

US DEPARTMENT OF DEFENSE BLAST INJURY RESEARCH PROGRAM COORDINATING OFFICE

Treatments for Neurotrauma Prophylactic Treatment of CN-105 Provides Neuroprotection in Small Animal Model of Traumatic Brain Injury

Researchers at Duke University (Durham, North Carolina) in conjunction with AegisCN, LLC (Durham, North Carolina), are working to identify an ideal neuroprotective therapeutic that can be prophylactically administered to protect the brain from the chronic effects of trauma. The proposed drug, CN-105, is a modified five amino acid apolipoprotein E (ApoE) mimetic which readily crosses the blood-brain barrier and provides anti-inflammatory and neuroprotective effects to the brain (*Laskowitz et al. 2017, Lei et al. 2016, Tu et al. 2017*). This study will determine the efficacy and most effective time frame to administer CN-105 before a traumatic brain injury (TBI) that will provide the optimal protection and mitigate cellular damage.

Animal studies have demonstrated that CN-105 is effective when administered prophylactically and post-injury in a closed head injury model, and that the optimal therapeutic window is dependent on the maintenance of sufficient concentrations of CN-105 in the body at the time of injury (*Laskowitz et al. 2017*).

CN-105 has an excellent safety profile in clinical single and multiple escalating dose studies (ClinicalTrials. gov Identifier: NCT02670824) and is currently being tested in a multicenter Phase 2 clinical trial evaluating outcome after intracranial hemorrhage (ClinicalTrials.gov Identifier NCT03168581) (*Guptill et al. 2017*). Current research efforts include preclinical work evaluating the efficacy of CN-105 in Alzheimer's disease, and neuroprotective efficacy offered by CN-105 when administered post-injury. Planning is underway for a follow-on first-in-man study on TBI.

Results from this research effort can be utilized to further develop an efficacious therapeutic for TBI and to protect from mild repetitive brain injury.

This study was funded by Defense Medical Research and Development Program, and is strategically aligned with Combat Casualty Care Research Program. This award (W81XWH-16-C-0142) was managed by Congressionally Directed Medical Research Programs. The current research efforts are funded by Food and Drug Administration orphan grant program (FD-R-5387), CURE-Alzheimer's fund, and philanthropy.



REFERENCES:

- Guptill, J. T., Raja, S. M., Boakye-Agyeman, F., Noveck, R., Ramey, S., Tu, T. M., and Laskowitz, D. T. 2017. "Phase 1 Randomized, Double-Blind, Placebo-Controlled Study to Determine the Safety, Tolerability, and Pharmacokinetics of a Single Escalating Dose and Repeated Doses of CN-105 in Healthy Adult Subjects." J Clin Pharmacol 57 (6):770-776. doi: 10.1002/jcph.853.
- Laskowitz, D. T., Wang, H., Chen, T., Lubkin, D. T., Cantillana, V., Tu, T. M., Kernagis, D., Zhou, G., Macy, G., Kolls, B. J., and Dawson,
 H. N. 2017. "Neuroprotective Pentapeptide CN-105 Is Associated with Reduced Sterile Inflammation and Improved Functional Outcomes in a Traumatic Brain Injury Murine Model." Sci Rep 7:46461. doi: 10.1038/srep46461.
- Lei, B., James, M. L., Liu, J., Zhou, G., Venkatraman, T. N., Lascola, C. D., Acheson, S. K., Dubois, L. G., Laskowitz, D. T., and Wang, H. 2016. "Neuroprotective Pentapeptide CN-105 Improves Functional and Histological Outcomes in a Murine Model of Intracerebral Hemorrhage." Sci Rep 6:34834. doi: 10.1038/srep34834.
- Tu, T. M., Kolls, B. J., Soderblom, E. J., Cantillana, V., Ferrell, P. D., Moseley, M. A., Wang, H., Dawson, H. N., and Laskowitz, D. T. 2017. "Apolipoprotein E Mimetic Peptide, CN-105, Improves Outcomes in Ischemic Stroke." Ann Clin Transl Neurol 4 (4):246-265. doi: 10.1002/acn3.399.

