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

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

Market Overview

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 an effective delivery platform for RNA interference (RNAi) therapeutics, a mechanism that can be used to silence oncogenes responsible for cancer progression. While a promising strategy for treatment, RNAi cargo requires an efficient delivery system to improve its bioavailability and delivery into cancer cells. Clemson University researchers have developed novel fusogenic peptides that facilitate efficient uptake and endosomal escape of RNAi therapeutics in ovarian cancer cells, resulting in enhanced bioactivity and therapeutic efficacy.

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 is bioactive. Due to this enhanced cytoplasmic delivery, gene silencing studies have proven the system's significant efficacy in silencing the target oncogene, resulting in significant antitumor activity in vivo. Therefore, these novel peptides demonstrate a highly efficient delivery system for RNAi therapeutic applications for cancer treatment.

Application

Gene silencing for cancer treatment

Development Stage

Preclinical and invivo proof of concept

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

App Type	Country	Serial No.	Patent No.	CURF Ref. No.	Inventors
PCT	United States EPO	US2023/061436	NA	2021-025	Dr. Angela Alexander-Bryant Dr. Timothy Samec

About the Inventors

Dr. Angela Alexander-Bryant

Associate Professor of Bioengineering and Director of Diversity and Inclusion at Clemson University

Dr. Angela Alexander-Bryant received her bachelor's and master's degrees in Materials Science & Engineering from Johns Hopkins University. She completed her Ph.D. in the Clemson-MUSC Joint Bioengineering Program in Charleston, SC in 2015. She has received many honors and awards, including the Gates Millennium Scholarship, honorary membership in the National Academy of Inventors, and a Minority Scholar in Cancer Research Award from the American Association for Cancer Research. In 2021, she received the NSF CAREER Award, supporting the development of peptide carriers for nucleic acid delivery. As PI of the Nanobiotechnology Lab at Clemson University, she leads her research team on the development of novel self-assembled biomaterials for delivery of chemotherapy and nucleic acid-based therapies to improve targeted treatment of aggressive and drug-resistant cancers.

Dr. Timothy Samec

Medical Writer and Adjunct Faculty at Abilene Christian University

Dr. Timothy Samec is a 2021 PhD graduate of Clemson University's Department of Bioengineering. He currently is a medical writer for Caris Life Sciences and adjunct faculty in the Department of Precision Medicine at Abilene Christian University. In 2022, he was recognized as a Distinguished Young Alumni of Slippery Rock University for his research contributions in bioengineering, his leadership and service roles at both Clemson and Slippery Rock University, and his continued mentorship of students at both universities as an alumnus.

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