

IMPROVED PE-BASED TARGETED TOXINS: A THERAPEUTIC WITH INCREASED EFFECTIVENESS

SUMMARY

The National Cancer Institute's Laboratory of Molecular Biology seeks interested parties to co-develop targeted toxins as therapeutic agents for cancer treatment.

REFERENCE NUMBER

E-269-2009

PRODUCT TYPE

- Therapeutics

KEYWORDS

- Immunotoxin
- Ligand-targeted toxin
- Toxin domain
- Lung
- Ovarian
- Breast
- Head
- Neck
- Hematological cancer

COLLABORATION OPPORTUNITY

This invention is available for licensing and co-development.

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DESCRIPTION OF TECHNOLOGY

Targeted toxins (e.g., immunotoxins) are therapeutics that have at least two important components: (1) a toxin domain that is capable of killing cells and (2) a targeting domain that is capable of selectively localizing the toxic domain to only those cells which should be killed. By selecting a targeting domain that binds only to certain diseased cells (e.g., a cell which only expresses a cell surface receptor when in a diseased state), targeted toxins can kill the diseased cells while allowing healthy, essential cells to

survive. As a result, patients receiving a targeted toxin are less likely to experience the deleterious side-effects associated with non-discriminate therapies such as chemotherapy or radiation therapy.

A particular toxin that has been used in targeted toxins is Pseudomonas exotoxin A (PE). The effectiveness of PE-containing targeted toxins has been demonstrated against various forms of cancer, including hairy cell leukemia (HCL) and pediatric acute lymphocytic leukemia (pALL). Although early variations these targeted toxins have demonstrated efficacy upon first administration, the continued administration of a targeted toxin often leads to a reduced patient response. The primary cause of the reduced response is the formation of neutralizing antibodies against PE by the patient.

Several variations of PE have been created to reduce the immunogenicity of PE as a means of increasing the therapeutic effectiveness of targeted toxins through multiple rounds of drug administration. This technology involves the identification of two important B-cell epitopes on PE, and the elimination of those epitopes by mutation. These new PE variants retain a sufficient cell killing activity while increasing their therapeutic effectiveness toward patients that receive multiple administrations. By further combining these new mutations with previously identified modifications that also improve the efficacy of PE-based targeted toxins, it may be possible to treat any disease characterized by cells that express a particular cell surface receptor when in a disease state.

POTENTIAL COMMERCIAL APPLICATIONS

- Treatment of diseases that are associated with the increased expression of a cell surface receptor
- Treatment for any disease associated with cells that preferentially express a specific cell surface receptor such as various cancers, including lung, ovarian, breast, head and neck, and hematological cancers.

COMPETITIVE ADVANTAGES

- Less immunogenic targeted toxin results in improved efficacy during multiple administrations
- Targeted therapy decreases non-specific killing of healthy, essential cells, resulting in fewer side-effects and healthier patients

INVENTOR(S)

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DEVELOPMENT STAGE

- Pre-clinical (in vivo)

PATENT STATUS

- **U.S. Issued:** US 8,936,792 (25 June 2012)
- **Foreign Filed:** Patents pending in India and Russia
- **Foreign Issued:** JP 5,795,765; EP 2475398; CH 1080049559.3

RELATED TECHNOLOGIES

- E-129-2001

THERAPEUTIC AREA

- Cancer/Neoplasm
- Cardiovascular Systems