

Possible Blood BIOMARKERS for TBI

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Traumatic Brain Injury (TBI) can be devastating not only to patients but to caregivers as well. According to the Centers for Disease Control and Prevention (CDC), approximately 1.7 million Americans sustain TBIs ranging from mild to severe every year.¹ Additionally, over 1.4 million are treated in emergency rooms and, unfortunately, 52,000 die from TBI related injuries each year.² These statistics are daunting but what is more concerning is there hasn't been an in vitro diagnostic test to properly identify and differentiate between the varying degrees of a mild to a severe concussion that could improve outcomes. A point of care blood test could greatly improve the diagnosis and treatment of brain injured patients.

Because of this critical unmet medical need, Banyan Biomarkers Inc. is conducting research to develop a simple point of care blood test for use in the emergency department. Ultimately the goal is to develop a field deployable handheld device. For example, if a high school football player were knocked unconscious, this device would test a small sample of blood and then be able to determine if an injury occurred and its severity. This type of information could help physicians and medical staff diagnose patients more effectively and therefore improve outcomes.

At the present time, sports concussions tend to be vastly under diagnosed and often poorly managed. The only diagnostic tests for brain injury available to physicians are expensive Computerized Tomography (CT) scans or Magnetic Resonance Imaging (MRI) studies. Unfortunately, these imaging studies are often not able to confirm mild TBIs and may only identify the very serious injuries that result in swelling and/or bleeding inside the brain. Moreover, not all hospitals or clinics have the technology or staff to conduct these studies and they are not available in the field.

●●● HOW IT WORKS

Biomarkers are proteins or other cellular components that relate specifically to injury or to disease and that can be found in body fluids such as cerebral spinal fluid (CSF) and blood. The presence and quantity of the biomarker in these fluids can be determined by antibody-based assays to assess the degree of injury or disease and in the best circumstances to determine recovery. To be specific for injury or disease, the presence of the biomarkers in body fluids must depend on the diseased state and they should not be present in these fluids under normal conditions.

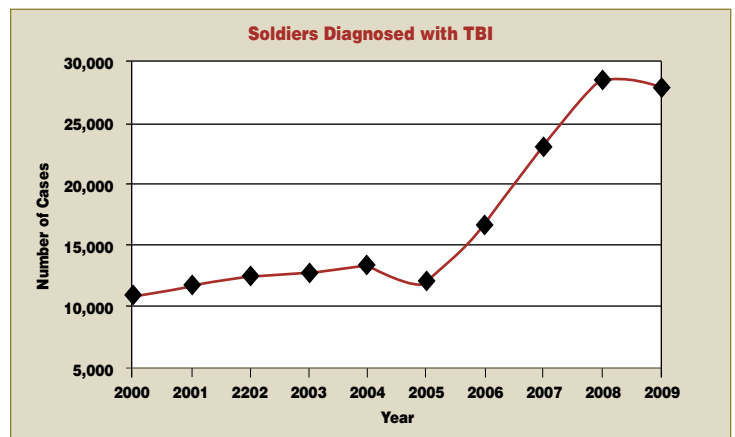
Banyan Biomarkers, Inc. has discovered unique biomarkers that are present in blood after a traumatic brain injury (TBI). These potential biomarkers for TBI could have important prognostic functions especially for patients who sustain mild TBIs. Accurate identification of these patients will facilitate development of guidelines for return to work or sports activities and also provide opportunities for patient and caregiver education. Mild TBI can make individuals at risk for several serious lifelong disabilities, such as impaired ability to form new memories, depression, headaches and personality changes.

●●● TBI IN THE US MILITARY



The US military has a keen interest in the development of a point of care test for TBI. Exposure to blast injuries from IED devices has made TBI the “signature injury” of the Iraq and Afghanistan conflicts. The U.S. Department of

Defense reported that between 2003 and 2008, 30 percent of patients with combat related injuries that were treated at Walter Reed Army Medical Center were, in fact, diagnosed with TBI.³ According to the Defense and Veterans Brain Injury Center (DVBIC), there were approximately 28,000 soldiers diagnosed with TBI in 2009, which is more than two times the number of soldiers diagnosed in 2005.⁴ A point of care test that would be able to determine and quantify a TBI would be very beneficial to physicians treating service members after a combat related injury.



Source: DVBIC (<http://www.dvbic.org/TBI>)

●●● TBI IN SPORTS



There have been startling new discoveries of the downstream health problems for individuals with mild TBI who did not receive proper treatment or were unaware of how serious the injury initially was. The CDC estimates that the number of mild TBIs has reached

300,000 cases per year in all sports.⁵ Recently, the National Football League (NFL) publicly acknowledged that players and former players were at a higher risk of acquiring specific neurological disorders. There are currently 2,000 current NFL players and more than 10,000 retirees, many of whom have sustained repetitive hits resulting in multiple concussions in short succession.⁶ What is more concerning is the fact that there are between 1.6 million and 3.8 million sports related concussions annually in the United States.⁷ Most of these concussions are minor, but some athletes return to play without allowing enough time for the brain to heal, which can result in very serious consequences.

Chronic traumatic encephalopathy (CTE) is a neurodegenerative disease that is caused by repetitive concussions. The trauma caused by these concussions triggers degeneration of brain tissue leading to neurological impairment. Groundbreaking neuropathological research conducted by the Center for the Study of Traumatic Encephalopathy (CSTE) at Boston University have confirmed a buildup of a specific protein, called tau, in the brains of retired football players and wrestlers. Chronic traumatic encephalopathy may result in memory loss, behavioral and personality changes, speech abnormalities, depression, Parkinson's Disease and Alzheimer's Disease. In 2007, the CSTE conducted neuropathological examinations of an 18 year-old football player and discovered the early stages of CTE already forming. This suggests that CTE could impact young, otherwise healthy teens that play contact sports in middle and high school. It is crucial that coaches, parents, trainers and athletes understand the risks involved and know that subsequent injuries could have lasting effects.

●●● THE PROBLEM

How does one determine the severity of a brain injury on the field or in the gym? The old approach was to simply ask the patient if they knew where he or she was or what his or her name was. If those questions were answered correctly, the usual next set of "testing criteria" was to ask how many fingers were displayed. Though some improvement has been made in understanding the seriousness of concussions or mild TBIs in sports, we have, unfortunately, not come a long way from the old methodologies of diagnosing a TBI. In progressive college and high school programs, neuropsychological testing is used on student athletes in the beginning of the season, and if the athlete suffers a concussion or brain injury, a follow up

test is performed. The idea is that only when the student can demonstrate that no physical or cognitive impairment is present and a doctor has given clearance, can he or she return to play.

The real problem is the "grey area" when a player takes a hard fall or is hit head on by another player's helmet and doesn't seem to be affected. How do we know the player has not sustained a serious injury? Should the coach send the player back in or bench him or her for the rest of the game? Should the decision be different based on the athlete's age? These critical questions might be answered by a readily available and objective brain injury measurement.

●●● THE FUTURE

To date, the Food and Drug Administration has not approved a biomarker for central nervous system (CNS) diseases or injuries like stroke, Parkinson's, Alzheimer's, depression or TBI. The primary reason is because of the blood brain barrier (BBB), which actively separates circulating blood in the body with the blood that is in the brain. Banyan Biomarkers has created proprietary technology that may be able to detect very small proteins that actually do pass through the BBB into the circulating blood in the body of patients that suffered from a TBI. In order for this investigational research to reach doctors and eventually patients, it must pass through the rigorous FDA approval process. Diagnostic tests have to endure a very similar process that a drug or device follows for approval and requires a clinical trial with detailed statistical analysis to prove that the test is truly safe and effective. Banyan Biomarkers, Inc. is in the developmental phase but hopes the research will improve the lives of individuals who sustain brain injuries throughout the world.

The Banyan Biomarker assays are for investigational and research use only and are not intended for clinical diagnostic purposes.

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