



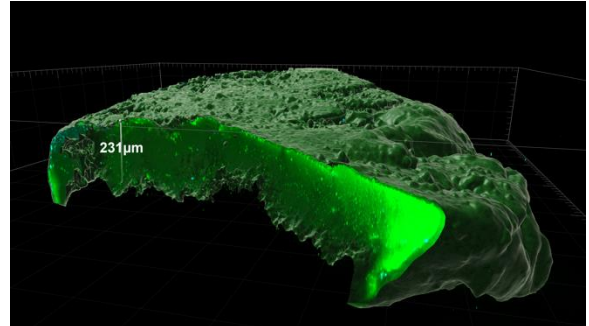
2023 IMPACT CIRCLE

Project Title

CARGO DELIVERY TO THE BRAIN

Investigator(s) and collaborations:

Lisa M. Ellerby, PhD; Barbara Bailus, PhD



Unmet Need/Primary Question:

The human brain has a structure to prevent molecules and proteins from entering the brain called the blood brain barrier. Effective delivery systems that cross the blood brain barrier represent a major challenge in the medical field. We have developed a protein-based technology to deliver the genome editing machinery CRISPR/Cas9 to the brain and into neuronal cells. Our approach was to design a novel cell penetrating protein based on a conserved sequence in the Zika virus. This newly designed protein crosses the blood brain barrier in C57BL/6J mice and shows the widespread distribution of Zika-Cas9 nickase (Zika-Cas9n) in the brain. This new delivery system to bring nucleic acid, RNA, peptide or proteins to the brain. To bring this technology to the clinic we would like to do key experiments to that would form the foundation of what is needed to start new company.

Novel Hypothesis:

Using the biology of ZIKA virus a novel delivery system to the brain can form the basis of cargo transport to this specialized organ of the body.

Project Proposal:

Effective delivery systems that cross the blood brain barrier represent a major challenge in the medical field. We have developed a protein-based technology to deliver the genome editing machinery CRISPR/Cas9 to the brain and into neuronal cells. Our approach was to design a novel cell penetrating protein based on a conserved sequence in the Zika virus. This newly designed protein crosses the blood brain barrier in C57BL/6J mice and shows the widespread distribution of Zika-Cas9 nickase (Zika-Cas9n) in the brain. To validate that the newly designed protein was functional, we evaluated editing in various Huntington's disease (HD) models. Delivery of Zika-Cas9n to neuronal cells, human brain organoids derived from HD induced pluripotent stem cells, and HD YAC18 mouse resulted in the contraction of the disease-causing CAG. We will now carry safety studies and validate multiple cargos can be delivered to the brain.

Description of Potential Impact:

Our protein-based technology provides a new method to deliver purified proteins and potentially other types of therapeutics including antisense oligonucleotides, siRNAs, viral vectors, and nanoparticles to the brain.