

INSTITUTE ON AGING

Special Edition - Fall 2009

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Coming of Age – The Evolution of the Institute on Aging

In 1979, the oldest baby boomers were in their early '30s, many of them raising families and building careers, not spending a lot of time thinking about their golden years that were still far off in the future. They had more immediate concerns to deal with: an accident at the Three Mile Island Nuclear Power Plant, the prime lending rate nearing 16%, and the cost of a gallon of gas soaring to 86 cents per gallon. But, if the baby boomers were not thinking about aging and the looming problem of a population where, by 2050, one in five would be age 65 years or older, others were, and some of those others were at the University of Pennsylvania.

One of these prescient thinkers was Thomas B. McCabe, former President of the Scott Paper Company and Chairman of the Federal Reserve from 1948-51. Mr. McCabe was in his mid-80s at the time, and naturally was interested in aging. He was also a long-time

friend and supporter of Penn, having established the Thomas B. and Jeannette E. Laws McCabe Fund Fellow and Pilot Awards in 1969 to support biomedical and surgical research for junior faculty at the medical and veterinary schools. His friend, Thomas Langfitt, MD, who was then the Vice President for Health Affairs at Penn, agreed that much more needed to be known about the state of aging research around the world. With Langfitt's support, Mr. McCabe asked Robert Doughty, MD, PhD, to investigate the problem. The two had become friends when Dr. Doughty attended Swarthmore College on a McCabe Scholarship. After graduating from Swarthmore, Dr. Doughty went to medical school and did a residency at Penn.

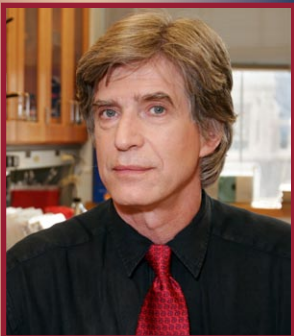
He recalled that one day, as he was finishing his residency in 1975, Mr. McCabe came up to him and said, "I think someone ought to go take a look at

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Basic Science
Clinical
Education & Policy
Translational

Research in aging at Penn ► ► ► ►

MESSAGE FROM THE DIRECTOR



Among the many events of this past year, the IOA has quietly reached a milestone - its 30th anniversary. As you read through this special edition of the newsletter, I hope you will appreciate both the historical perspective on the IOA and aging research at Penn, as well as the insights and comments shared by those who have been involved with the IOA, from its inception to its present, evolving form. It is amazing to think that the field of aging research is just over 30 years young. What has been accomplished by pioneers like Vince Cristofalo and what is being accomplished today - and what may be accomplished tomorrow - by this latest generation of researchers, clinicians, nurses, and social services personnel are equally amazing. I would like to extend a warm thank you to Lisa Bain, our writer for this special edition of the newsletter. Lisa took on the role of IOA historian and was the one reaching out to collect memories and thoughts from the many who have participated in shaping the IOA, as well as those who are guiding the IOA in the 21st century. It was no small task. To you, the readers, I invite you to step back with us through the history of the IOA and then to boldly step forward to meet those areas of basic science, education, public policy, clinical and translational research that will challenge us all in the coming years as the world copes with the unprecedented, explosive growth in the number of older adults.

Coming of Age – The Evolution of the Institute on Aging

Continued from page front cover

why people age. You're just about to graduate and become a faculty member at the Children's Hospital of Philadelphia. Can I convince you to take six months to a year off and study what is being done in the United States, and the world for that matter, about the cause of aging?" So with a modest stipend from Mr. McCabe, as well as introductions to people like Robert Butler, MD, who had just been appointed head of the nascent National Institute on Aging, Dr. Doughty started his research. He traveled to the International Congress of Gerontology in Jerusalem, Israel, and then spent six months studying the issues and writing a report. The report was embraced by Dr. Langfitt, who went on to appoint a steering committee to explore the idea of establish a center for aging at Penn.

During the course of Dr. Doughty's research, he came across the research of Vincent J. Cristofalo, PhD, who, at the time, was working at The Wistar Institute. Dr. Cristofalo was a cell biologist studying the mechanisms of cellular aging, and a leader in the field. He was a natural to chair the steering committee along with Dr. Stanley Brody, an expert in the social and health aspects of aging. In 1978, Dr. Cristofalo was named the first Director for the Center for the Study of Aging, which was established in early 1979.

The Center was designed to be multidisciplinary and to cut across Schools of Medicine, Veterinary Medicine, Nursing, Dental Medicine, Social Work, and the Leonard Davis Institute of Health Economics. Three core components were identified: basic research in animal models, a cell bank to pursue the study of cel-



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Coming of Age – The Evolution of the Institute on Aging

lular senescence, and a clinical arm, which included a geriatric research and education center at the Philadelphia Veteran's Administration Hospital and a program in geriatric nursing at the School of Nursing. As Cristofalo said in an interview for the IOA Newsletter in 2004, "We wanted to understand the fundamental properties of the aging process and to improve the quality of life for the elderly." This mission has not fundamentally changed through the years, although the Center continued to evolve.

Under Cristofalo's leadership, the Center began building collaborative relationships with the many Penn aging researchers that were scattered across the campus in the various schools. They



appointed both an internal steering committee and an External Advisory Board made up of directors from other aging centers in the United States. They established a seminar series that featured leaders in the field from across the country and another series with Penn-based speakers. Gradually, aging research at Penn began to grow and flourish.

The Institute on Aging is created

A turning point came after William N. Kelley, MD, became Executive Vice President for the Medical Center and Dean of the School of Medicine in 1989. "I viewed three scientific areas of high relevance to patient care, which were underdeveloped but whose development was crucial, and they were neuroscience, cancer, and aging. When I got to Penn, clearly we had a superb structure for both cancer and neuroscience. Both of them were well-established, outstanding programs and it was possible to help develop those and to build on them. But that was not quite the case in aging. And so as I thought about what would help it and allow us to infuse more resources and find the cutting-edge scientists that we wanted to bring into a program like that, the academic structure that seemed to be the most appropriate was the institute kind of structure, which cut across schools, cut across departments, and allowed a multidisciplinary approach to an extremely important problem. And so the University was very supportive, and it didn't

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Director

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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The Newsletter is published two times per year by the Institute on Aging at the University of Pennsylvania. Prior issues are available online.

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
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

February 4, 2010

Jesse F. Ballenger, PhD
Assistant Professor, Science, Technology and Society Program
Pennsylvania State University

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.

Support from the Top: A Conversation with Dean Rubenstein

Arthur H. Rubenstein, MBBCh, has served as Executive Vice President, University of Pennsylvania for the Health System and Dean of the School of Medicine since 2001. He is an internationally known endocrinologist, widely recognized for his groundbreaking research in diabetes, a highly regarded physician, and an accomplished leader in academic medicine. After being named Dean, Dr. Rubenstein appointed Dr. Trojanowski to be the Director of the IOA, and has continued to support the IOA both financially and administratively.

Q: When you first became Dean do you remember what your sense was at that time about the strengths and weaknesses of the IOA?

A: When I came here, it was a relatively small institute with a number of people of whom John (Trojanowski) and Virginia (Lee) were the leaders. But there were others in the institution, like Jerry Johnson, who was involved in a geriatrics program and an educational aging program, and Marge Bowman, who was interested in a variety of aging issues related to family practice. And of course aging permeates many other areas of the University. The Institute of Aging, because it is a trans-school program, had the ability to touch on many of these complementary programs relating to aging people.

John and Virginia were enthusiastic, to put it mildly, aggressive in the best sense; very ambitious, really unbelievably wonderful academic colleagues. Both of them were in my office telling me about all the wonderful things they were doing, which were plenty, and all the things I could do for them or should do for them, and all the worries they had about the kind of support they needed to fulfill their vision. So that was very impressive.

Q: What do you see now as the biggest strength of the IOA?

A: What distinguishes it at the moment is the whole interdisciplinary nature. John and Virginia have an enormous focus on translational research, which is how do we take all this basic sci-



“We know more and more about the science of aging...the big challenge will be to move those discoveries rapidly, and with care...so that we improve the lives of patients.”

ence research, which they are very, very good at, and move it as quickly as possible to the betterment of patients, either through prevention or treatment, which in Alzheimer's is in a very early state. There are also diseases such as vascular dementia, degenerative dementia, and Lewy body dementia, which are related to Alzheimer's disease but are difficult to distinguish, particularly at an early stage. And there's almost no effective way to treat them -- the drugs are really pretty inadequate. So John and Virginia recruited a colleague from industry who runs their high throughput screening lab with the hope of discovering new drugs. They have the ability to attract great people around them, to inspire them, and to have a vision. So you don't have to know everything yourself, you just have to have a vision and find great people to work with you and inspire them, and they do that really brilliantly.

Q: So how do you see things moving in the future?

A: I think the big issue will be whether we'll succeed in moving the science forward and rapidly apply it to the betterment of patients with either improved prevention or treatment. We know more and more about the science of aging and the science of Alzheimer's disease, but we know very little about prevention, diagnosis, and treatment. So I think that the big challenge will be to move those discoveries rapidly, and with care, into the human arena, so that we improve the lives of patients.

There are challenges of aging involved in cardiovascular disease, cancer, ophthalmology (macular degeneration), diabetes, and obesity. Then there are the unique core problems of aging such as Alzheimer's disease. There are also many associations with other conditions, such as diabetes, which is more common in obese people, more common in people who don't exercise, and more common in people who don't do mental exercise. You'll find 100 articles every week related to this issue because everyone is worrying about it now. These studies are useful, but they don't push the field forward very much, they just tell you about associations.

Q: As Dean of a place like Penn, are you able to bring these people together to start looking at these interrelationships?

A: I try. My job is to try to create the climate in which great faculty members can be more successful because of their interaction with other colleagues with complementary skills.

Q: Is Penn different in that way from other places you've been in the past?

A: I think Penn is a great academic medical center. The places we compete with - Columbia, Yale, Harvard, UCSF, Duke, etc. - are also outstanding places. Pittsburgh has an important center of aging. I think in some areas we are better, while in other areas we are not as good as others. It's no longer important

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Coming of Age – The Evolution of the Institute on Aging

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take much effort to establish the Institute on Aging and in a sense wrap in all the other programs that were the precursors of that into this one institute.”

At about this time, Dr. Cristofalo left Penn to start an aging institute at the Medical College of Pennsylvania, and Truman “Nipper” Schnabel, MD, became the Interim Director of the “new” Institute on Aging at Penn. A few years later, Risa Lavizzo-Mourey, MD, was recruited back to Penn after a two year term as Deputy Administrator of the federal Agency for Health Care Policy and Research (now the Agency for Healthcare Research and Quality), and she took the reins as the first Director of the Institute. “She was the perfect person to run it in my view,” said Dr. Kelley. “She was trained not only as a general internist but was also trained and board certified in geriatrics, and she was already one of the leaders in the world in health services research.”

Dr. Lavizzo-Mourey set out to further develop the Institute as a campus-wide institute that reflected the breadth of scholarly work that was going on in aging. “That meant that we needed to have a clinical arm, obviously, and be able to provide the kind of high-quality, cutting-edge, tertiary care within geriatrics that people associated with the University across disciplines and specialties. But we also needed to have a broad-based research arm, reflecting research that spans from the molecular level to the systems level. And third, we wanted to have a very strong educational component that was interdisciplinary and again reflected the interests of faculty all across campus.”

Dr. Lavizzo-Mourey envisioned an “institute without walls,” where even though the IOA offices and some faculty and staff were located at Ralston

House, the Fellows of the Institute would be drawn from across campus and even from other organizations and institutions in the region with Penn affiliations. Under her leadership, the Institute grew steadily and gained more national and international prominence. In 1998, research conducted within the IOA brought in more than \$2.3 million in research funding and, by 2000, the Institute included more than 150 Fellows conducting research ranging from a study of spirituality among elders to the neurobiology of various forms of dementia. There was an increasing focus on consumers, which coincided with Dr. Lavizzo-Mourey’s appointment to the U.S. Pre-

ventive Services Task Force in 1998. As she wrote in the IOA newsletter in the summer of 2000, “As we strive for the highest degree of excellence, we will work to cultivate our knowledge and understanding of our ‘consumers’ – who they are, what they need, and how we can meet their needs in the best way.”



Another turning point for the Institute

In early 2001, Dr. Lavizzo-Mourey left Penn to take on a new role as the Senior Vice President for Health Care at the Robert Wood Johnson Foundation. John Trojanowski, MD, PhD, was named Interim Director by then interim Dean Arthur Asbury, MD; in July, 2002, the new Dean and Executive Vice President, Dr. Arthur Rubenstein, named Dr. Trojanowski as Director of the IOA. Dr. Trojanowski’s appointment was coupled with a decision to split off the Division of Geriatric Medicine as a distinct entity under the direction of Jerry Johnson, MD. While the programs operate independently now, they are still closely linked, said Dean Rubenstein, as are many other aging related programs at Penn: not only the

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Giving

Providing support for Research

Aging was just beginning to be recognized as a distinct and important field of research in the early 1960s, when Vincent Cristofalo finished his postdoctoral fellowship and began his pioneering work in cellular aging as a new assistant professor at The Wistar Institute.

When Penn convinced him in 1979 to become the Director of the Center for the Study of Aging, Dr. Cristofalo had already established himself as a giant in the field, and continued to burnish those credentials over the next 25 years. Thus, when he passed away in 2006, the tributes poured in from far and wide.

His sisters, who are both older than he, said that when they read all the tributes they felt like they didn't know him, according to his wife, Mrs. Margaret (Peggy) Cristofalo. "I guess people like that don't talk a lot about what they have done," she said. "My friends have said that he was really a very modest man, because he didn't make waves about himself. So it was very heartening to read and hear from all these people. The accolades he received kind of say it all."

Among the many awards and lectureships established to honor him, the IOA established the Vincent J. Cristofalo, PhD, Annual Lectureship in 2007, endowed by a lead gift from Mrs. Cristofalo, as well as gifts from other family members and friends. Dr. Robert Pignolo, who had been a graduate student in Dr. Cristofalo's lab in the early '90s and is now an assistant professor of medicine at Penn, was one of the instigators in setting up the memorial lectureship. "It's more than a lecture, in the sense that the speakers not only are in an area of interest related to the work that Vince did, but are also people who actually knew him," said Dr. Pignolo.

Mrs. Cristofalo and several of her six daughters will be in attendance at this year's Cristofalo lecture on November 12th, when Dr. David Sinclair from Harvard University will deliver his lecture, "Finding Genes and Medicines That Extend Healthy Lifespans." Indeed, the Cristofalos are very much a part of the extended IOA family, which includes all of those who support the Institute through their gifts and service.

Another prominent member of the IOA family is Richard (Dick) Brown, who joined the IOA's External Advisory Board in 1990. Mr. Brown had previously served as Chairman of the Board of Trustees at the Penn Medical Center, and when his active trusteeship expired, he wanted to stay active at the University. "I knew about the Institute on Aging and I thought, well, I'm aging, so I would like to get involved. So I joined the board and have been on it ever since." As Chair of the Development Committee, Mr. Brown has played a significant role in raising funds for IOA programs and activities that are not supported by the NIH or private foundations. In addition to his service on the Board, he himself is also a major donor.

Mrs. Cristofalo and Mr. Brown are just two among the many community members who have advanced the mission of the IOA through both financial and other contributions. In summarizing Penn's legacy of excellence in aging research that began with her husband thirty years ago, Mrs. Cristofalo said, "I like to think my donations are going for research, which is what Vince was all about."

Make an Investment in Aging Research at Penn

Research is key to unlocking the mysteries of aging and aging-related diseases, and through your financial support you can help advance the health and quality of life for older adults. Despite substantial commitments by government agencies and foundations to support aging research at Penn, public funding has its limitations. The success of academic programs like ours in attracting major grants from the National Institutes of Health (NIH) rests on our investigators' ability to conduct preclinical studies that are the hardest to fund through conventional sources. Therefore, to pursue unexpected discoveries in greater depth and fast-track projects that are most likely to yield effective therapies for debilitating and costly diseases such as Alzheimer's, Parkinson's, Amyotrophic Lateral Sclerosis (ALS), Penn must rely on private support. To make a gift, please visit our website www.med.upenn.edu/aging or contact Irene I. Lukoff, Director of Development, at 215-573-0187, or via email at ilukoff@upenn.edu.

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Support from the Top

in a country where there are multiple excellent centers that one place should do it all. People are linked together if they need to be. So it's more important that many scientists focus on diseases of aging in the best way we can so that the sum is greater than the parts. I'm not a great believer in parochial things, because I don't think it usually works.

The IOA is an interdisciplinary institute, which means it doesn't have boundaries. In this case, healthy and disordered aging is the focus of attention of a multidisciplinary group of faculty and colleagues. The Institute also has a role in terms of education, which we hold dear here. So whether it's students, or house staff, or Fellows, or postdoctoral fellows, they all get linked into these programs and contribute to the mission. That's where the IOA is so wonderful: the problems are really internationally important, the leadership is inspired, and there are many opportunities to do good. In the end, we need people and resources to make it all work.

Learn more about our
partner programs at
www.med.upenn.edu/aging



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sections of Geriatric Psychiatry (within the Department of Psychiatry), but also the Center for Gerontologic Nursing Science/Hartford Center for Geriatric Nursing Excellence, the Advanced Center for Interventions and Services Research on Late Life Depression, the Population Aging Research Center, the Geriatric Sleep Research Lab, the Penn Memory Center, the Penn Alzheimer's Disease Core Center, Penn MARCH (Minority Aging Research and Community Health), the NewCourtland Center for Transitions and Health (in the School of Nursing), the Penn Udall Center for Parkinson's Disease Research, the Ralston-Penn Clinic for Osteoporosis and Related Bone Disorders, and the Center for Neurodegenerative Disease Research (CNDR). "These things are related and you can't look at them in isolation," said Dean Rubenstein. "While they aren't exactly the IOA, they all complement each other. Aging is very broad and it's important that all these programs are embedded in an institution that cares about aging. Everyone benefits from each other."

"It's like a complex mosaic or matrix of research, clinical care, education, that kind of all focuses on aging using different approaches," added Steven Arnold, MD, Associate Director of the IOA.

In 2002, the School of Medicine launched a Strategic Planning Initiative that identified aging and neuroscience as areas that should be targeted for "robust growth" over the next five years. With the IOA at the center of this effort, its mission statement was revised and a five-point plan was implemented to accomplish the mission. This plan focused on improving the visibility of the IOA at Penn, as well as locally, nationally, and internationally, and included establishing a visiting lecturer series. New research would be promoted through an annual pilot grant program and the recruitment of new faculty who would have joint appointments with School of Medicine departments. These new faculty recruits were expected to stimulate synergistic and multidisciplinary research in aging, particularly in the areas of human genetics (especially the genetics of complex traits including those related to successful and unsuccessful aging), animal models of normal and pathological ag-



{ Basic Science *Clinical* *Education & Policy* Translational

ing processes, oxidative stress and caloric restriction, patient oriented or translational research on normal aging and aging-related diseases, genomics, proteomics, and cell/gene therapy.

A new era in aging research

By all measures, the implementation of these plans has been hugely successful. Between July, 2002, and February, 2008, funding for aging research at Penn totaled nearly \$70 million, much of this in collaborative projects between the IOA, CNDR, various School of Medicine departments, and the School of Nursing. For example, an \$11.7 million grant to establish the Penn Udall Center for Parkinson's Disease Research supports a collaboration between IOA, CNDR, and the Departments of Biostatistics and Epidemiology, Neurology, and Pathology and Laboratory Medicine. Forty-three pilot grants have been awarded, and of those completed, 43% have gone on to receive additional funding. Five new faculty have been jointly recruited by the IOA in conjunction with the Departments of Pharmacology, Pathology and Laboratory Medicine, and Medicine. "This is the IOA at work, bringing new people, new ideas, and new technologies into the aging research arena at Penn. And this has gone from basic and clinical science to health services," said Dr. Trojanowski.

Indeed, the vitality of the IOA has been maintained despite funding cutbacks from both the federal government and private agencies. From 2003 on, funding for the NIH as a whole declined

in real dollars (adjusted for inflation) and the NIA was hit hard. In 2006, federal funding was eliminated - and then only partially restored - for geriatric education centers and fellowships for training new geriatricians, and the NIA cut grant budgets by 18 percent. Funding cutbacks have forced a slowdown in plans to recruit new faculty this year, but Dr. Trojanowski said he is not to be deterred. "We put in a P30 grant for the Obama stimulus package. So even though this is a year that has put financial constraints on recruiting, the P30 was successful." In addition, Dr. Trojanowski is partnering with Dr. Arnold to recruit a new faculty member in Psychiatry, who works on biomarkers, thus "adding bandwidth to our biomarker effort."

As federal funding has declined, private funding has become even more important. In 2004, Marian S. Ware, a long-time supporter of Penn with a special interest in aging, made a \$6 million gift to establish the Marian S. Ware Alzheimer Program with a three part mission: drug discovery, clinical research, and patient care. The program represents a collaboration between Penn's Alzheimer's Disease Core Center, the Center for Neurodegenerative Disease Research, and the Schools of Medicine and Nursing. "Her investment in the program had a kind of a catapulting role," said Dean Rubenstein. "It was the kind of money that really made a difference. It was just a transforming gift." Moreover, he said, the IOA leveraged the money to get more grants, expand programs, and fill in existing gaps.

Another private gift that has already yielded an impressive return on investment was a \$1 million grant from The Bingham Trust in 2006, which allowed the IOA to double the number of pilot research grants awarded, thus spurring even more high-risk/high-reward research. Yet even with these generous gifts, creative new mechanisms for funding essential research have clearly been



The Time to Act is Now: An interview with Risa Lavizzo-Mourey



Risa Lavizzo-Mourey, MD, MBA, was named the first Director of the Institute on Aging in 1995, succeeding Interim Director Truman “Nipper” Schnabel. She is a national leader in health care policy and reform, a geriatrician and former White House consultant.

Currently, she serves as the President and CEO of the Robert Wood Johnson Foundation.

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

A: When I got into the aging field I viewed it largely from the perspective of a clinician. I tried to deliver care to elders in a manner that met their clinical needs and also their emotional and social needs in what is now known as patient-centered care. But it certainly was not framed quite that way at that time. Over the years, I became much more interested in the research that would ultimately improve care for all older people, both through my greater understanding of the kind of work that the scientists at the IOA do (dementia, Alzheimer’s disease, cardiovascular disease) but also the work that is related to some of the ethical and systemic issues that affect the quality of care that older people receive. As I moved from an academic institution focused on clinical research to a large foundation focused on social change and how policy can improve the lives of people, I’ve come to think about aging as an important area for better understanding the fundamental changes in our policy that need to be put into place so that all vulnerable populations have a better quality of care and a better quality of life. So the way I think about aging has expanded. I now think about the lessons that we learn in aging as informing many of

the other policy changes that need to occur within our health care system.

Q: What got you interested in geriatrics as a specialty?

A: Geriatrics is one of the few specialties in which you actually expand your breadth of knowledge as you focus in on one aspect of care. You expand from a base of internal medicine, of family practice, to rehab, to neurology, to understanding the social service networks. This is not the way people typically approach a specialty, not to mention the need to use a team as opposed to an individual based practice. So for me the intellectual challenge of delivering high quality care for older people was fascinating and was what pulled me into it.

Q: Do you think that the major concerns in the field have changed much since when you were Director?

A: The science has gotten a lot more sophisticated and has continued to advance, but some of the challenges that the field faces sadly remain. One of them is the lack of people going into the field. That’s an across the board issue, whether you’re looking at physicians or nurses or social workers or basic researchers. It’s a field that is still underappreciated, and I think that, while sad, it is nonetheless a fact. The science that we’re starting to see in terms of understanding the fundamental mechanisms of aging is getting much better at appreciating some of the diseases that plague older people, like AD and other forms of dementia; it’s just more exciting than ever. But it still remains a field that people generally stumble upon rather than understanding that excitement from early in their careers.

So I would love to see better ways to expose young people when they are making career decisions to the excitement of aging across the spectrum of opportunities that it provides.

“It’s a field that is still underappreciated...”

Coming of Age

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Q: Do you think there's been a shift in emphasis within the aging community or the NIA or any of the other organizations toward basic molecular versus health services research over the years?

A: I do think there is a greater emphasis on some of the basic fundamental mechanisms at a molecular level because that area is moving so quickly, and there has been greater competition for health services resources and, frankly, fewer clinically oriented researchers that are going into that field. So over the years I have viewed more emphasis on the basic molecular mechanisms of aging and the diseases associated with aging.

Q: Is that something that you feel needs correcting?

A: To me a lot of the questions about how to improve care for older patients, and the health services questions generated, are questions that are applicable to many other populations. So to the degree that one can have an overlap between let's say, how to improve healthcare and the quality of care for people with 2 or 3 chronic problems at age 50 and how you address the same questions in someone who is 80 or 90, economies of scale become evident. So it may not be detrimental to the overall advancement of the improvement of quality of care if we are focusing on the molecular level. That said, I think it's hard for faculty who are trying to put together a clinically-focused career in the care of the elderly and a research career combined with their clinical interest if there is not a substantial amount of funding for that kind of work specifically focused on older people. I think that's been one of the key reasons that fewer people have been able to go into and sustain research careers combined with clinical work that focuses specifically on older people.

Q: What do you think are the most important issues that need to be confronted in the area of aging now?

A: The most important issue the field has to confront most directly is the urgency with which we have to find solutions to the questions that are facing us because of the population changes happening really all around the world. This has been articulated for a long time, but now the population has shifted. We used to talk about the coming shift in the population, but it really is upon us. Although we have been talking about the urgency for 20 years, the time is now.

Whether you are looking at the cost associated with caring for Alzheimer's patients in the next 20 years, the supply of high quality long term care services, or the ability of nations to provide care at a reasonable cost, all are going to be urgent issues. So from the molecular to the systems level, they're going to be even more urgent in countries and among populations that don't have as much wealth as the United States.

needed, including public-private partnerships such as the Alzheimer's Disease Neuroimaging Initiative (ADNI), which was launched in a 2005 as the largest public-private partnership on brain research.

ADNI was designed to search for imaging, biochemical, clinical, and neuropsychological biomarkers that could be used to detect mild cognitive impairment (MCI) and early AD, as well as assess the progression of disease. In addition to federal support from the NIA and the National Institute for Biomedical Imaging and Bioengineering, the project has attracted support from a number of private sector funders and non-profit partners. Drs. Trojanowski and Leslie Shaw, another IOA Fellow, were named Biomarker Core Directors.

ADNI and the Marian S. Ware Alzheimer Program both have expanded the IOA's leadership in translational medicine and efforts to move some of the fundamental discoveries made in IOA labs into the clinical space. Combined with existing and ever-expanding strengths in basic biomedical and health services research, these programs provide a more complete toolbox to address the important questions in the field. "Making things happen is what I see as the role of the IOA," said Dr. Trojanowski. "What we try to do is bring people together to spark new ideas and stimulate new initiatives."

Looking to the Future: A Conversation with John Trojanowski

John Q. Trojanowski, MD, PhD, the William Maul Measey-Truman G. Schnabel, Jr., MD, Professor of Geriatric Medicine and Gerontology, is the Director of Penn's Institute on Aging, Alzheimer's Disease Core Center, and Udall Parkinson's Research Center, and Co-Director of the Center for Neurodegenerative Disease Research and Marian S. Ware Alzheimer Drug Discovery Program. Along with his long-time colleague Virginia M.-Y. Lee, PhD, MBA, he is known around the world as a leader in neurodegenerative disease research.



Q: When you look into your crystal ball, how do you see the aging field evolving over the next several years, especially given the global economic crisis and all the pressures on scientific research?

A: I guess the place to start is with demographics and the fact that since 2006, a baby boomer turns 60 every 7 seconds, and this will continue for the next 20 years. So population demographics in the United States and around the world are changing dramatically. The message is that the globe is aging, and just taking Alzheimer's as an example of a potentially overwhelming aging related disease, there's going to be a relentless rise in Alzheimer's in the U.S., China, India, and in nearly every other country around the world. This dramatic fact, and the medical, social, economic and political dilemmas this is going to precipitate, will, I hope, catalyze decision making at the highest levels to implement an action plan with the understanding that we will only be able to sustain our economies by taking measures that will enable people to live healthier lives for a longer period of time. Thus, elimination of Alzheimer's alone will reduce health care costs by more than \$1.5 billion per year today, and of course

the financial impact of successfully eliminating Alzheimer's now means greater than \$1 trillion in savings over the coming 40 years.

We need more public and government recognition that aging is a problem about which we must do something now, just like global warming and energy and so forth. You can't wait until the last drop of oil to do something. We can't wait until everyone is in a nursing home with Alzheimer's to do something. And so I would predict that people will get that message and will begin

to act in more aggressive ways to do something about aging at the research and education level.

Q: Where are the big frontiers?

A: Certainly advances in understanding osteoarthritis and cardiovascular disease and Alzheimer's disease, which have come a long way, put us in a position now to think about interventions and therapies that were unthinkable 20 years ago. So right now the opportunities for drug discovery in Alzheimer's disease far exceed the available resources. If we talk about targets against which one can create a drug to disrupt the many steps, the hundreds of steps in the pathway from normal brain function to Alzheimer's disease, there are hundreds of potential drug targets to consider, and we're only going after a handful of them now. People in pharmaceutical and biotech companies mostly hedge their bets and go after what they think will be the most tractable Alzheimer drug targets in the shortest time, but it would be awful if the 100th target 100 years from now worked and the first 99 didn't. Can we afford to do Alzheimer drug discovery ad seriatum, or in a serial way, as opposed to ramping up drug discovery in massive parallel efforts? I don't think we can. I

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think we've got to bite the bullet and pull out all the stops to pursue the hundreds of potential targets rather than the 5 or 10, because we just can't afford to not get there soon. And the hundreds of targets are there. The science is in place. The people are in place, but we need more of a scientific cadre of investigators who are informed about aging and aging-related diseases. We need a lot more man- and woman-power behind the science to move it all forward. So we need to invest in people and projects and this is true for neurodegenerative diseases, basic mechanisms of aging, and how to do things that would delay the losses of function that come with aging. In short, we need massive resources now to combat Alzheimer's and other aging-related disorders.

Q: But how can this be accomplished given the enormity of the task?

A: By mobilizing people, catalyzing the coming together of public, private, and government entities to do something equivalent to building the transcontinental railway, building the Panama Canal, putting a man on the moon, or the Manhattan project. All of these things were recognized as national objectives that required the nation's attention and public/private consortia to get them done, and I think that's where we are with aging in general, that we need to address aging in the same forceful way that we built the transcontinental railway and the Panama Canal. We are entering an epoch in human civilization that is unlike any in the history of our species. It is colossal, and it needs to be understood and addressed and planned for with colossal resources, that's my view. And we are at a stage where you can talk about allocating colossal amounts of money to very wise and judicious areas of basic and clinical research, to patient-oriented research, discovery research, health services research, care and prevention research, integration of care research.

Q: What's the IOA's role in all of this?

A: It's what we're talking about right now, to issue

the clarion calls if you will -- locally, nationally, and globally -- to make our communities aware of what's at stake. That's one thing. And we have an educational mission. We have also a research mission and a care mission. So we are an Institute of over 200 Fellows, we're not a department, and the whole concept of an institute is to not operate in a department mode, which can be limited by operating in a silo. Instead IOA operates across departments and schools to bring people together around key critical issues.

There's no one solution to anything. There's no single technology that can resolve these issues. Instead, we have to "marry" genetics to cell biology, drug discovery, animal models, and patient studies, etc. to get the whole picture so one can move the entire field forward in unison to achieve our goal, that is, healthy or successful aging and a world without Alzheimer's and related disorders of our aging population.

Q: Does the Institute, because of the way it's structured, as an institute without walls, is it a better environment for doing exactly that, combining genetics with molecular biology, etc.?

A: I think so. It brings people together. The easy-to-do research studies that led to spectacular advances by harvesting the low hanging fruit have probably all been done in the last 50 years. There isn't going to be another Fleming sitting in his laboratory, who throws the Petri dish into the trash and has a Eureka moment, thereby discovering penicillin and changing the world of drug therapy for infectious diseases. It's going to be a much more complicated systems science that integrates all sorts of information. Genetics is an important aspect, but there are many other aspects to the problem. And to be multidisciplinary and interact collaboratively across departments and disciplines focused on aging, it is necessary to have an Institute on Aging. I think there would be a huge vacuum if many of our institutes and centers were not here, and aging is an area that would suffer without an aging

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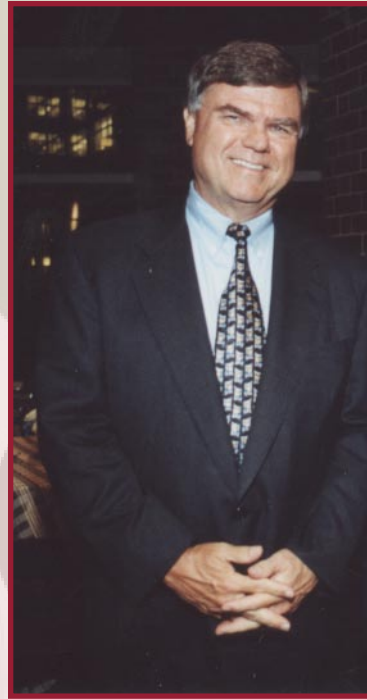
Attracting Top Talent: A Conversation with William Kelley

William N. Kelley served as CEO of the University of Pennsylvania Medical Center and Health System and Dean of the School of Medicine from 1989 to 2000 and was responsible for transforming the Center for the Study of Aging to the Institute on Aging in 1990.

Q: What do you think were the biggest challenges facing the aging field when you came on board in 1989?

A: I like to compare the aging field with cancer because it's similar in so many ways. If you go back to the '60s and early '70s, there was very, very little information in the whole geriatrics field and there was very, very little in the whole cancer field. Cancer was an unattractive discipline for clinicians to consider as a specialty. It was an unattractive field to entice scientists because there was so little known and the problems were so big and overwhelming that you hardly knew where to start. And the technology just wasn't there. I'm talking about the early '70s. And the same exact thing could be said about geriatrics and aging. Yet what happened in cancer was that molecular biology began to progress at a dramatic pace in the middle to late '70s, and since then all of a sudden tools were available to really look at cancer in terms of its etiology and pathogenesis and to begin to understand the diseases that we call cancer and what caused them. And then the molecular biology and molecular genetics of cancer became increasingly clear. Of course, there's a long way to go, but the progress has been astounding and some of that has been translated to improved survival with certain forms of cancer. I'm convinced that this progress will continue at an increasing pace. Also, as a result of the increasing science, the cancer field became much more attractive for scientists, clinicians, and physician-scientists.

Now having said all that, the geriatrics and aging field hasn't quite evolved in such a strong way, but it will, I believe. And I think it's a tougher problem.



If anything could be tougher than cancer, aging and geriatrics are. It's also an area that is critically important to understand, because the health benefits could be so dramatic once we do. It's one of those disciplines where the outcomes of improved understanding of treatment and prevention will be of incredible importance to the human race. So cancer is from my perspective a great

example of how changes have occurred. And it's also a great model for what I believe will happen in aging and geriatrics. But I think the problems are in some ways tougher in geriatrics, and we haven't reached that same point yet where the discipline is so attractive that scientists will put it at the top of their list in terms of their own interest. And the same thing is true in terms of the attractiveness of the field to clinicians.

Q: Why do you think it hasn't progressed the way the cancer field has?

A: I think it's a tougher problem to start with. Secondly, there hasn't been nearly as much money put into it by any federal agencies. There's some funding, but there hasn't been nearly what we've seen in cancer. And it hasn't yet attracted the same number of scientists that have gone into the cancer field. There probably are some other things that are also relevant. As one example, the reimbursement to physicians in geriatrics compared to cancer is just nowhere close. The reimbursement available

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to physicians and the incentives for pharmaceutical companies to move into the cancer field are substantial. New drugs represent a significant outcome for both patients and pharmaceutical companies, and cancer specialists are compensated well for being outstanding in their fields, and we haven't seen that happen yet in aging and geriatrics. So that's been a problem in my view.

Q: The field has probably changed a lot since 1989. Would you say that's true?

A: I'm not at all close enough to the field to reflect on that, but that's the whole reason we got things organized in the way we did and supported the Institute in the way we did. The purpose was to be in a position to be an outstanding institution for the investment of those resources and for attracting outstanding people. I'm not sure we're there yet, but if we are, it's fantastic, and if we aren't, we will be. We just need to keep hammering away at it.

The problems are the same. The solutions are the same. It really is a matter of making it a more attractive discipline both for the best people in science and medicine and for people that fund research.

institute. This is because a lot of the so-called "dots" wouldn't get connected, and a lot of the people who play together now in aging might not have met each other. I think one of the accomplishments of my tenure as IOA Director is that I've gotten people to interact and work together.

Q: How do you think the pressure to reform healthcare will affect your ability to move forward?

A: We need healthcare reform. So, for example, IOA Fellows try to address what is fair to say, are awful handoffs between different segments of the healthcare system, that lead to people bouncing back in the hospital. They also look at strategies to design a better way to allocate healthcare dollars, a better system. We don't have a healthcare system, we have a cacophony of systems, or a Balkanized healthcare system, where different parts of the healthcare enterprise don't talk to each other and are often not incentivized for efficiencies. We need a better system for how we pay for healthcare. We need public discourse on this. I'm not saying I know the right answers since there are religious, ethical, and a whole host of other things that get brought into the discussion of these issues, but we need to discuss them so we're on the same page.

I also believe prevention has not been invested in while it is more timely than ever to do so now. Our healthcare system is designed to treat diseases rather than prevent them. It's very hard to get funding for prevention. We brought people together around the issue of how to design and implement a comprehensive Alzheimer's center, and one of the "team units" we proposed is a healthy aging team unit, the goal of which is to recruit healthy people, 50 to 90 years old, for longitudinal studies, so we would have a cohort, a cadre of people, in whom we could try prevention interventions, i.e. to do prevention trials for Alzheimer's. Maybe all of us should be in clinical trials of one kind or another, for some lifestyle intervention, so that we'd know in 10 years rather than 1,000 years or 100 years the benefits of alpha omega fatty acids, curcumin powder, green tea, or other dietary regimens, as well as mental and physical exercise, social contacts and many other lifestyle options that appear to reduce risk for dementia. We'd have a rational way of understanding these lifestyle interventions. Prevention to me is one of the most exciting aspects of healthcare reform and I would love to see a huge investment in prevention science. That's obviously across the board for kids and adults and so forth, but especially for our aging population, since, I think, that's where large amounts of money can be saved. To understand these types of prevention trials, one also needs sci-

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Integrating and Improving Care: A Conversation with Steven Arnold

Steven Arnold, MD, is Associate Director of the IOA, and Director of the Penn Memory Center, the Cellular and Molecular Neuropathology Program, and the Geriatric Psychiatry Section. Dr. Arnold described the IOA as an umbrella under which all the various aging-related divisions, centers, and programs interact and collaborate. In addition, he said,



the IOA serves as a clearing-house for information on aging-related activities, such as grant announcements, seminars, research projects, and educational

initiatives, and it serves as a facilitator of activities that are based at Ralston House.

Q: In your role as the Associate Director of the IOA, how do you hope to shape the future of research?

A: My major focus is on clinical research, as well as clinical care, and what my vision has been since taking on this role, is to work here within Ralston House to facilitate more integrated care. More integrated research. To really make Ralston House as energized as it can be to provide truly integrated care with a shared infrastructure. You know, to use Ralston House as a base of operations for clinical studies, for clinical trials of treatment of Alzheimer's disease (AD), hypertension in the elderly, cardiovascular disease, osteoporosis, behavioral disorders, and so on. This requires a lot of integration which is difficult within the departmental structure. But perhaps we can develop a uniform infrastructure which would make it much easier for patients to negotiate

the system, get their medical care, if they're having some memory issues to be evaluated, to be invited to participate in some of the new and exciting clinical trials that actually offer the potential for stemming the course of AD or other dementias. I think that if we can work on the system level, and get things more integrated, that all boats rise.

A lot of this has to do with raising the funds to rehab the building because I think architecture really does promote interaction if done well. People have their little niches of research that they're involved in, but they need to be interacting more because I think that when you're trying to understand a complicated disorder like AD, which has all sorts of implications for not just neurology but psychiatry, for medical care, for health care decision making, and for end of life ethical issues, that by promoting more integration, we will have a much richer understanding of the health needs of older people. That's the intellectual and academic aspect although it also has a lot of practical implications.

Practically, you know the healthcare system is a nightmare for me to negotiate in terms of coordinating care among different physicians and all, or even trying to understand insurance. For older people who have even mild cognitive impairments, it's a nightmare. So if we can be a better integrated one-stop shop that allows people to get all their healthcare needs met in one place, that's huge. I think that's hugely important.

Q: Can you think of an example, some kind of clinical research study, where having a more integrated infrastructure led to a more productive study?

A: I think an example of this might be the Ware program. This is funded by a charitable gift that is supporting research at CNDR, in the School of Medicine, and the School of Nursing with Dr. Mary Naylor. In my portion of the Ware project, I'm looking at the effects of stress and psychological distress

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Improving the Quality of Care Provided to the Aged: A Conversation with Rachel Werner

Rachel Werner, MD, PhD, joined Penn and the IOA in 2005 as an Assistant Professor of Medicine in the Division of General Internal Medicine. Her research focuses on healthcare quality -- specifically quality measurement and interventions to improve quality -- and the impact of these interventions on healthcare delivery and outcomes. She also has a clinical practice in general internal medicine at the Veteran's Administration Medical Center.

Q: What are your biggest concerns in terms of healthcare quality for the aged?

A: Part of my research has been in the area of healthcare quality in nursing homes. There has been a large effort to improve quality of care in nursing homes through efforts such as public reporting or pay for performance. One of the things we're looking at is whether or not these initiatives really do improve quality, and if they don't, trying to investigate reasons they may not and approaches that may be more successful in improving quality. One of the things we find is that most of the quality measures used in these

initiatives are very specific to certain clinical problems, such as whether or not a nursing home resident has pain or whether or not a nursing home resident has pressure sores. But there are currently relatively few measures in quality improvement initiatives that assess globally how nursing home residents are doing through measures like quality of life. As a result, specific areas of care may improve, such as reducing the number of residents with pain or pressure ulcers, but broader measures of care don't change very much. So, we're looking into how to improve quality improvement initiatives to improve how residents are doing more globally.

Q: I assume this is becoming an increasing problem with the growing numbers of aging people. Is that right?

A: Yes. There are certainly an increasing number of people who are going to need long-term services of some sort and so the expectation is that this will become increasingly concerning. A

lot of the types of care that take place in the nursing home can certainly take place in other settings, such as in community-based or home-based care, and the issues we look at in terms of how to measure quality and improve quality in nursing homes I think are applicable for all these other long-term care settings.

Q: How does this research relate to your clinical practice at the VA? Do you see a lot of older people there?

A: I am a general internist and not a geriatrician, so I don't exclusively see older patients, but there is a lot of chronic disease in patients that I see at the VA, so many of the same issues

Conversation with Dr. Arnold *continued*

and how that effects the course of dementing illnesses like AD. Dr. Naylor is looking at transitions of care and the stress involved when older people, many of whom have AD or other dementias, get sick. These men and women are in the hospital and then transitioning back into the community - what kind of support services are available? what kind of stress are those people under? Dr. Jason Karlawish is looking at aspects of decision making as part of his Ware project. Well, you know, stress is a unifying theme in a number of these, so by bringing together different people interested in aging I can work closely with Jason, as well as Mary, so that we may all actually be able to share the same patients and learn that much more from each patient.

It's going to take some investment. We're struggling against a health system as well as an NIH system where, while everyone talks about integration of care, no one has really put their money where their mouth is about it.

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Searching for Alzheimer's Disease Genes: A Conversation with Gerard Schellenberg

Gerard D. Schellenberg, PhD, began studying Alzheimer's disease in 1984, looking for what he hoped would be a single gene that caused the illness. He and his colleagues at The University of Washington and other institutions quickly learned that there would be no easy answer to what turned out to be a group of complex diseases characterized by dementia. Now, 25 years later, Dr. Schellenberg continues his search at Penn, where he joined the IOA and the Department of Pathology and Laboratory Medicine in 2008.

What convinced Dr. Schellenberg to leave Washington? "One of the things Penn has is that there are so many people doing so many different things and it's so easy to collaborate and interact with people. It's a very collaborative atmosphere at Penn. And strangely enough, even though science, particularly medical science, is almost massively collaborative, that's not an attitude that's present everywhere, but it really is here at Penn. It's surprising that it's not everywhere else because it's so important."

Another factor contributing to Dr. Schellenberg's decision was that his wife, Dr. Mary Ersek, was recruited to the Penn School of Nursing. Dr. Ersek is also an IOA Fellow, working on pain and palliative care in older adults. "We all worked really hard to recruit both of them," said Dean Arthur Rubenstein, Penn School of Medicine. "They are both stars."

Better tools, better results

The tools for finding genes related to a particular disease have changed dramatically since Dr. Schellenberg first began his quest. In the 1980s, linkage studies allowed scientists to show that certain diseases or conditions were linked to particular segments of genes that had been mapped. While the scope of these studies was limited since only several hundred genes had been mapped at that time, they led to the identification of mutations responsible for more than 1,600 diseases, mostly those caused by a single genetic mutation, such as Huntington's disease. Com-

plex diseases such as Alzheimer's disease (AD), which are caused by multiple factors including multiple genes, were a much tougher nut to crack.

In 1990, the NIH initiated the Human Genome Project, and by the time the project was completed 13 years later, the entire human genome had been sequenced. Nearly 25,000 genes were discovered during this time at an estimated cost of \$300 million. Progress in gene mapping escalated dramatically as a result of the Project. In 2008, new technological developments led to the sequencing of three complete human genomes in less than a month, at a cost of only \$60,000. More importantly, the research tools developed in the Human Genome Project and later studies have made it possible to rapidly scan the genome for markers that are associated with particular diseases. Since 2005, genome wide association studies (GWAS) have identified genetic variations associated with more than 40 common diseases.

Dr. Schellenberg had been hunting for disease-causing genes since the 1980s, including the genes responsible for Werner's syndrome, a disease of premature aging, autism, and AD. In 1996, his team identified the gene responsible for Werner's syndrome using a technique called positional cloning. More recently, in June, 2009, Dr. Schellenberg and colleagues published a landmark paper identifying for the first time, genes that are linked to autism.

Just this year, he landed a huge NIH grant to conduct a genome-wide association study on AD, and he set up an Alzheimer's disease Genetics Consortium to gather data from large numbers of affected individuals and controls. "A large genetic study like this needs DNA samples from lots of well characterized patients and controls, and even before I started this consortium, all of the Alzheimer's Disease Centers (including the one at Penn), were seeing patients



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and normal elderly people, and also getting brains at autopsy and studying them. So that was all in place; it was just an issue of getting them all organized into one place and into a genetics study.”

The actual genotyping of samples collected for the study is being conducted at Children’s Hospital of Philadelphia, in the laboratory of Dr. Hakon Hakonarson. “We’ve only been funded for 2 ½ months, but we now have 2,000 DNA samples that are being genotyped, and in a week or two we’ll be ready to start analyzing the data,” said Dr. Schellenberg during an interview in August. Their plan is to analyze the entire genome, looking at individual sites along every chromosome and trying to identify particular genes or genetic variants that are associated with AD, or with particular symptoms of AD, such as depression, or characteristic neuropathological features, such as how many neurofibrillary tangles an individual has or how dense the plaques are.

Dr. Schellenberg said he hopes to have early results from the study within a couple of months. He added that the Alzheimer’s Disease Center at Penn works with the IOA to disseminate information, make sure people know about the study, and encourage them to participate. “That’s really important because even though Alzheimer’s is fairly common we still sometimes struggle to get the patient populations and the cognitively normal people that we need.”

ence -- genetics, molecular biology, biochemistry, biomarkers, etc. In short one needs all the same things, converging together to come up with an understanding of how to prevent Alzheimer’s disease and other aging disorders.

Q: Just one last question – how do you remain optimistic in the face of all these pressures?

A: I have a passion, and I believe in the future. I believe in the power of science, I believe in the power of people coming together. I believe in good luck, but I don’t believe in doing nothing while waiting for good luck to happen. I believe in trying to make good luck happen. And I’m an optimist. I’m a glass half full person I think by nature. And I just believe we can do things and I believe we will do things needed to solve aging, Alzheimer’s, and other aging-related disorders. I’m very determined.

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that you would think about in caring for older patients are true in any group of patients with chronic diseases. One of the other areas I’ve done research in relates to patients with multiple comorbid medical conditions and how you balance all these medical conditions against one another, especially in the setting of being asked to comply with guidelines or with quality measures in many areas.

Q: And I’d imagine that’s more of a problem as you get older?

A: Yes, you accumulate more comorbid medical problems. And I think patients’ priorities sometimes change as they get older. Things like preventative services, which were important at a young age to extend life, are less important to many people as they get older. So there really has to be evaluation at all steps along the way to balance patients’ needs and preferences against those clinical recommendations.

Q: Do you think your research impacts the care that you provide your patients?

A: Absolutely. It makes me much more aware of the need to prioritize care and take patients’ goals into account when deciding on a plan of care. It doesn’t really solve one of the things I’m most interested in, which is how health providers balance the needs of patients with the competing pressures from quality improvement initiatives that tell you that you have to do certain things and measure certain things. Achieving that balance is a difficult thing to do.

Healthy Aging - What *You* Can Do...

Although one cannot definitively predict what measures or lifestyle activities will prevent or delay Alzheimer's disease or other dementias, the research and medical literature provide evidence to support several strategies that further research may prove are effective for this purpose.

These strategies are summarized below, but they cannot be regarded as medical advice or recommendation, and, as always, one's physician should be consulted before adopting any of the strategies below.

1

1. First, what is good for your heart - controlling blood pressure, hypertension, and diabetes - is also good for your brain.



2

2. Second, exercise is beneficial even beyond its cardiovascular benefits.



3

3. Third, engaging in positive, meaningful activities will help your brain.



Prescription for the Future: Healthy Brain Aging

Research alone will not solve the problems that society faces as the population grows older. That's why IOA faculty have been taking their message out on the road, telling people that there are indeed things they can do to promote healthy aging and, in particular, healthy brain aging. Drs. Trojanowski and Lee, for example, have spoken to audiences from Philadelphia to as far away as Gabarone, the capital of Botswana, in southern Africa, on the topic of healthy brain aging. And they have delivered their message in a variety of forums – to Penn alumni at Alumni Weekend, senior citizens at several area retirement communities, and policy makers in Washington, D.C.

Geriatrician Jason Karlawish, MD, Director of the Alzheimer's Disease Center's Education and Information Transfer Core, and Associate Director of the Penn Memory Center, also speaks out frequently about healthy brain aging to the media, community groups, and at the annual research participant thank-you breakfast. In these talks, he makes three key points: first, that what is good for your heart - controlling blood pressure, hypertension, and diabetes -- is also good for your brain; second that exercise is beneficial even beyond its cardiovascular benefits, and third that engaging in positive, meaningful activities will help your brain.

Research backs up these claims, according to Dr. Karlawish. "There are really good data showing that exercise promotes learning, memory, and cortical thickness in animal models." Cortical thickness, he said, is a measure of healthy brain tissue. And there are great data about the benefits of social activities that engage you with other people, he said, noting that these activities should be ones that you enjoy.

"The classic one I like to pick on is crossword puzzles. I hate crossword puzzles. I find them tedious and stressful," he said. "The overarching theme is that chronic stress and anxiety have been shown to be associated with loss of brain function over time. And so the message I give people is that whatever you do, you ought to do in a way that you feel good about it, as opposed to feeling anxious about it, worrying about it."

The IOA's outreach efforts extend beyond these community talks. With support from the MetLife Foundation, Dr. Trojanowski and other IOA faculty worked with Carol Edwards and filmmaker Glenn Orkin of Motion, Inc., to produce the documentary "Al-

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zheimer's Disease Facing The Facts." The film won a CINE award and an Emmy award, and will be seen across the country on more than 80% of PBS stations throughout 2009 and 2010. "I hope as it circulates it will have an impact in mobilizing people, and catalyzing the coming together of public, private, government entities to do something along the lines as mentioned in the Alzheimer's Study Group that was prepared by Newt Gingrich and Bob Kerry," said Dr. Trojanowski. "It was something about which I had a passion because the message wasn't getting out."

Indeed, the IOA has been front and center in efforts to heighten awareness about the importance of healthy brain aging and ensure that it becomes a national priority. Dr. Kathryn Jedrzewski, Deputy Director of the IOA, worked with the Alzheimer's Association, the Centers for Disease Control, and experts around the nation to formulate 'The Healthy Brain Initiative,' a roadmap for the public on how to maintain cognitive health throughout the life span.

Bringing it back home

Outreach also includes programs at Penn that focus the attention of the Penn community, including the public, on Healthy Brain Aging. In 2008, for example, the IOA brought in a panel of national experts on healthy brain aging to the Sylvan M. Cohen Annual Retreat. This retreat, which each year highlights distinctive aging research and/or policy issues, was established in memory of Mr. Cohen, who was the founding Chair of the IOA. Alma Cohen, Sylvan's wife of 58 years and a supporter of the annual retreat named

in his honor, said she thought the topic of healthy brain aging was particularly appropriate for the Sylvan Cohen lecture. "He thought the Institute was very important because we're going to have a very large aging population," she said. "But aging has other problems that are not diseases, not physical disabilities, but the common occurrences of aging that don't require medical assistance. Healthy aging has different kinds of problems that you don't go and see a doctor about. Sometimes you don't even talk about them."

Speakers at the retreat included Dr. Marcelle Morrison-Bogorad, Director of the Division of Neuroscience at the National Institute on Aging; Dr. Marilyn Albert, Director of the Division of Cognitive Neuroscience at Johns Hopkins University School of Medicine; Dr. Carl Cotman, Director of the Institute for Brain Aging and the Alzheimer's Disease Research Center at the University of California, Irvine, and Dr. Hugh Hendrie, from the Center for Aging Research at Indiana University. They discussed both the science underlying brain aging as well as specific strategies that might reduce disabilities and enhance functional capacity. All of the speakers agreed that more data are needed to prove that a positive attitude, stimulating environment, and exercise can promote healthy brain aging; yet such large studies are difficult to conduct and enormously expensive.

Following the talks, a panel discussion was led by Nora Dowd Eisenhower, JD, (now former) Secretary of the Pennsylvania Department of Aging. Ms. Dowd Eisenhower asked the panelists what they would advise people to do today. Dr. Albert gave what was perhaps the most practical response. Shopping, she said, is the activity that best combines the three necessary ingredients for healthy brain aging. "This was inspired by my mother-in-law who is currently 97. She shops every day; she carries a heavy bag; she walks long distances, and she debates at great length, comparing and contrasting what she ought to buy. And when she finally makes a purchase she feels very good about herself!"

"...Aging has other problems that are not diseases, not physical disabilities... sometimes you don't even talk about them."

IOA Research Today: Investing now for future success

Ever since the Center for the Study of Aging was established in 1979, and throughout its evolution to become the Institute on Aging in 1990 and continuing on today, research has been at the heart of its mission. Recognizing even in the early days that improving the health of the elderly required research that spanned multiple fields in the basic and clinical sciences as well as in healthcare delivery and access, the Institute was designed to reach across all 12 schools at the University and beyond. Today, more than 200 Fellows and Associate Fellows contribute to the vibrancy of the Institute by sharing their expertise and collaborating across disciplines.

Building the faculty

Maintaining the vitality of research at the Institute requires the constant infusion of fresh blood in the form of new faculty recruits as well as seed funding for innovative ideas. Over the past five years, five new faculty have been recruited jointly by the IOA and the Departments of Pharmacology, Medicine, and Pathology and Laboratory Medicine, and their research ranges from studying healthcare delivery to the cellular and molecular basis of neurodegenerative diseases.

Benoît Giasson, PhD, was the first of this recent group of new faculty recruits, joining Penn's Department of Pharmacology and the IOA in 2004. Gias-

son has been investigating the mechanisms underlying Parkinson's disease (PD), the second most common neurodegenerative disorder in the developing world. Mutations in several proteins have been linked to PD; in particular, mutations in an enzyme called LRRK2 (leucine-rich repeat kinase 2) are the most common known cause of late-onset PD. These mutations can lead to the death of the dopaminergic neurons that are lost in PD patients. By understanding how LRRK2 mutations result in neuronal death, Giasson hopes to identify potential therapeutic targets. He is also collaborating with colleagues in the Departments of Pathology and Laboratory Medicine and Neurology to determine how different LRRK2 mutations result in different clinical and pathological outcomes.

In 2005, the IOA worked with the Department of Medicine to recruit Rachel Werner, MD, PhD, a physician at the Veteran's Administration Medical Center whose research examines healthcare quality and possible ways to improve it. Her research has demonstrated, for example, that publicly reporting on quality of care from physicians and hospitals, so called "healthcare report cards," does little to improve the quality of care and in fact may backfire if physicians begin to avoid high-risk patients in order to improve their "grades," thus worsening racial and ethnic disparities. (Read more about Dr. Werner's work on page 17.)

Bioinformaticist Li-San Wang, PhD, joined the Penn faculty as an Assistant Professor of Pathology and Laboratory Medicine in 2007, through a joint recruitment with the IOA. According to Dr. Trojanowski, bioinformatics was a completely untapped area for the IOA prior to Dr. Wang's arrival. "We advertised for someone who does bioinformatics in



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aging, but there was no one out there. They either knew aging or they knew bioinformatics, but they didn't know both. So we took Li-San Wang, who was terrific in bioinformatics, and he said, 'I will do everything in my power to bring aging and bioinformatics together,' and he's doing that."

While young investigators such as Giasson, Werner, and Wang have fueled the growth of IOA research in several important areas that were under-represented at the IOA, attracting established investigators was also essential in order to strengthen and expand the Institute's research portfolio. In 2008, the IOA landed an especially prized recruit, luring geneticist Gerard Schellenberg, PhD, from the University of Washington to Penn. Dr. Schellenberg had collaborated with Drs. Trojanowski and Lee many times over the years, particularly in their search for mutations in the protein tau that are associated with a group of neurodegenerative disorders collectively known as "tauopathies."

In his new role at the IOA, Dr. Schellenberg is leading a 5-year study to identify genes associated with an increased risk of developing

late-onset Alzheimer's disease. With a \$19.5 million grant from the National Institute on Aging (NIA) at the National Institutes of Health (NIH), Dr. Schellenberg put together a consortium of Alzheimer's disease (AD) geneticists to collect samples from more than 10,000 cases and 10,000 controls. In a collaborative effort, they will conduct a genome-wide association study (GWAS) to scan the entire genome in search of genes that are associated with AD. Earlier this year, he and his colleagues published a GWAS study that identified genetic variants that appear linked to autism and autism spectrum disorders. These findings provide new clues about the underlying causes of autism. Now, he hopes to repeat this success with AD. (Read more about Dr. Schellenberg and his research on page 18.)



Kick starting new research

Helping to kick-start their Penn careers, the IOA awarded Giasson, Werner, and Wang with pilot research grants of \$50,000. Indeed, the IOA pilot grant program is one of the most important functions of the IOA, a "crown jewel" in the IOA treasure chest. These grants provide seed money for new recruits who are in the early years of their research careers as well as for established investigators who have particularly novel or risky ideas that require an initial infusion of funds so they can collect preliminary data that may eventually lead to a larger, more long-term research grant. The table on pages 25-27 lists pilot grants that have been awarded over the past 7 years and illustrates the breadth of IOA research, as well as the success of many investigators in leveraging their pilot grants to get additional funding. Funding of this pilot research grant program was doubled from 4 to 8 grants beginning 4 years ago with a gift from the Bingham Trust for \$1,000,000. Unfortunately, this foundation does not renew grants to institutions it has funded, so the IOA is actively seeking potential donors to continue full funding of this important program. This certainly is fully justified by the fact that a stunning 43% of completed IOA pilot research projects have gone on to receive additional funding for their research, and many others are under review either at the NIH or with private funders.

For example, Robert Pignolo, MD, PhD, got a pilot grant in 2005, just two years after becoming a faculty member at Penn, and the results of his pilot grant led to his first R01 -- an individual investigator grant -- from the NIH in 2007. These grants are allowing him to elucidate the molecular mechanisms underlying osteoporosis in a mouse model of accelerated aging. Osteoporosis is one of the most debilitating conditions of aging, affecting some 200 million people around the world and leading to a high incidence of hip and vertebral fractures. "The pilot program has grown tremendously. I think this year 8 pilots were funded, which is an enormous number of pilot grants to give out," he said. Moreover, since so many of

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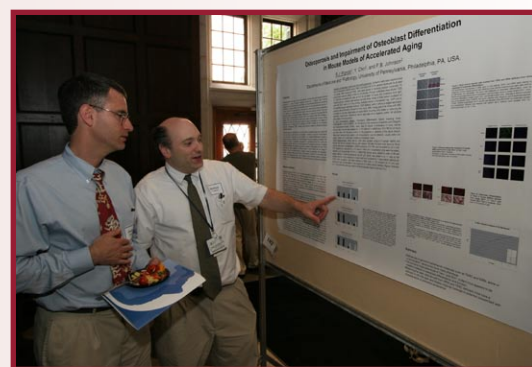
IOA Research Today: Investing now for future success

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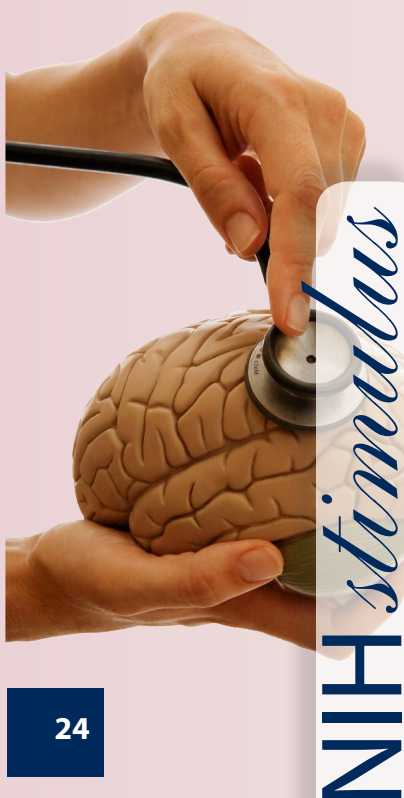
these pilots eventually result in some sort of extramural funding, the return on investment is fantastic, said Dr. Pignolo. “So to the extent that the mission of the IOA is to support research, I think the pilot program has been incredibly successful.”

While Dr. Pignolo credits the pilot grant program with helping him get that first R01, he said that the IOA helped build his research program in other ways as well. “The IOA Visiting Scholars Series program every year is outstanding. John brings in some of the most thoughtful and, I would say, cutting edge speakers across all areas of aging. The annual retreat is another highlight that I think everyone looks forward to – it’s a forum in which people at Penn get to know what others are doing in terms of aging research at Penn,” he said. “And John certainly introduced me to my now long-time collaborator Brad Johnson in Pathology. We collaborate not only on a basic science project but also teach a course on aging for medical students.”

Dr. Werner concurs on the value of both the pilot program (she received a pilot grant in 2009, and at this writing received a fundable score on a subsequent R01 proposal to the NIA) and the seminar series. “The IOA is a great resource to facilitate research and collaboration necessary to kick-start new projects, especially in these times when there is a large national interest in issues related to aging,” she said.




News from the outcome of Penn applications in response to the American Recovery and Reinvestment (ARRA) NIH stimulus package is that from among many NIH-funded applications, NIA will fund the P30 Center application Dr. Trojanowski submitted to recruit 2 new faculty to Penn, one in FY2010 and a second in FY2011. Briefly, according to Dr. Trojanowski, “This P30 (entitled NIA Core Center to Build a Multidisciplinary Community of Neurodegenerative Disease Research Faculty at the University of Pennsylvania) will provide >\$300,000 per faculty recruit to build further the multidisciplinary community of neurodegenerative disease researchers at Penn. The plan is to recruit 2 new faculty members whose expertise complements existing Penn programs while adding new content to these programs. This will lead to new job creation and enhanced capacity to reduce healthcare costs by improving the care of patients with aging related neurodegenerative disorders such as AD, Parkinson’s disease, amyotrophic lateral sclerosis, and frontotemporal lobar degeneration, thereby stimulating economic growth.”



2004-
2006

IOA Pilot Research Grant Program: Multi-Disciplinary Research in Aging

Begun in 2004, 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 will 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. Faculty from all twelve of Penn's schools are eligible.

In 2006, the Penn School of Nursing joined the IOA in sponsoring one additional Pilot Research Grant that was designated for nursing research in aging. Through the program, the IOA fosters the exploration of new directions in the field of aging on a broader, University-wide scale. Pilot Research Grants are funded at \$50,000 each for one year; those awardees who went on to receive further funding from other sources are noted below by the .

2004

Jennifer M. Kapo, MD

Can a Transitional Care Program (TCP) improve outcomes of elderly patients who are discharged from hospice?

Daniel Polsky, PhD

Lifecycle effects of health insurance on elderly health

John T. Seykora, MD, PhD

Mechanisms of impaired wound healing in murine models of aging



2005

Robert J. Pignolo, MD

Osteopenia and osteoblast differentiation in mouse models of accelerated aging

Amita Sehgal, PhD

Sleep:wake cycles and oxidative stress in aged *Drosophila*

Jennifer Tjia, MD

Comparing pharmacy refill records to PACE administrative claims to measure medication adherence



2006

Minghong Ma, PhD

Peripheral mechanisms of olfactory dysfunction in aging

Karen Hirschman, PhD, MSW

Improving advance care planning for dementia patients and their family members

Mark S. Forman, MD, PhD

Frontotemporal dementia and tissue microarrays: A novel method for identification of pathology-specific molecular probes for diagnostic and therapeutic applications

Jalpa Doshi, PhD

Impact of cost sharing on medication use in elderly patients with multiple chronic conditions



Continued on page 26

2007-
2010IOA Pilot Research Grant Program:
Multi-Disciplinary Research in Aging

In 2007, The Bingham Trust made a five-year commitment of support to the IOA to fund an additional four Pilot Research Grants each academic year. This added pool of funds, which began at a period of decreased available funding from such traditional sources as the National Institutes of Health, has enabled the IOA to award at least eight grants each year to promising investigators and research projects. Awardees represent the Penn School of Medicine, the School of Arts and Sciences, the School of Engineering and Applied Science, the School of Nursing Science, and the School of Veterinary Medicine. Pilot Research Grants are funded at \$50,000 each for one year; those awardees who went on to receive further funding from other sources are noted below. Abstracts for the grants listed can be found online at www.med.upenn.edu/aging.

2007

David Allman, PhD	Aging of hematopoietic stem cells	☑
Anne Cappola, MD, ScM	Ghrelin in the frailty syndrome: A pilot study	
Christopher Lance Coleman, PhD, MPH, APRN-BC, ACRN	Reducing HIV transmission behaviors among HIV sero-positive African American men 50 years and older	
Dawn M. Elliott, PhD	Intervertebral disc aging and degeneration: Pilot study to evaluate a novel treatment to restore mechanical function and structure	
Thomas F. Floyd, MD	Aging and the brain's hypoxic response to anemia	
Brad Johnson, MD, PhD	Tissue repopulation and phenotypic rescue by bone marrow derived cells in a mouse model of premature aging	☑
Paul S. Schmidt, PhD	<i>couch potato</i> aging in <i>Drosophila</i>	
Daniel Weintraub, MD	Use of ¹²³ I ADAM SPECT imaging to measure changes in serotonin transporter (SERT) binding with treatment of depression in Parkinson's disease	
Robert B. Wilson, MD, PhD	Screening assays for NADH-ubiquinone oxidoreductase deficiency	

2008

Aaron D. Gitler, PhD	A yeast TDP-43-opathy model	
Olena Jacenko, PhD	Hypomorphic perlecan mice: A model for osteoarthritis and osteonecrosis	
Jesse M. Pines, MD, MBA	The impact of emergency department (ED) crowding, ED waiting times, ED length of stay, and hospital occupancy on survival for older adults	☑
Barbara Riegel, DNSc, RN, FAAN, FAHA	Symptom recognition in elders with heart failure	
Kathryn H. Schmitz, PhD, MPH	Does adjuvant breast cancer treatment accelerate aging associated functional decline?: A pilot study	

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James Shorter, PhD	Elimination of alpha-synuclein amyloidogenesis and proteotoxicity using Hsp104	✓
J. Paul Taylor, MD, PhD	Histone deacetylase 6, autophagy and age-related neurodegeneration	✓
Li-San Wang, PhD	The role of G-quadruplexes in senescence through RecQ-dependent pathways	✓

2009

Hillary R. Bogner, MD, MSCE	Integrating depression services into Type 2 diabetes mellitus management	✓
Nalaka S. Gooneratne, MD	A novel method for the early detection of delirium in hospitalized patients with cognitive impairment using wrist and ankle accelerometry	
Michael Granato, PhD	Zebrafish as a model for peripheral nerve regeneration	✓
Frank S. Lee, MD, PhD	Targeting prolyl hydroxylase to treat anemia in the aging	
Robert L. Mauck, PhD	Age-dependence of functional ECM formation by MSCs for cartilage regeneration	✓
Giang T. Nguyen, MD, MPH, MSCE	Community connectedness and depression among South-east Asian immigrants in late life	
Richard M. Schultz, PhD	Live imaging of aged-induced aneuploidy during meiosis in mouse oocytes	✓
Rachel Werner, MD, PhD	Nursing home pay-for-performance in state Medicaid programs	

2010

Carlo Ballatore, PhD	Investigation of structure-activity relationship of novel 2-aminobenzothiazoles inhibitors of tau fibril formation	
Joseph A. Baur, PhD	Mitochondria as mediators of the protective effects of caloric restriction	
Eric. J. Brown, PhD	A critical role for p53 in facilitating tissue regeneration and suppressing age-related diseases	
Aureo De Paula, PhD	Overconfidence and decision making in aging	
Ravishankar Jayadevappa, PhD	Behavioral treatment for prostate cancer care	
Yuko Kimura, PhD	Role of properdin and complement activation in Alzheimer's disease	
Ling Qin, PhD	Osteoblastic epidermal growth factor receptor signaling and osteoporosis	
John H. Wolfe, VMD, PhD	iPSCs and NSCs from Alzheimer's disease patients	

INSTITUTE ON AGING

UPCOMING EVENT: SYLVAN M. COHEN ANNUAL
RETREAT WITH POSTER SESSION ON AGING



Osteoporosis

2010 Sylvan M. Cohen Annual Retreat with Poster Session on Aging

April 28, 2010

Houston Hall

University of Pennsylvania

save the date

The Sylvan M. Cohen Visiting Scholar is Clifford J. Rosen, MD, Senior Scientist at Maine Medical Center's Research Institute and former Director of the Maine Center for Osteoporosis Research and Education, presenting "Timekeeping and Its Impact on Bone and Fat." Our Penn School of Medicine Presenters are Robert J. Pignolo, MD, PhD, Assistant Professor of Medicine, and Director, Ralston-Penn Clinic for Osteoporosis & Related Bone Disorders, and Mary Leonard, MD, MSCE, Professor of Pediatrics and Epidemiology. Dr. Pignolo will present "The Biological Basis for Alternative Approaches to Osteoporosis Treatment"; Dr. Leonard will examine "Bone Structure, Muscle Function and Vitamin D in Adults with Chronic Kidney Disease." The 2010 Retreat with Poster Session on Aging is co-sponsored by the Penn Center for Musculoskeletal Disorders. For more information about the retreat and the poster session and to register to attend, visit the IOA's website.