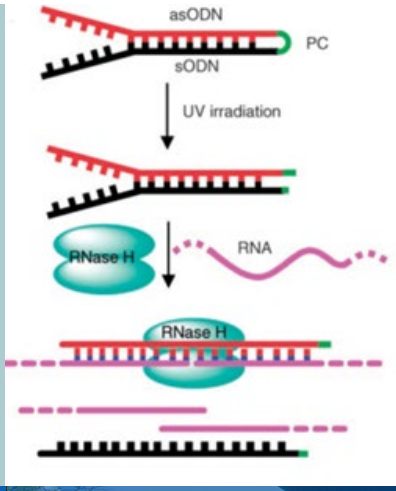

PENN CENTER FOR INNOVATION
Empowering Ideas

Photo-modulation of gene expression and RNA hydrolysis through photoactivatable oligonucleotide constructs

Brief Description

Light-activated DNA hairpin to control RNA digestion in gene silencing with mRNA-antisense complexes

Inventor

Ivan Dmochowski, Professor of Chemistry

STATE OF DEVELOPMENT

- Proof-of-concept
- *In vitro* and *in vivo* testing

INTELLECTUAL PROPERTY

UP Application (US20080227742 A1)

REFERENCE MEDIA

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Penn News highlight.

DESIRED PARTNERSHIPS

- License
- Co-development

LEARN MORE

Sarah Johnson
johnsa@upenn.edu
215-746-7253

Docket #S4240

Technology Overview

Gene silencing can be achieved by targeting messenger RNA (mRNA) during the transcription process. Antisense oligodeoxynucleotides can be designed to bind to a complementary mRNA sequence, where formation of the DNA-mRNA duplex recruits nucleases, such as RNase H, that degrade the target mRNA strand. Thus, a specific gene can be targeted for degradation, ensuring that the protein for which it encodes is not synthesized.

Researchers in the Dmochowski lab have created caged antisense hairpin molecules of DNA that bind to genes and are released upon activation with ultraviolet or infrared light. In order to exert this spatiotemporal control of mRNA degradation, the DNA antisense oligonucleotide is modified by attaching a short piece of the complementary sense strand via a photocleavable blocking group. The DNA oligo is prevented from binding to the target mRNA molecule until the blocking strand is released upon photo-activation. By altering protein expression within a cell and at particular times, a specific gene can be turned on or off to elucidate the role of the gene being studied. This approach was used to regulate two genes in zebrafish embryos, with controlled protein expression throughout the embryo. In another study, photoactivatable antisense oligodeoxynucleotides were demonstrated to downregulate the cancer-related gene c-myb in human K562 leukemia cells.

Advantages

- Straightforward chemical synthesis from commercially available reagents
- Control spatiotemporal patterns of gene expression
- High photoefficiency
- Reduced systemic toxicity in cells and tissues

Applications

- Uncover role of genes in embryonic development
- Regulate gene expression within cell using light
- Gene silencing
- Antisense oligodeoxynucleotides evaluated as cancer therapeutics in clinical trials
- Drug discovery