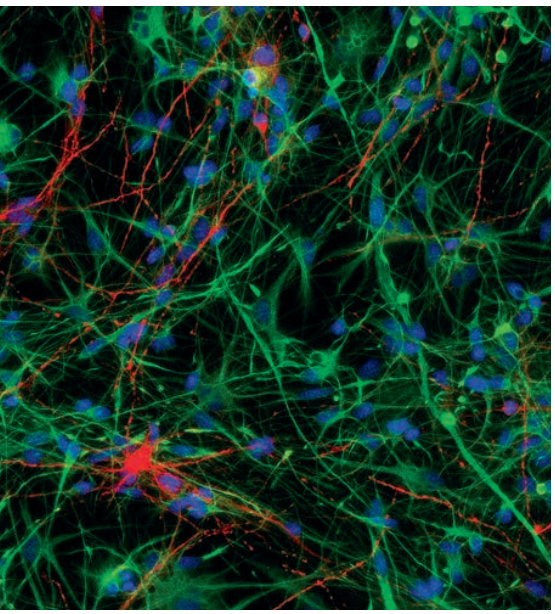
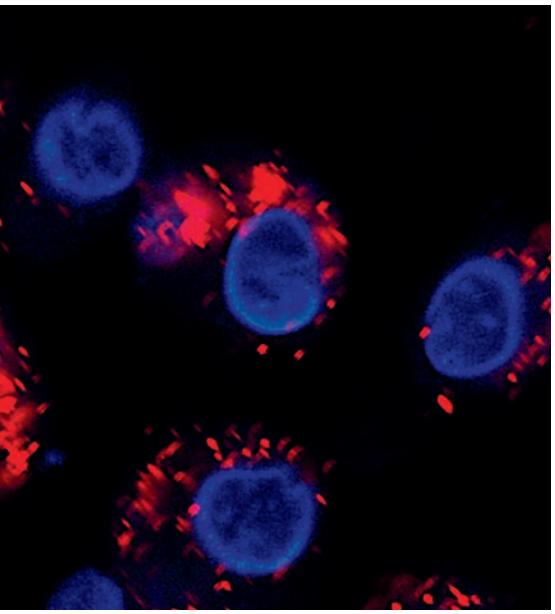
# ACCELERATING INNOVATION

BETTER CARE / GROWING ECONOMIC BENEFITS

# 2011/2012

ANNUAL REPORT





OICR
Ontario Institute for Cancer Research

# MESSAGE FROM THE MINISTER OF ECONOMIC DEVELOPMENT AND INNOVATION

On behalf of the government and people of Ontario, congratulations to the Ontario Institute for Cancer Research on another outstanding year. Thanks to the dedication and hard work of everyone involved, the Institute continues to advance the fight against cancer, improving the health and well-being of Ontario families.

Your leadership is helping us create a science-to-solution culture in Ontario. In areas like personalized medicine, our growing understanding of the disease at the individual level is helping identify which patients respond best to given treatments, enabling the health care system to deliver improved care while avoiding unnecessary treatments and costs.

The Institute continues to attract exceptional talent to the province, one reason Ontario is among the top three biotech sectors in North America. Meanwhile the work of your world-renowned scientists is enhanced through your partnerships with industry, academia and the international research community.

Once again, please accept my sincere thanks for your ongoing efforts and best wishes for the year ahead.

Sincerely,
Brad Duguid
Minister of Economic Development and Innovation

# THE ONTARIO INSTITUTE FOR CANCER RESEARCH

The Ontario Institute for Cancer Research (OICR) is an independent not-for-profit translational cancer research institute funded by the Government of Ontario. The focus of the Institute is on the translation of research findings into products, services and improved clinical practice related to cancer prevention, early detection, diagnosis and treatment.

OICR's research strategy was developed to have the greatest potential impact on patients and builds on Ontario's existing global strengths – medical imaging, clinical trials, cancer stem cells and bio-therapeutics. It includes small molecules, biologics, stem cells, imaging, genomics, informatics and bio-computing, pathology, health services and outcomes research.

The Institute has a variety of business models to help de-risk the commercialization of new technologies. OICR's Intellectual Property Development and Commercialization Fund provides capital and expertise to support the commercial development of technologies in areas such as therapeutics, medical technology and new technology platforms.

With an annual budget of more than $150 million (including contributions from partners and collaborators), the research strategy is advancing personalized medicine for cancer. The Institute is led by world-renowned scientists and supports more than 1,600 researchers, clinician scientists, research staff and trainees.

OICR is a province-wide research institute with headquarters in the MaRS Centre in Toronto, in the heart of Ontario's life sciences research community. Toronto has Canada's largest concentration of scientific research and is among the top three in North America in terms of its bioscience cluster.

For more information, please visit the website at **www.oicr.on.ca**

# FROM THE CHAIR OF THE BOARD OF DIRECTORS AND THE PRESIDENT AND SCIENTIFIC DIRECTOR

Left: Dr. Calvin Stiller, Chair, Board of Directors
Right: Dr. Tom Hudson, President and Scientific Director

OICR was established by the Government of Ontario as a strategic investment that would establish Ontario as a world leader in translational cancer research. The benefits that flow from this investment include attracting and retaining the brightest cancer researchers to the province, moving discoveries out of the lab and into the clinic for the benefit of cancer patients, as well as the attraction of private sector investment, company formation and the creation of high-quality jobs.

We were very pleased with two announcements made last year that ensure we have the capacity to meet our goals. The Government of Ontario confirmed funding of $420 million for a period of five years and construction re-started on Phase II of the MaRS Centre which will provide laboratory space we need to house our research programs.

The past year has seen great progress in our research and commercialization strategies, and in raising Ontario's international profile. In December 2011, *The Economist* twice featured the International Cancer Genome Consortium (ICGC), which was also covered by other international media. Dr. Tom Hudson, our President and Scientific Director, was key to the creation of the ICGC, a worldwide $800 million initiative, involving 47 project teams in 15 jurisdictions. It aims to sequence the genomes of 25,000 tumours from 50 different types of cancer. The knowledge created will facilitate personalized medicine by changing how cancer is diagnosed and treated. OICR hosts the ICGC's Secretariat and its Data Coordination Centre is based at OICR under the direction of Dr. Lincoln Stein.

The Ontario Health Study (OHS), which was launched in the fall of 2010, has seen more than 220,000 Ontarians sign up for what is one of the single largest health studies in Canadian history. It is the first large-scale, population-based study to take advantage of the reach of the Internet to recruit participants. The data derived from this study will help develop better strategies for dealing with cancer and chronic diseases. You can read more about the Study on page 22.

We have a unique translational research model that leverages Ontario's province-wide strengths in discovery research, translational medicine and commercialization to maximize the impact of discoveries for cancer patients. Last fall we set new priorities for our translational research mission. We are facilitating collaboration among our programs and platforms to capitalize on their expertise and increase the impact of our research.

The priorities include finding new ways to treat difficult cancers (therapeutic discovery), use of personalized medicine to optimize patient treatment decisions (clinical development) and improving cancer care through innovation in prevention, screening, diagnosis and delivery of treatment (population health).

The priorities align with the Institute's initiatives and capitalize on other ongoing OICR projects with high translational potential. Examples are the pancreatic cancer project for the ICGC, the Genomics Pathway Strategy's (GPS) clinical initiative, use of OICR's expertise to develop new imaging modalities to help distinguish aggressive from low-risk disease in breast and prostate cancer, and optimize screening and treatment delivery programs, with an initial emphasis on colon cancer.

We are confident that our priority setting and increased collaboration with Cancer Care Ontario and other government agencies will yield improved care.

# The past year has seen great progress in meeting our goals through our research and commercialization strategies, and in raising Ontario's international profile.

Benefits of our research and commercialization activities have flowed to the Ontario economy. More than 300 scientists, research technicians and support staff are employed at OICR's headquarters in the MaRS Centre in Toronto's Discovery District and more than 1,600 researchers, clinician scientists, technicians and trainees receive support from, and are integral members of OICR but located at research institutes across the province.

Base support from OICR has seeded and provided momentum to initiatives that were then able to attract funding from grants and partners, increasing research employment in Ontario. An example is the Centre for Probe Development and Commercialization (CPDC), which was developed out of OICR's imaging program. Under the leadership of Dr. John Valliant, a Centre of Excellence in Commercialization and Research was funded to establish the CPDC. Since 2008 it has grown to create a revenue generating and profitable pharmacy business which employs more than 60 people and had revenues in excess of $2 million in 2011. The CPDC has attracted $4.5 million in private sector funding. It has become a global destination for the development, commercialization and distribution of molecular imaging probes. CPDC is also working with a national team of experts to demonstrate that cyclotrons can be used to create substitute or supplementary supplies of Technetium-99, one of the most widely used medical isotopes.

OICR's commercialization activities continue to turn projects into commercialization opportunities. Spinout companies have been launched, two of which, DVS and Profound Medical, have set up manufacturing in Ontario. International companies, such as GE Healthcare, have been attracted to establish a footprint in Ontario. OICR's investment has led to the start-up of nine firms which would not have existed without OICR's support. Despite the recent slump in the life sciences venture capital community, OICR's commercialization team has attracted $35 million from private sector and other investors for OICR-supported commercialization projects. OICR's Intellectual Property Development and Commercialization Fund has made 17 investments since 2007 that resulted in six projects with prototypes, four projects with sales revenues, three private capital investments, three projects that started first-in-man studies and one large licensing deal.

This past year we welcomed the arrival of Ms. Karen Belaire as Chief Operating Officer. Ms. Belaire has an extensive background in finance, information technology and human resources gained in healthcare and academia. She is ensuring the efficiency and effectiveness of operations including quality control and regulatory compliance, forging effective partnerships and collaborative opportunities, development of strategic operating plans and development of financial strategies to grow the Institute.

As we close the year, we wish to thank Dr. Elizabeth Eisenhauer, who completed her term as a founding member of the Board of Directors and as co-chair of the Scientific Advisory Board, for her wise counsel and valuable contribution. It's hard to imagine anyone who has contributed more to cancer research in Ontario. We welcome Ms. Janet Davidson, Mr. Peter Fullerton and Mr. Douglas Squires, who joined the Board this year.

We are most grateful for the continuing excellent support of the Government of Ontario through the Ministry of Economic Development and Innovation. The Government's commitment to innovation has helped make the province a world leader in cancer research.

We are grateful to the staff of the Institute for their dedication and hard work. We have a very engaged and talented team and every member is responsible for our remarkable progress.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Ontario Institute
for Cancer Research

# RESEARCH STRATEGY AND SCIENTISTS

## The Ontario Institute for Cancer Research's mandate is to build innovative research programs that will have an impact on the prevention, early detection, diagnosis and treatment of cancer.

The mandate includes strengthening Ontario's cancer research capacity and developing the next generation of cancer researchers by attracting and retaining outstanding scientists. The Institute has a translational research mission which is to leverage Ontario's province-wide strengths in discovery research, translational medicine and commercialization to ensure promising technologies move to practical application in the clinic and realize economic benefits for Ontario.

The Institute created a blueprint (see page 6) to illustrate the relationships between programs and platforms for its research activities.

Innovation programs target different time-points in the clinical continuum, i.e., prevention, early diagnosis and therapeutics. OICR established an innovation theme called cancer targets because many new avenues for cancer screening, detection and drug discovery rely on the identification of specific components of cancer cells and biomarkers. Projects were selected for each theme, based on potential for impact and recognized strengths in Ontario. Technology platforms develop state-of-the-art knowledge and technologies in disciplines to enable OICR programs. Translation programs were created to ensure the Institute bridges the gap between discoveries and patients. They are aimed at the patient, the health care system and the general population.

OICR's program and platform leaders (see page 7) are internationally recognized scientists. They are meeting the cancer challenge with excellent science and a clear and focused strategic vision.

OICR congratulates Drs. John Bell and Ming-Sound Tsao, who were recognized by the Canadian Cancer Society for their significant contributions to cancer research in Canada.

Bell received the Robert L. Noble prize for work on oncolytic virus-based therapies. He is a Senior Scientist at the Ottawa Hospital Research Institute and leads OICR's Immuno- and Bio-therapies Program. In 2011, Dr. Bell published the results of a groundbreaking clinical trial that was the first in the world to show an intravenously-delivered viral therapy can consistently infect and spread in human tumours without harming surrounding healthy tissues. This was a major step in proving the efficacy of virus-based therapies and in bringing them closer to the clinic.

Tsao received the O. Harold Warwick Prize for work on use of molecular information to improve lung cancer treatment. He is a Senior Scientist at the Ontario Cancer Institute, the research arm of University Health Network's Princess Margaret Hospital and Director of Translational Research for Pancure, OICR's pancreatic project. Pancure integrates genomic, drug discovery, biology, pre-clinical and clinical efforts to develop new treatments for pancreatic cancer, one of the most lethal cancers. Pancure combines genome analyses (under the auspices of the International Cancer Genome Consortium), innovative screens (Selective Therapies Program led by OICR and the Terry Fox Research Institute), OICR's Early Drug Discovery Program, and the PMH Clinical Trials Consortium.

In 2002, OICR's predecessor organization funded Dr. Tsao's study on molecular aberrations in lung cancer tumours. This provided the first evidence that some patients whose tumours harbour the Ras mutation are not likely to benefit from chemotherapy post-surgery, allowing doctors to better tailor treatment to patients and sparing them unnecessary side effects.

# ONTARIO INSTITUTE FOR CANCER RESEARCH BLUEPRINT

| THEMES | INNOVATION PROGRAMS | TECHNOLOGY PLATFORMS |
|---|---|---|
| PREVENTION | Ontario Health Study | Genetic Epidemiology and Biostatistics |
| EARLY DIAGNOSIS | Smarter Imaging Program | Imaging Translation |
| CANCER TARGETS | Cancer Stem Cells<br>Cancer Genomics (ICGC) | Transformative Pathology |
| THERAPEUTICS | Selective Therapies (Terry Fox Research Institute, Ontario Node)<br>Immuno- and Bio-therapies | Genome Technologies<br>Medicinal Chemistry<br>Informatics and Bio-computing |

| TRANSLATION PROGRAMS |
|---|
| High Impact Clinical Trials |
| Health Services Research |
| Commercialization |

# OICR LEADERS

**TOM HUDSON**
President and
Scientific Director
—
Ontario Institute for
Cancer Research

**NICOLE ONETTO**
Deputy Director and
Chief Scientific Officer
—
Ontario Institute for
Cancer Research

**FRANK STONEBANKS**
Vice-President,
Commercialization and
Chief Commercial Officer
—
Ontario Institute for
Cancer Research

**KAREN BELAIRE**
Chief Operating
Officer
—
Ontario Institute for
Cancer Research

**RIMA AL-AWAR**
Platform Leader
Medicinal Chemistry
—
Ontario Institute for
Cancer Research

**JOHN BARTLETT**
Platform Leader
Transformative Pathology
—
Ontario Institute for
Cancer Research

**JOHN BELL**
Program Leader
Immuno-and Bio-therapies
—
Ottawa Hospital
Research Institute

**JANET DANCEY**
Program Leader
High Impact Clinical Trials
—
Queen's University

**JOHN DICK**
Program Leader
Cancer Stem Cells
—
Ontario Cancer Institute
Princess Margaret Hospital
University Health Network

**CRAIG EARLE**
Program Leader
Health Services Research
—
Cancer Care Ontario
Sunnybrook Health
Sciences Centre

**AARON FENSTER**
Co-Platform Leader, Imaging
Translation; Co-Program Leader,
Smarter Imaging Program
—
Robarts Research Institute
University of Western Ontario

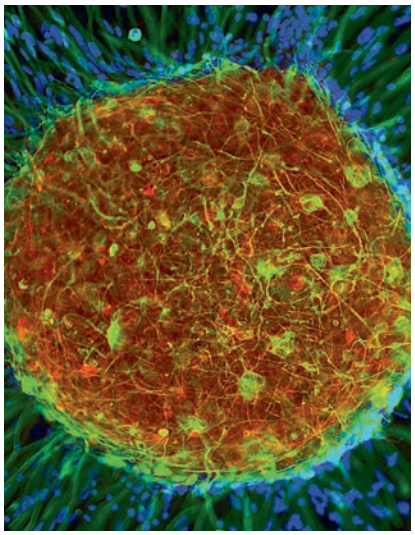
**JOHN MCPHERSON**
Platform Leader, Genome
Technologies; Program
Leader, Cancer Genomics
—
Ontario Institute for
Cancer Research

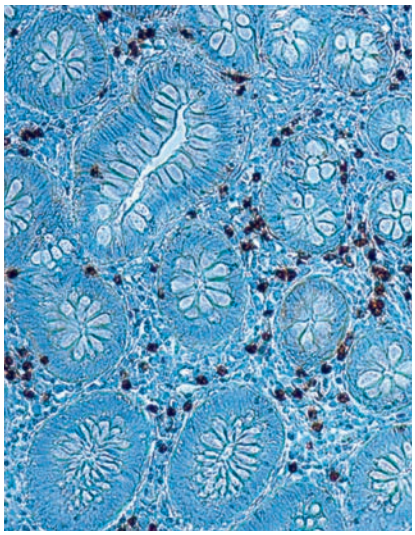
**LYLE J. PALMER**
Executive Scientific Director,
Ontario Health Study; Platform
Leader, Genetic Epidemiology
and Biostatistics
—
Ontario Institute for
Cancer Research

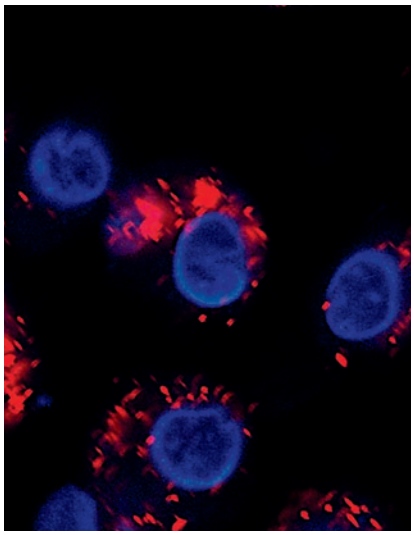
**ROBERT ROTTAPEL**
Program Leader, Selective
Therapies, Terry Fox Research
Institute (Ontario Node)
—
University Health Network
St. Michael's Hospital

**LINCOLN STEIN**
Platform Leader
Informatics and Bio-computing
—
Ontario Institute for
Cancer Research

**MARTIN YAFFE**
Co-Platform Leader, Imaging
Translation; Co-Program Leader,
Smarter Imaging Program
—
Sunnybrook Health
Sciences Centre





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# ACCELERATING INNOVATION – DISCOVERIES, TRANSLATION AND CLINICAL IMPACT

The Ontario Institute for Cancer Research has three translational research priorities and on the pages that follow you can read about projects that are making great progress in these important areas.

The first priority is therapeutic discovery – finding new ways to treat difficult cancers. You can read about Dr. Peter Dirks' cancer stem cells program that is working on an innovative approach to treating brain cancer. OICR scientists have found a new way to deliver drugs directly to the patient's tumour, using nanotechnology.

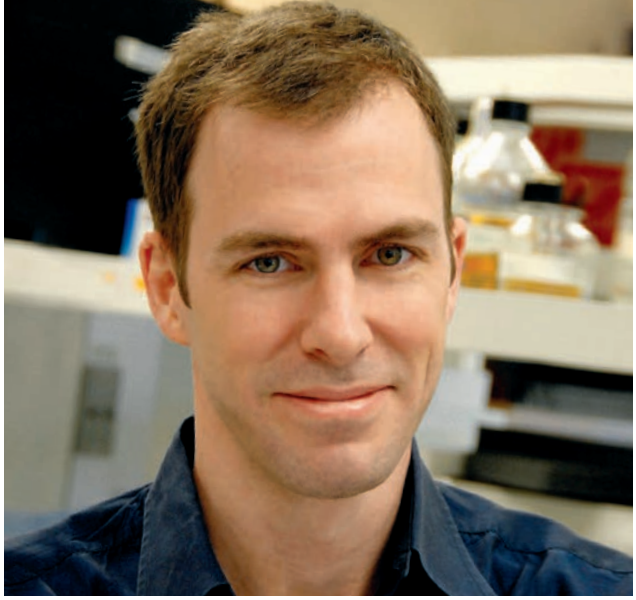
The second priority is clinical practice – the use of personalized medicine approaches to optimize treatment decisions. OICR aims to develop new biomarkers to stratify patients according to risk factors. The ASIST project is developing a new way to help distinguish aggressive from low risk prostate cancer. The Genomics Pathway Strategy is using genomics at the bedside to aid in decision-making regarding treatment and OICR's Transformative Pathology Platform is improving the understanding of cancer by identifying characteristics of the tumour specific to the individual patient.

The third priority is population health – the improvement of cancer care through innovation in prevention, cancer screening and treatment delivery. The Ontario Health Study is one of the largest health studies ever undertaken in Canada and a study has been done on how to prevent and better screen for cancer. The BETTER project is making prevention and screening strategies more accessible to patients.

The last two decades have seen a remarkable transformation in how scientific research is conducted. Examples are the innovations in genome sequencing and other high-throughput technologies. Large teams of scientists work collaboratively in interdisciplinary environments. The computer, the server farm and the Internet are the 21st century's essential tools for electronic communication and collaboration as well as storage and retrieval of the large volume of data generated by the new technologies. Highlighted in this report are OICR's scientists who are developing better informatics tools.

The last step in the discovery chain is the commercialization of the discovery, which translates the knowledge created into a product, a device or treatment, for use in the clinic. Read how Harmonic Medical has an innovative focus on patient care with the use of ultrasound technology to treat solid tumours.

# AN INNOVATIVE APPROACH TO TREATING ONE OF THE MOST AGGRESSIVE FORMS OF CANCER



Dr. Peter Dirks

Eight years ago, Dr. Peter Dirks published a groundbreaking paper confirming the existence of a small number of stem cells causing some brain cancers to grow and develop, even after treatment. It was a major discovery that, along with the work of stem cell pioneers such as Drs. James Till, Ernest McCullough and John Dick, has put Ontario at the forefront of stem cell research worldwide.

Now Dirks, today a neurosurgeon at The Hospital For Sick Children and a researcher in OICR's Cancer Stem Cells Program, has devised a new way of testing existing therapies that could create more personalized – and more effective – treatments for patients with one of the most aggressive forms of cancer: glioblastoma multiforme (GBM).

GBM accounts for about one fifth of all primary brain tumours in adults. The disease remains incurable and current therapies, which usually include a combination of surgery, radiation therapy and chemotherapy, can only offer patients improved care.

"It is clear that more innovative approaches to treatment for this disease are needed," Dirks says.

Dirks' recent research has focused on isolating and removing these stem cells from patients and culturing them *in vitro*: in other words, removing a selection of the patient's cells that are driving cancer growth and then growing these cells outside of the body. This is done so that selected drugs can be tested on the patient's unique cancer profile, without actually testing them on the patient. If successful, this could lead to a much safer, faster way to test and target multiple treatments, or combinations of treatments, for patients with GBM.

"Our goal with this project was to see if it would be feasible to test consecutive patient samples, come up with lists of drugs that showed activity on actual patient cells", says Dirks. "Then, theoretically, when we know which agent might block the proliferation of the patient's own tumour cells, maybe the next step would be to offer that back to the patient as part of a new way of running a clinical trial.

"We've been able to take human glioblastoma cells, plate them out in a culture system, and now we can get virtually every patient's glioblastoma cells growing out," he says. "That gives us an opportunity to not just look at the static biomarkers or signatures of a tumour, but to actually have patient cells that we can use for drug testing."

Over the past year they have generated cancer stem cell cultures for drug testing from a total of 27 patients. It takes about four weeks to culture these cells and a further four weeks to screen and validate drugs, meaning drugs could be potentially tested and ready for patient use in just two months. During this time patients could undergo regular therapies such as chemotherapy and radiation. Dirks sees this system potentially working well in conjunction with current treatments.

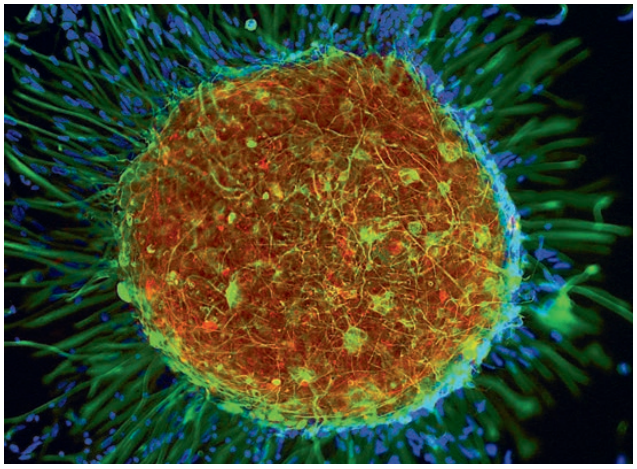
"There is always concern that what is measured *in vitro* is not necessarily correct, or won't apply if transferred back to the patient," Dirks says. He predicts there will be another year of *in vivo* validation to get a more complete understanding of the spectrum and to hone in on a dozen or so drugs, from which a small handful of drugs could be tested for use in humans and their safety profile could be fully defined.

Dirks' team has been focused on repurposing already tested, and in many cases off-patent, drugs that had some previous history of biologic activity on neural cell types, including drugs that have been used in the clinic to treat

"Our goal with this project was to see if it would be feasible to test consecutive patient samples, come up with lists of drugs that showed activity on actual patient cells."

depression, Parkinson's disease and epilepsy. Instead of testing many thousands of drugs, they focused on small clusters of about 50-100 that look especially promising. It currently looks like every patient's stem cells will require a slightly different repertoire of drugs. This creates an opportunity to generate more personalized treatments, but it will also create unique challenges in the clinical trial phase.

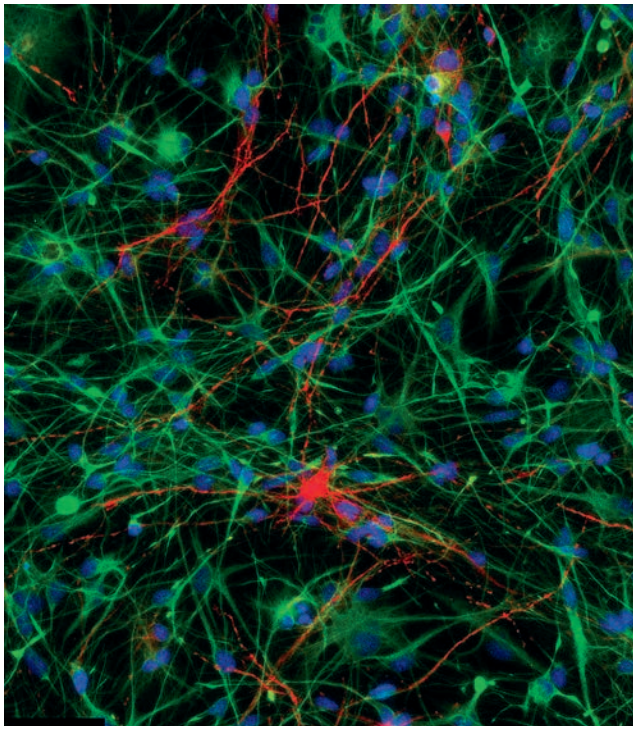
"The whole idea of personalized medicine may demand a major rethink of how we run clinical trials. It's no longer just drug A versus a placebo in a large group of patients. It might mean that theoretically every patient's tumour might need a different combination. We need to start to think about a different, more fluid way of running a clinical trial."



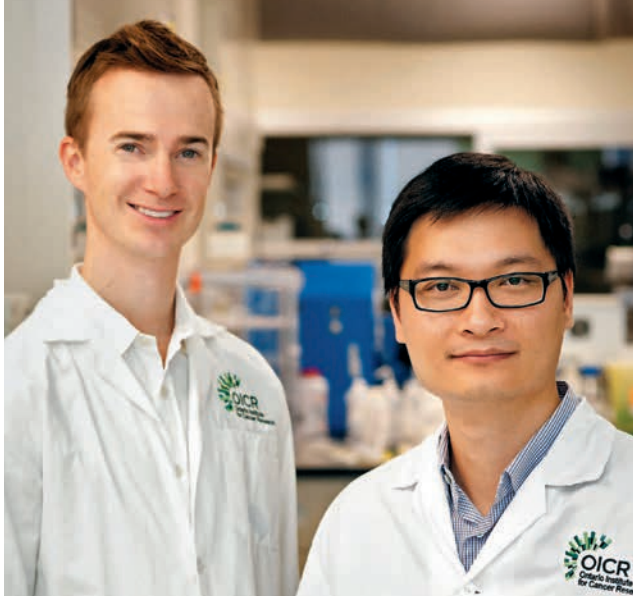
He admits this work will be complicated, but the approach would pay off because it could have major benefits for patients. "It's perhaps a different view of trying to think about drug discovery. There are things that can contribute to the growth of a tumour that don't show up as a biomarker experiment on a bulk tumour. We definitely wouldn't have predicted that some of the drugs that show efficacy were going to perform as well as they did."

He feels confident this can be done, especially with the collaborative nature of cancer research in Toronto. "A lot of the principles of stem cell research have been outlined in Toronto, so there's a great group of people established here who are looking at stem cell behaviour in cancer," he says.

"There's still a lot of work to be done. But one of the advantages here in Ontario with OICR is that these people have been put together in the same room, they are sharing information and they are learning from one another. Ontario is going to be a place where still a lot of new insights come and it will continue to be trailblazing well into the future."



# NANOTECHNOLOGY TO IMPROVE DRUG DELIVERY



Drs. Mark Ernsting and Shyh-Dar Li

With the ability to manufacture and manipulate particles around or smaller than 100 nanometres, scientists and engineers are deploying nanotechnology in diverse fields and transforming medicine. Nanoparticles are about the same size as a virus, smaller than bacteria, and can consist of materials such as metal, lipids and natural or synthetic polymers. At OICR, researchers have invented an innovative polymeric nanoparticle called Cellax™ that improves drug delivery and reduces toxicity.

"Cellax is a polymer-based nanoparticle drug delivery technology designed to transport non-toxic, water insoluble drugs into tumours," explains Dr. Shyh-Dar Li, a Principal Investigator working in the field of drug development and formulation in OICR's Medicinal Chemistry Platform.

Vessels supplying blood to tumours tend to be leaky and disorganized, allowing nanoparticles to permeate into the tumour but not into normal blood vessels. This prevents nanoparticles from affecting healthy tissue. This phenomenon is called the enhanced permeability and retention (EPR) effect and is the foundation science of nanomedicine. Researchers have used the EPR principle to develop technologies that administer drugs to passively target the tumour and avoid normal cells. Increasingly, these particles are being used to encapsulate imaging agents to visualize tumours. "By exploiting the processes of the EPR effect, we have developed a technology to improve the delivery of a drug to tumour sites," says Dr. Mark Ernsting, a Senior Biomedical Engineer at OICR. "We are involved in a global effort to leverage the EPR effect and are using our experience in polymer and nanoparticle design to build a more effective particle." The Cellax particle is built with biomedical materials, including cellulose and a generic drug. The combination of these elements gives the technology its unique properties.

The team aims to use the approach to tackle multiple types of cancer, including prostate, breast and pancreatic cancers. "The technology has the ability to target tumours and reduce adverse reactions," says Ernsting. "Cellax can deliver a sustained-released drug dosage inside the tumour to increase the chances of successful therapy."

Nanotechnologies exist in the clinic but do not always release the drug effectively. The drug may not be released inside the tumour or may be released too early in the bloodstream. "Cellax is designed to release the drug inside the tumour. We also have the ability to predict, monitor and adjust how much of the drug is delivered to a tumour," says Li. "This technology could mark a new direction in personalized medicine." The team also anticipates that Cellax can shorten drug infusion times and reduce the time spent in hospital.

The team initiated the project in 2009 and discovered by 2010 that Cellax greatly improved therapeutic efficacy and reduced toxicity in animal models. This strong preclinical evidence supported a move to clinical translation and researchers applied for a patent in 2011. "The results obtained from current projects will enable us to collaborate with other organizations to help advance Cellax. OICR has a strong and tangible commitment to translational research and we are working with the Commercialization team and MaRS Innovation to pursue the funding to drive this technology toward human clinical trials," says Ernsting.

# IMPROVING CANCER CARE THROUGH ADVANCED IMAGING TECHNOLOGY

Dr. Laurence Klotz

When a patient is diagnosed with cancer, first thoughts turn to how the cancer should be treated. Although this is the correct course of action for some cancers, it is not always ideal in the case of men with prostate cancer. Some prostate cancer tumours may pose little or no risk. However, it can be hard to distinguish between aggressive cancers and those that should go untreated while being monitored, a strategy known as active surveillance. This means that some men undergo radical treatments while active surveillance would be more suited to their particular case.

To help solve this clinical challenge, the Ontario Institute for Cancer Research has launched a Phase III clinical trial that will see if multi-parametric magnetic resonance imaging (MRI) coupled with transrectal ultrasound-guided biopsy (called fusion technology) can more accurately identify men with prostate cancer who are at risk of developing aggressive disease. The study is called the Active Surveillance Magnetic Resonance Imaging Study Trial (ASIST).

Dr. Laurence Klotz is chair of the study and Professor of Surgery at the University of Toronto and an Associate Scientist at Sunnybrook Health Sciences Centre. Klotz is no stranger to the use of active surveillance, as doctors at Sunnybrook pioneered the strategy in the late 1990s. He says that active surveillance is being used more than ever, "There has been concern and acknowledgment over the last 10 years or so that prostate cancer is being over-treated. Now the world has come around to our way of thinking and we have seen active surveillance become a viable option in 40 per cent of newly diagnosed cases of the disease." Klotz notes that 150,000 men in Canada and the United States could benefit from active surveillance each year. It has been widely adopted in Canada and Europe, but much less so in the U.S.

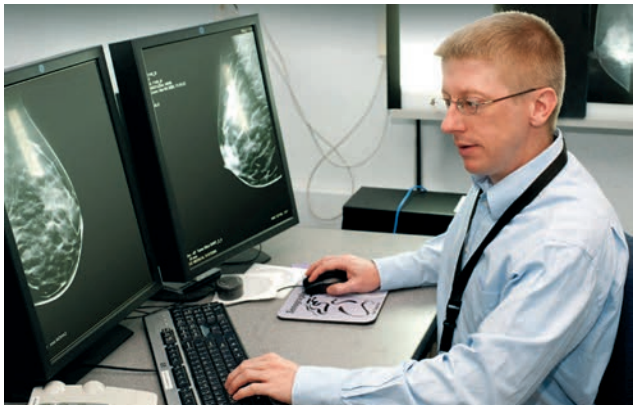
There is a however, a downside to active surveillance – it requires multiple biopsies and some patients end up being found to have worse cancers after years of follow-up. Klotz says that currently biopsies of the prostate are done without a target area because there has been no good way to image the cancers. Klotz says that biopsies also carry the risk of sepsis and this may negatively impact the quality of life of those who have chosen active surveillance. "Most of my patients would jump at the option of an MRI instead of a biopsy given a choice," says Klotz.

"Our goal with ASIST is to improve active surveillance using multi-parametric MRI which has the advantage of being able to identify large lesions at an early stage that can be missed on initial biopsies," says Klotz. ASIST is the first randomized trial to investigate the role of MRI in prostate cancer management and the first study into the use of MRI for active surveillance after a patient's initial biopsy. The study will evaluate MRI's ability to detect patients with intermediate or higher risk cancers in comparison to systematic biopsies, which is the current standard practice. It will also examine the side effects of the two approaches. In the long run, if the study confirms the accuracy of MRI, patients with a normal MRI may be able to even avoid a prostate biopsy altogether.

Klotz's group will also be looking for a molecular tool or biomarker that will facilitate the differentiation of aggressive and non-aggressive disease. Biomarkers are surrogate substances within, or introduced into an

organism that indicate the presence of a disease or other physiological condition. The ASIST team is trying to find a biomarker that will diagnose prostate cancers with a Gleason score of seven or higher. The Gleason scale is a standardized measure used by clinicians to grade the aggressiveness of a patient's prostate cancer.

The prevalence of prostate cancer makes being able to distinguish between aggressive and non-aggressive disease an urgent clinical need. "More than half of men over 50 have what I call microfocal prostate cancer. In most cases these microfocal cancers are just part of the aging process, but unfortunately some are eventually found to have worse forms of the disease," says Klotz. "Given the ability to identify these more aggressive cases we could treat them earlier and spare men with less aggressive forms of prostate cancer the negative, and sometimes long-term, side effects of



treatment. This is not only about saving lives but also increasing their quality."

Prostate cancer is the most common cancer in Canadian men. Each year more than 25,000 will be diagnosed with the disease, placing a large strain on the healthcare system. Klotz is cautiously optimistic that the use of MRI in active surveillance could result in a cost-savings for the healthcare system. "It is rare to have an innovation or discovery that improves patient care cost less than the alternative but it is plausible in this case," says Klotz. He says that this is because although MRIs are expensive, their costs are trending downwards and because biopsies are also expensive procedures and can have additional costs attached due to complications following biopsy. Further active surveillance results in significant cost savings compared to definitive treatment, and a means to follow patients non-invasively would enhance the appeal of this approach to patients.

The fusion technology, being used in the study was developed with funding from OICR by Dr. Aaron Fenster, Co-director of OICR's Smarter Imaging Program and Imaging Translation Platform and Director, Imaging Research Laboratories, Robarts Research Institute. Fenster's technology has been successfully commercialized and is now manufactured by a company called Eigen.

Fenster is pleased that his MRI fusion technology is being evaluated through ASIST. "Ontario researchers spent years perfecting this technology and now there is an opportunity to apply it in a way that will make a difference in lives of patients worldwide," he says. Fenster, with his counterpart Dr. Martin Yaffe of Sunnybrook Research Institute, oversees OICR's research initiatives in cancer imaging which comprise the Smarter Imaging Program and the Imaging Translation Platform.

"Our goal with ASIST is to improve active surveillance using multi-parametric MRI which has the advantage of being able to identify large lesions at an early stage that can be missed on initial biopsies."

The Smarter Imaging Program is tasked with increasing specificity of cancer imaging and to use information from images to help optimize selection of therapy to avoid over- or under-treatment of disease. The Imaging Translation Platform is aimed at accelerating the development of imaging tools and techniques for earlier detection, diagnosis and treatment of cancer.

"Being able to diagnose cancer using imaging technology is not enough, we need to be able to detect, as well as characterize, cancer at its early stages so that the most suitable treatment can be selected. This is what the Smarter Imaging Program is all about," says Yaffe.

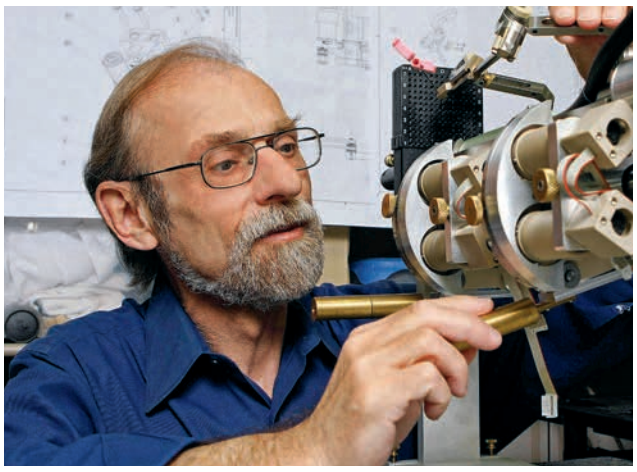
The Smarter Imaging Program is working to deliver solutions within the next five years that are focused on three of OICR's translational priorities in health: the over-diagnosis of prostate cancer, over aggressive treatment of early breast cancer and high-fatality rate associated with pancreatic cancer. To achieve its goals the Program has established major projects in radionuclides, x-ray and optical tomography, ultrasound and nuclear MRI. In addition, a small sub-component of the program will study imaging individual cancer stem cells with the use of MRI.

Ontario is recognized as a world leader in medical imaging technology, but there is concern that none of its research groups have, on their own, the capacity to push innovations through the development pipeline and into the clinic. The Imaging Translation Platform was created by OICR to address this need. The Platform's focus will be on the translation of research to creating new imaging probes for the early detection of cancer with projects in imaging probe translation, medical imaging instrumentation and software, pathology validation and imaging for clinical trials.

"Ontario is home to many of the world's best imaging scientists and organizations. The idea behind the Platform is to boost the ability of these innovators to move their projects through the pipeline, which can be a very complex and resource intensive process," says Fenster.

As part of its funding of the Imaging Translation Platform, OICR is supporting another initiative headed by Fenster and Yaffe called the Centre for Imaging Technology Commercialization (CImTeC), which has facilities in London and Toronto. CImTeC was established to help researchers and small and medium-sized enterprises to translate their research findings into clinical tools. CImTeC does this by providing business expertise and technical support and by providing access to clinicians and infrastructure.

"Providing Ontario's imaging researchers and businesses with the type of assistance offered by CImTeC means that they can take their world class research and make it internationally competitive in a commercial context," says Dr. Fenster who serves as Director and Acting CEO of CImTeC. "The innovative technologies being developed by Ontario's imaging community have great potential to help people around the world. CImTeC is about making that happen."



# USING GENOMICS TO GUIDE THE PERSONALIZED TREATMENT OF CANCER

Dr. Janet Dancey

For more than a decade, the possibilities stemming from the application of genomic research in health care have excited the world. Using genetic information to develop strategies for the prevention and treatment of diseases like cancer is at the heart of a concept called personalized medicine. Its use in treatment is often described as being "the right dose, for the right person, at the right time." Personalized medicine may enormously improve the outcomes of those with cancer and help to prevent its recurrence. The Ontario Institute for Cancer Research is working to bring the power of genomics and personalized medicine to the clinic and patients through its Genomics Pathway Strategy.

The GPS is the major project under OICR's initiative in personalized medicine. It aims to answer translational research questions that will have practical implications for the future of personalized medicine. The Strategy has been designed to align with three of OICR's priorities, as laid out in its strategic plan for 2010-2015. The study seeks to drive the adoption of personalized medicine for cancer, seeks solutions to critical issues in prostate and breast cancer and works to improve the digitization and interpretation of cancer data.

Dr. Lillian Siu, of the University Health Network (UHN), is leading the study and the co-principal investigators are Dr. Suzanne Kamel-Reid, also of UHN and Drs. Janet Dancey, leader of the OICR's High Impact Clinical Trials Program, John McPherson, leader of OICR's Genome Technologies Platform and Lincoln Stein, leader of OICR's Informatics and Bio-computing Platform.

The diverse set of expertise possessed by the study's investigators means that questions around the implementation of personalized medicine will be studied from a multi-disciplinary approach and lead to effective strategies for the clinical use of genomic next-generation sequencing approaches. OICR's strength in genome sequencing and analysis will be used to assist physicians in evaluating a patient's cancer and inform decision-making regarding treatment.

Recently the GPS reached a major milestone with completion of the first phase of a feasibility study. Dancey explains that this study was designed to "determine whether we can obtain patient consent, get samples, deliver them to the genomics platform for analysis, confirm the results in a clinical laboratory and forward a report that will describe the mutations, as well as their clinical significance and potential clinical trial availability, back to the clinician and the patient in less than three weeks." In essence, the study is testing the concepts of personalized medicine.

The feasibility study was initiated at UHN's Princess Margaret Hospital in Toronto but was expanded to include sites in London, Hamilton, Ottawa and Thunder Bay. The patients enrolled in the study have already exhausted the use of standard treatments, often leaving a clinical trial as their only treatment option. The GPS is employing personalized medicine to help these patients find suitable clinical trials and targeted treatments based on genetic mutations found through sequencing.

"What we are seeing from the first phase of this study is that personalized medicine has the potential to improve our decision-making about cancer treatment and guide patients to therapies that can have a great impact on their quality of life," says Dr. Tom Hudson, OICR's President and Scientific Director. "The advances we have seen in cancer treatment

in recent years have been great, but now we need to start focussing on how and when we use them."

Dancey says that it is often patients with rare tumours who are left with the fewest treatment options. To bridge this gap in treatment the Rare Tumour Clinical Trials Initiative was launched in August 2011, by the NCIC Clinical Trials Group, OICR and Pfizer Canada. "The Initiative was established to evaluate drugs in patients with rare tumours, which is an unmet need and a challenging task." Although the proper criteria would have to be met, Dr. Dancey says there is a possibility that a patient could be directed by the GPS to this clinical trial if genetic mutations that may be sensitive to the targeted drugs are identified in patient samples. OICR's Genomics Platform will be analyzing samples to identify disease or treatment markers.
"It's a bit of an unusual study," says Dancey of the Rare Tumour Initiative. "It deals with rare tumours, has a novel design and two cohorts of the study have gene mutation criteria for enrolment."

The study's design is unique in that it consists of 10 cohorts, in which patients are given one of two drugs; this results in 20 clinical trials being run within one protocol. Dancey points out that this makes it a highly efficient model which could, "be used in future studies of rare cancers in patients as well as rare subsets of cancer as might be identified, for example, by rare mutations in breast cancer patients."

The two cohorts with genetic mutation eligibility criteria were designed to allow researchers to evaluate targeting drugs based on molecular profile as opposed to traditional cancer diagnosis and histology, which serves as another test of the feasibility of personalized medicine. Patients with tumours that have mutations that are relevant to the drug's mechanisms of action can be enrolled.

So far the Rare Tumour Initiative has activated five trial centres across Ontario and has started to accrue patients. Dancey says that the Rare Tumour Initiative, like the GPS, will use genomics to help guide patients with few treatment options to therapies that may be of use.

"The GPS and the Rare Tumour Initiative are examples of how we are starting to move personalized medicine from the lab to the clinic. We are ushering in a new paradigm in health care by turning advances in genomics and bioinformatics into tools that can be used by clinicians to better treat their patients and improve decision making," says Dancey.

# CANCER DIAGNOSIS AND TREATMENT ADVANCE WITH MOLECULAR PATHOLOGY

Dr. John Bartlett

Molecular pathology is being used to advance cancer diagnosis and treatment by studying proteins, RNA and DNA to understand the molecular diversity of multiple cancer types (e.g., breast, ovarian and prostate) and to discover which gene is expressed in a particular cancer. Cancer is more complicated than previously thought, posing a challenge for molecular pathologists trying to properly diagnose and treat patients. Genomic research has shown that every patient's cancer is different – even for tumours of the same type of cancer. The Transformative Pathology Platform will use this better understanding of cancer to improve molecular and genetic approaches to the diagnosis and classification of human tumours. By identifying characteristics of the tumour that are specific to the individual patient, the Platform will pave the way for more personalized medicine.

OICR launched the Transformative Pathology Platform in July 2011 with a goal of bringing more personalized medicine to patients in Ontario and worldwide. The new Platform aims to develop novel molecular diagnostic approaches to cancer and train the next generation of clinicians and scientists to implement and develop further molecular companion diagnostic approaches. The Platform promises to play a leadership role in using personalized medicine to improve patient outcomes.

To pursue these goals, Dr. John Bartlett, who relocated from Edinburgh to join OICR as Director of the Transformative Pathology Platform, is developing a multi-disciplinary, multi-institutional plan to make Ontario a world leader in molecular pathology of cancer. He was appointed recently to the American Society of Clinical Oncology and College of American Pathologists Human Epidermal Growth Factor Receptor 2 (ASCO-CAP HER2) guidelines panel.

"The Transformative Pathology Platform is a personalized medicine initiative, which will develop a novel approach for cancer diagnosis," Bartlett says. "We will build diagnostic tools that integrate genomic alterations, which will improve therapeutic efficacy through the molecular selection of targets and tumours."

OICR is dedicated to integrating personalized medicine into everyday care and its new platform will equip physicians with more effective tools to determine how best to match patients to the most optimal treatments using genetic information. This will lead to improved treatment for patients with fewer side effects.

Since his move to Toronto, Bartlett has made significant progress in establishing a new platform. More than 18 researchers have been recruited, of which six have been recruited from Edinburgh. The group shares a common vision to work collaboratively with researchers within OICR and across provinces.

"OICR provides an exciting opportunity to work with other researchers and clinical trials groups in Ontario and across Canada," says Melanie Spears, Scientific Associate in the Transformative Pathology Platform. "The Institute is a great place to work and provides a lot of support for its scientists. OICR also has a strong translational focus, which is an essential aspect of our Platform."

"By empowering clinicians with novel diagnostic tools and knowledge in molecular pathology, we can accelerate the delivery of tailored treatments to individual cancer patients in the medium and long term."

The Platform has established collaborative links with OICR's Medicinal Chemistry Platform, Selective Therapies Program, Genome Technologies Platform and the International Cancer Genome Consortium. Bartlett has integrated the Ontario Tumour Bank biorepository and data bank into the Transformative Pathology Platform, and a new initiative of transforming sample collections into DNA, RNA and tissue microarray resources has commenced. This will help facilitate the use of samples by internal and external researchers interested in designing and validating new cancer biomarkers for disease progression and treatment response.

Over the years, there has been a nationwide shortage of pathologists and the discipline has become somewhat isolated. As more patient samples require validation, an increasing amount of expertise in pathology is required. This has resulted in the demand for more training programs. "Pathology, with its central role in accurate diagnosis, remains essential to the successful treatment of disease," he says. "As a community we also need to recognize the centrality of pathology and its applications." Bartlett will help fill in the gap by training a new generation of molecular pathologists and clinicians across the province. He will provide researchers with the tools required to implement and further develop molecular companion diagnostic approaches. He is also in the process of implementing pathology fellowships and student placements at OICR.

"Transformative pathology is about re-visiting the fundamental paradigm of medicine – that accurate diagnosis drives better treatment," says Bartlett. "By empowering clinicians with novel diagnostic tools and knowledge in molecular pathology, we can accelerate the delivery of tailored treatments to individual cancer patients in the medium and long term."

# A BETTER STRATEGY TO PREVENT AND SCREEN FOR DISEASE

Dr. Eva Grunfeld

When it comes to serious chronic diseases such as cancer, heart disease and diabetes, the healthcare system is often focused most heavily on ensuring successful diagnosis and treatment. Yet there is already a huge body of knowledge about how to prevent and better screen for these diseases that is currently underutilized. The problem isn't a lack of knowledge, but rather in ensuring this existing information is delivered to patients in a way that is clear, meaningful and that can be easily acted upon.

The BETTER project (Building on Existing Tools to Improve Chronic Disease Prevention in Family Practice), led by Dr. Eva Grunfeld, Director, Knowledge Translation Research Network (KT-Net) and a Clinical Scientist in OICR's Health Services Research Program, developed and tested an innovative new approach to help make prevention and screening strategies more accessible to patients.

"BETTER is a study based on the idea that the primary care setting is where the majority of evidence-based strategies to improve chronic disease prevention and screening take place," says Grunfeld. "But because of the realities of practice in primary care, where there is a huge demand for services and semi-urgent care, there isn't often enough attention paid to prevention and screening of chronic diseases."

The study, a pragmatic randomized controlled trial, took place in selected family practices in Edmonton and Toronto. In the practices assigned to the intervention, a member of the practice's team, such as a nurse practitioner or dietician, was trained in chronic disease prevention and screening. Patients at these clinics were then invited to come for a dedicated visit with that prevention practitioner, to develop an individualized strategy for preventing chronic disease. In the control practices, patients received the regular standard of care. Almost 800 patients in total were enrolled in the study.

Instead of thinking about diseases like heart disease and cancer in isolation, the team also considered common lifestyle factors that could lead to the development of more than one of these diseases, which Grunfeld refers to as an integrated approach.

"If you think about it from the patient's perspective or the family physician's perspective, it really needs to be an integrated whole," she adds. "It doesn't make sense to talk about heart disease and then have a separate conversation about diabetes and cancer, because in many ways it is a common pathway in terms of lifestyle factor that can improve all of these things."

Grunfeld and her team first identified 28 different maneuvers to include in the study, each of which is a lifestyle behaviour or screening technique directly linked, through evidence, to improved outcomes. "Weight control, exercise, smoking cessation, lipid and blood pressure monitoring are all factors that have been directly linked in large cohort studies and in some randomized trials to reducing the risk of diseases like diabetes, heart disease and cancer, and in that way reducing morbidity and mortality," says Grunfeld.

To reduce the chances of overscreening, no maneuvers were included in the study without a strong evidence base behind it. Grunfeld cites prostate-specific antigen (PSA) testing for prostate cancer and reducing sun exposure for skin cancer as two maneuvers with insufficient evidence to include. "We looked at the evidence behind PSA testing and

"BETTER is a study based on the idea that the primary care setting is where the majority of evidence-based strategies to improve chronic disease prevention and screening take place."

it was not strong – in fact, the current recommendation is for a discussion rather than routine testing. Similarly with reduction of sun exposure and prevention of skin cancer, there wasn't level one evidence that asking people to reduce their level of exposure to the sun would have an impact."

On average, patients involved in the BETTER study were eligible for seven prevention or screening interventions out of the 28 maneuvers identified for the study. Each patient received a prevention prescription tailored to his or her situation. The individualized prescription helped simplify prevention and screening for patients by showing them exactly what was needed to make them healthier.

"What we found is that the benefit of having a dedicated prevention practitioner in the family practice was highly significant. Compared to control patients, those patients who saw the prevention practitioner had accomplished far more of the prevention and screening maneuvers that they were eligible for compared to the control group," Grunfeld says.

In short, just by being given clear, individualized information about prevention and screening, patients were much more likely to follow up with further tests or lifestyle adjustments to improve their own health.

The study also made things easier for family physicians. "We developed this approach because we knew that family physicians are overworked and while they supported the idea of prevention and screening it is often hard for them to include all aspects in everyday practice. That's why we've taken a health professional member of their own team who they identified, and trained that individual. It should reduce their workload considerably."

Under the new model looked at in the BETTER study, physicians would still become involved when needed. If, for example, a patient found to have high blood pressure by the prevention practitioner, would go through the process of weight control and salt reduction to reduce blood pressure. But if the patient comes back and the blood pressure is still high, then an appointment would be scheduled with the family doctor for further evaluation.

The BETTER study is a major part of Grunfeld's clinician-scientist portfolio at OICR. She was able to attract $2.5 million in funding from the Canadian Partnership Against Cancer (CPAC) and the Heart and Stroke Foundation to run the study. CPAC has extended funding for a further six months to complete additional knowledge exchange activities to disseminate the findings more widely.

The goal is to use the results from the BETTER study to encourage more family practices across Canada to include prevention practitioners, and ultimately to make prevention strategies more accessible to patients nationwide. Already broad meetings have begun with decision makers in Alberta and Ontario, where Grunfeld says there has been a great deal of excitement about initial results. Leaders from the Northwest Territories and Newfoundland have both expressed interest in the study and are exploring how to adapt it to their settings.

"It's very early days and it is very new information," says Grunfeld, "but we are already seeing that there is a substantial amount of interest and enthusiasm about the study and its potential to really help patients."

# UNRAVELLING THE COMPLEX CAUSES OF CHRONIC DISEASES WILL AID FUTURE GENERATIONS

Dr. Lyle Palmer

How do diseases like cancer develop? The answer is complex – genes, lifestyle, environment and other factors play a role. Understanding risk factors and the chronic diseases they can lead to is the goal of the Ontario Health Study, one of the largest health studies in Canadian history. The health data from the Study will be used to improve the health of Ontarians and people around the world by helping researchers develop better strategies for the prevention, diagnosis and treatment of illnesses such as cancer, diabetes, heart disease, asthma and Alzheimer's.

The OHS is studying Ontario's large and diverse adult population using a unique online approach. Any resident of Ontario over 18 can participate in the Study by filling out an online questionnaire and participating in voluntary follow-up online surveys and physical measurements at assessment centres. The Study's first assessment centre is scheduled to open in downtown Toronto in summer 2012 with its first follow-up questionnaire, on the topic of psychosocial health, going out to participants late summer 2012. The Study is the first large-scale population-based health study in the world to take advantage of the reach of the Internet in this way. The response has been extraordinary – more than 220,000 people have completed the baseline questionnaire as of June 1, 2012.

"We have had a great response from Ontarians" says Dr. Lyle Palmer, Executive Scientific Director of the Ontario Health Study. "It is also very encouraging that we are seeing participation from people that reflects the cultural and geographic diversity of Ontario's population." The Study has been able to achieve good representation of age groups across the adult life span and socio-demographic indicators such as income.

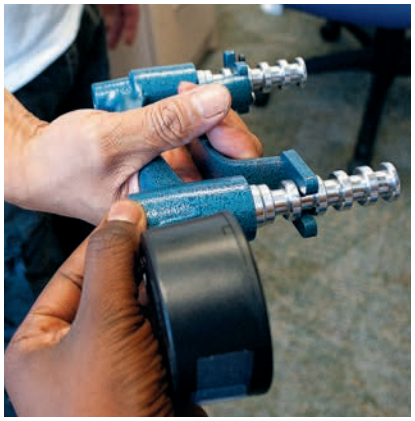
Ontario has many advantages for a population-based health study – one is the richness of administrative data collected by the healthcare system. "Ontario's health records infrastructure was a very attractive aspect of doing research here when I was deciding to move from Australia to lead the Study," says Palmer. "We will be able to take our data, and with the participant's consent, link it to their data from the health system to get a more complete picture and to follow people over their lifetime." Almost 90 per cent of participants agree to data linkage.

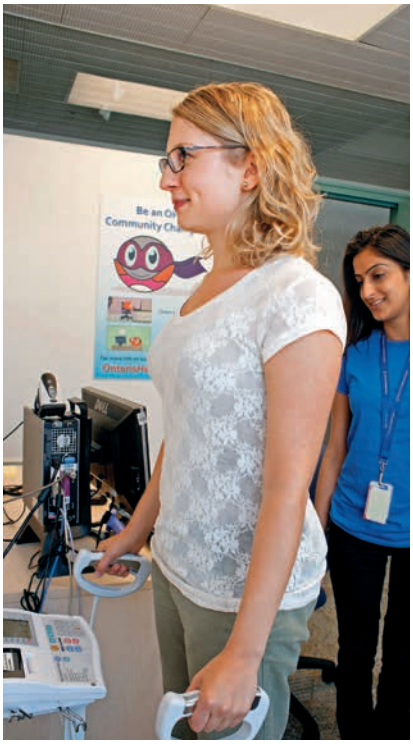
The data is particularly useful in the study of cancer. The Ontario Cancer Study (OCS) is an analytical sub-cohort of the OHS that focuses on cancer patients, survivors and family members participating in the OHS. The OCS is conducting high-impact research at a reduced cost by working within the OHS and using its online tools, databases and ethics and regulatory framework.

Researchers could use the OCS to track the experience and survivorship of patients, improve prevention and screening, use data linkage to support economic and policy research, characterize disease heterogeneity and re-contact participants for saliva DNA specimens to conduct genome-wide association studies.

"When you look at the possible research applications stemming from the OCS alone, you begin to realize how significant these types of population-based studies are," says Palmer. "I am very thankful to those who have completed the online questionnaire and encourage anyone who hasn't to do so. Most people don't realize how big an impact they can have with just a little bit of their time."


Ontario Health Study
Étude sur la santé Ontario






energy but is only 2% of its weight.
What will the Ontario Health Study
teach us? #HumansAreAwesome
ARTERY

# PROMOTING RESEARCH COLLABORATION THROUGH OPEN ACCESS DATABASES

Dr. Marc Perry and Abigail Cabunoc

The world's oldest glacier mummy, Ötzi the Iceman, lay frozen in the Italian Alps for over 5,000 years until his mummified remains were discovered in 1991. Scientists successfully mapped Ötzi's genome two decades later, revealing his entire genetic makeup – and with it, an enormous volume of sequenced data.

Without central organization, the data's interpretation would have been impossible. But thanks to the efforts of a group of collaborators, including Dr. Brian O'Connor, now a Senior Software Architect and Manager in OICR's Informatics and Bio-computing Platform, Ötzi's data was analyzed and his genetic information is now freely available to researchers around the world for study in a single online database hosted on the Amazon cloud. The Iceman genome data is available at icemangenome.net.

This type of research was unthinkable even a decade ago. Breakthroughs in genomics research, along with unprecedented advances in the genomics technologies used to screen, detect, monitor and diagnose cancer, have led to a new era in cancer research that promises to bring about improved, more personalized medicine for cancer patients.

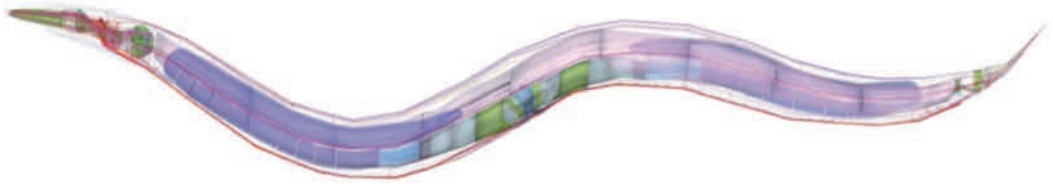
Databases are essential to this research. They can help to organize massive datasets and manage research results produced by these new technologies, turning large amounts of data into meaningful and accessible information for researchers. Open access databases provide the tools to freely share this information with other researchers, allowing them to collaborate on massive research projects that are global in scale.

Today, some of the most prominent open access databases in cancer research are housed at OICR and managed by OICR's Informatics and Bio-computing Platform, led by Dr. Lincoln Stein. A major part of the Platform's work involves maintaining these informatics tools and ensuring that they are all freely available online for the worldwide cancer research community. While the databases at OICR serve different functions, they are all connected by their ability to help researchers answer important questions about cancer genomics more efficiently, and help to bring answers to these questions to patients sooner.

"Organizations and jurisdictions can no longer afford to perform research in isolation," says Stein. "Providing open access to research data facilitates the sharing of knowledge, giving researchers the tools to collaborate rather than compete. This frees up valuable research time and dollars, allowing researchers to tackle larger, more complex and more far-reaching research problems."

One of the largest and most high-profile databases housed at OICR is the International Cancer Genome Consortium's Data Coordination Centre (DCC). The ICGC launched in 2008 with a goal of sequencing the genomes of 50 different tumour types and making the data freely available to researchers worldwide. There are currently 47 projects from 15 jurisdictions participating in the ICGC. All of their efforts are coordinated by the ICGC DCC and made available to researchers around the world through the ICGC's data portal at dcc.icgc.org.

"The ICGC DCC team at OICR coordinates data sent in by members, performs quality control and stores the data in a single database that is accessible through the ICGC's website," explains Dr. Vincent Ferretti, Principal Investigator, Senior Scientist and Associate Director, Bioinformatics Software Development. ICGC DCC staff members also develop the software required to share data with the community. "The ICGC DCC will help researchers



in efforts to gain a better understanding of how cancer works and is a fundamental tool to understand cancer genomics," says Ferretti.

Reactome is another prominent database housed at OICR that, since its inception, has been cited in over 1,200 research papers around the world. This database is an "online textbook" that helps users to access tools for visualizing pathway information and perform data analysis crucial to cancer research. "Reactome users can browse pathway diagrams and learn about reactions, genes, proteins and small molecules involved in different pathways," says Dr. Robin Haw, Scientific Associate, Informatics and Bio-computing and Manager, Outreach and Communication, Reactome. These tools assist researchers around the world, allowing them to work more efficiently and push their own research forward faster.

Model organisms are studied extensively because of their rapid rate of development and extremely short lifespan. These factors allow scientists to see genetic changes over generations that would be impossible with humans. There are surprising commonalities between humans and these model organisms on the genetic level – for example, it is estimated that 75 per cent of known human diseases have a recognizable match in the fruit fly genome. While the species themselves seem modest, the information they provide cancer researchers is extremely valuable, and OICR has databases that help share this valuable knowledge of these organisms with researchers around the globe.

The model organism ENCyclopedia of DNA Elements Project (modENCODE) is a continuation of the ENCODE Project, a public consortium launched by the National Human Genome Research Institute to identify all functional elements in the human genome. modENCODE aspires to identify all sequence-based functional elements in two model organisms: the common roundworm (*C. elegans*) and fruit fly (*Drosophila melanogaster*). modENCODE helps bridge the gap between research fields, explains Dr. Marc Perry, Scientific Associate, Informatics and Bio-computing and Data Liaison for 50 per cent of the modENCODE-funded projects. "modENCODE provides a platform to initiate collaboration between researchers working on human disease with researchers working with similar genes in model organisms," he says.

WormBase is another bioinformatics database that serves as a comprehensive resource for the genome and biology of the model system *C. elegans* and related types of roundworms. WormBase curates, stores and displays submitted genetic and genomic data. "The objective of WormBase is to capture the experimental data available from these organisms and place it into a rich information discovery space," says Abigail Cabunoc, Associate Technical Analyst, Informatics and Bio-computing and WormBase Web Developer. WormBase participates in the Generic Model Organism Database Project, which is a collection of open-source software tools for creating and managing genome-scale biological databases.

Bioinformaticians working in cancer research have been leaders in the movement towards open access databases – in part because of the complexity of the disease and in part because of the high costs of conducting cancer research. But other fields are now beginning to follow suit, seeing the advantages of sharing valuable research data and collaborating on research projects. The open access databases like those found at OICR provide models for researchers in other fields to build upon.

"This is the future of research," says Stein. "We can do far more working together and sharing results than we can ever do working in isolation."

# A NEW TECHNOLOGY USES ULTRASOUND TO DESTROY TUMOURS

Dr. Kullervo Hynynen

Ultrasound technology is widely known as a non-invasive way to help visualize pregnancy and muscles, organs or other soft tissues in the body. But it has many other applications, including the non-invasive destruction of diseased tissue. Harmonic Medical Inc., a start-up company founded by Dr. Kullervo Hynynen and colleagues at Sunnybrook Research Institute, is exploring the application of ultrasound technology to treat solid tumours.

The company is on the cusp of perfecting its unique tumour treatment system, which is precise and accurate. It is on the verge of starting clinical trials. "This technology will serve as a new paradigm in surgery and tumour therapy," says Hynynen.

The ultrasound technology developed by Harmonic Medical is a novel approach to image-guided, high-intensity focused ultrasound (FUS). The controlled procedure heats and destroys diseased tissue like tumours through focused beams of ultrasound energy. MRI is often employed in conjunction with FUS to confirm that the tumour has been destroyed. But MRI is expensive, the machines are cumbersome and they don't facilitate bedside treatment.

Recognizing the need for a low-cost MRI alternative, Hynynen set out to develop a technology to confirm tumour destruction. Using knowledge of the change in the physical properties of tissues during heating, Hynynen developed a proprietary ultrasound-based method to monitor tissue damage. This technique provides feedback on the effectiveness of the procedure, while ensuring there is no damage to surrounding tissue. In essence, this technology ensures safe treatment without the need for MRI. Hynynen is an internationally renowned expert in FUS therapy.

He was previously a scientist at Brigham and Women's Hospital, a teaching affiliate of Harvard Medical School. Hynynen applied for funding from OICR's Intellectual Property Development and Commercialization (IPDC) Fund in 2009 with the aspiration to build a device that could destroy tumours using FUS beams without using MRI technology to monitor the tumour. The IPDC Fund is designed to support early-stage development projects from the oncology research base in Ontario. It bridges the funding gap between traditional public granting agencies and private investors.

Hynynen qualified for IPDC funding and later created Harmonic Medical with Raphael Ronen who is now Director of Business Development. Harmonic Medical in-licensed the intellectual property developed by Hynynen at Brigham and Women's, and Sunnybrook. The company presented an opportunity to OICR for further investment in the technology through a convertible debenture in March 2011. This is a type of loan that can be converted into shares in the company. OICR's Executive-in-Residence, Frank Gleeson, serves as Harmonic's Chief Financial Officer and Bob Sutherland, OICR's Senior Investment Officer, serves on the company's board of directors. "I think OICR has the best model for helping small companies," says Ronen. "It's not just funding, it's funding that comes with help and expertise."

This additional investment allowed Harmonic Medical to further develop its technology, which is now nearing the clinical trial stage. In the next few months, Harmonic hopes to raise funds to build the clinical prototype. Once the prototype is ready, the technology can be further tested on large animal models and then enter clinical trials. The current technology will be focused on solid tumours, but future applications could extend to a variety of non-cancer medical applications.

The footprint of Harmonic Medical's focused ultrasound system will be far smaller and more affordable than current MRI-based systems, allowing it to be used in locations where it's impractical to use an MRI. One such application is the treatment of tumours that have metastasized to bone. Many patients with bone tumours receive palliative care and might be in a hospice. They often require radiation treatment to alleviate the pain of the metastasized tumours but it can be impractical for these patients to travel to the hospital. Additionally, there is a limit as to how much radiation therapy they can receive. Harmonic Medical's ultrasound technology will be portable and could treat a patient at the bedside with no theoretical limit on the number of treatments. The treatment is also non-invasive and requires little recovery time. "Ideally, we hope this is the type of treatment that could allow a patient to recover on the day of treatment", says Junho Song, a Research Associate at Harmonic Medical. Another application is in geographic locations where funds are not available for an MRI facility or there is little access to MRI machines.

"Not only will this technology improve outcomes for patients, it will also have a strong economic benefit with reduced recovery time. It will also provide emotional benefits by taking away the fear that goes with surgery," says Ronen. With the ability to change the status quo for treating tumours using ultrasound technology, Harmonic Medical is a bright prospect with potentially far-reaching future applications.

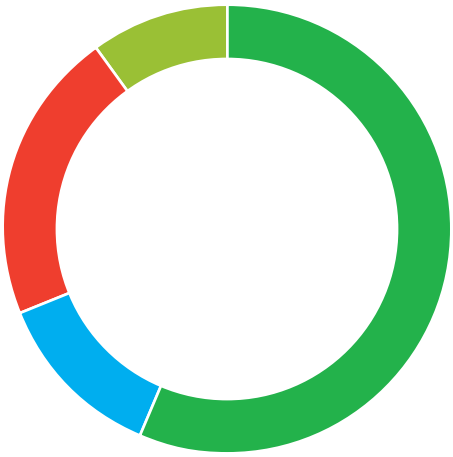
"Not only will this technology improve outcomes for patients, it will also have a strong economic benefit with reduced recovery time. It will also provide emotional benefits by taking away the fear that goes with surgery."

HARMONIC MEDICAL


POLO

# MONITORING RESULTS

OICR's strategic programs and the projects supported by OICR grants result in scientific discoveries, commercial activity, communications and the creation of jobs for highly qualified personnel.



## SOURCE OF FUNDING FOR OICR PROJECT EXPENDITURES 2011–2012 IN MILLIONS OF DOLLARS

$84.6 Ministry of Economic Development and Innovation

$18.5 OICR leveraged funding

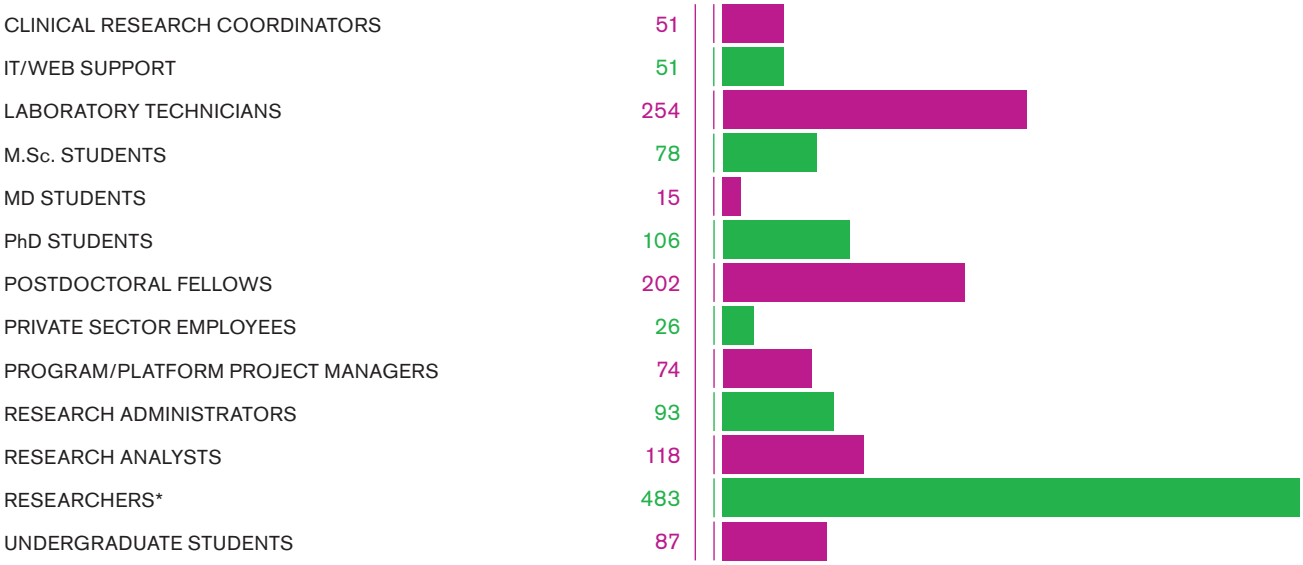
$31.9 Partner site leveraged funding

$14.6 IPDCP leveraged funding

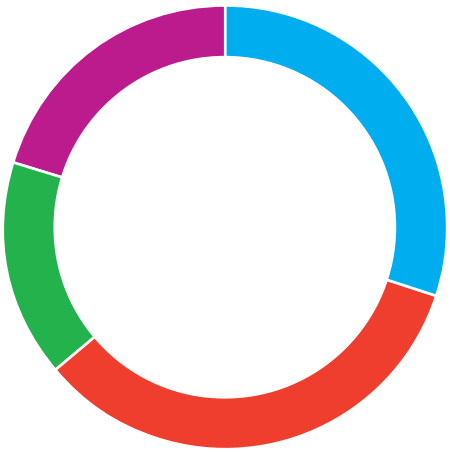
## COMMERCIAL ACTIVITY 2011–2012

| Commercial activity generated by funded projects | Cancer Research Fund | Cancer Research Program | Intellectual Property Development and Commercialization Program |
|---|---|---|---|
| DISCLOSURES | 1 | 7 | 0 |
| LICENSES GRANTED | 0 | 2 | 0 |
| PATENT APPLICATIONS | 4 | 17 | 1 |
| PATENTS AWARDED | 1 | 6 | 0 |
| START-UP COMPANIES | 0 | 1 | 2 |

## HIGHLY QUALIFIED PERSONNEL WORKING ON FUNDED PROJECTS 2011–2012




** includes principal investigators, program directors and project leaders*



## COMMUNICATIONS ARISING FROM FUNDED PROJECTS 2011–2012

229 Oral presentations in Canada

257 Oral presentations outside of Canada

123 Poster presentations in Canada

153 Poster presentations outside of Canada

## PUBLICATIONS IN JOURNALS 2011–2012

| PROGRAM | Journal impact factor range | Number in range |
|---|---|---|
| STRATEGIC PROGRAMS | 0-10 | 273 |
| | 11-20 | 29 |
| | 21-30 | 7 |
| | 31-60 | 10 |
| | NA** | 69 |
| GRANT SUPPORTED PROGRAMS | 0-10 | 40 |
| | 11-20 | 2 |
| | 21-30 | 1 |
| | 31-60 | 0 |
| | NA** | 6 |

*** NA = unrated journals*

## CANCER TYPES AND NUMBER OF PROJECTS 2011–2012

| CANCER TYPE | Translational grant competitions | Cancer Research Program | Intellectual Property Development and Commercialization Program |
|---|---|---|---|
| BRAIN | 2 | 5 | 0 |
| BREAST | 7 | 8 | 2 |
| COLORECTAL | 1 | 5 | 0 |
| HEAD AND NECK | 2 | 0 | 0 |
| HAEMATOLOGICAL | 3 | 2 | 1 |
| LUNG | 4 | 2 | 0 |
| MELANOMA | 1 | 1 | 0 |
| MULTIPLE CANCERS | 14 | 118 | 4 |
| OTHER | 3 | 3 | 0 |
| OVARIAN | 1 | 0 | 0 |
| PANCREATIC | 3 | 5 | 0 |
| PROSTATE | 7 | 3 | 0 |

## PROJECT TYPES 2011–2012

| PROJECT TYPE | Translational grant competitions | Cancer Research Program | Intellectual Property Development and Commercialization Program |
|---|---|---|---|
| CLINICAL TRIALS | 19 | 6 | 0 |
| COMPANION STUDIES | 6 | 0 | 0 |
| OTHER | 1 | 7 | 0 |
| TRANSLATIONAL | 22 | 139 | 7 |

## OICR GRANT-SUPPORTED PROJECTS

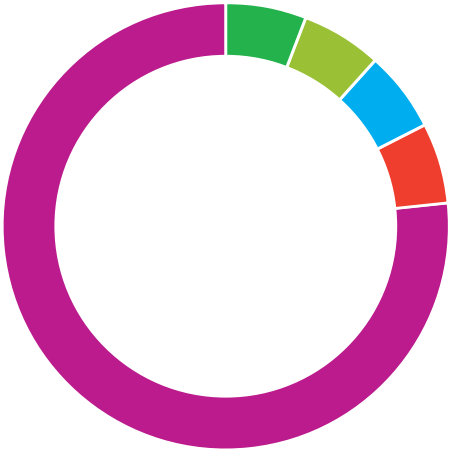
| DATE | Number of projects funded | Funds awarded (In millions of dollars) |
|---|---|---|
| 2002 | 34 | $ 15.6 |
| 2003 | 23 | $ 11.5 |
| 2004 | 12 | $ 7.0 |
| 2005 | 13 | $ 13.8 |
| 2006 | 21 | $ 7.9 |
| 2007 | 23 | $ 9.0 |
| 2008 | 13 | $ 6.4 |
| 2009 | 11 | $ 6.0 |
| 2010 | 11 | $ 5.6 |
| | 161 | $ 82.8 |

# INTELLECTUAL PROPERTY DEVELOPMENT AND COMMERCIALIZATION PROGRAM (IPDC)

## COMMERCIAL FUNDING 2007–2012

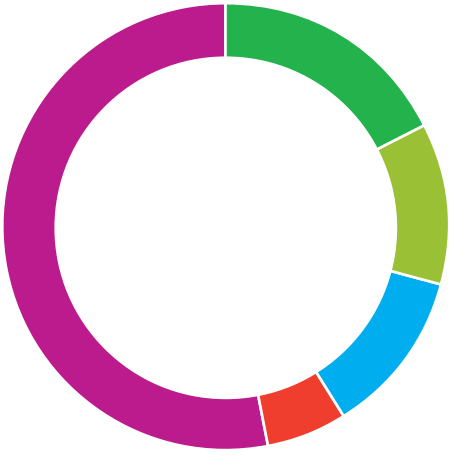
| | |
|---|---|
| NUMBER OF IPDC-FUNDED PROJECTS | 17 |
| OICR FUNDING | $12.5 million |

| LEVERAGED FUNDING | |
|---|---|
| FEDERAL GOVERNMENT (CASH) | $2 million |
| HOSPITALS (CASH) | $43,135 |
| NOT-FOR-PROFIT (CASH) | $3.2 million |
| PRIVATE SECTOR AND NOT-FOR-PROFIT (IN-KIND) | $390,135 |
| PRIVATE SECTOR (CASH) | $35.1 million |
| PROVINCIAL GOVERNMENT (CASH) | $5.7 million |
| TOTAL LEVERAGED FUNDING | $46.5 million |



## PROJECTS BY REGION 2011–2012

- 1 Hamilton
- 1 London
- 1 Ottawa
- 1 Thunder Bay
- 13 Toronto Area



## PROJECTS BY INTERVENTION 2011–2012

- 3 Diagnosis
- 2 Early detection
- 2 Other
- 1 Prevention
- 9 Treatment

## PROJECT BY CANCER TYPE 2011–2012

| | |
|---|---|
| 2 | Breast |
| 1 | Colorectal |
| 4 | Hematological |
| 2 | Liver |
| 5 | Multiple (platform technology) |
| 1 | Ovarian |
| 2 | Prostate |

## MILESTONES 2007–2012

| | |
|---|---|
| COMPANIES WITH PRODUCTS SOLD | 4 |
| EQUITY INVESTMENTS MADE BY OICR | 11 |
| FIRST-IN-MAN STUDIES COMMENCED | 3 |
| LARGE LICENSING DEALS | 1 |
| NEW ONTARIO START-UPS CREATED | 9 |
| PROJECTS WITH PROTOTYPES MANUFACTURED | 6 |
| VC DEALS | 3 |

# THE NEXT GENERATION

The Ontario Institute for Cancer Research has a mandate to strengthen Ontario's cancer research capacity and contribute to the development of the next generation of researchers. On the following pages you can read about some of the outstanding young investigators conducting research on OICR-funded projects.

# DR. GINA CLARKE

Dr. Gina Clarke

Dr. Martin Yaffe, Senior Scientist at Sunnybrook Research Institute and Co-Leader of OICR's Smarter Imaging Program and Imaging Translation Platform, was approached over a decade ago by a breast surgeon concerned about the limitations of the standard techniques used to evaluate lumpectomies. She was concerned about whether then-current lumpectomy techniques were accurately removing all cancer and was interested in the possibility of applying to pathology the advanced imaging techniques Yaffe's laboratory had previously developed for improving early detection of breast cancer with digital mammography. This collaboration evolved into the Biomarker Imaging Research Laboratory (BIRL), a state-of-the-art facility at Sunnybrook Research Institute.

The research team at the BIRL is today led by Dr. Gina Clarke, a Research Associate at Sunnybrook Health Sciences Centre. She completed a master's degree in upper atmospheric physics at York University. Motivated by the potential to help patients, her interests then shifted from imaging the atmosphere to imaging cancer. Consequently she pursued a PhD in the Department of Medical Biophysics at the University of Toronto, and in this program developed the basis for many of the methods employed routinely in the BIRL.

The BIRL provides researchers with advanced techniques for histopathology and immunohistochemistry imaging. These techniques are key in the accurate validation of novel techniques for cancer imaging. Clarke receives funding from OICR as an investigator in the Pathology Validation Platform, part of the Smarter Imaging Program led by Yaffe. A strong focus in the BIRL is application of the techniques to obtain more patient-specific molecular 'signatures' of cancer through tumour biomarkers.

Biomarkers are biological molecules that can be found in cells, which characterize an aspect of disease. They can provide information that helps to determine how aggressive a tumour is and could guide the most appropriate choice of treatment. However, for most cancer sites there are a highly limited number of biomarkers (if any) that are part of routine, diagnostic assays. As a result, when doctors are unable to accurately characterize the aggressiveness of the cancer, patients may receive more treatment than is actually required. "Breast cancer, for example, is very heterogeneous and only three biomarkers are routinely assayed to help determine the need for any secondary or adjuvant treatment," says Clarke. "But we believe that, in the near future, we will have a biomarker panel that will distinguish between the signatures of tumours that are likely to progress and those that will remain dormant."

Since biomarkers work in combination with each other, the team believes a major step in characterizing tumours to enable more patient-specific treatment is to develop techniques to image multiple biomarkers simultaneously on the same tissue section. The technology being developed by Clarke's lab will be a platform to discover new biomarkers, as well as help to avoid overtreatment. Clarke's lab is able to look at multiple biomarkers, co-localized in the same cell. "If you can look at multiple biomarkers co-localized in the same cell, you have a better framework to solve the problem of overtreating and recurrently treating patients," says Clarke.

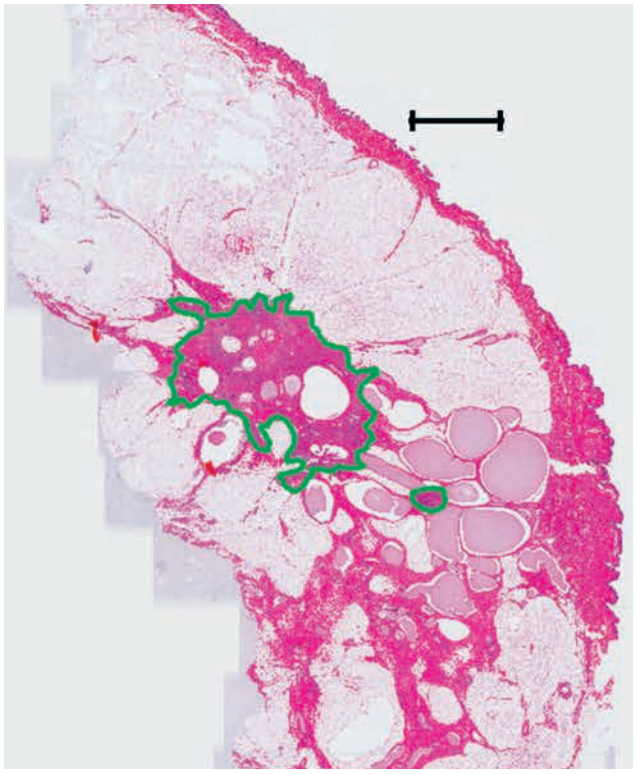
"But we believe that, in the near future, we will have a biomarker panel that will distinguish between the signatures of tumours that are likely to progress and those that will remain dormant."

Conventional pathology is based on a highly limited sampling of tissues. Clarke and her colleagues at the BIRL have developed an innovative technique called digitized whole-mount pathology imaging, in which large tissue sections are imaged. This is a specialty of this lab. "If we can do a better job of determining that there is no residual disease after surgery, then we could potentially spare patients adjuvant radiation therapy," she says.

The capacity to produce these whole-mount sections along with the imaging and image-processing capabilities makes this lab unique in the world. Another important feature is that the whole mount sections are produced in a way that maintains the three-dimensional conformation of the specimen.

Clarke's lab has a trial underway to validate the whole-mount technique compared to the conventional methods used in pathology, comparing key, prognostic tumour measurements. Preliminary data suggests that the whole-mount technique more accurately represents the full extent of disease and its relationship to the specimen margins.

Through OICR, Clarke is able to collaborate synergistically with other researchers. For example, using the whole-mount technology developed by the lab, she is able to support fellow researchers in pathology validation in trials of new systems for improved imaging of breast, prostate, colorectal and pancreatic cancer. "Our work through OICR allows us to extend the impact of our research well beyond what we could accomplish on our own," says Clarke.



# DR. KEVIN BROWN

Dr. Kevin Brown

Scientists first identified the existence of ribonucleic acid interference (RNAi) in 1998, a discovery for which a Nobel Prize was awarded. The naturally occurring process garnered a great deal of attention in the scientific community and is now viewed as a key drug discovery tool. Cells use RNAi to silence or turn down the activity of specific genes. Cancer is seen as one potential target for RNAi-based therapies because silencing the activity of certain genes could stop a cancer cell's activity. Dr. Kevin Brown, a Senior Research Associate in the Selective Therapies Program at the OICR, hopes to build on an advancement in RNAi technology to identify targets for new selective therapeutics in the treatment of cancer.

Brown works in Dr. Jason Moffat's lab, located in the Terrence Donnelly Centre for Cellular and Biomolecular Research. There he wears two hats – he is both a bioinformatician and computational biologist.

The Moffat lab performs lentiviral short hairpin RNA (shRNA) screens, mainly on pancreatic cancer cells. This method of screening is a recent advancement in RNAi technology. It uses a lentivirus (a type of virus widely used as a means to deliver genes to a cell) to deliver shRNA to cancer cells and pools of 80,000 different shRNAs are used to individually silence each of 16,000 genes in the cancer cells. Brown analyzes, interprets and manages the large dataset gained from these experiments, using computational tools, including some he has developed.

The screens are used to determine how a cancer cell's growth is affected when a given gene is removed from the cell. They are completed across a large series of cancer cell lines, which encompass many different tumour types. It is important to use many different cell lines from various tumours to account for the heterogeneity within pancreatic cancer. These cell lines are tumour cells that can be grown perpetually and are used to determine the behaviour of human tumours. They are important because they allow researchers to measure how a tumour will respond to drugs, without having to test them on humans. Brown's team explores the large dataset to determine which of the 16,000 genes across more than 100 cell lines might be important from a therapeutic perspective. "My main job is to take this large pile of data and essentially mine it to find these interesting needles in the haystack."

So, what makes a gene interesting or important? "If a gene disappears from the population during a screen, you know you have killed the cell," explains Brown. "Since these are tumour cells, this is a signal that this gene is important for that cell." However, it can be difficult to determine if the gene is important only for cancer cells or all cells in general. So the team references published copy number and gene expression datasets about portions of the genome that are amplified or deleted, and over- or under-expressed. "Then we overlay that data, to amplify the interest in some of those genes," says Brown. Knowing the gene is important to the tumour cell and that it is modified makes it interesting. The next question is if it's targetable by therapeutics.

"We want to find genes that will be good therapeutic targets. By doing large-scale data integration, hopefully we will determine that some of those genes are interesting targets. It's challenging because on one hand we have too much data but on the other hand we don't have enough. The challenge is to successfully look at the data we've gathered and pull out biologically meaningful patterns," says Brown.

Brown benefits from access to a large pool of experts at OICR who can provide assistance with analyzing sequencing data. "From a computational perspective, it's good to have a team of experts, including stem cell experts," he says. His lab, in terms of shRNA screens, focuses on pancreatic cancer and the synergy with OICR and the International Cancer Genome Consortium has been very important for Brown. "We are nearing the point where the ICGC can provide novel information about pancreatic cancer and the lab can integrate this with the data generated from the shRNA screens," he says.

"As a computational person whatever I find has to be validated by someone else, and I have a great lab with highly skilled people to make that happen," says Brown. "My wet lab experience allows me to filter out most of the noise from the data generated and I am able to present my team with information that is the most useful and important."

An exciting part of Brown's job is knowing that the work he and his lab produce will be tested very quickly and with a fast turnaround of their results. "The same people doing the tests are experts in the field who can look at our results and determine what makes sense." Brown hopes this dynamic will lead to another new and interesting discovery in cancer biology.

Brown completed a bachelor of science with a minor in computer science at the University of Waterloo, followed by a master of science in medical biophysics at the University of Toronto. He continued in the department to complete a PhD in medical biophysics, working in the bioinformatics realm.

"If a gene disappears from the population during a screen, you know you have killed the cell. Since these are tumour cells, this is a signal that this gene is important for that cell."

# DR. JAMES MAINPRIZE

Dr. James Mainprize

From a young age, Dr. James Mainprize was always interested in physics. After completing a summer position in Dr. Martin Yaffe's lab at Sunnybrook Health Sciences Centre, he realized physics was not just an application used to solve abstract problems, but also played a pivotal role in directly improving people's lives.

That persuaded him to start putting down roots in Toronto and complete graduate studies in medical biophysics at the University of Toronto. He later worked as a research associate with Yaffe. He now pursues research into digital breast tomosynthesis, imaging physics and 3D surgical planning.

Today, his team is developing new technologies to diagnose the most common type of non-invasive breast cancer, ductal *carcinoma in situ* (DCIS). With DCIS, abnormal cells are confined in the milk ducts of the breasts and have not spread into breast tissue or other parts of the body. DCIS isn't life threatening, but can increase the chances of developing a more aggressive form of breast cancer. Clinicians and researchers do not have tools to identify which cancers are fatal.

The number of DCIS cases detected has increased dramatically due to widespread use of mammography. Twenty per cent of breast cancers seen in screening are DCIS. Most patients are given two curative options, breast-conserving surgery and radiation therapy.

"There is a need to identify more personalized approaches to diagnosing patients with DCIS tumours to avoid over- and under- treatment," says Mainprize. "A study of autopsies has shown that some women have undetected DCIS at death. This supports the idea that not all DCIS occurrences will lead to an invasive or life-threatening cancer."

The team is using contrast-enhanced digital mammography to assess characteristics of DCIS and tumour size prior to biopsy. Vessels that supply blood to tumours are leakier than those feeding healthy tissue, allowing the contrast agent to build up and be visible to an x-ray camera. Mainprize will use this information to identify physiological and functional changes, including blood flow and metabolism, in the tumour.

"What we are learning is that the accumulation of a contrast agent at a tumour site is an indicator that the cancer might be more aggressive and likely to spread," he says." If successful, this cost-effective diagnostic tool could reduce overtreatment of DCIS and improve quality of life for many women."

In a related project, microbubble contrast ultrasound is being used to better determine aggressiveness of DCIS tumours. Microbubbles are tiny gas bubbles that flow through blood and into the smallest blood vessels. A simple ultrasound probe detects these microbubbles, providing an accurate picture of the blood supply surrounding the tumour. This could provide better, more personalized diagnostic standards and improved treatment options.

The information generated by the technologies will be used to develop imaging "fingerprints" that can be linked to the underlying genetic profiles of the tumours to address the specific needs of the individual patient.

Mainprize is excited to be playing a role in directly improving the lives of cancer patients. "Ontario's strong research infrastructure has given me the remarkable opportunity to use my background in physics to solve real medical problems," he says.

# DR. ANDREW BROWN

Dr. Andrew Brown

Dr. Andrew Brown's interest in science took him from his hometown of Markham, Ontario to McGill University in Montreal for an undergraduate degree in biochemistry. At McGill he developed a keen interest in genetics and decided to specialize in pharmacogenomics by pursuing his PhD at the Université de Montréal. Pharmacogenomics is concerned with the genetic basis for variation in drug response among patients. Brown's PhD was on the effects of genetic variation in drug metabolism pathways on efficacy and adverse drug reactions. Brown then moved back to Ontario to join OICR.

For Brown, the decision to join OICR was an easy one: "I wanted to stay in Canada after I finished my education, but more than anything I wanted to work with state-of-the-art technology and with world-class researchers," says Brown. "Ontario is one of only a few places in the country that can offer both of these." Brown is a postdoctoral fellow in OICR's Genome Technologies Platform and does research on a number of projects, including one under OICR's Genomics Pathway Strategy.

This study is using OICR's genome sequencing infrastructure to support a clinical trial involving the mutation profiling of cancer patients. The goal is to provide clinicians with detailed information about the mutations driving a patient's cancer that could potentially influence the choice of therapy. The GPS is testing the concepts of personalized medicine to help move it into the widespread clinical setting. Personalized medicine is moving the treatment of cancer beyond a one-size-fits-all approach.

Brown is overseeing the sequencing efforts in the study with a particular focus on the enrichment process, which determines how the sequencers will target the specific genes being examined in the study. "Initially we were targeting 19 genes which was fairly straightforward, but as we move towards hundreds or even thousands of gene targets, choosing the right method for enrichment is essential to the success of the project." explains Brown.

Brown's projects are highly complex, but he says that being at OICR makes it easier to achieve successful results. "We have all of the latest and greatest technologies and the notable investigators we have at OICR have attracted excellent partners for collaboration," says Brown. "It also helps that OICR's research model combines the best of both academic and industry settings."

Recently Brown presented the findings of the first 50 patients enrolled in the GPS study, which showed that 30 per cent of patients had reportable or actionable genetic variations. Patients were enrolled in the study at five sites across Ontario and the majority of patients were provided with a report about their genetic variations within three weeks. "We need to provide the report to the treating clinicians within a timeframe that is clinically relevant and I'm pleased to say we are meeting this goal," says Brown. Six of the first 50 patients had their course of therapy influenced by the results of the sequencing.

"The results of the study show that we are on the path to personalized medicine," says Brown. "Doing research at OICR places me on the leading edge of the personalized medicine revolution. The potential impact that our work could have on the lives of patients around the world is an exciting thing to consider."

# FINANCIAL STATEMENTS

# REPORT OF THE INDEPENDENT AUDITOR ON THE SUMMARY FINANCIAL STATEMENTS

To the Members of the Ontario Institute for Cancer Research

The accompanying summary financial statements, which comprise the summary statement of financial position as at March 31, 2012, the summary statement of operations and surplus, and the summary statement of cash flows for the year then ended, are derived from the audited financial statements of the Ontario Institute for Cancer Research for the year ended March 31, 2012. We expressed an unmodified audit opinion on those financial statements in our report dated June 21, 2012. Those financial statements, and the summary financial statements, do not reflect the effects of events that occurred subsequent to the date of our report on those financial statements.

The summary financial statements do not contain all the disclosures required by Canadian generally accepted accounting principles. Reading the summary financial statements, therefore, is not a substitute for reading the audited financial statements of the Ontario Institute for Cancer Research.

**MANAGEMENT'S RESPONSIBILITY FOR THE SUMMARY FINANCIAL STATEMENTS**

Management is responsible for the preparation of a summary of the audited financial statements in accordance with Canadian generally accepted accounting principles.

**AUDITOR'S RESPONSIBILITY**

Our responsibility is to express an opinion on the summary financial statements based on our procedures, which were conducted in accordance with Canadian Auditing Standard (CAS) 810, "Engagements to Report on Summary Financial Statements."

**OPINION**

In our opinion, the summary financial statements derived from the audited financial statements of the Ontario Institute for Cancer Research for the year ended March 31, 2012 are a fair summary of those financial statements, in accordance with Canadian generally accepted accounting principles.

Ernst & Young LLP

Chartered Accountants
Licensed Public Accountants
July 25, 2012
Toronto, Canada

# STATEMENT OF FINANCIAL POSITION

*Excerpt from the audited financial statements.*

| As at March 31 | 2012 | 2011 |
|---|---|---|
| **ASSETS** | | |
| **CURRENT** | | |
| Cash | **$ 13,012,946** | $ 16,466,759 |
| Investments | **4,275,000** | 4,275,000 |
| Receivables | **4,573,745** | 2,821,970 |
| Supplies | **729,745** | 359,906 |
| Prepaid expenses | **2,261,179** | 1,941,932 |
| Current portion of deferred lease incentive | **124,848** | 124,848 |
| **TOTAL CURRENT ASSETS** | **24,977,463** | 25,990,415 |
| Long-term portion of prepaid expenses | **770,855** | 1,268,223 |
| Deferred lease incentive | **322,526** | 447,374 |
| Property and equipment, net | **26,062,459** | 27,289,697 |
| Note receivable | **484,496** | 478,667 |
| | **$ 52,617,799** | $ 55,474,376 |
| **LIABILITIES AND DEFERRED CONTRIBUTIONS** | | |
| **LIABILITIES** | | |
| **CURRENT** | | |
| Accounts payable and accrued liabilities | **$ 10,700,101** | $ 11,345,169 |
| Current portion of unearned rental revenue | **4,255** | 127,691 |
| Current portion of deferred gain | **—** | 45,172 |
| Term loan | **500,000** | 500,000 |
| **TOTAL CURRENT LIABILITIES** | **11,204,356** | 12,018,032 |
| **TOTAL LIABILITIES** | **11,204,356** | 12,018,032 |
| **DEFERRED CONTRIBUTIONS** | **37,614,172** | 39,869,589 |
| **SURPLUS** | **3,799,271** | 3,586,755 |
| | **$ 52,617,799** | $ 55,474,376 |

# STATEMENT OF OPERATIONS AND SURPLUS

*Excerpt from the audited financial statements.*

| Year ended March 31 | Cancer Research Program | External Grants Programs | 2012 | 2011 |
|---|---|---|---|---|
| **REVENUE** | | | | |
| Grants from Ministry of Economic Development and Innovation | **$ 86,444,628** | **$ —** | **$ 86,444,628** | $ 83,433,669 |
| Other grants | **7,431,308** | **8,676,850** | **16,108,158** | 16,147,650 |
| Rent | **1,306,001** | **—** | **1,306,001** | 1,411,867 |
| Gain on sale of leasehold improvements | **45,172** | **—** | **45,172** | 180,689 |
| Fees and workshop | **316,300** | **—** | **316,300** | 339,633 |
| Overhead recovery and other income | **24,021** | **75,561** | **99,582** | 121,740 |
| | **$ 95,567,430** | **$ 8,752,411** | **$ 104,319,841** | $ 101,635,248 |
| **EXPENSES** | | | | |
| Amortization | **$ 7,915,408** | **$ 736,996** | **8,652,404** | 8,871,432 |
| Audit | **72,030** | **—** | **72,030** | 69,170 |
| Contracted services | **919,513** | **900,497** | **1,820,010** | 2,027,096 |
| Grants, Personalized Medicine Research Fund | **5,858,613** | **—** | **5,858,613** | 7,279,498 |
| Grants, Tumour Bank Operations | **712,672** | **—** | **712,672** | 669,627 |
| Honoraria | **209,976** | **—** | **209,976** | 282,608 |
| Information system support | **1,324,022** | **169,736** | **1,493,758** | 1,891,592 |
| Insurance | **94,810** | **—** | **94,810** | 114,415 |
| Investigator and research support, external | **34,266,839** | **2,183,504** | **36,450,343** | 40,595,110 |
| Legal | **375,539** | **45,545** | **421,084** | 226,591 |
| Marketing and communications | **319,708** | **10,141** | **329,849** | 390,366 |
| Maintenance, office and general | **3,123,416** | **35,972** | **3,159,388** | 2,323,154 |
| Rent | **5,289,889** | **—** | **5,289,889** | 4,934,486 |
| Research operations, internal | **10,460,853** | **2,256,531** | **12,717,384** | 10,034,381 |
| Salaries, benefits and recruiting | **23,425,281** | **2,291,262** | **25,716,543** | 20,471,610 |
| Travel | **833,381** | **122,227** | **955,608** | 885,930 |
| Workshops and conferences | **152,964** | **—** | **152,964** | 279,185 |
| | **$ 95,354,914** | **$ 8,752,411** | **$ 104,107,325** | $ 101,346,251 |
| Excess of revenue over expenses | **212,516** | **—** | **212,516** | 288,997 |
| Surplus, beginning of year | **3,586,755** | **—** | **3,586,755** | 3,297,758 |
| **SURPLUS, END OF YEAR** | **$ 3,799,271** | **$ —** | **$ 3,799,271** | $ 3,586,755 |

# STATEMENTS OF CASH FLOWS

*Excerpt from the audited financial statements.*

| Year ended March 31 | 2012 | 2011 |
|---|---|---|
| **OPERATING ACTIVITIES** | | |
| Excess of revenue over expenses | **$ 212,516** | $ 288,997 |
| Add (deduct) items not involving cash | | |
| Amortization | **8,652,404** | 8,871,432 |
| Gain on sale of leasehold improvements | **(45,172)** | (180,689) |
| Increase (decrease) in unearned rental revenue | **(123,436)** | 23,335 |
| Accretion of note receivable | **(5,829)** | (26,994) |
| Decrease in deferred lease incentive | **124,848** | 124,848 |
| | **8,815,331** | 9,100,929 |
| Net change in non-cash balances related to operations | | |
| Receivables | **(1,751,775)** | 248,155 |
| Supplies | **(369,839)** | 166,009 |
| Prepaid expenses | **178,121** | (444,752) |
| Accounts payable and accrued liabilities | **(645,068)** | 955,727 |
| Deferred contributions | **(2,255,417)** | (796,268) |
| **CASH PROVIDED BY OPERATING ACTIVITIES** | **$ 3,971,353** | $ 9,229,800 |
| **INVESTING ACTIVITIES** | | |
| Purchase of property and equipment | **$ (8,156,851)** | $ (12,592,703) |
| Proceeds on disposal of property and equipment | **731,685** | 1,834,180 |
| Proceeds on net disposal of investments | **—** | 5,725,000 |
| **CASH USED IN INVESTING ACTIVITIES** | **(7,425,166)** | (5,033,523) |
| **FINANCING ACTIVITIES** | | |
| Payments made on capital lease obligation | **—** | (5,425) |
| **CASH USED IN FINANCING ACTIVITIES** | **—** | (5,425) |
| **NET (DECREASE) INCREASE IN CASH DURING THE YEAR** | **(3,453,813)** | 4,190,852 |
| Cash, beginning of year | **16,466,759** | 12,275,907 |
| **CASH, END OF YEAR** | **$ 13,012,946** | $ 16,466,759 |

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# BOARD OF DIRECTORS, SCIENTIFIC ADVISORY BOARD AND SENIOR MANAGEMENT

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**For more information about the**
ONTARIO INSTITUTE FOR
CANCER RESEARCH
**please contact:**
–
**RHEA COHEN**
Director of Communications
rhea.cohen@oicr.on.ca
416-673-6642

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Telephone 416-977-7599
Toll-free 1-866-678-6427

info@oicr.on.ca
www.oicr.on.ca


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