

Mind MATTERS

SANDERS-BROWN PUBLICATION ON AGING | *Fall 2020*



 *in this issue*

**SCIENTISTS RETHINK ALZHEIMER'S,
DIVERSIFYING THE DRUG SEARCH**

 Sanders-Brown
Center on Aging



WE ARE FULLY INVESTED



Greetings from the University of Kentucky's Sanders-Brown Center on Aging—considered among the country's greatest enterprises for research into Alzheimer's and related dementias.

Sanders-Brown has had a hand in many important discoveries related to Alzheimer's disease, but we aren't yet finished making our mark. Sanders-Brown faculty continue to make pioneering contributions: characterizing new forms of dementia, identifying early warning signs, even exploring potential new treatments for the disease that affects more than 73,000 Kentuckians.

Yet even as we turn our eyes to the future, we are committed to helping people now. Education and outreach are key components of our mission. We have developed programs that educate the public about prevention and family/caregiver support.

In other words, our heads AND our hearts are fully invested.

I ask you to invest your heads and hearts, too. I welcome your questions about the disease or about the work we are doing. I encourage you to call us for a tour of our facilities and/or to meet our researchers. Above all, I urge you to consider a gift of any size to advance our mission. Without the generosity of people who share our passion, our work could not flourish.

Regards,
Linda J. Van Eldik, PhD
Director, Sanders-Brown Center on Aging

A handwritten signature in black ink that reads "Linda J. Van Eldik". The signature is written in a cursive style.

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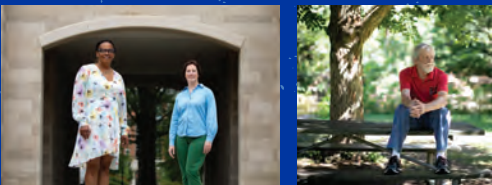


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Scientists Rethink Alzheimer's,
DIVERSIFYING *the* **DRUG SEARCH**



WASHINGTON (AP) - When researchers at the University of Kentucky compare brains donated from people who died with dementia, very rarely do they find one that bears only Alzheimer's trademark plaques and tangles—no other damage.

If they do, “we call it a unicorn,” said Donna Wilcock, an Alzheimer's specialist at the university's aging center. Contrary to popular perception, “there are a lot of changes that happen in the aging brain that lead to dementia in addition to plaques and tangles.”

That hard-won lesson helps explain how scientists are rethinking Alzheimer's.

For years researchers have been guided by one leading theory—that getting rid of a buildup of a sticky protein called amyloid would ease the mind-robbing disease. Yet drug after drug has failed. They might clear out the gunk, but they're not stopping Alzheimer's inevitable worsening.

THE NEW MANTRA: DIVERSIFY.

With more money—the government had a record \$2.4 billion to spend on Alzheimer's research this year—the focus has shifted to exploring multiple novel ways of attacking a disease now considered too complex for a one-size-fits-all solution. On the list, researchers are targeting the brain's specialized immune system, fighting inflammation, even asking if simmering infections play a role.

Some even are looking beyond drugs, testing if electrical zaps in the brain, along a corridor of neural connections, might activate it in ways that slow Alzheimer's damage. Tuesday, doctors at Barrow Neurological Institute in Phoenix

announced they had implanted a pacemaker-like “deep brain stimulation” device into the first of more than 200 patients for an international study.

Most of the fresh starts for drugs are in the earliest research stages. It's far from clear that any will pan out, but “the field is now much more open-minded than it ever was to alternative ideas,” Wilcock said.

BREAKING THE PLAQUE AND TANGLE LINK

No one knows what causes Alzheimer's but amyloid deposits were an obvious first suspect, easy to spot when examining brain tissue. But it turns out that gunk starts silently building up 20 years before any memory loss, and by itself it's not enough to cause degeneration.

Sometime after plaques appear, another protein named tau starts forming tangles inside neurons, heralding cell death and memory loss.

But again, not always: Autopsies show sometimes people die with large amounts of both plaques and tangles, yet escape dementia.

So something else—maybe several other things—also must play a role. One possible culprit: The brain's unique immune cells, called microglia (my-kroh-GLÉE'-ah).





No surprise if you've never heard of microglia. Neurons are the brain's rock stars, the nerve cells that work together to transmit information like memories. Microglia are part of a different family of cells long regarded as the neurons' support staff. But "it's becoming clear they're much more active and play a much more significant role," said Dr. Richard Hodes, director of the National Institute on Aging.

One microglial job is to gobble up toxic proteins and cellular debris. Recently, a mutation in a gene called TREM2 was found to weaken microglia and increase the risk of Alzheimer's. Dr. David Holtzman at Washington University in St. Louis took a closer look—and says microglia may be key to how the amyloid-tau duo turns toxic.

In donated human brains, his team found more tau tangles clustered around amyloid plaques when people harbored microglia-weakening TREM2 mutations. The researchers altered the TREM2 gene in mice and seeded their brains with a little human tau. Sure enough, more tangles formed next to plaques in mice with weak microglia than in those with functional immune cells, they recently reported in *Nature Neuroscience*.

Why? Normal microglia seem to restrict amyloid plaques, which limits damage to surrounding tissue—damage that can make it easier for tau to take hold, he explained.

While it was known that amyloid buildup drives tau tangles, "we never had a good clue as to how it is doing that," Holtzman said. The new findings "would argue that these cells are sort of a missing link."

Separately, biotech company Alector Inc. has begun first-step patient testing of a drug designed to boost TREM2 and better activate microglia.

THE GERM CONUNDRUM

Could gum disease or herpes be to blame? The idea that infections earlier in life could set the stage for Alzheimer's decades later has simmered on the edge of mainstream medicine, but it's getting new attention. It sounds weird, but both the germ that causes gum disease and different strains of herpes viruses have been found in Alzheimer's-affected brain tissue.

Researchers in New York are testing the herpes drug valacyclovir in 130 people with mild Alzheimer's who have evidence of infection with certain herpes strains.

And Cortoxyme Inc. is enrolling more than 500 early-stage patients around the country to test a drug that targets potentially neuron-damaging substances produced by gingivitis bacteria.

Whether the germ theory is a worthwhile pursuit was hotly debated at an international Alzheimer's Association meeting in July. One skeptic, Dr. Todd Golde of the University of Florida, cautioned that germs' mere presence doesn't mean they caused dementia—they could be a consequence of it.

Still, a 2018 study from Taiwan offered a hint that treating herpes infection might lower later dementia risk. And a U.S. study found certain herpes viruses affected the behavior of Alzheimer's-related genes.

"Maybe these are just opportunistic pathogens that have space to spring up in the brains of people affected with Alzheimer's disease," said Benjamin Readhead of Arizona State University, who co-authored that U.S. paper. But, "it looks at least plausible that some of these pathogens are capable of acting as accelerants of disease."

A COMMON DENOMINATOR

One key commonality among emerging Alzheimer's theories is how aggressively the brain's immune system defends itself—and thus how inflamed it becomes.

Inflammation is a normal part of the body's response to illness and injury, one method of fighting infection or healing wounds. But when inflammation is too strong, or doesn't go away, it's like friendly fire that harms cells. Remember how some people have lots of plaques and tangles but no dementia? A few years ago Massachusetts General researchers found strikingly little inflammation surrounded all the gunky buildup in the resilient brains—but the Alzheimer's-affected brains harbored a lot.

Research since has found similar inflammatory effects with other forms of dementia—like vascular dementia, where tiny blood vessels that feed the brain are lost or blocked, and dementias caused by Lewy bodies or other toxic proteins. A growing list of genes linked to inflammatory processes also may play a role.

A handful of drugs are being explored in the quest to tamp down inflammation's damaging side without quashing its good effects. Take those microglia, which Holtzman said "may be a two-edged sword."

Early on, before there's too much plaque, revving them up may be good. But later on, a hyperactive swarm around growing plaques spews out inflammatory molecules.

In addition to their immune system job, microglia also secrete molecules that help nourish neurons, noted Kentucky's Wilcock. The goal is to restore the natural balance of a healthy brain's environment, she said, so microglia "can perform their essential functions without damaging surrounding tissue."

AMYLOID'S STILL IN THE PICTURE

All those drug flops weren't a waste of time.

"Every time there's a failure it's absolutely clear that we learn a lot," Emory University neurologist Dr. Allan Levey recently told the government's Alzheimer's advisory council.

One lesson: Timing may matter. Most of the failed anti-amyloid drugs were tested in people who already had

at least mild symptoms. Some studies seeking to prevent memory loss in the first place still are underway. Several anti-tau drugs also are being tested.

Another lesson: Most people have a mix of different dementias, which means they'll need a variety of treatments.

“.....
Now we have an opportunity, a real opportunity, to expand and try all these avenues,” said Alzheimer's Association chief science officer Maria Carrillo.
“The triggers as we understand them are broad.” ■

.....
AP Chief Medical Writer Marilyn Marchione contributed to this report.



About DONNA

BIRTHPLACE

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EDUCATION/TRAINING

BSc Pharmacology
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Postdoctoral fellow
Duke University, Durham, NC

JOINED SANDERS-BROWN

2011

RESEARCH FOCUS

Vascular contributions to cognitive impairment and dementia.



healthy LIFESTYLE HEALTHY brain



1 in 3

cases of dementia could be prevented by addressing these

LIFESTYLE FACTORS

What is good for the heart, is good for the brain. We have heard this for many years, but now the science is backing this up. With new research emerging every day, we are finding that activities like exercise, a healthy, Mediterranean-style diet, and controlling blood pressure and cholesterol can all have positive impacts on the brain's ability to maintain healthy functioning as we age.

1



Take care of your heart



INCREASE

Education
Physical Activity
Social Contact



DECREASE

Hearing Loss
Hypertension
Obesity
Smoking
Depression
Diabetes

2



Be physically active

3



Follow a healthy diet

4



Challenge your brain

5



Enjoy social activity

While physical exercise is good for the heart and brain, we also know that exercising our brains is a great way to protect them from age-related cognitive decline and dementia. So, pick up a crossword puzzle, take a cooking class or try to learn a foreign language.

Try something new, and work out your brain!





PATIENT-FOCUSED FOR A CURE

Clinical trial volunteers see multi-fold benefits while helping advance a cure for Alzheimer's disease

The UK Alzheimer's Disease Research Center (UK-ADRC) at the Sanders-Brown Center on Aging (SBCoA) has a simple, unofficial motto, according to Gregory Jicha, MD, PhD, professor in the UK Department of Neurology and director of the Clinical Core at the UK-ADRC. "We do not have research participants. We have patients who take experimental medicines." The distinction is a subtle but important one. "When you say 'research participants,' research comes first and the person comes second. But when you say 'patient who takes an experimental medicine,' that patient is always number one, and the science has to take a second seat to that," explains Dr. Jicha.

A focus on patients and finding a cure is the motivation behind the clinical trials program at SBCoA, which seeks to understand the aging process and age-related brain diseases.



Gregory Jicha, MD, PhD





One such patient is Eva Elam. A 75-year-old retired occupational health nurse, Elam considers herself fairly healthy. She stays active by volunteering and doing water aerobics. But, Elam has a family history of Alzheimer's disease and dementia. Her mother, brother and several cousins all suffered from it.

"I cared for my mother at home until I couldn't care for her anymore," she says. "It takes such a toll on the family, and I guess that is what triggered me to want to volunteer for Sanders-Brown."

Shortly after Elam retired in 2012, she saw an ad in the newspaper for a clinical trial at SBCoA, and she and her husband volunteered. They did not qualify for that study but were referred to another one and have been participating in trials ever since.

A STUDY FOR EVERYONE

The research program at SBCoA translates research from the laboratory into practice. A part of SBCoA, the UK-ADRC is one of 10 original Alzheimer's Disease Research Centers funded by the National Institutes of Health and draws patients not only from across Kentucky, but the region. In partnership with several national and international consortiums and pharmaceutical companies, the center has access to the world's leading clinical trials on Alzheimer's disease and related disorders.

"I am really working to find cures for these diseases and when a cure is found, we will be part of that cure here at the University of Kentucky," says Dr. Jicha.

The center has two clinical research focuses: healthy brain maintenance as people age and interventions for memory problems associated with Alzheimer's disease or related disorders. "We typically have some studies along the cognitive continuum for everyone. So, there's usually some sort of prevention study, some sort of mild cognitive impairment study and some Alzheimer's disease study," says Shani Bardach, PhD, assistant professor and director of clinical trials outreach and recruitment.

VOLUNTEERING FOR SELF AND OTHERS

Elam has participated in five or six trials. She is part of the Longitudinal Study (see related article) and is currently enrolled in the INCREASE Study.

The INCREASE Study looks at the effects of changing medications that may be inappropriate for older adults on the onset of memory and thinking problems caused by Alzheimer's disease or related disorders. Elam's participation has included meeting with a pharmacist and nurse practitioner who made medication recommendations to her doctor.

"Frankly, they have been great. One of the medications I had been taking for years was causing so much mouth dryness. So, I just take another one, the same medication, but in a lower dose and extended release. It was a miracle," she says.

Although her cognitive abilities are currently normal, given her family history, Elam is concerned about the potential for future decline. Volunteering for clinical trials has helped her understand the importance of doing small things to maintain her health. She is managing her weight, exercising, keeping her brain agile and staying socially active. "I'm doing all the things they tell you will help you at least delay it," she says.

Staying involved at SBCoA is also giving her a level of monitoring and attention she knows she would not be getting from routine medical visits. This is one of the reasons she continues to volunteer. "If they see any signs coming on, they will tell me. That is my selfish reason. The other reason is that it makes me feel good to know that I might be helping find a cure for this," she says.

Volunteer participation is necessary to make a difference, says Dr. Bardach. "I think one of the biggest things is just recognizing that that's how we learn anything, recognizing the important role that participants play in helping develop better ways to prevent and treat Alzheimer's disease."

Dr. Jicha believes it is not just about this generation but "the ability to go beyond, the ability to create the legacy for our children and our children's children, that they inherit a world without Alzheimer's disease," he says.

Elam hopes others will take an interest.

“.....
Everybody needs to feel needed. And I think that's one of the reasons that people would find it rewarding is the fact that you are volunteers, you are needed.” ■



SANDERS-BROWN

RESEARCH *by the numbers*

DID YOU KNOW?

Sanders-Brown Center on Aging researchers support research in the fields of **cardiovascular, cancer, diabetes and obesity, genetics, social work, and pharmacy**, as well as conducting their research on Alzheimer's disease and dementia.

42

CLINICAL TRIALS

in prevention and treatment of Alzheimer's disease and related dementias between **2015 and 2020**

MAJOR RESEARCH AREAS INCLUDE

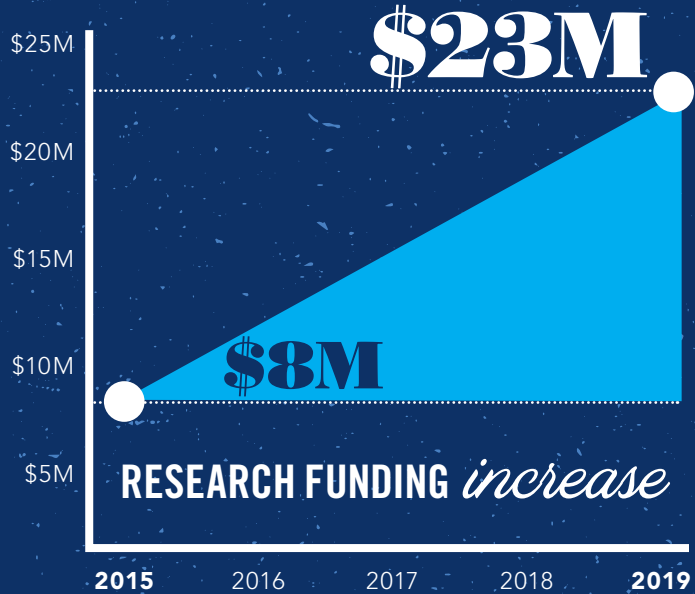
Inflammation in Dementia

New **Biomarkers**

Causes of Dementia that **Mimic** Alzheimer's disease

Developing **New Therapies**

Genetic & Environmental **Risk Factors**



BETWEEN 2015 & 2020

15,567

 SAMPLES
to

50

 LABORATORIES
at the University of Kentucky.

SANDERS-BROWN CENTER ON AGING
RESEARCHERS ACCOUNTED FOR ALMOST

10%

 of the entire
College of Medicine
research funding
received in 2019.



Student PROFILE

WRITTEN BY HILLARY SMITH | PHOTOGRAPHY BY MARK CORNELISON



COURTNEY KLOSKE

As a doctoral candidate at the University of Kentucky's Sanders-Brown Center on Aging, Courtney Kloske finds motivation in studying Alzheimer's disease mainly through her experiences in volunteer work. This motivation began during her undergraduate studies when Kloske was a member of Sigma Kappa Sorority, where the main philanthropic focus was the Alzheimer's Association.

"I've seen the connection people in my sorority had to Alzheimer's disease and saw how much the disease affected them. I thankfully don't have that family connection, but I could see how much it impacted those around me. The way I felt I could contribute to the disease was through research, so I felt like that would be a path I should take in graduate school. Then coming here, it felt like this was meant to be."

Kloske joined the Wilcock lab at the University of Kentucky in 2018 to work on her doctoral degree in the Department of Physiology. Her research focuses on Alzheimer's disease and the role inflammation plays with disease progression through the lens of genetic risk factors.

In addition to her research, Kloske remains involved in the community—a core value she picked up during her time in college. One of her roles outside of the lab is being the Alzheimer's Association ambassador for public policy for her congressional representative. Kloske and her team tirelessly advocate for increases in Alzheimer's disease research funding and improved legislation to help patients

and caregivers. Her first-hand connections with the local community also are shown through her work as a community educator with the Alzheimer's Association.

“.....
I've been able to talk with patients and caregivers, getting to know their stories, and they are the main motivator for my research. Being able to make these connections and hear the stories of these people helped me see how awful this disease is and that this is the way I can give back to their communities.”
.....

Kloske says one of her favorite memories as a member of Sanders-Brown is from the Walk to End Alzheimer's, held in Lexington to raise money for the Alzheimer's Association. "We are all fighting for the same thing—but being able to see people donate, raise money and show up for our team ... showed that they don't just care about the science. They care about actually curing this disease."

Through her time at Sanders-Brown, Kloske says she has learned the importance of working in a collaborative and engaging environment. Due to that and her experiences volunteering with the Alzheimer's Association, Kloske plans to pursue a career in science leadership for Alzheimer's disease once she completes her doctorate. ■



Patient & CAREGIVER

WRITTEN BY RENA BAER | PHOTOGRAPHY BY MARK CORNELISON



LOOKING FOR ANSWERS

When Micki Hillgen's life partner, Jackie, was diagnosed at age 59 with early onset Alzheimer's six years ago, the two women turned to Sanders-Brown Center on Aging for answers.

"You can go to a neurologist who can look at your brain and give you a diagnosis, but they don't have the Alzheimer's training to tell you what might be helpful unless they specialize in that field," says Hillgen. "Going to Sanders-Brown gives you access to those experts."

It also provided the two women the opportunity to participate in Sanders-Brown's internationally known Longitudinal Study, which follows volunteers over their

lifetime, usually from age 70 on, examining cognitive changes related to aging, and concludes with a brain autopsy to further research those changes.

One of the original Alzheimer's Disease Research Centers funded by the National Institutes of Health, Sanders-Brown began the study in the 1980s and by the end of the decade was following a large group that has since grown upward of 700 people. "We thought that while it might not benefit us short term, it would benefit a lot of others long term, and the fact that participating allows access to some of the best experts in the field made it a foregone conclusion that we wanted to be a part of their research," says Hillgen.

Every year they return for a three- to four-hour panel of neurological tests. In addition to cognitive function and memory, researchers examine biomarkers, neuroimaging, bloodwork, tissue samples, DNA, genetics and inventory the medications they are taking, according to Dr. Peter Nelson, an experimental neuropathologist at Sanders-Brown who focuses on Alzheimer's disease.

The results have yielded incredible insights into the dementia continuum, from normal cognition through severe dementia and cognitive impairment. The findings are helping researchers figure out who is more at risk for developing dementia and how to better treat Alzheimer's disease in its earlier stages, before regions of the brain become too degenerated for the medications to be useful.

Participants in the Longitudinal Study who develop Alzheimer's often want to do everything they can to slow down the disease, says clinical research assistant Justin Barber. "So that may mean getting into a clinical trial or starting a regimen of the established medications that can help with memory and thinking," says Barber.

"We tend to do this more aggressively than you might see in the primary care setting because these drugs that are available don't necessarily alter the disease, but they can extend that period of time people can think clearly and remember things and make new memories. They can decide how they want to be cared for and how they want to live in the event they don't have the capacity to make those decisions for themselves."

Jackie, after overcoming a few reservations, became involved in a separate clinical drug trial through the University of Kentucky that Hillgen says seems to be helping.

"Getting Jackie on the medication early [in the progression of Alzheimer's] seems to have slowed down the decline of her short-term memory, though she has had executive function and cognitive thinking loss," she says. "I think people are reluctant in joining a clinical trial or research study, thinking that they'll lose control and have to do something that they don't want to. Jackie had that fear initially. But it's not that way. You retain your freedom of choice; if you don't want to do something, you don't have to."

Today's drugs are more focused on trying to prevent the damage in the first place, says Dr. Nelson. "That means that a cohort like ours, which is based upon a large number of older individuals who have been carefully followed, we know who is at risk for developing dementia, and we know who the candidates are for drug trials," he says. "That allows us to have the highest level of research participation in clinical trials in the country."

After every visit for the Longitudinal Study, the participant's data is reviewed among the group of medical professionals in Sanders-Brown, and if there are concerns over changes in memory and thinking, they are contacted and asked whether they want to follow up with an appointment, says Barber.

Hillgen says that additional appointment has been important in helping them manage Jackie's symptoms. She had noticed Jackie's anxiety levels increasing and was able to talk about medication adjustments that might help at her last appointment. The pair, who have been together 45 years, have always loved to travel, but the anxiety has made it more difficult. Still, they plan to take their usual trip to Indian Rocks Beach in Florida and watch the dolphins and manatee swim, with Hillgen knowing they are managing the best they can.

“.....
It's very comforting to me as a caregiver to know I have people who are supportive of both the caregiver and the patient,” says Hillgen.
“I trust the information I get from the people at Sanders-Brown and at UK, and that they are going to be there when I need something from them.”
.....

In return, Hillgen says, they are happy to participate in research studies and donate their brains to Sanders-Brown's autopsy program, which is world renowned and receives requests for samples from around the world to further study Alzheimer's.

"We agreed to donate our brains, which I think is awesome," says Hillgen.

Dr. Nelson says research, including the autopsies, has helped them to discover that there is no garden variety of dementia, and treatment approaches need to be adapted depending on the specific cause of dementia, much like what scientists discovered about cancer in the 1990s.

"One scientific phenomenon has become clear: Brain changes in the impaired individual are much more complicated and you can have more than one disease," he continues. "There are hundreds of different molecular signatures, each with its own natural history and different potential to be manipulated by different drugs. And it's not until you grapple with that complexity that you have any hope of changing the course of that disease."

This discovery, Dr. Nelson says, provides a lot of optimism. "We have a great chance of cracking the case and developing the first therapies for these diseases." ■





Patient SUPPORT

WRITTEN BY LYNN DAVY | PHOTOGRAPHY BY MARK CORNELISON

SOCIAL WORKERS: AT THE HEART OF IT ALL

Sanders-Brown's social workers help patients and their families handle health and research demands

At the center of much of what the Sanders-Brown Center on Aging does in Kentucky and on the national brain health research front, are two social workers who keep in touch with the cluster of patients and families who provide the important medical information needed to advance brain science in the U.S.

Social workers Julia Johnson and Kelly Parsons work with hundreds of patients and families who come to Sanders-Brown for help navigating an Alzheimer's, dementia or other cognitive disorder diagnosis. They also play a role in keeping the center's Alzheimer's clinical core work on track. Since 1985, Sanders-Brown has been collecting patient data as part of a longitudinal study on Alzheimer's disease sponsored by the National Institute on Aging. The center also manages clinical trials for new medications and techniques to maintain optimal brain health.

When a trial participant visits the center for his or her checkup, the appointment can take several hours. Johnson and Parsons, along with nurse practitioners, psychometricians and nursing assistants, help to manage the visits and talk patients and their families through the next steps in treatment and care. They also help families find support and resources in their community, which can be difficult in rural areas of the state.

"I couldn't ask for a more rewarding job," said Julia Johnson, MSW, who has worked at Sanders-Brown for six years. "The families we work with endure so many challenges, and so if I'm able to make their lives less stressful, I count it as a major blessing."

Johnson's colleague, Parsons, who has been part of the Alzheimer's Disease Clinical Core Center at Sanders-Brown for three years, is also passionate about her work.

"I wanted to work with older adults because I realized that they go through the most loss," said Parsons, CSW. "They lose their friends, their spouses, their physical and sometimes mental abilities, and, eventually, for most, their homes. When I started working with Alzheimer's patients, I saw that it's not only the person with the diagnosis that is affected, but also the people who love them. There's no cure for Alzheimer's disease, so how do you ensure autonomy and self-determination of the person with the diagnosis? What is the best way to provide support?"

Parsons grapples with these questions, and more, on a daily basis.





CONNECTING WITH FAMILIES, CAREGIVERS

Families dealing with a dementia or Alzheimer’s diagnosis are often desperate for information and resources. At Sanders-Brown, social workers meet with families individually as often as possible so that they “feel heard.” When working with a family, Parsons and Johnson encourage caregivers to create a plan for how to best care for their father or mother, brother or sister, aunt or uncle. They provide education on the stage of the disease and find out what behavioral symptoms the person is experiencing. Discussions can include instructions on medication safety, driving intervention, wandering, or aggressive behavior management. Depending on the stage of disease, social workers talk to families about home safety plans, advanced-care and end-of-life care directives, and Power of Attorney directives.

“.....
To know that someone is paying attention and that possible relief is available is huge for many of our families,” said Johnson.
.....

The social workers also plan quarterly outreach meetings and webinars for families who live in rural areas of the state. Since the start of the COVID-19 pandemic, all outreach meetings have shifted to webinars.

Outreach meetings are often led by Dr. Gregory Jicha, MD, PhD, Professor of Neurology and Associate Director of the Alzheimer’s Disease Research Center at Sanders-Brown Center on Aging. Social workers also attend these meetings to connect families with local resources. They talk with caregivers about the importance of taking a break from their duties of looking after a loved one with a cognitive disorder.

Sanders-Brown partners with the Alzheimer’s Association for the rural community caregiver webinars. The sessions focus on different topics involving Alzheimer’s and dementia, and provide rural residents with a much-needed forum to ask specific questions about caring for someone with a cognitive disorder.

“The webinars are an easy way to make sure people, even in rural areas, are connected to experts,” said Johnson. “Rural caregivers can feel isolated, especially if other family

members aren’t supportive. There are so many challenges in caring for someone with Alzheimer’s—they lose their ability to taste, they lose their ability to say that they have a tooth ache, or some other problem, and they become agitated, but no one knows why.”

HELPING FAMILIES DECODE ALZHEIMER’S

Johnson and Parsons say that caring for an Alzheimer’s patient can mean a lot of “detective work,” in that family members have to piece together clues to understand the root cause of a specific behavior. Patients with dementia or Alzheimer’s also tend to have a certain hour of the day, usually near sunset, when they become agitated. Social workers, with help from Sanders-Brown nurses, work with families to calm patients.

“Often it’s a matter of helping the patient connect with something from their past,” said Parsons. “With one patient, it was songs from 70s rock bands; another patient, it was talking about cars because they used to love working on vintage cars.”

When working with families, social workers often use the Best Friends Approach, a relationship-centered method to dementia care that builds on the essential elements of friendship—respect, empathy, support, trust, and humor. The Best Friends Approach was created by Sanders-Brown’s first social worker, Virginia Bell, and it is recognized around the world as one of the most effective ways to care for someone with dementia or Alzheimer’s.

Working with Dr. Jicha in the Alzheimer’s Disease Clinical Core, there is never a typical day, the social workers say, but they appreciate the sense of working together with other experts toward a common goal.

“Everything we do is 100 percent patient-first,” said Parsons. “We’re all working together to help our patients fight this disease, but we’re also fighting for our own families and future generations. We are getting closer and closer to a cure, but will it be a pill or a vaccine? I don’t know, and that’s why I’ll come back to work tomorrow and the next day and the next.

“This disease is devastatingly isolating, and we will be here for patients diagnosed and their loved ones to ensure they know they are not alone.” ■



Faculty PROFILE

WRITTEN BY HILLARY SMITH | PHOTOGRAPHY BY MARK CORNELISON



PETER NELSON

MD, PhD



Dr. Pete Nelson is an experimental neuropathologist focusing on Alzheimer's disease. The motivation behind his work is personal. His own grandmother, Sylvia "Tib" Becker, died with Alzheimer's disease and he says his mother grew terrified of the disease. "It gives me purpose in life to attack that."

That, coupled with his experiences once in a lab in medical school, set him on his life's mission of helping find a cure. "It absolutely galvanized me," explained Nelson. "It is like a pandemic that has been going on for years and it is going to keep going until we find a cure." He understands the disease is not only harsh on the patients themselves, but also on caregivers.

Dr. Nelson and his family moved to the Bluegrass State in 2006 after spending time in Philadelphia. He says he loves being at the Sanders-Brown Center on Aging because there are many people that have the same passion, they work collaboratively, and have a long track record of success. Dr. Nelson likens the prestige of the center to another

powerhouse that calls Lexington home—University of Kentucky basketball. "There is a talent magnet here that is just as good as Coach Cal's, and I don't just say that... that is what brought me here."

He wears numerous hats at the University of Kentucky and the Sanders-Brown Center on Aging. Dr. Nelson is the Director of the Neuropathology Division of the Pathology Department, and he also directs the brain bank and the Neuropathology Core of the University of Kentucky Alzheimer's Disease Research Center. He is responsible for the Alzheimer's Disease Research Center brain autopsies. These autopsies are performed with profound respect for the volunteers who are enabling researchers to combat this dreadful disease. "Research volunteers make this place tick," said Dr. Nelson.

Respect for research volunteers is Dr. Nelson's top goal throughout his work. He says the second goal is to cure the disease and thirdly he is striving to be the best in the world.





In addition to duties as a neuropathologist, Dr. Nelson is an experimental researcher focusing on the molecular neurochemistry of the human brain—in health and in neurodegenerative disease—particularly in the context of RNA biology. The study of small regulatory RNAs is a relatively new and unexplored research field with much potential. Dr. Nelson’s work has focused upon microRNAs (miRNAs). He invented new techniques to analyze and manipulate these small molecules and studies how miRNA biology is altered in neurodegenerative diseases. Dr. Nelson seeks both to understand how miRNAs contribute to disease pathogenesis, and to explore how specially-designed RNAs may be applied for therapeutic strategies.

Work in Nelson’s lab has led to various important discoveries in the fight to find a cure. A multi-institutional study co-led by Dr. Nelson defined and established criteria for a new neurological disease called primary age-related tauopathy (PART). Patients with PART develop cognitive impairment that can be indistinguishable from Alzheimer’s disease, but

lack amyloid plaques that are a hallmark of Alzheimer’s disease. Awareness of this neurological disease will help doctors diagnose and develop more effective treatments for patients with different types of memory impairment.

Most recently, in the spring of 2019, an international group of experts led by Dr. Nelson characterized a different form of dementia that is now called LATE. The discovery was recognized as one of the top science stories of 2019 by Discover magazine. It also was named the number one advancement in 2019 in the field of neurodegenerative neuropathology.

The study came about after noticing that a large number of people who died in advanced age had symptoms of dementia without the telltale signs of amyloid or another common culprit, tau, in their brains at autopsy. Emerging research seemed to indicate that the protein TDP-43 contributed to that phenomenon.





“More than 200 different viruses can cause the common cold,” explained Dr. Nelson. “So why would we think there is just one cause of dementia?”

With that question in mind, Nelson and the group set out to define diagnostic criteria and other guidelines for advancing future research into this newly named dementia, called LATE.

“Our ongoing work is aimed at stopping or reversing problems in thinking and memory in the elderly. It turns out that the diseases that cause these symptoms are fairly complex. Workers at Sanders-Brown have worked for decades to tease out what causes those diseases and possible therapeutic strategies,” said Nelson, who notes that this work has always been important but more so now than ever as the population is aging. “Now that we recognize LATE, we can not only generate therapies for this disease, but we can now better perform clinical trials for Alzheimer’s disease as well. Since the University of Kentucky has an extraordinary group of research volunteers and great researchers, we are uniquely situated to perform these studies.”

LATE, which tends to appear in the oldest-old, may seem the same as Alzheimer’s to the lay person, but the disease inside the brain looks very different. The incidence of LATE is almost as prevalent among the oldest-old as Alzheimer’s.

Dr. Nelson and the group’s work established that, like Alzheimer’s disease, LATE affects multiple areas of cognition, ultimately impairing activities of daily life, but it appears that LATE progresses more gradually than Alzheimer’s. However, LATE combined with Alzheimer’s—which is a common combination—appears to cause a more rapid decline than either would alone.

Nelson likens this work to Benjamin Franklin’s “discovery” of electricity.

“People had seen lightning before of course, but Franklin helped formalize a concept that augmented our ability to study electricity,” he said. “By developing a sense of scientific focus around these data, we hope to jump-start a broad field of work to advance our understanding of this form of dementia and, ultimately, to open new opportunities for treatment.”

Most importantly, Nelson adds, it’s time to stop thinking of dementia as a “one-size-fits-all” disease.

“LATE probably responds to different treatments than AD, which might help explain why so many past Alzheimer’s drugs have failed in clinical trials,” he said. “Now that the scientific community is on the same page about LATE, further research into the ‘how’ and ‘why’ can help us develop disease-specific drugs that target the right patients.” Since the discovery, Nelson and others at Sanders-Brown have acquired the first clinical trial for LATE. He calls it an opportunity to help the world.

To make these discoveries, researchers need the funding and flexibility to pursue new leads, Nelson said. Science occurs at the edges, and typical grants, which are awarded for a specific project or purpose, don’t give researchers freedom to innovate and explore new ideas.



About PETER

BIRTHPLACE

Washington, D.C.

EDUCATION/TRAINING

BA in Biology and Economics
Rice University

MD—University of Chicago

PhD—University of Chicago

AP Residency
University of Pennsylvania

Neuropathology Fellowship
University of Pennsylvania

JOINED SANDERS-BROWN

2006

RESEARCH FOCUS

Neuropathology

Endowed positions do. The R.C. Durr Foundation Chair in Alzheimer’s was established in 1998 to further dementia research. Though Durr died in 2007, his legacy lives on through his foundation, funded by his estate. Nelson has held the Durr position since 2012. He uses the endowed funds to do research that is not “cookbook.” It allows him to explore new ground and be more innovative in his research.

“

What I am doing is not abstract,” Nelson said. “My mother’s mother had Alzheimer’s, and she saw how devastating the disease could be. I am privileged to work every single day to find a cure for a disease that haunts my own mother.” ■



IN THE *Community*

WRITTEN BY HARDIN STEVENS | PHOTOGRAPHY BY MARK CORNELISON



COMPASSION. GUIDANCE. SUPPORT.

Helping families within the African-American community who are affected by memory loss and dementia.

The Sanders-Brown Center on Aging is acutely aware of the overwhelming numbers and projections for those whose lives will be touched by Alzheimer's disease in the future. As elsewhere, that number is set to increase in Kentucky unless treatments and cures are discovered. Alzheimer's disease knows no distinction in who it afflicts. This can be clearly seen in the African-American community.

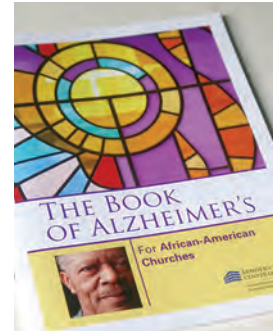
African Americans make up the largest minority group in Kentucky at approximately 8.5% of the population. Yet African Americans are twice as likely to be diagnosed with Alzheimer's disease and other dementias. No single reason for this higher risk has been identified. Many doctors speculate that health disparities (including access to health care), education, income and stress levels contribute. Delaying medical intervention due to cultural stigmas, such as believing that memory and thinking problems are "normal" for older people, plays a role as well. In addition, the African-American community has higher rates of high blood pressure, diabetes and other conditions that raise the risk for dementia.



“
By raising awareness of memory and thinking issues and their impact on families, we inform African-American communities in Kentucky about the many free services that Sanders-Brown provides in the battle against Alzheimer's disease.”

.....
—**Derrick Hord**, Community Outreach and Engagement Director





Due to this high rate of Alzheimer's disease and related dementias, Sanders-Brown has been intentional in reaching out to the African-American community, especially to churches and faith communities. For many years, Sanders-Brown has worked with leaders and interested individuals through a program called the African-American Dementia Outreach Partnership (AADOP). The mission of the AADOP council is to help us to provide compassion, guidance and support to families within the African-American community who are affected by memory loss and dementia.

THIS COUNCIL HAS THREE MAIN GOALS:

- Increase awareness of Alzheimer's disease through community education.
- Provide culturally sensitive care to patients and support to families at a Memory Care Clinic located in the African-American community.
- Work with churches and community organizations to offer support for family caregivers and provide free memory checkups to identify this disease early on when current drugs are most effective on a person's symptoms.

Out of this partnership came a successful resource, "The Book of Alzheimer's for African-American Churches." This resource is written for church leaders interested in helping families cope with dementia. The manual is designed to share what Sanders-Brown has learned in order to build awareness and support related to Alzheimer's disease in the Lexington/Bluegrass area of Kentucky.

Due to our collective work on the local level in central Kentucky, Sanders-Brown was contacted by the international organization, Balm in Gilead, Inc. On their website, The Balm in Gilead highlights the disparities of Alzheimer's disease in the Black community. "Alzheimer's disease impacts African Americans and Hispanics disproportionately. African Americans are impacted worse being twice as likely to have Alzheimer's. Other health conditions like high blood pressure and socioeconomic factors contribute to the challenges of addressing Alzheimer's in the African-American community. African Americans and minorities are also more likely to be diagnosed with Alzheimer's in the later stages of the

disease or to be misdiagnosed due to other illnesses, a lack of awareness, and a lack of access to appropriate medical care. There is a strong need for more data and information that is specific to the African-American community in terms of not only disease but more research is needed to get a better picture of not only the state of the disease in minority communities but also to identify culturally appropriate strategies to address them." Through this partnership, Sanders-Brown has contributed to the Balm in Gilead's initiatives of Memory Sunday, Healthy Churches and the National Brain Health Center for African Americans. Under the leadership of Dr. Perness Seele, founder and CEO, and Ms. Pamela Price, RN, from Balm in Gilead and our Sanders-Brown team, "The Book of Alzheimer's for African-American Churches" has now been made available nationally and internationally.

Sanders-Brown participated in the Memory Sunday program beginning in June 2017 with 25 churches. Since then, they have worked with many churches in central Kentucky and Louisville. Memory Sunday Weekend is held annually in June. "It is a weekend where we provide local church and faith community leaders resources about dementia and our 'Healthy Brain' Campaign," says Community Outreach and Engagement Director Derrick Hord. "By raising awareness of memory and thinking issues and their impact on families, we inform African-American communities in Kentucky about the many free services that Sanders-Brown provides in the battle against Alzheimer's disease." Free memory screens are a critical part of the weekend, and Sanders-Brown encourages all people of color to join our "fight" by considering involvement in any of our treatment and research studies. "A breakthrough might just come from one of these demographics," says Hord.

Until there are effective treatments, the Sanders-Brown Center on Aging at the University of Kentucky is committed to continuing its work, research and outreach for all persons affected by Alzheimer's disease, their families and loved ones.



ALZHEIMER'S *in* KENTUCKY

Alzheimer's disease is a growing public health crisis in Kentucky. Without an effective treatment or cure, the impact of Alzheimer's will continue to rise, and the numbers in Kentucky are escalating.

75,000
PEOPLE
AGED 65 AND OLDER
living with Alzheimer's in Kentucky

274,000
family caregivers
bear the burden of the disease in Kentucky

\$803
MILLION
is the cost of Alzheimer's to the state Medicaid program

12.1%
OF PEOPLE AGED 45 AND OLDER
have subjective cognitive decline

\$4
BILLION IS THE
VALUE
OF THE
UNPAID
CARE

312 *million*
HOURS OF UNPAID CARE
provided by Alzheimer's caregivers

These numbers show that a public health approach is necessary to lessen the burden and enhance the quality of life for those living with cognitive impairment and their families.



Faculty PROFILE

WRITTEN BY HILLARY SMITH | PHOTOGRAPHY BY MARK CORNELISON



DANIEL LEE

PhD

Like many others who work at the University of Kentucky's Sanders-Brown Center on Aging, the drive behind Daniel Lee's research comes from a direct impact on his family. Lee shared many things with his grandfather, including a name. While Lee completed his undergraduate degree in chemistry, his grandfather was diagnosed with Parkinson's disease. Due to that, he went on to pursue his PhD degree while studying the disease. His grandfather was later diagnosed with Alzheimer's disease or some form of dementia, leading Lee to focus his postdoctoral training on Alzheimer's disease.

"To me, he was one of the smartest people. He put himself through medical school, served in the army, traveled and navigated a successful career by giving back to his community. I wanted to learn more about this terrible disease."

Lee joined Sanders-Brown in 2019. His primary research centers around neurodegenerative diseases. He shares a lab with his wife, Dr. Maj-Linda Selenica, who also recently joined Sanders-Brown. Lee says his favorite part about Sanders-Brown is the faculty, staff and students.

"Everyone is welcoming, collaborative and selfless. The leadership, including the associate directors, have been extremely helpful. They provide mentorship, are open and exude a genuine desire to see colleagues succeed."

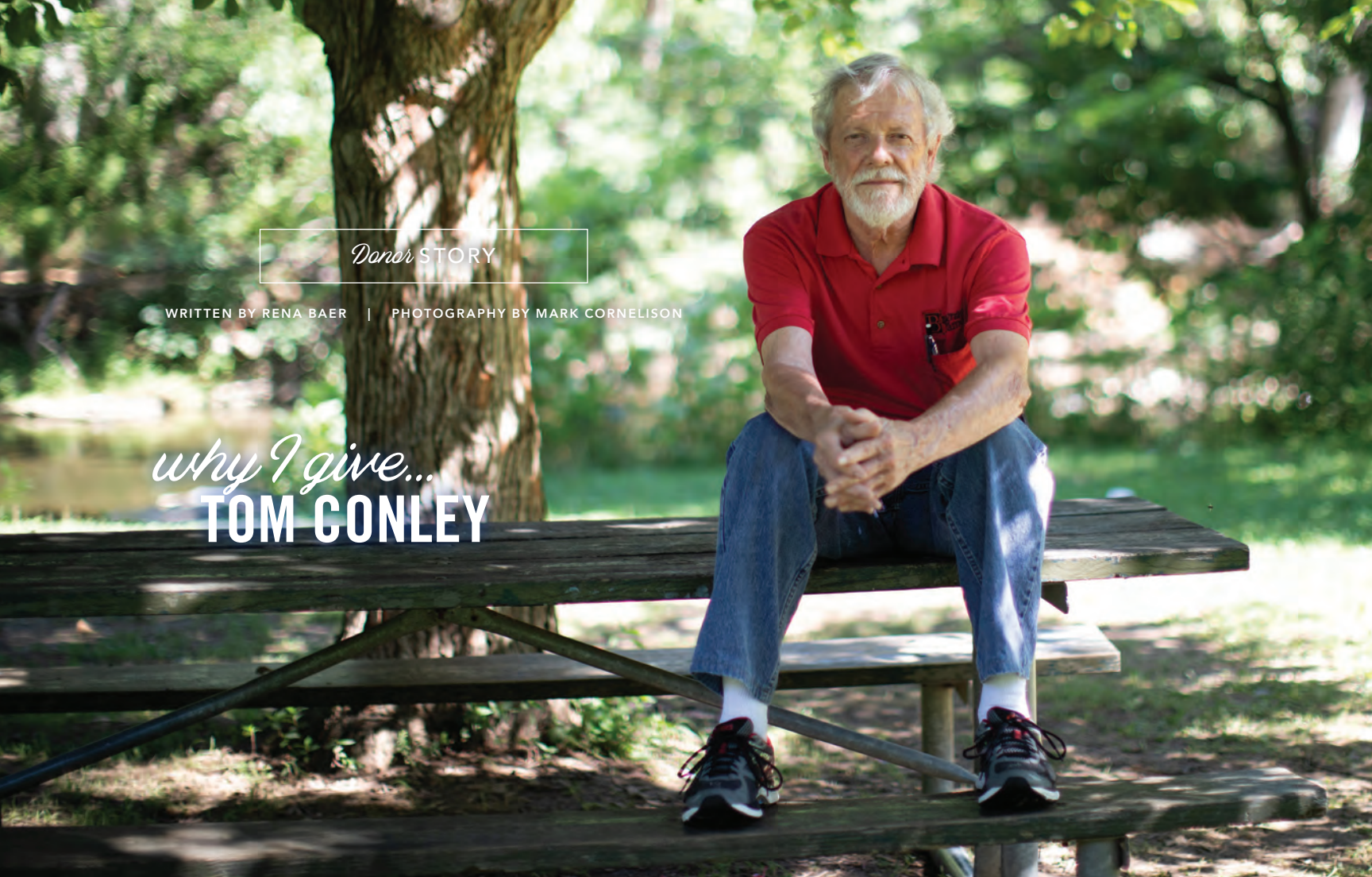
This is why we chose to join Sanders-Brown. A favorite part of my job is the collaborative discoveries with colleagues. Different perspectives provide new understanding to the problems we face in fighting these diseases."

Lee's long-term goal is to develop therapeutics that could eventually lead to safe treatments for Alzheimer's disease or related dementias. He also hopes to mentor and inspire the next generation of independent scientists, particularly those serving in his lab and at Sanders-Brown.

In all of Lee's work, he not only strives to keep his grandfather's memory alive but also others he has met that are impacted by the disease.

“
It's important to talk to patients, various communities and others affected by Alzheimer's disease and related dementias. To hear their stories, and to see the disease up close creates a face to the disease.” ■
.....





Donor STORY

WRITTEN BY RENA BAER | PHOTOGRAPHY BY MARK CORNELISON

why I give...
TOM CONLEY

It took only one appointment at Sanders-Brown Center on Aging Clinic for Tom Conley to observe a notable difference in the care his wife, Nancy, received there. She'd visited a local neurologist in Louisville after Tom noticed she kept forgetting appointments and birthdays. The neurologist diagnosed her with Alzheimer's disease, but the brevity of the appointment had put Tom ill at ease.

On the advice of a friend, he took Nancy to Sanders-Brown at the University of Kentucky, where over the course of an afternoon she underwent tests for both memory and logic, as well as having spinal fluid and blood drawn for analysis. Though the conclusion was the same, that she did have Alzheimer's, Conley noted their meticulous care, their thoroughness, and their willingness to answer questions. He immediately trusted their diagnosis and felt more at ease. So did Nancy, who'd undergone a double mastectomy for breast cancer a year earlier.

The couple, married over 45 years, opted to continue her follow-up care and be part of the research taking place at Sanders-Brown. This included also making the 90-minute trip each way to participate in four separate clinical trials for Alzheimer's drugs. Tom says he doesn't know for sure,

but he credits those drug trials with helping keep Nancy's Alzheimer's at a mild-to-moderate level for six years, until her breast cancer returned and she died in 2014. At the very least, he says, the interest, studies and care provided at Sanders-Brown kept his wife more engaged through a difficult time.

Tom, who at age 80 is still working at the picture-framing shop Nancy started in 1975, continues to be involved with Sanders-Brown. He has volunteered for studies and supports Sanders-Brown through donations. He says he remains involved because he holds out hope Sanders-Brown's research will one day help his two daughters who have a higher genetic risk for Alzheimer's, and if not them, his grandchildren.

“.....
I believe in what they are doing at Sanders-Brown,” says Tom. “The problem they are trying to solve is immense and growing. And if there's anything I can do to help them, I'm all in.” ■
.....



THE SANDERS-BROWN CENTER ON AGING IS A LEADER IN THE FIGHT AGAINST ALZHEIMER'S.

However, in order to continue the fight
and reach the ultimate goal of finding a cure,

we need your help.


**Philanthropy is essential to continue the
groundbreaking and life-changing work of SBCoA.**

To secure the direction of these programs, endowments
are needed to provide core support to make today's
dream tomorrow's reality. We have set a goal of \$10
million to advance our clinical operations/facilities,
expand resources for outreach and education, and recruit
and retain the most talented faculty and staff in the field.

**TO LEARN MORE OR TO MAKE A GIFT
TO SUPPORT SANDERS-BROWN CENTER ON AGING,
PLEASE CONTACT THE UKHC OFFICE OF PHILANTHROPY AT**

859-562-1602





“
It’s important to talk to patients, various communities
and others affected by Alzheimer’s disease and related
dementias. To hear their stories, and to see the disease
up close creates a face to the disease.”

—*Daniel Lee, PhD*