

The 2013 Harvard / Paul F. Glenn

Symposium on Aging

June 17, 2013



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

Welcome to the 8th 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 educate the wider research community about advancements in this fast-paced field and to stimulate collaborative research in this area. 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, whose unwavering support for aging research for over 30 years has allowed it to grow into the cutting-edge field it is today. Today we are joined by Mark Collins, President of the Glenn Foundation for Medical Research and K. Leonard Judson, the Foundation's Executive Vice President. Since the inception of the Paul F. Glenn labs at Harvard in 2005, the network of Paul F. Glenn Laboratories have grown into a consortium that includes Princeton University, Buck Institute, Massachusetts Institute of Technology, Salk Institute, Stanford University, and Albert Einstein College of Medicine.

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 is going to place an unprecedented burden on the families and the economies of those nations. Because chronic illness in the elderly is a major medical cost, enormous savings would be achieved if mortality and morbidity could be compressed within a shorter duration of time at the end of life. 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. Many leaders in the aging field predict that significant strides will be made in understanding how human health and lifespan are regulated, leading to novel medicines to forestall and treat 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 the Harvard/Paul F. Glenn Symposium on Aging, 2013.

David Sinclair and Bruce Yankner

Co-Directors, The Paul F. Glenn Laboratories at Harvard Medical School

Symposium on Aging
Agenda

June 17, 2013
9:00 - 5:00

- 9:00 - 9:15 **Welcome**
Jeffrey S. Flier, M.D., Dean of the Faculty of Medicine
Harvard Medical School
Mark Collins, President,
Glenn Foundation for Medical Research
- 9:15 - 10:00 Bruce Yankner, M.D., Ph.D.
Systems Biology of the Aging Brain
- 10:00 - 10:45 Tomas Prolla, Ph.D.
**Mechanisms of Age-Related Hearing Loss and its
Prevention by Caloric Restriction**
- 10:45 - 11:30 Yousin Suh, Ph.D.
Functional Genomics of Human Aging
- 11:30 - 12:15 Martin W. Hetzer, Ph.D.
You Are Only as Old as Your Proteins
- 12:15 - 1:30 Lunch
- 1:30 - 2:15 Amy Wagers, Ph.D.
Reversing Aging-Related Pathology
- 2:15 - 3:00 Angelika Amon, Ph.D.
Gametogenesis Induces Rejuvenation
- 3:00 - 3:45 Irina M. Conboy, Ph.D.
Intrinsic and Extrinsic Aging of Stem Cells
- 3:45 - 4:15 Thomas E. Johnson, Ph.D.
**Genetic and Epigenetic Modulation of Stochastic
Effects on Aging**
- 4:15 - 5:00 Public Social

Bruce A. 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. Recent work from his laboratory has defined the transcriptome of the aging human brain, its evolution from mouse to man, and a role for DNA damage in age-related cognitive changes and pathology. 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 Ellison Medical Foundation Senior Scholar Award, the Nathan W. Shock award from NIA and the NIH Director's Pioneer Award.

Tomas Prolla, Ph.D.

Dr. Tomas A. Prolla received a B.A. in Biochemistry from the University of California at Berkeley in 1990. He continued his studies at the Department of Molecular Biophysics and Biochemistry at Yale University, receiving a doctoral degree in 1994. While at Yale, Dr. Prolla contributed to the discovery of the molecular mechanism of DNA mismatch repair in eukaryotic organisms, a discovery that was the basis for the identification of human DNA mismatch repair genes involved in cancer.



Following his doctoral work, he completed a research fellowship at the Human and Molecular Genetics Department at Baylor College of Medicine. Dr. Prolla joined the faculty of the Department of Genetics & Medical Genetics at the University of Wisconsin-Madison in 1997, where he is currently a Professor. Dr. Prolla's work focuses on understanding the genetic basis of aging. Areas of interest include the role of mitochondrial dysfunction in aging, as well as understanding the mechanisms of aging retardation by caloric restriction. Recent studies from the Prolla laboratory have focused on understanding the mechanisms of age-related hearing loss and its prevention by caloric restriction.

Yousin Suh, Ph.D.



Yousin Suh, Ph.D., is a Professor of Genetics and Medicine at Albert Einstein College of Medicine. She investigates the genetic component that underlies the interface of intrinsic aging and disease. The approach she follows is based on the identification of genome sequence variants associated with age-related disease risk or its opposite, i.e., an unusual resistance to such disease. For this purpose her target populations are either cohorts of middle-aged individuals followed longitudinally for signs of all major age-related diseases, or cohorts of extremely long-

lived individuals who managed to ward off such diseases. To tackle the key problem of identifying the functional impact of any observed association, she applies specific functional tests, including *in silico* modeling, cell culture assays and mouse models. Discoveries thus far made include novel, rare alleles associated with extreme longevity and sirtuin variants that confer risk for heart disease. Her contributions in the field have been recognized by the Glenn Award for Research in Biological Mechanisms of Aging. She has organized numerous international symposiums on functional genomics of aging, had served as the Associate Editor for the Mechanisms of Aging and Development, and participates on advisory committees for several research institutions and companies. She is a supervising editor for *Aging Cell* and is on the Editorial Boards of numerous Journals. She is a Distinguished Professor at the GuangDong Medical College in China.

Martin W. Hetzer, Ph.D.

Martin W. Hetzer is the Jesse and Caryl Philips Professor of Molecular and Cell Biology and Director of the Waitt Advanced Biophotonics Center at the Salk Institute for Biological Studies in La Jolla. Dr. Hetzer received his PhD in biochemistry and genetics from the University of Vienna, Austria, and completed postdoctoral work at the European Molecular Biology Laboratory (EMBL) in Heidelberg, Germany. He joined the faculty at the Salk as an Assistant Professor in 2004. His research focuses on the functional organization of the cell nucleus, developmental gene regulation and protein homeostasis during aging. Dr. Hetzer has received a number of awards including a Pew Scholar Award, an Early Life Scientist Award from the American Society of Cell Biology, a Senior Scholar Award for Aging from the Ellison Medical Foundation, a Senior Scholar Award from the American Cancer Society and a Royal Society Research Merit Award.



You Are Only as Old as Your Proteins

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.

Angelika Amon, Ph.D.

Dr. Amon obtained her PhD in 1994 from the University of Vienna for her work on the molecular mechanisms governing cell cycle progression in budding yeast. She then joined the laboratory of Dr. Ruth Lehmann at the Whitehead Institute as a Helen Hay Whitney Postdoctoral Fellow to investigate germ cell formation in *Drosophila*. In 1996 Dr. Amon accepted a Whitehead Fellow position to study the mechanisms governing chromosome segregation and exit from mitosis. Dr. Amon joined the faculty of the Department of Biology and the Koch Institute for Integrative Cancer Research at MIT in 1999 and the Howard Hughes Medical Institute in 2000. At the Koch Institute Dr. Amon studies the molecular mechanisms that prevent chromosome mis-segregation during mitosis and meiosis. When these mechanisms fail cells become aneuploid. Dr. Amon's laboratory also investigates the consequences of aneuploidy on cell physiology and proliferation. As aneuploidy is a key characteristic of cancer, her discovery of an aneuploidy associated stress response has important implications for our understanding of tumorigenesis.



In recognition of her contributions towards our understanding of the cause and consequences of aneuploidy Dr. Amon has received numerous awards. Dr. Amon is the 1999 Presidential Early Career Award for Scientists and Engineers recipient, the 2003 Alan T. Waterman awardee, the 2003 Eli Lilly and Company Research Award recipient, the 2007 ASBMB Amgen Prize awardee, the 2007 Paul Marks Prize recipient, the 2008 recipient of the National Academy of Sciences Award in Molecular Biology and the 2013 Ernst Jung Prize for Medicine awardee. In 2010 Dr. Amon was elected to the National Academy of Sciences.

Gametogenesis Induces Rejuvenation

Irina M. Conboy, Ph.D.

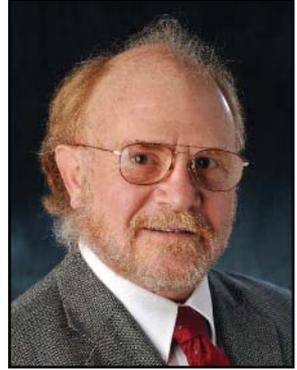


Irina Conboy is Associate Professor of Bioengineering at UC Berkeley. She received numerous awards in Regenerative Medicine and Aging Research, including Ellison's Medical Foundation, Glenn Foundation, Stem cell Research Foundation and CIRM New Faculty award, and commendation for her services as a referee for high impact journals, such as Nature. She is a long-standing mentor of Student Society for Stem Cell Research and a reviewer for the American Federation of Aging Research. Irina's laboratory focuses on the high-impact areas of

stem cell engineering and molecular medicine, aimed at the enhancement and rejuvenation of tissue maintenance and repair. Her work is published in Science, Cell and Nature, is highly cited and is highlighted in the popular press. She has patented methods for enhancing and rejuvenating tissue regeneration.

Thomas E. Johnson, Ph.D.

The ability to predict future health outcomes has been a long-time goal of medical research, especially in aging. There is an urgent need in aging to be able to predict future mortality and morbidity, two major components determining the rate of aging. For many diseases, biomarkers have been established that facilitate rapid detection and subsequent clinical intervention, not true for aging, despite an intense multi-year effort by the NIA. In 2005 (Rea *et al.* 2005), we put forth just such a marker: expression of a “GFP reporter” that is expressed in response to heat stress and can be used as a surrogate of HSP-16. *C. elegans*, a nematode worm, have been genetically engineered to carry this “reporter,” which is an indicator of level of response to environmental stress; moreover GFP can be seen in living cells and worms. On the second day of adult life, we are able to predict whether an individual will be long-lived or short-lived, with as much as 2.8-fold differences between their mean life spans following selection solely based on GFP brightness in living animals. Knowledge of future health prospects well before problems are encountered could be quite important in decisions as to appropriate medical interventions for the individual patient. The proposal was to develop a molecular understanding of the underlying mechanisms responsible for the relationship between biomarker expression and lifespan. We have disrupted the HSP-16.2 gene and its homologs and asked whether the GFP expression levels are still able to predict subsequent life span. We have used microarray analysis to detect differentially-expressed genes and ask if genetic manipulations of these targets disrupt the predictive power of the *Phsp-16::gfp* reporter. Interestingly, we also see inheritance of level of expression, consistent with an epigenetic component in their expression. (This work was supported by a BIG grant from the American Federation for Aging Research.)



Thomas E. Johnson, James Cypser, David Kitzenberg, Alex Mendenhall, Breanne Newell, Shane Rea*, Pat Tedesco*

Department of Integrative Physiology, Institute for Behavioral Genetics, University of Colorado, Boulder; Current addresses, AM: Hutchinson Institute and SR: San Antonio

Genetic and Epigenetic Modulation of Stochastic
Effects on Aging

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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

