A Microtubuli Modifying Compound

A therapeutic cytotoxic immuno-fusion protein which binds specifically to target body cells and has reduced immunogenic effect

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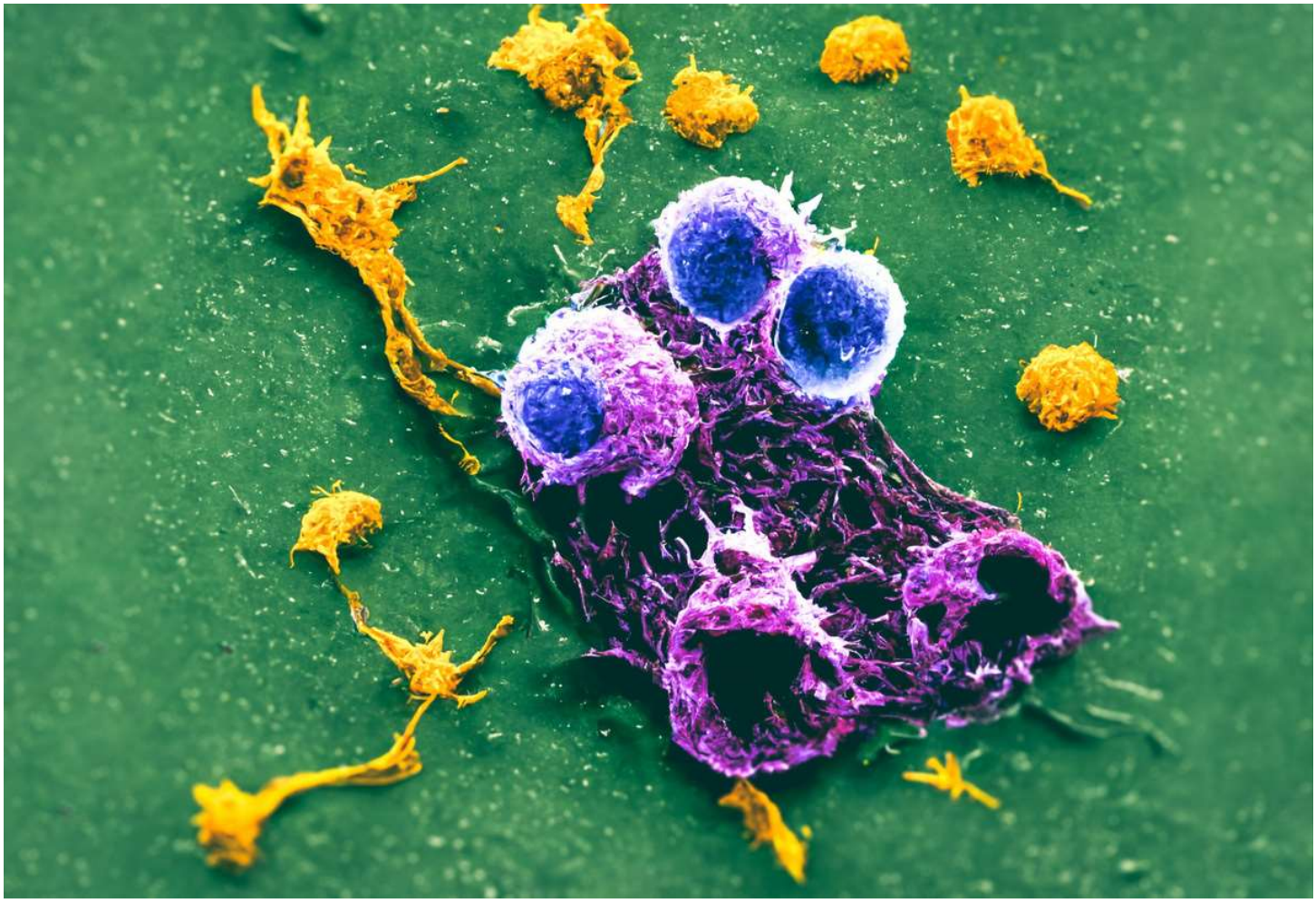

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Background

Recombinant immunotoxins are chimeric proteins predominantly used to treat cancer. These proteins are composed of a binding domain, which is commonly an antibody or a fragment thereof, and a toxic domain, which is a protein usually derived from bacteria or plants. After binding of the antibody to a target cell antigen, the immunotoxin is internalized followed by endosomal processing and the final release of the toxin into the cytosol, where it exerts its toxic activity. In addition to antibodies as targeting units, several ligands including growth factors have been used.

In the beginning of immunotoxin development, antibodies were conjugated to the toxin via chemical coupling, which, however, bore many disadvantages, such as a required separate production and purification of targeting and toxic unit, low yields after conjugation, and an undirected coupling leading to a heterogeneous protein preparation.

To overcome these drawbacks and to allow the commercial development of immunotoxins, recombinant immunotoxins were generated by genetically fusing the ligand and the protein- based toxin resulting in a single chain DNA construct.

Technology Overview

For use in immunotoxins, truncated versions of ETA and DT were generated by deletion of the cell-binding domain. This has reduced the size of ETA and DT, respectively, making them even more suitable to be used as fusion proteins and it has increased their specificity preventing unwanted binding to healthy cells.

Benefits

An effective medicament for treating proliferative diseases based on a compound having reduced side effects.

The predominant toxins used in immunotoxins are plant and/or bacteria derived. There is very little activity around the use of human toxins. The novel immunotoxins disclosed herein are distinct in their use of human cytotoxic payloads to create fully human cytolytic fusion proteins. The human toxins have a reduced immunogenic effect when compared with foreign (i.e., bacterial or plant) toxins.

Applications

An immuno-fusion protein, which binds specifically to target cells in the body and has a cytotoxic microtubule-associated protein (MAP, tau) which causes cell death, for use as a therapeutic agent (in cancers but scope includes inflammatory/autoimmune diseases as well). The invention includes the use in the treatment of cancer disease, in particular proliferative diseases.

The invention involves a fully human immunotoxin comprised of 2 parts:

- Binding domain for extra-cellular surface of diseased cells that internalizes the compound upon binding
- Protein with MAPs or relevant fragment that can bind microtubules.

Novelty: MAPs (tau) being used as the cytotoxic component.

Opportunity

Seeking licensing opportunities, or collaboration/development partners to take the invention into clinical practice.

Patents

- PCT/EP2013/072257

IP Status

- Patented

Seeking

- Development partner
- Commercial partner
- Licensing
- Seeking investment