

The 2010 Harvard / Paul F. Glenn

Symposium on Aging

June 21, 2010



Paul F. Glenn Laboratories for the Biological Mechanisms of Aging

Welcome to the 5th 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 these 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.

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 in 2006 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. Thus, a major goal in the coming years is to understand healthy aging, and to translate this understanding into therapeutic approaches to postpone and treat diseases of aging.

On this, the 5th anniversary of the Paul F. Glenn labs at Harvard Medical School, we acknowledge Paul F. Glenn and Mark Collins, President of the Glenn Foundation for Medical Research, for their vision and generosity. Since the inception of the labs at Harvard Medical School in 2005, the network of Paul F. Glenn Laboratories has grown to include the Massachusetts Institute of Technology and the Salk Institute. On behalf of The Paul F. Glenn Laboratories and Harvard Medical School, we welcome you to the 2010 Harvard/Paul F. Glenn Symposium on Aging, 2010.

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

Symposium on Aging Agenda

June 21, 2010

9:00 - 5:00

9:00 - 9:30 **Opening Remarks**

Jeffrey S. Flier, MD, Dean of the Harvard Faculty of Medicine

Paul F. Glenn, Founder, Glenn Foundation for Medical Research

Mark R. Collins, President, Glenn Foundation for Medical Research

9:30 - 10:10 Elaine Fuchs, Ph.D.

Stem Cells and Skin Aging

10:10 - 10:50 Li-Huei Tsai, Ph.D.

Longevity Pathways in Preventing NeuroD

10:50 - 11:30 Wade Harper, Ph.D.

The Human Autophagy System

11:30 - 12:10 Pinchas Cohen, M.D.

The New World of Mitochondrial Peptides

12:10 - 1:30 **Lunch**

1:30 - 2:10 Gerald Shulman, M.D., Ph.D.

ROS and Mito Function in Aging, Diabetes

2:10 - 2:50 Raul Mostoslavsky, M.D., Ph.D.

Sirtuins Regulating Metabolism

2:50 - 3:30 Gary Ruvkun, Ph.D.

Xenobiotic Detection and the Control of Lifespan

3:30 - 4:10 Alexander Meissner, Ph.D.

Epigenetics, Stem Cells and Aging

4:15 - 5:00 **Public Social** – Cheese & Crackers

Elaine Fuchs, Ph.D.



Elaine Fuchs is the Rebecca C. Lancefield Professor in Mammalian Cell Biology and Development at The Rockefeller University. She is also an Investigator, Howard Hughes Medical Institute. Fuchs has published >250 papers and is internationally known for her research in skin biology and associated human genetic disorders, which include skin cancers and life-threatening genetic syndromes such as blistering skin disorders. Fuchs' current research focuses on the molecular mechanisms that underlie how multipotent stem cells respond to external cues, change their program of gene expression, exit their niche and adopt specific fates to make the epidermis, sebaceous glands and hair follicles of the skin, and how this goes awry in squamous cell carcinomas and in aging.

Fuchs received her Ph.D. in Biochemistry from Princeton University, and after her postdoctoral research at the Massachusetts Institute of Technology, she joined the faculty at the University of Chicago. She stayed there until 2002 when she relocated to The Rockefeller University. Fuchs' awards and honors include the Presidential Young Investigator Award, the Richard Lounsbery Award from the National Academy of Sciences, the Novartis-Drew Award for Biomedical Research, the Dickson Prize in Medicine, the FASEB Award for Scientific Excellence, the Beering Award and most recently, the National Medal of Science, the L'Oreal-UNESCO Award and the Charlotte Friend Memorial Lecture and Award from the American Association for Cancer Research. She is a member of the National Academy of Sciences, the Institute of Medicine of the National Academy of Sciences, the American Academy of Arts and Sciences and the American Philosophical Society, and she holds honorary doctorates from Mt. Sinai/New York University School of Medicine and from the University of Illinois, Champaign-Urbana. Fuchs is also a past President of the American Society of Cell Biology and in June 2010, she will become President of the International Society for Stem Cell Research.

Dr. Li-Huei Tsai was born in Taipei, Taiwan. In 1986, she started her Ph.D. at the University of Texas Southwestern. Under the direction of Bradford Ozanne, she graduated in 1990 and joined Ed Harlow's laboratory at Cold Spring Harbor Laboratory and Massachusetts General Hospital for postdoctoral training. She was appointed Assistant Professor of Pathology at Harvard Medical School in 1994, elected Investigator of Howard Hughes Medical Institute in 1997, and promoted to Professor of Pathology in 2002. In 2006, she relocated her lab to MIT and became the Picower Professor of Neuroscience. Li-Huei began directing the Neurobiology Program at the Stanley Center for Psychiatric Research in 2007 and she was named Director of the Picower Institute for Learning & Memory in 2009.



Li-Huei is on numerous editorial boards, has been awarded the Young Investigator Award from Metropolitan Life Foundation, the Outstanding Contributor Award from the Alzheimer Research Forum. She serves on the China Strategy Working Group and the Neuroscience Council, as well as for NIH Study Sections. In addition to being a member of The Republic of China's Academia Sinica, Li-Huei sits on the scientific advisory boards and committees for NINDS, Gruber Foundation, Alzheimer Research Forum Foundation, and the Hotchkiss Brain Institute at the University of Calgary, among other organizations. She was named a fellow of the American Association for the Advancement of Science in 2008.

Wade Harper, Ph.D.



J. Wade Harper received both his B.S. and Ph.D. in chemistry from the Georgia Institute of Technology in 1980, and 1984. He was a post-doctoral fellow at Harvard Medical School from 1984 to 1988, when he joined the faculty of Baylor College of Medicine. He has been the B. and N. Vallee Professor of Molecular Pathology at Harvard Medical School since 2003.

Work in the Harper lab is focused on the interplay between protein ubiquitination and control of signaling pathways ranging from cell division to DNA damage and repair. We have contributed to the understanding of cullin-ring ubiquitin ligases and their role in protein turnover, the role of Cdks and their inhibitors in cell cycle control, and the role of deubiquitinating enzymes in control of protein ubiquitination. The laboratory integrates genetic, proteomic and enzymological approaches to elucidate signaling control mechanisms, primarily in mammalian systems.

Dr. Cohen graduated with highest honors in 1986 from the Technion Medical School in Israel, and trained in Pediatrics, Endocrinology and Diabetes at Stanford University until 1992. He was until 1998 an Associate Professor and Program Director at the University of Pennsylvania & Children's Hospital of Philadelphia. He is currently a Professor and Chief of Pediatric Diabetes and Endocrinology at UCLA and the associate director of the UCSD/UCLA Diabetes/Endocrinology Research Center. He was inducted into both the Society for Pediatric Research and the American Pediatric Society. He is the recipient of Juvenile Diabetes Association, American Diabetes Association, Pediatric Diabetes & Endocrinology Society, Eli Lilly, CaPCURE, & Ross awards, and most recently, the American Pediatric Society Best Science Award. Dr. Cohen published over 250 papers focusing on diabetes, growth disorders, cancer, aging, GH/IGF biology and the emerging science of humanin and other mitochondrial peptides. He received grants from the National Institutes of Health, the FDA, the Juvenile Diabetes Association, and the American Diabetes Association. Recently, he received two prestigious "roadmap awards": a EUREKA-RO1 grant and an NIH-Director Transformative-RO1 award. His editorial services include being an associate editor of Pediatric Research and a member of the editorial boards of JCEM and Endocrinology as well as being an executive officer of the GH Research society, the IGF society the and Endocrine Society Steering Committee.



Gerald Shulman, M.D., Ph.D.



Dr. Shulman is the George R. Cowgill Professor of Physiological Chemistry Medicine and Cellular & Molecular Physiology at Yale University as well as an Investigator of the Howard Hughes Medical Institute. He is also Associate Director of the Yale Diabetes-Endocrinology Research Center and Associate Director of the Yale Medical Scientist Training Program. Dr. Shulman completed his undergraduate studies in biophysics at the University of Michigan, and he received his M.D. and Ph.D. degrees from Wayne State University. Following internship and residency at Duke University Medical Center, he did an endocrinology fellowship at the Massachusetts General Hospital and additional postdoctoral work in molecular biophysics and biochemistry at Yale before joining the faculty at Harvard Medical School. He was subsequently recruited back to Yale and has remained there ever since. Dr. Shulman has pioneered the use of magnetic resonance spectroscopy (MRS) to non-invasively examine intracellular glucose and fat metabolism in humans. His work has been recognized with numerous honors and awards including the Outstanding Investigator Award from the American Federation for Clinical Research, the Diabetes Care Research Award from the Juvenile Diabetes Research Foundation, the Novartis Award in Diabetes, the Outstanding Scientific Achievement Award and the Distinguished Clinical Scientist Award from the American Diabetes Association and the Stanley J. Korsmeyer Award from the American Society for Clinical Investigation. Dr. Shulman has been elected to the Association of American Physicians, Fellow of the American Association for the Advancement of Science, the Institute of Medicine and the National Academy of Sciences.

Raul Mostoslavsky, M.D., Ph.D.

Dr. Mostoslavsky received his M.D. Degree from the University of Tucuman, Argentina in 1993. He then went to Israel to pursue Ph.D. studies under the Supervision of Howard Cedar and Yehudit Bergman at the Hebrew University in Jerusalem. He received his Degree in 2001, after studying the role of chromatin dynamics in antigen receptor rearrangement. In 2001 he moved to Boston, where he did his post-doctoral studies in the laboratory of Fred Alt, at the Children's Hospital. During his post-doc, Dr. Mostoslavsky became interested in mammalian sirtuins, and among other things, he generated and studied knock-out animals for all the mammalian sirtuins. Since 2007, he is an Assistant Professor of Medicine at the Massachusetts General Hospital Cancer Center-Harvard Medical School, where he continues his work on sirtuins and chromatin dynamics. Lately, he has focused his research on understanding the role of the histone deacetylase SIRT6 in glucose homeostasis. For his work, Dr. Mostoslavsky received numerous awards, among them the 2002 Science-Amersham Prize for Young Scientists, the 2009 American Federation for Aging Research (AFAR) Award, and the 2009 Howard M. Goodman Award.



Gary Ruvkun, Ph.D.



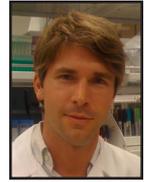
Gary Ruvkun is a professor of genetics at Harvard Medical School. Dr. Ruvkun is a graduate of UC Berkeley (AB, Biophysics, 1973) and Harvard (PhD Biophysics, 1982). Dr. Ruvkun began to work on genetics in the nematode *C. elegans* in 1982 as a Harvard Junior Fellow working with Bob Horvitz at MIT and Walter Gilbert at Harvard.

Dr. Ruvkun's laboratory discovered that an insulin-like signaling pathway controls *C. elegans* metabolism and longevity. The Ruvkun laboratory also identified the *daf-16* gene product as a highly conserved Forkhead transcription factor and the signal transduction components from the DAF-2 insulin receptor. The Ruvkun lab has also used full genome RNAi libraries to reveal a comprehensive set of genes that regulate aging and metabolism. Many of these genes are broadly conserved in animal phylogeny and are likely to reveal the neuroendocrine system that assesses and regulates energy stores and assigns metabolic pathways based on that status.

Dr. Ruvkun's research has also elucidated the regulation of developmental control genes by microRNA (miRNA) genes and other small RNAs, and control of longevity and metabolism. Between 1989 and 1993, Dr. Victor Ambros of Harvard University and Dr. Ruvkun reported that graded levels of the developmental timing control gene *lin-14* are generated by the production of a regulatory RNA of unprecedented size, the 21 nucleotide *lin-4* RNA, which basepairs to complementary regulatory elements in the *lin-14* 3' untranslated region. In 2000, the Ruvkun lab reported the identification of second microRNA (miRNA), *let-7* and provided the first indication that miRNA regulation via 3' UTR complementarity is a general phenomenon in biology. Dr. Ruvkun has identified many of the proteins that collaborate with miRNAs and siRNAs and other small RNAs which, in addition to revealing fundamental regulatory axes in biology, some of these may be developed as drug targets to enhance RNAi in mammals, a technical improvement that may be necessary to elevate a laboratory tool to a therapeutic modality.

Dr. Ruvkun's honors and awards include a Harvey Lecture at Rockefeller University, the Rosenstiel Award from Brandeis University (with Victor Ambros, Andy Fire, and Craig Mello), the Warren Triennial Prize from Massachusetts General Hospital (with Victor Ambros), the Benjamin Franklin Medal (with Victor Ambros and David Baulcombe), the Gairdner International Award (with Victor Ambros), the Albert Lasker award (with Victor Ambros and David Baulcombe), the Louisa Horwitz Prize from Columbia University (with Victor Ambros), the Shaul and Meira Massry Prize (with Victor Ambros), and the National Academy of Sciences.

During his Ph.D. in Rudolf Jaenisch's laboratory Alex trained in developmental biology, nuclear transfer and stem cell technology using mouse as a model system. In addition he has worked extensively on developmental and disease related aspects of DNA methylation.



Alex was author and co-author of several papers that have demonstrated the conversion of fibroblasts into pluripotent cells through overexpression of defined transcription factors. This field of induced pluripotent stem cells has received wide attention and raises the prospects of generating patient-specific stem cells without the need for embryos.

Alex joined the Harvard University Department of Stem Cell and Regenerative Biology in February 2008. He is a member of the Harvard Stem Cell Institute and Associate Member of the Broad Institute. He is also Co-Director of the Broad Institute Reference Epigenome Mapping Center.

Along with colleagues at the Broad Alex is developing and applying high-throughput bisulfite sequencing technologies for DNA methylation analysis. This should ultimately lead to generating reference epigenomes for many cell types and a better understanding of normal and diseased cellular states. His group also continues to investigate the mechanisms of transcription factor mediated reprogramming.

The Paul F. Glenn Laboratories Steering Committee

Lewis C. Cantley, Ph.D.



Dr. Cantley joined the faculty of Harvard Medical School in 1992, when he was also appointed Chief of the Division of Signal Transduction in the Department of Medicine at Beth Israel Hospital. He graduated summa cum laude from Wesleyan College and earned his Ph.D. from Cornell University in 1975. His postdoctoral research and first faculty appointment were in the Department of Biochemistry and Molecular Biology at Harvard University.

Although Dr. Cantley has made major contributions to numerous fields, he is best known for his discovery of the phosphoinositide 3-kinase (PI3K) pathway, which opened a window on the way biochemical signaling pathways control normal cell growth and how they can trigger the development of cancer when they are defective. Dr. Cantley's discoveries formed the foundation for the elucidation of longevity pathways in the worm *C. elegans*. His work has also enabled researchers to use the genetic blueprints of signaling proteins to predict their cellular targets, with a view to finding new cancer therapies.

Dr. Cantley has received numerous awards in recognition of these achievements. He received the Caledonian Prize of the Royal Society of Edinburgh in 2002. He has well over 300 publications to his name, including research papers, reviews, and book chapters. Cantley was elected to the National Academy of Sciences in 2001.

Stephen J. Elledge, Ph.D.

Stephen J. Elledge, Ph.D. is The Gregor Mendel Professor of Genetics and Professor of Medicine at Harvard Medical School and Senior Geneticist at Brigham and Women's Hospital. He is also an Investigator of the Howard Hughes Medical Institute, and is a Pew Scholar in the biomedical sciences. He is a recipient of the G.H.A. Clowes Memorial Award, the Paul Marks Prize in cancer research, the Michael E. DeBakey Award for research excellence, and the 2002 National Academy of Sciences Award in molecular biology. Dr. Elledge was elected to the National Academy of Sciences in 2003.



The Elledge lab uses model organisms to characterize cell cycle control and the cellular response to DNA damage. They have identified and characterized a signal transduction pathway that senses and responds to DNA damage. The lab is interested in technology development to aid in gene and drug discovery, and most recently applied a screen to identify transcriptional regulators of telomerase, an important player in human cancer. Currently they are initiating genome wide siRNA screens for regulators in cell cycle, checkpoint signaling tumorigenesis and cell proliferation. Until recently large-scale genetic screens have not been possible in mammals. The Elledge Lab initiated a genetic screen to find transcriptional regulators of human telomerase, an important player in human cancer. Using a technique that places endogenous genes under the control of a regulated promoter, we uncovered multiple negative regulators of this pathway.

Judith A. Glaven, Ph.D.



Judith A. Glaven, Ph.D. – Dr. Glaven is the Director of Basic Science Programs at Harvard Medical School. Dr. Glaven came to HMS with over four years of experience as a Senior Scientific Editor at the journal *Cell*, where she evaluated and recruited scientific papers and worked closely with the scientific community in the areas of basic Cell Biology, Immunology, Cancer Biology and Aging. Previous to being at *Cell* her own research focused on basic molecular mechanisms of cell proliferation and migration. She brings a broad perspective of basic biomedical science to the steering committee and represents the involvement and commitment of the Medical School to this initiative.

Marcia Haigis, Ph.D. is the Assistant Professor of Pathology at Harvard Medical School. Dr. Haigis's lab is focused on understanding the role that mitochondria play in mammalian aging and disease. Mitochondria are dynamic organelles that provide cells with energy even during dramatic changes in diet, stress and development. Mitochondria are also a major site for reactive oxygen species production, ion homeostasis, and apoptosis. Not surprisingly, mitochondrial dysfunction has been implicated in aging, neurodegeneration and metabolic diseases, such as diabetes.



The regulation of aging is highly conserved. For example, an extra copy of SIR2 (silent information regulator; sirtuins) significantly increases the lifespan of yeast, worms and flies. Mammals have seven homologs of SIR2, three of which are found in mitochondria. Recent studies have shown that sirtuins affect mitochondrial biogenesis and energy production. Our lab is interested in understanding how sirtuins mediate the interplay between mitochondrial activity and aging.

The main goals of the lab's research are: 1) to identify signals generated by mitochondria that contribute to aging and to identify those regulated by mammalian sirtuins, 2) to determine molecular mechanisms for these signals, and 3) to understand how these pathways regulate biological functions that decline during normal aging. To accomplish these goals, the lab's research integrates biochemistry, proteomics, cell biology and mouse genetics. These studies have the potential to lead to novel therapies that could treat a spectrum of human diseases.

Peter M. Howley, M.D.



Peter M. Howley, M.D., is the Shattuck Professor of Pathological Anatomy and Chairman of the Department of Pathology at Harvard Medical School. Research in the Howley laboratory is focused on the molecular biology of cancer and the role of viruses in its formation. The lab studies “high risk” HPV types such as HPV16 and HPV18 encode two oncoproteins, E6 and E7, which target the important cellular growth regulatory proteins p53 and pRb, respectively. They have previously shown that E6 promotes the ubiquitination and degradation of p53, and are now interested in the general question of how proteins are recognized within cell by the ubiquitin proteolytic machinery. The E6 promoted ubiquitylation of p53 is mediated by a cellular protein, called the E6 Associated Protein (E6AP), that binds to E6 and participates directly in its ubiquitination. We are interested in how E6AP is regulated and the identification of additional cellular proteins that E6AP targets in cells, either in the presence of or absence of the viral E6 protein.

C. Ronald Kahn, M.D.

C. Ronald Kahn, B.A., M.D., M.S., D.Sc. is President and Director of the Joslin Diabetes Center in Boston. Dr. Kahn received his M.D. from The University of Louisville School of Medicine (with highest honors) and holds honorary doctorates from University of Louisville (Honoris Causa) (1984), Universite de Paris Pierre et Marie Curie (1994) and The University of Geneva (2000). He has received over 60 awards and honors and is the author of over 170 publications. The Kahn lab seeks to understand the link between metabolism and aging. Recent studies from the lab showed that a reduction of fat mass without caloric restriction can be associated with increased longevity in mice, possibly through effects on insulin signaling. Work in the lab is also aimed at defining the roles of each of the IRS-proteins and isoforms of PI 3-kinase in insulin signaling and insulin resistance, the same pathway that regulates aging in *C. elegans* and *Drosophila*. The Kahn lab has also found interesting links between SIRT1-3 and the control of metabolism and longevity. Ronald Kahn has also been recognized for his pioneering work in the field of diabetes, including seminal discoveries that have defined the molecular and cellular mechanisms of insulin action and have yielded critical information about insulin resistance in obesity and diabetes. His recent work has made important contributions to the aging field by demonstrating that a mutation of the insulin receptor gene in adipocytes and that the hormone Klotho, which down-regulates insulin and IGF-1 signaling, extends mouse lifespan.



Gary B. Ruvkun, Ph.D.



Gary B. Ruvkun, Ph.D., is a Professor in the Department of Genetics at Harvard Medical School. The Ruvkun lab identified some of the first ever longevity genes using the nematode *C. elegans* as a model and have been instrumental in deciphering the insulin/IGF-1 pathway of longevity regulation. The lab showed that longevity is regulated by insulin signaling within the nervous system, suggesting that it is the metabolism within particular neurons that are key to regulation of lifespan. They study how these neuroendocrine pathways are coupled to sensory inputs. For example, the insulin pathway is coupled to a thermosensory pathway, allowing metabolism to be coupled to temperature. We are now exploring the neural signaling pathways that couple these systems. They have used powerful genetic selections to identify signaling molecules downstream of insulin-like receptors, as well as a novel insulin reception pathway that may act more broadly in animals. Another Glenn Lab Associate, Dr Ron Kahn, showed that disruption of the same insulin-signaling pathway can extend the lifespan of mice.

Pamela A. Silver, Ph.D. is a Professor in the Department of Systems Biology at Harvard Medical School and a member of the Department of Cancer Biology at the Dana Farber Cancer Institute. She studied translocation of proteins across membranes as a graduate student with Bill Wickner at the University of California and nuclear transport as an ACS Postdoctoral Fellow with Mark Ptashne at Harvard University. First as a faculty member at Princeton University, and later at Harvard Medical School, she developed novel genetic and cell biological approaches to study movement of macromolecules in eukaryotic cells. Her current interests range from the systems biology of the nucleus to the use of genomics, chemical genetics, cell-based screening and proteomics in the study of diseases and the brain. She has been the recipient of an NSF Presidential Young Investigator Award, an Established Investigatorship from the American Heart Association, the BBS Mentoring Award from Harvard Medical School and an NIH MERIT award. The Silver group focuses on several major areas in biology from a systems-wide point of view. They model and design biological circuits and parts with well-defined properties for engineering biological systems with an emphasis on intracellular spatial programming. Their recent work has identified new aging regulatory genes in yeast and has led to “cellular oscillator” technology for analyzing cellular aging. The system allows researchers to determine the lifespan of individual yeast cells based on nuclear/cytoplasmic localization.



David A. Sinclair, Ph.D.



David Sinclair, Ph.D. is Co-Director of the Paul F. Glenn Laboratories for the Molecular Biology of Aging, Professor of Pathology at Harvard Medical School. Dr. Sinclair's research aims to identify conserved longevity control pathways and devise small molecules that activate them, with a view to preventing and treating diseases caused by aging. His lab has discovered key components of the aging regulatory pathway in yeast and is now focused on finding genes and small molecules that extend healthy lifespan in simple organisms and in mammals.

Dr. Sinclair obtained a BS with first-class honors at the University of New South Wales, Sydney, and received the Commonwealth Prize for his research. In 1995, he received a Ph.D. in Molecular Genetics. He worked as a postdoctoral researcher with Dr. Leonard Guarente at M.I.T. being recruited to Harvard Medical School in 1999. Dr. Sinclair has received several awards including a Helen Hay Whitney Postdoctoral Award, and a Special Fellowship from the Leukemia Society, a Ludwig Scholarship, a Harvard-Armenise Fellowship, an American Association for Aging Research Fellowship, and is currently a Senior Scholar of the Ellison Medical Foundation.

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

Bruce A. Yankner, M.D., Ph.D. is Professor of Pathology 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 potential 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, and the 2009 Nathan W. Shock award for aging research from the National Institute on Aging.



Junying Yuan, Ph.D.



Junying Yuan, Ph.D. is a Professor in the Department of Cell Biology at Harvard Medical School. Dr. Yuan received a Ph.D. in Neuroscience from Harvard University in 1989. Dr. Yuan carried out her postdoctoral research at the Massachusetts Institute of Technology where she made seminal discoveries about apoptosis that formed the basis of a Nobel Prize for Medicine in that field. She was first appointed as Assistant Professor at Harvard Medical School in 1992, when she became a Principal Investigator of the Cardiovascular Research Center at Massachusetts General Hospital. She joined the Department of Cell Biology in 1996 and was appointed a Professor of Cell Biology at Harvard Medical School in 2000. The Yuan lab aims to understand the basic mechanisms of cell death as well as their implications in neurodegenerative diseases using cellular, genetic, molecular and chemical biological approaches. The lab has developed a high throughput assay for ER stress and identified a small molecule inhibitor of ER stress induced cell death, which they named salubrinal (sal). They have identified a new form of cell death called “necoptosis” and identified a small molecule inhibitor named necrostatin-1 (Nec-1). Nec-1 reduced ischemic brain injury with an extended time window for treatment and thus may be very important for mediating acute neurological injury.

