THE SCIENCE OF AGING

SPRING 2016 // *an Institute on Aging Publication*

THE JOSEPH A. PIGNOLO AWARD IN AGING RESEARCH

John Q. Trojanowski, MD, PhD (IOA Director), Bruce A. Yankner, MD, PhD (2016 Pignolo Awardee), and Robert J. Pignolo, MD, PhD (Founder of the Pignolo Award in Aging Research).

On Tuesday, March 1, 2016, the Institute on Aging hosted their annual Joseph A. Pignolo Award in Aging Research lecture. This year's awardee was Bruce A. Yankner, MD, PhD, professor of Genetics and Neurology and Co-director of the Glenn Center for the Biology of Aging at Harvard Medical School, for his 2014 publication in Nature on "REST and Stress Resistance in Aging and Alzheimer's Research."

This award-winning paper analyzes gene expression changes that occur in the aging brain and shows the pattern of changes in genes that turn on or off in neurons of the brain as it ages. The greatest impact was seen in REST (RE1 neuron-silencing transcription factor), a gene originally thought only to function during fetal brain development. However, Dr. Yankner and his team found that the REST gene is also expressed in the adult human brain, dramatically up-regulating in neurons as the brain ages.

The significance of this in neurodegenerative research is their discovery that in the brains of individuals with Alzheimer's disease, the protein is actually much less up-regulated — and sometimes completely absent. Using both mouse models and culture dishes in a laboratory, they found that regular stressors encountered by an aging brain such as oxidative stress—a disturbance in the balance between the production of reactive oxygen species and antioxidant defenses—and amyloid stress associated with AD had a significant impact on sustaining the REST gene.

Dr. Yankner assumes there is a potential genetic underpinning, but believes that environmental factors contribute as well.

> "This was a galvanizing observation for us. It suggested that some people can resist the onslaught of Alzheimer's because they're able to up-regulate this intrinsic defense mechanism [REST]. So, a very important question is why some people can do it and some people can't..."
>
> - Bruce A. Yankner, MD, PhD

For more information, including a video interview with Dr. Yankner, visit: www.penninstituteonaging.wordpress.com

INTRODUCING REACT!

REACT! Africana Culture Education/Discussion group participant creates her own African mask during an art & history class.

THE RHYTHM EXPEREINCE & AFRICANA CULTURE TRIAL (REACT!)

The University of Pennsylvania is excited to announce that they have officially kicked off their first round of **The Rhythm Experience and Africana Culture Trial** (REACT!) led by Kathy Jedrziewski, PhD, Deputy Director of the Institute on Aging.

This Alzheimer's Association-funded study is being conducted in collaboration with the University of Pittsburgh's Brain Aging & Cognitive Health (BACH) Lab, led by the study's Principal Investigator Kirk I. Erickson, PhD, Associate Professor, Department of Psychology at the University of Pittsburgh. This research study will compare two activities, African Dance and an Education/ Discussion group, which Drs. Jedrziewski and Erikson believe could be beneficial for older African Americans (ages 65-75).

... Introducing REACT *continued inside // + much more!*

INTRODUCING REACT! ...continued

The goal of the REACT! Study is to examine whether brain health, fitness levels or quality of life improve as a result of participating in dance or education activities three times per week for six months. However, after the first week of classes, participants were already noticing the benefits.

With just a few short days under their belts, several members from both the education and the dance groups said they had already learned so much and look forward to seeing what is to come. This study not only provides an opportunity to enhance socialization and perhaps physical and cognitive health, but it also allows participants to help others in the aging African American community by providing evidence about potentially effective ways to improve and maintain quality of life as we age.

While the study has already started, coordinators will continue to recruit on a rolling basis.

If you or anyone you know is interested in participating in the REACT! Study, contact:

Philadelphia - Penn Campus
Shardae Williams, Project Coordinator
215-573-8153

Pittsburgh – The BACH Lab at the University of Pittsburgh
412-302-6679

REACT! African Dance group participants warm up before a class led by African Dance instructor Patricia (Peaches) Jones.

REACT! Africana Culture Education/Discussion group participants and Shardae Williams, REACT! Project Coordinator at the Penn Campus (far right) show off their individual style and creativity.

To learn more about the REACT! Study and to view a highlight video from the first week of classes, visit: www.med.upenn.edu/aging/react.html

COULD TOO MUCH IRON BE BAD FOR OUR EYES?

New research from Penn Medicine's Joshua Dunaief, MD, PhD, Adele Niessen Professor of Ophthalmology, shows that people with age-related macular degeneration (AMD), the leading cause of blindness in the elderly, have higher levels of iron than those in the same age group without the disease. Learn more ...

"Too much? Too Little? The Goldilocks Story of Iron in the Eye" // a Penn Medicine News Blog

via Karen Kreeger, Penn Medicine Communications

"The body needs just the right amount of iron, otherwise all manner of havoc happens. Too little iron and the body malfunctions because it carries oxygen to all the cells. Roughly two-thirds of the mineral resides in hemoglobin, the oxygen-transporting protein in red blood cells. And if the body doesn't make enough healthy red blood cells, which leads to anemia, it can't get enough oxygen.

However, this is a story of excess. Too much iron is also toxic, especially in the brain and eyes. In a recent *FASEB Journal* article from his lab, they showed that mice with a mutation in the iron transporter protein called ferroportin have increased iron levels in the retina, which causes degeneration. The retina is a layer of light-sensitive cells at the back of the eye that trigger impulses to the optic nerve and on to visual centers, where images are formed.

> " Like any food we eat, it's all about balance. But iron levels increase in the body with age, and excess iron is a major source of oxidative stress. "
>
> - Joshua Dunaief, MD, PhD

Normally, ferroportin carries excess iron out of cells – and, it's the only molecule that can do that. Using a mouse model of AMD, developed in the Dunaief lab, in which iron accumulates specifically in the retina, they verified that ferroportin is located in the retina and showed exactly where and how it's regulated. Answering these questions is important to understand why it accumulates. They found that retinas from people with AMD obtained from post-mortem donated eyes have higher iron levels than people without the disease, but how that iron accumulation affects an individual depends on their specific environmental and genetic features. On the other hand, the team also found that higher iron levels do not lead to an up- regulation of ferroportin in the cells affected by AMD, so they can't get rid of the excess iron. "Ferroportin in retina is not regulated the same way as in the rest of the body," Dunaief explained."

To read the full Penn Medicine News Blog, visit: news.pennmedicine.org/blog

what's new in *aging research*?

PENN MEDICINE RESEARCHERS including IOA Director, John Q. Trojanowski, MD, PhD WIN NIH AWARD TO STUDY **PROGRESSIVE BRAIN DAMANGE**

– From Concussions & More Severe Traumatic Brain Injuries –

A nearly $3 million, five-year grant from the National Institute of Neurological Disorders and Stroke (NINDS) has been awarded to an international team of investigators led by Institute on Aging Director, John Q. Trojanowski, MD, PhD, and co-lead researcher Douglas Smith, MD, Robert A. Groff Professor of Teaching and Research in Neurosurgery at Penn and director of the Penn Center for Brain Injury and Repair.

This grant will support the establishment of diagnostic criteria for chronic traumatic encephalopathy (CTE). CTE is a progressive neurodegenerative disease that afflicts the brains of people who have primarily suffered repeat concussions and in some individuals with a history of a single severe traumatic brain injury.

> " We want to see which pathological changes consistently occur in CTE and assess whether they are similar to or different than those in other major neurodegenerative diseases. "
> - Douglas Smith, MD

The Penn-led team will look for common pathological changes in post-mortem brains of over 200 patients with a history of traumatic brain injury compared to post-mortem brains from patients with other neurodegenerative diseases. Researchers plan to identify proteins that show evidence of neurodegenerative damage, document gross anatomical changes such as brain atrophy, and uncover underlying biochemical and genetic alterations.

For more information on this grant and to read the full Penn Medicine News Release visit: www.med.upenn.edu/aging/news.html

ANTIPSYCHOTIC DRUGS LINKED TO INCREASED MORTALITY AMONG PARKINSON'S DISEASE PATIENTS

A recent Penn Medicine News Release highlights new research linking the use of antipsychotic drugs such as quetiapine, a common treatment for symptoms of psychosis in Parkinson's disease (PD), to increased mortality in PD.

This collaborative study between researchers at the Perelman School of Medicine at the University of Pennsylvania, the University of Michigan Medical School, and the Philadelphia and Ann Arbor Veterans Affairs (VA) Medical Centers suggests that these drugs may actually do significantly more harm than good in a subset of PD patients. That raises an important question for patients, family members, and clinicians alike – is this treatment worth it?

"I think that antipsychotic drugs should not be prescribed to Parkinson's patients without careful consideration," explained Daniel Weintraub, MD, Associate professor of Psychiatry and Neurology at Penn Medicine and Institute on Aging Fellow.

According to the news release, these findings are not the first to undercover a link between antipsychotic drugs and increased mortality.

> " Treatment with antipsychotics should be reserved for those cases where the benefits exceed the risks. "
> - Helen C. Kales, MD

Studies dating back to the early 2000s, including a number from a group led by Helen C. Kales, MD, senior author of the study and Professor of Psychiatry at the University of Michigan, "have found increased mortality with antipsychotic use among patients who have dementia in the general population. Since 2005 the FDA has mandated "black box" warnings on antipsychotic drug packaging, noting the apparent increased risk of death when these drugs are used in dementia patients." However, a later study from Weintraub, Kales, and their colleagues found that this warning had very little effect on antipsychotic prescriptions for Parkinson's disease with dementia (PDD) patients.

For the full Penn Medicine News Release visit: www.med.upenn.edu/aging/news.html

2017 PILOT RESEARCH AWARDS

INSTITUTE ON AGING

Exploring functional and structural neuroimaging biomarkers of Huntington's disease progression // **Pedro Gonzalez-Alegre, MD, PhD**

Multiplexed fluorescent microscopy for quantification of tau-mediated neurodegeneration // **David Irwin, MD, MSTR**

Mitochondrial NAD, redox state and aging biomarkers // **Lin Li, PhD**

Genetic risk factors associated with coincident Alzheimer and Parkinson Disease in neuropathologically confirmed cases // **Adam Naj, PhD & Jon Toledo, MD, PhD**

ALZHEIMER'S DISEASE CORE CENTER (ADCC)

Family matters: How does Alzheimer's Disease genetic testing impact relationships? // **Angela Bradbury, MD**

Statistical and experimental fine mapping of Alzheimer's disease loci // **Christopher Brown, PhD**

For more information, visit: www.med.upenn.edu/aging/pilotawards.html

Institute on Aging
University of Pennsylvania

Institute on Aging
3615 Chestnut Street
Philadelphia, PA 19104-2676

THE SYLVAN M. COHEN ANNUAL RETREAT // 06.08.16

"To sleep, per chance to age... and avoid Alzheimer's disease"

Presented by the Institute on Aging & Penn's Center for Sleep and Circadian Neurobiology

Keynote Speaker: David M. Holtzman, MD // Professor & Chairman, Department of Neurology, Washington University School of Medicine
Penn Presenters: David M. Raizen, MD, PhD // Assistant Professor of Neurology; Matthew S. Kayser, MD, PhD // Assistant Professor of Psychiatry; Nirmala Nirinjini Naidoo, PhD // Research Associate Professor of Medicine; & Sigrid C. Veasey, MD // Professor of Medicine | *Center for Sleep and Circadian Neurobiology*

* Poster Session to follow | Poster submission deadline: May 27, 2016
* Registration deadline: June 2, 2016

For more information, visit: www.med.upenn.edu/aging/annualretreat.html

5K FOR THE IOA & THE MEMORY MILE WALK // 09.25.16

Penn Medicine's 5th annual 5K for the IOA & The Memory Mile Walk to support Alzheimer's and aging-related research and care at the IOA! *More details to come.*

Make a Gift

To support aging-related research and care at Penn's Institute on Aging, contact:
Aubre Naughton, Penn Medicine Development
aubren@upenn.edu or 215-898-9174

Become an IOA Fellow

Learn more about becoming an IOA Fellow at:
www.med.upenn.edu/aging/fellows.html

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The mission of the Institute on Aging 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 aging-related diseases across the entire Penn campus.