



SILENT

BANYAN BIOMARKERS PROMISES A QUICK TEST

EPIDEMIC

FOR TRAUMATIC BRAIN INJURY

BY JOSEPH KAYS

Actress Natasha Richardson's seemingly harmless fall on a ski resort bunny slope last March and her tragic death days later shocked fans the world over, but it didn't shock the researchers at Banyan Biomarkers.

The traumatic brain injury, or TBI, that Richardson suffered is exactly the type of injury the Alachua-based company was created to address.

"It's a silent epidemic," says Ron Hayes, a former researcher at UF's McKnight Brain Institute who is co-founder and clinical programs director of Banyan Biomarkers.

In fact, the Centers for Disease Control and Prevention estimates that 1.4 million people sustain a TBI each year in the United States and 50,000 die. TBIs are the leading cause of disability among young people and the most common injury on the battlefield.

Hayes has spent a quarter century seeking a greater understanding of the physiological changes that occur after a head injury. What he's learned is that, after the initial impact, a "destructive cascade" of biological events occurs over the subsequent hours or days. This cascade involves the activation of two enzymes — calpain and caspase — which break down proteins in brain cells, resulting in progressive damage and death of brain tissue.

But these events leave a telltale sign in the patient's bloodstream, Hayes says, and it is that sign that offers hope for more effective treatment.

"When the brain is injured, cells are injured and die," Hayes says. "When they disintegrate, ultimately the blood or cerebrospinal fluid will pick up pieces of proteins. These proteins can be specific markers — clues to the death of the cell — telling us what caused it and where it happened."

Hayes, co-founder Kevin Wang and the team at Banyan Biomarkers have identified more than 40 of these biomarkers thus far. Now they're working to get a quick test for the condition into the hands of first responders and military medics.

"The Natasha Richardson tragedy certainly illustrated the need for something that is readily available and can be used not only in an emergency-room environment but also in the field by an EMT," says Banyan Biomarkers CEO Gary Ascani.

According to news reports, the 45-year-old Richardson seemed to suffer no ill effects from her fall and declined medical treatment, but within hours she had slipped into unconsciousness and within days she was dead.

"Mild injury is very difficult to diagnose and, in extreme cases, it can progress very quickly to something much more serious," Ascani says.



ABC NEWS ANCHOR **BOB WOODRUFF** FOCUSED ATTENTION ON THE PLIGHT OF SOLDIERS WITH TBI AFTER HE SUFFERED A HEAD INJURY IN 2006 WHILE REPORTING FROM IRAQ. IN AN ABC NEWS SPECIAL AND A BEST-SELLING BOOK, WOODRUFF CHRONICLED HIS OWN RECOVERY AND THAT OF THE MANY OTHER SOLDIERS HE MET ALONG THE WAY.



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An estimated 200,000 sport-related traumatic brain injuries are treated annually in U.S. emergency rooms. Children aged 10-19 suffer the most injuries. The most common causes are bicycling, football, playground activities and basketball.

-Centers for Disease Control and Prevention



About 33 percent of patients who needed medical evaluation for battle-related injuries at Walter Reed Army Medical Center in 2008 had traumatic brain injury.

-Defense and Veterans Brain Injury Center

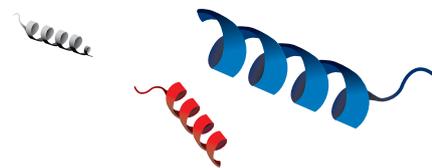
The population most vulnerable to these injuries right now is soldiers in Iraq and Afghanistan, where explosive devices have become the enemy's weapon of choice. That's why the U.S. Department of Defense has provided the company more than \$20 million in funding to date to support the research and work toward developing a test.

"The problems in Iraq and Afghanistan are driving commercialization of this test for TBI," says Ascani. "For the most part, the injuries our soldiers are suffering today are not penetrating injuries like in Vietnam but explosive injuries, and the traumatic brain injuries associated with these blasts, have been of great concern to the Department of Defense and to the Veterans Administration."

ABC News Anchor Bob Woodruff focused attention on the plight of soldiers with TBI after he suffered a head injury in 2006 while reporting from Iraq.

In an ABC News special and a best-selling book, Woodruff chronicled his own recovery and that of the many other soldiers he met along the way.

"In this war it is not clear how many are injured. Mine was obvious, but others are not," Woodruff said in a 2008 commencement speech at Syracuse University. "A recent report by the Rand Corporation found that more than 300,000 soldiers are suffering from some kind of brain injury. That includes physical injuries or mental stress from combat. Some of them have obvious wounds — scars that mark them as brain injured, But others are more hidden from the outside and are, in a way, invisible."



Rendering of caspase enzymes.

Ascani says Banyan Biomarker's work for the military should give civilian doctors confidence in the technology.

"We have these types of tests to objectively identify heart injury, but nothing exists like that for TBI," Ascani says. "Currently, doctors use a subjective test based on the patient's cognitive responses, but what has been missing is a reliable test that is more objective."

Typically, if doctors aren't sure, they'll order a CT scan.

"Mild injury is very difficult to diagnose even with a CT," Ascani says. "As a clinical diagnostic company, we see the need for an objective measure that is inexpensive compared to a CT scan."

In addition to the cost — Ascani estimates the Banyan Biomarkers test could cost just \$50-75, compared to \$1,000 for a CT scan — CT exposes the patient to significant amounts of radiation.

The company is currently validating the biomarkers in a large study at hospitals in the United States and Europe. Doctors are collecting blood and spinal fluid from patients with head injuries upon admission and every six hours for 10 days.

"We're building a profile of what these biomarkers look like in a severe situation," Ascani says.

Ascani says the current study is part of the clinical pathway of getting physicians in emergency rooms comfortable with the idea that the test has value in determining whether a patient has no injury or mild-to-severe injury.

That same educational process is going on within the diagnostic device industry.

"TBI has not been recognized by the diagnostic industry as a market opportunity," Ascani says. "We are working to educate the industry to the market potential."

He says Banyan Biomarkers most likely will partner with a company that already makes diagnostic devices.

"We've met with a number of platform manufacturers whose devices will work nicely with our markers," he says. "We don't strive to be an instrument company. We'll identify the biomarkers, then provide the critical raw materials to put on an instrument. It's kind of like software and hardware. We're the content, they're the tool."

Banyan Biomarkers has about 30 employees continuing the search for biomarkers in its labs at UF's Sid Martin Biotechnology Development Incubator.

For Ascani, who came to Banyan Biomarkers after several years in a venture capital firm in Birmingham, Ala., and a short stint running one of the companies in which the firm invested, the incubator is essential to Banyan Biomarker's continued success.

Because most federal grants don't permit new construction, he says, having access to high-quality laboratory space is essential.

"Having quality space at UF's biotechnology incubator available to us has made all the difference in the world," Ascani says. "In exchange for allowing us to rent here, UF owns a piece of the company, so everyone has an opportunity to win."

Because destructive cascades are not limited to the brain, Banyan Biomarkers is also researching new tests for other organs, including the liver.

Based on his more than 30 years in the biotechnology and medical products industry, Ascani has promoted a unique organizational structure at Banyan Biomarkers that allows basic and applied science to proceed simultaneously.

Corporate structures often don't allow for the kind of basic research typically conducted in academia, Ascani says, so in late 2007, when Hayes and Wang joined Banyan Biomarkers full-time after careers at UF, the team decided to create Banyan Biomarker's Center of Innovative Research — a place where fundamental science continues apace with developing commercial products.

"A fundamental challenge in biotechnology and pharmaceutical companies is to foster research supporting product pipelines without inhibiting the creative processes essential for scientific discovery," Ascani says. "Banyan's Center of Innovative Research was created to address that challenge."

One day soon, Hayes hopes the work Banyan Biomarkers has done for the military will result in first responders everywhere having a quick, easy, inexpensive way to determine if someone has suffered traumatic brain injury.

"TBI is a scandalously ignored health problem," he says. "It's the biggest killer of kids. This research is where homeland defense provides a service for the soccer mom." ❌

