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PROJECT TEAM

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Developing a Novel CAR Macrophage Therapy to Treat Glioblastoma



Glioblastoma

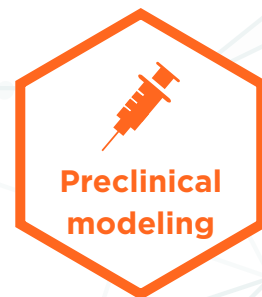
TARGETED CANCERS

RESEARCH PRIORITIES



Discovery & Innovation

RESEARCH ENABLERS



Preclinical modeling



Biobanking



Synthetic immunology

Previous enablers:
• Vectorology

PROJECT SUMMARY

Glioblastoma creates a tumour microenvironment that suppresses the immune system. While T cells, a type of immune cell, have difficulty infiltrating glioblastoma tumours, another type of immune cell called macrophages are abundant in these tumours.

Researchers at UCalgary, led by Dr. Jennifer Chan, are exploring a potential new therapy that harnesses these macrophages to fight glioblastoma. The team is developing a treatment called CAR macrophage (CAR M) therapy. CARs are special molecules that can be engineered into immune cells to help them recognize and destroy cancer cells. In this project, researchers are engineering macrophages to express CARs that target a specific marker on glioblastoma cells called EGFRvIII. These engineered macrophages are designed not only to kill cancer cells, but also to release signals that recruit other immune cells, such as T cells, to join the fight against the tumour.

The team has created and tested a number of different CAR M designs that target EGFRvIII. They

discovered that designs including specific signalling molecules were particularly effective at triggering macrophages to release pro-inflammatory signals, which are important for reactivating the immune system.

Next, the team tested a standard chemotherapy alone and in combination with immune-checkpoint inhibitors (a form of immunotherapy) in their preclinical model of EGFRvIII glioblastoma. They found these therapies had limited success in improving survival in their preclinical models, underscoring the need for novel therapies like CAR M. More recently, the team began studying delivery methods of CAR M into preclinical models and has started experiments evaluating the presence of the engineered CAR M in the tumour. Future experiments will explore whether CAR M therapy can change the tumour microenvironment to make it more supportive of immune activity and test the therapy's effectiveness on its own and in combination with other treatments.

OVERALL IMPACT

The researchers are working toward creating a powerful new therapy for glioblastoma by using macrophages that can penetrate deep into the tumour and reprogram it, this approach holds the potential to improve survival for patients with this difficult-to-treat cancer.