

Therapeutic Immunotoxins with Increased Half-Life and Anti-Tumor Activity

Summary

The National Cancer Institute (NCI) seeks research co-development partners and/or licensees for mesothelin targeting Recombinant Immunotoxins (RITs). These RITs have been engineered by site specific modification with polyethylene glycol (PEG) to have an increased serum half-life, while maintaining high cytotoxicity and have greatly improved anti-tumor activity.

NIH Reference Number

E-179-2019

Product Type

- Therapeutics

Keywords

- Mesothelin, Mesothelioma, Immunotherapy, Recombinant Immunotoxins, RITs, Pastan

Collaboration Opportunity

This invention is available for licensing and co-development.

Contact

- David Lambertson
NCI TTC

david.lambertson@nih.gov (link sends e-mail)

Description of Technology

Recombinant Immunotoxins (RITs) are chimeric molecules composed of an antigen binding domain and toxin. The antigen binding domain component targets the cancer cell and delivers the toxin component to the cell. However, the efficacy of RITs is limited by their short half-life once they are in the patient. To address this problem, investigators at the National Cancer Institute (NCI) increased the half-life of RITs using polyethylene glycol (PEG).

In specific embodiments, the antigen-binding fragment targets mesothelin, and the toxin is a fragment of Pseudomonas exotoxin (PE). Mesothelin is highly expressed in many human cancers including mesotheliomas, ovarian cancers, squamous cell carcinoma and pancreatic cancers - making it an excellent candidate for targeted therapies. The resulting PEGylated RITs have an increased half-life while retaining cytotoxic activity, thus

increasing anti-tumor activity in mouse models. This indicates that site-specific modification with PEG can improve the therapeutic utility of RITs. Furthermore, the ability of PEGylation to increase the half-life of RITs can be applied to other RITs directed against different targets.

The NCI [Laboratory of Molecular Biology](#) is seeking parties interested in co-development research collaborations and/or licensing of this technology for commercialization in the field of recombinant immunotoxins and cancer therapeutics.

Potential Commercial Applications

- Cancer therapeutics
 - Specific therapeutic targets include mesothelin-expressing cancers, such as mesothelioma, ovarian cancer, squamous cell carcinoma and pancreatic cancer

Competitive Advantages

- Circulating half-life of RIT's improved 10-30-fold while retaining cytotoxic activity
- In vivo proof-of-concept mouse studies demonstrate that increased half-life allows the agent to exert a therapeutic effect for a longer duration
- Delayed uptake by kidney and liver leads to greatly increased AUC

Inventor(s)

[Ira Pastan M.D. \(NCI\)](#), [Zeliang Zheng Ph.D. \(NCI\)](#)

Development Stage

- Pre-clinical (in vivo)

Publications

Zheng Z, et al. Site-specific PEGylation of anti-mesothelin recombinant immunotoxins increases half-life and antitumor activity. [[PMID 31871266](#)]

Patent Status

- **U.S. Provisional:** U.S. Provisional Patent Application Number 62/935,822 , Filed 15 Nov 2019

Related Technologies

- E-292-2007

Therapeutic Area

- Cancer/Neoplasm

Updated

Sunday, September 11, 2022

Source URL: <https://techtransfer.cancer.gov/availabletechnologies/e-179-2019>