TAKE 3: Revolutionizing Cancer Therapy with New Generation TR3 Biologics

**Background:** Cancer reoccurrence is a major concern for the 14 million cancer survivors within the U.S. Traditional treatments often miss cancer cells, fail to perform in cases of metastasis and may present broad side-effects. Targeted therapies in oncology have the potential for fewer side effects, elimination of all cancer cells from the body and the potential to target disseminated cancers. Unique differences between cancer cells and healthy cells make targeted therapies attractive in cancer treatment plans. Patented research technology at Washington University provides a new therapeutic for specific targeting and destruction of cancer cells.

**Technology Description:** Unique differences in cancerous and healthy cells are apparent at the cellular level, such as the over-expression of the mucin protein MUC16 (CA125). TR3 Technology delivers a new generation of TNF superfamily TRAIL (TNF-related apoptosis-inducing ligand, designated TR3) directly to MUC16-expressing cancer cells. The TR3 molecule is a unique bioactive trimer that has been developed with a highly targeted affinity for cancer cells. This unique fused TR3 overcomes historical challenges faced by TRAIL therapies. When fused with a mesothelin peptide (Meso64-TR3), it directly binds MUC16 with high affinity and delivering a strong apoptosis signal, resulting in efficient cancer cell death. The MUC16-targeted Meso64-TR3 molecule exhibits highly aggressive killing efficacy of cancer cells compared to healthy cells *in vitro* and exhibits remarkably specific action compared to existing recombinant TRAIL technologies.

**Key Advantages:**
- New Generation of TRAIL: High Affinity TR3 family with linked deliverables
- Strong, sustained death receptor signaling
- Modular drug design: easy incorporation of delivery moieties at both of the TR3 trimer
- Stoichiometric, stable drug delivery
- Targeted therapy for primary and metastatic cancers
- Potential to prevent dissemination of metastatic cells via MUC16 blockade
- Used as stand-alone and in combination with other anti-cancer agents

**Patents:** [US9,127,081]: Tumor targeted TNF-related apoptosis inducing ligand fusion polypeptide and nucleic acids encoding the same; [US8,461,311]: TRAIL trimers, methods and uses therefor.


**Lead Inventor:** Dirk Spitzer, PhD, Assistant Professor of Surgery, Division of General Surgery, Washington University School of Medicine at Washington University School of Medicine in St. Louis.

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