NATIONAL CANCER INSTITUTE
Technology Transfer Center

Inducible Activation Nucleic Acid Hybrid Switch for Conditional Generation of Oligonucleotides

Summary

Researchers at the National Cancer Institute (NCI) developed a potential nucleic acid-based therapy using an inducible activation nucleic acid hybrid switch for conditional generation of oligonucleotides. The NCI seeks innovative companies interested in co-developing and/or licensing this technology.

NIH Reference Number

E-065-2019

Product Type

- Therapeutics

Keywords

- RNA, RNA Logic, Conditional Activation, Functional RNA, Nucleic Acid Therapeutic, In Silico Design, Nanoparticle, Gene Silencing, Shapiro

Collaboration Opportunity

This invention is available for licensing and co-development.

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Description of Technology

Gene therapy research has yielded FDA-approved treatments for an array of diseases. However, challenges facing nucleic-acid based therapeutics include non-specific delivery and degradation of the nanoparticles. NCI investigators have developed a solution to address these challenges in their novel nucleic-based therapy based on the conditional activation strategy.

The inducible activation nucleic acid hybrid switch overcomes the drawbacks of current technologies through its unique design. The implementation of nucleic acid logic elements in these constructs circumvents off-target effects. The functional oligonucleotide constructs would only be generated and activated in environments denoted by the presence or absence of a specific cognate RNA trigger, ensuring context-sensitive

function. The systems were also optimized to be resistant to nuclease degradation yet inexpensive for commercial production. Furthermore, this collection of logic-based systems can accommodate different trigger/target sequence pairs, enhancing its diversity of application, and serves as a novel paradigm for conditionally regulated therapeutics against cancer, genetic disorders, or infectious diseases. The NCI is looking for innovative companies interested in co-developing and/or licensing this technology.

Potential Commercial Applications

- Cancer
- Infectious diseases
- Genetic disorders

Competitive Advantages

- Resistant to nuclease degradation
- Specificity of action based on environmental context, minimizing off-target effects
- Amenable to alterations to accommodate different trigger/target sequence pairs without the need for sequence overlap or similarities
- A set of context sensitive drugs that separate diagnosis (disease state – e.g. over or under expression of particular genes) from the therapeutic state (targeting specific genes – e.g. Dicer substrate RNAs that induce apoptosis)

Inventor(s)

Bruce Shapiro (NCI), Paul Zakrevsky (NCI)

Development Stage

- Pre-clinical (in vivo)

Publications

Zakrevsky P, et al. A Suite of Therapeutically-Inspired Nucleic Acid Logic Systems for Conditional Generation of Single-Stranded and Double-Stranded Oligonucleotides. [PMID 30991728]

Patent Status

- **U.S. Provisional:** U.S. Provisional Patent Application Number 62/832,171 , Filed 10 Apr 2019
- **PCT:** PCT Application Number US2020/27637, Filed 10 Apr 2020

Related Technologies

- E-059-2009 - In silico design of RNA nanoparticles
- E-039-2012 - Nanoparticles for the targeted treatment of infected cells
- E-765-2013 - Multifunctional RNA Nanoparticles as Cancer and HIV Therapeutics
- E-156-2014 - Nucleic Acid Nanoparticles for Triggering RNA Interference
- E-078-2016 - RNA/DNA Nanoparticles as Cancer Therapeutics
- E-277-2016 - Functionally-Interdependent Shape-Switching Nucleic Acid Nanoparticles

- E-075-2018 - siRNA Delivery Using Hexameric Tetrahedral RNA Nanostructures for Gene Silencing

Therapeutic Area

- Cancer/Neoplasm

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