Near-IR Light-Cleavable Antibody Conjugates and Conjugate Precursors

Summary (1024-character limit)
Researchers at the National Cancer Institute (NCI) developed novel groups of cyanine (Cy) based antibody-drug conjugate (ADC) chemical linkers that undergo photolytic cleavage upon irradiation with near-IR light. By using the fluorescent properties of the Cy linker to monitor localization of the ADC, and subsequent near-IR irradiation of cancerous tissue, drug release could be confined to the tumor microenvironment.

NIH Reference Number
E-245-2016

Product Type
- Diagnostics
- Therapeutics

Keywords
- Chemical linkers
- Fluorescent linker
- Antibody-Drug Conjugate
- ADC
- Targeted drug release
- Photodynamic Therapy
- PDT
- Targeted therapy
- Personalized medicine

Collaboration Opportunity
This invention is available for licensing and co-development.

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Description of Technology

This invention describes a general way to trigger the release of a bioactive small molecule from a

targeting antibody. The key "trigger" is a fluorescent linker that is chemically disassembled upon irradiation with light in the near-IR range (~800 nm).

This linker technology is a dramatic step forward for the field. The molecules can be tracked using conventional fluorescence imaging technology, and with the application of a higher light dose, drug-release can be initiated in a targeted manner. In current clinical practice, a bulk tumor is often removed through a guided surgical approach with the tumor margins cleared by targeted irradiation. This technology promises fewer side-effects and the potential to pre-empt resistance issues by achieving higher, otherwise unattainable, drug doses. Compared to existing photodynamic therapy approaches, this technology relies on the activity of highly potent drug molecules, leading to dramatically improved potency.

To date, the inventors have demonstrated the ability to synthesize and use antibody conjugates that release the bioactive molecule duocarmycin. These ADCs display potent and highly selective activity in cellular assays. *In vivo* imaging has proven the ability to track and subsequently release the compounds with external irradiation from a continuous wave laser source. Significant antitumor efficacy has been observed following a single dose. Future studies are aimed at optimizing the physical properties of the conjugates and detailed *in vivo* efficacy and toxicology studies.

Potential Commercial Applications

- To deliver a potent ADC payload with otherwise unattainable control through local irradiation
- Targeted cancer therapy
- In a basic research context, could be used to test the effect of timing, dose, and location of *in vivo* activity of payloads

Competitive Advantages

- These studies are the first to illustrate *in vivo* drug delivery using antibody and light-based targeting
- Light in the near-IR range exhibits meaningful tissue penetration (up to several cms) and is non-toxic
- Enhanced potency compared to existing photodynamic therapies (PDT) that rely on the use of ROS as the major mediator of biological function
- In comparison to other ADCs, this approach should provide reduced off target release, while providing highly controlled delivery to irradiated areas of interest. These features should reduce toxicity, while providing improved efficacy for certain solid tumor applications (e.g. head and neck, bladder, and glioblastoma)

Inventor(s)

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Development Stage

- Pre-clinical (in vivo)

Publications

Nani RR, et al. In Vivo Activation of Duocarmycin-Antibody Conjugates by Near-Infrared Light. [PMID 28470051]

Nani RR, et al. Near-IR Light-Mediated Cleavage of Antibody-Drug Conjugates Using Cyanine Photocages. [PMID 26403799]

Gorka A, et al. A Near-IR Uncaging Strategy Based on Cyanine Photochemistry. [PMID 25211609]

Patent Status

- **U.S. Provisional:** U.S. Provisional Patent Application Number 62/373,666, Filed 11 Aug 2017
- **U.S. Provisional:** U.S. Provisional Patent Application Number

Related Technologies

- E-204-2015

Therapeutic Area

- Cancer/Neoplasm