Arnie Charbonneau Cancer Institute
The Riddell Centre for Cancer Immunotherapy

University of Calgary | Alberta Health Services

Precision CAR T Cell Therapy for Glioblastoma: Developing Safe, Multi-Targeted Treatments with Logic-Gated CAR T Cells

TARGETED CANCERS

Glioblastoma

RESEARCH PRIORITIES

Discovery & Innovation

PROJECT TEAM


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RESEARCH ENABLERS

- Genomics
- Proteomics
- Synthetic immunology
- Preclinical modeling

PROJECT SUMMARY

Glioblastoma is an extremely aggressive brain cancer with very limited treatment options. Current approaches, such as chimeric antigen receptor (CAR) T cell immunotherapy, target specific markers on the surface of cancer cells. However, the inherent complexity of glioblastoma has posed significant challenges to these therapies. Within a single patient's tumour, the cancer cells can vary greatly, with some cells expressing the target marker while others do not. This lack of uniformity allows the cancer to evade treatment and develop resistance, leading to regrowth and progression despite therapy.

Recent research indicates that targeting multiple markers could enhance the effectiveness of CAR T cell therapies. However, this approach introduces new challenges. Many markers present on glioblastoma cells are also found on healthy brain cells, which could lead to unintended damage to normal tissues and result in toxic side effects.

To address these challenges, our team is developing an innovative solution with "logic-gated" CAR T cells. These engineered cells are designed to precisely target and eliminate cancer cells that display a unique combination of characteristics. By employing a logic-gated mechanism, this approach enhances the accuracy of distinguishing cancer cells from healthy tissue, thereby minimizing the risk of collateral damage to normal cells. For instance, we have designed "logic-gated" CAR T cells that require both a signal derived from the unique environment of the glioblastoma tumour “AND” the presence of a specific marker on the glioblastoma cells themselves before unleashing their cancer killing activity.

The markers utilized in this project to safely and effectively target glioblastoma were identified through the Riddell Centre’s discovery program. A "logic-gated" CAR T platform has been developed, and we have engineered several glioblastoma environment-glioblastoma cell "logic-gated" CAR constructs. Our next steps include evaluating these "logic-gated" CARs in appropriate models of glioblastoma. If successful here, and upon expansion of the glioblastoma target repertoire, we anticipate the creation of a safety-gated CAR T cell library that can address the complexity of glioblastoma.

OVERALL IMPACT

The objective of this work is to develop CAR T therapies that specifically target glioblastoma within its tumour environment. By addressing challenges such as safety, tumour diversity, and drug resistance, this approach aims to contribute to the advancement of CAR T therapy in glioblastoma and other solid tumours.