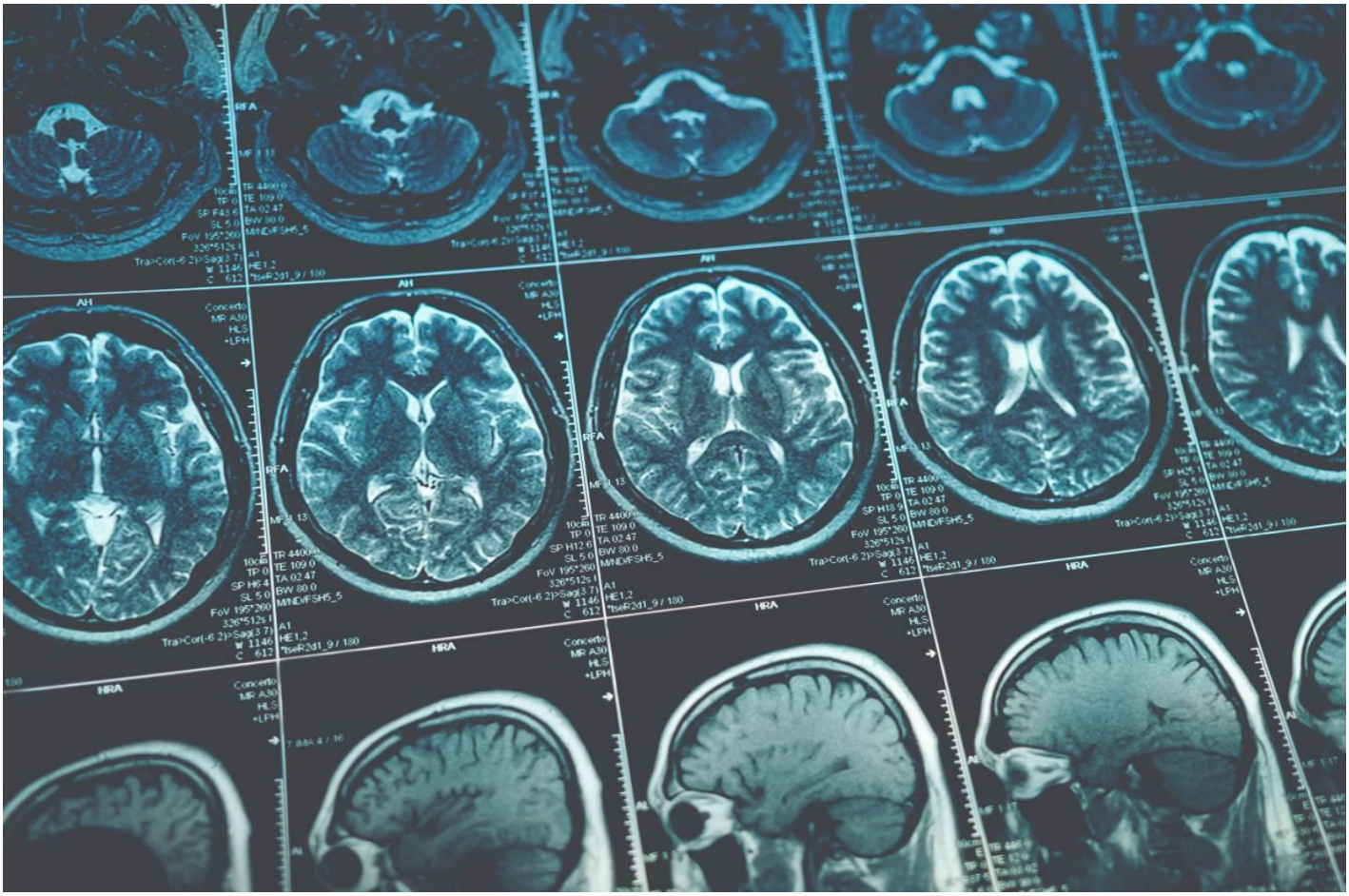
Florida Researchers Develop The First Blood Test To Diagnose Brain Injuries

McKnight Brain Institute
University of Florida



When actress Natasha Richardson died of an epidural hematoma after an accidental fall on a ski slope in 2009, many people were shocked. How could something like this happen? Why didn't the doctors *do* something?

The fact is, head trauma is frustratingly difficult to diagnose. Traumatic brain injury (TBI) creates a perplexing set of circumstances for medical staff for many reasons.

As was the case for Richardson, patients frequently remain conscious after a head trauma and underreport their discomfort because the injury can impact thinking, memory and objectivity. Emergency room personnel check vital signs such as heart rate and blood pressure but can easily misdiagnose whether it's a brain injury, stroke or something entirely different. Medical staff may incorrectly prescribe unnecessary tests, fail to order a necessary test like a CT scan or recommend no treatment when it is required.

More than a million people suffer from TBI every year, resulting in more than 50,000 deaths. According to the Centers for Disease Control and Prevention, each year, 1.7 million people sustain a traumatic brain injury. Many more TBI-related disability cases are unreported. TBI contributes to a third of all injury-related deaths in the United States, and there was an increase in TBI-related ER visits and hospitalizations between 2002-2006.

Perhaps most disturbing is that after a natural disaster, children are susceptible to TBI inflicted by their parents as a consequence of the high level of stress. According to a study published by researchers in the Department of Social Medicine at the University of North Carolina in the American Journal of Preventive Medicine in April 2004, the incidence of TBI is higher for children living in areas recovering from severe, weatherrelated adversity.

Making Patients Better by Better Diagnosing

With the number of traumatic brain injuries so large, why hasn't there been a better way to diagnose them?

This was the question that Ron L. Hayes, Ph.D., a tenured professor of neuroscience at the McKnight Brain Institute of the University of Florida, was asking in the late 1990s and early 2000s, almost a decade before Richardson's death.

"We weren't diagnosing brain injury very well," says Hayes, who was the former director of the University of Florida Center for Traumatic Brain Injury Studies. "It occurred to me that in the 35 years I had worked in this area, I hadn't done anything to make patients better."

Hayes thought that, just as heart specialists revolutionized cardiology care by discovering protein biomarkers in people experiencing a heart attack, a similar biomarker could exist in an injured person's blood, postinjury. His theory was that TBI wasn't simply an immediate injury but a disease process, and the sooner it was diagnosed and treated, the better the outcome for patients.

With the help of his colleague, Kevin K. W. Wang, Ph.D., an associate professor at the McKnight Brain Institute and former scientific director of the Center for Traumatic Brain Injury Studies who also has a doctorate in pharmaceutical sciences, Hayes conducted research to assess proteins produced after a brain injury.

They found correlations between the degree of brain injury and certain levels of brain biomarkers. They were able to show that the levels of the protein UCH-L1 were 16 times higher in patients' blood following injury to the brain than in noninjured patients. The results of these tests were published in Critical Care Medicine in 2010. The reliability rate was sufficient enough to provide an accurate diagnostic tool.

There it was: A blood test that could possibly have helped save Natasha Richardson's life. In addition to detecting certain biomarkers in the blood, Hayes' and Wang's research also focused on the potential treatment of brain injury using compounds that blocked two enzymes that cause additional brain cell death following injury.

"By blocking the action of these enzymes," says Hayes, "subsequent tissue damage can be reduced or eliminated, which greatly improves patient outcomes."

A More Elegant Solution Surfaces

In the early 2000s, Hayes received funding from the Department of Defense and the National Institutes of Health to pursue the diagnostic biomarker. The Office of Technology Licensing at University of Florida entered into a licensing agreement with Hayes, Wang and Nancy Denslow, Ph.D., a University of Florida professor of biochemistry in the Department of Physiological Sciences and Center for Environmental and Human Toxicology who was also director of a Proteomics Laboratory at the university, for a development-stage company based on the biomarker technology.

Denslow collaborated with Hayes and Wang to help discover the protein biomarkers of TBI.

By 2002, Hayes and Wang had left their posts at the university to build the University of Florida startup company that ultimately became known as Banyan Biomarkers, after the tree under which Buddha received enlightenment, says Hayes. The banyan tree, native to India, was first planted in the United States in Florida by Thomas Edison.

"The University of Florida is very supportive of startup biotechnology companies," says Denslow. "We have a wonderful business incubator building in Alachua — the Biotechnology Development Incubator — that offers a great deal of support to startup companies, including shared instrumentation, computer services and meetings with prospective investors. It is a win-win situation for both the university and the startup companies. In the case of Banyan Biomarkers, the University of Florida has been a very helpful partner."

Hayes became chairman of the board and Wang was named chief operations and scientific officer. Once the company was formed, Banyan was supported by congressional funding and secured two Small Business Innovation Research grants to continue their research efforts.

According to John Byatt, licensing officer at the Office of Technology Licensing at the University of Florida, the university has equity in Banyan and will earn royalties on sales of the biomarkers. "It's great that the university will earn royalities, but what's more satisfying is to be a part of the birth of a new company and knowing that the research is making a real difference to the health and well-being of people everywhere," says Byatt.

Located in Alachua, Fla., just 13 miles from the university, the company is focusing on the development of a simple, point-ofcare blood test for use by physicians in the emergency room and hospital.

"[The financial support] gave everyone confidence to fund work in humans and get to work on a more elegant solution," says Jackson Streeter, M.D., an experienced medical device executive who joined the team as CEO in 2010. To date, the company has received more than $70 million in grants from the United States Department of Defense and the National Institutes of Health.

"With Hayes and Wang on board, funding from the U. S. Department of Defense and National Institutes of Health and 65 employees, the company is in a good position to continue to discover and commercialize," says Byatt.

> *The company anticipates that three to five biomarkers will be used in detecting and monitoring patients sustaining TBI, translating into a potential market in excess of $250 million in the United States alone, says Streeter.*

Hayes is hoping that the diagnostic will ultimately be a portable device much like a handheld glucose strip. This small device would be optimal for testing not only in the playfields as a sports medicine application but also on the battlefield and be able to provide information within 20 minutes.

Athletic, Pediatric and Other Applications

After Banyan completes clinical validation (expected in 2013), the company will seek Food and Drug Administration approval to market the biomarkers as an in vitro diagnostic test for detection and monitoring of TBI. Hayes says that the test will be used for military personnel after blast injuries like those occurring from improvised explosive devices in Iraq and Afghanistan. The test will also be used for sports concussion injuries during athletic events. A future application also includes pediatric TBI, especially for shaken baby syndrome and for children who are victims of TBI inflicted by a parent such as in the stressful aftermath a natural disaster.

Currently, Banyan has three U.S.-issued patents and three patent applications broadly covering the use of biomarkers, and international patents have been filed. The firm has also secured grants to develop biomarkers for stroke and liver injury.

If this is the case, and a handheld device could be used on the slopes by ski patrol, head trauma patients would never again be solely responsible for identifying and communicating the severity of their condition. The chance for a definitive diagnosis could eradicate the question, "Why didn't the doctors do something?

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