BioCanRx
Canada's Immunotherapy Network
Le réseau canadien d'immunothérapie

Catalyst Program

In vivo genome-wide CRISPR/Cas9 screen to identify genes that limit curative checkpoint blockade immunotherapy in triple negative breast cancer

Jan. 31, 2018 to Mar. 31, 2020

Highlights

- The results of the proposed study have the potential to revolutionize checkpoint blockade immunotherapy in breast cancer.
- These treatment strategies can bring a long-term solution to control metastatic and relapsing tumor types owing to the establishment of immunological memory in the body.

Biotherapeutics
CRISPR, Checkpoint blockades

targeted cancers
Triple negative breast cancer

Develop targeted combination immunotherapy for TNBC and metastatic forms of breast cancer, and to generate foundational knowledge that can inform other cancer types.

Project value
$198,650
BioCanRx contribution:
$98,650

Partners
2

About the project

Emerging clinical data indicate that checkpoint blockade immunotherapies show limited efficacy in non-immunogenic cancers, such as ~20% efficacy in Triple Negative Breast Cancer (TNBC), a form of breast cancer that currently lacks effective treatment. Dr. Mossman and team propose to use a high throughput genetic screen to identify molecules used by tumors to escape immune attack.

The molecules used by cancer cells to escape the immune system will be pharmacologically inhibited to enhance the antitumor effects of checkpoint blockade immunotherapy. The study will use a preclinical Triple Negative Breast Cancer model. Combination strategies will be tested for tumor regression, prevention of metastatic tumors, survival and long-term protection. Future experiments will also determine the mechanisms of biological interaction that results in improved antitumor immune response.

The screen proposed here uses an unbiased genome wide approach to identify the various mechanisms tumors evolve to escape checkpoint blockade immunotherapy. Findings will not only provide a basic understanding of immune escape mechanisms but also a translational benefit for next generation immunotherapies. Using these preclinical findings, the team can design future clinical trials aimed at increasing the proportion of cancer patients that respond to checkpoint immunotherapies. Current therapies are generally toxic and cancer cells often develop resistance. As immunotherapy targets multiple types of cancer with minimal adverse side effects, including drug-resistant cells, these treatment strategies improve the quality and duration of life of patients.

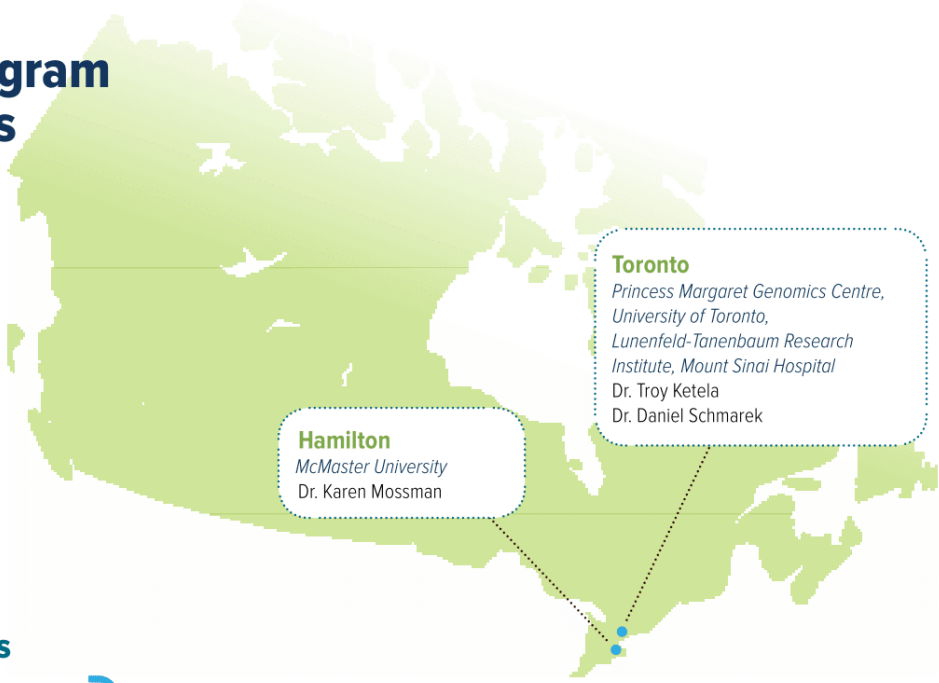
Canadian Breast Cancer Foundation

The Terry Fox Research Institute
L'Institut de recherche Terry Fox

Key investigator

Project lead:
Dr. Karen **Mossman**
McMaster University

Catalyst Program Investigators



Toronto
Princess Margaret Genomics Centre, University of Toronto, Lunenfeld-Tanenbaum Research Institute, Mount Sinai Hospital
Dr. Troy Ketela
Dr. Daniel Schmarek

Hamilton
McMaster University
Dr. Karen Mossman

Partners

Canadian Breast Cancer Foundation
$50,000

Terry Fox Research Institute
$50,000

Key Milestones

0-4 months
- Perform primary genome-wide screen
- Generate shortlist of potential hits

4-10 months
Generate E0771-SIY cell lines deleted individually for top 10 genes hits.

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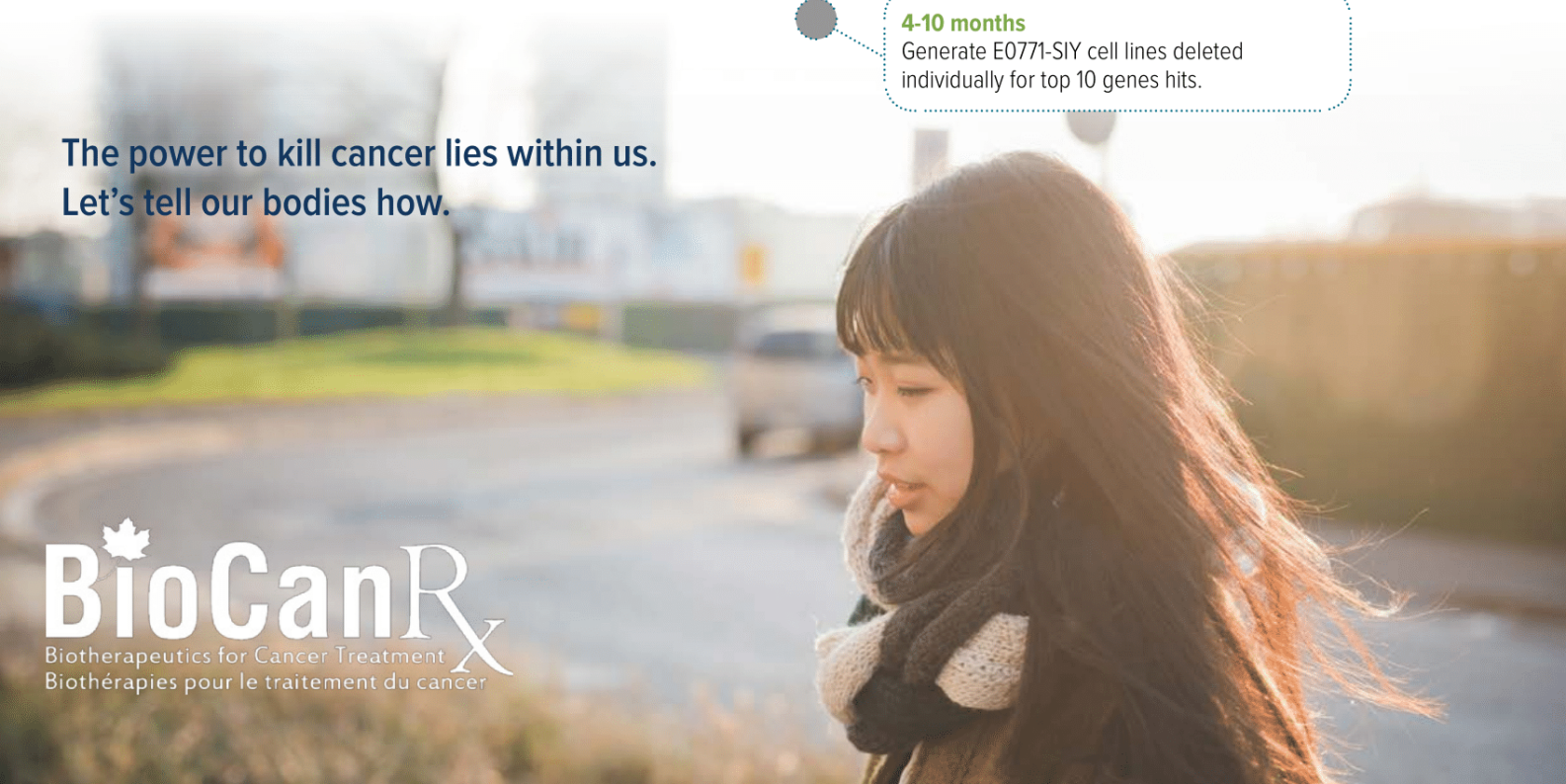
The power to kill cancer lies within us. Let's tell our bodies how.



BioCanRx
Biotherapeutics for Cancer Treatment
Biothérapies pour le traitement du cancer