



Spring / Summer 2014

## Innovative new investigators to study cancer growth and response to treatment

Three promising Canadian cancer researchers, two in Ontario and one in Quebec, have been awarded a total of \$1.35 million under the Terry Fox Research Institute's 2013 New Investigator Awards.

University Health Network researchers Drs. Paul Boutros and Catherine O'Brien, and Dr. Francis Rodier, Centre de recherche du Centre hospitalier de l'université de Montréal (CRCHUM), were selected by a committee of international scientific experts in a competitive application process. Each is now being mentored within a team of Terry Fox-funded discovery or translational research projects working with leading cancer researchers.

Each investigator uses a different approach and technique to try to uncover more about how cancers grow and respond to treatments. Their goal is to learn why some cancers respond better to therapy than others.

Dr. Victor Ling, TFRI president and scientific director, explains why their work is important.

"There can be big differences not only between cancers, but within a cancer tumour and between single cancer cells. I'm very excited to see how these three young investigators progress and what they find out."

The funding for the three investigators will be provided over the next three years. The New Investigators program is an annual competition and provides research operating grant support to future leaders as they develop their independent careers in cancer research.

Please see page 2 for profiles of these New Investigators.

## MARK YOUR CALENDARS!

TFRI's 6th Annual Scientific Meeting  
May 7-9, 2015 | St. John's, NL

Help us celebrate the 35th Anniversary of the Terry Fox Marathon of Hope



### Important finding for lymphoma patients

The discovery of a new, recurrent genetic mutation in two kinds of lymphoma is promising for patients who have these mutations, say Terry Fox-funded researchers, whose findings were published recently in *Nature Genetics*. "It provides potential new targets for treating the disease with new therapeutics," says Dr. Christian Steidl, shown above right with his PhD student Jay Gunawardana, the study's first author. Dr. Steidl is an investigator with the Terry Fox-funded Program Project Grant (PPG) in lymphoma. The work was done at the BC Cancer Agency in Vancouver. Read the complete story on page 3. Photo credit: Cameron Heryet/BC Cancer Agency

### 2015 PPG RFA Coming Soon!

Watch our web site mid-May for the posting of our 2015 RFA for the Terry Fox New Frontiers Program Project Grants. LOIs will be due **July 2, 2014**. Award decisions stemming from the 2014 competition will be made known in late May. Visit [www.tfri.ca/en/research/program-project-grants](http://www.tfri.ca/en/research/program-project-grants) for details.

### 2014 RFA for New Investigators

Applications for our 2014 competition for New Investigator awards are now being accepted. These awards, worth approximately \$450K over three years, are given to outstanding young researchers who work in close collaboration with established TFF/TFRI research teams. Full applications are due Monday, **June 2, 2014**. Visit [www.tfri.ca/en/research/new-investigators/new-investigator-2014](http://www.tfri.ca/en/research/new-investigators/new-investigator-2014) for details.

NOTICES

# 2013 Terry Fox **New Investigators**

## DR. CATHERINE O'BRIEN



**Where:** Ontario Cancer Institute  
**Project Title:** Understanding Cancer Stem Cell Heterogeneity and Dynamics: Implications for Therapy in Human Colorectal Cancer  
**Award:** \$450,000  
**Mentoring Program:** The Terry Fox New Frontiers Program Project Grant: Addressing Tumour Heterogeneity By Identifying Subgroup-Specific Shared Maintenance Genes  
**Mentor/PI:** Dr. Sean Egan

Dr. Catherine O'Brien is a scientist with the Ontario Institute for Cancer Research and a general surgeon with the University Health Network. She is studying colorectal cancer at the level of single cells to identify which cells cause metastases and are resistant to chemotherapy.

"We have known for a long time that not all cells in any given cancer are the same – some cancer cells are more aggressive than others. We also know that cancer cells from the same tumour can demonstrate differential responses to chemotherapy. Our goal is to study colorectal cancer at the single-cell level. By doing so we can begin to understand what makes certain cells so aggressive. The ultimate goal is to devise therapies directed at these specific cells."

Being part of a TFRI Program Project Grant (PPG) has given Dr. O'Brien many new opportunities

to work with a wider research community. For example, she will track the growth of different cancer cells using a bar-coding method developed by fellow TFRI researcher Dr. Jason Moffat (University of Toronto).

"TFRI is unique within Canada, and working within the PPG is an incredible opportunity for me. The other investigators are all world-class researchers. I wouldn't have the opportunity to interact with them otherwise. I can discuss my work and get their input and learn from their different areas of research."

TFF PPG principal investigator Dr. Sean Egan, University of Toronto, says "Dr. O'Brien's proposed work is particularly exciting; by studying cell composition before and after treatment she will be able to answer questions regarding how colorectal cancers respond to both standard chemotherapeutic agents and stem cell-targeted therapies."

## DR. PAUL BOUTROS



**Where:** Ontario Institute for Cancer Research  
**Project Title:** Systems Biology of Tumour Hypoxia  
**Award:** \$450,000  
**Mentoring Program:** The Terry Fox New Frontiers Program Project Grant: Hypoxia in Tumours: Clinical and Experimental Studies  
**Mentor/PI:** Dr. Bradley Wouters and Dr. Robert Bristow

Dr. Paul Boutros is a computational biologist and principal investigator with the Ontario Institute for Cancer Research. Using his mathematical expertise, Dr. Boutros will take a computational approach to modelling the internal structure or "micro-environment" of a tumour, with the goal of predicting how a tumour will respond to therapy.

"Tumours that look superficially very similar can have very different responses to treatment," he explains. "Some areas within a tumour grow quickly and others grow slowly. In particular, different parts of a tumour show differences in blood circulation and in oxygenation. Tumours with blood vessels that are inefficient at providing oxygen respond very poorly to many therapies. By creating models of the tumour micro-environment and bringing different data sets together, I hope to find a link between genetics and tumour oxygenation."

As part of the TFRI Hypoxia in Tumours Program Project Grant, Dr. Boutros will have access to 15

years' worth of unique data collected from several projects. "By combining everything we know about a tumour, in the future we may be able to predict how a patient will respond to treatment, potentially enabling us to modify existing therapies and treat patients more effectively."

Being part of TFRI is critical to Dr. Boutros' work. He says "I am able to learn so much from colleagues with more experience and scientific backgrounds that are different from mine. They help me apply clinical meaning to my mathematical work. Being part of the TFRI community not only helps me, but my research team and trainees all benefit greatly as well."

Dr. Rob Bristow, Princess Margaret Cancer Centre, says "The merging of our many datasets collected over the years will lead to a better understanding of tumour biology and prognosis. Dr. Boutros is an outstanding addition to our PPG team and he fills an important gap in bioinformatics across all our projects."

## DR. FRANCIS RODIER



**Where:** Centre de recherche du Centre hospitalier de l'université de Montréal (CRCHUM)  
**Project Title:** Understanding the Impact of Cancer Cell Fate Decisions During Ovarian Cancer Treatment  
**Award:** \$450,000  
**Mentoring Program:** TFRI's Translational Cancer Research Project: A Pan-Canadian Platform for the Development of Biomarker-Driven, Subtype-Specific Management of Ovarian Carcinoma (COEUR)  
**Mentor/PI:** Dr. Anne-Marie Mes-Masson, Dr. David Huntsman and Dr. Diane Provencher

Dr. Francis Rodier, an associate professor of molecular and cell biology at the department of radiology, radio-oncology and nuclear medicine at the University of Montréal, is studying how ovarian cancer cells respond to the damage caused by radiotherapy and chemotherapy.

In response to treatment, damaged cells have many options; they can repair themselves, they can die, or they can enter a state of permanent growth arrest called "senescence".

Dr. Rodier is particularly interested in this process of senescence, where cells stop growing but don't die. "Nobody really knows what is going on inside tumours during treatment. We know if a tumour is regressing or not, but we don't really understand what's going on inside," explains Dr. Rodier. "By analyzing tissue samples from patients pre- and post-treatment, we can characterize different cancer cell responses to therapy and whether senescence has an impact on treatment success and patient survival."

Dr. Rodier is now mentored by TFRI's Translational Cancer Research Project, led by Drs. Anne-Marie Mes-Masson and Diane Provencher, at the Centre de recherche du Centre hospitalier de l'université

de Montréal (CRCHUM), and David Huntsman (BC Cancer Agency). Using the COEUR project's biobank of tissue samples, his initial goal is to determine how much senescence occurs within cancer cells in response to treatment and to identify some biomarkers that could label this process. Any biomarkers found could potentially be used to follow-up treatment evolution in real time or even predict how well a patient will respond to a given treatment.

"Being part of the TFRI network is a huge advantage. It allows me an opportunity to collaborate with other established Canadian researchers that I wouldn't otherwise have had. I am trying to focus more and more on applying my research to the patient. Learning from Anne-Marie, David and Diane is incredibly important as my background is in a completely different type of science," says Dr. Rodier.

TFRI project co-leader Dr. Anne-Marie Mes-Masson, director of cancer research at CRCHUM, is delighted that Dr. Rodier has taken an interest in ovarian cancer. "Our CRCHUM biobank has a rich resource in terms of cell lines, cultures, and tumour samples, and Francis's research will make excellent use of this data."

## Federal funding to new \$15M centre of excellence for personalized medicine a boost for TFRI's investment in colorectal cancer

TFRI's efforts to improve outcomes for colorectal cancer patients received a vote of confidence in January 2014 with the announcement that a pan-Canadian initiative comprising colorectal researchers supported by TFRI, received \$15-million from the federal government to establish a Business-Led Network of Centres of Excellence (BL-NCE) in Precision Therapeutics.

**Colorectal cancer is the second leading cause of cancer in Canada. One in 14 men and one in 15 women is likely to develop the disease.**

"We extend hearty congratulations to this team – which includes our C4 clinicians and scientists – for their success in securing this new NCE and federal funding for PreThera. We are extremely delighted to see that TFRI-funded translational research is now attracting the attention of and investment from partners in government, the biotech and pharma industries, and other not-for-profits within the research sector. We look forward to working with these new partners and we see this as a great opportunity to bring better, safer treatments to patients through an expanded network of both funders and partners," said TFRI president and scientific director Dr. Victor Ling.

In October 2012 TFRI awarded \$1.2 million to the Canadian Colorectal Cancer Consortium (C4) to support its creation and purpose: to reduce incidence and mortality for colorectal patients while increasing survival and improving quality of life. Co-led by Dr. Gerald Batist



TFRI's C4 team held a project meeting last year to discuss their pan-Canadian work in colorectal cancer.

(Segal Cancer Centre and Jewish General Hospital, Montreal) and Dr. Steven Gallinger (Mount Sinai Hospital and University Health Network, Toronto), C4 has built pan-Canadian linkages over the last 19 months with leading colorectal cancer clinicians and scientists across the country to jointly collaborate on the development of state-of-the-art diagnostics and therapeutics for these patients.

To date, the team has focused on creating a pan-Canadian high-risk colorectal cancer registry with the goal of detecting colorectal cancer earlier, and is also studying tissue and biomarkers to identify new therapies where there is tumour resistance to existing treatments.

Dr. Batist says he is delighted by the NCE and is also grateful to TFRI for its initial support. "TFRI funding has provided us with a scaffold to reach out and spread across the country and build the needed infrastructure to undertake population-based observational

studies of all cancer patients and to develop a database to identify patients who will respond to a particular treatment. We can (now) find the extraordinary responders and understand what they look like at the proteomic and genomic levels."

In supporting C4's NCE application, TFRI advised that it will provide nearly \$3.9 million (over approximately four years) to support the work of the C4, subject to the project's successful review.\*

The TFRI funding will support clinical trial work at 10 sites across five provinces where more than 2,000 colorectal cancer patients and relatives will be recruited to participate in studies to help identify new treatments and diagnostics.

\*In April 2014 TFRI advised C4 that funding for Phase II has been awarded following a successful project review.

## Important discovery for Terry Fox-funded lymphoid cancer group

Researchers funded by the Terry Fox Foundation and based at the BC Cancer Agency's Centre for Lymphoid Cancer in Vancouver have discovered a new, recurrent genetic mutation in two kinds of lymphoma – Hodgkin lymphoma and primary mediastinal B-cell lymphoma (PMBCL).

Their findings, published February 16 in *Nature Genetics*, provide scientific proof that the altered gene PTPN1 plays a role in human cancer and point to the possibility of a new way to personalize treatment for lymphoma patients. PMBCL is a distinct subtype of aggressive B-cell lymphoma which affects predominantly young females but may also occur in children and adolescents. Lymphoma is the fifth most common cancer in Canada.

Study lead Dr. Christian Steidl, department of experimental therapeutics at the BC Cancer Research Centre and an assistant professor of pathology at the University of British Columbia, says the discovery is a world first. "Our work

identifies, for the first time, the entirety of genetic mutations in primary mediastinal B-cell lymphoma and first-of-its kind-mutations in the PTPN1 gene." He says the study shows how cancer cells profit from these genetic mutations to the detriment of affected patients through activation of cellular signaling that ultimately leads to tumour growth.

The discovery is promising for lymphoma patients who carry these mutations because it provides potential new targets for treating the disease with new therapeutics, including for those who do not respond to standard treatment, says Dr. Steidl.

For the study, investigators used high-throughput sequencing to analyze the whole-genome and whole transcriptome of 10 index samples, which was followed by targeted sequencing of about 100 human samples and lab-developed cell-lines which revealed "highly recurrent and novel gene mutations in the PTPN1 gene." The Vancouver Centre has one of the largest collections of these samples in the world.

Dr. Steidl is a principal investigator on the Terry Fox New Frontiers Program Project Grant in Molecular Correlates of Treatment Failure in Lymphoid Cancers (2013-2106). The New Frontiers Program Project Grants are now managed by TFRI.

### TFRI Executive & Node Leaders

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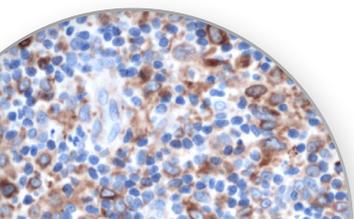
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675 West 10th Ave  
Vancouver, BC  
Canada V5Z 1L3  
T 604.675.8222

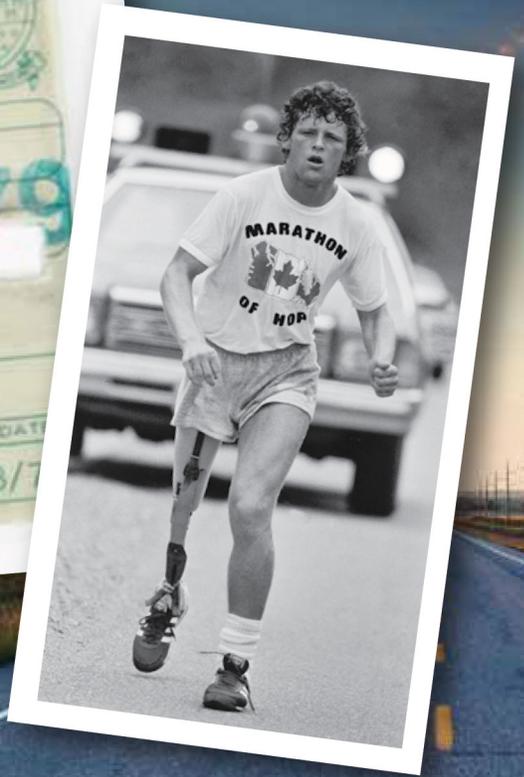
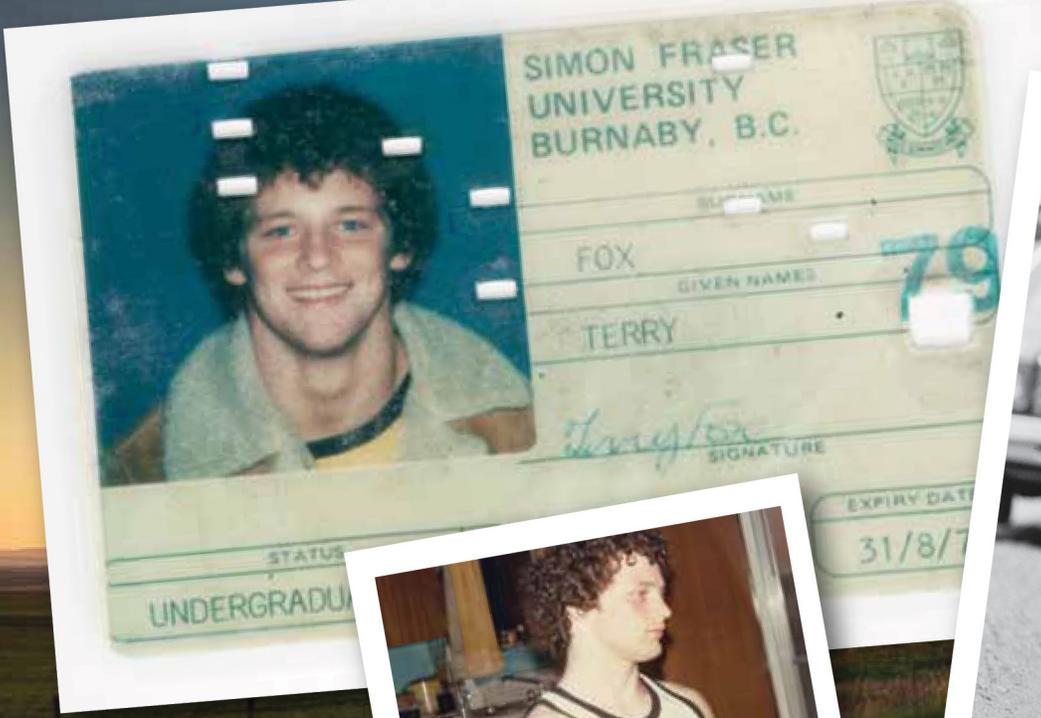
info@tfri.ca | [www.tfri.ca](http://www.tfri.ca)



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Under the microscope: lymphoid cancer cells (larger brown-coloured cells)



At 18 Terry Fox was a university student.  
At 19 he was a cancer patient.  
At 21 he was a hero.

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### Want to get involved?

All of our researchers and trainees are welcome to join our campus CAUSE events - or start one if there currently isn't one on your campus! Visit the web site to learn what campuses are participating this year! The list is growing!

