. In 2009, she returned to Stanford University, where she became the Chief of Rheumatology and Immunology and the Director of the Center for Translational Medicine. Dr. Weyand remains a faculty member at Stanford University as Professor Emerita.



Daniel Winer, M.D.

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Dr. Winer is an Associate Professor at the Buck Institute for Research on Aging, with cross appointments to the University of Southern California, School of Gerontology, to the University of Toronto, Department of Immunology and Department of Laboratory Medicine and Pathobiology, to the Toronto General Research Institute, and to the Dominican University of California. Dr. Winer is known as an early pioneer in three emerging fields of immunology: immunometabolism, mechanoimmunology, and astroimmunology. In immunometabolism, the Winer lab studies how the immune system inside tissues, including adipose, liver and the intestinal tract, control aging and obesity-related chronic diseases such as insulin resistance and type 2 diabetes. In addition, they study how nutrient availability signals that are also tied to aging, like insulin receptor signaling, control immunological function, especially in adaptive immune cells.



Qiuyang (Lisa) Zhang, Ph.D.

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Dr. Qiuyang Zhang is an Assistant Professor in the Department of Structural and Cellular Biology at Tulane University School of Medicine. She is affiliated with both the Tulane Center for Aging and the Tulane Cancer Center. Dr. Zhang earned her Ph.D. from Xi'an Jiaotong University in China and completed her postdoctoral training in the United States. She began her tenure-track position in June 2021. Her research focuses on aging and prostate cancer, specifically investigating the role of inflammation in these conditions, particularly during aging and obesity. One of her key projects examines “inflammaging” and its effects on prostate cancer, particularly through the Th17/Treg axis, utilizing innovative mouse models. In addition, Dr. Zhang’s lab explores the connection between inflammaging and Alzheimer’s disease, with a particular emphasis on its impact on gut microbiota. She also studies the effects of deubiquitinating enzymes, specifically USP26, on prostate cancer metastasis and treatment resistance. Her work employs CRISPR/Cas9 technology and proteomics to inform the development of targeted therapies.



Rugang Zhang, Ph.D.

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Dr. Zhang received his Ph.D. in Cell Biology from the Institute of Biochemistry and Cell Biology, Shanghai Institutes of Biological Sciences, Chinese Academy of Science. His postdoctoral training came from the Institute for Cancer Research, Fox Chase Cancer Center, where he later became an Assistant Professor. He joined The Wistar Institute as an Associate Professor in 2012, was promoted to Professor in 2015 and later became holder of the Christopher M. Davis Endowed Professor & Leader, Immunology, Microenvironment and Metastasis Program. He assumed various leadership roles during his time at Wistar and was appointed Deputy Director in 2017. He joined The University of Texas MD Anderson Cancer Center as a Professor and Chair of Department of Experimental Therapeutics in 2023. He holds the John M. O’Quinn Endowed Chair in Cancer Research and serves as Associate Director for Discovery Science, MD Anderson Cancer Center Supporting Grant.

Zhang’s research program focuses on development novel therapeutic strategies for gynecological cancers. In addition, he investigates the aging process of normal mammalian cells and its role in both tissue aging and cancer development for the discovery of therapeutic applications.

Abstracts

Day One Keynote Speaker

Vishwa Deep Dixit, D.V.M., Ph.D.

All biological activities require energy through the intake and generation of metabolites. Unresolved chronic inflammation originating from innate immune cells and loss of naïve T cells with restriction of T cell receptor repertoire diversity emanating from age-related thymic involution are some of the mechanisms that limit healthspan and even lifespan. In this presentation I will provide evidence that energy metabolism and aging of the immune system are intimately linked to health and disease. The presentation will give an overview of the hallmarks of immunological aging and synthesize how the immune system, coupled to cellular and organismal metabolism, controls disease susceptibility. Furthermore, I will highlight potential unifying immunometabolic mechanisms that may underlie lifespan-healthspan extension. Given that immune and metabolic systems are modifiable and targetable, understanding the role of myriads of organ-resident immune cells and the underlying metabolic mechanisms that cause dysfunction can have transformational potential for the health of older adults. Based on our new data, we posit that harnessing the checkpoints of healthspan and longevity may require awakening the dormant enantiostatic pathways that maintain and restore tissue function.

Session 1: Molecular Mechanisms of Inflammaging

Rugang Zhang, Ph.D.

Sterile inflammation, also known as “inflammaging”, is a hallmark of tissue aging. Cellular senescence contributes to tissue aging in part through the secretion of proinflammatory factors known as the senescence-associated secretory phenotype (SASP). Thioredoxin reductase 1 (TXNRD1) genetic variability is associated with aging and age-associated phenotypes such as late-life survival, activity of daily living, and physical performance at old age. TXNRD1's role in regulating tissue aging has been attributed to its enzymatic role in regulating cellular redox. Here we show that TXNRD1 drives the SASP and inflammaging through the cyclic GMP-AMP synthase (cGAS)-stimulator of interferon genes (STING) innate immune response pathway independently of its enzymatic activity. TXNRD1 localizes to cytoplasmic chromatin fragments and interacts with cGAS in a senescence status dependent manner, which is necessary for the SASP. TXNRD1 enhances the enzymatic activity of cGAS. TXNRD1 is required for both the tumor-promoting and immune-surveillance functions of senescent cells, which are mediated by the SASP *in vivo* in mouse models. Treatment of aged mice with a TXNRD1 inhibitor that disrupts its interaction with cGAS, but not an inhibitor of its enzymatic activity alone, downregulated markers of inflammaging in several tissues. In summary, our results report TXNRD1 promotes the SASP via the innate immune response with implication in inflammaging. This suggests that TXNRD1 and cGAS interaction is a relevant target for selectively suppressing inflammaging.

Bimal Desai, Ph.D.

Age-associated chronic low-grade inflammation, termed inflammaging, is a major driver of aging-related diseases, yet its molecular mechanisms remain poorly understood. We discovered that reduced mitochondrial calcium (mCa^{2+}) uptake in macrophages is a central mechanism driving inflammaging. Analysis of 700 human blood transcriptomes revealed that expression of the mitochondrial calcium uniporter (MCU) and its regulatory subunit MICU1 correlates inversely with age. Indeed, macrophages from aged mice exhibit significantly decreased mCa^{2+} uptake capacity, which amplifies cytosolic Ca^{2+} oscillations and potentiates NF κ B activation, rendering them hyper-inflammatory. Using genetic models, we demonstrated that loss of MCU mimics this aging phenotype in young macrophages. Beyond inflammaging, we uncovered that mCa^{2+} signaling serves as an electrometabolic switch essential for antifungal immunity. Upon pathogen detection, macrophages use a rapid two-phase Ca^{2+} relay, cytosolic Ca^{2+} elevation followed by MCU-mediated mitochondrial Ca^{2+} influx, to reprogram macrophage metabolism. This mCa^{2+} signaling activates pyruvate dehydrogenase, fueling NADPH production necessary for phagosomal reactive oxygen species generation and pathogen killing. MCU-deficient macrophages show impaired fungal killing, and mice lacking myeloid MCU are highly susceptible to disseminated candidiasis. Our findings reveal MCU as a keystone molecular apparatus linking mitochondrial dysfunction to both inflammaging and antimicrobial immunity. These discoveries suggest that restoring mCa^{2+} uptake capacity in tissue-resident macrophages could simultaneously combat inflammaging and enhance antimicrobial defense, offering novel therapeutic strategies for age-associated inflammatory and infectious diseases.

Emily Goldberg, Ph.D.

Neutrophils are short-lived cells that are produced by the billions every day to circulate throughout the body. As a key component of the innate immune system, they play essential roles in antimicrobial immunity, but also instigate sterile inflammatory diseases. Immunometabolic paradigms developed by studying T cells and macrophages establish that cellular metabolism dictates immune function. Neutrophils have long been known as glucose-reliant. But roles for lipids have been reported in granulopoiesis and mature neutrophil function. Therefore, we set out to uncover how neutrophils acquire lipids, how this influences their functionality, and what role this might play in chronic inflammatory diseases. We found that neutrophils take up free fatty acids and complex lipoproteins, but that their uptake is regulated through different signaling pathways. Remarkably, after lipid uptake, neutrophils show evidence of actin depolymerization and expression of adhesion molecules. In line with these observations, neutrophils with high lipid content also migrate less. Physiologically, neutrophils help drive chronic inflammation in the setting of atherosclerosis, and conditionally ablating TLR pathways involved in their lipid uptake also protects against vascular plaque growth. Our work highlights an important understudied role for lipids in neutrophil biology and how this controls inflammation and disease progression.

Yuxiang Sun, M.D., Ph.D.

Chronic low-grade inflammation (“inflammaging”) contributes to many age-related diseases. Aging is marked by elevated systemic and tissue inflammation, as well as reduced disease

resistance. Growth hormone secretagogue receptor (GHS-R) is the receptor of nutrient-sensing gut hormone ghrelin, ghrelin-GHSR system has multifaceted functions in energy-homeostasis and metabolism. We have observed that GHS-R is highly expressed in macrophages, and the expression is upregulated during aging and correlated with inflammatory responses to high-fat diet (HFD), carbon tetrachloride (CCl₄), and dextran sulfate sodium (DSS).

To define the roles of GHSR in macrophages, we studied myeloid-specific GHS-R knockout *LysM-cre;Ghsr^{f/f}* mice. Under HFD, macrophage GHS-R activated IRS2–AKT2 signaling, promoting pro-inflammatory polarization. In CCl₄-induced liver fibrosis, GHS-R, via Foxo1–TGF-β1 pathway, reprogrammed the tissue microenvironment to exacerbate fibrosis. Aging is known to be associated with weakened intestinal barrier (“aging leaky gut”) and microbial dysbiosis. We found that GHS-R expression in colon increases with age and is negatively correlated with epithelial gap junction proteins. FITC-dextran assay in young (2 mo) and old (22 mo) mice revealed reduced gut permeability in old knockouts, indicating protection of aging leaky gut. Under DSS-induced colitis, old control mice developed severe symptoms, whereas old knockouts showed mitigated disease activity index, immune profiles, and reduced tissue injury. Consistently, bone marrow–derived macrophages from old knockouts exhibited enhanced mitophagy, reduced ROS, and suppressed inflammasome activation. In summary, GHS-R is a critical regulator of macrophage programming. Targeting macrophage GHS-R may represent a novel immunotherapeutic strategy to improve metabolic health and enhance immune fitness in aging.

Session 2: Hallmarks of Inflammaging

Daniel Winer, M.D.

A dysregulated adaptive immune system is a key feature of aging, and is associated with age-related chronic diseases and mortality. Most notably, aging is linked to a loss in the diversity of the T cell repertoire and expansion of activated inflammatory age-related T cell subsets, though the main drivers of these processes are not fully understood. Here, we find that T cell aging is directly influenced by B cells. Specifically, B cells are a major cell type that contributes to the age-related reduction of naive T cells, their associated differentiation towards pathogenic immunosenescent T cell subsets, and for the clonal restriction of their T cell receptor (TCR). Concurrently, mice lacking B cells display marked improvements in healthspan and lifespan. Mechanistically, we uncover a role for B cell specific insulin receptor signaling in influencing age-related B cell pathogenicity that in turn induces CD4⁺ T cell dysfunction; this process is in part driven by MHCII expression. These results establish intercellular communication and nutrient sensing mechanisms as hallmarks of aging utilized by B cells to drive age-associated adaptive immune dysfunction and healthspan outcomes. Furthermore, this study suggests new modalities to manage aging and related health decline.

Gaylia Jean Harry, Ph.D.

Aging represents a set of fundamental and interconnected biological processes for which the development can set the stage for modifications across the lifespan. The culmination of

structural and functional changes requires continual adaptation with an accumulation of molecular and cellular deficiencies or damage. This may shift normal immune and metabolic homeostasis, increasing the potential for numerous aging-related diseases, frailty, and early mortality. Inflammation is a common hallmark of numerous age-related diseases reflecting such dysregulation or immunosenescence of immune cells, resulting in compromised elimination and accumulation of pathogens, pre-malignant cells, senescent cells, cellular debris, and/or aberrant proteins. Tissue resident macrophages (TRMs) represent a potential target to consider in such processes. They uniquely serve as immune sentinels providing day-to-day functions essential for tissue homeostasis as regulated by specific tissue “niches”. The early development, long-life, reliance on self-renewal of these cells may reflect cellular alterations that contribute to the latent or later in life adverse effects observed with inflammaging. Alternatively, an elevated inflammatory state with aging can compromise the normal regulatory functions of TRM contributing to adverse health effects. Thus, a functional alteration in TRMs could result in a spectrum of secondary adverse effects influencing and interacting with aspects of inflammaging. Findings will be presented from various studies as well as experiments examining the brain TRM to set a framework for considering TRMs as critical components in the process of inflammaging and how they may be modified by environmental factors.

Jie Sun, Ph.D.

Tissue-resident alveolar macrophages (AMs) rely on intrinsic stem-like programs for self-renewal and maintenance, yet the transcriptional networks that support these functions and their relevance to post-viral lung disease remain largely unknown. Here, we identify TCF4 (*Tcf7l2*) as a critical transcription factor that governs AM maturation and stemness. Loss of TCF4 impaired AM proliferation, shifted their identity toward a pro-inflammatory phenotype, and exacerbated host morbidity following influenza or SARS-CoV-2 infection. Conversely, enforced TCF4 expression promoted the expansion of mature AMs, and supported lung recovery, thereby protecting against severe acute viral disease. Mechanistically, TCF4 antagonized β -catenin-driven inflammatory transcription while preserving oxidative phosphorylation, defining a reciprocal regulatory axis essential for AM function. Notably, respiratory viral infections and exuberant interferon signaling suppressed TCF4 expression, which remains chronically reduced in murine and human lungs with post-COVID fibrosis. This downregulation is associated with persistent KRT8^{hi} dysplastic epithelium and collagen deposition. Moreover, aging diminished TCF4 expression and enforced TCF4 expression dampened age-associated decline of AM self-renewal. Furthermore, *in vivo* TCF4 overexpression after viral clearance promoted mature AM presence, attenuated chronic lung fibrosis and restored pulmonary function in aged lungs after acute infection. These findings have established TCF4 as a key regulator of AM stemness and identified a promising therapeutic target for long COVID and related chronic lung diseases through modulation of macrophage regenerative capacity by targeting TCF4.

Session 3: Measures of Inflammaging

Yang Mao-Draayer, M.D., Ph.D.

Dr. Yang Mao-Draayer’s presentation will review her research on immunosenescence and inflammaging for prognosis and therapeutic consideration in MS.

1. Comprehensive deep immunophenotyping in progressive MS.
2. SASP--cytokine and gene expression changes in progressive MS as compared to nonprogressive benign MS.
3. Recent work on specialized pro-resolving mediators (SPMs) enhance efferocytosis as potential treatment of inflammaging in MS.
4. Metabolites and microbiome work demonstrating short-chain fatty acid (SCFA) and unique gut microbiome links disease progression in MS.

Corina Amor Vegas, M.D., Ph.D.

Cellular senescence, a stress response program characterized by stable cell cycle arrest and a proinflammatory secretome, is a key hallmark of the aging process. While in younger organisms senescent cells are effectively cleared by the immune system; in the elderly they accumulate in tissues and are thought to contribute to aging pathobiology. Yet how do they build up and how do they contribute to aging remains unclear. Two key limitations that have held the field back in answering these questions have been the lack of: 1) surface markers to isolate and characterize senescent cells from aged tissues and 2) specific somatic approaches to target them without the need to breed and age for years genetically engineered mouse models (GEMMs) or employ unspecific chemical approaches. In a departure from these strategies we develop cell-based senolytic therapies based on chimeric antigen receptor (CAR) T cells. Harnessing them, we here explore the profile and characteristics of senescent cells that accumulate during physiological aging and their functional impact on aging phenotypes. In addition, we explore the preventive and therapeutic potential of immune-based cell therapies for age-related pathologies.

Day Two Keynote Speaker

Janko Nikolic, M.D., Ph.D.

Loss of immunity with old age underlies dramatic increases in vulnerability against new, previously not encountered, infections. In response to primary infections, old T cell responses are lower, slower and less diverse. We examined what factors critically contribute to these defects. While a numerical decline in naïve T cells with aging (60-75% reduction) is one contributing factor, we found that the remaining naïve T cells (T_n) from the old organism show no cell-intrinsic defects in activation, proliferation or differentiation. Indeed, old T_n cells can function on par with T_n cells from younger individuals, as long as they are activated in the young environment.

Instead, we have mapped many defects in T_n cell maintenance and activation to age-related changes in lymph node stroma. Specific and discrete numeric and architectural defects in the old lymph nodes affect distinct stromal subpopulations, as evidenced by confocal microscopy and single-cell transcriptional analysis. A combination of cell subset loss, decline in extracellular matrix component synthesis and metabolic dysregulation at the level of cellular respiration was found in fibroblastic reticular cells (FRC) and lymphoid endothelial cells (LEC), with less prominent defects in blood endothelial cells (BEC). These defects all synergize to profoundly change structure and function of old stromal LN cells. Correction of stromal function by

improved redox balance and mitochondrial respiration was achieved in vitro and in vivo and needs to be considered in the context of rejuvenation treatments.

Session 4: Technologies for Detecting and Monitoring Inflammaging

Mohammad Rashidian, Ph.D.

Imaging inflammation offers tremendous opportunities to transform how we diagnose, treat, and monitor a wide range of diseases. However, the field has long faced a critical challenge: the absence of a sensitive and specific PET probe that can reliably capture immune-driven inflammation in vivo. To address this need, we have developed CD45-PET imaging, a strategy that leverages the pan-leukocyte marker CD45 to visualize inflammation with exceptional clarity across multiple preclinical models. CD45-PET not only outperforms 18F-fluorodeoxyglucose (FDG)-PET, the current clinical standard, but also provides a dynamic, whole-body view of inflammation that directly correlates with disease severity in models of lung and bowel inflammation. Its ability to longitudinally track immune responses enables precise monitoring of inflammatory progression and resolution over time. We have now extended CD45-PET to cardiovascular disease, using it to image myocarditis with early and highly promising results. Finally, we engineered a human CD45-PET probe suitable for clinical translation, which successfully detects human immune cells in humanized mouse models. Together, these advances position CD45-PET as a powerful next-generation tool for precision imaging of inflammation, with strong potential to guide diagnostic and therapeutic decision-making in diverse clinical settings.

Amanda Latham, Ph.D.

Aging profoundly alters tissue structure and cellular function, driving the emergence of dysregulated cells that reduce protective, homeostatic processes while upregulating damaging, pro-inflammatory signaling. These maladaptive changes contribute to the pathogenesis of age-associated diseases, including neurodegenerative disorders. Although recent advances have expanded our understanding of age-altered cell fates, the precise molecular changes that underly these shifts remain poorly defined, particularly within complex tissues like the brain. Spatial transcriptomic mapping has emerged as a transformative technology for characterizing cell states in distinct tissue microenvironments, providing high-resolution, subcellular gene expression profiles while preserving spatial context. These technological advancements are especially critical in aging tissues, which often exhibit pronounced phenotypic heterogeneity. We applied single-cell CosMx Spatial Molecular Imaging to hippocampal sections from young adult (4-5-month-old) and old (23-24-month-old) female mice, leveraging a 1,000-gene panel enriched for markers of cellular senescence and inflammation. Using this approach, we successfully classified major cell populations within the hippocampus, including neurons, astrocytes, oligodendrocytes, oligodendrocyte precursor cells (OPCs), multiple vascular cell types (endothelial cells, smooth muscle cells, pericytes, and ependymocytes), and immune cells such as microglia and infiltrating cells. We developed a 'SenBrain' panel, comprised of 103 brain-expressed genes identified in senescent cells covering distinct senescence domains, including the senescence associated secretory phenotype (SASP), cell cycle regulation, nuclear

stress, organelle stress, anti-apoptotic pathways, and senescence cell surface markers. We identified distinct subpopulations of age-altered cells, including microglia that express transcriptional overlapping signatures of disease-associated microglia (DAM) and senescence. In addition, mapping gene expression at single-cell resolution within spatially intact tissue enables us to interrogate cell-cell interactions and microenvironment disruptions using proximity analysis and ligand-receptor pairing tools. These data offer critical insights into how aging alters cellular communication and spatial organization across vulnerable brain regions. Importantly, extending this platform to postmortem human brain tissue from patients diagnosed with mild cognitive impairment and age-matched cognitively unimpaired controls allows us to identify the translationally conserved and unique transcriptional profiles and cellular interactions that drive cognitive decline. Collectively, this work demonstrates the power of spatial transcriptomics to uncover the cellular aging landscape and to identify therapeutic targets within vulnerable tissues.

Duygu Ucar, Ph.D.

Aging and infection-induced inflammation fundamentally reshape the immune system, influencing baseline immune states, transcriptional programs, and vaccine responsiveness. These factors contribute to the heterogeneity of protection observed in older and vulnerable populations.

In a recent study of pneumococcal vaccination in older adults, we vaccinated 39 participants (>60 years) with either PPSV23 or PCV13 and performed serology, flow cytometry, bulk RNA-seq, and single-cell RNA-seq. While both vaccines elicited comparable antibody titers and plasmablast responses, baseline immune predictors of responsiveness differed by platform. For PCV13, weaker responses were linked to a cytotoxic and pro-inflammatory immune state with elevated CD16⁺ NK cells, increased IL-17–producing helper T cells, and reduced type 1 helper T cells, a phenotype more common in men. PPSV23 responsiveness was predicted by a distinct gene set, underscoring the value of precision vaccinology for tailoring strategies to baseline immune profiles.

In another study, we investigated whether severe COVID-19, an acute inflammatory state, leaves lasting imprints on hematopoietic stem and progenitor cells (HSPC). Using enriched circulating HSPC from survivors, we identified persistent epigenomic alterations (lasting up to one year) associated with altered transcription factor activity, inflammatory program regulation, and sustained myelopoiesis. These changes were propagated to progeny innate immune cells and were partly driven by early IL-6 activity, as we showed in mouse models. Together, these studies reveal how aging and infection-induced inflammation remodel immune architecture, from progenitor cells to vaccine responses. Understanding these processes will inform biomarker-driven personalized strategies and the design of interventions to restore immune resilience.

Qiuyang (Lisa) Zhang, Ph.D.

Cancer predominantly affects aging populations; however, research frequently relies on younger animal models and often excludes older adults from clinical trials. This creates a significant gap

in our understanding of the disease. Given the growing elderly demographic, it is crucial to investigate the relationship between aging and cancer. Mouse models play a vital role in studying the molecular mechanisms of aging and cancer, yet few have been specifically designed for this purpose. We have developed a novel method to create age-related cancer models in mice to understand better how aging influences cancer development and progression. Aging is characterized by "inflammaging," which involves the activation of immune cells, particularly a shift towards pro-inflammatory Th17 cells. Therefore, we further generated a double knockout mouse model for Batf (a transcription factor for Th17) and Pten at different ages to investigate how Th17-related inflammaging contributes to prostate cancer. Our findings revealed that Batf knockout prostates exhibited less invasive cancer, lower cell proliferation, higher apoptosis, reduced inflammatory infiltration, and decreased angiogenesis compared to Batf wild-type (WT) mice, especially significant in aged mice. RNA sequencing indicated that tissues from aged Batf WT mice showed substantial enrichment in pathways such as inflammatory responses linked to TNF α signaling via NF- κ B, when compared to Batf knockout tissues. These results suggest that age-related Th17 inflammaging promotes the progression of prostate cancer, potentially through effects on the activation of age-related key signaling pathways. Therefore, these novel age-related mouse models represent a new approach for studying inflammaging in cancer progression.

Session 5: Role of Inflammaging in Age-Related Diseases

Danica Chen, Ph.D.

Aging leads to chronic inflammation that is linked to aging-associated conditions and diseases. Multiple immune pathways become activated during aging, posing a challenge to effectively reduce aging-associated inflammation. SIRT2, an NAD⁺-dependent deacetylase, suppresses several immune pathways that become activated during aging and may represent an attractive target to broadly dampen aging-associated inflammation. SIRT2 deficiency leads to increased inflammation governed by multiple immune pathways and tissue function decline at an old age, while NAD⁺ boosting with 78c suppresses aging-associated inflammation and improves tissue function. These findings highlight SIRT2 as a master regulator of aging-associated inflammation and support NAD⁺ boosting as an effective strategy to counteract aging-associated inflammation and tissue function decline.

Mohamed Abdel-Mohsen, Ph.D.

Chronic low-grade inflammation, known as inflammaging, is a hallmark of biological aging and a major driver of several age-related diseases. An emerging yet underappreciated contributor to inflammaging is disruption of the glycome, the repertoire of glycans (sugars) decorating the surface of all living cells, as well as circulating glycoproteins and glycolipids, including antibodies. Glycan structures are powerful regulators of immune responses: those containing terminal sialic acid or galactose exert potent anti-inflammatory effects, while their loss generates pro-inflammatory glycan patterns. With advancing chronological and biological age, these protective glycans decline systemically, accompanied by an accumulation of pro-inflammatory forms such as hyposialylated (lacking sialic acid) and agalactosylated (lacking galactose) glycans. Our data show that living with chronic conditions, including chronic HIV

infection, accelerates these age-related glycomic shifts. Longitudinal and cross-sectional analyses show that the loss of anti-inflammatory glycans predicts the development of multiple aging-associated comorbidities. Mechanistically, we show that senescent cells, which accumulate with age and chronic disease, contribute to these changes by producing elevated levels of glycan-degrading enzymes such as sialidases and β -galactosidases, well-established markers of cellular senescence. Importantly, these detrimental glycomic alterations are reversible. We show preclinical evidence that pharmacologic inhibition of glycan-degrading enzymes, as well as targeted dietary supplementation, can restore protective glycans, dampen inflammation, and mitigate virus-mediated cognitive decline. Together, these findings position glycomic alterations as both powerful prognostic biomarkers and mechanistic drivers of inflammaging, and targeting the glycome offers a promising, tractable strategy to delay or prevent age-related pathologies.

Curtis J. Henry, Ph.D.

Aging is the single most important prognostic factor for developing cancer, and mortality rates for most cancer subtypes significantly increase with age. This relationship is multifactorial with inflammaging postulated to be a major driver of aging-associated cancers.

We tested this relationship using murine models of B-cell acute lymphoblastic leukemia (**B-ALL**). We found that aging B-lymphopoiesis is characterized by impaired metabolism, loss of nucleotide anabolism, attenuated IL-7 receptor signaling, and cell cycle defects. The introduction of oncogenic mutations in old, but not young, B-progenitor cells corrected aging-associated defects and led to leukemia development only in aged mice. Like humans, we found that circulating and bone marrow localized levels of the pro-inflammatory cytokines IL-1 β , IL-6, and TNF were significantly elevated with aging in mice. Notably, elevating TNF levels in young mice recapitulated aging-associated defects in B-progenitor cells. Counteracting inflammaging with the anti-inflammatory cytokine IL-37 augmented IL-7 receptor signaling and improved nucleotide anabolism in aged B-progenitor cells which prevented the expansion oncogene-bearing cells.

Treating aged mice with recombinant IL-37 also augmented T-cell function by reducing tonic NF- κ B signaling. This boost in the function of murine T-cells was also observed in CD19-directed CAR T-cells engineered from humans aged 60 and older. Notably, both co-administration of IL-37 with aged CAR T-cells and engineering aged T-cells to secrete IL-37 improved the function of the engineered product.

In summary, inflammaging is a major driver of B-ALL and anti-inflammatory strategies should be further explored as treatment for this cancer in older populations.

Marta Rodriguez-Garcia, M.D., Ph.D.

As women age, susceptibility to urogenital infections increases, including sexually transmitted infections and HIV infection. However, very little is known about how mucosal immune protection changes in the genital mucosa with age. Further, the initial interactions between

pathogens and the mucosal immune cells that allow or prevent infection and how these interactions change in the female genital tract with age remain largely unknown. Using human endometrial, endocervical and ectocervical tissues obtained from women undergoing hysterectomies we have investigated key aspects of innate immune protection in the female genital tract, including characterization of changes in genital innate immune cell distribution and function with age, mechanisms for antiviral responses, and we have uncovered innate immune mechanisms that protect against HIV infection but become dysfunctional as women age.

Understanding how immune protection against infections changes in the female genital tract with age is key to develop prevention strategies for women throughout their lifespan. The study of this mucosal surface is complex as the immune system is compartmentalized and regulated by multiple factors, including hormonal regulation and changes after menopause.

Session 6: Interventions

Lisa Lesniewski, Ph.D.

US census data demonstrates that the percent of the population 65 and over increased from 5% in 1920 to 17% in 2020, and among these higher numbers of older adults there is an increased prevalence of both cardiovascular and metabolic disease contributing to a staggering healthcare burden and cost. Understanding the mechanisms underlying the increased risk of chronic diseases with aging may help direct the development of therapeutics to improve physiological function and reduce disease burden in this population. Increases in cellular senescence is one potential mechanism that may underlie age-related dysfunction and disease. Cellular senescence is characterized by stable cell cycle arrest induced by a number of factors that are associated with advancing age, including DNA damage, telomere dysfunction, oncogene activation, mitochondrial damage, etc. With aging, senescent cells accumulate and contribute to tissue dysfunction through the release of pro-inflammatory mediators that are termed the senescence associated secretory phenotype (SASP). Clearing senescent cells can improve lifespan/healthspan in mice, generating interest in developing of therapeutics that can selectively eliminate senescent cells, termed senolytics. Pre-clinical studies exploring the efficacy of senolytic drugs have provided evidence that the clearance of senescent cells may prevent or improve age-related dysfunction/disease. Here, I will present work from our laboratory demonstrating that the senolytic cocktail of dasatinib and quercetin (D&Q) improves age-related phenotypes in mice, including metabolic and vascular dysfunction.

Elizabeth Kovacs, Ph.D.

Clinical studies show that people aged 65 and older experience higher rates of morbidity and mortality after traumatic injuries, such as burns, when compared to younger patients. This includes greater incidence of pulmonary infections and cognitive impairment, both of which are thought to be mediated by inflammation originating in the intestines. Ongoing studies in the laboratory reveal that, relative to young mice who sustain burn injuries, aged burn injured mice have less DNA expression of Bacteroidetes in the feces, an unhealthy Firmicutes/Bacteroidetes ratio, and reduced intestinal barrier function. The shift in the gut microbiome and breach of the

intestinal epithelial barrier coincides with heightened expression of inflammatory mediators in the gut, lungs, and brains of aged burn injured mice. We chose to use our clinically relevant model of scald burn injury in young and aged mice to determine whether targeting the gut would provide protection against systemic inflammation and multi-organ damage after burn injury. We tested whether the transfer of fecal material between age groups and administration of agents that restore intestinal epithelial barrier integrity are sufficient to protect the intestine and other organs. These results highlight the importance of the intestinal microbiome and gut epithelial cells in mediating inflammation and triggering multi-organ responses, giving insights into potential future treatments in the clinic. Funding Sources NIH: R01 AG018859 (EJK).

Christina Camell, Ph.D.

Aging is characterized by amplified inflammation, including pro-inflammatory macrophages, and increased susceptibility to sepsis and endotoxemia. In this study we uncover a mechanism by which macrophages maintain their inflammatory phenotype through autocrine GDF3-SMAD2/3 signaling that increases chromatin accessibility, ultimately promoting worsened endotoxemia. We show that inflammatory CD11c⁺ adipose tissue macrophages (ATMs) display an age-dependent increase in GDF3, a TGF β -family member. Lifelong systemic or myeloid-specific deletion of *Gdf3* leads to reduced endotoxic inflammation, with decreased inflammatory ATMs and inflammatory cytokines, and protection from hypothermia. Pharmaceutical treatments to old mice link the inflammatory ATM phenotype with SMAD2/3 signaling and lethality during endotoxemia. We also validate the relevance of GDF3 using human AT and data from the Atherosclerosis Risk in Communities (ARIC) longitudinal study. Mechanistically, scRNA-seq and ATAC-seq analyses suggest that GDF3 shifts the chromatin accessibility towards an inflammatory state by limiting methylation-dependent chromatin closing. These findings position the GDF3-SMAD2/3 axis as a critical driver of age-associated chromatin remodeling, amplifying inflammation in ATMs and contributing to heightened susceptibility to endotoxemia during aging. Overall, our results highlight this axis as a promising therapeutic target for mitigating macrophage-related inflammation in the aged.

Payal Ganguly, Ph.D.

Age-related changes in the bone impacts movement, presents musculoskeletal challenges and is associated with pain, stiffness, frailty and age-related diseases (ARDs) like osteoarthritis (OA). Bone marrow mesenchymal stromal cells (BM-MSCs) are multipotential cells that differentiate into bone, fat, cartilage, support hematopoiesis, and are increasingly used for cellular therapies. However, with advancing age their numbers and functions decline due to cellular senescence. Cellular senescence is the irreversible loss of a cell's proliferative capacity, which along with inflammaging (accumulated inflammation with advancing age), is a potential target for interventions to combat ARDs. We found a significant decline in the number BM-MSCs (n=62) with advancing age. Remarkably, several interventions were applied for combating cellular senescence and inflammaging in BMMSCs over the last nine years. Treating older donors BM-MSCs with younger donor serum, significantly enhanced proliferative capacity (p<0.05*). We also observed a regenerative effect of platelet rich plasma (PRP) on BM-MSCs from older OA patients indicating higher proliferation (14.5%) post PRP treatment. More recently, our work with shell nacre cement (SNC) suggested that the biomaterial was able to demonstrate higher

proliferation in old donor BM-MSCs when compare to 2D model. With these findings, we observed the anti-ageing potential of interventions including biologics like PRP and biomaterials like SNC on BM-MSC proliferative capacities. With the aim of enhancing the health-span of the elderly, we outlined the common pathways and different types of interventions investigated to combat cellular senescence in bone in our review article in 2024, that will be presented in this workshop.