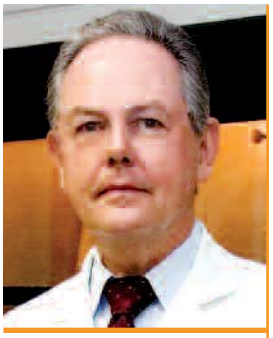
It's Not Just Brain Science

John H. Dougherty, MD conducts research on Alzheimer's disease that may affect 15 million people by 2050.

If asked to explain the word "neuroscience," most of us would likely use the words "brain science" somewhere in our simple description. However, as you might guess, this branch of the life sciences is much more complex, concerning itself with the anatomy, physiology, biochemistry, or molecular biology of the entire nervous system, including the brain, spinal cord, and network of sensory cells throughout the body.

Scientists are fascinated by neuroscience research, in particular studies focused on several well-known diseases—Alzheimer's, Huntington's, Parkinson's. Each of these diseases can significantly impact quality of life, and researchers at the University of Tennessee Medical Center's Cole Neuroscience Center and UT Graduate School of Medicine are making discoveries that can detect, and sometimes delay, their onset.

Research in fighting these crippling diseases starts at the smallest level: the molecule. A research team led by George Kabalka, PhD, professor, Robert H. Cole Chair in Neuroscience, and director, Basic Research, Department of Radiology, UT Graduate School of Medicine, builds molecules that have never existed before to target the causes of these diseases.


George Kabalka, PhD

"We work with physicians and biologists to discover molecules that naturally target organs or diseases," says Kabalka, "and with that knowledge, we can envision how to put a short-lived radioisotope into the molecule, which travels straight to the tumor or diseased area within the body."

That's when imaging, namely positron emission tomography (PET), becomes invaluable.

"Using modern medical imaging, physicians can evaluate the activity level of the disease, which enables them to both diagnose and monitor the disease prior to, during and after treatment," says Kabalka. "We've already successfully used this technology in patients, and with additional medical funding, our research can continue to expand."

The molecules created in Kabalka's labs are used for research in oncology and amyloid diseases and in the fight against Parkinson's and Alzheimer's.

Patients with Parkinson's disease have a decrease in the activity of neuroreceptors in the brain, leaving victims incapable of initiating or controlling movement. Kabalka's team has created isotopically labeled neuroreceptor molecules that travel to the neuroreceptors, and using PET imaging, can show physicians the activity—or lack of activity—in the brain.

Similar research with promising results is being conducted for Alzheimer's.

Alzheimer's disease is a condition that cripples the ability of millions of older Americans to think and manage their lives. However, says John Dougherty, MD, director of the Cole Neuroscience Center, because of the soaring numbers of people with the disease, the search for a cure for Alzheimer's promises breakthroughs in patient care across the board.

"It's a disease that has great impact, because people live for a long time with it and they slowly get worse," says Dougherty. "Because the population of people 85 and older is going to grow tremendously, by the year 2050 there will be 14 or 15 million people with Alzheimer's disease."

This is why researchers at the Cole Neuroscience Center, in the UT Graduate School of Medicine Human Immunology and Cancer Program run by Alan Solomon, MD, in the UT Graduate School of Medicine Molecular Imaging and Translational Research Program headed by David Townsend, PhD, and in Kalbalka's group, are leading several research initiatives focused on Alzheimer's and other neurological disorders.

One of the largest research efforts in neuroscience is just getting under way. A $300 million study of the use of monoclonal antibodies, disease-fighting agents reproduced from a single cell,

to battle Alzheimer's disease is enrolling patients at some 100 sites across the United States, including the University of Tennessee Medical Center. Initially approved for the treatment of about 16 patients in the study, the Medical Center could eventually contribute data on up to 50 patients, Dougherty says.

Researchers believe Alzheimer's disease affects patients' brains through clusters of protein fragments, known as amyloid. It is believed these clusters accumulate and attract other proteins to form abnormal plaques in brain tissue, which cause degeneration. Monoclonal antibodies engineered to neutralize amyloid have been proved to work in laboratory studies.

"In laboratory models," says Dougherty, "the monoclonal antibody produces a spectacular response. It sucks the amyloid out of the brain and improves memory." Early clinical tests were so promising that the FDA approved moving forward with the multi-center trial of the monoclonal antibody.

Solomon's group at the Graduate School of Medicine has been researching amyloid-related diseases—including Alzheimer's, Parkinson's, Lou Gehrig's, Huntington's, type 2 diabetes, amyloidosis, and others—for decades. One recent study reported a link between foie gras prepared from goose or duck liver and the type of amyloid found in arthritis or tuberculosis; another identified a structurally unique protein in a rare dental tumor that may assist in targeting therapy for other cancers such as breast, lung, and gastrointestinal.

Work by Brian O'Nuallain, PhD, a member of Solomon's team, may also be useful in delaying Alzheimer's disease. He discovered an intravenous antibody product that is used as antibody-replacement therapy for patients with autoimmune disease contains naturally occurring human antibodies that bind to A-beta, the protein fragment believed to be the chief culprit in Alzheimer's disease. Antibodies are proteins that attach to foreign proteins and remove or neutralize them.

Dougherty says success in the treatment of other neurological disorders, such as Parkinson's disease, could be models for the fight against Alzheimer's. "The new mantra in Alzheimer's disease is prevention and delay," he says. "If you can put off the symptoms of Alzheimer's disease three to five years, you can decrease the number of people with the disease by half."

And prevention and delay of these diseases ultimately improves your quality of life—for life.

John Yates

Exercise Your Brain

It is always good to exercise your brain. Performing daily brain tests will help keep your brain active and healthy. Try this brain test now:

1. Say the days of the week backwards, then in alphabetical order.
2. Say the months of the year in alphabetical order. Easy? well, why don't you try doing so backwards, in reverse alphabetical order.
3. Find the sum of your date of birth, mm/dd/yyyy. Want more exercise? Do the same with friends' and relatives' date of birth.
4. Name two objects for every letter in your complete name. Work up to five objects, trying to use different items each time.
5. Wherever you are, look around and within two minutes, try to find 5 red things that will fit in your pocket, and 5 blue objects that are too big to fit.

Harriet Vines, PhD

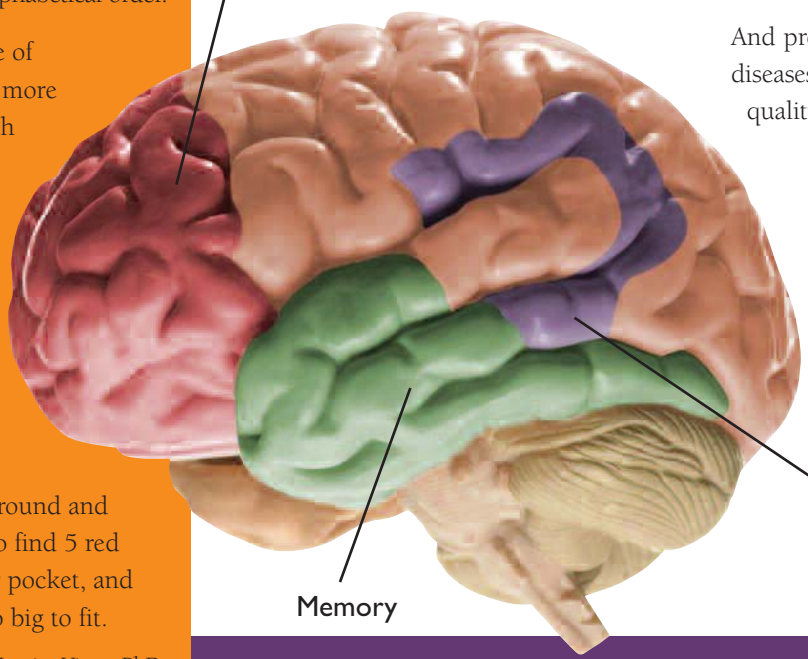


Illustration of the areas of the cerebral cortex commonly affected by Alzheimer's disease.