

The 2012 Harvard / Paul F. Glenn

# Symposium on Aging

June 18, 2012

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

Welcome to the 7th 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 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. This year we welcomed Amy Wagers as a new member of the Glenn Laboratories at Harvard Medical School. Amy's research is aimed at understanding the role of blood-forming and muscle-forming stem cells in aging and finding factors that may allow the reversal of aging by reactivating stem cell function. These cells may also be exploited for the treatment of diseases such as cancer, anemia, muscular dystrophy, and diabetes.

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, 2012.

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

# Symposium on Aging Agenda

June 18, 2012  
9:00 - 5:00

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| 9:00 - 9:15   | Welcome<br>Jeffrey S. Flier, M.D., Dean of the Faculty of Medicine<br>Harvard Medical School  |
| 9:15 - 10:00  | Pier Paolo Pandolfi, M.D., Ph.D.<br><b>Aging, Metabolism and Cancer</b>   |
| 10:00 - 10:45 | Gerald S. Shadel, Ph.D.<br><b>Mitochondrial ROS Signaling in Disease and Aging</b>  |
| 10:45 - 11:30 | Jan van Deursen, Ph.D.<br><b>Does Cell Senescence Cause Aging?</b>  |
| 11:30 - 12:15 | Norbert Perrimon, Ph.D.<br><b>Organ communication and Regulation of Insulin<br/>Signaling in <i>Drosophila</i>: Implications to Aging</b> |
| 12:15 - 1:30  | Lunch   |
| 1:30 - 2:15   | Eric Verdin, M.D.<br><b>Mitochondrial Protein Modifications and Aging</b>   |
| 2:15 - 3:00   | Ana Maria Cuervo, M.D., Ph.D.<br><b>Selective Autophagy and Aging: Cleaning with a Spin</b>   |
| 3:00 - 3:45   | Bradley T. Hyman, M.D., Ph.D.<br><b>Multiphoton Imaging and the Natural History of<br/>Alzheimer's Disease</b>                            |
| 3:45 - 4:15   | Rafael de Cabo, Ph.D.<br><b>Dietary Interventions for Aging</b>   |
| 4:15 - 5:00   | Public Social   |

## Pier Paolo Pandolfi, M.D., Ph.D.



Pier Paolo Pandolfi received his M.D. in 1989 and his Ph.D. in 1996 from the University of Perugia, Italy, after having studied Philosophy at the University of Rome, Italy. He received post-graduate training at the National Institute for Medical Research and the University of London in the UK. He became an Assistant Member of the Molecular Biology Program and the Department of Human Genetics at Memorial-Sloan-Kettering Cancer Center in 1994. Dr. Pandolfi rose to become a Member in the Cancer Biology and Genetics Program at

the Sloan Kettering Institute; Professor of Molecular Biology and Human Genetics at the Weill Graduate School of Medical Sciences at Cornell University; Professor, Molecular Biology in Pathology and Laboratory Medicine, Weill Medical College at Cornell University; and Head of the Molecular and Developmental Biology Laboratories at MSKCC. Dr. Pandolfi presently holds the Reisman Endowed Chair of Medicine, and is Professor of Pathology at Harvard Medical School. He serves as the Director of Research, Beth Israel Deaconess Cancer Center; Director, Cancer Genetics Program; and Chief, Division of Genetics in the Department of Medicine, Beth Israel Deaconess Medical Center, and is a Member of the Department of Pathology, Beth Israel Deaconess Medical Center. The research carried out in Dr. Pandolfi's laboratory has been seminal to elucidating the molecular mechanisms and the genetics underlying the pathogenesis of leukemias, lymphomas and solid tumors as well as in modeling these cancers in the mouse.

Dr. Pandolfi has been the recipient of numerous awards including the Pezcoller Foundation–AACR International Award for Cancer Research (2011). In 2006, Dr. Pandolfi was elected as a member of the American Society for Clinical Investigation (ASCI) and the American Association of Physicians (AAP), and in 2007 as Member of the European Molecular Biology Organization (EMBO).

## Gerald S. Shadel, Ph.D.

Dr. Shadel earned a B.S. in Chemistry from the University of Nevada, Las Vegas in 1986 and received his Ph.D. in Biochemistry from Texas A&M University in 1991. Following this, Dr. Shadel was a postdoctoral fellow with Dr. David Clayton in the Department of Developmental Biology at Stanford University, where his mitochondrial research career began. He was an Assistant Professor of Biochemistry at Emory University from 1997-2003 and was promoted to Associate Professor with tenure there in 2003. He joined the faculty at Yale University in 2004 as an Associate Professor of Pathology and has held a secondary appointment in the Department of Genetics since 2008. In 2008, he was promoted to full Professor with tenure at Yale.



Dr. Shadel's research today is directed toward understanding the mechanism of gene expression in human mitochondria, as well as delineating signaling pathways that regulate mitochondrial function and biogenesis. The ultimate goal is to gain a comprehensive understanding of how defects in these processes contribute to aging and human disease that might in turn lead to novel therapeutic strategies. He has made numerous contributions to this field such as identifying and characterizing key factors and mechanisms that regulate human mitochondrial gene expression, defining signaling pathways that control mitochondrial homeostasis, and elucidating how mitochondria affect aging and pathology in yeast, mouse and human cell culture models. In doing so, previously unappreciated roles for mitochondria in disease pathology and aging have been elucidated, including deafness, ataxia-telangiectasia, cancer, and life span regulation. To date, Dr. Shadel has authored 60 peer-reviewed primary research articles, 6 book chapters/symposium contributions and 21 review articles/commentaries. He serves on the editorial boards of "Aging Cell," "Aging," "Frontiers in Genetics" and "Mitochondrion." He has received honors and awards at every academic level, including the "Damon Runyon-Walter Winchell" Postdoctoral Fellowship and, most-recently, the prestigious "Amgen: Outstanding Investigator Award" in 2007.

Mitochondrial ROS Signaling in Disease and Aging

## Jan van Deursen, Ph.D.



Dr. Van Deursen received his PhD in Cell Biology at the University of Nijmegen and is currently a professor of Biochemistry, Molecular Biology and Pediatrics at Mayo Clinic. He is the Vita Valley Professor of Cellular Senescence and Director of the Senescence Program in the Robert and Arlene Kogod Center on Aging.

The aging related work of the van Deursen lab focuses on the progeroid gene BubR1, which encodes a core component of the mitotic checkpoint whose level of expression markedly declines with aging. About 10 years ago, the lab discovered that BubR1 hypomorphic mice that begin life with low amounts of the mitotic checkpoint protein BubR1 protein die early and develop multiple progeroid and age-related disorders. Shortly thereafter, others demonstrated that loss of function mutations in BubR1 cause mosaic-variegated aneuploidy, a human syndrome that is characterized by aneuploidy, cancer predisposition and several progeroid traits. These observations led to the idea that depletion of BubR1 with age is a key determinant of longevity and age-related disorders. His lab went on to test this hypothesis using BubR1 transgenic mice in which age-related decline of BubR1 is prevented. These mice are resistant to tumorigenesis, have an extended lifespan and delayed age-related decline in several tissues and organs important to human health in the absence of any overt negative side effects. These findings identify BubR1 and its regulator(s) as therapeutic targets for treatment of a broad spectrum of human cancers and key age-related disorders that dictate health- and lifespan.

Does Cell Senescence Cause Aging?

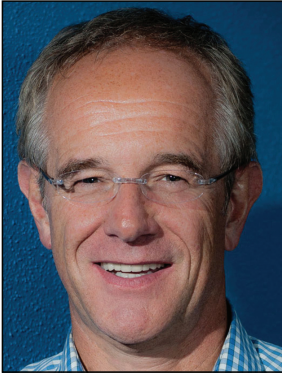
## Norbert Perrimon, Ph.D.

Perrimon is the James Stillman Professor of Developmental Biology at Harvard Medical School and an Investigator of the Howard Hughes Medical Institute. He has made a number of contributions to the fields of Genetics, Developmental Biology, signal transduction and functional genomics. His group developed many methods that have significantly improved the *Drosophila* toolbox. His contributions include the characterization of the maternal effects of zygotic lethal mutations; the logic of head patterning; the identification of cell polarity complexes; the discovery of adult gut stem cells; and the mechanisms of muscle growth and aging. His lab has characterized many signaling components of receptor tyrosine kinases, Wnt and JAK/STAT pathways. Currently, his laboratory is applying large-scale RNAi and proteomic methods to obtain a global understanding of the structure of a number of signaling pathways and their cross-talks. In addition, he is studying the roles of signaling pathways in homeostasis and tissue remodeling in *Drosophila* muscles and gut stem cells.



Perrimon was a Lucille P. Markey Scholar in Biomedical Sciences. He received the George W. Beadle Medal from Genetics Society of America, and is a fellow of the American Academy of Arts and Sciences and of the American Association for the Advancement of Science.

## Eric Verdin, M.D.



Dr. Verdin received his MD degree from the University of Liege, Liege, Belgium. He trained as a diabetologist/endocrinologist and held positions at the Joslin Diabetes Center and Harvard Medical School, the University of Brussels, the NIH, and the Picower Institute for Medical Research. He joined the Gladstone Institute of Virology and Immunology in 1997 and became its Associate Director in 2004. He is also Professor of Medicine, University of California, San Francisco. Dr. Verdin was Senior Scholar in Aging from the Ellison Medical

Foundation and was recently elected a fellow of the American Association for the Advancement of Science. He has served as the organizer of international meetings and as the editor of several books and reviews. He has published more than 160 papers and is associated with 11 published patents. His laboratory focuses on the biology of mitochondrial protein modifications and aging.



## **Ana Maria Cuervo, M.D., Ph.D.**

Ana Maria Cuervo is the Robert and Renee Belfer Chair for the Study of Neurodegenerative Diseases, a Professor in the Departments of Developmental and Molecular Biology and of Medicine of the Albert Einstein College of Medicine, co-director of the Einstein Institute for Aging Studies, and member of the Liver and Cancer Centers at the same institution. She obtained her M.D. degree and a Ph.D. in Biochemistry and Molecular biology from the University of Valencia (Spain) in 1990 and 1994, respectively. After her postdoctoral training at Tufts University in Boston, she started her laboratory at the Albert Einstein College of Medicine at the end of 2001, where she continues her studies in the role of protein-degradation in aging and age-related disorders, with emphasis in neurodegeneration.



Dr. Cuervo's group is interested in understanding how altered proteins can be eliminated from the cells. Her group has linked alterations in lysosomal protein degradation with different neurodegenerative diseases including Parkinson's, Alzheimer's and Huntington's disease. They have also proven that restoration of normal lysosomal function prevents accumulation of damaged proteins with age, demonstrating this way that removal of these toxic products is possible.

Dr. Cuervo is considered a leader in the field of protein degradation in relation to biology of aging. She is currently co-Editor-in-Chief of Aging Cell and associate editor of Autophagy. She has served in NIH advisory panels, special emphasis panels and study sections and has been recently elected member of the NIA Scientific Council. She was the recipient of the 2005 P. Benson Award in Cell Biology, the 2005/8 Keith Porter Fellow in Cell Biology, the 2006 Nathan Shock Memorial Lecture Award, the 2008 Vincent Cristofalo Rising Start in Aging Award, the 2010 Bennett J. Cohen Award in Aging Biology and the 2012 M. Hortwitz Prize for Excellence in Research.

**Selective Autophagy and Aging: Cleaning with a Spin**

## **Bradley T. Hyman, M.D., Ph.D.**



Bradley T. Hyman, M.D., Ph.D., is the John B. Penney, Jr. Professor of Neurology at Harvard Medical School and Massachusetts General Hospital where he has a clinical practice in the Memory and Disorder Unit and is the Director of the Massachusetts Alzheimer Disease Research Center.

His clinical career is devoted towards the care of patients with dementia. His research laboratory is pursuing research in Alzheimer's disease, and other neurodegenerative diseases, with a goal of

understanding the neuropathophysiologic and genetic factors that underlie dementia.

Dr. Hyman's laboratory is developing methods to examine clinical-pathological correlates and biomarkers in AD, as well as animal and cell models to explore the natural history of the diseases. A recent focus has been the use of advanced microscopy methods – including multiphoton microscopy for in vivo imaging of plaques, tangles, and synuclein aggregates, as well as FRET methods to detect protein-protein interactions and protein conformation.

Dr. Hyman received a B.A. in chemistry from Northwestern University and a Ph.D. in Biochemistry and M.D. from the University of Iowa, where he also did residency in neurology and fellowships in Behavioral neurology and neuropathology. He joined the faculty at Harvard Medical School in 1989. Dr. Hyman has received the Potamkin Award, a Metropolitan Life Award, a Brookdale Foundation fellowship, an Alzheimer Association Faculty Scholar Award, an Alzheimer Association Pioneer Award, and a National Institute on Aging Merit Award.

**Multiphoton Imaging and the Natural History of  
Alzheimer's Disease**

## Rafael de Cabo, Ph.D.

Dr. Rafael de Cabo is Senior Investigator, Laboratory of Experimental Gerontology, National Institute on Aging, National Institutes of Health, USA. He has extensive training as a biogerontologist with expertise in nutrition, biochemistry, molecular biology and animal interventions. After completing his PhD on nutrition at Purdue University, West Lafayette he became a Postdoctoral Fellow, Laboratory of Neurosciences, at the National Institute on Aging. Subsequently he has achieved his tenured position at the NIA, NIH as Senior Investigator in 2009.



His research has focused on the molecular mechanisms for the effects of caloric restriction on aging, and interventions that act on these pathways including resveratrol, rapamycin, metformin and deoxyglucose. Honours and awards include Fellow of the Gerontological Society of America (2010), Elected Member of the Board of Directors, American Aging Association, Nathan Shock New Investigator Award of the Gerontological Society of America (2006), Paul E. Glenn Runner-Up Award for Meritorious Research from The American Aging Association (2003) and Paul E. Glenn Award for Meritorious Research from The American Aging Association (2001). Dr de Cabo is Editor in Chief, Journal of Gerontology Biological Sciences and on the editorial boards of Aging Cell, BBA-Mol Mech of Disease and AGE.

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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

