We have a talent for seeing the future

*a letter from Jeffrey Kaye, M.D.*

In the late 1980's Senator Mark Hatfield realized that Alzheimer’s disease would be a great challenge for coming generations of Oregonians. He recognized that the way to meet this challenge was through research. It would take the best and brightest to lead the way. He advocated recruiting leaders of the future as key to creating a highly productive, nationally recognized Alzheimer’s research program in Oregon. My recruitment and that of other key faculty and clinicians was the direct result of his forward-thinking advocacy.

The leadership of OHSU and the citizens of Oregon rose to the challenge with their support. Oregonians helped create and support the state tax check-off for Alzheimer’s disease research A tax check off grant supported my first project: the now internationally recognized Oregon Brain Aging Study. The Layton family joined the cause with unwavering and generous support over the years. This vision has led to the blossoming of innovation and discovery that we see today, and resulted in the Alzheimer’s research powerhouse known as the Layton Center at OHSU.

As I prepare to lead the international Professional Society of Alzheimer’s Scientists this year, I realize that we have a unique vision, born of the many Oregonians who enabled the creation and sustained the growth of our Center and its superb community of clinicians and scientists now recognized throughout the world.

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We now stand at a transformative moment.

We need to apply our insights and talents toward seeing Alzheimer’s in new ways: in the way its damaging processes take over the brain, in the way we identify these changes before it is too late, in accelerating how we take these insights and prove that treatments work and are safe, and in the way that we bring these discoveries into the homes and the daily fabric of life of every Oregonian facing the challenge of Alzheimer’s.

In this and following issues of Update, we present a series of initiatives to change the way we see Alzheimer’s. Launching this plan will ensure that by 2020 every Oregonian can have access to meaningful assessment and promising treatments.

By changing the way we see Alzheimer’s we will fundamentally and radically transform Alzheimer’s from a hopeless disease to a preventable disorder.

Jeffrey Kaye, M.D.

Layton Professor of Neurology and Biomedical Engineering
Director, Layton Aging & Alzheimer’s Disease Center
Director, NIA ORCATECH:
Oregon Center for Aging & Technology
Oregon Health & Science University
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OHSU Alzheimer’s research: an unparalleled resource

Recognizing our exceptional science and clinical expertise, the National Institutes on Aging (NIA), beginning in 1990, designated OHSU as home to one of its national Alzheimer’s Disease Centers (ADC). Since then, the center has been continuously funded through competitive peer review, consistently achieving among the highest scores of any ADC in the US.

In 2001, the Layton family provided a generous gift to the Center, helping sustain and stimulate further promising research.

Major features of our work:

- A unique focus on understanding and treating Alzheimer’s dementia in the oldest old. We maintain a large comprehensive database of data on over 1000 participants. The power of this database resides in its longitudinal nature with over 3000 follow-up visits, the largest number among all national Alzheimer’s centers.

- A leading-edge neuroimaging laboratory dedicated to brain analysis maintains one of the largest MRI data sets for brain research in the world.

- Memory Assessment and Alzheimer’s clinics provide exceptional dementia care from experienced multidisciplinary staff.
• Brain and Biomarker Banks, among the largest repositories for dementia research in the US.

• A novel model for conducting clinical research using home-based assessment assisted by technology. Our technical expertise promises to revolutionize the way clinical research is conducted.

• Participation in the majority of national collaborative clinical trials, as a lead enrolling center of the NIA Alzheimer’s Disease Cooperative Study group and the Alzheimer’s Disease Neuroimaging Initiative, as well as in unique studies of alternative treatments.

Our clinical research expertise is complemented by the extraordinary basic neuroscience research community at OHSU, where over 30 neuroscientists are engaged in basic dementia research. All contribute research that directly informs clinical care for Oregonians, making meaningful treatments a reality.

Changing the way we see and assess the Alzheimer’s brain

A profoundly important insight has been gained in recent years: The brain changes that lead to the development of dementia begin many years before we are aware of them. This presents us with an opportunity: if these changes are addressed early, we may be able to prevent the development of disease. This means that we need to develop better ways to detect dementia in people as early as possible.

Our first challenge is to develop ways to detect disease even in people who have no symptoms. We can improve our identification of the biomarkers of brain change. Among the revolutionary methods now available are not only detection of classic AD pathologies (plaques and tangles), but most importantly for the majority of older adults, identifying vascular pathology in living patients.

Layton Center scientists were among the first to show that vascular disease signatures seen on MRI are a first marker of risk for dementia. The fundamental need for the brain to be nourished by oxygen and nutrients is compromised in vascular disease. The degree to which this process can be precisely defined during life is a key to not only diagnosing what is going awry, but in calculating the effect of therapies.

Next steps: MIND-It

To change the way we see Alzheimer’s will require support for MRI and PET brain imaging. We call this dynamic program proposal "MIND-IT": “Multi modal Imaging of Neurodegenerative Disease In Transition.” The program would, for the first time, employ MRI and PET imaging of each patient to map all the known contributors to cognitive decline. We’ll also include continuously acquired behavioral biomarkers never before incorporated into assessment.

MIND-IT will also benefit from the many volunteers who have gifted their brains to research after death. We have an opportunity to assess the post-mortem brain utilizing our 12T MRI scanner—one of the highest strength available in the world—to detect brain lesions previously too small to be seen, allowing researchers to determine the contribution of such lesions to the development of Alzheimer’s disease and other dementias.

We are well on the way to changing the way we see Alzheimer’s disease. With continued investment in leading-edge tools and teams, we can carry the work forward.
Research by Oregon Health & Science University’s Jeffrey Iliff and his colleagues, which gives scientists new insight into sleep, Alzheimer’s and the human brain, received national attention last year, from National Public Radio to the Huffington Post and beyond.

Iliff and colleagues from New York University and the University of Rochester found that when mice sleep, their brains clear out harmful toxins and other waste that built up during waking hours. The findings give a tantalizing hint at how lack of normal sleep might contribute to Alzheimer’s disease.

Now, Iliff will be using money from a special fund of donations from Oregon taxpayers to continue his research at OHSU — and to advance that research into human brains.

“My grant from the Oregon Partnership for Alzheimer’s Research (OPAR) will allow us to see whether this process works similarly in human brains,” said Iliff, now an assistant professor of anesthesiology and perioperative medicine at OHSU. “That may allow us to figure out whether problems in the brain-clearing process might contribute to the onset of Alzheimer’s.”

Iliff is only the latest in a long line of Oregon Alzheimer’s researchers who have benefitted from the special fund, part of Oregon’s Income Tax Charitable Check-off Program that lists state charities as possible beneficiaries of tax refund dollars on Oregonians’ tax returns. The Oregon Tax Checkoff Alzheimer’s Research Fund was among the first to be included in the Oregon check-off program in 1990. Since then, the fund has awarded about $2 million to Oregon Alzheimer’s researchers.

Jeff Kaye, M.D., professor of neurology and director of OHSU’s Layton Aging & Alzheimer’s Disease Center, whose scientists have received several of the grants, points out that the amounts generally aren’t huge — about $15,000 to $30,000. “But they’ve packed a huge punch — because they are often important startup grants to Alzheimer’s researchers at the beginning of their careers.”

Over the 20 years of the program, scientists who started with tax check off pilot grants, have been awarded a total more than $65.5 million in subsequent funding. Many of these Oregon projects have been supported by larger grants from the National Institutes of Health.

“That’s more than 30 times what was donated through the tax check off program,” Kaye said. “It has been an incredibly successful investment by Oregonians in Oregon scientists working to find ways to treat and cure Alzheimer’s disease.”

Small grants lead to productive careers and local expertise

- Kaye won a $15,000 grant in 1997 that, he said, “was instrumental in helping start the landmark Oregon Brain Aging Study.” The study recruits healthy older people who yearly receive a battery of neurological tests: of concentration and memory and MRI scans of their brain. Subjects commit to donate their brains after death so that those brains can be examined to improve understanding of neurological function.
- Jaggiebultowicz, PhD, Professor at Oregon State University’s Center for Healthy
in Alzheimer’s research in Oregon

times more research funding than the original tax refunds invested

Aging Research, won a $25,000 grant in 2009 to study the links between brain aging and biological (circadian) rhythms which control sleep and activity. “OPAR funds helped me to secure more than $1 million from NIH for related research. These funds launched me into research on fruit flies which carry human Alzheimer-causing mutations. Our studies have already revealed that Alzheimer-like pathologies disrupt sleep activity rhythms; we are now testing interventions to improve these rhythms.”

• Joseph Quinn, M.D., professor of neurology and director of OHSU’s Parkinson Center of Oregon, won a $24,873 grant in 2004 to study how anti-inflammatory drugs affected neurological tangles in animals that are a hallmark of dementia in humans.

“My application for the tax check-off grant was the first grant proposal I had ever written,” Quinn said. “The grant allowed me to generate the preliminary data and establish a track record necessary to secure larger and longer-term federal grants.

I am grateful for that tax check-off grant for literally making my research career possible.”

Oregonians who contribute to the Tax Check-off Alzheimer’s Research program will help direct some of the additional $100 million for Alzheimer’s allocated by Congress this year to Oregon neuroscientists.

Charitable Check-off fund

The Oregon Tax Check-off Alzheimer’s Research Fund is a unique program, created by the Oregon State Legislature to fund vital early stage research and position researchers in Oregon to leverage larger grants from national sources. The fund is administered by the Oregon Partnership for Alzheimer’s Research (OPAR), a community advisory board of volunteers from research and health care institutions. OPAR makes funding decisions based on scientific reviews of applications.

“Alzheimer’s disease is a devastating disease — for the 76,000 Oregonians 65 and older who have it, for their 167,000 caregivers, and for everyone touched by it,” says Kathleen Cody, executive director of the Alzheimer’s Association Oregon Chapter.

“The Oregon Alzheimer’s research fund has helped find effective ways to address the myriad impacts of Alzheimer’s disease on our state’s families, and we are always proud to remind Oregon taxpayers that every donation makes a difference in what Oregon researchers can learn about this disease.”

You can also support grants to new Alzheimer’s disease researchers in Oregon by donating directly to the Oregon Partnership for Alzheimer’s Research. To do so, visit www.opar.ohsufoundation.org.
Prevention of dementia through diet and lifestyle.

Professor Gene Bowman and OHSU colleagues in the Layton Aging & Alzheimer’s Center report new results (December 2013, Frontiers in Aging Neuroscience) showing how good fats tailored to the individual might be our best chance to preserve brain health as we age. The team found that higher blood levels of certain fats called omega 3 fatty acids (EPA and DHA) while not related to changes in broader mental and thinking abilities over time, did affect one area of mental function - executive function and speed of processing in older adults participating in the Oregon Brain Aging Study. They also present evidence that suggests higher blood omega 3’s can preserve the small blood vessels and the highly active parts of the brain cells that support these executive and processing speed skills.

Other studies have also found that people with higher blood omega 3’s have healthier small blood vessels in the brain and better executive function, but this is the first study to suggest omega 3’s can prevent future mental decline by supporting the “vascular tree” in our brain.

“We may have identified the individuals who should and should not benefit from omega 3 therapy. The critical next step, of course, is to formally test this new theory. In fact, I am happy to announce that we have funding now secured in order to pursue this principle of personalized nutrition to prevent dementia” Bowman said.

Bowman’s work at OHSU has attracted international attention; he was recently recruited as head of research in aging and cognitive health at the Nestlé Institute of Health Sciences in Lausanne, Switzerland. The institute, on the campus of the Swiss Federal Institute of Technology, focuses on facilitating and prolonging healthy life through nutrition and lifestyle. They carry out research on aging, neurological disorders, diabetes, heart disease and obesity, with a goal to develop targeted, personalized nutritional interventions.

Concurrent with his new position in Lausanne, Professor Bowman will continue as Principal Investigator (PI) on the omega 3 dementia prevention study at OHSU along with co-PI Lynne Shinto, N.D., M.P.H. For information about volunteering for the study, contact James Dursch, 503-494-7823.

Choose healthy fats
Omega-3 fatty acids are important for a number of functions in the body. The best way to get omega-3’s is from food sources, rather than supplements.

Some suggested foods to include in your diet:
- salmon
- tuna
- shellfish
- vegetable oils such as canola, olive and soy
- walnuts
- flaxseed
Highlights of current work at the Layton Center

Clinical Trials

The Layton Center Clinical Trials Team, led by Dr. Erten-Lyons, is currently engaged in 11 clinical trials ranging from prevention to treating established symptomatic disease. These trials will involve hundreds of volunteers over several years. Of particular note are three dementia prevention trials that focus on identifying risk for dementia in cognitively normal volunteers using imaging and genetics to identify individuals for preventative treatments.

Biomarkers

Several projects are underway to measure the progress of treatment or diagnose those with pre-symptomatic or early disease and find markers that identify these patients. Key to this effort is use of neuroimaging. Dr. Lisa Silbert, supported by a NIH grant, is following volunteers with varying degrees of cognitive function to identify the earliest brain changes preceding dementia. She has uncovered unique blood-flow and white matter connection (the long fibers that connect the nerve cells from one part of the brain to another) disruption that is present when people are asymptomatic.

Dr’s Julie Saugstad and Joe Quinn are investigating a new marker in the cerebral spinal fluid (CSF) called microRNA that may provide a means to early diagnosis. The large CSF biobank of the Layton Center facilitates this work, as do new volunteers who are having spinal taps for this innovative research.

Clinical Care

Optimal clinical care is key for those facing the challenges associated with Alzheimer’s. One new approach is the Layton Center’s development of telemedicine for managing Alzheimer’s disease. Many patients and families travel hours to see us for follow-up care. Some spend the night in a motel for an appointment the next day. We are beginning to apply our technology expertise to provide remote visits via the Internet using video telephone direct to families’ homes. The first such visit by Dr. Erten-Lyons was conducted recently through a Veteran’s Administration program. We intend to initiate this service for our patients over the coming year. Another project is the first ever to investigate cognitive changes that occur in real-time while people go about their daily lives. Using unobtrusive sensing technologies developed at OHSU we measure activities such as sleep, walking, medication taking and socialization to detect the earliest disruption of life changes before they come to conventional clinical attention. This data will provide insight to the patient, care team and family that may be used to improve care decisions.

To find out more about our current clinical studies, contact Lisa Loree: 503-494-7615.

2014 pilot grants:

Our pilot program provides modest support to allow new investigators to develop preliminary data sufficient to form the basis for application for on-going support.

This year’s awardees are:

Katie Schenning, MD, MPH
House Officer, OHSU Anesthesiology & Perioperative Medicine
Topic: Effect of Surgery and Anesthesia on Cognitive Outcomes in the Elderly

Rebecca Lunsford, PhD
Postdoctoral Researcher, OHSU Center for Spoken Language Understanding
Topic: Whether spoken language characteristics differ between people with MCI and healthy age-matched adults.
Oregon Health & Science University
Mail code: CR 131
3181 S.W. Sam Jackson Park Road
Portland, OR 97239-3098

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Oregon Brain Institute
2014 BRAIN AWARENESS Lectures
Building Brain Bridges

MONDAY, APRIL 7
The brain and the adolescent mind: Why is it so special and vulnerable at the same time?
Bonnie Nagel, Ph.D.
OHSU Division of Child and Adolescent Psychiatry, OHSU Doernbecher Children’s Hospital

MONDAY, MAY 12
The brain and cancer: How does your brain affect cancer — and its future treatments?
Joe Gray, Ph.D.
Gordon Moore Endowed Chair, OHSU Department of Biomedical Engineering; Associate Director for Translational Research, OHSU Knight Cancer Institute

The OHSU Charitable Gift Annuity
Make a Gift and Help Fight Alzheimer’s Disease

A charitable gift annuity supporting the OHSU Layton Aging & Alzheimer’s Disease Center will help us lead vital research, sustain essential support programs and provide a dependable income stream for you.

Visit giftplanning.ohsufoundation.org or contact Lori Sweeney at 503.494.7455 or sweeneyl@ohsu.edu to learn more.

The C. Rex & Ruth H. Layton Aging & Alzheimer’s Disease Center UPDATE
OHSU Brain Institute (OBI) is a national leader in neuroscience patient care, research and education. We provide the most comprehensive care of the brain, spine and central nervous system in the Pacific Northwest. Our nationally recognized neurological programs and centers offer comprehensive care, advanced research and clinical trial opportunities.

The Layton Aging & Alzheimer’s Disease Center is one of 28 NIH Alzheimer’s Disease Centers in the United States and the only one of its kind in Oregon. Our Center is recognized as a national leader in dementia care and research, and is committed to serving the needs of people throughout the Northwest.