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Antibody Fusion Protein and Compositions for Targeting Cancer

Glioblastoma (GBM) is a common and highly aggressive brain tumor that affects over 11,000 patients every year in the US alone. Standard of care includes surgical resection, radiation therapy, and chemotherapy. Even with these aggressive treatments, outcomes remain poor, with a 5 year survival rate of approximately 5%. Many small molecule chemotherapeutics are ineffective at treating GBM due to the presence of the blood-brain barrier, which blocks the delivery of more than 98% of systemically administered agents. Thus, alternatives to traditional chemotherapy are desperately needed.

The last few years have seen an explosion of impressive clinical results in the field of cancer immunotherapy, representing some of the most promising advancements in cancer treatment. Bispecific antibodies are one class of cancer immunotherapies that have been shown to harness a patient's own immune system to target and kill tumor cells. To date, though, no bispecific antibody capable of effectively targeting GBM has been developed.

Researchers at Dignity Health in collaboration with researchers at Arizona State University have developed a novel bispecific antibody fusion protein comprising an anti-CD3 antibody fragment, which is an immune stimulator, and a targeting peptide, which enables the construct to localize with cancer cells, even across an intact blood-brain barrier and with little to no specificity for normal tissue. The targeting peptide belongs to a class of chlorotoxin-like peptides, which are derived from the venom of scorpions. These peptides have been extensively studied for their cancer targeting abilities in vitro, particularly for GBM, and versions have already been tested in the clinic in Phase 2 trials for targeted imaging and radiotherapy. With this novel fusion protein, CD4+ T cells, CD8+T cells, and NK T cells can be engaged to attack cancer cells. T cells in the vicinity of even small numbers of malignant cells can be activated to direct their cytotoxic effects specifically against those cells. The fusion protein does not activate T cells unless it is bound to a cancer cell, thus reducing unwanted side effects and enabling a potent specific therapeutic.

Further, this fusion protein can overcome immune evasion by circumventing the need for MHC expression on the target, allowing any T cells in the tumor periphery to directly kill tumor cells. This targeted immunotherapy could effectively treat tumors and decrease rates of recurrence.

Applications

- Cancer therapeutics

o Particularly promising for glioblastoma but of interest for other cancers including: melanoma, SCLC, neuroblastoma, medulloblastoma, ganglioneuroma, pheochromocytoma, Ewing sarcoma, ependymoma, and more

Benefits of Technology

- The targeting molecule binds to tumors of neuroectodermal origin
- Significantly more selective to malignant versus healthy cells
- Broadly able to target different types of cancer
- Capable of directing the immune response to very small numbers of malignant cells (potentially individual cells)
- Can reach areas in the brain where the blood-brain barrier is intact or partially intact
- Can overcome immune evasion by circumventing the need for MHC expression on the target cells
- Versatile production methods – has been stably expressed in E. coli and plants. Expression in human cells is being developed and other expression systems are also possible
- The chlorotoxin-like peptide selectively binds to glioma cells, with binding capability increasing with tumor grade
- Individual components have validated safety profiles

Additional Information

Dignity Health ID: DN 2016-001

Inventors: Rebecca Cook, Rachael Sirianni, PhD; Tsafrir Mor, PhD; Joseph Blattman, PhD

Stage of Development: Compositions were tested on GL261-LucNeo mouse glioma cells

IP: WO2017143259A1

Status: Seeking corporate partner to license and develop this technology

Contact: Michael Donovan, IP Manager, 602.307.2989,