The 2009 Harvard / Paul F. Glenn

Symposium on Aging

June 8, 2009

Paul F. Glenn Laboratories for the Biological Mechanisms of Aging

Welcome to the 4th 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. As a result, attendees come not only from the Harvard research community but from across the nation and from overseas for this one day event. We are pleased to have with us today Dr. Lenny Guarente, and Dr. Andrew Dillin, directors of the newly established Glenn Laboratories at M.I.T. and The Salk Institute.

The reasons for accelerating research 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 are likely to be more cost-effective than any other type of medical breakthrough.

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 how healthy lifespan is expended and to translate these discoveries into medicines that could postpone and treat diseases of aging.

The Paul F. Glenn Laboratories at Harvard Medical School are located on two floors of the New Research Building at Harvard Medical School. To promote aging research at Harvard and foster collaboration, the Glenn Labs Steering Committee awards two pilot research grants each year to investigators with innovative approaches to addressing critical questions in the aging field. The graduate course on the biology of aging run by Glenn Lab member Marcia Haigis continues to be one of the most popular courses, and the bi-monthly "Boston Aging Data Club" has become a regular event where aging labs from around New England gather. On behalf of The Paul F. Glenn Laboratories, we welcome you to the Harvard Symposium on Aging, 2009.

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

Symposium on Aging Agenda

June 8, 2009
9:00 - 5:00

9:00 - 9:30	**Introductions:** Jeffrey S. Flier, M.D., Dean of the Faculty of Medicine Paul F. Glenn, Founder, Glenn Foundation for Medical Research
9:30 - 10:10	Ronald A. DePinho, M.D. **Axes of Aging**
10:10 - 10:50	Dan Gottschling, Ph.D. **Cellular Aging and Genome Instability: New Clues from Yeast**
10:50 - 11:30	Leanne Jones, Ph.D. **Mechanisms Regulating Size and Maintenance of a Stem Cell Niche**
11:30 - 12:10	Bruce Yankner, M.D., Ph.D. **Evolution of the Aging Brain Transcriptome and Cognitive Decline**
12:10 - 1:30	**Lunch**
1:30 - 2:10	Arlan Richardson, Ph.D. South Texas Veterans Health Care System, Audie L. Murphy Division The Univ. of Texas Health Science Center at San Antonio **Is the Oxidative Stress Theory of Aging Dead?**
2:10 - 2:50	Frank Slack, Ph.D. **MicroRNAs in Aging**
2:50 - 3:30	Shin-ichiro Imai, M.D., Ph.D. **Invitation to the NAD World - SIRT1, Systemic NAD Biosynthesis, and Their Importance for Metabolism and Aging**
3:30 - 4:10	Irv Weissman, M.D. **Normal and Neoplastic Stem Cell**
4:10 - 4:50	Andy Dillin, Ph.D. **Deciphering the code of Longevity**
5:00 - 5:45	**Public Social** – Cheese & Crackers

Ronald A. DePinho, M.D.

Dr. DePinho has contributed to the fields of cancer and aging. His work in the area of tumor suppressors revealed that p53 suppresses tumorigenesis via activation of apoptosis in aberrantly cycling cells, that both products of the Inkta/Arf locus function to suppress cancer, that Arf blocks MDM2 induced degradation, and that Mxi1-mSin3-HDAC1/2 constitutes a key tumor suppressor pathway. He also developed and utilized inducible oncogene to establish and prove the concept of tumor maintenance, which laid the foundation for use of inducible cancer model in industry for preclinical drug development. His work in telomeres revealed their essential roles in aging, cancer and stem cells – establishing that telomere dysfunction may drive or suppress cancer's development depending on status of DNA damage checkpoint responses, that telomere dysfunction is a key pathogenetic element in activating the premature aging phenotypes of Werner's syndrome and A-T and in precipitating end-stage liver failure in cirrhosis (a leading cause of death worldwide), and that telomere dysfunction and p53 loss drives epithelial carcinogenesis and genomic alterations such as non-reciprocal translocations, amplifications and deletions, thus illuminating the intimate link between advancing age and cancer in humans. He has developed many new mouse models of human cancer and has utilized these faithful models to facilitate the analysis of the human cancer genome and serum proteome, resulting in the discovery of many new cancer genes and candidate biomarkers for early disease detection and management. He has served on numerous advisory boards in the public and private sector, has founded several biotechnology companies, and co-chairs the human cancer genome advisory board. Dr. DePinho is the Director of the Belfer Institute for Advanced Cancer Science at the Dana-Farber Cancer Institute, a fully integrated cancer drug discovery program. He is a member of the IOM and has received numerous awards such as the American Society of Clinical Investigator (Korsmeyer) Award, American Cancer Society Research Professorship, AACR Clowes Memorial Award, Harvey Lecture, Helsinki Medal, Albert Szent-Gyorgyi Prize, and Distinguish Alumnus Award from the Albert Einstein College of Medicine.

Dan Gottschling, Ph.D.

Dr. Gottschling is a member of the Basic Sciences Division at Fred Hutchinson Cancer Research Center, and the Affiliate Professor of Genome Sciences at the University of Washington School of Medicine.

Dr. Gottschling studies baker's yeast, a simple, single-celled organism, to understand basic aspects of biology, such as why age is the greatest cancer-risk factor in humans. Although yeast do not get cancer, Dr. Gottschling and his colleagues found that after a certain age yeast do exhibit one of cancer's major hallmarks: a condition known as "genetic instability" in which cells have missing or damaged chromosomes. The discovery that an age-dependent switch somehow triggers genetic instability in yeast means scientists can use this simple organism as a tool to learn more about age-related cancer in humans. He discovered the first system for detecting and destroying abnormal proteins in the cell nucleus, where flawless proteins are essential to maintaining and copying the genetic code. The finding could shed light on diseases like Huntington's and Alzheimer's that result from the accumulation of defective proteins in brain cells.

Dr. Gottschling earned his Ph.D. in chemistry from the University of Colorado in 1984. After graduating, he completed postdoctoral work at the Hutchinson Center before joining the faculty of the University of Chicago in 1989. In 1996, he returned to the Hutchinson Center as a faculty member.

Dr. Gottschling was named a Pew Scholar in 1991 and a Fletcher Scholar of the Cancer Research Foundation in 1995. He received the National Academy of Sciences Award in Molecular Biology in 1995 and an Ellison Foundation Senior Scholar Award in 1999.

Leanne Jones, Ph.D.

Adult stem cells are responsible for tissue homeostasis and repair throughout life, and a decline in stem cell function is a likely contributing factor to the loss of tissue homeostasis in older individuals. We are using the Drosophila gonad as a model system to study the effects of aging on an adult stem cell system. In addition to a moderate loss of stem cells, we observe significant changes to the stem cell micro environment (niche), including an aging-related decline in the expression of a key stem cell self-renewal factor. Our studies suggest genetic programs are in place to regulate maintenance of a functional stem cell niche over time. Therapeutic strategies that manipulate the size and activity of stem cell niches will complement stem cell transplantation in regenerative medicine and the treatment of cancer.

Dr. Jones received her Ph.D. in Microbiology and Molecular Genetics from Harvard University. She then carried out her postdoctoral work at the Department of Developmental Biology at Stanford University as a Lilly Fellow of the Life Science Research Foundation. She is currently an Assistant Professor in the Laboratory of Genetics and the William Scandling Developmental Chair at the Salk Institute for Biological Studies.

Mechanisms Regulating Size and Maintenance of a Stem Cell Niche

Bruce 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.

Evolution of the Aging Brain Transcriptome and Cognitive Decline

Arlan Richardson, Ph.D.

Dr. Arlan Richardson earned his Ph.D. in biochemistry from Oklahoma State University and for the past 35 years has been involved in aging research. He is the founder and director of the Barshop Institute for Longevity and Aging Studies at the University of Texas Health Science Center at San Antonio.

Dr. Richardson has mentored and directed the research of more than 50 Ph.D. graduate and postdoctoral students and junior faculty and is the author of more than 200 peer-reviewed, scientific articles. He has served as president of both the Gerontological Society of America (GSA) and the American Aging Association, has chaired a Gordon Conference on the Biology of Aging, and in 2008 organized and chaired the Keystone Symposium on Aging. Among his many honors and awards are the GSA's Robert W. Kleemeier Award and the NIA Nathan W. Shock Award. In 2005, the NIA honored his research with the highly competitive MERIT award, and in November 2008, he received the Irving Wright Award of Distinction from the American Federation for Aging Research, the organizations highest award to honor exceptional contributions to research in the field of aging by members of the scientific community. This past July, Dr. Richardson was honored with the 2008 Lord Cohen Medal for Services to Gerontology, the highest honor form British Society for Aging Research.

Dr. Richardson's laboratory is a major contributor in studying the role of gene expression in aging, showing for the first time that caloric restriction, a manipulation that retards aging, alters gene expression at the level of transcription and that these changes in gene expression enhance the ability of animals to respond to stress. The present focus of Dr. Richardson's research is developing novel genetically modified mouse models to study the roles of oxidative stress and damage in aging and age-related diseases, such as cancer, neurodegeneration, and diabetes.

Frank Slack received his B.Sc from the University of Cape Town in South Africa, before completing his Ph.D. in molecular biology at Tufts University School of Medicine. He started work on microRNAs as a postdoctoral fellow in Gary Ruvkun's laboratory at Harvard Medical School, where he co-discovered the second known microRNA, *let-7*. He is currently an Associate Professor in the Department of Molecular, Cellular and Developmental Biology at Yale University. The Slack laboratory studies the roles of microRNAs and their targets in development, disease and aging.

The Slack lab works to provide an understanding of how organs are specified at the correct time during development of higher animals. They are using molecular, genetic and genomic approaches to understand the roles of the *lin-4* and *let-7* microRNAs, the LIN-14, LIN-42 and HBL-1 transcription factors, and the LIN-41 RING finger protein in the control of developmental timing and aging. Their work may also lead to a better understanding of human cancer since cancer is often caused by the inappropriate adult redeployment of developmental pathways utilized previously in the embryo.

Dr. Slack has won numerous awards including the Dean's Postdoctoral Fellowship (Stanford University), a Fund for Medical Discovery Postdoctoral Fellowship (MGH) and an NIH NRSA Individual Fellowship and The Robert Leet And Clara Guthrie Patterson Trust Award.

Shin-ichiro Imai, M.D., Ph.D.

Shin-ichiro Imai received his M.D. and Ph.D. degrees in 1989 and 1995, respectively, from Keio University School of Medicine in Tokyo, Japan, where he studied cellular aging-associated transcriptional regulation in human fibroblasts and proposed his "Heterochromatin Island Hypothesis of Aging." To expand his aging research, he joined the laboratory of Leonard Guarente at the Massachusetts Institute of Technology as a Human Frontier Science Program Long-Term Fellow in 1997. During his postdoctoral period, he made a phenomenal discovery of the NAD-dependent protein deacetylase activity of yeast and mammalian Sir2 proteins and published his landmark paper in the journal Nature in 2000. In 2001, Shin-ichiro Imai joined the faculty of Washington University School of Medicine in St. Louis, Missouri. His laboratory has been devoted to studying the roles of mammalian SIRT1 and NAMPT-mediated NAD biosynthesis in the systemic regulation of metabolism and aging in mammals. Based on his research, he has recently proposed a novel concept of a systemic regulatory network for mammalian aging, named "NAD World." His long-term goal is to achieve "productive aging," which aims to maintain good health and spirit in our later life, by understanding the spatial and temporal dynamics of our physiological system and developing nutriceutical/pharmaceutical interventions for age-associated complications. He has received many prestigious awards for his works including the American Society for Cell Biology/Glenn Foundation Award, the Ellison Medical Foundation New Scholar Award in Aging, the American Diabetes Association Innovation Award, the Juvenile Diabetes Research Foundation Innovation Award, the Glenn Award for Research in Biological Mechanisms of Aging, the WUSM 2008 Distinguished Investigator Award, the Longer Life Foundation Pilot & Feasibility Award, and the Ellison Medical Foundation Senior Scholar in Aging Award. He is living with his wife in the suburb of St. Louis and enjoying his Midwest life.

Irving L. Weissman, M.D., is the Director of the Stanford Institute for Stem Cell Biology and Regenerative Medicine, Director of the Stanford Ludwig Center for Stem Cell Research, as well as Professor of Pathology, Developmental Biology and, by courtesy, of Biological Sciences and Neurosurgery. Dr. Weissman was a member of the founding Scientific Advisory Boards of Amgen, DNAX, and T-Cell Sciences. He co-founded several companies, SyStemix, StemCells and Cellerant Therapeutics, in 2001. Dr Weissman did his undergraduate work at Montana State College (now a University), and was awarded his medical degree from Stanford University in 1965.

Dr. Weissman has many first discoveries to his credit that opened fields in which he has participated. His most important achievement is developing the general method to identify and to isolate stem and progenitor cells. Using that method he and his lab and collaborators were first to isolate prospectively any stem cell from any tissue in any species. At StemCells, Inc., he co-discovered a human central nervous system stem cell. The neural stem cell is currently being investigated in clinical trials for treatment of a lethal lysosomal storage disorder, Batten's disease. In addition, the Weissman laboratory has pioneered the study lymphocyte homing to lymphoid organs in vivo, either as a normal function or as events involved in malignant leukemic metastases.

His current research encompasses the biology and evolution of stem cells and progenitor cells, mainly blood-forming and brain-forming. He is also engaged in a large effort to isolate and characterize the cancer stem cells from a wide variety of solid tumors and leukemia.

Professor Weissman has received numerous prestigious awards during his career.

Andy Dillin, Ph.D.

Andrew Dillin wants to modify the aging process to slow or prevent aging-related diseases like Alzheimer's. When he finished graduate school, Dillin was eager to address a big biological question. University of California, San Francisco, biologist Cynthia Kenyon had shown that altering a single gene in the nematode *Caenorhabditis elegans* doubled its life span. That presented the big question Dillin had been looking for: Why do cells age? He joined Kenyon's lab for a postdoctoral fellowship and has studied aging ever since.

Recently, his lab at the Salk Institute discovered that the nematode gene pha-4 (called Foxa in mammals) is essential for the increased longevity seen in mice and other animals kept on near-starvation diets.

The single greatest risk factor for many neurodegenerative diseases is age, and Dillin has surmised that known cellular pathways associated with aging may interfere with protein folding. He discovered that reduced insulin/IGF-1 signaling suppressed the toxic effects of human beta-amyloid—the protein linked to Alzheimer's disease—in worms. Even more intriguing, his lab found that the insulin/IGF-1 signaling pathways regulate two key proteins that influence how the cell handles toxic jumbles of proteins called aggregates: One protein breaks them up, while the other sequesters them in even bigger clumps.

Dillin suggests that a principal cause of aging and aging-related diseases is a person's declining ability to manage these protein clumps in their cells. His group is working to understand how the two proteins they discovered confer their protective effects. They are also looking for other aggregation and disaggregation pathways that are conserved in worms and mice in the hopes of finding clues that one day will help patients with neurodegenerative disease.

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. 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, 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. 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.

Notes

Notes

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