Washington University in St. Louis
Office of Technology Management

SCFV-TR3: TRAIL TRIMERS TARGETED TO MESOTHELIN

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Technology Description

Researchers at Washington University in St. Louis have developed an additional targeting strategy to provide more flexibility and improve the bioactivity of the anticancer therapeutic TR3. This strategy targets TR3 to mesothelin, a tumor biomarker frequently overexpressed in pancreatic cancer, ovarian cancer and mesothelioma, by fusing single chain antibody fragments (scFvs) to TR3. Here, scFvs for P4 or HN1 (anti-human scFvs that bind mesothelin with high affinity) are fused to TR3 to form, P4-TR3 or HN1-TR3. Unlike prior attempts at this strategy, these fusions do not require a spacer between the scFv and TR3 to allow direct cancer cell killing. This technology enables superior cancer cell killing and provides much needed therapeutics to treat pancreatic cancer, ovarian cancer and mesothelioma.

Schematics of TR3 and mesothelin-targeted TR3. Far left: unlinked TRAIL monomers. Left: TR3- genetic fusion of 3 TRAIL monomers. Center and right: TR3 fused to mesothelin targeting scFvs. (Hu= human, Ms=mouse).

Stage of Research

Preliminary studies show P4-TR3 and HN1-TR3 mediate strong direct killing of the targeted cancer cells.

Applications

- Anticancer therapeutic for:
  - Pancreatic cancer
  - Ovarian cancer
  - Mesothelioma
  - Additional cancers

Key Advantages

- Targeted anticancer therapeutics- provide greater treatment efficacy and reduced systemic toxicity
- Spacer is not required
- Can directly induce cancer cell death
- Fully human peptide sequence- low immunogenicity

Publications

- Tatzel K, Kuroki L, Dmitriev I, Kashentseva E, Curiel DT, Goedegebuure SP, Powell MA, Mutch DG, Hawkins WG, Spitzer D. Membrane-proximal TRAIL species are incapable of inducing short circuit apoptosis signaling: Implications for drug development and basic cytokine biology. Sci Rep. 2016 Mar 3;6:22661. doi: 10.1038/srep22661.

Patents

- PCT patent application has been filed

Related Web Links

- Dr. Spitzer profile
- Dr. Hawkins profile