

THE SCIENCE OF AGING

FALL 2017

PENN MEDICINE'S

6th ANNUAL 5K FOR THE IOA & THE MEMORY MILE WALK

- ▶ Meet our New IOA Associate Director
- ▶ New Retina Test May Help Detect Frontotemporal Degeneration
- ▶ "Simplifying Science"

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.

It was a warm Fall morning on Sunday, September 24, 2017 as 371 runners and walkers and 70 volunteers gathered for Penn Medicine's 6th Annual 5K for the IOA and Memory Mile Walk.

The fundraiser, which takes place throughout Penn Park and the University of Pennsylvania campus, raised a total of \$49,260 this year for Alzheimer's and aging-related disease research efforts at Penn's Institute on Aging.

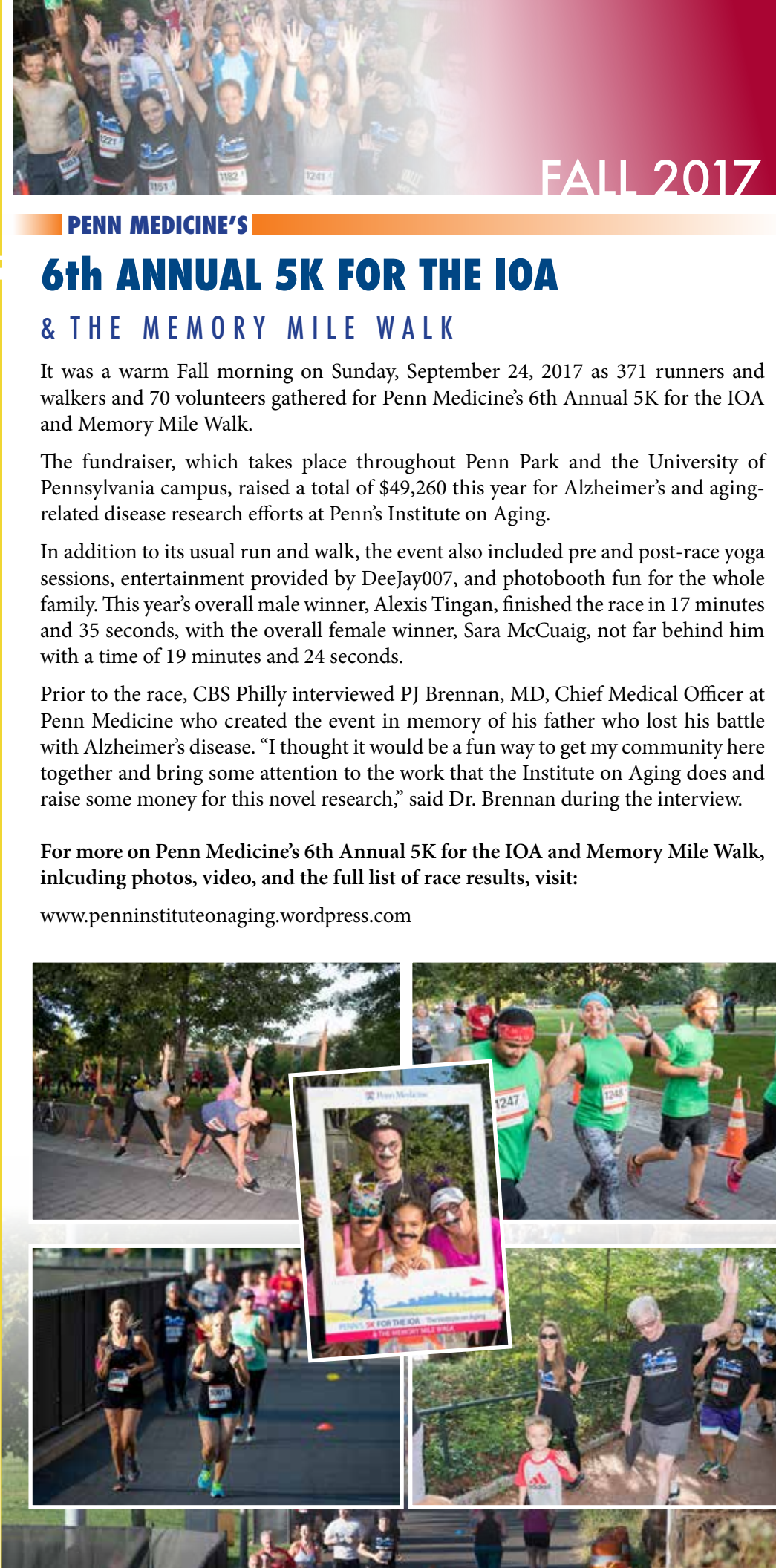
In addition to its usual run and walk, the event also included pre and post-race yoga sessions, entertainment provided by DeeJay007, and photobooth fun for the whole family. This year's overall male winner, Alexis Tingan, finished the race in 17 minutes and 35 seconds, with the overall female winner, Sara McCuaig, not far behind him with a time of 19 minutes and 24 seconds.

Prior to the race, CBS Philly interviewed PJ Brennan, MD, Chief Medical Officer at Penn Medicine who created the event in memory of his father who lost his battle with Alzheimer's disease. "I thought it would be a fun way to get my community here together and bring some attention to the work that the Institute on Aging does and raise some money for this novel research," said Dr. Brennan during the interview.

For more on Penn Medicine's 6th Annual 5K for the IOA and Memory Mile Walk, including photos, video, and the full list of race results, visit:

www.penninstituteonaging.wordpress.com

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Q&A with F. Bradley Johnson, MD, PhD

The Institute on Aging (IOA) at the University of Pennsylvania is pleased to introduce our new Associate Director, F. Bradley Johnson, MD, PhD! In addition to this new title, Dr. Johnson is also an Associate Professor of Pathology and Laboratory Medicine at the University of Pennsylvania. His research is focused primarily on the biologies of telomeres, genome stability, and cellular senescence, and how they impact age-related diseases. Dr. Johnson's clinical duties include serving as Assistant Director of the Clinical Immunology Laboratory at the Hospital of the University of Pennsylvania, where he helps oversee tests facilitating solid organ and bone marrow transplantation. Related to these clinical activities, he is also investigating roles for the major histocompatibility complex in the regulation of RNA biology and Alzheimer's disease. **Full Q&A available at www.penninstituteonaging.wordpress.com**

Q: How did you first get involved with the Institute on Aging?

A: I first learned about the IOA from John Trojanowski and Virginia Lee when I was interviewing for faculty positions back in 2001. The fact that Penn had such a well-established and active aging institute was one of the key features that attracted me to join the university.

Q: What goals do you hope to achieve as the new Associate Director?

A: First, I hope to learn more from current IOA leaders, particularly John Trojanowski and Kathy Jedrzejewski, about how they run things, and where they see problems and opportunities for growth. Second, I'd like to see how we might enhance interactions among people studying features of aging at Penn in disciplines that have traditionally been considered separate. We have a remarkable breadth of expertise, and an unusually collegial environment, so there are many opportunities for cooperation. Finally, I'd like to expand our efforts to inform the public about new findings in gerontology, and to involve them in debates on related issues.

Q: How has your thinking about aging changed over the years?

A: Quite a bit. I first began to wonder about how aging happens when I was a young kid. Some of my great-grandparents and grandparents were lucky enough to live to exceptional ages with few health problems and I wondered what explained their good fortune. My mom's mom's mom, who I got to know well, was given a ceremonial cane by the town government in recognition of her 100th birthday, and the newspaper reported her remark that what she'd really have enjoyed was a motorcycle, and that upon leaving the ceremony she carried the cane in a fashion that conspicuously avoided it touching the floor! At the same time, other family members and older friends were suffering from various age-related problems, and it started to become apparent to me how much aging increases the risk of many different diseases and, ultimately, death. As a kid, it was the death aspect that really got my attention, but as I came to recognize and accept the transient nature of all things, I became increasingly motivated by the idea that the more that people understand how aging works, the better we can minimize its negative impacts. Today, I believe aging is in fact complicated - it involves lots of little problems that affect different people to various extents, and which can sum into bigger problems. All of these problems can be addressed in principal, and indeed great strides are being made, but there's no single "magic bullet." Mostly, I think of aging as something that changes individual strengths and weaknesses over time. I hope that by understanding more about how aging works, we can expand the tools available for people to use as they wish to enhance their own happiness.

Q: What do you find most interesting and/or challenging about the field of aging?

A: Worldwide, people are living to older ages than ever before. This is because we've made progress in solving many of the problems that have plagued people for most of our history - especially starvation, infectious disease, political instability and violence, and, more recently, cardiovascular disease and cancer. Therefore, aging has become one of the ultimate barriers to physical health. You can do everything possible to follow a healthy lifestyle, and if - like most people these days, you avoid death by things like automobile accidents, natural disasters or violence - you will get old, likely get sick, and will most certainly die...

Aging is now the biggest risk factor for most of the diseases that still affect us. The challenge now is to understand the details of how aging does this so as to minimize disease.

Q: What do you think are the most important issues that need to be addressed in the area of aging right now? And how do you, if at all, see this evolving in the next several years?

A: One important issue is to extend the successes the aging research community has had in model organisms, e.g. flies and mice, to human biology. It's become apparent that there are some conserved mechanisms impacting aging, that is, there are biological processes that operate similarly in different species to regulate the pace of aging. However, important aspects of aging will be different in different species, and so if we really want to understand how human aging works, we can't rely solely on model organisms, and ultimately we have to study it in human systems. Fortunately, the tools for doing this type of work are developing rapidly, e.g. growing human tissues in culture or using new bioinformatics tools to study the impact of natural human genetic variation on health, and thus there are many opportunities to make progress. Another challenge is to dispell negative perceptions of aging research. The point is that the aging research community is not focused on immortality, but is rather aimed at using an understanding of aging to improve wellbeing. I think this is in line with what innovators in the fields of science, medicine, and government have always tried to do. A third challenge is to address some of the hype surrounding things like "anti-aging" therapies. I know from interactions with friends and family members that people are remarkably willing to spend resources on special foods, supplements, and other types of regimens that are advertised to slow or reverse aging. Mostly these therapies are unproven, and are even potentially harmful, and I think organizations like the IOA can help people understand what really is known, what's plausible, and what's more likely to be snake oil. On a more positive note, there really are some potential "anti-aging" therapies that have arisen from recent research, for example metformin, which is being studied in a clinical trial. It will take time and effort to see if any of these therapies prove worthwhile for broadly protecting people from age-related diseases, but the only way to know is to do the work.

Q: You've received two separate IOA Pilot Awards as a Co-Principal Investigator (PI). How has this pilot award program helped to shape or guide your career as a researcher?

A: My Co-PIs and I are very grateful for the support we've received from the IOA pilot grant program. It is one of the most impactful functions of the IOA, because it helps provide seed money to explore high risk/high reward avenues of investigation, which if successful can be turned into more substantial support from outside sources. For example Chris Lengner (at the Penn Vet School) and I received an IOA pilot in 2015 to study the possibility of treating the rare disease dyskeratosis congenita using a novel approach to improved telomere maintenance. Things went well, and we have obtained NIH funding to continue our work. With our new IOA pilot, Dimitri Monos (at CHOP) and I are investigating connections between Alzheimer's disease and a part of the human genome called the major histocompatibility complex, which plays important roles in the immune system. We're excited to see where these studies lead us.

SIMPLIFYING SCIENCE

// from A Penn Medicine News Blog by Abbey Anderson

Whether it's explaining common illnesses to help people better understand terms they may hear all too often or detailing the inner-workings of proteins and cells construction, even the most advanced minds in science and medicine lean on everyday analogies to break down and describe their work.

In fact, as highlighted in a recent Penn Medicine New Blog, many researchers and scientists here at Penn, including IOA Director, John Q. Trojanowski, MD, PhD, often rely on this tactic to help explain the complexities of what they do.

Crumpled Paper

One of Dr. Trojanowski's most frequently used examples is a demonstration comparing the concept of misfolded tau proteins to crumpled pieces of paper. He uses this example "to help explain how pathological changes in tau affect its function and behavior in Alzheimer's disease and related disorders."

"The main underlying problem behind neurodegenerative diseases such as Parkinson's and Alzheimer's is the misfolded proteins, which effects the information being carried from one cell to the next," Dr. Trojanowski said. "Imagine you have two pieces of paper with text on each. Normally, when the two pieces of paper are smooth and flat, you're able to read the information written on both. But when you crumple one of the papers up into a ball, you can no longer read the copy easily, if at all. When disease spreads, it is like the crumpled paper encountering the smooth paper and corrupting it or templating it to misfold, and we speculate that the continuation of this process is what causes the spread of disease."

Train Tracks

Dr. Trojanowski also uses an analogy of train tracks when discussing his work in Alzheimer's research on tau amyloids -- "misshaped, insoluble proteins that clump in the brain and elsewhere and cause a host of debilitating diseases." As described in the blog, tau typically binds to structures called microtubules which are responsible for various movements in cells and are key elements in the transport of neurons. When a mutation occurs in the tau gene, it no longer binds to the microtubule causing it to lose its ability to send and carry vital signals to other cells.

"Think of tau as the cross-ties of train tracks. The tracks will handle the traffic as long as they are parallel and there are substrates for transport," explains Dr. Trojanowski. "If the cross-ties are missing, the tracks will wobble and the train will run off the tracks."

However, unlike a train derailing, there is a way to reverse the effects of this loss of function in these genes. There are currently drugs -- including one by Dr. Trojanowski's team which made its way to a phase 1 clinical trial -- being developed that can be used as treatments for Alzheimer's disease wherein tau function was lost due to misfolding.

For more analogies used by Penn Medicine researchers to "simplify science," read the full Penn Medicine News Blog at: www.pennmedicine.org/news/news-blog/2017/august

Can a simple eye test help detect Frontotemporal Degeneration (FTD)?

Penn study suggests that a quick, non-invasive retina test may help diagnose FTD // A Penn Medicine News Release by Queen Muse

Frontotemporal degeneration (FTD) is a progressive neurodegenerative condition that is present in tens of thousands of Americans, but is often difficult to diagnose accurately. Now in a study recently published in *Neurology*, researchers from the Perelman School of Medicine at the University of Pennsylvania have found evidence that a simple eye exam and retinal imaging test may help improve that accuracy. Using an inexpensive, non-invasive, eye-imaging technique, the Penn Medicine scientists found that patients with FTD showed thinning of the outer retina—the layers with the photoreceptors through which we see—compared to control subjects.

The retina is potentially affected by neurodegenerative disorders because it is a projection of the brain. Prior studies have suggested that patients with Alzheimer's disease and ALS may also have thinning of the retina—although a different part of the retina. Thus, imaging the retina may help doctors confirm or rule out FTD. Neurodegenerative diseases in general are challenging to diagnose, and often are confirmed only by direct examination of brain tissue at autopsy. Now that science appears to be on the brink of developing effective treatments for these diseases, the need for better diagnostic methods is becoming acute.

"As we enter an era of disease-modifying treatments for neurodegenerative disorders, it is essential for us to have tools that can identify the specific pathologies accumulating in the brain so that we can administer the appropriate treatments to patients who are likely to benefit," said study senior author Murray Grossman, MD, a professor of Neurology and director of the Penn FTD Center.

For the full Penn Medicine News Release, visit: www.pennmedicine.org/news/news-releases



"Our finding of outer retina thinning in this carefully designed study suggests that specific brain pathologies may be mirrored by specific retinal abnormalities."

- Benjamin J. Kim, MD,
Assistant professor of Ophthalmology
at Penn's Scheie Eye Institute & study lead author

NOVEMBER 10, 2017**Speaker: Tom Montine, MD, PhD // Visiting Scholars Series**12:30 - 1:30pm | Smilow Center - Rubenstein Auditorium
3400 Civic Center Blvd., Philadelphia, PA 19104**NOVEMBER 29, 2017****Speaker: Nathan Basisty // Joseph A. Pignolo Award in Aging Research**3:00 - 4:00pm | Smilow Center - Rubenstein Auditorium
3400 Civic Center Blvd., Philadelphia, PA 19104**NOVEMBER 30, 2017****Speaker: Richard Mayeux, MD, MSc // Visiting Scholars Series**9:30 - 10:30am | Medical Alumni Hall - 1st Floor Maloney Building
3600 Spruce Street, Philadelphia, PA 19104**JANUARY 24, 2018****Speaker: Anne Newman, MD, MPH // Visiting Scholars Series**3:00 - 4:00pm | Smilow Center - Rubenstein Auditorium
3400 Civic Center Blvd., Philadelphia, PA 19104**FEBRUARY 6, 2018****Speaker: Tom Misteli, PhD // Vincent J. Cristofalo Annual Lectureship**3:00 - 4:00pm | Smilow Center - Rubenstein Auditorium
3400 Civic Center Blvd., Philadelphia, PA 19104**APRIL 3, 2018****Speaker: Edward Huey, MD // Visiting Scholars Series**3:00 - 4:00pm | Biomedical Research Building
421 Curie Blvd., Philadelphia, PA 19104**MAY 1, 2018****Speaker: Kenneth M. Langa, MD, PhD // Sylvan M. Cohen Annual Retreat**11:30am - 5:00pm | Smilow Center - Rubenstein Auditorium and Lobby
3400 Civic Center Blvd., Philadelphia, PA 19104**Make a Gift**

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