

The 2014 Harvard / Paul F. Glenn

# Symposium on Aging

June 23, 2014



## The Paul F. Glenn Laboratories for the Biological Mechanisms of Aging

Welcome to the Harvard/Paul F. Glenn Symposium on Aging at Harvard Medical School, an annual event hosted by the Paul F. Glenn Laboratories. We are pleased you could join us. The event is now in its 9th year, serving to educate the wider community and foster collaborations to accelerate knowledge about the biology of aging. We have been fortunate to have many leaders in the aging field speak at the symposia and today is no exception.

In the mid-1960's, when aging was considered to be intractable to biology, Mr. Glenn thought differently. He realized that if we understood the root causes of aging, we could find medicines to keep us healthier for longer. He teamed up with lobbyist Florence Mahoney and together they convinced Congress to establish The National Institutes on Aging (NIA) at the National Institutes of Health, signed into law on May 31st 1974. Because of this monumental achievement and his unwavering philanthropic support of aging research, we are far closer to being able to forestall some of the disabilities of aging and treat common diseases cause by it. On this occasion, we thank Mr. Glenn for his unwavering belief in medical research for the common good.

On behalf of The Paul F. Glenn Laboratories and Harvard Medical School, we welcome you to the Harvard/Paul F. Glenn Symposium on Aging, 2014.

David Sinclair and Bruce Yankner  
Co-Directors, The Paul F. Glenn Laboratories at Harvard Medical School

## Symposium on Aging Agenda

June 23, 2014  
9:00 - 5:00

9:00 – 9:15 a.m.	<b>Welcome</b> Harvard Medical School Mark Collins, President Glenn Foundation for Medical Research
9:15 – 10:00 a.m.	<b>Accelerated Aging in HIV Infection</b> Dana H. Gabuzda, MD
10:00 – 10:45 a.m.	<b>Hypothalamic Inflammation in Neural Control of Aging</b> Dongsheng Cai, MD, PhD
10:45 – 11:30 a.m.	<b>Transcriptome analysis of age-associated neurodegeneration</b> Asa Abeliovich, MD, PhD
11:30 – 12:15 p.m.	<b>Cognitive Aging Versus Preclinical Alzheimer's Disease: Does Amyloid Matter?</b> Reisa Sperling, MD
12:15 – 1:30 p.m.	Lunch
1:30 – 2:15 p.m.	<b>From Yeast Cells to Patient Neurons: A Powerful Discovery for Combating Neurodegeneration</b> Susan Lindquist, PhD
2:15 – 3:00 p.m.	<b>Insights into Impaired Antibody Responses in Aging</b> Arlene Sharpe, PhD
3:00 – 3:45 p.m.	<b>Mouse Model to Help Understand Mammalian Aging</b> Toren Finkel, MD, PhD
3:45 – 4:15 p.m.	<b>From naked mole rats to sirtuins: ways to extend lifespan</b> Vera Gorbunova, PhD
4:15 – 5:00 p.m.	Public Social

## Dana Gabuzda, M.D.



Dana Gabuzda is Professor of Neurology with affiliation in Microbiology and Immunobiology at Dana-Farber Cancer Institute and Harvard Medical School. She received her M.D. from Harvard and did her internship and neurology residency at Massachusetts General Hospital followed by postdoctoral training at Johns Hopkins and Dana-Farber. Her lab has studied HIV and associated comorbidities for over 20 years, contributing to the understanding of pathogenic mechanisms underlying immune system and metabolic dysfunction, accelerated

aging, and neurocognitive decline in affected populations. Her recent work uses systems biology approaches to analyze and integrate heterogeneous types of big data. Using metabolomics, her lab identified metabolite alterations indicative of accelerated aging in HIV, and characterized metabolite signatures linked to age-related cognitive decline and “inflammaging” mechanisms. She has received several awards including a Howard Temin Award for Basic Science, Elizabeth Glaser Scientist Award from the Pediatric AIDS Foundation, Avant-Garde DP1 award for HIV/AIDS Research from NIH/NIDA, and Women in Neuroscience Lectureship Award from the International Society for Neurovirology.

## Dongsheng Cai, Ph.D., M.D.



Professor of Molecular Pharmacology, Department of Molecular Pharmacology, Diabetes Research Center, Institute of Aging, Albert Einstein College of Medicine.

In this talk, I will discuss the relationship between hypothalamic inflammation and neuroendocrine pathways in aging development as well as related metabolic syndrome. First, I will provide an overview on neuronal control of aging and lifespan in different species. Second, I will describe the involvement of hypothalamic pro-inflammatory IKK-beta and NF-kappaB pathway and resulting neuronal stresses in development of aging and metabolic syndrome. Finally, I will discuss the impact of hypothalamic inflammation on hypothalamic neuroendocrine systems, and influences on hypothalamic regulation of physiology which contribute to aging and lifespan changes. Altogether, inflammation-induced hypothalamic dysfunction represents a neural mechanism of aging.

## Asa Abeliovich M.D. Ph.D.



Dr. Abeliovich joined the Columbia University College of Physicians and Surgeons in 2000, and is an Associate Professor of Neurology and Pathology and Cell Biology. The overall goal of his research program is to develop effective therapeutic strategies for Parkinson's disease and Alzheimer's disease. There are 2 interrelated themes to the laboratory's research efforts: (i) one focus is the pursuit of mechanisms that underlie these neurodegenerative disorders, with an emphasis on genetic approaches; and (ii) a second focus is the development of

novel human brain cell models in which to study disease mechanisms and test potential lead therapeutics. Dr. Abeliovich obtained undergraduate degrees in Life Science and in Humanities at MIT, and then earned MD and PhD degrees from Harvard Medical School and MIT, respectively, through a joint Medical Scholar Training Program Fellowship. At MIT, Dr. Abeliovich undertook thesis research in the laboratory of Dr. Susumu Tonegawa, where he pioneered studies on the molecular mechanisms of learning and memory in mammals. Dr. Abeliovich completed his Medicine Internship, and subsequent clinical training Residency in Neurology, at UCSF. At Genentech, Inc., in South San Francisco, he undertook research on molecular mechanisms of Parkinson's disease in the laboratory of Dr. Arnon Rosenthal. In addition to his research efforts, Dr. Abeliovich is an Attending Physician in the Neurology Clinic at NYPH. He was awarded the Lamport award for excellence in basic science research at Columbia University in 2005.

## Reisa Sperling, M.D.



Dr. Reisa Sperling is a neurologist, specializing in Alzheimer's disease and imaging research. She is a Professor in Neurology at Harvard Medical School. She is the Director of the Center for Alzheimer Research and Treatment at Brigham and Women's Hospital, and the Director of the Neuroimaging Core of the Massachusetts Alzheimer's Disease Research Center at Massachusetts General Hospital. Dr. Sperling's research is focused on the early diagnosis and treatment of early Alzheimer's disease (AD). She is the Principal Investigator of the Harvard Aging Brain Study, funded by a NIA Program Project grant. Dr. Sperling led the National Institute on Aging-Alzheimer's Association workgroup to develop guidelines for the study of "Preclinical Alzheimer's disease". She is the Project Leader for the ADCS Anti-Amyloid Treatment in Asymptomatic AD (A4) study, a three-year secondary prevention trial in 1000 clinically normal older individuals with biomarker evidence of early AD pathology.

Transcriptome Analysis of Age-Associated  
Neurodegeneration

Cognitive Aging Versus Preclinical Alzheimer's  
Disease: Does Amyloid Matter?

## Susan Lindquist, Ph.D.



Susan Lindquist is a pioneer in the field of protein folding. Her work has provided transforming insights into the role of protein folding in the evolution of new traits and the devastation of human disease. Her seminal work on the role of Hsp90 in folding mutant oncogenic kinases led to the development of Hsp90-based therapeutics. Her work in fruit flies, mustard plants and yeast established that Hsp90 pervasively influences the manner in which genotypes are read out into phenotypes by chaperoning the folding of key players in signal transduction pathways. This work provided the first explanation for the rapid evolution of complex traits in response to environmental stress. She established the biochemical basis of protein-based inheritance in yeast and created a new understanding of amyloid protein function and assembly. Most recently, her group has developed new platforms for dissecting the protein-folding problems that drive neurodegenerative diseases, with the aim of discovering new therapeutic strategies based on stopping the precipitating causes of such protein-folding disorders. Susan Lindquist is a Member and former Director of the Whitehead Institute. She is a member of the National Academy of Sciences, the American Academy of Arts and Science, the American Philosophical Society, and the Institute of Medicine. Her honors also include the E.B. Wilson Award, Dickson Prize in Medicine, the Otto-Warburg Prize, the Genetics Society of America Medal, the FASEB Excellence in Science Award, the Max Delbrück and the Mendel Medals. In 2009, she was the recipient of the National Medal of Science. Susan Lindquist is also a member of the Board of Directors of Johnson & Johnson, and a co-founder of FoldRx, a biotech company (recently acquired by Pfizer) that develops drug therapies for diseases of protein misfolding and amyloidosis. She became an Investigator of the Howard Hughes Medical Institute in 2006. Previously she was on the faculty of the University of Chicago where she was the Albert D. Lasker Professor of Medical Science. She received her PhD in Biology from Harvard University, and was a postdoctoral fellow of the American Cancer Society at the University of Chicago.

From Yeast Cells to Patient Neurons: A Powerful  
Discovery for Combating Neurodegeneration

## Arlene H. Sharpe M.D. Ph.D.

Arlene Sharpe M.D. Ph.D. is the George Fabyan Professor of Comparative Pathology at Harvard Medical School, Head of the Division of the Division of Immunology in the Department of Microbiology and Immunobiology, and Co-Director of the Harvard Institute of Translational Immunology at Harvard Medical School, and a member of the Department of Pathology at Brigham and Women's Hospital. Dr. Sharpe earned her M.D. and Ph.D. degrees from Harvard Medical School, and completed her residency training in Pathology at Brigham and Women's Hospital. Dr. Sharpe is interested in mechanisms that regulate immune responses in young and aged individuals. Her laboratory has discovered and elucidated the functions of T cell costimulatory pathways, including the immunoinhibitory functions of the CTLA-4 and PD-1 pathways, which have become exceptionally promising targets for cancer immunotherapy. Her laboratory currently focuses on the roles of T cell costimulatory pathways in regulating T cell tolerance and effective antimicrobial and antitumor immunity. Her laboratory also is involved in studies aimed at translating fundamental understanding of T cell costimulation into new therapies for autoimmune diseases, chronic viral infections, and cancer.



Insights into Impaired Antibody Responses in Aging

## Toren Finkel, Ph.D., M.D.



Toren Finkel received his undergraduate degree in Physics and his MD and PhD degree from Harvard Medical School in 1986. Following a residency in Internal Medicine at the Massachusetts General Hospital, he completed a fellowship in Cardiology at Johns Hopkins Medical School. In 1992, he accepted a position as an Investigator within the Intramural Research Program of the National Heart, Lung and Blood Institute (NHLBI) at the National Institutes of Health in Bethesda, Maryland. In 2001, he became the Chief of the Cardiology

Branch and in 2010 he assumed his current position as the Chief of the Center for Molecular Medicine within the NHLBI. His current research interests include the role of reactive oxygen species and mitochondrial function in aging and age-related diseases.

## Vera Gorbunova, Ph.D.



Vera Gorbunova is a Professor of Biology at the University of Rochester and a co-director of the Rochester Aging Research Institute. Her research is focused on understanding the mechanisms of longevity and genome stability and on the studies of exceptionally long-lived mammals. Dr. Gorbunova earned her B.Sc. degrees at Saint Petersburg State University, Russia and her Ph.D. at the Weizmann Institute of Science, Israel. Dr. Gorbunova applied comparative biology approach to study aging and identified rules that control evolution of tumor suppressor mechanisms depending on the species lifespan and body mass. Dr. Gorbunova also investigates the role of Sirtuin proteins in maintaining genome stability. More recently the focus of her research has been on the longest-lived rodent species the naked mole rats and the blind mole rat. Dr. Gorbunova identified high molecular weight hyaluronan as the key mediator of cancer-resistance in the naked mole rat. Dr. Gorbunova has over 50 research papers including publications in *Nature* and *Science*. Her work received awards of from the Ellison Medical Foundation, the Glenn Foundation, American Federation for Aging Research, and from the National Institutes of Health. Her work on cancer-resistance in the naked mole rat was awarded the Cozzarelli Prize from PNAS for outstanding scientific excellence and originality. Most recently she was awarded a prize for research on aging from ADPS/Aliaz, France and Prince Hitachi Prize in Comparative Oncology, Japan.







## Nearby locations for lunch:

### 1. Elements Café

located at Harvard Medical School, New Research Building

### 2. Bertucci's

(at Children's), 1 Blackfan Circle (Exit rear of Harvard Medical School)

### 3. Galleria Longwood Food Court

342 Longwood Avenue

