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Potential therapeutic for traumatic brain injury (TBI)
Testing cathepsin B as a therapeutic target for TBI

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Researchers at the Walter Reed Army Institute of Research (WRAIR) are conducting studies to investigate a possible new therapy for traumatic brain injury (TBI). The studies—conducted in collaboration with San Diego-based company- ALSP, Inc.—are focused on the effects of cathepsin B, which is an enzymatic protein that has been found to be elevated in some trauma patients and in animal models of TBI. The researchers hope to devise the first-ever drug therapy for TBI by developing compounds which inhibit cathepsin B enzymatic activity.

TBI is called the "signature injury" of the wars in Afghanistan and Iraq. While most traumatic brain injuries are mild and outwardly observable symptoms resolve quickly, a small percentage of those who've sustained TBIs experience persistent problems and adverse outcomes. The brain may succumb to cell death, inflammation, breakdown of blood vessel walls, lack of oxygen, aneurysms, hemorrhage, and swelling. Research has not yet revealed how all of these events are regulated and how they may be prevented, but cathepsin B may be important in causing those pathologies.

A treatment strategy, focused on cathepsin B, suggested by a recent review published by Dr. Greg Hook, of ALSP Inc., and colleagues,* which presents supporting evidence for a potentially important therapy that inhibit cathepsin B to treat traumatic brain injury.

Cathepsin B, is a member of the cysteine protease family of enzymes, known for degrading proteins. It is likely cathepsin B escapes its normal, controlled environment in a cell because of trauma and enters the cell's liquid interior or exits the cell completely. Once free within the cell or outside the cell, the enzyme's protein-destroying power causes cellular destruction and inflammation in the brain. Adverse outcomes from TBI include behavioral dysfunction and pathology in pre-clinical models as a result of TBI.

Dr. Angela M. Boutté of the Brain Trauma Neuroprotection and Neurorestoration Branch at WRAIR, is conducting experimental trials to better understand cathepsin B and how its inhibitors may change the course of injury in pre-clinical studies of specialized, militarily relevant models of TBI. Certain cathepsin B inhibitors show encouraging results as therapeutics, as they have been used in TBI-related epilepsy and Alzheimer's disease models. A review of the literature shows that this research is quite promising in mitigating adverse outcomes caused by TBI.

The collaboration between ALSP, Inc. and the WRAIR leverages the research advances by ALSP scientists and WRAIR's extensive capabilities for pre-clinical trials of experimental therapeutics.

*Front. Neurol., 02 September 2015, http://dx.doi.org/10.3389/fneur.2015.00178, Cathepsin B is a New Drug Target for Traumatic Brain Injury Therapeutics: Evidence for E64d as a Promising Lead Drug Candidate, Gregory Hook *et al.*

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