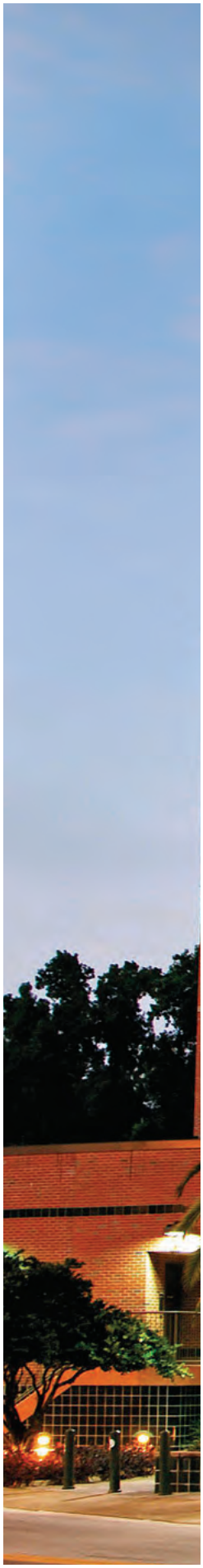
CHECK YOUR HEAD

Brain Institute

A Cure for Brain Cancer Might Come From Within

WRITTEN BY MICHAEL STONE



Along Newell Drive on the University of Florida campus, at the bottom of a rare steep slope in Gainesville, stands an imposing, six-story structure in which minds of great intelligence study the mind, hoping to make life better — or longer — for those suffering from mental illness or injury.

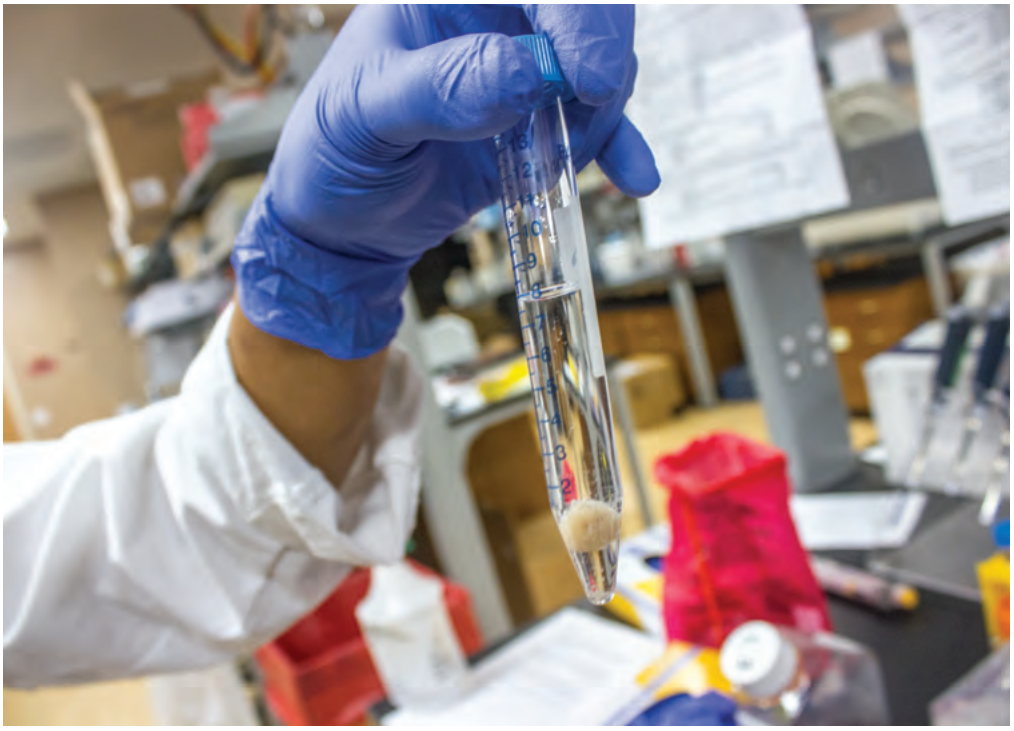
More specifically, research in the 200,000-square-foot building, the McKnight Brain Institute, focuses on memory loss from age or injuries to the brain or spinal cord; brain tumors; drug addiction; and diseases that cause brain degeneration, such as Alzheimer's, Parkinson's and ALS.

Developing solutions for these general categories and their multitudes of sub-problems is a Rubik's Cube of colossal proportion, and research is further complicated, experts say, by the secrets of their causes and even the brain itself.

"The brain is the least understood organ in the human body. I consider it the last frontier of medicine," Dr. Tetsuo Ashizawa, the institute's executive director, wrote to *Our Town* in an email. "In the next decade, further inventions of new technologies, discoveries of new neurobiological mechanisms, and integration of different disciplines and knowledge will advance neurosciences to open the mystery of the brain little by little."

With 50-plus laboratories at the institute and roughly 300 UF faculty members from more than four dozen academic departments involved in its work, lifting particular research projects, current or past, above the rest becomes a near impossible task.


Evelyn F. & William L.
McKnight Brain Institute



(Clockwise, from top left) Yu Long, a UF research scholar in neurosurgery, examines DC cells, part of the immune system, as part of the Brain Institute's brain cancer immunotherapy research. Lab manager Jeff Drake holds tumor tissue samples from patients with brain cancer. Rat brains, like this one, are used in the immunotherapy research.

But there is one niche area of study — brain cancer immunotherapy, or stimulating the patient's body to be a primary weapon in fighting against a tumor — that has particularly blossomed at the institute over the past few years.

Such work is rooted in the 2006 donation of $5 million from the Wells Foundation to UF to establish the Center for Brain Tumor Therapy. Other donations and grants have followed, including another $10 million from the Wells Foundation that brought Dr. Duane Mitchell from Duke University to UF in 2013 to serve as co-director of the center and director of the university's Brain Tumor Immunotherapy Program.

Duke and UF are the only two U.S. institutions studying immunotherapy specifically as a treatment for brain cancer, and when Mitchell came to Gainesville, he brought a team of five other researchers from Duke with him.

"Scientifically, it's very interesting," one of those five, Dr. Catherine Flores, said of using immunotherapy to fight brain cancer. "But also, on a human level, it's a lot more satisfying."

Including those five, Mitchell's lab at the Brain Institute has about 20 researchers studying brain cancer immunotherapy.

While the team believes their research could eventually apply to other cancers and illnesses, teaching the body to fend for itself becomes especially important for brain cancer. The cancer may be in areas necessary to running the body's essential functions, striking out surgery as an option, and bigger tumors often produce additional ones that might be too small to detect.

The most recent published findings from Mitchell's team, in the March issue of the journal OncoImmunology, detail how immunotherapy has proven successful in fighting brain tumors in mice and could be applied to children.

Current treatment for children with brain cancer includes giving them stem cells that replenish their blood cells after chemotherapy destroys them.

In studying mice, the team found that also introducing immune cells familiarized with brain-tumor material helped treat the animals' cancer.

This particular method of immune cells learning to fight brain tumors is called adoptive cellular therapy.

"Your own body is unable to recognize the tumor," said Flores, the study's lead author, "so what we do is essentially take those immune cells and engineer them to be tumor-specific and put them back into you."

In skin cancer, the patient's immune system recognizes it should produce antigens that attack the tumor because blood is always running through the tumor, according to background information on the study from UF Health, the network of the university's medical facilities.

But the brain has a barrier that blocks harmful substances from entering in blood — and this same defense mechanism could be preventing the immune system from recognizing the tumor and thus producing antigens to fight it.

From the mice — which had glioblastoma, an aggressive type

Fernanda Guimaraes, a Ph.D. candidate in biomedical sciences at UF, works with samples at the Brain Institute's brain cancer immunotherapy lab.

of brain tumor — Mitchell's team extracted tumor samples and, outside the body, taught immune cells to attack tumor cells for when they'd return inside.

With the specially trained cells, the mice's bone barrow began to produce more cells that would fight the tumor, and they migrated to the brain to kill the tumor cells.

This technique is being tested on children in a clinical trial by the team and partner medical institutions across the country.

There's urgency for these brain cancer patients wanting to participate in immunotherapy trials to seek them out soon after being diagnosed. Firstly, the patients can't have had the cancer removed because, without tumor cells, antigens can't be taught to fight the tumor. Secondly, immunotherapy is individualized to each patient, meaning it takes time to develop the appropriate therapy.

If immunotherapy does transition out of trials and research and into widespread treatment, it could provide hope against an illness that, while rare among cancer types, presents dire statistics for those diagnosed. Patients with brain or other cancers that affect the nervous system have only a 33 percent chance of living for five-plus more years, according to the National Cancer Institute.

The median lifespan after developing brain cancer is roughly 12 months, Flores said.

About 150,000 people in the U.S. have brain or another nervous-system cancer, and 2015 is estimated to bring 23,000 new cases and 15,000 deaths from it, the National Cancer Institute reports.

But Flores is hopeful that the team's progress, from Duke and now at UF, will be able to assist in taking the numbers down.

The findings in OncoImmunology are the latest in research and trial studies on brain cancer immunotherapy that have been building off each other, Flores said, and they've all seemed to suggest it's working. She noted the success story of a 70-something-year-old California man who received treatment at Duke, has survived brain cancer for nine years, and even runs in marathons.

"In our long-term survivors, they have perfectly normal lives," Flores said.

For Ashizawa, the Brain Institute's executive director, the work being done with immunotherapy and everything else at the institute has the aim of turning the irremediable into something patients can move past and still enjoy life.

"Many neurological injuries and diseases are currently incurable," he wrote to *Our Town*, "but advances in neuroscience give a chance for better quality of life to victims of brain injuries and diseases." **OT**