Perelman School of Medicine
University of Pennsylvania

Institute on Aging

Summer 2013 www.med.upenn.edu/aging @PennAging

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Protecting the Genome in the Longevity Revolution: Cancer and Aging

This year's Sylvan M. Cohen Annual Retreat with Poster Session on Aging explored the relationship between cancer and pathways related to genome protection and aging, from basic model organism systems to patient research.

Held on May 22, 2013, in the Arthur Rubenstein Auditorium of the Smilow Center for Translational Research, the IOA partnered with the Abramson Cancer Center and the Tumor Biology Program at the Abramson Cancer Center to present "Protecting the Genome in the Longevity Revolution: Cancer and Aging."

2013 Sylvan M. Cohen Visiting Scholar Dr. Norman Sharpless

Dr. John Trojanowski began the day with a welcome and recognition of the continued support of Mrs. Alma Cohen for the retreat, named and endowed in honor of her late husband, Sylvan M. Cohen. Pennsylvania Secretary of Aging Brian Duke addressed the audience, discussing his department's committment to improving the quality of life and aging for Pennsylvanians and encouraging Penn clinicians and researchers to continue to take the lead and make a tangible difference in the health and care of older Pennsylvanians. Dean J. Larry Jameson praised the interdisciplinary focus of the day and scope of science to be presented by the presenters from Penn and the invited guest, Dr. Norman Sharpless. Dr. Chi Van Dang, Director of the Abramson Cancer Center, set the stage for the speakers, wondering about the secrets of cellular mechanisms and mysteries of aging and links to cancer that the speakers would touch on throughout the day.

Anil Rustgi, MD, Co-Program Leader of the Tumor Biology Program at the Abramson Cancer Center, introduced the Syl-

Continued on page 4

Research in Aging and Age Related Diseases at Penn


John Q. Trojanowski, MD, PHD
Director, Institute on Aging

A Message from the Director

As the fourth 'oldest' state in the country, issues of aging and age related disease greatly affect Pennsylvania and its citizens. On February 7th, we here at Penn were honored to host Governor Tom Corbett as he signed an Executive Order establishing the Pennsylvania Alzheimer's Disease State Planning Committee. The goal is to create a comprehensive Pennsylvania State Plan on Alzheimer's disease.

In June, the kick off meeting for this group gathered individuals from around the state of Pennsylvania - from diverse backgrounds and areas of specialization - to lay the groundwork and offer guidance on the development of the plan's details, addressing the impact and needs of both those who have Alzheimer's disease and those who are caring for them. In a state the size of Pennsylvania, with its unique urban-rural mix, a disease as complex and as devastating as Alzheimer's presents wide-ranging, new challenges to families, caregivers, physicians, nurses, medical support staff, first responders, and others with no 'easy' fix.

On August 15th, Penn hosted a public hearing for the committee to provide a forum for Pennsylvanians to offer testimony on Alzheimer's disease and the committee's planning efforts. We commend the Pennsylvania Department of Aging and its dedicated and experienced staff, led by Secretary Brian Duke, for advocating so strongly to improve the quality of life for all aging Pennsylvanians.

Given the enormity of the neurodegenerative disease issues, Penn is taking the lead in tackling areas outside of the research lab. Dr. Jason Karlawish will be leading a new program in neuroethics - the first in the nation. The Penn Memory Center will also be offering new rounds of Cognitive Fitness classes, an educational program designed for older adults who want to improve their memory and thinking; see page 13 for the website to learn more. For professionals, the Penn Behavioral Health MIND series will hold a two-day seminar. See below for more details.

Support the IOA

www.med.upenn.edu/aging/gift.shtml

Course Information

Event starts:
10/4/2013 at 7:00 am
Event ends:
10/5/2013 at 12:30 pm
Cost: $135.00

Healthy Aging, Cognitive Impairment, and Dementia: Diagnosis, Care, Treatment, and Prevention

This overview of cognition and aging will include cognitive impairment and dementia, the neuropsychological assessment, assessing capacity and decision-making abilities in the cognitively impaired, and neuropsychiatric symptoms in neurodegenerative disease. Participants will learn about managing behaviors in patients with dementia, counseling and supporting the dementia family caregiver, about mild cognitive impairment, the future of diagnosing dementia, new treatments, preventing dementing illness, and successful aging through positive lifestyle changes. The last day to register for this symposium is Tuesday, October 1, 2013. **This course is designed for psychologists, social workers, therapists and other mental healthcare practitioners. For more information, visit www.pbhmind.com/memory-symposium-13.**

Another Penn First: First Program in the U.S. to Focus on Ethical and Policy Issues in Neurodegenerative Diseases

The Penn Provost's Office, in collaboration with the Department of Medical Ethics and Health Policy at University of Pennsylvania, has created a unique program, the Penn Neurodegenerative Disease Ethics and Policy Program. The program will support research, education, and training to identify and address the ethical, legal, social, and policy implications of advances in the diagnosis and treatment of neurodegenerative diseases. Dr. Jason Karlawish, Professor of Medicine, Medical Ethics and Health Policy and Associate Director of the Penn Memory Center, has been named the program's inaugural director.


Jason H. Karlawish, MD

As part of the program, researchers will also be working to form best practices for how the diagnostic and treatment advances can be successfully translated into clinical practice around the country. The growing number of individuals living with a neurodegenerative disease - like Alzheimer's or Parkinson's - gives rise to intriguing questions about loss of function and decision-making capacity. With the potential for biomarkers to provide early, potentially pre-clinical diagnosis and treatment, new ethical challenges arise for clinicians, researchers, policymakers, families, and individuals.

A web-based resource developed by the program, Making Sense of Alzheimer's Disease, will seek to educate patients, families, and clinicians about the changing diagnostic criteria surrounding Alzheimer's and current ethical and clinical challenges. The site will answer questions like "What is a biomarker?" "What is pre-clinical Alzheimer's disease?" and "Things to think about before you order biomarker testing."

"As the diagnosis and treatment of neurodegenerative diseases expands from the bedside of the person with dementia, to now include the desktop with the person at risk of becoming demented, not only medicine but society as well face a host of ethical, legal and social challenges," explains Dr. Karlawish. "This program will take those challenges on, and it will do this with a keen respect for making sense of the continuum of the disease: from the person at risk, to the patient dying of end-stage disease."

Support for the program is being provided by the Provost's Office, the MetLife Foundation, the Michael J. Fox Foundation, and the Robert Wood Johnson Foundation.

e-News from the IOA

Interested in staying connected to what's happening in aging?

Sign up today to receive our new, monthly e-newsletter with details on all of the latest age-related news and events going on within the University of Pennsylvania community.

Email ebonyfen@mail.med.upenn.edu to subscribe.

2013 Sylvan Cohen Annual Retreat with Poster Session on Aging: "Protecting the Genome in the Longevity Revolution - Cancer and Aging" (continued from front cover)

van Cohen Visiting Scholar, Norman E. Sharpless, MD, Wellcome Distinguished Professor in Cancer Research and Associate Director for Translational Research at the University of North Carolina's Lineberger Comprehensive Cancer Center.

Pictured above: Anil Rustgi, Shelley Berger, John Trojanowski, Eric Brown, Ned Sharpless, Doug Wallace, Brad Johnson, and Chi Van Dang.

Dr. Sharpless presented "INK4a/ARF Locus: Cancer, Aging, and RNA Circles." Dr. Sharpless' talk focused on his research on the cancer-aging hypothesis and the importance of the gene p16 in cellular senescence.

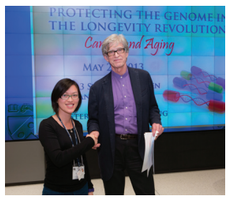
The Penn portion of the day began with Shelley Berger, PhD, PIK Professsor, Daniel S. Och University Professor and Director of the Penn Epigenetics Program at the Perelman School of Medicine, who explored the epigenetic landscape of cellular aging in "Profound Epigenetic Changes During Senescence and Aging."

Brad Johnson, MD, PhD, Associate Professor of Pathology and Laboratory Medicine, discussed the basic science research that he and his lab have undertaken in "Connecting Aging to Cancer with Telomeres" and specifically the dysfunction caused when the telomeres shorten with age.

Eric Brown, PhD, Associate Professor of Cancer Biology and Associate Investigator at the Abramson Family Cancer Research Institute, took the podium to review his research and findings about how replication stress influences the initiation and progression of cancer and how it can also influence aging in "Replication Stress as a Cause of Age-Related Disease."

Doug Wallace, PhD, Professor of Pathology and Laboratory Medicine; Michael and Charles Barnett Endowed Chair in Pediatric Mitochondrial Medicine, and Director of the Center for Mitochondrial and Epigenomic Medicine at The Children's Hospital of Philadelphia, closed the day with "A Mitochondrial Etiology of Aging and Age-Related Diseases," a look at bioenergetics in complex diseases, proposing a new bioenergetic paradigm for understanding complex age-related diseases.

Following the lectures and Q&A sessions, attendees moved to the lobby for the Poster Session on Aging. Over 65 posters were on display as Penn faculty, staff, students, and researchers in aging were joined by colleagues from other area colleges and universities and community groups.



Hien Tran and John Trojanowski

Judges nominated the following poster presenters for awards:

Basic Science

1st Prize: *Alpha-Synuclein Immunotherapy as a Potential Therapeutic for Parkinson's Disease*, presented by Hien Tran, Perelman School of Medicine.

2nd Prize: *Distinct Alpha-Synuclein Strains Differentially Promote Tau Inclusions in Neurons*, presented by Dustin Covell, Perelman School of Medicine.

Clinical Research

1st Prize: *Individually-Targeted Direct Current Stimulation Enhances Language Recovery in Patients with Chronic Non-Fluent Aphasia*, presented by Gabriella Garcia, Perelman School of Medicine.

Gabriella Garcia and John Trojanowski

Sheila Shanmugan and John Trojanowski

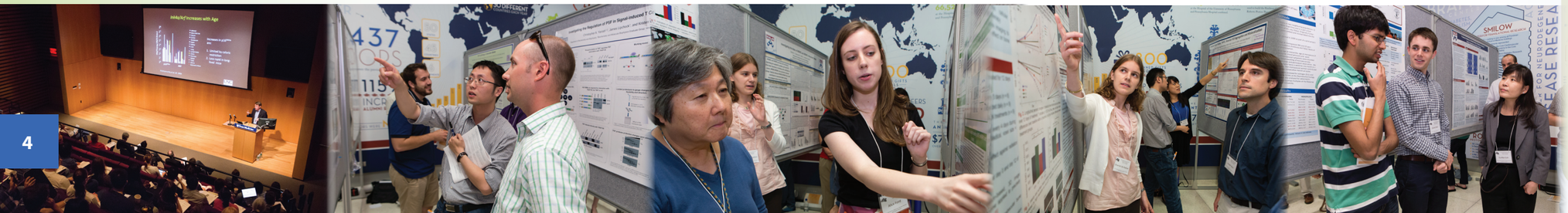
2nd Prize: *Psychostimulant Effects on Executive Function, Prefrontal Cortex Activation, and Glutamate in Menopausal Women*, presented by Sheila Shanmugan, Perelman School of Medicine.

Diane Menio and John Trojanowski

Honorable Mention: *The State of Guardianship in Pennsylvania*, presented by Diane Menio, Center for Advocacy for the Rights and Interests of the Elderly (CARIE).

Video of the event is available on the IOA website at **www.med.upenn.edu/aging/video.shtml**.

Photos courtesy of Mark Garvin



Institute on Aging
University of Pennsylvania

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John Q. Trojanowski, MD, PhD

Associate Director
Steven E. Arnold, MD

Deputy Director
Kathryn Jedrziewski, 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 Perelman School of Medicine at the University of Pennsylvania and across the entire Penn campus.

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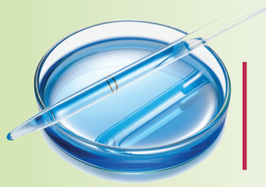

Funding the Next Generation of Aging Research: $200,000 in Pilot Research Grants

The IOA Pilot Research Grant Program supports new faculty entering the field of aging, assists Penn faculty in obtaining critical, preliminary data which serve as the basis for grant applications to agencies funding aging research, and stimulates multidisciplinary projects that focus the diverse expertise at Penn toward aging research. The Pilot Research Grant Program awarded four pilot grants to investigators and research projects in the Perelman School of Medicine and the Penn School of Veterinary Medicine. Visit us online for complete abstracts.

The Role of COX-2 in Aged Fracture Healing and Implications for Therapeutics

Jaimo Ahn, MD, PhD, and
Kurt Hankenson, PhD
Perelman School of Medicine and
Penn School of Veterinary Medicine

Fragility fractures in the elderly are already a substantial source of morbidity and mortality to our aging population. As well, the ability to heal fractures decreases with age; whereas an eighteen year-old may heal a fracture in several weeks, an eighty year-old may take several months to heal the same fracture.

Many biological pathways can affect fracture healing. However, there are few that are well-characterized to be involved in aging and fracture healing in humans and for which we already have potential therapeutic interventions. The cyclooxygenase 2 (COX-2) pathway is one such pathway. Therefore, we propose to examine the role of COX-2 in a validated geriatric mouse fracture model and to determine whether therapeutic delivery of the COX-2 gene can enhance geriatric fracture healing.

The results of our proposal will lead to: 1) a better understanding of key mechanism (COX-2) implicated in human aged fracture healing that is mimicked in a mouse model, and 2) characterization of the causal relationship between that pathway and aged fracture healing.

Improving Care for Injured Older Adults

Brendan G. Carr, MD, MS, and
Nabila Dahodwala, MD, MS
Perelman School of Medicine

Trauma is the fourth leading cause of death in Americans aged 55-64 and the seventh leading cause for adults over 65; falls are the primary driver of injury-related death in this population. Rates of mortality and complications are higher for injured older adults than for similarly injured younger patients. Multiple studies have described improved survival among younger adults treated at certified trauma centers as compared to non-trauma center hospitals. The benefit of trauma care for older adults, however, is substantially less clear, with the largest study to date demonstrating no benefit associated with care at a trauma center for adults 55+. Clinical practice guidelines exist for the care of injured older adults, and the success of targeted interventions and multidisciplinary treatment teams have been described, but many questions remain about the structures and process of care that describe ideal trauma care for older adults. The broad objective of this study is to better understand the variability in outcomes that exists for injured older adults and to identify structures and processes that might contribute to improved outcomes in this population. The pilot data will support a larger proposal to develop a cohort of geriatric trauma centers and test their impact on injury outcomes for older adults.

2014 Pilot Research *Grants in Aging*

RNA Binding Proteins That Cause ALS and FTLD Regulate Synaptic Activities

Zissimos Mourelatos, MD, and
Marc A. Dichter, MD, PhD
Perelman School of Medicine

About 20% of amyotrophic lateral sclerosis (ALS) patients develop frontotemporal lobar degeneration (FTLD), characterized by dementia due to degeneration of cortical and subcortical neurons. Recent studies have shown that RNA binding proteins (RBPs) are at the heart of ALS and FTLD pathogenesis, implicating that dysregulation of RNA pathways leads to neuronal toxicity that causes disease. Dominant mutations in genes coding for four hnRNPs are found in familial and sporadic cases of ALS and FTLD. Studies have recapitulated TDP-43 and FUS mediated neurodegeneration in animal models and reveal that the RNA binding activity of TDP-43 and FUS is required for toxicity, suggesting that neurotoxicity is manifested by their impact on RNA targets. We have identified the in vivo RNA targets for TAF15 and FUS in human and mouse neurons, which regulate targets with synaptic activities and glutamergic receptors. One hypothesis is that altered regulation of the synaptic receptors for glutamate or other molecules related to these synapses plays a significant functional role in the neurodegenerative process. This would be consistent with numerous studies relating to the pathophysiology of ALS that implicate dysregulation of glutamate in neurotoxicity. The research will attempt to determine the functional consequences on synaptic function and excitotoxicity of FUS and TAF15 and of patient mutations causing ALS.

Cytoplasmic Sequestration of RNA by Abnormal TDP-43

Edward B. Lee, MD, PhD
Perelman School of Medicine

Amyotrophic lateral sclerosis (ALS) and frontotemporal lobar degeneration (FTLD) are characterized pathologically by the presence of neuronal cytoplasmic TDP-43 protein aggregates. TDP-43 is an RNA-binding protein and under normal conditions is nearly exclusively nuclear. However, various stressors cause a redistribution of TDP-43 from the nucleus into the cytoplasm in relatively insoluble foci called stress granules (SGs). SGs sequester and protect vital RNAs during periods of stress and have been postulated to represent a precursor to neuronal cytoplasmic inclusions (NCIs). NCIs have been hypothesized to be toxic through an abnormal gain-of-function, and TDP-43 toxicity in a variety of models is linked to its ability to bind to RNA. Thus, I hypothesize that sequestration of vital RNAs within NCIs contributes to neurodegeneration. Within the nucleus, TDP-43 binds to predominantly intronic RNA to regulate splicing. The cytoplasmic RNA targets of TDP-43 must be a unique set of RNAs but are currently unknown. I propose methods to identify RNAs bound to cytoplasmic TDP-43 in stressed neuronal cultures to better understand the composition of TDP-43-positive SGs. I further propose biochemically isolating and sequencing RNAs bound to pathologic TDP-43 in human brains. These experiments will provide pilot data which will serve as the basis for further extramural funding and will address hypotheses about how SGs and RNA sequestration contribute to the pathogenesis of ALS and FTLD.

Dr. Ahn: Clues from Mice on Better Bone Healing in Older Adults

IOA Fellow Dr. Jaimo Ahn and Penn colleagues are studying differences in gene expression between young and older mice as they heal after a bone fracture. Mesenchymal stem cells (MSCs) participate in the mending of fractures; some of the problems older adults experience after bone fractures can be attributed in part to the compromised functioning of MSCs.

Penn researchers suspected that Notch, a receptor that is critical in relaying the signal to MSCs to differentiate into cartilage, fat, or bone cells, played a vital role in healing aged, broken bones.

Comparing five month-old mice (considered 'young') and twenty-five month old mice (considered 'geriatric') from the same strain, researchers looked

for progression of tissue and healing and the expression of Notch pathway genes, as well as ligands and Notch receptors. Young mice were found to produce a more robust healing response than the geriatric mice - a condition that persisted throughout healing. While baseline levels of Notch signaling were reduced in the geriatric mice, MSCs in both mice were able to be stimulated by Jagged1, one of the main ligands of Notch. This response to Jagged1 provides a potential basis for delivery of Jagged1 as a potential therapeutic option for aged fractures.

Cerebrovascular Disease Associated with Dementia

Penn researchers have found that cerebrovascular disease affecting blood circulation in the brain was significantly associated with dementia, across a variety of neurodegenerative diseases. The link appears strongest with Alzheimer's and had the most pronounced effect in younger Alzheimer's patients.

Individuals showing clinical features of Alzheimer's and other memory impairments may benefit from therapies currently available to reduce vascular problems, such as monitoring high blood pressure and cholesterol levels, following a heart healthy diet, exercise, and other lifestyle changes.

Dr. Weintraub: Connection Between Parkinson's and Impulsivity?

IOA Fellow Dr. Dan Weintraub and colleagues released findings from their study in January on the perceived connection between Parkinson's disease and impulsivity. The study used a large sample of people with untreated Parkinson's disease and showed that these individuals were no more likely to have increased impulsivity than people without Parkinson's.

"When looking at newly diagnosed Parkinson's patients who had yet to be treated with drugs targeting the dopamine system, we saw no difference in impulsivity than what we found in healthy people without the disease," said Dr. Dan Weintraub, lead study author. "Now knowing that the disease itself is not driving impuslive behaviors (gambling, shopping, etc.), we can follow newly diagnosed patients over time to see if we can predict how exposure to dopamine-related drugs and other factors play a role in impulse control disorders." Data was pulled from those enrolled in the Parkinson's Progression Markers Initiative (PPMI). The study also found an increasing severity of depression associated with impulse control disorders among both groups, particularly with the presence of compulsive eating symptoms.

Research and News in *Aging*

Dr. Lee: Parkinson's Protein Interferes with Cell Clean Up

IOA Fellow Dr. Virginia Lee and colleagues at the Penn Center for Neurodegenerative Disease Research (CNDR) have demonstrated that clumps of the protein alpha-synuclein in cells resist degradation and impair the function of macroautophagy, the process by which a cell's lysosome breaks down unnecessary or dysfunctional cellular material. Dr. Lee and her CNDR colleagues used a new neuron model system of Parkinson's disease pathologies that they had recently developed.

Alpha-synuclein clumps in nerve cells are present in many degenerative brain diseases, such as Parkinson's disease (PD) and related disorders, PD with dementia, dementia with Lewy bodies, and multiple system atrophy. The clumps persist even after soluble alpha-synuclein levels within the cell are substantially reduced; this suggests that the clumps, once formed, are resistant to being cleared. Additionally, the clumps impede the autophagy degradation process by delaying the maturation of autophagosomes; this may contribute to the increased cell death seen in clump-filled nerve cells.

Get involved in research.

Find a Penn Medicine study to enroll in by visiting:

www.pennmedicine.org/health-system/research/

Find special aging studies at:

http://www.med.upenn.edu/aging/ParticipateinaStudy.shtml

Dr. Grossman: Improved Detection of Frontotemporal Degeneration

IOA Fellow Dr. Murray Grossman, Director of the Penn FTLD Center, and Penn colleagues presented data from three recent studies that offer more diagnostic specificity for frontotemporal degeneration (FTD), the second most common form of dementia.

The first study showed that a multimodal neuroimaging approach was more accurate than using either MRI or DTI alone to detect FTD versus Alzheimer's. The study was conducted to assist in better screening patients for FTD clinical trials. The second study demonstrated that a brief series of neuropsychological tests of memory, word generation, and creative problem-solving helped distinguish people with very mild behavioral variant FTD (bvFTD) and those with mild cognitive impairment, at the early stages of disease.

The third study centered on hereditary forms of FTD and indicated that these seem to have a more rapid cognitive decline and differing tau profiles as compared with sporadic forms of FTD. Differences in speed of disease progression may impact clinical trial results for those trials testing whether a potential drug can delay damage caused by tau.

New Findings in Neurodegenerative Diseases from the Center for Neurodegenerative Disease Research (CNDR)

Shifting Proteins and Variability in Neurodegenerative Diseases

IOA Fellow Dr. Virginia Lee and colleagues at Penn's CNDR have uncovered interesting new information about alpha-synuclein, the protein that forms clumps in several neurodegenerative diseases like Parkinson's. In the mouse models studies, alpha-synuclein can exist in at least two different structural "strains" - despite having the same chemical composition. The two "strains" do differ in how they fold into different shapes and in their ability to promote fibril formation of normal alpha-synuclein and tau. Additionally, the "strains" evolve so that fibrils that initially cannot promote tau tangles acquire that ability. Dr. Lee and colleagues suggest that this shape shifting may occur as the alpha-synuclein passes from cell to cell, acquiring the ability to entangle other proteins as well. This could explain the distinct types of alpha-synuclein pathologies observed in different brain regions of Parkinson's patients - with different strains promoting formation of different types of alpha-synuclein clumps that may or may not induce tau pathology in different areas of the brain and in different patients.

Pathological Proteins Are Not Transmitted Between Humans

IOA Director Dr. John Trojanowski and Penn colleagues have determined that while pathological proteins, linked to neurodegenerative diseases like Alzheimer's and Parkinson's, can spread from cell to cell and thus region to region within an affected brain, there is no evidence that these proteins could be considered 'infectious' or could be transmitted from human to human or from animal to human. Researchers analyzed data from a cohort of U.S. patients who had received human growth hormone from cadaveric patients (chGH) prior to the synthetic version being available. A set number of such patients worldwide had received chGH contaminated with prion proteins from affected donor tissue. They went on to develop Creutzfeldt-Jakob disease, a degenereative, fatal brain disorder that is caused by pathological prion proteins. The U.S. cohort was examined for signs of elevated Alzheimer's, Parkinson's, frontotemporal lobar degeneration, or ALS; none were found to have developed any of the above diseases.

Staging System in ALS Indicates Disease Progression

IOA Director Dr. John Trojanowski and colleagues at CNDR have shown, through post-mortem review, that amyotrophic lateral sclerosis (ALS) progresses in a sequential pattern or stages from a starting point in the nervous system and moves to other regions of the brain and spinal cord. The study suggests that, just as with other neurodegenerative diseases, disease-specific pathological proteins, in this case TDP-43, may be trasmitting from cell to cell and damaging motor neurons in the brain and spinal cord of ALS patients. Stage 1 is marked by the presence of TDP-43 pathology in the primary motor cortex, in neurons in the spinal cord, and in nerves in the brainstem that are involved with swallowing, breathing, and movement. In stage 2, TDP-43 progresses forward in the brain and into brainstem areas that deal with balance and posture. TDP-43 pathology continues to move further forward in the frontal cortex in stage 3 and also into areas just behind the primary motor cortex. Once in stage 4, TDP-43 lesions have spread more widely to the temporal lobe and hippocampus, involved in memory and language comprehension. Additionally the research team found that those with the genetic mutation C9orf72 had a shorter duration of the disease and a greater buildup of pathology.

Research and News in *Aging*

Dr. Shorter: Pinpointing Proteins at Work in Brain Diseases

IOA Fellow Dr. James Shorter and research colleagues from several institutions have found new candidate disease proteins for neurodegenerative disorders. The research group found that mutations in prion-like segments of two RNA-binding proteins are associated with a rare, inherited degeneration disorder that affects muscle, brain, motor neurons, and bone and with one case of the familial form amyotrophic lateral sclerosis (ALS).

Previous studies have identified two RNA-binding proteins, TDP-43 and FUS, as causing some forms of ALS. As there are over 200 human RNA-binding proteins, it raises the possibility that additional proteins may contribute to ALS pathology. 'Candidate proteins' were narrowed down to about ten proteins with prion-like segments. Two proteins, TAF15 and EWSR1, proved toxic to yeast, the model being used, but mutations of these two proteins were detected in ALS patients. Two additional proteins, hnRNPA1 and hnRNPA2B1, cause familial cases of brain disease. The mutations accelerate the formation of fibrils that recruit normal protein to form even more fibrils, likely contributing to disease.

Dr. Karlawish: Genetic Risk Carriers Take Positive Steps After Learning Risk Status

IOA Fellow Dr. Jason Karlawish and research colleagues have uncovered more information about the post-informed state of those with uncommon risk for Alzheimer's disease (AD). As part of the NIH-funded REVEAL study, 648 people were tested for the AD risk marker, APOE4. Of those tested, 4% had the highest risk with two copies of the gene; 34% had a single copy of the gene, and 62% had no genetic risk marker. Following participants for one year after learning their risk status, there was no inflated perceived risk of getting AD and no significant difference in anxiety, depression, and test-related distress. In fact, they were more active in engaging in efforts to reduce their risk of AD by exercising, eating a healthy diet, and taking recommended vitamins and medications.

Dr. Schellenberg: Increased Late-Onset Risk of Alzheimer's for African Americans

IOA Fellow Dr. Gerard Schellenberg, who leads the Alzheimer Disease Genetics Consortium (ADGC), and fellow researchers compared genetic data from close to 6,000 African Americans 60 years of age and older, with and without Alzheimer's disease, and found that a variation in the ABCA7 gene causes a twofold increase in the risk of late onset Alzheimer's disease (LOAD) among African Americans. This link is 60% stronger among African Americans than observed among those of European descent. As with other groups, presence of the APOE gene is also associated with an increased risk.

Dr. Davatzikos: Promise in Early Biomarker for Alzheimer's Disease

IOA Fellow Dr. Christos Davatzikos and research colleagues at Penn Medicine Department of Radiology, the NIA, and Johns Hopkins University conducted a study looking at the relationship between amyloid plaque buildup in the brain and memory decline. Amyloid plaques are the abnormal proteins that are linked to Alzheimer's disease.

The study found that amyloid plaque that starts to accumulate relatively early in the temporal lobe of the brain was associated with cognitively declining individuals, and the patterns of the amyloid plaques can be used as a diagnostic marker to predict whether an individual will cognitively decline.

While previous studies have focused on the amount of amyloid plaque found in the brain and drawn associations to greater risk for developing Alzheimer's, Dr. Davatzikos and colleagues suggest that focusing more on the patterns of the plaque progression and the spatial distribution of the plaques in the brain may prove to be more important as studies have shown that nearly a third of people with plaque on their brains never show signs of cognitive decline. In Dr. Davatzikos' study, differences were noted in the plaque distribution between cognitively declining patients and stable patients: the overall amounts of amyloid plaque was similar, but the placement or location of the plaques was different. Thus it may be the pattern growth of the plaques that ultimately determines whether an individual's memory will decline and not just the presence of amyloid plaque.

PET PiB scans were reviewed from participants in the Baltimore Longitudinal Study of Aging's Imaging Study. The scans were compared to California Verbal Learning Test (CLVT) scores, among other tests, to determine the individuals' longitudinal cognitive decline.

New Research Study Recruiting: Ghrelin Plus Resistance Training in Frail Elderly

Older People Who May Be Experiencing Weight Loss, Decreased Activity or Muscle Loss with Aging

Penn is conducting a research study to see if the combination of a hormone called "Ghrelin" and a home-based strength training program is able to improve physical function in older people who may be frail (or experiencing weight loss, decreased activity or muscle loss with aging). You must be at least 70 years of age to participate. Volunteers will be asked to come to the Clinical and Translational Research Center at the Hospital of the University of Pennsylvania for one visit and our physical function testing center on Market Street for three visits. Participants will be asked to take ghrelin or a placebo once daily and will receive weekly in-home visits from a fitness professional as a part of the strength training program. There is no cost for being in the study. Participants will receive a total of $500 plus free exercise equipment if they are eligible to participate. Transportation will be provided.

Those interested should contact Terry Scattergood via email at **Terry.Scattergood@uphs.upenn.edu** or by phone at 215-898-5664.

Basic Science
Clinical
Education & Policy
Translational

Cognitive Fitness Class

Learn more online at www.pennadc.org

From the Chair…

Got your running or walking shoes handy? Bring a friend and join us at the 2013 5K for the IOA and 1 Mile Memory Walk on September 22nd. With our success at last year's inaugural event, we're hoping to top last year and increase the participants and awareness for aging and age related diseases with a hearty crowd in 2013. Individuals, teams, families, friends - all are welcome to participate. More information is available on the back cover of this edition of the IOA newsletter.

Why should you join us? As many of those of us who serve on the IOA's External Advisory Board can attest, research matters. From pinpointing potential biomarkers to uncovering improved clinical methods of diagnosing disease, research makes a difference in the lives of us all. You've no doubt read some of the latest findings in this edition of the newsletter. All of this new knowledge came as a result of research. The differences it will make are priceless.

So, join us. Come out and learn more about the IOA, about aging research here at Penn, about some of the community groups in the Philadelphia area that are working with and for older adults and their concerns. Research shows that the exercise will do your mind and body good! See you on September 22nd!

What's New in Aging Research?
2013-2014 Visiting Scholars Series

Join us for another year of insights into the latest research in aging and age related diseases. Registration is requested. To learn more about speakers' lectures as it is available and to obtain directions to the locations, visit the IOA website **at www.med.upenn.edu/aging**. Lecture locations will be announced unless otherwise listed below. Select lectures will be available as podcasts. To subscribe, visit **www.med.upenn.edu/aging** or **www.upenn.edu/cgi-bin/itunes/itunes**.

October 15, 2013

Vincent J. Cristofalo, PhD Annual Lectureship
"Towards Productive Aging: The Systemic Regulatory Network for Mammalian Aging and Longevity"

Shin-ichiro Imai, PhD
Washington University in St. Louis
3:30 to 5:00pm
BRB Auditorium, BRB 2/3

October 29, 2013 - Visiting Scholars Series
Topic: Translational Research in Neurotherapeutics and Clinical Care

Jeffrey Cummings, MD
Cleveland Clinic Lou Ruvo Center for Brain Health
2:30 to 4:00pm
BRB Auditorium, BRB 2/3

November 20, 2013 - Visiting Scholars Series

Joseph A. Pignolo, Sr. Award in Aging Research
Topic: Rapamycin-Induced Insulin Resistance, mTORC2 Loss, and Longevity

Joseph Baur, PhD
University of Pennsylvania
2:30 to 4:30pm
BRB Auditorium, BRB 2/3

January 23, 2014 - Visiting Scholars Series
Topic: Palliative Care

Diane E. Meier, MD
Mount Sinai School of Medicine
2:30 to 4:00pm
co-sponsored by the Penn Hospice and Palliative Care Program

March 27, 2014 - Visiting Scholars Series:
Topic: Improving Physician Prescribing Practices and Medication Policy

Jerome Avorn, MD
Harvard University
2:30 to 4:00pm
co-sponsored by the Penn Center for Pharmacoepidemiology Research and Training and the Pennsylvania Department of Aging

April 1, 2014 - Visiting Scholars Series:

Topic: Long-Term Care for People with Dementia

Sheryl Zimmerman, PhD
University of North Carolina

May 14, 2014
Sylvan M. Cohen Annual Retreat with Poster Session on Aging
Topic: Gender Differences and Longevity

10:00am to 5:00pm
Rubenstein Auditorium, Smilow Center for Translational Research

June, 2014 - Visiting Scholars Series
Topic: Developing Dementia Screening Methods and Modeling Cognitive Change

James E. Galvin, MD, MPH
New York University

Date to Be Announced - Visiting Scholars Series:

Topic: Osteoporosis
Neil Resnick, MD, University of Pittsburgh

Building Awareness
Aging Matters

Awards and Honors: News from the IOA Fellows and Associate Fellows

Perelman School of Medicine

Dr. Shelley Berger, Penn Integrates Knowledge Professor, Daniel S. Och University Professor, and Director of the Epigenetics Program, was elected to the 2013 class of members of the American Academy of Arts and Sciences.

Dr. Virginia M.-Y. Lee, Director of the Center for Neurodegenerative Disease Research, the John H. Ware 3rd Professor in Alzheimer's Research, and Professor of Pathology and Laboratory Medicine, was elected to the 2013 class of members of the American Academy of Arts and Sciences.

Dr. Amita Sehgal, John Herr Musser Professor of Neuroscience and a Howard Hughes Medical Institute Investigator, received the 2013 Outstanding Scientific Achievement Award from the Association of Professional Sleep Societies for her discoveries in circadian biology and her work with the *Drosophila* fruit fly. The award is given to honor researchers for a single research contribution based on novel and seminal discoveries of basic, clinical, or theoretical nature.

Dr. Brian Strom, Executive Vice Dean for Institutional Affairs and George S. Pepper Professor of Public Health and Preventive Medicine, Professor of Biostatistics and Epidemiology, Medicine, and Pharmacology, was honored with a National Award for Career Achievement and Contribution to Clinical and Translational Science by the Association for Clinical and Translational Science and the American Federation for Medical Research. Dr. Strom was also named a 2013 Career Distinguished Investigator.

Dr. Rachel Werner, Associate Professor of Medicine and LDI Senior Fellow, was awarded the 2013 American Federation of Medical Research's (AFMR) Outstanding Investigator Award, given to a researcher, age 45 or younger, who is judged to be the most outstanding medical scientist in any field. Dr. Werner was cited for her innovative insight and the impact of her work in clinical and translational science.

Penn Nursing

Dr. Pamela Cacchione, Associate Professor of Geropsychiatric Nursing and Associate Director of the Center for Integrative Science in Aging, has been named a Fellow in the American Academy of Nursing.

Catch up with the IOA.

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http://www.med.upenn.edu/aging/social-media.shtml

Perelman School of Medicine
University of Pennsylvania

Institute on Aging
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Save the Date: September 22, 2013

open to all

Penn's 5K for The IOA and 1 Mile Memory Walk raise awareness and support for the Institute on Aging at the University of Pennsylvania. The 5K race will be held on a unique course on the campus of the University of Pennsylvania, starting on Shoemaker Green between the Palestra and Franklin Field and running through Penn Park with its skyline views of the City.

The registration fee is $20 prior to September 7th and $15 with Penn student ID. Registration after September 7th and the day of the race is $25. There is an online surcharge for registration that is added to the above fees. Registration closes at midnight September 18th and is limited to the first 500 runners and walkers. The 5K Run will begin at 8:00 AM on Shoemaker Green. The 1 Mile Memory Walk will begin at 8:10 AM. Medals will be given to top (3) male and female runners in each age bracket.

Penn's 5K for The IOA

(The Institute on Aging)

& the 1 Mile Memory Walk

Penn Medicine

For information and to register, visit www.med.upenn.edu/aging