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

PROJECT TEAM


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TARGETED CANCERS

- Glioblastoma

RESEARCH PRIORITIES

- Discovery & Innovation

RESEARCH ENABLERS

- Synthetic immunology
- Genomics
- Proteomics
- Preclinical modeling
- Data science

Previous enablers:
- Vectorology

PROJECT SUMMARY

Glioblastoma has very limited treatment options. Current approaches, such as CAR T-cell therapy, work by targeting specific markers on the surface of cancer cells. However, the complex nature of glioblastoma presents major challenges for 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 suggests 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 harmful side-effects.

To address these challenges, a team at UCalgary led by Dr. Franz Zemp recruited Dr. Snow Guo as a staff scientist to help develop an innovative solution using "logic-gated" CAR T-cells, which are like high-tech immune cells with built-in decision making. They only activate when they detect a very specific combination of signals — both from the tumour's environment and from unique markers on the cancer cells. This double-check system helps ensure only the cancer cells are targeted, leaving healthy brain cells unharmed.

The markers used in this project were discovered through the Riddell Centre's Discovery and Innovation Program. Using this information, the team has already created several versions of these logic-gated CAR T-cells. The next step is to test them in models that closely mimic glioblastoma. If these tests are successful, the team hopes to build a library of safe and effective CAR T-cells that can adapt to the complex nature of this disease.

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.

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