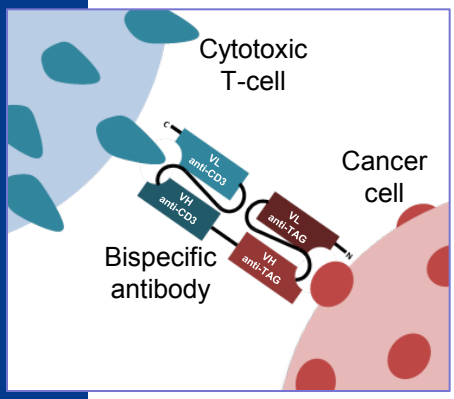
TAG72-CD3 Bispecific T-cell Engager Antibody for Targeted Cancer Immunotherapy



Our technology is a bispecific T-cell engager antibody that can activate T-cells while simultaneously binding TAG-72 expressing cancer cells, bringing the two within close proximity. The process enhances the cancer killing ability of the activated T-cell. In ovarian and breast cancer cell lines, addition of this antibody alongside naïve T-cells significantly increases cancer cell death ($p<0.05$). Our 2nd generation bispecific T-cell engagers are engineered with increased, single digit nanomolar affinity for TAG-72, which should optimize cancer-killing ability. Our antibody can be used as an immunotherapy against breast and ovarian cancer, but may potentially be used to treat any TAG-72-expressing tumor.

COMMERCIAL OPPORTUNITY

- Tumor associated glycoprotein 72 (TAG-72) is a pancarcinoma marker expressed on the surfaces of many cancer tissues including those of the breast, prostate, ovary, endometrium, stomach, esophagus, and pancreas. It is not expressed in normal tissues making it an ideal cancer therapy target.
- Bispecific T-cell engager antibodies have binding activity against two targets, an immune cell receptor (such as CD3) and an antigen. Thus, our bispecific T-cell engager antibody will bind CD3 to activate the T-cell while simultaneously binding TAG-72 on the surface of the cancer cell. The T-cell will be held in close proximity to more effectively kill the cancer. Our particular 2nd generation bispecific T-cell engagers are strategically designed to have enhanced, single digit, nanomolar affinity for TAG-72.
- Our *in vitro* data indicate our bispecific T-cell engager may be effective in the treatment of breast and ovarian cancers. Application of the antibody alongside naïve T-cells significantly increases cancer cell death ($p<0.05$). The treatment of these two populations brings the market size to ~271,500 cases/year in the US. However, this technology can potentially be applied to treat any TAG-72 expressing cancer.
- The CD19-CD3 bispecific T-cell engager (BiTE®) antibody Blinatumomab was approved in December 2014 for the treatment of acute lymphoblastic leukemia, and had been obtained by Amgen through acquisition of Micromet for $1.6 billion. Blinatumomab binds both CD3 and a tumor antigen, suggesting that utilizing CD3 binding to recruit cytotoxic T cells will also work with TAG72-CD3 antibodies.

TECHNOLOGY

A bispecific T-cell engager antibody (CC49-OKT3) contains a proprietary linker to enhance half-life of the antibody and minimize immunogenicity of the therapy. The antibody can bind the TAG-72 and MCF-7 doxorubicin resistant (DOX), SKBR3 HER2+, and ovarian OVACAR-3 cancer cell lines. Flow cytometry data show the addition of the bispecific T-cell engager antibody to naïve CD8 T-cells significantly increases cancer cell death as indicated by the Annexin/PI+ signal from DOX (52.4% vs. 41.4% CD8 alone), SKBR-3 (47.9% vs. 30% CD8 alone), and OVACAR3 cells (31.1% vs. 23.8% CD8 alone) respectively ($p<0.05$). Furthermore, significant levels of IFNγ secreted by activated T-cells are only detected in the bispecific T-cell engager Ab+ CD8 conditions. Finally, 2nd generation bispecific T-cell engager antibodies are being generated with the scFv region engineered to have a 2-6 fold increased affinity for TAG-72—changes expected to optimize the targeting and killing of cancer cells.

PUBLICATION/PATENT

- U.S. patent application filed on 8/18/16 for Dr. Hatem Soliman.

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