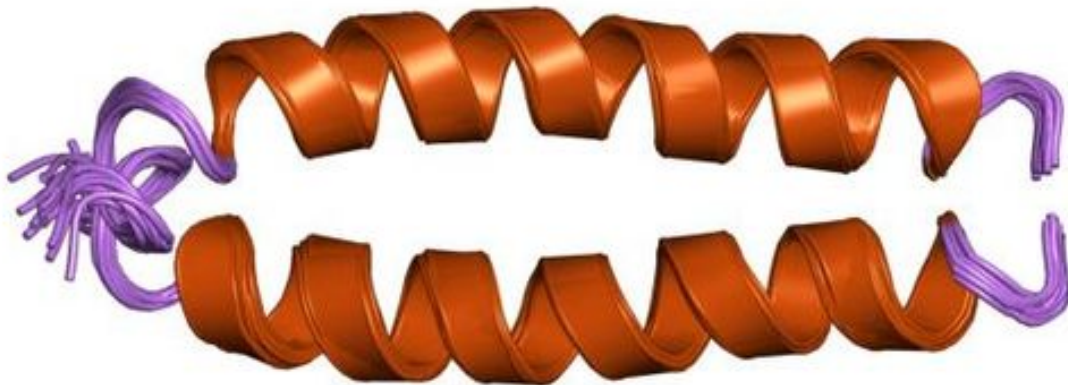


TRAIL Fusion Protein: Novel Gene Therapy for Oncology

A novel genetic construct encoding a CD40LTRAIL fusion protein which kills cancer cells selectively and with high potency.



Please note, header image is purely illustrative. Source: Jawahar Swaminathan, European Bioinformatics Institute, CCO

IP Status

Patented

Seeking

Development partner

About **University of Liverpool**

By facilitating access to our expertise, facilities and networks, the University of Liverpool offers the means to transform ideas into creative solutions, improved performance, new technologies, strategies, applications, products or skills.

Tech Overview

University of Liverpool researchers are developing a novel gene therapy, which kills cancer cells selectively and with high potency . The invention consists of a novel genetic construct encoding a CD40LTRAIL fusion protein.

The TRAIL death receptor pathway is a well validated target for cancer therapeutics, with multiple agonistic antibodies entering clinical trials in the last 10 years. However many of these mAbs failed in the clinic due to poor efficacy. This novel fusion protein overcomes these issues by generating a more potent apoptotic signal.

The improvements employ the use of membrane-anchoring moieties to amplify the effectiveness of this modality of TRAIL-based therapeutic inventions. Significantly improved cancer cell-killing activity has been observed compared to the natural derivatives or soluble equivalents.

Features:

- CD40LTRAIL fusion protein induces cell death in DR4- and DR5- positive carcinomas (**Figure 1**).
- CD40LTRAIL fusion protein induces more potent growth inhibitory effects compared to wild type TRAIL or treatment with soluble TRAIL ligand in a range of cancer cell lines (pancreatic, cervical and bladder).
- CD40LTRAIL fusion protein induces caspase 3/7 activation suggesting specific activation of the death receptor pathway.

Benefits

- TRAIL is a member of TNF superfamily that upon binding to its receptors induces cell death with high specificity for carcinoma cells
- Novel construct tethers the death receptor ligand TRAIL to the cell membrane
- Membrane anchorage increases the cytotoxicity of TRAIL in a range of TRAIL receptor-positive carcinomas

Applications

Significant market opportunity:

- Widespread TRAIL expression in cancer tissue suggests this therapy has the potential to treat various forms of cancer.
- Potential to combine with other chemotherapies and targeted therapies in difficult-to-treat cancers.

Opportunity

Stage of Development - early stage project:

- Preliminary in vitro results suggest great potential for this approach in overcoming efficacy issues with TRAIL mAbs
- Ongoing studies to trial different delivery vehicles for gene construct

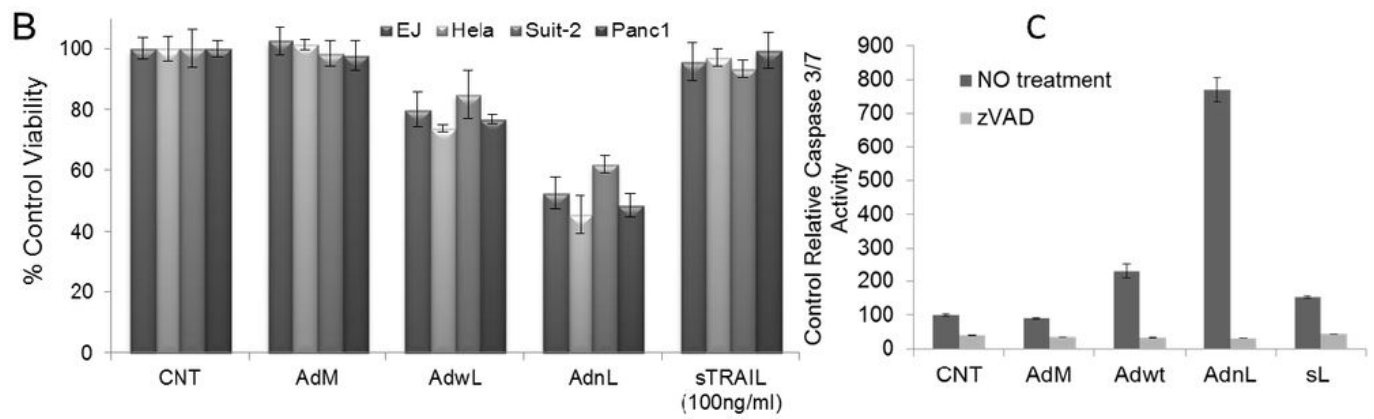
Seeking partners to advance project through preclinical and clinical development. The technology is most applicable to those companies developing viral delivery vector based oncology products.

Patents

- Patent protected technology (Intl. Patent No. PCT/GB2015/051145)
-

Appendix 1

Figure 1



AdM= mock; **AdwL** = recombinant adenoviral WT TRAIL; **AdnL**= recombinant adenoviral CD40LTRAIL fusion; **CNT**= negative control; **SL**= soluble TRAIL ligand