The 2024 Harvard / Paul F. Glenn

Virtual Symposium on Aging

June 17, 2024

GLENN FOUNDATION
FOR MEDICAL RESEARCH

BLAVATNIK INSTITUTE
HARVARD MEDICAL SCHOOL

The Paul F. Glenn Center for the Biology of Aging Research

The Paul F. Glenn Center for the Biology of Aging

Welcome to the Annual Harvard/Paul F. Glenn Symposium on Aging. Each year, the Paul F. Glenn Center for Biology of Aging Research hosts the Harvard Symposium on Aging with a mission to present new advances in aging research and to stimulate collaborative research in this area. The symposium has grown to be a significant forum for aging research at Harvard Medical School over the years.

We wish to acknowledge the generosity and vision of Paul F. Glenn, Leonard Judson, and Mark Collins for their unwavering support of aging research. Thanks to their help, we now have a vibrant community of researchers who study aging and age-related diseases at Harvard Medical School.

The reasons for accelerating research into the molecular biology of aging are clear. First, the number of aged individuals in developed countries is increasing dramatically, which will place unprecedented burdens on medical care and economic infrastructure. A major goal is to extend the healthy lifespan through a greater understanding of age-related diseases. A study by the RAND Corporation concluded that advances in medicine arising from aging research would be one of the most cost-effective approaches to age-related disease. Indeed, extending healthy lifespan by one year has been calculated to be worth $86T in the USA alone. Advances in our understanding of aging have shown that it is possible to extend the healthy lifespan of laboratory animals and reduce their risk of and treat major age-related diseases, such as diabetes, cancer, Alzheimer's, and heart disease. With dozens of human clinical trials in progress testing the efficacy of these interventions, there has never been a more exciting time for the field.

On behalf of The Paul F. Glenn Center for Biology of Aging Research and Harvard Medical School, we welcome you to the 2024 virtual Annual Harvard/Paul F. Glenn Symposium on Aging.

Marcia Haigis and Bruce Yankner

Co-Directors, Paul F. Glenn Center for Biology of Aging Research

Symposium on Aging
Agenda

June 17, 2024
1:00 PM - 4:30 PM

1:00 PM to 1:15 PM	Introductions by: Mark R. Collins, President *and* K. Leonard Judson, Chief Executive Officer, Glenn Foundation for Medical Research
1:15 PM to 1:45 PM	Maria Mittelbrunn, Ph.D. **Immune control of aging**
1:45 PM to 2:15 PM	Xiaowei Zhuang, Ph.D. **Spatial genomics of the brain**
2:15 PM to 2:45 PM	Saul Villeda, Ph.D. **Mechanisms of cognitive rejuvenation**
2:45 PM to 3:15 PM	Amy Wagers, Ph.D. **Aging stem cells**
3:15 PM to 3:45 PM	Ashani Weeraratna, Ph.D. **Aging and cancer progression**
3:45 PM to 4:15 PM	Judith Frydman, Ph.D. **Proteostasis decline during aging**
4:15 PM to 4:30	Closing Comments

Maria Mittelbrunn, Ph.D.

Maria Mittelbrunn received the degree of Doctor in Biomedicine, Biochemistry and Molecular Biology from the School of Medicine at the Autonomous University of Madrid in 2006, and performed postdoctoral work at Spanish National Center for Cardiovascular Research (CNIC) (Madrid, Spain). Since 2017, she is Group Leader of the Immunometabolism& Inflammation Laboratory at the Molecular Biology Center (Madrid) as Research Scientist of the Spanish Research Council (CSIC) . Since 2024, she is Visiting Professor of Medical Sciences, Columbia Center for Translational Immunology and Center for Human Longevity

Among her original contributions as PI are the demonstration that the deterioration of immune system function with aging not only compromises the response to infection, cancer, vaccination, or predisposes to autoimmunity but also increases the risk for cardiovascular, metabolic, and cognitive decline, thereby placing the immune system as a controller of healthy aging. Dr. Mittelbrunn has contributed to decoding the molecular mechanisms by which aged T cells contribute to inflammaging and age-related diseases. Additionally, she has proposed new therapeutic targets to delay age-related multimorbidity and to reverse aortic aneurysms, thus preventing sudden death due to aortic dissections.

She has obtained funding from the major European and Spanish funding organizations, including an European Research Council Starting Grant in 2016, and Consolidator Grant in 2022.

For her scientific achievements, she has been awarded with Doctoral thesis Extraordinary Prize (2006), LÓREAL UNESCO for Women in Science (2015), BANCO SABADELL AWARD for Biomedical Research (2022), and Royal Spanish Academia of Science for young researchers among others. Since 2024, she is Visiting Professor at CCTI, Columbia

Xiaowei Zhuang, Ph.D.

Xiaowei Zhuang is an investigator of Howard Hughes Medical Institute and the David B. Arnold Professor of Science at Harvard University. She pioneered the development of super-resolution imaging and genome-scale imaging methods. She invented STORM, a super-resolution imaging method, and discovered novel molecular structures in cells using STORM. She invented a single-cell transcriptome and genome imaging method, MERFISH, which enabled spatial genomics. Using MERFISH, she made discoveries in the areas ranging from the cellular organization and functions in the brain and the 3D genome organization and gene regulation in cells.

Zhuang received her B.Sc. degree in physics from the University of Science and Technology of China, her Ph.D. in physics under the supervision of Prof. Y. R. Shen from University of California at Berkeley, and her postdoctoral training in biophysics in the lab of Prof. Steven Chu at Stanford University. She joined the faculty of Harvard University in 2001 and became a Howard Hughes Medical Institute investigator in 2005.

She is a member of the National Academy of Sciences, National Academy of Medicine, and the American Academy of Arts and Sciences, a fellow of the National Academy of Inventors, a member of the American Philosophical Society, and a foreign associate of the Chinese Academy of Sciences and the European Molecular Biology Organization. She received honorary doctorate degrees from the Stockholm University, the Delft University of Technology, and the Icahn School of Medicine at Mount Sinai. She has received many awards, including the National Inventors Hall of Fame, the Dreyfus Prize in Chemical Sciences, the Heinrich Wieland Prize, the J. Allyn Taylor International Prize in Medicine, the FNIH Lurie Prize in Biomedical Sciences, the Vilcek Prize in Biomedical Science, the Breakthrough Prize in Life Sciences, the Pearl Meister Greengard Prize, the National Academy of Sciences Award for Scientific Discovery, the Heineken Prize for Biochemistry and Biophysics, the National Academy of Sciences Award in Molecular Biology, the Raymond and Beverly Sackler International Prize in Biophysics, the Max Delbruck Prize in Biological Physics, the MacArthur Fellowship, etc.

Decoding the contribution of the immune system to aging

Spatially resolved single-cell genomics and cell atlas of the brain

Saul Villeda, Ph.D.

Dr. Saul Villeda is an Associate Professor in the Department of Anatomy and Endowed Chair in Biomedical Science at the University of California San Francisco and serves as Associate Director of the Bakar Aging Research Institute. He obtained his B.S. degree from the University of California Los Angeles, his PhD degree in Neuroscience from Stanford University, and started his independent career at the University of California San Francisco as a Sandler Fellow. Dr. Villeda has made the exciting discovery that the aging process in the brain can be reversed by altering levels of circulating factors in blood. Dr. Villeda's research is best known for the use of innovative heterochronic parabiosis and blood plasma administration approaches to investigate the influence that exposure to young blood-derived or exercise-induced circulating factors has in promoting molecular and cellular changes underlying cognitive rejuvenation. His work has garnered accolades that include a National Institutes of Health Director's Independence Award, the W.M. Keck Foundation Medical Research Award, the Glenn Award for Research in Biological Mechanisms of Aging, and the McKnight Innovator Award in Cognitive Aging.

Deciphering the mechanisms of cognitive rejuvenation

Amy Wagers, Ph.D.

I am an established investigator who has led a research laboratory studying aging and regenerative biology for almost 20 years. Research in my group focuses primarily on defining cellular and molecular mechanisms that regulate the migration, expansion, and repair potential of blood-forming and muscle-forming progenitors, with a particular emphasis on how stem cell activities in these tissues change with age and how they can be exploited for regenerative medicine. Studies from my lab have helped to develop a model in which circulating factors, immune and inflammatory cells, metabolic regulators and intrinsic transcriptional programs that change during aging play a crucial role in determining stem cell function and modulating tissue repair and homeostasis. Our work also has provided exciting proof-of-concept evidence demonstrating the utility of gene editing in mature cells and stem cells in vivo. In recently published studies, we developed CRISPR-based systems to enable robust genome modification of endogenous muscle stem cells, as well as multinucleated muscle fibers and cardiomyocytes, and adapted this system to target other stem cell populations, including hematopoietic (blood-forming) progenitors. These efforts have been continuously funded from both philanthropic and government sources, including a Scholars Award from the WM Keck Foundation (2007-2010), an NIH New Innovator Award (2008-2013), HHMI Early Career Award (2009-2015), and multiple NIH R01 and P01 and P30 awards from the NIDDK, NEI, NHLBI, and NIA (2008-present). Our current work is supported by an NIH Pioneer Award (DP1 AG063419) and R01 (AG048917), as well as collaborative research grants from the Paul F. Glenn Foundation and Sarepta Therapeutics. Overall, my research program has established unique systems for generating, identifying and isolating gene-edited stem cells in vivo for the investigation of disease-causing mutations in complex organ systems and offers a unique perspective on the fields of gene therapy and geroscience, opening new opportunities for regenerative medicine in aging tissues.

Pancreatic beta-cell senescence and SASP in type 2 diabetes

Ashani T. Weeraratna, Ph.D.

Dr. Weeraratna is the Bloomberg Distinguished Professor of Cancer Biology, E.V. McCollum Chair of Biochemistry and Molecular Biology at the Johns Hopkins Bloomberg School of Public Health, as well as the Associate Director for Laboratory Research at the Sidney Kimmel Cancer Center, Johns Hopkins School of Medicine. She is a Past President of the Society for Melanoma Research, and was recently appointed by President Biden as a member of the National Cancer Advisory Board. Prior to joining Johns Hopkins, she was the Ira Brind Professor and Co-Program Leader, Immunology, Microenvironment & Metastasis Program Member at the Wistar Institute. Born in Sri Lanka and raised in Lesotho in Southern Africa, Weeraratna first came to the United States in 1988 to study biology at St. Mary's College of Maryland. She earned a Ph.D. in Molecular and Cellular Oncology at the Department of Pharmacology of George Washington University Medical Center. From 1998 to 2000, she was a post-doctoral fellow at The Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins Oncology Center, before joining the National Human Genome Research Institute as a staff scientist. In 2003, she moved to the National Institute on Aging, where she started her own research program, before joining the Wistar Institute from 2011-2019.

Dr. Weeraratna is an expert in melanoma metastasis, Wnt signaling, and aging, and her research focuses heavily on the effects of the tumor microenvironment on metastasis and therapy resistance. She is one of the first to study how the aging microenvironment guides metastasis and therapy resistance in melanoma. For this innovative work, she was selected by Nature to be a part of their "Milestones in Cancer Research" video series and in 2021 the NCI selected her as one of their "Top 5 Cancer Researchers Accelerating Cancer Research Into the Future". Moreover, the quality and impact of Dr. Weeraratna's research is further recognized by the award of numerous peer-reviewed grants and awards.

Finally, Dr. Weeraratna has been a champion of increasing diversity for many years, and this is evident in her writings which call for gender and racial equity (e.g., Nature, Nature Medicine, Nature Reviews in Cancer, Cancer Cell and Cancer Discovery). She mentors junior faculty all over the world, and is spearheading efforts to increase the diversity among the Hopkins faculty. In her own department she has successfully implemented strategies to increase diversity both through faculty recruitment, and in her student body. She has written a book for the lay public called "Is Cancer Inevitable?" meant to highlight the progress made in the field, and the importance of diversity in cancer research. She is also heavily invested in Public Health, with multiple calls for sun protection and awareness through her social media presence, and community outreach.

The Ravages of TiME: How the aging tumor immune microenvironment impacts cancer progression

Judith Frydman, Ph.D.

Judith Frydman is currently the Donald Kennedy Chair in Humanities and Sciences at Stanford University and a professor in the Departments of Biology and Genetics.She grew up in Buenos Aires, Argentina, where she majored in Chemistry and received her PhD in Biochemistry from the University of Buenos Aires. She carried out her postdoctoral training with Ulrich Hartl at the Sloan Kettering Institute in New York, where she made major contributions to the field of cellular protein folding that shaped current thinking of protein folding in vivo. She is an elected member of the National Academy of Sciences and of the American Academy of Arts and Sciences.

The central theme of Dr. Frydman's research is to understand how cells maintain a healthy and functional proteome by focusing on biological mechanisms controlling cellular protein folding, aggregation and quality control. Her research aims to uncover basic principles of chaperone action during de novo protein folding, i.e. when proteins are synthesized on ribosomes, as well as during quality control, i.e. when folded proteins get misfolded or damaged during normal function or during stress. Her lab also applies this knowledge to understand neurodegenerative diseases and aging, as well as the forces shaping viral proteins. These insights may lead to novel therapeutic strategies against neurodegeneration, cancer and viral infectious diseases. Work in the Frydman lab has also identified specific interventions that disfavor the production of toxic protein species; efforts are now focused on the link between aging and loss of cellular robustness.

Proteostasis decline during aging: mechanisms and questions