

The 2015 Harvard / Paul F. Glenn

Symposium on Aging

June 19, 2015



**The Paul F. Glenn Laboratories for the Biological Mechanisms of Aging
10th Anniversary Symposium**

Welcome to the 10th Annual Harvard/Paul F. Glenn Symposium on Aging. Each year, the Paul F. Glenn Laboratories host 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 over the past 10 years to be one of the biggest events at Harvard Medical School. We have been fortunate to have many of the leaders in the aging field speak at the symposia and today is no exception.

We wish to acknowledge the generosity and vision of Paul F. Glenn, Mark Collins and Leonard Judson for their unwavering support of aging research through the Paul F. Glenn Foundation. Thanks to their support, we now have a vibrant community of researchers who study aging and age-related diseases. Since the inception of the Paul F. Glenn labs at Harvard in 2005, this network has grown to include aging studies at the Albert Einstein College of Medicine, the Buck Institute, the Mayo Clinic, Massachusetts Institute of Technology, Princeton University, Stanford University, the University of California San Francisco, the University of California, Berkeley, and the University of Michigan Geriatrics Center.

The reasons for accelerating research into the molecular biology of aging are clear. First and foremost, the number of aged individuals in developed countries is growing rapidly, which will place an unprecedented burden on the social fabric and economic infrastructure. Because chronic illness in the elderly is a major medical cost, enormous savings would be achieved if the healthy lifespan were extended 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. Advances in aging research have shown that it is possible to extend the healthy lifespan of laboratory animals through genetic and pharmacological means. We anticipate that significant strides will be made in understanding how human health and lifespan are regulated, leading to novel therapeutic approaches to the diseases of aging, such as diabetes, cancer, Alzheimer's and heart disease.

Today's attendees come not only from the Harvard research community, but from across the nation and from overseas for this one day event. On behalf of The Paul F. Glenn Laboratories and Harvard Medical School, we welcome you to this Special 10th Annual Harvard/Paul F. Glenn Symposium on Aging.

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

Symposium on Aging
Agenda

June 19, 2015
9:00 - 5:00

- 9:00 – 9:45 a.m. **Introduction**
- 9:45 – 10:15 a.m. **Ensuring the Health of the Germ-line**
Cynthia Kenyon, Ph.D.
- 10:15 – 10:45 a.m. ***C. elegans* Surveillance of Core Cellular Components to Detect and Defend Pathogen Attacks, and How This Relates to Longevity**
Gary Ruvkun, Ph.D.
- 10:45 – 11:15 a.m. **Regulation of Brain Aging and the Onset of Alzheimer's Disease**
Bruce Yankner, M.D., Ph.D.
- 11:15 – 11:45 p.m. **Telomere Maintenance in Human Life Trajectories**
Elizabeth H. Blackburn, Ph.D.
- 11:45 – 1:30 p.m. Lunch
- 1:30 – 2:00 p.m. **Mitochondria, Flexibility and Aging**
Marcia Haigis, PhD
- 2:00 – 2:30 p.m. **On the reversibility of aging**
David A. Sinclair, Ph.D.
- 2:30 – 3:00 p.m. **Sirtuins and Adult Stem Cells**
Leonard Guarante, Ph.D.
- 3:00 – 3:30 p.m. **Local and systemic regulators of aging in mammalian tissues.**
Amy Wagers, PhD
- 3:30 – 5:00 p.m. Public Social

Cynthia Kenyon, Ph.D.



Cynthia Kenyon's discovery in 1993 that a single-gene mutation could double the lifespan of healthy, fertile *C. elegans* roundworms sparked an intensive study of the molecular biology of aging. Her discoveries led to the realization that a universal endocrine network influences the rate of aging in many organisms, apparently including humans, and that the same genes that affect basic aging also affect age-related disease. Dr. Kenyon graduated valedictorian in chemistry from the University of Georgia in 1976. She received her Ph.D.

from MIT in 1981 and was a postdoctoral fellow with Nobel Laureate Sydney Brenner in Cambridge, England. In 1986, she joined University of California, San Francisco, where she was the Herbert Boyer Distinguished Professor and an American Cancer Society Professor. Dr. Kenyon is a member of the US National Academy of Sciences, the American Academy of Arts and Sciences and the US Institute of Medicine. She has received many scientific awards. Dr. Kenyon was president Genetics Society of America, 2003, and she directed the Hillblom Center for the Biology of Aging at UCSF. In 2014 she became a UCSF Emeritus Professor, and Vice President of Aging Research at Calico Life Sciences, a new basic- and applied-sciences company initiated by Google whose aim is to maintain healthy youthfulness and increase the quality of life as we age.

Gary Ruvkun, Ph.D.



Gary Ruvkun is a professor of genetics at Harvard Medical School. Dr. Ruvkun is a graduate of UC Berkeley (AB, Biophysics, 1973) and Harvard (Ph.D. Biophysics, 1982).

Converging TGF-beta and insulin-like neuroendocrine signaling pathways control a developmental decision that *C. elegans* makes between larval arrest at the dauer stage, generally induced by crowding and stresses, or development to the fertile adult stage. Dauer arrest in nematodes is a specific example of the much more general phenomenon of diapause arrest, a developmental or reproductive arrest observed for example, in overwintering insects or amphibians or fish in dessicated lakes induced by dessication or day length changes. Other developmental arrest points are also programmed responses to a deficiency in a core cellular function that in the natural world would be caused by toxins. A genetic defect in the core cellular components are read as a toxic or microbial attack: they also induce aversive behaviors and induce anti-bacterial and detoxification genes. We have discerned new genetic pathways that surveil the ribosome or mitochondria or proteasome and couple to the induction of innate immunity and detoxification pathways. Using a panel of GFP-fused xenobiotic and immune response genes, we identified protective pathways upregulated by gene inactivations that disrupt core cellular pathways. Variation in human cellular surveillance and endocrine pathways controlling behavior, detoxification and immunity selected by past toxin or microbial interactions could underlie aberrant responses to foods, medicines, and microbes, and the difference in lifespan between males and females.

Bruce Yankner, M.D., Ph.D.



Bruce A. Yankner, M.D., Ph.D. is Professor of Genetics and Neurology at Harvard Medical School, Director of the Harvard Neurodegeneration Training Program, and Co-Director of the Paul F. Glenn Laboratories for Biological Mechanisms of Aging. Dr. Yankner graduated from Princeton University, received his M.D. and Ph.D. from Stanford University, and did a residency at Massachusetts General Hospital. His work has contributed to understanding pathogenic mechanisms in Alzheimer's disease, Down's syndrome and

Parkinson's disease, beginning with the initial observation that amyloid beta protein is a toxic molecule, and later with investigations into the roles of presenilin proteins, notch and wnt in neuronal signaling and pathology. Work from his laboratory has also defined the transcriptome of the aging human brain, its evolution from mouse to man, and a role for DNA damage in brain aging. More recently, his laboratory has identified a gene network controlled by the REST transcription factor that promotes survival and stress resistance in aging neurons, and may protect against Alzheimer's disease. He has received the Major Award for Medical Research from the Metropolitan Life Foundation, the Derek Denny-Brown Neurological Scholar Award from the American Neurological Association, the Irving S. Cooper Award from the Mayo Clinic, the Zenith Award from the Alzheimer's Association, the Ellison Medical Foundation Senior Scholar Award, the Nathan W. Shock award from NIA and the NIH Director's Pioneer Award.

Elizabeth H. Blackburn, Ph.D.



Dr. Elizabeth H. Blackburn, Morris Herzstein Professor in Biology and Physiology in the Department of Biochemistry and Biophysics at the University of California, San Francisco, is a leader in the area of telomere and telomerase research.

She discovered the molecular nature of telomeres - the ends of eukaryotic chromosomes that serve as protective caps essential for preserving the genetic information - and the ribonucleoprotein enzyme, telomerase. Blackburn and her research team at the University of California, San Francisco are working with various cells including human cells, with the goal of understanding telomerase and telomere biology.

Blackburn earned her B.Sc. (1970) and M.Sc. (1972) degrees from the University of Melbourne in Australia, and her Ph.D. (1975) from the University of Cambridge in England. She did her postdoctoral work in Molecular and Cellular Biology from 1975 to 1977 at Yale.

In 1978, Blackburn joined the faculty at the University of California at Berkeley in the Department of Molecular Biology. In 1990, she joined the Department of Microbiology and Immunology at UC San Francisco, where she served as Department Chair from 1993 to 1999. Blackburn is currently a faculty member in Department of Biochemistry and Biophysics at UCSF. She is also a Non-Resident Fellow of the Salk Institute.

Throughout her career, Blackburn has been honored by her peers as the recipient of many prestigious awards. She was elected President of the American Society for Cell Biology for the year 1998. Blackburn is an elected Fellow of the American Academy of Arts and Sciences (1991), the Royal Society of London (1992), the American Academy of Microbiology (1993), and the American Association for the Advancement of Science (2000). She was elected Foreign Associate of the National Academy of Sciences in 1993, and was elected as a Member of the Institute of Medicine in 2000. She was awarded the Albert Lasker Medical Research Award in Basic Medical Research (2006). In 2007 she was named one of TIME Magazine's 100 Most influential People and she was the 2008 North American Laureate for L'Oreal-UNESCO For Women in Science.

In 2009, Dr. Blackburn was awarded the Nobel Prize in Physiology or Medicine.

Regulation of Brain Aging and the Onset of Alzheimer's Disease

Telomere Maintenance in Human Life Trajectories

Marcia Haigis, Ph.D.



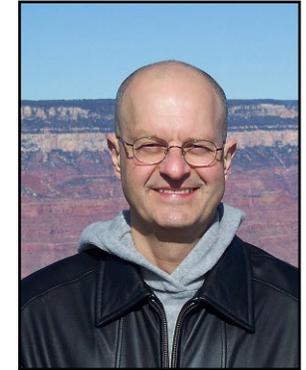
Marcia C. Haigis, Ph.D. is an Associate Professor in the Department of Cell Biology at Harvard Medical School and a member of the Paul F. Glenn Laboratories for Medical Research. Dr. Haigis received her Ph.D. in Biochemistry from the University of Wisconsin in 2002 studying protein chemistry. She performed postdoctoral research at MIT in 2006 where she made fundamental discoveries connecting sirtuin function to mitochondrial metabolism. Dr. Haigis joined the Harvard faculty as an Assistant Professor in 2006.

The Haigis lab seeks to understand the role that mitochondria play in human aging and age-associated diseases. In particular, the lab uses cellular and mouse models to study the mitochondrial and metabolic responses to cellular stresses, such as DNA damage or nutrient challenge. Recent studies have identified roles for the sirtuin family of NAD-dependent deacylases in regulating the metabolic response to DNA damage. Additionally, the lab has used proteomic and metabolomic approaches to identify novel sirtuin targets, further defining how mitochondria adapt to stress.

In recognition of these scientific achievements, Dr. Haigis has received a Brookdale Leadership in Aging Award, the Ellison Medical Foundation New Scholar Award and an American Cancer Society Research Scholar Award.

Mitochondria, Flexibility and Aging

Leonard Guarante, Ph.D.



Dr. Leonard P. Guarante is the Novartis Professor of Biology at MIT, Director of the Glenn Labs at MIT, and affiliate of the Koch Institute for Integrative Cancer Research. His lab is responsible for showing that a novel set of proteins termed sirtuins slow the aging process in a wide variety of organisms from yeast to mammals. Moreover he discovered the novel biochemical activity for yeast and human sirtuins Sir2 and SIRT1 -- NAD-dependent deacetylation. This finding led to the hypothesis that sirtuins mediate the healthful effects of calorie restriction, which has been amply corroborated. It also provided an assay for screening for drugs that can activate SIRT1. These include drugs under development by GSK to activate the human SIRT1 protein allosterically. In addition it has emerged that NAD⁺ levels decline in an aging population, and the use of NAD⁺ precursors offers a promising treatment to restore NAD levels, sirtuin activity and health benefits to an aging population. It is likely that such drugs would represent a new strategy to delay or ameliorate the major diseases of aging, including diabetes, cancer, neurodegenerative diseases, and cardiovascular disease. He was elected to American Academy of Arts and Science in 2004 and the French Academie des Sciences in 2009. He is the recipient of the AFAR Irving Wright Award of Distinction in 2015, the Feodor Lynen Award, Miami Winter Symposium in 2012, and the Dart/NYU Biotechnology Achievement Award in 2009.

Sirtuins and Adult Stem Cells

David A. Sinclair, Ph.D.



David A. Sinclair, Ph.D. is a tenured Professor of Genetics at Harvard Medical School, co-Director of the Paul F. Glenn Laboratories for the Biological Mechanisms of Aging at Harvard, and a Professor at the University of New South Wales. His postdoctoral training was with Dr. Lenny Guarente at M.I.T., where he worked on the cause of yeast aging and a family of longevity regulators that become known as the sirtuins. He is known for his work on understanding why we age and how to slow its effects, including molecules that can slow or reverse aspects of

aging in mammals. He has founded a number of biotechnology companies in areas of aging, diabetes, vaccines, and bioinformatics. He also co-founded and serves as co-chief editor of the scientific journal *Aging* and has received awards including the Australian Commonwealth Prize, the Thompson Prize, a Helen Hay Whitney Postdoctoral Award, a Charles Hood Fellowship, a Leukemia Society Fellowship, a Ludwig Scholarship, a Harvard-Armenise Fellowship, an American Association for Aging Research Fellowship, The Nathan Shock Award from the National Institutes of Health, Ellison Medical Foundation Junior and Senior Scholar Awards, The Merck Prize, a Genzyme Outstanding Achievement in Biomedical Science Award, the Bio-Innovator Award, the David Murdock-Dole Lectureship, the Fisher Honorary Lectureship at UCLA, the Les Lazarus Lectureship, the ASMR Medal, and TIME 100, TIME magazine's list of the "100 most influential people in the world."

Amy Wagers, Ph.D.



Amy Wagers earned a B.A. in Biological Sciences from Northwestern University in 1994 and received her Ph.D. in Immunology and Microbial Pathogenesis in 1999, also from Northwestern University. Dr. Wagers then pursued postdoctoral training with Dr. Irving Weissman at Stanford University, where her work in stem cell biology and regenerative medicine began. In 2004, Dr. Wagers joined the faculty at Harvard Medical School as an Assistant Professor of Pathology and an Investigator at the Joslin Diabetes Center. She moved to Harvard's Department of Stem Cell and Regenerative Biology upon its founding in 2008, and was promoted to Associate Professor in 2009. In 2012, Dr. Wagers became the first incumbent of the Forst Family Professorship in Stem Cell and Regenerative Biology. She is also an Early Career Scientist of the Howard Hughes Medical Institute and a Senior Investigator at the Joslin Diabetes Center.

Dr. Wagers' current research is aimed at understanding how changes in stem cell activity impact tissue homeostasis and repair throughout life. Her work focuses particularly on the circulatory system as a source signals that modify stem cell function. Work from her lab provides evidence for the existence of a conserved systemic regulatory axis that modulates tissue maintenance and regeneration across a wide variety of tissues that vary significantly in their intrinsic repair capacity, and her ongoing studies have begun to identify the molecules responsible for age-variant regulation of regenerative potential.

Dr. Wagers has authored 91 primary research and review articles and she has been recognized with awards from the Burroughs Wellcome Fund, Beckman Foundation, and WM Keck Foundation, as well as, most recently, the HHMI Early Career Scientist Award and Presidential Early Career Award for Scientists and Engineers.

On the Reversibility of Aging

Local and Systemic Regulators of Aging in Mammalian Tissues.



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

