

HIGH THROUGHPUT SCREENING AND DRUG DISCOVERY PROGRAM ACCELERATES WITH DONOR GIFT

Research into drug discovery may seem a bit like finding a needle in a haystack - in a very large field of haystacks. Making the process more complex, and more rewarding, there may well be more than one needle hiding in that hayfield. Those who specialize in drug discovery efforts frame the search a bit differently. It's simply a matter of finding, testing, and refining the most promising 'needles.'

Recognizing the growing number of Americans with neurodegenerative diseases like Alzheimer's disease (AD), the Center for Neurodegenerative Disease Research (CNDR) moved to open a Drug Discovery Center with a High Throughput Screening (HTS) robot and large compound screening library in 2005, as part of the Marian S. Ware Alzheimer Program, to improve its ability to find the most promising 'needles' and enhance the drug discovery process. "Using assays specially developed at CNDR, at its peak the HTS robot can screen about 15,000 compounds in a given day," recounts Kurt Brunden, PhD, Scientific Director, Marian S. Ware AD and Benaroya Parkinson's Disease Drug Discovery Programs. "The primary aim of the HTS facility is to identify compounds with activity against relevant AD drug targets that have been discovered or characterized at CNDR. These early prototype compounds subsequently undergo many cycles of further medicinal chemistry optimization and testing, with the ultimate goal of identifying small molecule compounds that are safe and which ameliorate AD brain degeneration."

In fact, finding the 'needles' within the various haystacks is really just the beginning of the drug discovery process. Molecules identified from HTS must be further developed through chemical modifications to yield compounds that have greater potency and other desirable drug-like properties for use in AD patients, including an absence of toxicity, good oral absorption, adequate stability in the bloodstream and, importantly for AD drugs, an ability to gain access to the brain. "Compounds that have been further refined are then studied in CNDR's specially developed transgenic mouse

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Message from the Director



John Q. Trojanowski, MD, PhD

Congratulations are in order. The program mentioned in my last Message from the Director, "Alzheimer's Disease: Facing the Facts," which aired on PBS stations nationally, was awarded a 2009 Emmy for Documentary Program from the National Academy of Television Arts & Sciences, Boston/New England, as well as a CINE Golden Eagle Award for Independent Documentary Short. We are extremely proud of the dedication and hard work that Carol Edwards, Associate Director of the Education Core at the Penn Alzheimer's Disease Center, and others put into this program. For more information on this program, please visit the website at www.alzheimersfacingthefacts.org.

As the topics of investments and healthcare continue to receive a great deal of news and attention - and deservedly so - it is the perfect time to evaluate your investment in your health, from your brain to your bones to everything else.

Aging doesn't happen overnight. While we in the lab are making progress in teasing out the causes

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John Q. Trojanowski, MD, PhD

Associate Director
Steven E. Arnold, MD

Deputy Director
Kathryn Jedrzewski, PhD

MISSION:

The mission of the Institute on Aging (IOA) at the University of Pennsylvania is to improve the health of older adults by increasing the quality and quantity of clinical and basic research as well as educational programs focusing on normal aging and age-related diseases at the University of Pennsylvania School of Medicine and across the entire Penn campus.

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HTS, DRUG DISCOVERY AND THE HAAS GIFT

Continued from front cover

models of AD to gain insights into the fundamental mechanisms of disease," continues Dr. Virginia M.-Y. Lee, Director of CNDR. "The use of our mouse models also serves as a preclinical analysis that will guide our decision making about the human therapeutic potential of compounds and their possible future evaluation in human clinical trials."

To date, the HTS facility has conducted multiple screens with its chemical library of ~60,000 small molecule compounds. In addition, an AD assay that was developed at CNDR was recently transferred to the NIH Chemical Genomics Center, where their larger library of 290,000 compounds was screened. This led to the identification of a number of interesting and unique chemical structures that are presently undergoing further optimization. Furthermore, CNDR scientists have identified a lead compound in another AD drug discovery project that has recently advanced to testing in a transgenic mouse model of AD.

The recent gift from John O. and Dr. Janet Haas will provide a critical boost to CNDR's advanced drug discovery efforts by funding early stage research studies. Working closely with Dr. Lee and Dr. John Trojanowski, co-Director of CNDR, Dr. Haas, a physician trained in physical medicine and rehabilitation of neurologically-impaired patients, helped develop the new Penn Innovative Pilot Program for Alzheimer's Drug Discovery. The Pilot Program will give researchers the greatest possible scientific freedom to pursue AD therapies and allow researchers to amass the preliminary data needed to successfully apply for long-term funding from more traditional sources, like the National Institutes of Health (NIH). "By providing substantial support for early stage AD drug discovery efforts through this gift to support pilot studies," explains Dr. Trojanowski, "John and Janet Haas have made a significant investment in hastening the day when we will have more effective ways to treat and help AD patients."

The Program will support two types of pilots. In the first, each pilot will be conducted by a postdoctoral fellow or senior investigator and will run for 1-2 years, following the process outlined above but using new AD drug target assays. A second type of pilot may focus on experimental therapeutics and drug discovery that target co-morbid pathologies in AD that are signatures of other related disorders like Parkinson's, Dementia with Lewy Bodies, and Frontotemporal Dementia, which commonly co-occur with AD. As compounds from the pilot projects are identified and found to be suitable for additional studies, CNDR will seek to further develop the compounds through a combination of government grants and collaborations with pharmaceutical companies. The ultimate goal is to advance drug candidates to the stage where an Investigational New Drug (IND) application can be filed with the Food and Drug Administration (FDA) to take the most promising compounds forward to clinical trial in AD patients.

In Memoriam

TRUMAN G. "NIPPER" SCHNABEL, JR.
FORMER ACTING DIRECTOR, INSTITUTE ON AGING

Truman G. "Nipper" Schnabel, Jr., MD, C. Mahlon Kline Professor Emeritus of Medicine and Distinguished Professor Emeritus of Medicine, passed away on March 10th at the age of 90.

Dr. Schnabel was a beloved member and a much honored legend of the Penn School of Medicine and the larger Penn community. He served on the Penn Medicine faculty for more than 50 years, receiving its Distinguished Graduate Award in 1988 and its Lifetime Achievement Award. The University similarly honored Dr. Schnabel with its Alumni Award of Merit.



Dr. Schnabel earned his BS from Yale University and then his MD from Penn in 1943. After serving as an Army captain in a medical battalion in the Philippines during World War II and completing his residency at Massachusetts General, he returned to Penn as a cardiology fellow and helped establish the first cardiac catheterization unit at the Hospital of the University of Pennsylvania. He was appointed to the School of Medicine faculty in 1954 and was made a full professor in 1963. In addition to his teaching duties, Dr. Schnabel served first as Ward Chief and then Chief of the University service at Philadelphia General Hospital until it closed in 1977, coordinating Penn's medical staff schedules there and at VA Medical Center.

After three decades of outstanding service, Dr. Schnabel retired from teaching in 1989. He later assumed the role of Acting Director of the Institute on Aging and Acting Director of the Division of Geriatric Medicine in the early 1990s. He was accorded emeritus status in 1994 and retired in 2002. In recognition of his service, Penn Medicine established the William Maul Measey-Truman G. Schnabel, Jr. Chair in Geriatric Medicine and Gerontology in 2001.

In addition to his decades of service at Penn, Dr. Schnabel was the 50th President of the American College of Physicians, by which he was named a master in 1975 for his "scholarship, humanistic attitudes, and superb leadership." On two occasions, in 1977 and 1982, he was asked by students to deliver the commencement address for the School of Medicine. He published numerous articles in medical journals and also co-authored the book, *It's Your Body: Know What the Doctor Ordered - Your Complete Guide to Medical Testing*, with Marion Fox, a nurse, in 1979.

Dr. Schnabel is survived by his wife, Mary; his children, Ann Gignac, Paul Schnabel, and Brooke Schnabel; seven grandchildren, and three great-grandchildren. Memorial donations may be made to a fund established to honor his father: the Truman G. Schnabel, Sr. Fund, University of Pennsylvania School of Medicine, 3400 Spruce Street, Philadelphia, PA 19101.

Continued from front cover

Message from the Director

behind some aging-related diseases and working to pinpoint biomarkers to possibly provide earlier detection for other aging-related diseases, there are measures that everyone can take to improve how they age. There are very real health crises facing our nation and the world as it grows older. Preventative measures - like exercise, adopting a well-balanced diet, and addressing stress - cannot be overlooked as vital tools in what can only be called 'better aging.' It is an investment, yes, of time, attention, dedication, persistence, and enthusiasm even. But it is an investment that produces a real return.

I encourage you to also consider a different kind of investment in your health and that is participating in a research study or supporting research efforts if you are able. As much as we can accomplish in the lab, it only gets us so far. Beyond that point we need the participation of people who share our interest and passion for discovering the how, the why, the when, and the 'what can be done.' So, please consider getting involved in research - and then spread the word and let others know, through your social networking tools like Facebook, MySpace, and LinkedIn, how they too can make an invaluable contribution.





RESEARCH AT PENN: NEWS FROM IOA FELLOWS AND IOA-SUPPORTED RESEARCH

Dr. David Casarett: Investigating End of Life Care

In January of this year, Dr. David Casarett, Associate Professor of Medicine in the Division of Geriatric Medicine, IOA Fellow, and Staff Physician, Core Investigator at the Center for Health Equity Research and Promotion (CHERP) and Director of the Palliative Care Service at the Philadelphia VA Medical Center, was named to lead a major initiative by the Department of Veterans Affairs that is designed to help improve the quality of health care veterans receive at the end of life. Called the PROMISE Center (the Performance Reporting of Outcome Measures to Improve the Standard of care at End of life), the program will help the VA identify best practices in palliative care and develop strategies for improving care at the end of life throughout the VA healthcare system. The PROMISE Center currently involves 12 Veterans Integrated Service Networks (VISN) and will be VA-wide at all 21 VISNs next year.

Working with Dr. Jessica Fishman, also part of CHERP at the Philadelphia VA Medical Center, Dr. Casarett also published a study online in January that found that racial disparities in end of life cancer care may be caused by a preference for continuing aggressive treatment. African American patients with advanced cancer were more likely to choose to continue treatment rather than opting for comfort care, which would make them ineligible to receive care from most hospice programs. The study was published by *CANCER*, a peer-reviewed journal of the American Cancer Society. Given that African-American patients also reported greater needs for hospice services - such as counseling, respite care, chaplain, and nurse, the study suggests that the eligibility criteria for hospice services should be reconsidered.

Dr. Aaron Gitler: Link Between Parkinson's Disease Genes and Manganese Poisoning

A Penn Medicine research team, led by Dr. Aaron Gitler, Assistant Professor of Cell and Developmental Biology, IOA Fellow and IOA Pilot Research Grant awardee, has discovered a connection between genetic and environmental causes of Parkinson's disease. The research uncovered a genetic interaction between alpha-

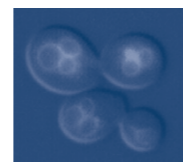


Image at left courtesy of Alessandra Chesi and Aaron Gitler



synuclein and PARK9, two Parkinson's disease genes, and determined that the PARK9 protein protects cells from manganese poisoning, an environmental risk factor for a Parkinson's disease-like syndrome.

Building on his postdoctoral work that looked for genes that could prevent cell death caused by misfolded alpha-synuclein in yeast and recent published research from Europe on a form of early-onset Parkinson's and mutations in the PARK9 gene, Dr. Gitler and colleagues sought the closest yeast gene to the human PARK9 gene. Dr. Gitler was familiar with that gene, YOR291W (renamed YPK9 or Yeast PARK 9), from his aforementioned postdoctoral research.

Looking into the function of YPK9, post-doctoral fellow Alessandra Chesi discovered that its sequence looks like other proteins that are known to transport metals. YPK9-deficient yeast showed hypersensitivity to the presence of manganese in that they did not grow as well in its presence. Additionally, the loss of neurons that occurs with manganese poisoning affects the brain's motor center - the same location that loses neurons in European patients found with the PARK9 gene mutation.

Additional research showed that the protein made by the YPK9 gene is localized to the vacuole membrane. Given the vacuoles' role in walling off toxic substances for later disposal, the team's hypothesis is that the vacuoles take in and sequester manganese for detoxification, but having the mutation in the PARK9 gene causes problems for this process in yeast and possibly in humans. Further investigation will look at how PARK9 protects against alpha-synuclein toxicity and how it helps to prevent manganese poisoning.

Dr. Jerry Schellenberg: Funding for Alzheimer's Disease Genome-Wide Association Study

The National Institute on Aging has awarded Dr. Jerry Schellenberg, Professor of Pathology and Laboratory Medicine and an IOA Fellow, an \$18.3 million, five-year grant to lead a genome-wide association study (GWAS) to identify genes that may affect the risk of Alzheimer's disease (AD).

Dr. Schellenberg joined Penn in September, 2008, from the University of Washington, where he had been a longtime and successful researcher in neurogenetics

- investigating autism, neurodegenerative diseases, and schizophrenia in addition to the genetics of premature or accelerated aging in patients with Werner Syndrome.

GWAS studies are important in that they take a large number of samples and carefully sift through the DNA in order to detect significant genetic changes that are associated with increased risk for AD in the general population. This AD GWAS study will use existing phenotype data and DNA samples that have been gathered by the NIA-funded Alzheimer's Disease Centers (ADCs). The Alzheimer's Disease Genetics Consortium has been formed to both analyze the existing samples and to collect additional samples for this very comprehensive GWAS project which will be looking for susceptibility genes that potentially influence the age of AD onset and the rate of progression through the various disease phases - from the earliest symptoms in patients with Mild Cognitive Impairment to those with overt AD.

"We are at a very exciting point in Alzheimer's disease research, especially for genetics," explains Dr. Schellenberg. "Recent advances in technology have made it possible to search the entire genome for the genes responsible for this disease. Now, with this grant, we can assemble the large number of subjects needed for this type of experiment."

Given the work that Penn colleagues have been doing in the area of pinpointing AD biomarkers, Dr. Schellenberg and his colleagues involved in this new GWAS project are hoping to identify genes that influence specific AD-related biomarkers. These biomarkers include the amount of amyloid plaques or neurofibrillary tangles, concentrations of amyloid beta and tau in cerebral spinal fluid, rate-of-disease progression, and responses to environmental factors.

"By including a large number of autopsy confirmed AD patients and controls from the network of NIA-funded ADCs across the United States, the probability that Dr. Schellenberg and his team will find novel and significant new insights into genetic risk factors for AD is very high," says Dr. Virginia M.-Y. Lee, Director of the Center for Neurodegenerative Disease Research, "and the impact of his GWAS will be enhanced very substantially by the wealth of clinical and biomarker data that the ADCs can provide to enrich the genetic findings from this GWAS. The outcome of this GWAS is likely to accelerate efforts to find better ways to diagnose and treat AD."

GERIATRICS: NEWS FROM THE DIVISION OF GERIATRIC MEDICINE

In support of comprehensive projects in academic health centers to train medical students, residents and practicing physicians in geriatrics, The Donald W. Reynolds Foundation has awarded Penn a \$1.93 million grant to create the Penn CARES (Community and Academic Resources for Education about Seniors) Program. Jerry Johnson, MD, Chief of the Division of Geriatric Medicine, will lead the program with Richard Shannon, MD, Chair of the Department of Medicine, and Gail Morrison, MD, Vice Dean for Medical Education, as co-leaders.

"Penn CARES is designed to have a pervasive and lasting impact on medical education at our institution," explains Dr. Jerry Johnson, "building on foundations in geriatrics education established over the past 20 years. It will strengthen the capacity of physicians trained in the University of Pennsylvania Health System to care for elders and create new models of community-based service learning. Penn CARES represents a substantive, sustainable change in the current geriatrics education."

The Program will target three groups of trainees: 1) medical students; 2) residents in family medicine, internal medicine, orthopaedic surgery, physical medicine and rehabilitation, psychiatry, and urology, and 3) faculty preceptors of medical students and residents in the aforementioned residencies. The Program will also add a chief resident immersion training program.

Internal medicine and family medicine residents will undertake a 'transitions of care' program for patients admitted to the Hospital of the University of Pennsylvania; primary care medicine residents and family medicine residents will partner with community organizations to deliver health education topics in aging to seniors in community settings. Senior medical students will be offered a new elective geriatrics track focused on community health.

"At the conclusion of the four-year period, Penn Medicine will have established a comprehensive longitudinal curriculum for all medical students, substantially increased the expertise in geriatrics among key faculty teachers and chief residents, and infused training in the fundamental domains of geriatrics for residents of the aforementioned specialties," says Dr. Johnson.



IOA VISITING SCHOLARS SERIES 2009-2010

The IOA Visiting Scholars Series is dedicated to bringing national leaders in aging research, policy, and clinical care to Penn. Sessions promote interdisciplinary discussion and debate and are free and open to the public. Registration is requested. Select series lectures are available as podcasts. For information on subscribing to the free podcasts, visit the IOA website at www.med.upenn.edu/aging.

November 4, 2009

Michele K. Evans, MD
Deputy Science Director, Intramural Research Program
National Institute on Aging
Topic: HANDLS Study (Healthy Aging in Neighborhoods of Diversity Across the Life Span)

January 7, 2010

Russell Katz, MD
Director, Division of Neurology Products
Food and Drug Administration

April 8, 2010

Luigi Ferrucci, MD, PhD
Senior Investigator and Chief, Longitudinal Studies Section
National Institute on Aging

April 28, 2010

Sylvan M. Cohen Annual Retreat with Poster Session on Aging
Topic: Osteoporosis
Venue: Houston Hall

Presented in conjunction with the Penn Center for Musculoskeletal Disorders

For more information and updates, visit www.med.upenn.edu/aging, or contact us at aging@mail.med.upenn.edu or 215-898-3163.

THE 2009 SYLVAN M. COHEN ANNUAL RETREAT WITH POSTER SESSION ON AGING: INTERFACE OF THE AGING BRAIN AND METABOLIC DISORDERS

Partnering this year with the Institute for Diabetes, Obesity, and Metabolism (IDOM), the IOA presented the 2009 Sylvan M. Cohen Annual Retreat with Poster Session on May 12, 2009, in Houston Hall. This year's focus was on the interface between the aging brain and metabolic disorders.

Dr. John Trojanowski, Director of the IOA, opened the afternoon's retreat and lectures in Houston Hall and recognized Mrs. Alma Cohen, who generously supports the day's activities in memory of her husband and founding chair of the IOA's External Advisory Board, Sylvan M. Cohen. Dr. Trojanowski read a letter of congratulations from Dean Arthur Rubenstein, Penn School of Medicine.



Dr. Mitchell Lazar, Director, Institute for Diabetes, Obesity and Metabolism; Sylvan H. Eisman Professor of Medicine & Genetics and Chief, Division of Endocrinology, Diabetes & Metabolism, introduced the Sylvan M. Cohen Visiting Scholar, Dr. Bruce Yankner, 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 spoke on "Epigenetic Reprogramming of the Aging Brain and Pancreas" to a full house.

In order to better understand the genetic basis of aging- and disease-related changes in cognitive function, Dr. Yankner and his lab study the regulation of genes in the aging brain across multiple species. They have shown that neuronal gene downregulation is a hallmark of human, but not mouse, aging. Their findings suggest that repression of genes in neurons may be caused by DNA damage that increases with age. Dr. Yankner's lab has established a mouse model of DNA damage in the brain and found that this causes memory loss, consistent with the idea that age-related DNA damage in humans may play a role in memory loss. Going further, they have studied gene regulation in the brains of individuals with Alzheimer's disease and in muscle from patients with adult-onset diabetes. The studies have identified, at a molecular level, several key differences between normal aging, AD, and diabetes in genes that protect against oxi-

dative damage, providing a conceptual link between the aging process and diseases that are dependent on aging, such as Alzheimer's and diabetes.

Serving as Penn Presenters were Dr. Anne Cappola, Assistant Professor of Medicine; Director of Research Education for the Division of Endocrinology, Diabetes, and Metabolism; Assistant Director of IDOM's Type 2 Diabetes Unit, and Director of Research Programs for FOCUS on Health and Leadership for Women, and Dr. Joseph A. Baur, a new Penn and IDOM faculty member and an Instructor in the Department of Physiology. Dr. Cappola, a past recipient of an IOA Pilot Research Grant and an IOA Fellow, presented "Metabolic Changes in the Frailty Syndrome." With an IOA Pilot grant, Cappola conducted a small intervention study in which she treated women with ghrelin, a naturally-occurring hormone that stimulates appetite. Her study showed that when frail women received ghrelin rather than placebo, they ate more protein and carbohydrate and had higher blood levels of growth hormone, suggesting that this agent could combat the unexplained weight loss that may lead to frailty, one of the greatest risk factors for increased hospitalization and mortality.

Dr. Baur, whose research centers on the interface between aging and metabolism, discussed his work in "Caloric Restriction, Metabolism, and Aging." While malnutrition can lead to frailty in the elderly, lowering caloric intake with adequate nutrition has been shown in animal studies to increase longevity and slow the development of age-related diseases. Dr. Baur believes that the life-extending effect of calorie restriction may result from increased numbers of mitochondria, the cell's energy factories. He has been working to tease out the signaling pathways that are upregulated during calorie restriction, hoping to identify targets along these pathways that could lead to novel therapies for age-related diseases.

Following the lectures and Q&A sessions, attendees moved to the Hall of Flags for the Poster Session on Aging. Over 50 posters were on display in basic science, clinical research, and education/community programs. Penn faculty, staff, students, and researchers in aging

Photos by Mark Garvin

were joined by colleagues from area community groups and colleges/universities. Judges nominated the following poster presenters for awards:

Basic Science



1st Prize: *Expression of TDP-43 C-Terminal Fragments in Vitro Recapitulates Pathological Features of TDP-43 Proteinopathies*, presented by Lionel Muller Igaz, School of Medicine.

2nd Prize: *SUM and Smc5/6 Ensure Proper Registration and Resolution of Recombination, Thus Impacting Telomeres*, presented by Alejandro Chavez, School of Medicine.



Clinical Research



1st Prize: *Validity of the Montreal Cognitive Assessment (MoCA) and Mini-Mental State Examination (MMSE) for the Detection of Mild Cognitive Impairment and Dementia in Parkinson's Disease*, presented by Staci Stewart, School of Medicine.

2nd Prize: *A Pilot Study on Factors Related to Post-Operative Weight Loss and Health Outcomes in Older Adults Following Cardiac Surgery*, presented by Rose Ann DiMaria-Ghalili, School of Nursing.



Education/Community Programs



1st Prize: *Bringing Our Democracy to Long Term Care Facilities: The Benefits of Mobile Polling*, presented by Jason Karlawish, Paige Brookstein, Kristin Harkins, and Elizabeth Sullo, School of Medicine.

2nd Prize: *Community Connectedness and Depressive Symptoms Among Older Vietnamese Immigrants*, presented by Ethan Nguyen, School of Medicine.





FUNDING PROMISING NEW RESEARCH: IOA AWARDS \$400,000 IN PILOT GRANTS FOR 2010

The IOA Pilot Research Grant Program is designed to support new faculty entering the field of aging, to assist Penn faculty in obtaining critical, preliminary data which serve as the basis for grant applications to agencies funding aging research, and to stimulate multi-disciplinary projects that focus the diverse expertise at Penn toward aging research. Through this, the IOA fosters the exploration of new directions in the field of aging on a broader scale. With the generous support of The Bingham Trust, the Pilot Research Grant Program awarded eight pilot grants to investigators and research projects in the School of Medicine, the School of Arts and Sciences, and the School of Veterinary Medicine.



CARLO BALLATORE, PHD
School of Medicine, Department of Pathology and Laboratory Medicine
"Investigation of Structure-Activity Relationship of Novel 2-Aminobenzothiazoles Inhibitors of Tau Fibril Formation"

The research plan presented in the IOA Pilot Grant proposal entitled "Investigation of Structure-Activity Relationship (SAR) of Novel Inhibitors of Tau Fibril Formation" is focused on SAR elucidation as well as optimization of a novel class of small-molecule inhibitors of tau aggregation that exhibit a promising combination of biological activity as well as drug-like physical-chemical properties. These medicinal chemistry efforts will provide data to support a R01 grant proposal aimed at developing agents for in vivo efficacy studies in a transgenic animal model of tauopathy to test the hypothesis that compounds capable of slowing/preventing the formation of tau aggregates can delay significantly the onset and/or progression of neurodegeneration.



JOSEPH A. BAUR, PHD
School of Medicine, Division of Endocrinology, Diabetes, and Metabolism
"Mitochondria as Mediators of the Protective Effects of Caloric Restriction"

Age is the most important risk factor for conditions associated with morbidity and mortality in Western societies, including cancer, cardiovascular disease, and neurodegenerative disorders. Restricting energy intake while maintaining adequate nutrition (caloric restriction, CR) improves health and delays or prevents the onset of age-related diseases. In laboratory rodents, this results in a 20-50% increase in mean lifespan. There is currently no consensus as to how CR works. Several treatments that increase lifespan, including CR, have intriguingly been shown to boost the number of mitochondria, the tiny organelles responsible for converting fat, carbohydrates, and proteins into usable energy. Since the effect is common to several lifespan-extending treatments, the signals that trigger an increase in mitochondrial number, or the mitochondria themselves, may play a key role in longevity. Cells in a dish can be induced to make more mitochondria simply by exposing them to serum from calorie-restricted animals, suggesting that it will be possible to study these signaling pathways and assess the effects of "extra" mitochondria on cellular physiology prior to initiating studies on animals. If some of the protective effects of CR can be attributed to changes in mitochondria, this may offer new opportunities for interventions to slow the onset and development of age-related diseases.



ERIC J. BROWN, PHD
School of Medicine, Department of Cancer Biology
"A Critical Role for p53 in Facilitating Tissue Regeneration and Suppressing Age-Related Diseases"

Mammalian aging is characterized by a steady decline in tissue regenerative potential. Accumulation of DNA damage in the stem cells that maintain these tissues contributes to this loss. Recent research into factors that influence the ability of stem cells to contribute to tissue homeostasis have focused predominantly on genes that affect their long-term potential. We propose to investigate a less explored paradigm, the role of efficient cellular clearance of terminally damaged cells as a significant contributor to tissue regeneration. To do so, we are utilizing conditional deletion of an important genome maintenance regulator (ATR). Our prelimi-

nary evidence indicates that p53, a protein with integral roles in DNA damage-induced cellular clearance, is required for immediate tissue reconstitution after ATR deletion. Importantly, the regenerative failures observed in ATR/p53-deleted mice are associated with the persistence of terminally damaged cells that are unable to contribute productively to tissue function or renewal. We will explore the hypothesis that persistence of these damaged cells, both within the stem cell niche and in downstream differentiated progeny, poses a significant barrier to tissue homeostasis and leads to age-related pathologies. These studies will further define p53's function in tissue renewal following catastrophic replication-associated DNA damage and may demonstrate a pivotal role for damaged-cell clearance in countering premature aging.



AUREO DE PAULA, PHD
School of Arts and Sciences, Department of Economics
"Overconfidence and Decision Making in Aging"

older persons frequently are called upon to make financial and other decisions that directly impact their ability to live independently in the community. This pilot study will capitalize on and supplement the longitudinal clinical-pathologic study of aging conducted by the Rush University Memory and Aging Project and is motivated by recent theoretical findings in economics suggesting that lack of recognition of memory loss (as opposed to memory loss itself) is an important factor in the formation of overconfidence. Since many studies indicate that overconfidence is a leading cause of impaired decisions, the above studies suggest a potential link between lack of memory loss recognition and faulty decisions. In collaboration with Drs. David Bennett and Patricia Boyle at Rush and Dr. Alvaro Sandroni, a renowned economic theorist, I will develop, refine and collect measures of overconfidence and lack of memory loss recognition and study their relation to decision-making by older individuals. We will collect data for approximately 300 older participants without dementia from the Rush Memory and Aging Project. This empirical analysis will not only allow the testing of the theoretical results mentioned above but will also help develop novel theoretical models of behavior relating aging with quality of decisions to further aid empirical and policy work on aging.



RAVISHANKAR JAYADEVAPPA, PHD
School of Medicine, Division of Geriatric Medicine
"Behavioral Treatment for Prostate Cancer Care"

The incidence of prostate cancer increases with age and is an important cause of disability in the elderly. Stress is a critical factor implicated in the pathogenesis and progression of prostate cancer as stress and related problems contribute to disease burden and impaired health related quality of life (HRQoL). This study will evaluate the efficacy and physiological mechanisms of Transcendental Meditation (TM), a complementary alternative medicine-based behavioral intervention; HRQoL; psychological well-being, and health resource utilization in elderly prostate cancer patients with intermediate risk of cancer recurrence and treated with radiation therapy. We believe that TM will be beneficial as a secondary prevention tool in improving HRQoL and psychological well-being. This three-arm, single blinded, randomized control trial will recruit 30 newly diagnosed elderly (65 years+) prostate cancer patients from the University of Pennsylvania Health System. Subjects will be randomized to a Transcendental Meditation group, Healthy Eating Education group, or usual care control group and will continue to receive their usual treatment. We will collect demographic, clinical, cost and HRQoL data at baseline and at three and six months of follow-up and compare the three groups on objective and subjective parameters. Comparisons will be made on the following outcomes: functional status; physiologic stress; perceived stress; HRQoL; sleep quality; depression; anxiety; distress, and cost of care. This study will aid in improving the care and outcomes for elderly prostate cancer patients.



YUKO KIMURA, PHD
School of Medicine, Department of Pharmacology
"Role of Properdin and Complement Activation in Alzheimer's Disease"

Alzheimer's disease (AD) is a progressive neurological disorder, affecting over 5 million people in the USA. It is now recognized that inflammation plays a role in the pathogenesis of AD, but how inflammation is initiated in this condition is not well understood. In this project, we will study the possible role of a protein in the blood, called properdin, in AD and explore if properdin can be exploited as a therapeutic target in AD. Properdin is normally involved in initiating an immune response called complement to defend the host from pathogen infection. However, under certain conditions, properdin may initiate abnormal immune response against self tissues.

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AWARDS AND HONORS
Fellows

Pathology Awards: Dr. Gonatas



Dr. Nicholas Gonatas, Professor of Pathology and Laboratory Medicine, was recognized with two awards this spring. He received the American Society for Investigative Pathology (ASIP) Gold Headed Cane Award, presented in recognition of long-term contributions to pathology – including meritorious research, outstanding teaching, general excellence in the field, and leadership in pathology. Dr. Gonatas also received the Meritorious Award from the American Association of Neuropathologists, given in honor of his contributions to neuropathology.

Endowed Term Professor: Dr. Kagan



Dr. Sarah Hope Kagan, Professor of Gerontological Nursing-Clinician Educator, was appointed as the Ralston House Endowed Term Professor in Gerontological Nursing. The appointment was founded in 1995 by a gift from The Ralston House to support Gerontological Nursing.

State-of-the-Art and Provost Awards: Dr. Naylor



Dr. Mary Naylor, Marian S. Ware Professor in Gerontology and Director of the NewCourtland Center for Transitions and Health, is the first nurse to receive the American Geriatrics Society's 2009 Henderson State-of-the-Art Award, which is given annually to an individual whose work helps healthcare providers better understand and respond to problems inherent in elder care. Dr. Naylor was also selected to receive a University of Pennsylvania Provost's Undergraduate Research Mentorship grant for Summer 2009 to support "Transitions in Health

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FELLOW IN THE SPOTLIGHT

A PROFILE OF DR. JAMES SHORTER

The IOA Fellows program brings together researchers, clinicians, and educators with varied interests and remarkable achievements in the field of aging. The IOA Fellows are University of Pennsylvania faculty, representing the 12 schools within the University. Associate Fellows represent Penn staff, as well as colleagues from other institutions, who have demonstrated a keen interest in aging-related research, education, or services. The IOA is honored to include nationally-recognized members of Penn's faculty, such as James Shorter, PhD, in the Fellows program.

James Shorter, PhD



Assistant Professor, Department of Biochemistry and Biophysics, Penn School of Medicine

Dr. Shorter received his BA in Biological Sciences from Keble College, University of Oxford. He went on to pursue a PhD in Cell Biology at University College London and a predoctoral fellowship at the Imperial Cancer Research Fund (ICRF, now Cancer Research UK), working with Dr. Graham Warren. His PhD thesis, "Molecular mechanisms regulating Golgi architecture during the mammalian cell division cycle," earned him the Pontecorvo Prize for best PhD thesis at ICRF in 2000. Dr. Shorter moved to Yale that same year as a postdoctoral fellow. He was awarded the Charles A. King Trust postdoctoral fellowship at the Whitehead Institute for Biomedical Research at MIT in 2002, where he studied with Dr. Susan Lindquist. In 2005, now a Senior Research Associate at Whitehead, Dr. Shorter received the American Heart Association's National Scientist Development Grant. He left Whitehead in 2007 to come to Penn as an Assistant Professor in the Department of Biochemistry and Biophysics in the Penn School of Medicine.

Shortly after arriving at Penn, Dr. Shorter was named as one of the first group awarded the NIH Director's New Innovator Award. Given to "exceptionally innovative investigators, many of whom are in the early stages of their careers...and who are well-positioned to make significant — and potentially transformative — discoveries in a variety of areas," the New Innovator Award provides Dr. Shorter with funding, over five years, for his research to develop biochemical methods to combat diseases caused by nerve degeneration, such as Parkinson's, Alzheimer's, and Huntington's. Just this year, Dr. Shorter was nominated for and will receive an Ellison New Scholar Award in Aging. New Scholar candidates are investigators who are nominated by U.S. medical institutions and universities for their outstanding promise in aging research.

His research within the last year has led to interesting findings on Hsp 104, a protein identified and introduced into animal models of Parkinson's disease which has been shown to reverse protein aggregation. Given the

potential of Hsp104, Dr. Shorter's lab is also working to identify a meta-zoan AAA+ protein that can perform a similar function to Hsp104. They are also studying the mechanisms by which 4,5-dianilinophthalimide, which dissolves Aβ42 fibers that occur in Alzheimer's disease, eliminates the fibers' neurotoxicity and disrupts prion structure and function.

Dr. Shorter serves on the Editorial Board of *The Biochemical Journal* and as a reviewer for a number of periodicals, including *The Journal of Cell Science*, *Science*, *Molecular and Cellular Biology*, and *Prion*. He has published over 30 journal articles to date.

IOA: The primary focus of your research is protein folding and the formation of prion and amyloid fibers. What led you into biochemistry and research in aging and in particular neurodegenerative diseases?

JS: I've always wanted to acquire an accurate mechanistic understanding of key biological processes at the molecular level. Naturally, this desire has drawn me to biochemistry. Biochemists have a massive role to play in research concerning aging and neurodegenerative disease. Many neurodegenerative disorders are essentially problems of protein biochemistry. I'm driven to understand how certain proteins seem prone to accessing toxic misfolding trajectories that can selectively and severely devastate specific regions of the brain. Moreover, as a biochemist I want to develop methods to inhibit or reverse these misfolding events.

IOA: You made the move from London to Yale to the Whitehead Institute at MIT to Penn. What brought you to Penn Medicine?

JS: Among several offers, I chose Penn Medicine with a mission. The truly world-class and cutting-edge expertise at Penn in neurodegenerative disorders provides an optimal venue to achieve my goals using a multi-disciplinary approach. My strengths and expertise will synergize with the expertise of my collaborators to help realize goals much greater than the sum of their parts.

IOA: Within the last two years, you've received the NIH Director's New Innovator Award and an Ellison New Scholar Award in Aging. How have these awards aided your research?

JS: I'm delighted, but also surprised to have won these awards. When you consider the quality of the other awardees, it's clearly a great privilege. The Ellison New Scholar Award in Aging is particularly special because I am following in the footsteps of some very cool scientists like Ana Maria Cuervo and David Sinclair. These awards have been invaluable and instrumental in launching my group here at Penn.

IOA: As part of the next generation of researchers, do you have any thoughts on the future directions in aging research?

JS: Aging is a major risk factor for many neurodegenerative disorders, including Alzheimer's disease. The key to these disorders will be to truly understand how the continuum of misfolded forms encodes the continuum of disease phenotypes. In particular, how does a particular complement of misfolded species induce such selective neuronal dysfunction? As biochemists, a major future direction must be to develop methods to eradicate entire spectra of misfolded forms, and not to become entangled with only a single, pure misfolded form.

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AWARDS AND HONORS

Care for Older Adults with Cognitive Impairment," a project with Dr. Karen B. Hirschman, Research Assistant Professor of Nursing, and her student, Jeffrey Lee.

Hamdan Award: Dr. Sweeney



Dr. H. Lee Sweeney, William Maul Measey Professor of Physiology, was honored for his research efforts in degenerative muscle diseases like muscular dystrophy and pharmacogenomics with international recognition as one of three recipients of the Hamdan Award for Medical Research Excellence. The Award is given by the Deputy Ruler of Dubai and the Minister of Finance and Industry of the United Arab Emirates to individuals whose medical research has helped to improve the lives of thousands of people worldwide.

Outstanding Investigator Award: Dr. Armstrong



Dr. Katrina Armstrong, Associate Professor of Medicine, Epidemiology, and Obstetrics and Gynecology, and Chief, Division of General

Internal Medicine, has been given the Outstanding Investigator Award from the American Federation for Medical Research, the organization's highest research honor.

Steering Committee on Care Coordination: Dr. Bowles



Dr. Kathryn Bowles, Associate Professor, Penn Nursing, was appointed to the National Quality Forum Steering Committee on Care Coordination, which is tasked with developing, endorsing, and devising measurements for a

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AWARDS AND HONORS

Fellows

list of preferred practices in care coordination. The National Quality Forum is a not-for-profit organization, created to develop and implement a national strategy for healthcare quality measurement and reporting.

Distinguished Researcher Award: Dr. Ersek



Dr. Mary Ersek, Associate Professor in the School of Nursing, is the recipient of the 2009 Distinguished Researcher Award, which is presented by the Hospice and Palliative Nurses Association (HPNA) in recognition of a nurse who has demonstrated longevity and consistency in hospice and palliative nursing research presentations and publications in a variety of peer-reviewed journals.

Dr. Ersek is also the recipient of the 2009 Distinguished Researcher Award, which is presented by the Hospice and Palliative Nurses Association (HPNA) in recognition of a nurse who has demonstrated longevity and consistency in hospice and palliative nursing research presentations and publications in a variety of peer-reviewed journals.

Banks Award for Mentoring: Dr. Gallo



Dr. Joseph Gallo, Associate Professor of Family Medicine and Community Health, was awarded the Steven Banks Award for Mentoring in Mental Health Research at the American Public Health Association's annual conference. The award recognizes and honors those who have given freely and generously of their time in mentoring others.

Dr. Gallo is also the recipient of the 2009 Distinguished Researcher Award, which is presented by the Hospice and Palliative Nurses Association (HPNA) in recognition of a nurse who has demonstrated longevity and consistency in hospice and palliative nursing research presentations and publications in a variety of peer-reviewed journals.

New Investigator Award: Dr. Volpe



Dr. Stella Volpe, Associate Professor of Nursing and Miriam Stirl Term Associate Professor in Nutrition, has received funding for her study on "Magnesium and the Metabolic Syndrome Trial from the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK). The study will assess the effects of magnesium on the metabolic syndrome.

Dr. Volpe is also the recipient of the 2009 Distinguished Researcher Award, which is presented by the Hospice and Palliative Nurses Association (HPNA) in recognition of a nurse who has demonstrated longevity and consistency in hospice and palliative nursing research presentations and publications in a variety of peer-reviewed journals.

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MEET THE BOARD

The Institute on Aging External Advisory Board is comprised of dynamic and dedicated individuals from all walks of life who share a common goal - to improve the quality of life for older adults. Meeting several times a year, this body of informed, hands-on volunteer advisers is instrumental in forwarding the mission of the Institute on Aging.

News from the Board



Passing the Baton: Welcoming the new Chair

The position of Board Chair functions both as a conduit and a spark, working with new and long-time board members to assist the IOA in executing its mission by lending collective expertise and advice as needed. The IOA would like to thank Dr. Bruce A. Kehr, MD, for serving as the Institute on Aging's External Advisory Board Chair since March, 2006, and welcome new Chair, Orien Reid Nix.

"We appreciate Dr. Kehr's exemplary leadership of the IOA Board during his tenure as Chair of the Board and are gratified that he will continue to contribute to IOA and the Board through his continued membership on the Board," says Dr. John Q. Trojanowski, Director of the IOA.

In April, Orien Reid Nix was appointed as the Institute on Aging's External Advisory Board Chair. Ms. Reid was the first woman to ever hold the position as Chair of the National Board of Directors of the Alzheimer's Association and is currently the Vice Chair of Alzheimer's Disease International - in addition to being a respected advocate and media personality in the Philadelphia area. She is also a Member of the National Advisory Council on Aging and an Advisory Board Member for the National Institutes of Health Council of Councils. In addition to being a Charter Member of the Montgomery County of Pennsylvania Chapter of Jack and Jill of America, Inc. and a Member of Philadelphia Alumnae Chapter of Delta Sigma Theta Sorority, Inc., Ms. Reid works with Jefferson Hospital's Farber Institute for Neurosciences and the Dickens Auxiliary Board of Abington Memorial Hospital.



"I am so proud of the work of IOA and the world-class research being done in understanding the aging process, treatment of age-related diseases and developing environmental models with supportive services that improve the quality of life for our aging population," says Ms. Reid. "The IOA is more important than ever now with increasing longevity in our society and with 70 million baby boomers joining our rapidly aging population. It is my hope that IOA will receive greater national and international media attention it so richly deserves."

Ms. Reid, who often characterizes herself as a baby boomer with a family history of dementia, learned first-hand the struggles and sacrifices of caring for a person with a chronic neurological disorder. She was

her mother's primary caregiver while also looking after her own young children. She has testified before Congress about the need for increased funding for Alzheimer's research and patient-care programs. Ms. Reid's mother died of Alzheimer's at 75 years old; her grandmother, aunt and uncle also had Alzheimer's. Ms. Reid earned her Bachelor of Arts Degree from Clark College and a Master's Degree from the Atlanta University School of Social Work in Atlanta, Georgia.

Icon of the Industry Award

This May, IOA External Advisory Board member Barbara Kleger, an associate member of National Association of Home Builders (NAHB), was presented the prestigious 2009 Icon of the Industry award from NAHB's 50+ Housing Council. Ms. Kleger was honored as "an outstanding industry leader, who has made a lasting impact on the seniors housing industry" during the 2009 Best of 50+ Housing Awards gala. Ms. Kleger serves as President of 55+ Consulting, a division of KD Partners, LLC, and has served over 300 clients/communities and surveyed over 1 million households.



Lending Their Expertise: Four New Board Members

The Institute on Aging would like to welcome four new External Advisory Board members: Nora Dowd Eisenhower, JD; Steven C. Quay, MD, PhD; Donna Marie Seyfried, and Daniel M. Skovronsky, MD, PhD.

Former Secretary of the Pennsylvania Department of Aging, **Nora Dowd Eisenhower, JD**, managed an extensive network of services provided in part through a statewide system of 52 Area Agencies on Aging. Ms. Dowd Eisenhower worked to enhance important programs that protect the health and safety of older Pennsylvanians, such as expanding the PACE/PACENET pharmaceutical assistance programs. Before joining the Department of Aging, she served as the AARP Executive Director for Pennsylvania, directing the advocacy for almost two million Pennsylvanians over age 50 and also directed AARP's nationwide campaign designed to combat telemarketing fraud aimed at older consumers.

While at CARIE (The Center of Advocacy for the Rights and Interests of the Elderly), Ms. Dowd Eisenhower directed a federal project designed to fight health care fraud among the Medicare beneficiaries, coordinated education and outreach, and acted as the liaison with federal and state law enforcement authorities. She is a graduate of the State University of New York at Stony Brook and received her Jurist Doctorate degree from Antioch University.

Steven C. Quay, MD, PhD, is the Founder and President of Ensisheim Partners LLC, a biotechnology company. Dr. Quay will be featured in the IOA's Fall 2009 newsletter.



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FELLOWS

Welcome to New Fellows

The IOA would like to welcome several new Fellows and Associate Fellows.

Penn Medicine: Dr. Kim



Dr. Sangwon F. Kim is Assistant Professor of Psychiatry in the Penn School of Medicine. Dr. Kim's lab is interested in cellular signaling

casades in the brain but particularly in two areas right now: oxidative stress-mediated neurodegeneration and nutrient sensing mechanisms.

Penn Medicine: Dr. Yushkevich



Dr. Paul Yushkevich is a Research Assistant Professor in the Department of Radiology in the Penn School of Medicine. His research focuses on the

application of shape analysis to neuroimaging, automatic segmentation, and open source imaging software.

New IOA Associate Fellows

Dr. Gail Towlsey is a Postdoctoral Fellow at the Polisher Research Institute, part of the Madlyn and Leonard Abramson Center for Jewish Life.

Chamith Rajapakse, PhD, is a Post-Doctoral Fellow in Radiology at Penn Medicine.

Andrew B. Rosenzweig, MD, is a Geriatrician at Abington Memorial Hospital.

Irving E. Vega, PhD, is an Assistant Professor of Biology at the University of Puerto Rico - Rio Piedras.

Harleah Buck, PhD, RN, is a Post-Doctoral Research Fellow at the Hartford Center of Geriatric Nursing Excellence in Penn Nursing.

Linda Herrmann, MSN, RN, is a Pre-Doctoral Scholar at the Hartford Center of Geriatric Nursing Excellence in Penn Nursing.



ADC PILOT RESEARCH GRANTS AWARDED

The Penn Alzheimer's Disease Core Center has awarded two Pilot Research Grants for 2009-2010. Each grant provides \$50,000 in support for research at Penn investigating areas of Alzheimer's disease and related disorders. The two awardees are:



Thomas A. Jongens, PhD, Penn Medicine, Department of Genetics

"Testing for Calcium Dysregulation in a New Fly AD Model"

We have developed a new *Drosophila* model for Alzheimer's disease (AD) that is based on haplo-insufficiency for the *Drosophila* presenilin (psn) gene. In studying this psn-het model, we have found age dependent deficits in learning and memory that can be rescued by treatment with mGluR antagonists or by genetic reduction of the inositol-triphosphate receptor calcium release channel (InsP3R) pathway. Since the observed rescue occurs through pathways that should reduce intracellular calcium levels, they provide support for a growing body of literature that suggests that sustained disruption of intracellular Ca²⁺ signaling processes may play an early proximal, and perhaps central, role in the pathogenesis of AD.

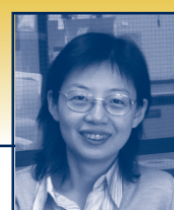
Therefore, our goal is to develop and examine calcium regulation in cells derived from our fly model to determine if the observed age onset cognitive deficits and the rescue of these defects correlates with detectable changes in calcium regulation. If successful, our studies will provide evidence that directly links calcium dysregulation due to mutation of the presenilin gene to the occurrence of age onset cognitive deficits. They will also indicate that correction of this dysregulation is a potential route to take to ameliorate at least some aspects of AD.

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IOA PILOT RESEARCH GRANTS AWARDED FOR 2010

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We recently obtained evidence to suggest that b-amyloid, the abnormal protein deposit commonly found in the brains of AD patients can trigger properdin-dependent complement activation. This project will extend our recent studies and determine in animal models if properdin plays a critical role in AD and whether blocking properdin function might be therapeutically beneficial.



LING QIN, PHD
School of Arts and Sciences, Department of Orthopaedic Surgery
"Osteoblastic Epidermal Growth Factor Receptor Signaling and Osteoporosis"

Osteoporosis is a silent disease due to the imbalance of bone resorption and bone formation. It makes bone prone to fracture and occurs mostly in the aging population. Today, it is a major public health threat for an estimated 44 million Americans, or 55 percent of the people over age 50. In the past several years, studies in our laboratory and others revealed that epidermal growth factor receptor (EGFR) and its growth factor ligands strongly influence bone metabolism in multiple ways by regulating both osteoblasts, the bone forming cells, and osteoclasts, the bone destroying cells. Our recent preliminary data suggest that lack of EGFR signaling in bone results in bone loss in mice. We hypothesize that osteoblastic EGFR signaling plays a vital role in normal bone metabolism and therefore deficiency in EGFR activity results in osteoporosis. In this project we will develop two animal models to study the physiological roles of EGFR in bone in both adult and old mice. These studies should exploit the possibility of whether EGFR could be used as a therapeutic target for treatment of osteoporosis, an aging-related disease.



JOHN H. WOLFE, VMD, PHD
School of Veterinary Medicine, Department of Pathobiology
"iPSCs and NSCs from Alzheimer's Disease Patients"

Our understanding of what is wrong in the brain in Alzheimer's Disease (AD) has been limited by the inability to obtain live brain cells from patients for study. It has recently become possible to reprogram skin cells from individual patients into stem cells, which can form all types of human tissues. The reprogrammed cells (called induced pluripotent stem cells, iPS cells) can be differentiated into mature cells of specific organs, including brain cells. The iPS cells have potential uses for therapy but also open new avenues to study the mechanisms of human disease. In our study, the iPS cells from AD patients and their unaffected family members will be converted into brain cells. We will examine the human genome program characteristic of these brain cells to look for AD-specific changes that may implicate a specific cellular process in the disease.

NEWS FROM THE IOA EXTERNAL ADVISORY BOARD

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Donna Marie Seyfried is an independent consultant in business development and strategic planning focused on advanced molecular diagnostics and personalized medicine. She has over 25 years of corporate experience in the development of emerging markets in biotechnology and healthcare and has been instrumental in directing strategic investments, market development, and mergers and acquisitions in high growth, profitable businesses in life sciences, molecular diagnostics, and women's health. Ms. Seyfried previously served as Vice President, Business Development and Intellectual Property and was an Officer of Digene Corporation. Ms. Seyfried was a key member of the Corporate Executive team which built the company and established HPV testing as the new standard of care for cervical cancer screening in women over 30 years old. Ms. Seyfried received her BS in Biology from Lehigh University.

Daniel M. Skovronsky, MD, PhD, founded Avid Radiopharmaceuticals, a clinical-stage, product-focused molecular imaging company, in 2005 and currently serves as President and CEO. Prior to establishing Avid, Dr. Skovronsky served as Scientific Director of High Throughput Screening and Drug Discovery at the Center for Neurodegenerative Disease Research at Penn. Dr. Skovronsky trained as a resident in Pathology and completed a fellowship in Neuropathology at the Hospital of the University of Pennsylvania; he received his MD and PhD in Neuroscience from the University of Pennsylvania and did his undergraduate training in molecular biochemistry at Yale. Dr. Skovronsky now serves as an adjunct faculty member in the Department of Radiology at Penn. He has more than 20 peer-reviewed publications and has served as principal investigator or co-principal investigator on seven NIH-funded grants since 2005.



Rotating Off the Board

The IOA would like to thank **Ms. Diane Linen Powell** for her three years of service as an IOA External Advisory Board member. Ms. Powell's media and publishing expertise was an important contribution to the Board's Public Affairs subcommittee, which has collaborated successfully over the past year with Penn Medicine Communications to promote the IOA's expertise in national media outlets such as *The New York Times*, *USA Today*, and *The Today Show*. Thanks to board members like Ms. Linen Powell, the IOA has benefitted from expert advice, strategic direction, and a broad network of personal and professional contacts – all of which are instrumental in advancing its mission and reputation. We are most grateful to Ms. Linen Powell for her years of service.

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ADC PILOT RESEARCH GRANTS AWARDED



David Wolk, MD, Penn Medicine, Department of Neurology

"Exploration of Episodic Memory Enhancement in Aging with Transcranial Direct Current Stimulation"

Normal aging is associated with decline in a number of cognitive functions, particularly memory for life's prior events and experiences. Evidence has suggested that functional changes in the prefrontal cortex (PFC) play a major role in cognitive decline with aging, but a more specific understanding of the underlying neural mechanisms is lacking. While some functional imaging studies have reported reductions in PFC recruitment in elderly relative to young subjects, some have reported increases in activation. There is debate as to whether they reflect compensatory activity or inefficient/nonselective recruitment that may actually have a deleterious effect on task performance.

Brain stimulation techniques offer a potential avenue for addressing these issues and more directly testing brain regions involved in cognitive functions. Transcranial direct current stimulation (tDCS) involves the application of a low level direct current to the scalp, which, by depolarizing (cathodal stimulation) or hyperpolarizing (anodal stimulation) the underlying tissue, modulates the likelihood that neurons will fire. In this project, we will use this technique to assess the functional significance of altered recruitment patterns in elderly subjects during both memory encoding (study) and retrieval (test). Two main questions will be addressed: 1) does excitatory stimulation (anodal) of hypo-recruited regions enhance memory performance in aging and 2) do regions of hyper-recruitment represent neural compensation or inefficiency/non-selective recruitment?

UPCOMING EVENTS: CNDR ANNUAL RESEARCH RETREAT AND 2009 CRISTOFALO LECTURESHIP

OCTOBER 16TH & NOVEMBER 12TH

save the dates

CNDR 9th Annual Marian S. Ware Research Retreat

The Center for Neurodegenerative Disease Research will hold its annual research retreat on October 16, 2009. The focus will be on "Current Research in Alzheimer Biomarkers."

8:30am - 5:00pm

*Biomedical Research Bldg. 2/3 Auditorium
421 Curie Boulevard - University of Pennsylvania*

This year's scheduled speakers will include Holly Soares, PhD, from Pfizer; David Holtzman, MD, and Randy Bateman, MD, from Washington University; Harald Hampel, MD, MSc, from Trinity College and the University of Munich; Douglas Galasko, MD, from UC San Diego; Tony Wyss-Coray, PhD, from Stanford University VA Palo Alto Health Care System, and Daniel Skovronsky, MD, PhD, from Avid Radiopharmaceuticals.

From Penn School of Medicine, Leslie Shaw, PhD, and Christos Davatzikos, PhD, will discuss their respective research in AD biomarkers and neuroimaging and chemical biomarkers. For more information about the retreat and the poster session, visit CNDR's website at www.med.upenn.edu/cndr.

**Vincent J. Cristofalo, PhD
Annual Lectureship**

Join the IOA on November 12th as we celebrate the spirit of our colleague, mentor and friend, Dr. Vincent J. Cristofalo. The 2009 Lectureship will be held at:

3:30 - 5:30pm

*Biomedical Research Bldg. 2/3 Auditorium
421 Curie Boulevard - University of Pennsylvania*

This year's Cristofalo Lecturer is David A. Sinclair, PhD, Professor of Pathology and Co-Director of the Paul F. Glenn Laboratories for the Biological Mechanisms of Aging at Harvard Medical School. Dr. Sinclair's research centers on the biology of lifespan extension and research towards treating diseases of aging. He is best known for his investigation of the SIR2 and related genes, as well as his co-discovery of and his work with sirtuin activating compounds, like resveratrol, that extend lifespan. His lab is currently focused on working to more fully understand which tissues are important for the regulation of mammalian lifespan and to discover whether it is possible to create a molecule that can activate longevity pathways and treat age-related diseases.



INSTITUTE ON AGING

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