Fusogenic Peptides for Delivery of RNAi Therapeutics to Ovarian Cancer (2021-025)

Novel fusogenic peptide drug delivery to enhance bioactivity of therapeutics through efficient cellular delivery and endosomal escape.

Market Overview
The novel fusogenic peptides improve the delivery of therapeutics for ovarian cancer through their ability to enhance endosomal escape and delivery of bioactive therapeutics. Epithelial ovarian cancer is the 5th leading cancer among women, with a 49% five-year survival rate. Current treatment strategies for ovarian cancer include surgical removal, chemotherapy, and radiation; however, these treatments often prove ineffective or toxic to patients. Global News Wire expects the nanotechnology drug delivery market to have an 18.7% CAGR growth rate from 2022 to 2032. Current chemotherapies are limited due to the toxicity of therapeutic and resistance to treatment. Furthermore, there has been increased attention to reducing systemic effects and therapeutic concentration. This technology fills this gap by providing a means of delivery for therapeutics of RNA interference (RNAi), a mechanism used to silence genes responsible for cancer prognosis. While a promising strategy for treatment, RNAi cargo needs a delivery system to improve its bioavailability and delivery into cancer cells. Clemson University researchers have developed novel fusogenic peptides that have efficient delivery into ovarian cancer cells and enable the endosomal escape of therapeutic.

Technical Summary
The peptides’ design is composed of alternating residues of hydrophobic and hydrophilic amino acids, highlighted by repeating aspartic acid residues. Due to the inclusion of a cationic tail, these peptides have shown effective electrostatic complexation and protection of RNAi cargo. High biocompatibility and cellular internalization have been shown both in vitro and in vivo. These sequences have proven to enhance endosomal escape through the protonation of hydrophobic amino acids, which leads to a conformational change in a more acidic pH to disrupt the endosomal membrane. Upon release from the endosome, the siRNA is released into the cytoplasm of the cell, where it can be bioactive. Due to this enhanced delivery, gene silencing studies showed the systems’ efficacy in silencing the target oncogene. Therefore, these novel peptides demonstrate a highly efficient delivery system for RNAi therapeutic applications for cancer treatment.

Application
The fusogenic peptides are a delivery system designed to improve the intracellular delivery and endosomal escape of RNAi cargo to improve gene silencing for cancer treatment.

Development Stage
Provisional Patent

Advantages
- Facilitates endosomal release of cargo, increasing the bioavailability of therapeutic
- Electrostatic complexation of cargo, resulting in a wide range of potential cargo
- High biocompatibility and tumor localization, lower adverse systemic effects compared to current treatments
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About the Inventors

**Dr. Angela Alexander-Bryant**
Assistant Professor of Bioengineering and Director of Diversity and Inclusion at Clemson University

Dr. Angela Alexander-Bryant is an Assistant Professor of Bioengineering and Director of Diversity and Inclusion in the College of Science at Clemson University. She earned his Ph.D. in Bioengineering from the Clemson-MUSC Joint Bioengineering Program in Charleston, SC. Among her many accomplishments, she has been awarded the Gates Millennium Scholarship, honorary membership in the National Academy of Inventors, the National Science Foundation Early Career Award, and the Minority Scholar in Cancer Research Award from the American Association for Cancer Research. At Clemson, Dr. Alexander-Bryant leads the Nanobiotechnology Lab as the Principal Investigator in developing novel self-assembled biomaterials for delivery of chemotherapy and nucleic acid-based therapies to improve targeted treatment of aggressive and drug-resistant cancers. Her current research focuses on drug and gene delivery, biomaterial design, and targeted therapy and controlled releases.

**Dr. Timothy Samec**
Medical Writer and Adjunct Faculty at Abilene Christian University

Dr. Timothy Samec is a 2021 Ph.D. graduate of Clemson University’s Department of Bioengineering. He currently works as a Medical Writer for Caris Life Sciences and adjunct faculty in the Department of Precision Medicine at Abilene Christian University. Dr. Samec earned his undergraduate degree in Physics from Slippery Rock University of Pennsylvania, Master’s degree in Data Analytics from Slippery Rock University of Pennsylvania, and Master’s degree in Bioengineering from Clemson University. In 2022, he was recognized as a Distinguished Young Alumni of Slippery Rock University for his research contributions in bioengineering, leadership and service roles at both Clemson and Slippery Rock, and continued mentorship of students at both universities as an alumnus.

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