



The Faces of Cancer Research

summer 2010

Terry Fox: A legend who transformed cancer research in Canada

For us – and millions of Canadians including school children – Terry Fox **is the face** of cancer research. His *Marathon of Hope*, now a 30-year legacy, continues to inspire people here at home and around the world.

Terry's vision and courage have helped to change and reshape Canada in many ways. Importantly, it transformed cancer research here – establishing a new attitude and threshold regarding what kind of investment was necessary to support cancer research. Through the National Cancer Institute of Canada (NCIC), Terry Fox Foundation funds were allocated to researchers and teams for nearly three decades.

The NCIC was able to provide individual awards worth up to one million dollars to recognize the needs of individual investigators and their team members. This helped to ensure that Canadian investigators would be able to compete on a world stage and came at a time when funding to individual investigators was substantially less. Additionally, the funds were used for very specific needs such as the recruitment and training of medical experts. "These two activities were only possible through the availability of Terry Fox funds and I believe they had a major impact on how health research is supported in Canada," reflects former NCIC head Dr. Peter Scholefield (assistant executive director (1969-1980) and executive director (1980-1991)).

"The Terry Fox Foundation has always insisted on funding the best research no matter where it was. By insisting on extremely high levels of excellence, they ended up focusing on a limited number of people, but this has led to huge advances in science and some of those are now

on the cusp of being translated," said Dr. Bob Phillips, also formerly with NCIC.

This transformation continues today. The research institute that now bears Terry's name will play a key role in translating these findings into the clinic. Giving hope. Reducing the pain and suffering. Finding a cure. This is the dream.

Terry's vision for a world free of cancer is alive in the hearts and minds of the bright, talented researchers, scientists, clinicians, post-doctoral and graduate students and support staff who work every day under his name in cancer laboratories, hospitals, clinics and academic facilities across this country.

More than half a billion dollars – \$553 million – has been raised for cancer research by Terry's *Marathon of Hope* and The Terry Fox Foundation. Three decades later, we know more about cancer today thanks to biological, molecular and genomic discoveries, and new technologies, tests and treatments made possible with funding from The Terry Fox Foundation. We have better ways to detect, diagnose and treat it. This is helping cancer patients to live, to live longer and with a better quality of life.

Many challenges still remain, but we are making a difference. In this issue (and future ones), we highlight some results:

- The life expectancy for men with advanced prostate cancer is improving
- Scientists have discovered a new mutation that may lead to new treatments for lymphoma
- Today's health-care imaging tools and techniques are built on Terry Fox-funded research

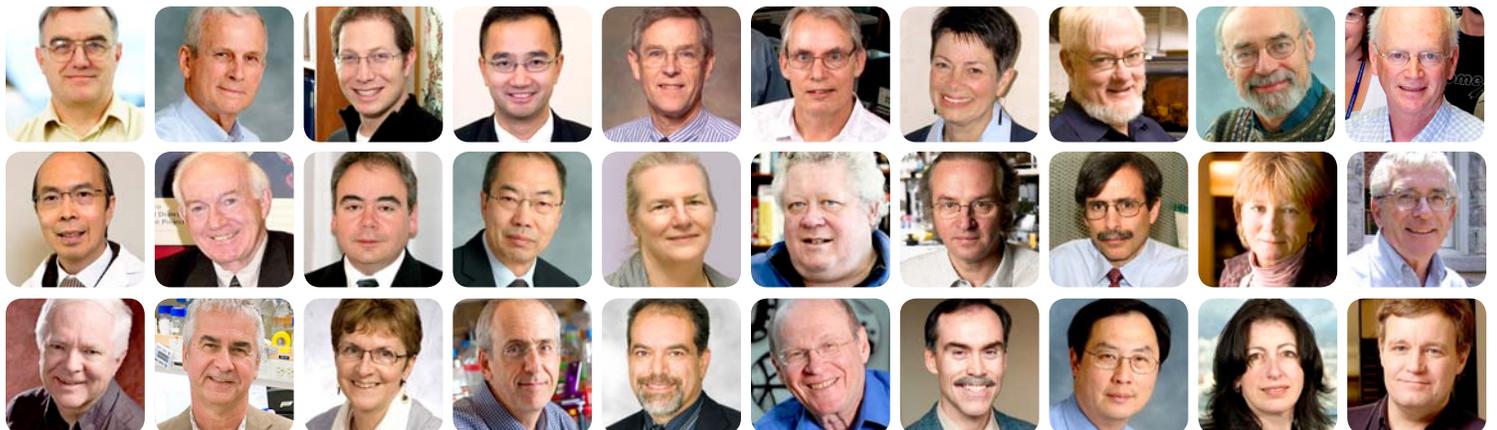
- Early screening holds great potential for improving survival from lung cancer, the number one cancer killer worldwide
- New selective therapies are being explored to provide treatment that is "personalized"
- Translational research is helping to close the gap between discovery and application
- Terry Fox funding has helped to build the nation's research capacity
- Young and promising new investigators will ensure Canada continues to lead discovery and innovation both nationally and internationally
- We have built, and continue to build, a critical mass of talent and expertise through team science to address cancer's many complexities

There is still much for us to do to achieve Terry's vision. "Thirty years ago, Terry brought people together, inspiring them to achieve more than they can imagine. Today we know that cancer is a huge challenge – perhaps far greater than anyone had imagined – representing more than 100 different diseases. We are making progress and the future is very promising; much of this is because of Terry Fox," said Dr. Victor Ling, president and scientific director of The Terry Fox Research Institute, which oversees the Foundation's research investment portfolio.

"With the continued support of donors, run organizers and volunteers, and this team of world-class researchers, we will meet these challenges head on and, like Terry, we will not quit."



Dr. Victor Ling



Terry Fox Investigators

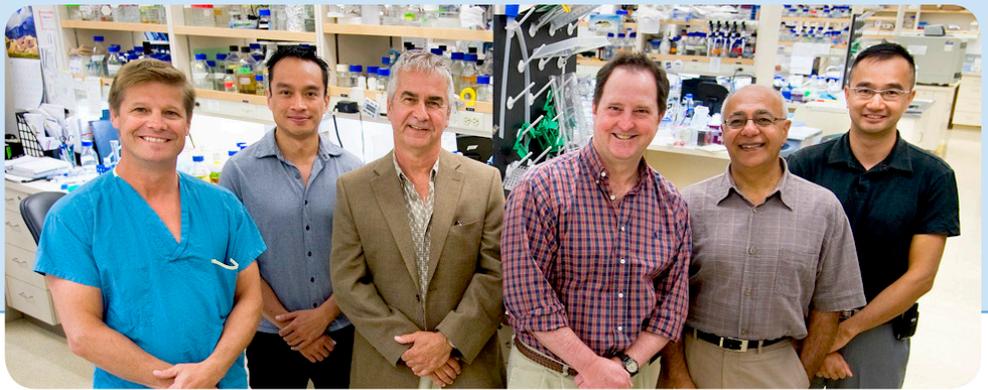
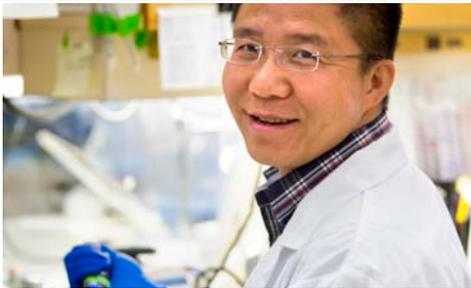
These are many of the investigators who head discovery and translational research programs and projects funded by The Terry Fox Foundation. (L-R) Dr. J. Bell • Dr. N. Boyd • Dr. J. Bramson • Dr. K. Chi • Dr. J. Connors • Dr. S. Foster • Dr. B. Gallie • Dr. M. Henkelman • Dr. R. Hill • Dr. K. Humphries • Dr. S. Lam • Dr. N. MacDonald • Dr. T. Magliocco • Dr. T. Mak • Dr. A-M. Mes-Mason • Dr. W. Muller • Dr. A. Nagy • Dr. C. Paige • Dr. M. Park • Dr. J. Pater • Dr. T. Pawson • Dr. P. Rennie • Dr. J. Rossant • Dr. R. Rottapel • Dr. F. Saad • Dr. N. Sonenberg • Dr. D. Stewart • Dr. M. Tsao • Dr. D. Waterhouse • Dr. J. Wrana

TRAINING FUTURE LEADERS IN CANCER RESEARCH

Dr. Xuesen Dong is a newly funded investigator at the Vancouver Prostate Centre who was mentored by Drs. Paul Rennie and Martin Gleave, and completed post-doctoral studies at the centre with Terry Fox funding. The Foundation makes awards to new and promising researchers like Dr. Dong, who now oversees a staff of 17, and is a recipient of a four-year Canadian Institutes for Health Research grant.

Originally conducting research in reproductive endocrinology in Toronto, Dr. Dong relocated to Vancouver three years ago to embark on a research path focused on understanding how nuclear receptors, such as androgen and progesterone receptors, control gene expressions that promote tumour cell growth. Research training has been an important component of the Terry Fox research portfolio for three decades, providing support to bright and talented researchers and clinicians through studentships, fellowships, grants and awards to new investigators.

Dr. Dong in his Vancouver laboratory.



Prostate researchers in Vancouver (L-R): Drs. Martin Gleave, Christopher Ong, Paul Rennie, Michael Cox, Shoukat Dedhar and Kim Chi.

Helping to extend life expectancy for prostate cancer patients

Prostate cancer is the second-largest cancer killer among men in North America. One out of every six men will be diagnosed with prostate cancer in their lifetime. For those with advanced stages of the disease, the work of a Vancouver-based research team funded by the Terry Fox Foundation is helping to increase life expectancy.

The prostate gland controls the normal growth and function of the male sex hormones. Drugs used to block these sex hormones are the main treatments for advanced prostate cancer. Unfortunately, when the cancer becomes resistant to these drugs, the patients usually die within 16-18 months.

Dr. Paul Rennie and his colleagues at the Vancouver Prostate Centre (VPC) work to understand the molecular and cellular events that underlie resistance to these drugs. Team member Dr. Martin Gleave developed a new drug which is effective in targeting clusterin, a protein which is involved in the survival of cancer cells. Use of this drug helped add over nine months to the lives of patients with advanced prostate cancer. "Men who are diagnosed with prostate cancer usually undergo surgery or radiation treatment as the first line of treatment and then are given anti-hormone therapy if the cancer recurs" says Dr. Rennie.

The team has also discovered a way to block the activity of another critical cell-survival protein called Hsp27 and this treatment is also currently undergoing clinical trials. This trial, which is being led by Dr. Kim Chi (BC Cancer Agency/ VPC), will consider the effectiveness of the drug in fighting prostate tumour growth as well as its toxicity in patients. "We always hope that any drug or new discovery will lead to a cure, but the disease usually comes back. Perhaps a more realistic goal is to extend the life of a patient such that he eventually dies of something else," says Dr. Rennie.

Another avenue of their research is the application of viruses to treat cancer. By genetically engineering viruses such as the herpes simplex virus, the group has demonstrated the ability to selectively kill prostate and bladder tumour cells while sparing normal tissues. This approach offers the potential for avoiding the unpleasant side effects that often come with many conventional anti-cancer treatments.

Many of the findings and contributions this program has made would not have been possible without funding from The Terry Fox Foundation. The funding has had a broader impact as well. Over the past 12 years, with support from The Terry Fox Foundation, Dr. Rennie and his colleagues have developed an internationally renowned centre for prostate cancer research.

"We have been able to establish a multidisciplinary program to attack advanced prostate cancer and which has provided a nucleus for the development of the Vancouver Prostate Centre. The Centre is the largest of its kind in the world, and has become a hub for national and international collaborations within the field," said Dr. Rennie.



Terry Fox is also funding other studies in prostate cancer, separate from this program at VPC. In Montreal, Quebec, Terry Fox Research Institute investigator Dr. Fred Saad (Centre hospitalier de l'Université de Montréal) and co-investigators are conducting studies to identify biomarkers that will assist in the development of better therapies across all stages of prostate cancer.

OUR INVESTMENT – BY THE NUMBERS

For 30 years, funds have been provided to support cure-oriented, biomedical cancer research around the globe. Here's a look at some significant numbers:

\$383 million directly provided for cancer research over three decades (1980 – 2010) as follows:

- \$311 million provided to the National Cancer Institute of Canada (1980 – 2010)
- \$63 million provided by the Terry Fox International Run program (1991 – 2010)
- \$8.8 million provided to The Terry Fox Research Institute (2008 – 2010)
- \$1 million to the Canadian Institutes for Health Research

1,164 cancer research projects funded in Canada allocated as follows:

- 440 cancer research grants
- 625 awards made specifically to support researchers directly through fellowships and scholarships to study in Canada and abroad
- 22 cancer research capacity-building grants, and
- 54 grants to support cancer research meetings

Translational Research

In 2007, the Foundation created The Terry Fox Research Institute as a pan-Canadian virtual institute to support translational research with the potential to significantly improve the health of cancer patients.

With an initial \$50 million commitment from the Foundation, the Institute has:

- Invested over \$40 million in 23 translational cancer research projects
- Leveraged an additional \$65 million from provincial and national partners
- Established partnerships with over 40 universities, cancer research institutions and hospitals across Canada

A SYMBOL OF HOPE

"Terry showed me that one person with determination can make a difference. He far exceeded his expectation of raising \$1 for every Canadian, and generated half a billion dollars. The amazing thing about Terry and his story is that it ignited the passion of a nation, and has become a legend that will transcend time as a symbol of hope and inspiration for future generations. People with cancer are living today because of research funded by Terry's dream."

Rick Hansen (Man in Motion) Rick Hansen Institute, Friend of Terry





World leaders: The world-class medical imaging team at the Sunnybrook Health Sciences Centre in Toronto.

Imaging technology used worldwide has a Terry Fox connection

Enter any cancer research and treatment facility around the world today and you'll find that the imaging technology that is used has a connection to Terry Fox. Through its "Imaging for Cancer Program," The Terry Fox Foundation has supported substantial advances in this area since the mid-80s. It has also helped to create world leaders in this area of research.

"Imaging is a cornerstone for health care delivery related to cancer," sums up Dr. Stuart Foster, who leads this team of 10 fellow investigators in the department of medical biophysics at Sunnybrook Health Sciences Centre in Toronto. TFF's investment has enabled these researchers to continue to push beyond the boundaries of what is presently known about imaging technology to find new ways to apply knowledge and discovery, and to translate these ideas into the clinic to reduce the burden for cancer sufferers here and around the world.

"It is really hard to think about treatment of cancer patients in 2010 without the use of medical imaging," remarks scientist and team member Dr. Mark Henkelman.

The team's work is focused on four areas: diagnostics, which provides valuable information on the anatomy of tissues; functional imaging, which, for example, allows for the study of how blood flows in tissue; molecular imaging, which enables scientists to examine the molecular aspects that are part of disease processes; and, more recently, image-guided therapeutics.

With fellow scientists, and the support of about 200 trainees and staff, this group is developing radically new therapeutic strategies and

imaging systems that will help to prevent, or to detect early, breast, prostate, brain and renal cell carcinoma.

One interesting focus is a minimally invasive technique to study a vascular tumour network by injecting "micro bubbles" into a vein and watching these bubbles "percolate" through the vascular network of tumours so scientists can study the flow of blood through a living tumour before, during and after therapy. The TFF is supporting an ongoing clinical trial of renal cell carcinoma using this technique.

The longest running of the Terry Fox *New Frontiers* Program Project Grants (PPG), this PPG is responsible for an impressive list of achievements and advances in medical imaging, including the development of:

- magnetic resonance breast imaging and intervention tools that are the standard of care for breast cancer patients and are marketed by all of the top, multi-national imaging companies (Dr. D. Plewes et al);
- fundamental detection strategies using contrast imaging for ultrasound; a technology that is a part of virtually every U.S. scanner in the world (Dr. P. Burns et al);
- digital mammography for screening for breast cancer (Dr. M. Yaffe et al); and
- trans-urethral, high-intensity, focused ultrasound therapy (for prostate cancer) (Drs. M. Bronskill and R. Chopra et al).

As well as: The Creation of a Mouse Imaging Centre (Dr. M. Henkelman et al); the invention, development and translation of micro-ultrasound

for use in pre-clinical imaging and eye cancer (Dr. S. Foster et al); and the invention, development and translation of image-guided, high-intensity, focused ultrasound therapy for the treatment of uterine fibroids initially, but now, for application in brain and other cancers (Dr. K. Hynynen et al).

These advances in imaging technology have helped to "change the game" in terms of helping researchers worldwide to understand, diagnose and treat cancer as well as other illnesses, such as cardiovascular disease; further, they have also led to the creation of successful Canadian imaging companies as well as hundreds of high-tech jobs in industry to ensure these new imaging tools move from bench to clinic.



AN INSPIRATION TO ALL

"Terry is *the* example of the distance that the human spirit can go. He shows us how self-motivation can be used to surpass any expectations we might have of ourselves. Terry takes selflessness to everyone, and his convictions touch everybody."

Jasey Jay Anderson
Canadian Olympic Gold Medalist, Vancouver 2010
Snowboard – Men's Parallel Giant Slalom



TFL director Dr. Keith Humphries (second from right) with TFF investigators, trainees and staff in the Terry Fox Laboratory in Vancouver.

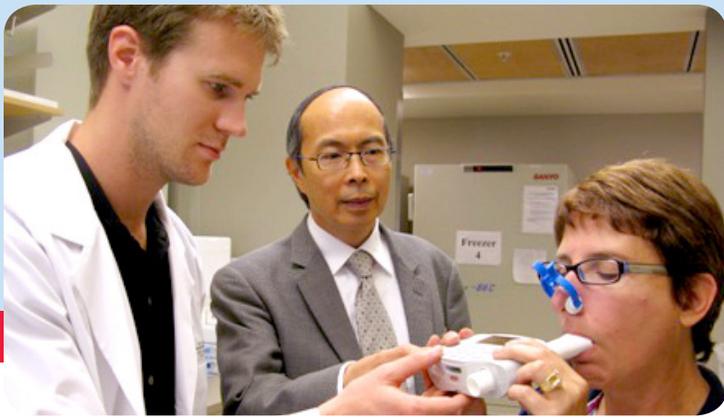
Building national capacity

Research capacity-building grants given by The Terry Fox Foundation in the early 1980s have helped to create cancer research laboratories such as the Terry Fox Laboratory (TFL) at the BC Cancer Agency in Vancouver. Today, 13 faculty and over 150 research trainees and staff work in the facility.

Dr. Keith Humphries, a long-time member of the lab (1984), took up duties as TFL Director in July 2010. The TFL was led for its first 25 years by Dr. Allen Eaves and subsequently by Dr. Connie Eaves. The BCCA lab was started with a \$1 million award from the Foundation in 1981 and officially opened in 1983.

Dr. Humphries was part of an NCIC-C Group grant team before receiving a *New Frontiers* Program Project grant in 1989, led then by Dr. Connie Eaves. His team of collaborators today includes Dr. Connie Eaves, Dr. Gerry Krystal, Dr. Peter Lansdorp, and Dr. Andrew Weng.

In Saskatchewan, a 1990 Terry Fox Regional Development grant helped to establish the Cancer Research Unit of the Saskatchewan Cancer Agency and the University of Saskatchewan. The funding supported scientists in the unit. Today this dynamic research centre employs 50 people.



Wil Cottingham (right), an administrative co-ordinator at the BC Cancer Agency's Research Centre, demonstrates a lung capacity test under the guidance of research technician Jamieson Best (left) and Dr. Stephen Lam, co-director of the Pan-Canadian Lung Cancer Early Detection Study.



Pan-Canadian lung study detects 39 cases of cancer

The Terry Fox Research Institute Pan-Canadian Lung Cancer Early Detection Study has diagnosed 39 cases of cancer (as of July 2010) since it began recruiting patients in September 2008. To date, there are over 2,000 participants enrolled in this study, which is co-funded by the Canadian Partnership Against Cancer. The study is aimed at early detection and treatment of lung cancer using readily accessible and affordable detection techniques.

In June 2010, the TFRI announced the expansion of the nationwide lung cancer detection study to Newfoundland & Labrador.

INSTITUTE FORMS ATLANTIC PARTNERSHIP

On April 12, the TFRI launched a new partnership with cancer research, academic and health care organizations in the four Atlantic provinces. The announcement was made in St. John's on the 30th anniversary of the Terry Fox *Marathon of Hope*.

Atlantic Canada has the highest incidences of and mortality from cancer in the country. The six institutions (Memorial University of Newfoundland, Dalhousie University, University of New Brunswick, New Brunswick Cancer Network, Atlantic Cancer Research Institute and University of Prince Edward Island) and TFRI have agreed to work toward the common goal of improving cancer outcomes for citizens of Newfoundland & Labrador, Nova Scotia, New Brunswick and Prince Edward Island.

"This Atlantic node represents an important step forward for us to work together to improve outcomes for cancer patients in Atlantic Canada. We look forward to, in the spirit of Terry Fox, a great partnership with the research and clinical communities in these provinces," said TFRI scientific director Dr. Victor Ling.

Cutting the ribbon (L-R): Dr. Michael Johnston (TFRI Atlantic node leader), Darin King (Government of Newfoundland & Labrador Education Minister), Betty & Rolly Fox and Dr. Victor Ling.

Based in St. John's, organizers aim to recruit 200 participants – including current and former smokers. TFRI is providing \$472,907 for this new site study and will work with health care and research partners at Memorial University of Newfoundland and Eastern Health. The total money invested to date in the eight-site study is \$7.16 million. The study is being led by Drs. Stephen Lam (BC Cancer Agency) and Ming Tsao (Princess Margaret Hospital).

"These are people without symptoms who took part in our program, so if they had not participated in the program, they would have appeared later on with symptoms. By that time, I would suspect that most of them would have a more advanced disease," said Dr. Lam. The study uses a risk assessment tool developed by Dr. Martin Tammemagi (Brock University) which helps efficiently identify those who are at high risk of developing lung cancer.

"This is much better than the other models we have used before. Based on age and smoking history, this model is very unique because we incorporate things like family history, educational level, body mass index, and also if there's a history of chronic obstructive lung disease. This is a very accurate model that we are testing," explained Dr. Lam.

Lung cancer still has the highest death rates compared to other cancers in Canada and around the world. It is estimated that 1.2 million people die from this cancer each year, and only 16% of lung cancer patients will live more than five years. If it is detected and treated at an early stage, the survival rate is over 70 per cent. Current and former smokers between the age of 50 and 75 who are interested in participating, can call 1-888-505-TFRI (8374).

"If you've given a dollar, you are part of the Marathon of Hope"

– TERRY FOX

Never-before-seen mutation discovered in lymphoma study

In January 2010, Drs. Joseph Connors, Randy Gascoyne and Marco Marra and fellow team scientists discovered a never-before-seen DNA "spelling mistake", or mutation, in the EZH2 gene of the diffuse large B-cell lymphoma and follicular lymphoma, the two most common types of non-Hodgkin lymphoma. The researchers were working in collaboration with the BC Cancer Agency and on research grants funded in part by The Terry Fox Foundation (TFF).

Their study identified a mutation found in exactly the same location in samples from different lymphoma patients. Based on previous research, the mutated site is known to be one of the most important amino acids in the proper functioning of EZH2.

"While we know EZH2 is involved in certain types of breast and prostate cancer, it has never before been found mutated in any cancer and was not previously implicated in having a role in lymphomas," said Dr. Connors, who conducted work in this area under a TFF PPG and is clinical director of the Centre for Lymphoid Cancer at the BC Cancer Agency. "The presence of this mutation can be considered a marker that will aid in diagnosing these lymphomas and identifying new therapies for their treatment."

In addition to decoding thousands of genes in malignant cells from 31 patients with diffuse large B-cell lymphoma, the entire genome of a patient with follicular lymphoma was decoded.

It is hoped that treatments can be developed to target cancer cells with this particular characteristic, including drugs that would specifically affect cancer cells without side effects to healthy cells.

Screening and selection processes for drugs affecting the EZH2 mutation have already begun.



A single dream. A world of hope.
The Terry Fox Foundation



The Terry Fox Research Institute
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