Arnie Charbonneau Cancer Institute
The Riddell Centre for Cancer Immunotherapy

University of Calgary | Alberta Health Services

Improving CAR T Therapy with Gene Editing Technologies

TARGETED CANCERS

- Cancer agnostic

RESEARCH PRIORITIES

- Discovery & Innovation
- Biomanufacturing

PROJECT TEAM

Dr. Pierre Billon (PI)

Dr. Lou Baudrier (Co-I)

Dr. Douglas Mahoney (Co-I)

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RESEARCH ENABLERS

- Genomics
- Synthetic immunology
- Preclinical modeling

PROJECT SUMMARY

Over the past 40 years, two groundbreaking approaches, CAR T cell therapies and CRISPR gene editing, have revolutionized modern medicine. CAR T cell therapies, or chimeric antigen receptor T cell therapies, involve collecting immune cells from a patient, genetically modifying them in a lab, and reintroducing them to the patient's body, where they can seek out and destroy cancer cells. CRISPR gene editing, on the other hand, is a powerful tool that acts like molecular scissors, allowing scientists to precisely cut and change DNA to fix genetic problems or insert desired genes. This project combines these two transformative technologies to improve cancer treatment, aiming to create the next generation of highly effective and precise cancer therapies.

To reach this goal, a team of scientists at the University of Calgary are working on three main strategies:

1. **Enhanced Gene Editing of CAR T Cells:** The team is using advanced CRISPR tools to edit multiple genes in immune cells, with the intention to boost the cells' cancer-fighting abilities. So far, the team has developed the tools and protocols for editing genes in immune cells, using protein and mRNA-based delivery systems. The team has also edited specific genes in T cells that enhance their durability and ability to fight cancer.
2. **Improved Delivery Systems:** To streamline and expedite the manufacturing process, the team is developing methods to modify T cells directly within the body (in vivo) rather than in a lab (ex vivo). Currently T cells are modified in the lab which can take several weeks, and cost thousands of dollars. To address this, the team has developed a nanoparticle delivery system, which has shown success in editing different types of immune cells and could eventually allow CAR T cells to be modified inside the body. The team is working to fine-tune this system so that it can target specific cell types, which would further boost CAR T therapy effectiveness and simplify the manufacturing process.
3. **Efficient Selection System:** To improve efficiency, the team has created a selection system that quickly identifies successfully edited cells. This allows the team to filter out only the most effective CAR T cells for use in treatment.

OVERALL IMPACT

The project aims to significantly enhance CAR T therapies, enabling them to tackle a wider range of cancers, potentially including difficult-to-treat solid tumours. Additionally, the advancements in delivery and manufacturing processes could pave the way for affordable, "off-the-shelf" CAR T therapies. These innovations would reduce the need for extensive patient-specific preparation, minimize associated risks, and make this cutting-edge treatment accessible to more patients.