Development of a novel orthotopic brain tumor murine model for pre-clinical evaluation of CAR T cells

Mike Hart-Matyas[1,2], Alaina Jarisz[2,3], Vijay Ramaswamy[1] and Juan Carlos Zúñiga-Pflücker[2,3]
1. The Hospital for Sick Children, Divisions of Haematology and Oncology; 2. Department of Immunology, University of Toronto; 3. Biological Sciences Platform, Sunnybrook Research Institute

GOAL

There is growing excitement about using chimeric antigen receptor (CAR) T cells to treat deadly brain tumors in children based on success in leukemia. However, there's a big gap between the promising results seen in mouse models and the more limited success seen in early human clinical trials.[1,2] This disconnect suggests that the current preclinical models, which rely on mice without functioning immune systems, don't fully represent what happens in children with brain and solid tumors.

To address this critical gap in pediatric brain tumor research, we aim to develop a new preclinical model that better mimics the human body by allowing a human brain tumor to grow alongside a human immune system.

OBJECTIVES

- Development of a pre-clinical brain tumor mouse model with human microenvironment.
- Leverage this new model to benchmark CAR T cell responses.
- Develop new CAR T cells for the treatment of brain tumors

STUDY METHODS

RESULTS

IMPACT/OUTCOMES

PROJECT TIMELINES

Complete timeline: May 01, 2025 – March 31, 2026.

First quarter: Development of HSPC model

Second and third quarter:

- Evaluation of humanized mice and development of tumor/immune microenvironment.
- Development of conventional and novel CAR constructs.

Fourth quarter:

- Planning for CAR T cell treatment of humanized mice with orthotopic brain tumors.

REFRENCES

1. Monje M, Mahdi J, Majzner R, et al: Intravenous and intracranial GD2-CAR T cells for H3K27M(+) diffuse midline gliomas. Nature 637:708-715, 2025.
2. Vitanza NA, Ronsley R, Choe M, et al: Intracerebroventricular B7-H3-targeting CAR T cells for diffuse intrinsic pontine glioma: a phase 1 trial. Nat Med 31:861-868, 2025.
3. Voillet, V. *et al.* An In Vivo Model of Human Macrophages in Metastatic Melanoma. J. Immunol. 209, 606–620, 2022.

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