BATTLE FOR THE BRAIN

SANDERS-BROWN CENTER ON AGING AIMS TO SOLVE THE RIDDLES OF AGE-RELATED NEURODEGENERATIVE DISORDERS

By William Bowden / Photos by Lee Thomas

Jerry Raider came to Lexington in 1976 when his employer, IBM, transferred the highly skilled engineer from its upstate New York facility to its operation in the Bluegrass. With an undergraduate degree from Purdue University and a master's in automatic control, he specialized in electric motors.

Now retired, Raider might be seen as someone who simply tinkers in his basement workshop long after his high-achieving days at IBM ended, but that characterization would miss the mark by a long shot. He has not stopped searching for the ultimate efficient electric motor.

"I still have this great interest in electric motors, which has gotten me interested in the relationship between motors and generators," Raider says. "A possible application I've come up with is a generator in a wind turbine. I hope to get a patent on my idea."

With all that in mind, it might surprise people to learn that Raider has early and very mild cognitive impairment. He is being treated by clinicians with the University of Kentucky's Sanders-Brown Center on Aging, where he also participates in the center's long-term research group.

Center, Jerry Raider, a patient and a research group participant, meets with his doctor, Gregory A. Jicha, left. Janet Raider accompanies her husband.

At the Sanders-Brown Center on the University of Kentucky campus, scientists in the lab and scientists working with patients collaborate as they seek to understand disease processes of the aging brain.

Making a difference

Faculty members and staff at the Sanders-Brown Center are dedicated to improving the lives of people such as Raider through the center's world-class research, the clinical care it offers to all Kentuckians, and its educational outreach programs.

The center, opened in 1979, has earned an international reputation for its pioneering research on a variety of aging problems, from mild forms of cognitive impairment to the aggressive and ultimately fatal Alzheimer's disease. The facility's Alzheimer's Disease Center, one of only 27 in the nation, is a true gem for UK and Lexington. It was established in 1985 as one of the first 10 such centers to be funded by a National Institutes of Health/National Institute on Aging grant. Faculty members take part in collaborative research with scientists in the nation's other Alzheimer's centers.

The faculty includes professors with advanced degrees from, and prior professional experience at, such prestigious institutions as The Mayo Clinic, Duke University, the University of Chicago, the University of Pennsylvania, Cornell University, Johns Hopkins University, Harvard University, and Vanderbilt University, among others. "We have all come here to Lexington because of the success of the center and because, in horse-racing lingo, we want to back a winner," said faculty member Dr. Peter T. Nelson, who holds an M.D.-Ph.D. degree from Chicago's Pritzker College of Medicine.

Among its major research accomplishments, the center has:

- developed a new understanding of pathological changes in the brain as individuals transition from cognitively normal to impaired;
- defined major risk factors and molecular mechanisms underlying disease progression in Alzheimer's and related dementias; and
- worked with the national Alzheimer's consortium, foundations, and pharmaceutical companies to perform clinical trials of new drugs.

One of the studies conducted under the leadership of the center's founder, Dr. William Markesbery, was the Nun Study, which followed a group of sisters over the age of 75 from the School Sisters of Notre Dame. It examined the autobiographical essays the sisters wrote upon entering the order in their late teens and early 20s. The study concluded that the nuns who showed intellectual vigor through strong language and writing skills early in life were less likely to develop dementia in later life. These groundbreaking results generated considerable publicity for the center at the time. The study also showed that those who expressed positive emotions in their essays lived significantly longer than those with

Adam Bachstetter, PhD, is examining microscopic images of a thin section of mouse brain (right) and nerve cells in a culture (left) to test for specific changes that occur in the brain as disease progresses.

fewer positive emotions. Although the Nun Study is no longer active, the data from the research are still being used in new studies.

Sanders-Brown research takes two forms: basic and clinical. Center director Dr. Linda J. Van Eldik, who earned a Ph.D. from Duke, offered this explanation:

"Basic scientists are usually using some kind of model systems. They may grow cells from the brain of an animal or look at animal models such as mice. They're trying to dissect out mechanisms that might be involved in the disease. Clinical scientists are studying human subjects or human tissue. They are looking at the actual disease or the person with the disease."

Christopher Norris, PhD, and Jennifer Furman, PhD, are preparing brain tissue for microscopic analysis.

In practice the two types of research often overlap. In fact, it's the interaction between the scientist in the lab and the clinical scientist working directly with patients that fuels the entire research engine, according to Van Eldik.

"We typically take something we have discovered in the lab and ask the clinical person, 'Is this mechanism relevant? Is this something you see in your practice?' Conversely, the clinical person can come back to us and say, 'I've noticed this really interesting thing about our patients. Can you try to figure out why that happens?' "

The center speaks of these interactions as "transitions," i.e., the study of movement from normal cognitive aging to cognitive impairment, and "translation," or the application of those findings to intervention strategies.

Nelson and Dr. Gregory A. Jicha, who earned an M.D.-Ph.D. degree from Yeshiva University's Albert Einstein College of Medicine, are currently collaborating on a project that perfectly illustrates the relationship between the two forms of research. Nelson's research on microRNAs has led to an NIH-funded project to see if his findings can make a difference in the treatment of Alzheimer's patients, and Jicha is supervising the clinical trial aspect.

As it celebrates the 35th anniversary of its founding, the center is benefiting greatly from having had a pool of approximately 700 research volunteers for more than 30 years. "Because we have this longitudinal information from over three decades now, we know a tremendous amount of information about what's going on in the brain as people progress from normal to dementia, or stroke, or whatever the disease is," Van Eldik said.

Among the center's other research projects is a study of learning and memory changes in aging adults with Down syndrome, implemented by Dr. Elizabeth Head and Dr. Frederick Schmitt. One of just two such NIH-funded programs in the nation, the study explores new ways of detecting Alzheimer's disease by

Sanders-Brown Center on Aging MILESTONES

1972

Awarded a $1-million grant from the Eleanor and John Y. Brown Jr. Foundation, with matching funds from the state of Kentucky and additional funds from the University of Kentucky, for construction of the Sanders-Brown Research Building.

1979

The 32,000-square-foot Sanders-Brown building opens with three faculty members and a budget of $250,000. Dr. William Markesbery is named director.

1984

Awarded a groundbreaking multimillion-dollar program/project grant from the National Institutes of Health/National Institute on Aging that was continuously funded through March 2014.

1985

Named one of the original 10 NIH/NIA-funded Alzheimer's Disease Centers in the nation. Also became one of 19 initial national Geriatric Education Centers.

1987

Designated a Center of Excellence in Stroke by the Kentucky legislature and named a Kentucky Center of Excellence.

1989

Initiated normal longitudinal control study with subjects followed yearly and agreeing to brain autopsy. Seven hundred volunteers are in the cohort; 1,500 brain autopsies have been performed; and 14,000 biospecimens sent worldwide to support research.

1997

Another 34,000 square feet added to original building at a cost of $9.5 million, with $1.75 million from the NIH and the remainder from private and university funds.

2010

Dr. Linda Van Eldik named the second center director upon the death of Markesbery.

2014

The center now has 19 faculty members, 11 faculty associates, 75 staff members and students, nine endowed chairs/professorships, $8 million in NIH grants, and several gift accounts to support cutting-edge research.

Linda Van Eldik, PhD, director of the Sanders-Brown Center on Aging, and Stephen Scheff, PhD, the associate director, discuss experimental results.

monitoring changes in cognitive function, measuring physical brain changes using MRIs, and profiling protein patterns in the plasma.

In the community

When the Sanders-Brown Center interacts with the community in Lexington and throughout Kentucky, it offers patient treatment at the clinic in Lexington, consultation through telemedicine, and educational outreach programs aimed at the general public as well as at caregivers.

Clinical care includes medicine that can have a limited effect on Alzheimer's disease, clinical trials of other promising medicines, testing for early signs of dementia, and personal and social counseling to help patients deal with the disease. For patients in other parts of the state who cannot come to Lexington for treatment, a telemedicine program links them and their doctors with Sanders-Brown clinicians in Lexington.

Patients and caregivers alike benefit from ongoing educational programs that include caregiver workshops, town hall meetings, and an annual symposium. The center also participates in the African-American Dementia Outreach Partnership, a council of leaders from government, the religious community, and others that meets regularly to discuss the needs of minorities.

Of course, it takes a great deal of money to make the Sanders-Brown Center possible. Funding comes from federal grants (NIH/NIA mainly), UK, philanthropic giving, and the Sanders-Brown Center on Aging Foundation, whose current chair is Steve Matherly, vice president, wealth management advisor with Fifth Third Private Bank. He brings a personal background to his service, having lost his paternal grandfather to Alzheimer's disease.

"The commitment and the quality of the people doing the research at Sanders-Brown is phenomenal," he said. "They could literally work anywhere, and they choose to come here. They are the real heroes. Some people have a hard time believing this kind of research facility is here in Lexington, but the word is getting out. My job is to help with awareness of the center's mission and accomplishments."

The foundation raises funds from other foundations, corporations, and individuals. It sponsors an annual dinner, coming up this fall, that recognizes donors and promotes the values of the center.

Steven Estus, PhD, and Irfan Baig, PhD, look at protein bands analyzed by a technique called gel electrophoresis that separates proteins based on their size and charge. This technique can help identify abnormal proteins isolated from Alzheimer's disease brain extracts.

Building on good news

The good news about Jerry Raider's recent visit to the Sanders-Brown clinic is that his mild impairment has remained just that — mild. "Dr. Jicha and I reviewed my memory on this visit, and it seems like there's not a lot of change, and that's good," Raider says. "I'm happy with that."

Raider is also pleased that his participation in the center's research can help with the long-term battle against age-related diseases of the brain.

"I know that what is going on here right now is helping me, and I certainly hope it can help society even more down the road to get a better understanding of what it's all about," he says. "They have a lot of images of my brain to use in studying the process. Whatever knowledge they can get from that is the least I can do."

"Jerry is a valuable member of our research group," Jicha says. "They come from all walks of life and from a history of very impressive occupations and accomplishments."

Raider is also a prime example of the benefits of staying intellectually active as a means of delaying the onset of aging disorders of the brain, including Alzheimer's disease.

"It's tremendously helpful to stay active the way Jerry is with his continued research on electric motors," Jicha says. "His engagement with creative thinking is one of the keys to brain health over time."

Janet Raider sometimes accompanies her husband to clinic appointments and is a valuable partner in the treatment process.

"Jerry's mother was a patient at the clinic in the 1980s, so we already had a buy-in to the center," she says. "We both feel that the care available here is as good or better than anywhere in the country. We couldn't be living in a better place."

The Raiders' relationship with the center illustrates what Jicha, Nelson, and Van Eldik feel is at the heart of the Sanders-Brown Center's role in Kentucky:

"It's a privilege to serve this community," Nelson said. "There's a synergy between us, where we give of our knowledge and services and the community gives back to us by participating in our research group and by other means of support. That's one of the reasons the center is so strong. The community is backing a winner, and as they keep doing that, we're going to take them places we've never been before." **KM**