

## **North Carolina Companies Conducting Brain Injury-Related Research**

**by Suzanne McKenna, PhD**

Each year an estimated 1.5 million Americans sustain a traumatic brain injury (TBI). This is eight times the number of people diagnosed with breast cancer and 34 times the number of new cases of HIV or AIDS. TBI is the leading cause of disability for adults and children in the United States with an annual cost to society of over \$60 billion. The Center for Disease Control has acknowledged that these figures underestimate the scope of the problem because they are derived only from patients treated in hospital and emergency room settings and therefore, do not take into account TBIs treated in federal, military, VA hospitals, physician offices, outpatient settings, or those with negative MRI/CT scans or those for whom loss of consciousness is uncertain. This number also does not include the several hundred thousand individuals with mild TBI each year. Despite its name, mild TBI can result in significant permanent post-injury impairment. In addition to the enormous socioeconomic toll of TBI in the civilian population, TBI is the signature wound of the wars in Iraq and Afghanistan, with over 30% of the soldiers at Walter Reed being diagnosed with a TBI. Therefore, TBI represents a major public health problem and a significant unmet medical need.

Since the initial traumatic event produces irreparable primary brain injury, the goal in care of the head injured patient focuses upon the prevention of the inevitable secondary wave of brain injury. However, there are currently no therapies to treat these secondary brain injuries. Despite the best efforts of doctors and researchers to date, doctors are left to try to maintain adequate cerebral blood flow, oxygenation, and intracranial pressures and, in the most severe cases, wait for the patient to regain consciousness. Over the past 30 years a great deal of research has focused on understanding this secondary brain injury cascade and how to best target it with a therapeutic compound. However, of the 20 compounds tested in late phase II/phase III clinical trials none have been successful for all of the patients receiving the drug compared to those receiving the placebo, the standard in judging the efficacy of compounds in clinical trials.

There is still a great deal that is unknown about TBI and how to best replicate it in a laboratory setting in order to test candidate compounds. In addition, each TBI is very different. If it were possible to give two people the exact same TBI they would respond differently. It is very difficult to evaluate the effectiveness of a compound on patients in clinical trials when they have TBIs that were sustained in very different ways, e.g., different types of car accidents, falls, gunshot wounds, blast injuries sustained in war, etc. This makes it difficult to form treatment groups and to interpret the resulting data after treatment. These barriers to the successful development of therapeutics for the treatment of TBI discourage companies from going into TBI drug development because the likelihood of success is much slimmer than that for other diseases with well worked out research models with clearly defined end points such as high cholesterol and depression. Despite the significant challenges involved in TBI research, there are a few companies right here in North Carolina that are engaged in drug development for TBI.

Durham-based **Aldagen** <http://www.aldagen.com/> is a biopharmaceutical company developing proprietary regenerative stem cell therapies that target significant unmet medical needs. The company has four product candidates which consist of specific populations of adult stem cells isolated from umbilical cord blood. Products are currently in clinical trials for the treatment of inherited metabolic diseases, leukemia, critical limb *ischemia* (restricted blood flow) and ischemic heart failure.

Aldagen is currently evaluating the activity of their proprietary adult stem cells in a preclinical animal model of *ischemic stroke* (rapidly developing loss of brain function(s) due to restricted blood supply to the brain). Researchers have demonstrated that these cells can restore functional nerves and ameliorate symptoms in mouse models of human nervous system disorders. These repair capabilities are important for treating ischemic stroke typically caused by clots that cut off the supply of oxygen to the brain, damaging surrounding blood vessels and brain tissue. These same mechanisms damage brain tissue in TBI as well. Therefore, adult stem cells hold promise in the treatment of TBI and other neurological disorders, including Parkinson's disease, amyotrophic lateral sclerosis, and cerebral palsy.

Research Triangle Park-based **Cognosci Inc.** <http://www.cognosci.com/> is an established pharmaceutical company developing proprietary multi-dimensional inhibitors of the brain inflammation and injury associated with TBI, Stroke, Subarachnoid Hemorrhage, and Multiple Sclerosis. Cognosci has tested their lead compound in multiple models of TBI which replicate the cortical brain contusion, diffuse neuronal injury, and death of vulnerable nerve cells seen in the clinical setting of blunt head trauma. In all TBI models tested, this compound reduced neuronal cell loss and improved functional behavior when administered 2 hours following TBI. Cognosci is currently seeking venture funding in order to conduct Phase I/II clinical trials.

Research Triangle Park-based **NeuroScience Pharmaceuticals** <http://www.neurosciencepharma.com/> is a clinical stage company dedicated to the development of a pipeline of brain-disorder therapies based on neurosteroids. Neurosteroids are hormones that affect nerve cells in the brain and body that show promise as treatments for a range of conditions, including anxiety, depression, schizophrenia, cognitive impairment, Alzheimer's, Post Traumatic Stress Disorder, epilepsy and TBI. Their future product pipeline includes a variety of delivery mechanisms and second generation neurosteroid compounds. Funding has been received from the VA for a Proof of Concept Clinical Trial in 20 patients using the neurosteroid Pregnenolone for treatment of veterans with TBI. Outcome measures will target cognitive symptoms. A grant has been submitted to conduct a larger study in this population. NeuroScience Pharmaceuticals is seeking a partnership to evaluate the safety and effectiveness of Pregnenolone and other neurosteroids for the treatment of TBI.

Winston-Salem-based **Targacept** <http://www.targacept.com> is a biopharmaceutical company spun out from RJR Tobacco engaged in the design, discovery, and development of neuronal (brain cell) nicotinic receptors which are proven therapeutic targets for nervous system disorders. One lead candidate affects the activity of a receptor that plays a key role in protecting neurons from inflammatory activity that arises from injury and improves cognitive

functioning in schizophrenics. This candidate has potential to treat other conditions characterized by inflammation and cognitive impairment, e.g., TBI.