

# The Aging & Alzheimer's Update

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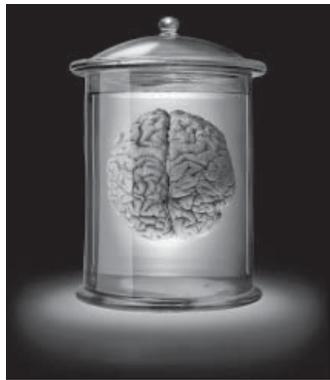
## Oregon Alzheimer's Disease Center Neuropathology Core

What it does and how it serves to advance our understanding of dementing illnesses

Dr. Randal Nixon, Director, Oregon Alzheimer's Disease Center

Discussing the Oregon Alzheimer's Disease Center Neuropathology

Core may be uncomfortable for some, since with very few exceptions we are dealing with the examination of tissues obtained at autopsy from loved ones. Nonetheless, the services provided by the core are essential both to establish the diagnosis in these individuals and for the scientific studies performed by the OADC. The need for the neuropathologic examination stems from the significant overlap in the clinical presentations of the various neurodegenerative disease that in turn reflects the sites of degeneration. Since multiple neurodegenerative diseases



may affect the same regions of brain, and given the immense complexity of the human

nervous system it's not surprising that overlap exists. Clearly, such overlap may complicate the interpretation of results obtained from participants in the myriad of

OADC studies examining new diagnostic tests and therapies. It is therefore imperative to have a "gold-standard" with which to classify these processes. For the neurodegenerative diseases, that standard is the neuropathologic examination which thus defines the primary function of the OADC Neuropathology Core. However, in addition to providing a diagnosis to the families and clinicians, the

Neuropathology Core also has a number of other responsibilities that are discussed below.

### *Oregon Brain Bank*

Managing the Oregon Brain Bank is an important function of the NP Core. The brain bank is provides tissues to researchers in the fields of neuroscience and neurodegeneration. By working closely with the clinicians in the Oregon Alzheimer's Disease Center, we are able to provide tissues that have been well-characterized both pathologically as well as clinically. Donated materials from the brain bank are currently being used in studies in North America and Europe.

### *PaNDA*

The OADC Neuropathology Core has been working in close collaboration with the

University of Washington Alzheimer's Disease Brain Bank in an attempt to standardize the harvesting, processing, and storage of tissues to increase the number of samples available for researchers. This joint venture has been called PaNDA (Pacific Northwest Dementia

and Aging); the utility of this approach was recently recognized by the National Institute of Aging in our successful grant renewals for both institutions.

#### *Research*

Research activities of the Neuropathology Core range

from molecular genetic studies performed in collaboration with the OADC Genetics Core to studies examining the molecular mechanisms underlying the prion diseases (a.k.a. "madcow disease") to classic pathologic studies of patients with the lesions of Alzheimer's disease but without dementia. These collaborative studies have resulted in a number of peer-reviewed publications.

#### *Teaching*

It is critical that we continue to train the next generation of physicians regarding dementia. To this end, the Core is involved in activities ranging from conferences with clinicians to projects with undergraduate students. It is generally accepted that even today in this era of remarkable neuro-imaging that an appreciation of the underlying pathology remains fundamental to an understanding of the processes causing dementia.

The Neuropathology Core provides a variety of services to patients, clinicians, and researchers both locally and internationally. The strength of the program stems from the generous donations made by the patients and families affected by these devastating diseases.

### **Establishing a diagnosis through brain autopsy**

To establish the neuropathologic diagnosis more than 20 brain regions are sampled. These tissues are preserved, embedded in wax, and then cut to approximately 1/100th millimeter thickness. The sections are then further processed by one of three general techniques to allow microscopic examination; either staining with various dyes to allow discrimination of the cell types and components, reacted with a combination of chemicals to look for the presence of unusual deposits (much like the reaction of developing a photograph), or tested with antibodies to detect the presence of specific proteins; in rare cases electron microscopy may be performed. Once complete, the pattern of tissue changes, the distribution of the

lesions, the types of deposits as well as the types of proteins allows classification into one of the more than 20 neurodegenerative disorders. For several of these disorders, it's not only a matter of determining the type of disease, but also giving an estimate, based on published guidelines, of the relative severity of the lesions and the probability that the observed pathologic changes account for the patients clinical presentation. In many cases, it's found the patient suffered from not one but perhaps several disorders. A common example would be Alzheimer's disease and vascular disease. This information is then compiled and reported to the clinicians as well as to the National Alzheimer's Coordinating Center.

Although the cell culture and animal model experimental systems developed over the years have provided unique insights into the pathologic processes involved in these disorders, they must always be compared to the human condition. This is the value and strength of the contributions made by the participants in the Center. Their importance cannot be over stated, and we are profoundly grateful.

### **ORCATECH Holds First Council Meeting**

On May 3<sup>rd</sup> 28 experts from diverse disciplines gathered in the Hatfield Research Center at OHSU for the first Council meeting of the Oregon Roybal Center for Aging, Technology, Education and Community Health (ORCATECH). Included were representatives from diverse academic disciplines and institutions, community organizations, residential communities, and industry partners. The Roybal Council listened with intense interest in the tremendous potential of this collaborative endeavor, as Dr. Jeffrey Kaye, Director of the Layton Center, Eric Dishman, Chief Scientist from Intel, and others presented their vision and goals for ORCATECH.

The National Institute on Aging awarded funding in 2004 to OHSU to establish the Roybal center to develop and translate basic social, behavioral and biological knowledge about aging independently using state-of-the-art technology and engineering.

ORCATECH is working to establish a 'living laboratory' for technology-based health monitoring and support of independent aging. This concept proposes that continuous and unobtrusive assessment in the home will lead to earlier detection of memory impairment and help elders live independently for as long as possible.

At this first and successful Roybal Council meeting, the overall goals and operations of ORCATECH were reviewed and pilot investigators from the first round of pilot grants presented their progress and preliminary results. The Council also discussed directions for new research, workgroups, and collaborations. The Council plans to meet quarterly. Future meetings will be focused around key topics related to innovation and challenges in this field of technology research.

Council activities will also include reviewing and guiding our pilot project program, advising on the development of a community-based 'living laboratory', establishing targeted work groups to tackle critical issues, and building a community to stimulate and foster translational research on aging and technology.

One of the key elements of ORCATECH is its pilot core, which awards funding and support for innovative research. ORCATECH pilot projects for 2005-2006 have been announced, and include:

- Tamara Hayes, PhD (Oregon Graduate Institute, Biomedical Engineering), Medication adherence in MCI and normal aging
- Brian Roarke, PhD (Oregon Graduate Institute, Center for Spoken Language Understanding), Automated analysis of spoken story recall tests
- Carmen Steggell, PhD (Oregon State University, Department of Design and Human Environment), The role of technology for healthy aging among rural and minority older women
- [funded by Intel] Jay Lundell, PhD (Intel, Proactive Health Research), Medication adherence, sleep, and patterns

of morning activity in healthy elders and MCI patients

For more information about ORCATECH, please visit the Roybal website ([www.ohsu.edu/research/alzheimers/roybal](http://www.ohsu.edu/research/alzheimers/roybal)), or contact Tracy Zitzelberger ([zitzelbe@ohsu.edu](mailto:zitzelbe@ohsu.edu) or 503.494.9635).

### Scientist Studying Herb as Possible Alzheimer's Therapy

*Study of gotu kola among projects funded this year by state tax check-off grants*

A study of the potential therapeutic effects of the dietary supplement gotu kola is among seven research projects being funded this year by Oregon's Tax Check-Off Program for Alzheimer's Disease Research. The Oregon Alzheimer's Disease Research Small Grants Program, funded by the Tax Check-Off Program for Alzheimer's Disease Research, is administered by the Education/Information Transfer Core of the Layton Aging & Alzheimer's Research Center. The program provides grants ranging from \$21,100 to \$25,000.

Amala Soumyanath, Ph.D.,

associate professor of neurology, Oregon Health & Science University School of Medicine, will use the \$25,000 grant to continue her work on gotu kola, also known as *Centella asiatica*. Previous studies, in collaboration with Joseph Quinn, M.D., neurologist with the Layton Aging & Alzheimer's Disease Center, and Bruce Gold, Ph.D., at OHSU, have shown that gotu kola extracts

reverse behavioral deficits in a mouse model for Alzheimer's disease and had protective effects on neuronal cells cultured in the laboratory. The title of her project is "*Centella asiatica* – a potential therapy for Alzheimer's disease."

As a pharmacognosist, Soumyanath is an expert in the study of medicines derived from botanicals. She said gotu kola was chosen for closer study from a group of herbs she was examining because "this particular herb came out showing some interesting effects in animals and cell

models. This tax check-off grant supports the follow-up to that."

A slender plant with fan-shaped leaves that's found primarily in the swampy regions of India, Madagascar and other tropical

climates, gotu kola has traditionally been used in the ancient Hindu system of healing known as Ayurveda and in Chinese medicine as a nerve tonic and memory-enhancing agent. It's often prepared as a tea and can be dried for use in capsules.



*gotu kola*

Soumyanath's laboratory uses a water or alcohol extract of the herb.

Dr. Soumyanath's ultimate aim is to "be able to carry out clinical trials in human beings. We want to see if gotu kola is of benefit in Alzheimer's patients to relieve or delay cognitive impairment." Herbal products can vary considerably in composition depending on the geographical origin, climatic factors and production method. Information from the current project will help researchers conduct well-designed trials for which the gotu kola preparations have

been confirmed to contain the relevant active components.

Other recipients of the Oregon Tax Checkoff Grants for Alzheimer's Research for 2005 include:

- "Annotation and Automatic Approximation of Language-use Metrics for Detection of Mild Cognitive Impairment," Brian Roark, Ph.D., assistant professor of computer science and engineering, Center for Spoken Language Understanding, OHSU OGI School of Science and Engineering, \$25,000.
- "The In Vivo Role of N-terminal peptides from APP-related proteins," Doris Kretzschmar, Ph.D., assistant professor of molecular and medical genetics, OHSU School of Medicine, and assistant scientist, OHSU Center for Research on Occupational and Environmental Toxicology, \$25,000.
- "Rapid Estrogen signaling modulates receptor localization," Laird C. Sheldahl, Ph.D., postdoctoral fellow in physiology and pharmacology, OHSU School of Medicine, \$24,995.
- "Genetics and Successful Brain Aging," Deniz Erten-Lyons, M.D., instructor in neurology, OHSU School of Medicine, \$24,300.
- "Unobtrusive in-home activity assessment for multi-person homes," Tamara Hayes, Ph.D., assistant professor of biomedical engineering, OHSU OGI School of Science & Engineering, \$24,882.
- "Distribution and trafficking of mutant PrP," Randal Nixon, M.D., Ph.D., assistant professor of pathology, OHSU School of Medicine, director of the neuropathology core, OHSU Layton Aging & Alzheimer's Disease Center.

Grant recipients are determined by the Alzheimer's Research Partnership, an alliance of scientists and administrators from OHSU, Providence Health System in Oregon, Kaiser Permanente, the Oregon chapter of the Alzheimer's Association, Portland State University and Oregon State University. The Layton Aging & Alzheimer's Disease Center serves as steward for the program's funds.

Grants are awarded to clinical investigators and

basic scientists for clinical, biological, behavioral or health system research that will advance understanding, treatment and prevention of Alzheimer's disease. Appropriate fields include the neurosciences, nursing, social work, epidemiology, sociology, psychology, psychiatry, economics, counseling, delivery of health care services and others relevant to Alzheimer's research or practice. Applicants are evaluated on scientific merit, but priority is given to investigators just entering the field of dementia research and to new or innovative projects.



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**OHSU Center for Diversity & Multicultural Affairs honors Layton Center researcher**

At its 6th Annual Awards Ceremony the OHSU Center for Diversity & Multicultural Affairs presented Fred Miller, MS, the director of the African American Dementia and Aging Project (AADAPT) for his support for diversity and multiculturalism through his work both at OHSU and Portland Community College, where he is a professor of psychology. The Faculty Award recognizes and honors a faculty member within OHSU's educational network who exemplifies dedication to education and sets the mark for credibility, flexibility, and maintains interest in the well being of our minority communities.

Fred was selected based on his work in serving diverse communities and in supporting minority students who are interested in the health and science professions. According to Leslie D. Garcia, MPA, Director of OHSU's Center for

Diversity & Multicultural Affairs, "Fred has been instrumental in getting the word out to students at Portland Community College, as a speaker, and in many other ways. He was a great resource for the Center."

Congratulations Fred!

