

## New generation chimeric antigen receptors for improved adoptive T-cell therapy for cancer

Jan. 17, 2017 to Dec. 31, 2018

### Highlights

- Produces new generation CAR constructs for tumor antigens other than CD-19
- Generates intellectual property that will lead to important and effective therapeutics for cancer patients in Canada and beyond
- Preclinical data critical for the rapid launching of first-in-human clinical trials to treat Canadian cancer patients with CAR T-cell therapy

Biotherapeutics  
**Adoptive cell therapy – engineered T cells**

targeted cancers

### All cancers (tumours)

Generate new generation CAR constructs and validate their in vitro and in vivo function in comparison with their previous generation counterparts. Successful completion will provide preclinical data to launch first-in-human clinical trials to treat cancer patients in Canada with new generation CARs in the near future.

Project value

**\$475,001**

BioCanRX contribution:  
**\$200,001**

Partners

**1**

### About the project

Adoptive T-cell therapy is a type of personalized cancer immunotherapy that utilizes the patient's own T cells to attack their cancer. The results of recent clinical trials show that the adoptive transfer of anti-CD-19 chimeric antigen receptor (CAR) T cells can induce dramatic clinical responses in patients with relapsed or refractory B cell malignancies. Importantly, these responses are often durable and long lasting. Encouraged by this, CAR T-cell therapy has been tested in other blood cancers and various solid tumors. However, CAR T-cell therapies targeting antigens other than CD-19 have not yet achieved the same level of success. New strategies need to be developed.

The goal of this proposal is to produce new generation CAR constructs for targets other than CD-19 and test these constructs in CAR gene therapy clinical trials for cancer patients. The team recently developed a new generation CAR construct with improved quality compared to the conventional CAR constructs currently used. It will produce new generation CAR constructs for tumor antigens other than CD-19 and test their function in comparison with their conventional orthologues. Successful completion of this study will provide preclinical data critical for the rapid launching of first-in-human clinical trials to treat Canadian cancer patients with CAR T-cell therapy.

Collectively, this project can provide an integrative platform where new generation CAR T cells can be made for any given antitumor single-chain variable fragment (scFv) gene in the laboratory and then test its safety and effectiveness in CAR gene therapy clinical trials at Princess Margaret. These clinical trials will be extended to centers throughout Canada. This project will also generate intellectual property that will lead to important and effective therapeutics for cancer patients in Canada and beyond.

The overarching goal of this research is to treat patients with various types of tumors via the adoptive transfer of anti-tumor CAR T cells. The objective is to generate new generation CAR constructs and validate their in vitro and in vivo function in comparison with their previous generation counterparts.

# TakaRa

Key investigator

**Project lead:**

**Dr. Naoto Hirano**

 **UHN** The Princess Margaret Cancer Foundation

# Catalyst Program Investigators



## **Hamilton**

*McMaster University*  
Dr. Jonathan Bramson

## **Toronto**

*Princess Margaret Cancer Centre,  
University Health Network*  
Dr. Naoto Hirano  
Dr. Marcus Butler

## **Partners**

**Takara Bio**  
**\$275,000**

## **Key Milestones**

### **Year 1**

Produce the pre-clinical data package needed for pre-CTA meeting with Health Canada:

- Robust murine data that demonstrates dosing and schedule of the ILCV.
- Robust murine survival data that demonstrates efficacy, safety and manufacturing of the ILCV under immune compromising conditions.
- Understanding of host factors that may be important for patient inclusion criteria at time of trial
- In vitro data demonstrating the immunogenicity of the ILCV.
- Based on immune studies, a potency assay to test patient specific ILCV.

### **Year 2**

Results from aim 3. The key milestone will be to have a straightforward process design procedure for GMP manufacturing of a patient specific ILCV. Deliverables at this stage will include:

- The understanding of key methods and parameters for manufacturing ILCV including processing of cells, infection with MG1, irradiation, storage and administration
- Validating the potency assay in patient specific samples to allow straightforward process design procedure for development of this GLP assay.
- The understanding of key methods and parameters to measure anti-leukemia specific T cell immune responses to facilitate the process design for development of a GLP assay to be used as an outcome measure in a clinical trial.

**The power to kill cancer lies within us.  
Let's tell our bodies how.**