

The 2011 Harvard / Paul F. Glenn

Symposium on Aging

June 20, 2011



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

Welcome to the 6th 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. Today's attendees come not only from the Harvard research community but from across the nation and from overseas for this one day event.

We wish to acknowledge the generosity and vision of Paul F. Glenn and Mark Collins, whose unwavering support for aging research has allowed it to grow into the cutting-edge field it is today. Today, thanks to their support, we 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, the network of Paul F. Glenn Laboratories has grown to include the Massachusetts Institute of Technology, the Salk Institute and, most recently, Stanford University.

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.

On behalf of The Paul F. Glenn Laboratories and Harvard Medical School, we welcome you to the Harvard/Paul F. Glenn Symposium on Aging, 2011.

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

Symposium on Aging
Agenda

June 20, 2011
9:00 - 5:00

- 9:00 - 9:30 **Welcome**
- 9:30 - 10:10 Bruce Spiegelman, Ph.D.
Transcriptional Control of Adipogenesis and Metabolism in Age-related Disease
- 10:10 - 10:50 Tomas Prolla, Ph.D.
Mitochondrial Mechanisms of Aging and its Retardation by Caloric Restriction
- 10:50 - 11:30 Anne Brunet, Ph.D.
Aging and Stem Cells
- 11:30 - 12:10 John M. Sedivy, Ph.D.
Cellular Senescence and the Aging of Organisms
- 12:10 - 1:30 Lunch
- 1:30 - 2:10 Leonard Guarente, Ph.D.
New Findings on Sirtuins
- 2:10 - 2:50 Jonathan L. Tilly, Ph.D.
Rewinding the Female Biological Clock for Fertility Reasons: An End to Menopause as Well?
- 2:50 - 3:30 Edward G. Lakatta, Ph.D.
Stress of Aging Viewed from the Arterial Wall
- 3:30 - 4:10 Judith Campisi, Ph.D.
Cellular Senescence Links Cancer to the Degenerative Diseases of Aging
- 4:15 - 5:00 Public Social

Bruce Spiegelman, Ph.D.



Bruce M. Spiegelman is the Stanley J. Korsmeyer Professor of Cell Biology and Medicine at Harvard Medical School and Dana-Farber Cancer Institute. Dr. Spiegelman received a B.S. with highest honors from the College of William and Mary in 1974, his PhD in biochemistry from Princeton University in 1978, and completed postdoctoral work at MIT. He joined Harvard Medical School and Dana-Farber Cancer Institute in 1982. His research focuses on fat cell biology, diabetes and muscular diseases. Dr. Spiegelman has been honored with

many awards including Bristol-Myers Squibb Award for Distinguished Achievement in Metabolic Research; the Solomon Berson Award, American Physiological Society; the Rolf Luft Award in Endocrinology, Karolinska Institute (Sweden); the Trans-Atlantic Medal, British Endocrine Society; the Naomi Berrie Award for Outstanding Achievement in Diabetes Research, Columbia University. In 2002 Dr. Spiegelman was elected to the American Academy of Arts and Sciences and the National Academy of Science.

Transcriptional Control of Adipogenesis and
Metabolism in Age-related Disease

Tomas Prolla, Ph.D.

Dr. Tomas A. Prolla, received his B.S in Biochemistry from the University of California at Berkeley in 1990, and his Ph.D from the Department of Molecular Biophysics and Biochemistry at Yale University in 1994. He was a HHMI postdoctoral fellow in the Department of Human and Molecular Genetics at Baylor College of Medicine (1994-1997). He is currently Professor of Genetics & Medical Genetics at the University of Wisconsin-Madison. Dr. Prolla is internationally recognized for research in two research areas, gene expression changes associated with aging, and the role of mitochondria in aging. Dr. Prolla's research group was the first to employ large-scale gene expression profiling using DNA microarrays to the analysis of aging and its retardation by caloric restriction. These studies have generated the first detailed analysis of the aging process at the gene expression level. More recently, Dr. Prolla and his research group have focused on understanding the relationship between mitochondrial function, aging, and its retardation by caloric restriction.



Anne Brunet, Ph.D.



Anne Brunet is an Associate Professor in the Department of Genetics at Stanford University. Dr. Brunet obtained her B.Sc. from the Ecole Normale Supérieure in Paris, France and her Ph.D. from the University of Nice, France. She did her postdoctoral research training in Dr. Michael Greenberg's lab at Harvard Medical School. Dr. Brunet is interested in the molecular mechanisms of aging and longevity, with a particular emphasis on the nervous system. Her lab studies the molecular mechanism of action of known longevity genes, including

FOXO transcription factors, in mammalian cells and organisms. She is particularly interested in the role of longevity genes in neural stem cells during aging. Another goal of the Brunet lab is to discover novel genes and processes regulating longevity using two model systems, the invertebrate *C. elegans* and an extremely short-lived vertebrate, the African killifish *N. furzeri*. Dr. Brunet has received several grants from the National Institute on Aging to study the importance of FOXO transcription factors in aging neural stem cells, the molecular mechanisms of dietary restriction, and to develop genetic tools for the short-lived fish *N. furzeri*. She has published over 50 peer-reviewed papers, reviews, and book chapters. She has received a number of awards, including the Pfizer/AFAR Innovations in Aging Research Award, a Junior Investigator Award from the California Institute for Regenerative Medicine, a Glenn Foundation Award, and an Ellison Medical Foundation Senior Scholar Award.

John M. Sedivy, Ph.D.

Dr. John M. Sedivy, PhD, is the Hermon C. Bumpus Professor of Biology at Brown University. He received his PhD from Harvard University in 1984 and pursued postdoctoral studies at MIT. Dr. Sedivy has had a long standing interest in mammalian genetics, signaling and cell cycle control. As a postdoc he developed one of the first methods for targeted homologous recombination, which he established into a specialized method for gene targeting of somatic cells. In 1995 his lab isolated the first homozygous knockout of *c-myc*, which led to his career-long interest in this proto-oncogene. In 1997 his lab was the first to achieve a homozygous gene knockout in nonimmortalized human cells. An ongoing interest has been the study of signaling pathways responsible for the establishment and maintenance of the senescent state. Dr. Sedivy has pioneered single-cell assays of cellular senescence, which his lab used to document and quantify senescent cells in aging primates. More recently his group developed new single-cell assays showing age-associated *in vivo* expansion of facultative heterochromatin, leading to current efforts to study genome-wide chromatin changes. Other projects in the lab include regulation of chromatin states by the polycomb pathway, the role of Wnt signaling in cellular senescence and organismal aging, and the regulation of the important cell cycle inhibitor and senescence effector p16^{Ink4a}. Dr. Sedivy was a founding member of the CMAD study section, where he currently serves as permanent member. He has been actively involved with the journal *Aging Cell* since its inception in 2002, serving as one of the Editors-in-Chief since 2006. In 2007 he received the Senior Research Scholar in Aging Award from the Ellison Medical Foundation, and in 2009 was recognized with a MERIT award from the NIA.



Leonard Guarente, Ph.D.



Leonard Guarente is the Novartis Professor and Director of the Paul F. Glenn Lab for the Science of Aging at MIT. He discovered that a group of related proteins termed sirtuins slow aging in model organisms and mitigate aging and diseases in mammals. Critically, he showed that sirtuins are NAD-dependent protein deacetylases. This finding links protein acetylation, metabolism, and aging. It also indicates that sirtuins mediate the benefit of calorie restriction on health and longevity. More recently, the Guarente lab has shown that genetic activation of the mammalian

sirtuin SIRT1 mitigates major diseases, such as Alzheimer's Disease, in appropriate murine models.

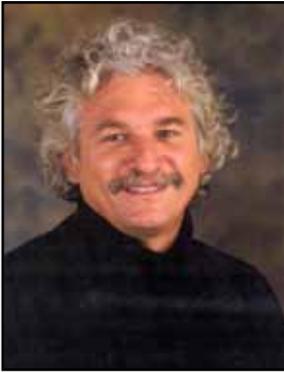
Jonathan L. Tilly, Ph.D.

Dr. Tilly obtained his PhD in 1990, and completed postdoctoral training at the University of California-San Diego and Stanford University Medical Center. Dr. Tilly joined the faculty of Johns Hopkins University as an Assistant Professor in 1993, and moved to Massachusetts General Hospital in 1995 to direct the Vincent Center for Reproductive Biology. He was promoted to Professor of Obstetrics, Gynecology and Reproductive Biology at Harvard Medical School in 2010. Dr. Tilly's primary area of research is on the development of methods for preserving or reviving fertility and prolonging or restoring ovarian function in young girls and women. These studies have greatly expanded our understanding of such basic processes as menopause, infertility resulting from cancer treatments, and premature ovarian failure caused by exposure to toxic chemicals in the environment. In addition to reporting the first animal model that fails to undergo its equivalent of menopause with age, Dr. Tilly and his associates developed the first therapy that protects ovaries from the ravages of cytotoxic therapies. Recently, Dr. Tilly has taken a much different approach to new methods of fertility preservation based on his discovery of a population of stem cells in the ovaries of adult mice that are capable of generating new eggs. Following publication of this ground-breaking study in *Nature* in 2004, Dr. Tilly re-focused his entire lab on characterization of egg-producing stem cells to demonstrate that ovarian failure can be reversed through germline (egg) stem cell-based technologies. He has also discovered a similar population of egg stem cells exists in humans. Dr. Tilly is a member of the National Scientific Advisory Committee of the American Federation for Aging Research. His work, published in over 100 research articles, 18 reviews, and 18 book chapters, and 2 edited books, is currently supported by a 10-year MERIT Award from the NIA.



Rewinding the Female Biological Clock for Fertility
Reasons: An End to Menopause as Well?

Edward G. Lakatta, Ph.D.



Dr. Lakatta is the founder and Director of the Laboratory of Cardiovascular Science, National Institute on Aging, National Institutes of Health. He also holds adjunct appointments as Professor, Department of Physiology, University of Maryland School of Medicine, and Professor, Cardiology Division, Johns Hopkins School of Medicine.

He has made a sustained 30-plus-year commitment to a broad-based research career.

His studies range from molecules to humans, including translation of novel findings into the clinical realm. The overall goals of his research program are 1) to identify age associated changes that occur within the cardiovascular system and to determine the mechanisms for these changes; 2) to determine how aging of the heart and vasculature interacts with chronic disease states to enhance the risk for CV diseases in older persons; 3) to study basic mechanisms in excitation-contraction coupling and how these are modulated by surface receptor signaling pathways in cardiac cells; 4) to elucidate mechanisms of pacemaker activity in sinoatrial nodal cells; 5) to elucidate mechanisms that govern cardiac and vascular cell survival; 6) to establish the potentials and limitations of new therapeutic approaches such as changes in lifestyle, novel pharmacologic agents or gene or stem cell transfer techniques in aging or disease states.

Dr. Lakatta is recognized as both nationally and internationally as an expert in cardiovascular research. He has authored over 350 original publications in top peer-reviewed cardiovascular journals, written over 200 invited reviews/book chapters, and delivered over 300 invited lectures. He is a member of multiple scholarly societies and journal editorial boards. Based upon his accomplishments, Dr. Lakatta has received numerous awards, among which are the Allied Signal Achievement Award in Aging, the Novartis Prize in Gerontology, the Irving Wright Award of Distinction of the American Federation for Aging Research (AFAR) and the Distinguished Leader Award of the International Society of Heart Research (ISHR).

Stress of Aging viewed from the Arterial Wall

Judith Campisi, Ph.D.

Judith Campisi received a PhD in Biochemistry from the State University of New York at Stony Brook, and postdoctoral training in cell cycle regulation and cancer at the Dana-Farber Cancer Institute and Harvard Medical School. As an Assistant Professor at the Boston University Medical School, she became interested in the control of cellular senescence and its role in tumor suppression and aging. She left Boston University as an Associate Professor to accept a Senior Scientist position at the Lawrence Berkeley National Laboratory in 1991. In



2002, she established a second laboratory at the Buck Institute for Age Research, where she is a Professor. At both institutions, she established a broad program to understand various aspects of aging, with an emphasis on the interface between cancer and aging. The Campisi laboratory has made several pioneering discoveries in these areas, and her research continues to challenge and alter existing paradigms. In recognition of the quality of her research and leadership in the field, she received numerous awards, including two MERIT awards from the US National Institute on Aging, awards from the AlliedSignal Corporation, Gerontological Society of America and American Federation for Aging Research, the 2010 Longevity prize from the IPSEN Foundation. She currently serves on numerous national and international editorial and advisory boards.

Cellular Senescence Links Cancer to the
Degenerative Diseases of 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

