

# Ontario Institute for Cancer Research

ANNUAL REPORT 2010/11

# Message from the Minister of Research and Innovation



It is my pleasure to thank the Ontario Institute for Cancer Research (OICR) for the outstanding work it has done over the past year to improve the health and wellbeing of the people of Ontario.

The work you do has a direct impact on the lives of everyone in the province. It offers hope to the nearly 70,000 Ontarians who will be diagnosed with cancer in 2011 and to many millions more around the world. The survival rate for most types of cancer is constantly improving – and your work is helping to make that happen.

OICR is recognized around the world for its leadership in cancer research. The Institute's high profile role – and that of its President and Scientific Director, Dr. Tom Hudson – in the International Cancer Genome Consortium is just one example of that leadership.

This could not happen without your strong commitment, not only to research, but to moving the resulting discoveries quickly from the lab through clinical trials and into the commercial marketplace where doctors around the world can use them to save lives.

Your work also contributes greatly to Ontario's economic prosperity. Over the past year you have helped to commercialize Ontario technologies that promise to advance the field of personalized cancer medicine. The payback for Ontario goes well beyond the obvious health benefits. These investments strengthen our innovation-based economy and create skilled jobs for Ontarians.

On behalf of both the government and people of Ontario, congratulations on your achievements over the past year, and my best wishes for your continued success in the years ahead.

Sincerely, Glen Murray Minister of Research and Innovation

### The Ontario Institute for Cancer Research

THE ONTARIO INSTITUTE FOR CANCER RESEARCH IS AN INNOVATIVE TRANSLATIONAL RESEARCH ORGANIZATION DEDICATED TO RESEARCH ON THE PREVENTION, EARLY DETECTION, DIAGNOSIS AND TREATMENT OF CANCER. IT IS CREATING TANGIBLE HEALTH BENEFITS FOR CANCER PATIENTS WORLDWIDE AS WELL AS ECONOMIC BENEFITS FOR THE PEOPLE OF ONTARIO.

### The Institute:

- Is an independent, not-for-profit corporation;
- Focuses on the translation of ideas into products, services and improved clinical practice;
- With its collaborators and partners has an annual budget of more than \$160 million;
- Is headquartered in the MaRS Centre in the heart of Toronto's Discovery District;
- Along with its collaborators and partners, supports more than 1,400 researchers, clinician scientists, research staff and trainees at MaRS and at Ontario's leading universities and hospital-based research institutes.

The Institute's clinical and translational research activities are strategically chosen to focus on areas of the highest

potential impact on patients. They build on Ontario's existing global strengths – medical imaging, clinical trials, cancer stem cells and bio-therapeutics. OICR has complemented these strengths with world-leading programs and facilities in genomics, bioinformatics and high-throughput screening (see page 5).

In addition to supporting research OICR maintains its translational pipeline through shared infrastructure, resources and world-class expertise along with sufficient funding for these activities. Staff on OICR's commercialization team engages directly with scientists to advance their inventions to clinical application. OICR also actively seeks industry partners and private investors to participate in bringing discoveries to market (see page 9 for a description of OICR's commercialization resources and activities).

## Message from the Chair of the Board of Directors and the President and Scientific Director

THIS HAS BEEN A MILESTONE YEAR. THE INSTITUTE CELEBRATED ITS FIFTH ANNIVERSARY AND LAUNCHED ITS SECOND FIVE-YEAR STRATEGIC PLAN.

OICR was established with a mandate to act as a catalyst, working with cancer research institutions across the province, to undertake a strategic approach in Ontario and to focus on translation, development and commercialization of cancer research findings resulting in health and economic benefits for the province. Through the first five years, the Institute has been a strategic enabler and played a significant role in raising the international profile of Ontario.

OICR has enriched the cancer research community in the province by supporting the recruitment of leading international scientists and the retention of a significant number of bright, accomplished young investigators in Ontario. The Program and Platform leaders are an outstanding team of internationally recognized scientists. Most recently, we have welcomed Dr. John Bartlett, who joined OICR this year as the leader of the Transformative Pathology Platform. He is developing a multi-disciplinary, multi-institutional plan to make Ontario a world leader in molecular pathology of cancer. He was Professor of Molecular Pathology in the Department of Pathology at the University of Edinburgh's School of Molecular and Veterinary Medicine and has played key roles in the design and analysis of multi-centre clinical trials, several of which played pivotal roles in establishing new therapeutic regimens for breast cancer in the U.K. and Europe.

In total, OICR, with its partners and collaborators, now supports 1,400 investigators, clinician-scientists, research staff and trainees located at our headquarters and in research institutes and academia across the province of Ontario, in Hamilton, Kingston, London, Ottawa, Sudbury, Thunder Bay, Toronto and Waterloo. OICR is a new model of translational medicine that sits between academic institutions and receptors of scientific innovation in the private sector.

Through its program and platforms, OICR has effectively established a therapeutic target through to drug pipeline. Its drug development program, staffed with 30 scientists, is unique in Canada outside of pharmaceutical companies. OICR plays an international leadership role in genomics and the Genome Technologies Platform is a critical element of the Institute's translational program. It is a fundamental tool in evolving our understanding of cancer and the basis of personalized medicine in the clinic.

OICR has been instrumental in the support of important national and international collaborations. The International Cancer Genome Consortium, now has 40 projects underway around the world (see page 20) hosted by 13 countries. OICR's informatics team is already disseminating cancer genome data for over 3,000 tumours to researchers around the world using web-based tools.

Through its Commercialization program OICR is supporting the development of promising research applications to ensure that the discoveries of Ontario's cancer researchers move out of the lab and into the clinic. The 15 investments made by the Commercialization program's Intellectual Property Development and Commercialization Fund over a period of three years have resulted in:

- 8 new start-up companies;
- 6 industry co-development deals;
- 6 projects with manufactured prototypes;
- 3 private capital (VC) investments;



#### LEFT TO RIGHT

Dr. Tom Hudson President and Scientific Director

**Dr. Calvin Stiller** Chair, Board of Directors

- 3 technologies licensed or partnered;
- 4 projects with sales revenues;
- 3 projects started first-in-man studies (devices).

A major event this year was the launch of the Ontario Health Study, which will grow over the next decades to be one of the largest population-based health studies ever conducted. Close to 40,000 Ontarians over the age of 18 have already registered with the Study to help researchers investigate the complex interplay of environmental, lifestyle and genetic components that increase the risk of developing cancer and other chronic diseases such as diabetes.

The Ontario Health Study will be supported by the newly created Genetic Epidemiology and Biostatistics Platform, which will develop the tools to analyze data for new knowledge about the causes and progression of cancer and related conditions. It will also assist in the translation of this new knowledge into prevention and health promotion strategies.

The plan for the future is to build on the foundation established and to continue to lead the translation of cancer discoveries into health services and products. The Institute is expanding its network of collaborations with both academia and the private sector, nationally and internationally, and is working with clinical leaders to bring results to the clinic for the benefit of patients worldwide.

We have entered into a period of exciting transformation that is leading to a new model to prevent, detect, diagnose and treat cancer. OICR, in a short time, has taken a lead role in meeting the cancer challenge and with its focus on personalized medicine, which is highlighted in this year's report, is positioned to play a key part in this transformation. As we close the year, we wish to thank Dr. Joseph Pater, who stepped down as a member of the Board of Directors for his wise advice and counsel. We welcome Mr. Allan Rock, Dr. Ben Neel, Dr. Michael Sherar, Ms. Susan Thompson and Dr. David Williams, who joined the Board this past year.

We also wish to thank Drs. Tony Pawson and John Potter, who completed their terms on the Scientific Advisory Board (SAB) for their valuable contribution and welcome Drs. Karen Gelmon and David Mankoff to the SAB.

We gratefully acknowledge the continuing excellent support of the Government of Ontario through the Ministry of Research and Innovation. As champions of research and development in Ontario, they are helping to establish Ontario as a world leader in cancer research and innovation.

Our success would not be possible without the talent, dedication and hard work of the staff of the Institute. Their engagement and commitment to excellence drive the innovation that has made OICR an internationallyrecognized model for cancer research.

The Government of Ontario began this initiative five years ago to stimulate collaborations across the research institutions in the Province, reverse the "brain-drain", accelerate the translation of medical discoveries from theory to practise, and to reduce the suffering and loss of life of patients with cancer. We are proud of the progress that our wonderful staff has made on all these fronts. We hope that you enjoy reading this report about the remarkable advances made.



# Discoveries, translation, and clinical impact

OICR'S RESEARCH STRATEGY BUILDS ON THE STRENGTHS IN THE ONTARIO CANCER RESEARCH COMMUNITY AND ENHANCES ITS CAPABILITY.

Cancer is an old disease, first documented thousands of years ago. It currently strikes approximately 11 million people a year around the world and each year about seven million people die of the disease. The challenge to find the cause and develop preventive measures and effective treatments for cancer is daunting.

OICR was launched by the Government of Ontario in December 2005 to tackle the big questions in cancer research. Since its inception, the Institute has forged multi-disciplinary, multi-institutional teams to tackle the incidence, diagnosis, management, morbidity and mortality of cancer.

The Institute's research strategy builds on the strengths in the Ontario cancer research community and aims at enhancing its capability. OICR created a blueprint (see page 6) for its research activities from 2007-2010, which identified the themes of OICR's research – prevention, early diagnosis, cancer targets and therapeutics – and inaugurated the programs and platforms that would enable OICR to achieve its goals. New platforms in transformative pathology and genetic epidemiology have been launched this year.

In its first five years, OICR focused on creating or enhancing existing infrastructure, recruiting outstanding scientists, and launching new programs and technology platforms to establish the foundation necessary to fulfil its translational research and commercialization missions.

Partnerships and collaboration have played a large role in advancing the Institute's research. They include the California Institute for Regenerative Medicine, the Canadian Partnership Against Cancer, Cancer Care Ontario, GE Healthcare, MaRS Innovation, Pfizer Global and the Terry Fox Research Institute.

The largest international collaboration has been the International Cancer Genome Consortium (ICGC), co-founded by Dr. Tom Hudson, OICR's President and Scientific Director. Launched in 2008, it will sequence the genes of 50 different cancer tumour types. OICR houses the Data Coordination Centre for the Consortium, which links to worldwide data and makes it available in a single secure location, conducts quality assessment, provides data curation services and manages data releases. The projects conducted by Consortium members are expected to produce 25,000 times the amount of data generated by the Human Genome Project. OICR also hosts the ICGC Secretariat, which manages its networking activities.

The High Impact Clinical Trial (HICT) program, a joint program of the Ontario Institute for Cancer Research and Cancer Care Ontario, is designed to support hypothesisdriven translational research in clinical trials and facilitate the evaluation of personalized medicine strategies and interventions. Through integrative, multi-disciplinary Translational Research Teams, the HICT program engages academic clinical trial investigators throughout Ontario to support studies involving experimental therapeutics, bio-specimen-based diagnostics and biomarker evaluations.

Last year, OICR released its second Strategic Plan outlining the Institute's four main objectives for 2010 to 2015. These are:

- 1. Facilitate the adoption of more personalized medicine for cancer.
- 2. Seek solutions to critical issues that could benefit patients in the next five years.
- 3. Enhance and facilitate the digitization and interpretation of cancer data.
- 4. Accelerate OICR's Patents to Products (Commercialization) Program.

OICR's six innovation programs are each structured as a province-wide, often international, collaboration with central leadership by a principal investigator accountable to OICR's President and Scientific Director. The six technology platforms are similarly organized with teams and leaders focused on advancing technology as well as providing the highest quality, cutting-edge infrastructure. One of OICR's greatest strengths is bridging the gap between discoveries and patients. The three translation programs will ensure the movement of promising technologies to practical applications in the clinic and marketplace and realize economic benefits for Ontario.

In formulating OICR's Strategic Plan for 2010-2015, OICR's scientific leaders identified five clinical challenges of high priority for cancer patients, physicians and public health. OICR's goal is to make an impact in these areas in five years.

**1. Pancreatic cancer.** The five-year survival rate for pancreatic cancer is only five per cent. It is usually diagnosed too late when surgery is not possible and it does not respond well to treatment. OICR is leading a large-scale analysis of the genome of pancreatic cancer as a member of the ICGC and is supporting the creation of the new cell lines and mouse xenograft models needed to screen for and test potential new drugs.

2. Prostate cancer. Extensive PSA testing has resulted in over-diagnosis of prostate cancer. Since treatment involves life-altering risks, there is a need for screening and surveillance methods that allow for better characterization of the prognosis and to determine the best treatment strategy. OICR is working with Prostate Cancer Canada and Cancer Research UK to identify biomarkers that can be used to develop better tools. In collaboration with three Ontario institutions, OICR is launching a study to optimize selection of patients for active surveillance by using a new imaging/biopsy approach. **3. Early stage breast cancer.** No reliable method currently exists to identify aggressive breast cancers. Current pathology tools do not provide sufficient information with which to make treatment decisions. OICR is working with breast cancer biologists and imaging probe developers to improve diagnosis. The Institute is also supporting development of improved quantitative pathology to validate new biomarker-based imaging techniques.

4. Population-based screening programs for colon cancer. Colorectal cancer is the second most frequent cause of cancer death in Canada yet most patients can be cured if the tumour is found early. OICR is partnering with Cancer Care Ontario on programs to increase screening rates. The Institute is studying the genetic and environmental causes of the disease and new imaging methods for earlier and more accurate detection.

**5. Long-term adverse effects affecting children and young adults.** While cancer is sometimes thought of as a disease primarily affecting the elderly, 10,000 children and young adults will be diagnosed with the disease this year. There are long-term health consequences for these patients. OICR pharmaco-vigilance research is examining the long-term effects of cancer therapy and the impact of follow-up. •

OICR BLUEPRI	NT		
Themes		Innovation Programs	Technology Platforms
Prevention	•	Ontario Health Study	Genetic Epidemiology
Early Diagnosis	•	One Millimetre Cancer Challenge	Imaging Pipeline Transformative Pathology
Cancer Targets		Cancer Stem Cells	Genome Technologies Medicinal Chemistry
		Cancer Genomics (ICGC)	
		Selective Therapies (Terry Fox Research Institute, Ontario Node)	
		Immuno- and Bio-therapies	
		+	
		Translation Programs	
		High Impact Clinical Trials	
		Health Services Research	
		Patents to Products (Commercialization)	

### **OICR** leaders



Thomas Hudson President and Scientific Director Ontario Institute for Cancer Research



Rima Al-awar Platform Leader Medicinal Chemistry Ontario Institute for Cancer Research



John Dick Program Leader Cancer Stem Cells Ontario Cancer Institute Princess Margaret Hospital University Health Network



Lyle J. Palmer Executive Scientific Director Ontario Health Study; Platform Leader, Genetic Epidemiology Ontario Institute for Cancer Research



Nicole Onetto Deputy Director Ontario Institute for Cancer Research



John Bell Program Leader Immuno- and Bio-therapies Ottawa Hospital Research Institute



Craig Earle Program Leader Health Services Research Cancer Care Ontario Sunnybrook Health Sciences Centre



Robert Rottapel Program Leader, Selective Therapies Terry Fox Research Institute (Ontario Node) University Health Network St. Michael's Hospital



Frank Stonebanks Vice-President, Commercialization and Chief Commercial Officer Ontario Institute for Cancer Research



John Bartlett Platform Leader Transformative Pathology Ontario Institute for Cancer Research



Aaron Fenster Co-Platform Leader, Imaging Pipeline; Co-Program Leader One Millimetre Cancer Challenge Robarts Research Institute University of Western Ontario



Lincoln Stein Platform Leader Informatics and Bio-computing Ontario Institute for Cancer Research



Janet Dancey Program Leader High Impact Clinical Trials Queen's University



John McPherson Platform Leader, Genome Technologies; Program Leader, Cancer Genomics Ontario Institute for

Cancer Research



Martin Yaffe Co-Platform Leader, Imaging Pipeline; Co-Program Leader, One Millimetre Cancer Challenge Sunnybrook Health Sciences Centre



### Patents to products: commercialization

OICR FINDS INDUSTRY PARTNERS AND PRIVATE INVESTORS TO PARTICIPATE IN THE DEVELOPMENT AND COMMERCIALIZATION OF CANCER RESEARCH.

OICR, with its network of outstanding researchers and facilities located at the MaRS Centre and at Ontario's leading universities and hospital-based research institutes, is well positioned to advance the next generation of drugs, therapeutic products and health services for the benefit of cancer patients in Ontario and worldwide.

The Institute actively seeks industry partners and private investors to participate in development and commercialization of cancer research. Its industry-focused commercialization program is staffed by a very experienced team with a mandate to foster an effective and collaborative approach. The team works with both OICR-sponsored research and external Ontario-based scientists and inventors. It is nimble and moves quickly once it identifies intellectual property (IP) suitable for development. It facilitates the management of IP, engages industry in collaborative arrangements and promotes value creation for Ontario.

Four years ago OICR created a targeted investment and commercial development program called the Intellectual Property Development and Commercialization (IPDC) Fund to address the critical need for funding and expertise to enable proof-of-concept activities. The IPDC Fund de-risks and accelerates the advancement of promising cancer innovations by providing meaningful, timely funding and expert commercial and regulatory guidance. To date, the IPDC Fund has supported 15 projects across a wide spectrum of technologies including medical devices, imaging, therapeutics, diagnostics and software. OICR also makes equity investments in selected start-up companies that have successfully matured their technology through the IPDC Fund, including the formation of new start-up companies owned jointly by OICR and its research partners.

In addition, OICR has initiated a novel private-public partnership, cancer-focused accelerator called Triphase. It is an Ontario holding company co-founded by OICR and MaRS Innovation that will in-license cancer-related assets at the Clinical Trial Application – Phase I stage and carry them through to Phase II clinical proof-of-concept. Triphase will provide proof-of-concept funding, start-up company space, industry advisory and other resources to help companies move from late pre-clinical to clinical proof-of-concept in less than three years at a cost of less than \$10 million per product. When clinical proof-of-concept is achieved the technology will be sold, licensed or spun out.

The tax regimes of both the federal and Ontario governments are very generous for investment in R&D and among the best worldwide. They offer substantial tax credits for foreign investors and provisions for easier foreign venture capital investment. The federal government's requirement for tax withholding by non-resident investors in high-tech businesses has been repealed, creating a favourable environment for the investment community.

THE COMMERCIALI	ZATION TEAM IS INVOLVED	AT EVERY STEP OF KNOWLED	GE TRANSLATION
Idea	Т	ranslation	Product
Early engagement with scientists	• IPDC Fund	Triphase Corp. and private financing	Regulatory advice and OICR clinical trials
Basic research	in-licensing	First private investment	<ul> <li>Human trials and proof-of-concept</li> </ul>
Proof of principle	development	• Product development	Regulatory approval



Dr. Scott Tanner President and CEO DVS Sciences

### **DVS Sciences**

When Dr. Scott Tanner and colleagues founded DVS Sciences in 2004, they knew they were facing an immense and very risky challenge. Private capital for life sciences is difficult to secure even for established technologies and the instrument Tanner was developing, while extremely promising, was new and still unproven. He had experience working in industry but navigating the regulatory and financing side of the business requires a great deal of money and expertise.

DVS Sciences was one of OICR's earliest commercialization ventures. It first benefited through funds that OICR's predecessor organization, the Ontario Cancer Research Network (OCRN), provided to Tanner's group at the University of Toronto, which leveraged substantial development funds from other sources. At a later critical stage, OICR's Cancer Stem Cells Program purchased the first commercial prototype of the instrument from DVS. This sale enabled the company to gain complementary funding to bring the technology to market entry. OICR then provided direct funding and business development mentoring through the IPDC Fund.

"OICR's IPDC Fund investment effectively bridged the 'valley of death' – that period of transition between invention and the market," said Tanner, who is now President and CEO of DVS. "And without that initial support from OCRN, the development of the technology is unlikely to have happened."

This year the company opened its global R&D and manufacturing centre in Markham, Ontario with 14,000 square feet of space designed to enable the production of 100 instruments per year. It has additional room to support research and engineering development. The company currently has 23 employees and plans to expand to 35 by the end of 2011. Six of the instruments, which cost more than a half million dollars each, have been sold to buyers in Canada, Japan, Taiwan and the U.S., and the company is opening an additional 11,000 square foot facility in Sunnyvale, California that will house global sales and marketing.

### **TORCell Therapeutics**

TORCell Therapeutics was formed last year around a technology developed at the University Health Network's (UHN) Princess Margaret Hospital by Dr. Li Zhang. The technology could provide a new form of treatment for acute myeloid leukemia, a disease that currently has very few treatment options. OICR first became involved in the company through a \$500,000, two-year investment from the IPDC Fund that was used to assist in advancing the technology and proof-of-concept.

"At the end of that initial funding period, we felt that the technology had sufficient promise that we should try to further develop it toward commercialization," says Frank Gleeson, an Executive-in-Residence in OICR's Commercialization Program. "This represents an area where OICR is really trailblazing because we're dealing with a technology that is profoundly important but, because of the type of research, raising private capital is particularly challenging."

OICR partnered with UHN and Zhang to form TORCell. OICR then provided seed funding to the company to enable it to assess the likelihood of whether the treatment, which involves using a sub-population of the patient's own cancer-killing T cells to treat the disease, could be approved for clinical development. OICR's Commercialization team spent several months providing regulatory and drug development expertise for a successful presentation of the technology to Health Canada. When the clinical development plan was found to be viable, OICR made a follow-on investment to prepare the preclinical package in anticipation of a first-in-man Phase I clinical trial in 2012.

"We're recognizing that point on the translational spectrum where there's a need that cannot be filled by the existing infrastructure and capital markets," Gleeson says. "OICR is unique in having the understanding of what is required, bringing the expertise to the table in a collaborative spirit and having some of the capital necessary to build a bridge to the private sector investment markets."

He points out that a willingness to work together with other funders is also crucial. In the case of Xagenic Inc., another company formed last year with assistance from OICR, an even larger funding partnership was established. Based on technology developed by Drs. Shana Kelley and Ted Sargent at the University of Toronto, it was a broader partnership between OICR, MaRS Innovation, the Health Technology Exchange and the Ontario Centre of Excellence Centre for Commercialization of Research. Combined, these partners were able to offer \$1.04 million in capital for the new startup. The money will be used to develop a new, chip-based molecular diagnostic technology that has the potential to detect many conditions, from bacterial infections to genetic disease and cancer.

"It is important to point out that to support these companies to the next stage does not always require a huge amount of money," Gleeson says. "It's the right amount at the right time, used efficiently on the right tasks. Timing and clear priorities are the keys. This can make a tremendous difference in the future of these companies. Working with them in the areas outside of their expertise, namely the financing and business-building aspects of translating research to the marketplace, has paid huge dividends and has been an area where we're collectively making a significant contribution."

Gleeson sees TORCell as a model of company formation that OICR can use to help develop other successful collaborative investments. OICR took a similar approach in the founding of DLVR Therapeutics, also in partnership with UHN, and in financing Harmonic Medical, a spin-off from Sunnybrook Health Sciences Centre. They are both new Ontario-based startups developed over the past year. OICR is flexible, offering different investment options to ensure that any investment it makes is tailored to best suit the technology involved.

"In every one of these examples the principles are the same but the details are quite different," says Gleeson. "Essentially, our challenge is to single out those special technologies that might have profound impact from all the other technologies that are simply interesting. Many technologies are compelling, but some are more commercially relevant and have more potential. These are the ones that we try to identify and advance."

Tanner, meanwhile, is optimistic that his partnership with OICR can be used as a model for OICR to develop and commercialize other promising technologies around the province.

"A successful partnership involves not just the funding but also the business mentoring that builds confidence. It is by no means an easy path, and requires incredible commitment from both parties. But with the right team in place and the right drive, I believe that it can be replicated – and hope that it will be, over and over." •



LEFT TO RIGHT

Dr. Li Zhang Founder and Principal Scientific Advisor TORCell Therapeutics

Mr. Frank Gleeson Executive-in-Residence Ontario Institute for Cancer Research



### Personalized medicine

CANCER IS A COMPLEX DISEASE THAT DIFFERS EVEN AMONG PATIENTS WITH THE SAME TYPE OF TUMOUR. IMPROVING PATIENT OUTCOMES AND REDUCING THE BURDEN OF DISEASE ON SOCIETY REQUIRES AN UNDERSTANDING THAT TREATMENT SHOULD BE GUIDED NOT ONLY BY CLINICAL SYMPTOMS BUT BY KNOWLEDGE OF MOLECULAR, GENETIC AND FUNCTIONAL ALTERATIONS SPECIFIC TO THE PATIENT.

Predictive genomic tests will identify those patients who will respond to a particular treatment. This will avoid unnecessary treatment and be more cost-effective for the health care system.

Advances in imaging, genomics, bioinformatics and nanotechnology are providing the knowledge and tools necessary to develop the next generation of personalized cancer interventions. OICR's translational and clinical research activities have been strategically chosen to focus on areas of the highest potential impact. Over the last year, work has been done to implement genomic tools in a clinical setting, develop targeted drugs, train bioinformatics specialists, enhance imaging technologies, identify the genetic mutations in different types of cancer, and on how new knowledge can be used to change clinical practice.

# Evaluating pharmacogenetic tests



Pharmacogenetic tests are important new tools in personalized medicine. They have shown great potential in assisting clinicians in estimating the prognosis of cancer for individual patients and determining if certain treatments will work. They are evaluated in clinical trials to determine whether they should be implemented on a large scale.

"Genetic tests enable physicians to choose the most effective treatment for each patient. They can also prevent the administration of therapies that would be of no use, thereby avoiding treatment without clinical benefit and the side effects of the therapy. Genetic testing offers rational utilization of resources in the health care system," explains OICR's Deputy Director, Dr. Nicole Onetto. "The big question facing Ontario and many other jurisdictions right now, is how and when to administer these tests."

In Ontario, new health care technologies and pharmaceuticals are evaluated by the Medical Advisory Secretariat (MAS), a branch of the Ministry of Health and Long-Term Care (MOHLTC). The use of pharmacogenetic tests in the province currently is often inconsistent and is supported by a variety of funding mechanisms, from pharmaceutical companies to government.

OICR was approached for help in early 2010. The Provincial Expert Panel on Pharmacogenetics (PEPP) was struck and chaired by Onetto. The panel's 12 experts include medical oncologists, pathologists, geneticists, pharmacoeconomists, health-policy experts and other medical specialists. OICR's Director of Genome Technologies, Dr. John McPherson, participated as an expert on genomic technologies. Work began in April to evaluate three tests including Oncotype Dx, which guides the treatment of breast cancer, the most common cancer among Canadian women. "The incidence of breast cancer in Ontario makes it crucial to have access to new technologies as soon as possible by evaluating their benefits and establishing best practices for their use," says Onetto.

Chemotherapy can be an effective form of treatment for early stage breast cancer. Oncologists estimate the risk of

reoccurrence to determine if the benefit gained outweighs the potential side effects. Many women are still receiving chemotherapy for early stage breast cancer when they may not need it.

Oncotype Dx is the only test commercially available to determine response to chemotherapy for breast cancer. Testing is performed only in the U.S. and the US\$3,000 cost is covered by MOHLTC's "out of province" funding program.

PEPP conducted a thorough review of all available clinical evidence regarding the test's clinical utility and economic impact. The review focused on use in newlydiagnosed early stage estrogen-receptor positive or progesterone receptor positive breast cancer. This represents over half of all breast cancer cases in Ontario.

The findings of the PEPP and the MAS were presented to the Ontario Health Technology Advisory Committee, the provincial body responsible for making recommendations to the MOHLTC on the adoption of new health care technologies. Response to PEPP's recommendations was positive and has resulted in planning for a field study involving 1,000 patients to test the impact of Oncotype Dx in the reality of clinical practice in Ontario.

"The work that the Panel performed in its review of Oncotype Dx was an important step," says Onetto. "Driving the adoption of personalized medicine in a clinical setting in Ontario will help more patients. We have shown that OICR's expertise can facilitate the implementation of new health care technologies." •



Dr. Nicole Onetto Deputy Director Ontario Institute for Cancer Research

### High Impact Clinical Trials



CLINICAL TRIALS WILL CHANGE HOW CANCER IS PREVENTED, DIAGNOSED, TREATED AND MONITORED.

Ontario has one of the most advanced networks of clinical trial organizations in the world. OICR, in partnership with Cancer Care Ontario (CCO) created the High Impact Clinical Trials (HICT) program, which is leveraging this to support clinical trials that will change how cancer is prevented, diagnosed, treated and monitored. Working with OICR's Genome Technologies Platform, the University Health Network's (UHN) Princess Margaret Hospital (PMH) and UHN, OICR/CCO launched the Genomics Pathway Strategy (GPS), to answer translational research questions that will have practical implications for the future of personalized medicine.

"The GPS is OICR's major personalized medicine initiative," says HICT program leader Dr. Janet Dancey. It determines how to incorporate sequencing technologies into clinical practise by identifying markers of response to therapy or risk of toxicity. Patient specimens are genetically profiled and the program develops tools so that clinicians can use the information for patient care. The lead principal investigator is Dr. Lillian Siu, of UHN and the co-principal investigators are Dr. Suzanne Kamel-Reid of UHN, Drs. Dancey, John McPherson, and Lincoln Stein, of OICR, Dr. Fiona Miller of the University of Toronto and investigators in Hamilton, London, Ottawa and Thunder Bay.

One GPS project used next generation technology to identify potential genetic abnormalities and confirm their presence using standard technologies in PMH/UHN's molecular diagnostics laboratory. This involved cross validating the Pacific Biosciences platform, a third generation machine that allows for rapid and cost-effective sequencing of tumour samples at OICR, and the Sequenom platform at UHN. They are used for genetic analysis and for comparing 30 samples of fresh frozen and paraffin-embedded tissues. It confirmed both platforms would produce similar enough results and that both sample types would be of sufficient quality for the larger study. The next step is a feasibility study.

Dancey explains that this study "will 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 describing the mutations, their clinical significance and potential clinical trial availability, to the clinician and patient in less than three weeks."

After the feasibility study, the large validation study, the Cancer Genomics Assessment Trial (CGAT) will start clinical trials. Data from CGAT will be used to determine whether genetic stratification based on genetic markers within and between histologies leads to better patient outcomes. "In the validation study we are trying to prove that personalized medicine works," says Dancey. "If we can identify a patient's mutation and provide comprehensive, actionable information to clinicians for treatment, we will succeed in improving health care and patient outcomes."

Dancey hopes that the validation study will boost participation in clinical trials in Ontario. Initial proposals for these trials focus on advanced, previously treated breast, colon, lung and ovarian cancer. The goal is to recruit 800 patients with OICR's industry partners.

The GPS aligns with two of OICR's strategic priorities – the adoption of personalized medicine and the improvement of the digitization and interpretation of cancer data. Dancey notes that the GPS will be on the leading edge of the second strategic priority because "the marriage of –omic, imaging and clinical data will have to occur in the context of these clinical trials."



Dr. Janet Dancey Program Leader High Impact Clinical Trials Queen's University

# Drug discovery



OICR'S MEDICINAL CHEMISTRY PLATFORM IS FILLING THE GAP BETWEEN INDUSTRY AND ACADEMIA.

Many scientists worldwide are engaged in drug discovery, but OICR's Medicinal Chemistry Platform has a unique approach. "Often the research is done either in industry or academia. Both have their advantages, but OICR has captured the best of both worlds," explains Dr. Rima Al-awar, director of the Platform and senior principle investigator. Having a group with drug discovery expertise, working in an academic setting, fills a critical translational gap in the Ontario scientific community.

Al-awar likens the Platform to a miniature version of the drug discovery groups found in large pharmaceutical companies, but adds that the Platform's interface with academia and the OICR-Terry Fox Research Institute (TFRI) Selective Therapies Program (STP), led by Dr. Robert Rottapel, of the University Health Network and St. Michael's Hospital, gives it a distinctive approach. "Our people have immense knowledge of the drug discovery process and combined with the expertise available from the academic community, we are extremely productive," says Al-awar.

Since it is much smaller than an industry group, the Platform must be more selective about its projects. This is where the flexibility afforded by its unique model comes into play. "Between our group and academic labs there is more openness. We look for natural alignments in our collaborations and principle investigators who have a desire to pursue new therapies. There is a lot of excitement in academia about working with an experienced team like ours," says Al-awar.

One collaboration illustrates how the Platform has effectively linked the interests of multiple research groups in the STP. Al-awar's team began collaborating with a team at Mount Sinai Hospital, led by Drs. Frank Sicheri and Dan Durocher on a project to study a biological pathway known as the unfolded protein response. This pathway is thought to be critical in the development and maintenance of many types of tumours. Because it has been shown that a protein known as IRE-1 plays a key role in driving this pathway, Al-awar and her team are working closely with them to identify small molecules that selectively block the protein's function. With these molecules in hand, they are working with Dr. Brad Wouters at the University Health Network's Princess Margaret Hospital, to understand how the drugs can be used to treat tumours.

Another member of the STP, Dr. David Stojdl at Ottawa's Children's Hospital of Eastern Ontario, independently developed an interest in the same protein. Stojdl researches oncolytic viruses that target and kill cancer cells. Because this approach may show limited efficacy against some tumours, he looked for new biological targets that would enhance the activity of the viruses. Stojdl's team applied a systematic screening method that revealed that knocking down the IRE-1 protein was particularly effective.

Stojdl turned to the Medicinal Chemistry Platform for confirmation. Through its collaboration with the Mount Sinai team, the Platform was able to provide small molecule inhibitors for IRE-1 that enhanced the activity of the oncolytic virus in several experiments. Stojdl validated the importance of the IRE-1 target to fully harness the oncolytic viruses to treat cancer because of the Platform's ability to deliver sufficient quantities of a potent compound.

"Our success shows that OICR's model is working and that we are making significant progress towards new cancer treatments," says Rottapel.

Al-awar agrees, "These two examples clearly demonstrate how our team effectively collaborates with scientists in our community to positively impact the identification of new cancer targets."



Dr. Rima Al-awar Platform Leader Medicinal Chemistry Ontario Institute for Cancer Research

### Canadian Bioinformatics Workshops

BIOINFORMATICS WORKSHOPS ARE TRAINING RESEARCHERS TO VISUALIZE, ANALYZE AND EXTRACT VALUABLE INFORMATION FROM COMPLEX DATASETS.

Continuous improvements in genomic sequencing and other high-throughput technologies have resulted in a dramatic increase in the rate at which data is produced. With new cancer research technologies producing larger and more complex datasets, an increasing amount of expertise in bioinformatics is required by Canadian researchers. This demand has resulted in a need for bioinformatics training programs.

The Canadian Bioinformatics Workshops (CBW) organized by Dr. Michelle Brazas, OICR's Manager, Research and Knowledge Exchange, are bridging the knowledge gap by providing training opportunities in specialized bioinformatics topics.

The CBW is a series of two-day training sessions designed to equip researchers with the knowledge and skills required to visualize, analyze and extract valuable information from complex datasets. "Today, highthroughput technologies are generating staggering amounts of data," says Brazas, "Scientists must be skilled and have the computational skills to sift through and integrate massive datasets, and make discoveries from their research projects."

Since 2008, Brazas has been involved with the development and implementation of advanced bioinformatics education programs for the CBW series. Now hosted by OICR, the CBW has been operating since 1999 under the direction of Francis Ouellette, OICR's Associate Director, Informatics and Bio-computing and Principal Investigator, with ongoing support from the Canadian Institutes of Health Research and Genome Canada. Since their inception, the workshops have trained more than 1,500 participants at the undergraduate, graduate and professional levels in cities across Canada.

A steady rise in the number of applicants has resulted in an increase in the number of workshops offered by the CBW from four to nine per year between 2008 and 2011. Brazas is committed to keeping registration costs at a minimum to ensure that workshops remain accessible to everyone. Recognizing that bioinformatics skill development is needed to advance research, the CBW offers award opportunities to eligible participants.

"Currently, the CBW series can only meet the demands of 30 participants per workshop," says Brazas, "However all of the materials presented in the workshops are free and accessible online to the public." The content online (www.bioinformatics.ca) extends bioinformatics training opportunities to the larger research community.

Brazas anticipates that the CBW series will continue to offer more specialized workshops in the future. "For example, cancer research projects have been early adopters of sophisticated research technologies that generate enormous amounts of data that require computational skills to evaluate," she says. "This year, we are offering a focused five-day cancer genomics workshop to provide researchers with the tools and approaches to visualize and interrogate their cancer specific datasets."

The CBW series also trains researchers in communities outside Canada. Brazas has made three trips to Nigeria to provide bioinformatics training opportunities to Nigerian researchers. With minimal infrastructure requirements, Nigerian researchers can also engage in bioinformatics based research.

"The training program in Nigeria focuses on empowering researchers with the tools to analyze research collected from their own community," says Brazas. "By empowering researchers with computational skills and exposing them to various bioinformatic tools, they can accelerate the research efforts within their own countries." •



Dr. Michelle Brazas Manager, Research and Knowledge Exchange Ontario Institute for Cancer Research



### Imaging technologies

CUTTING-EDGE IMAGING TECHNOLOGIES ARE BEING DEVELOPED TO AID IN THE EARLY DETECTION OF CANCER AND THE DELIVERY OF TREATMENT.

These technologies not only locate tumours but can also help assess the biochemical changes in tumour cells, enabling physicians to identify abnormal organs and tissues and select the most appropriate form of treatment.

Dr. John Valliant, CEO and Scientific Director, leads the Centre for Probe Development and Commercialization (CPDC) in Hamilton, which develops and supplies radiopharmaceuticals - tools used for imaging cancer patients. OICR is funding the development of the next generation of molecular imaging probes by CPDC. Probes are chemical compounds that are used to non-invasively visualize cancer at its earliest stage, identify patients that are best suited for a particular treatment and help monitor the response to treatment. Tagged with a short-lived, radioactive isotope and injected into the patient, probes seek out and bind to specific markers at the site of the disease. When viewed by imaging equipment such as positron emission tomography (PET) or single photon emission computed tomography (SPECT) cameras, the accumulation of molecular probes at the tumour clearly distinguishes it from healthy cells while providing information on the biochemical makeup of the cancer. This information is critical in properly managing cancer patients.

CPDC is one of the province's largest distributors of <sup>18</sup>F-Fludeoxyglucose (<sup>18</sup>F-FDG), the most widely used molecular imaging probe for PET scans. The Centre manufactures <sup>18</sup>F-FDG under the trade name Glucovision<sup>®</sup> and reliably delivers it daily for important, often life-saving, imaging procedures throughout Ontario.

Valliant's team at CPDC uses the Glucovision program to support the development of the next generation of probes to aid in the early diagnosis of cancer, accelerate and support drug discovery and the development of new treatments.

"Emerging probes will be used to detect tumours earlier than is currently possible and to visualize cancers that are highly aggressive," says Valliant. "The next generation of agents will be used to help guide the best choice of therapy



"Emerging probes will be used to detect tumours earlier than is currently possible and to visualize cancers that are highly aggressive. The next generation of agents will be used to help guide the best choice of therapy for the individual patient and to aid in biopsy and surgical resection of tumours."



Dr. John Valliant CEO and Scientific Director Centre for Probe Development and Commercialization

for the individual patient and to aid in biopsy and surgical resection of tumours."

CPDC is working to expand the offering of molecular probes in Ontario through its own development pipeline and by manufacturing probes that are successfully used in other parts of the world. Clinical trials are an important part of this process and CPDC is actively involved in several such initiatives through OICR, Cancer Care Ontario, the Ontario Clinical Oncology Group, and leading institutions in Hamilton, London, Toronto and Thunder Bay.

The Centre is currently supplying <sup>18</sup>F-Fluorothymidine (<sup>18</sup>F-FLT) a probe used to determine the rate of cell division within a tumour. <sup>18</sup>F-FLT PET is designed as a non-invasive tool to indicate the presence and location of a tumour and reveal whether or not a tumour has stopped growing in response to treatment. Unlike a biopsy, these real-time images are of the whole tumour (or tumours) not small tissue samples. The images provide physicians with critical information on the effectiveness of the chosen therapy over the course of the treatment. <sup>18</sup>F-FLT is being evaluated in a clinical trial for its ability to detect response to chemotherapy in breast cancer patients. The OICR-funded trial is a collaborative effort initiated by Dr. Mark Levine, a medical oncologist at the Juravinski Cancer Centre, Dr. Karen Gulenchyn, Chief of Nuclear Medicine at Hamilton Health Sciences and St. Joseph's Healthcare Hamilton, and Valliant.

CPDC has also started to manufacture <sup>18</sup>F-Fluoroazomycin Arabinoside (<sup>18</sup>F-FAZA), a probe designed to identify hypoxic tumours. When tumours grow, certain types can rapidly outgrow their blood supply, leaving parts of the tumour deprived of oxygen. Hypoxic tumours are more resistant to chemo- and radiation therapy. <sup>18</sup>F-FAZA PET could be an effective probe to detect hypoxic tumours and help physicians prescribe the most effective treatment for the patient. CPDC is supplying <sup>18</sup>F-FAZA for use in a trial of patients with cervical cancer, conducted by Dr. Michael Milosevic of the University Health Network's Princess Margaret Hospital.

Valliant also played a key role in bringing OICR, GE Healthcare and Hamilton Health Sciences together to evaluate a new technology that could help identify breast cancer in high-risk patients that are not well served by mammography.

"Mammography is the current screening method for breast cancer but it has limitations identifying tumours in women with dense breast tissue," says Valliant. "When breast tissue is dense, which is often the case in younger women, small tumours can be hidden from view in mammography images."

The team is one of only a handful of sites in the world evaluating new molecular breast imaging (MBI) technology against conventional mammography. In conjunction with the trials, CPDC is working on the next generation of breast cancer imaging probes for the MBI technology and for positron emission mammography devices. Levine and Gulenchyn are currently leading two clinical trials to determine the utility of this technology. MBI has already been approved for use in clinics and hospitals in the U.S.

"Our goal for the next generation of probes is to provide information that can help physicians guide the choice of therapy and evaluate its effectiveness within a short period after the treatment starts," says Valliant. "This is a critical goal because new therapies are extremely expensive and are designed to work on very specific types of cancer. Imaging probes that help guide therapy would be a tremendous step forward because treatments, which are increasingly costly, Current screening methods involve two-dimensional devices that are unreliable. More than 30 per cent of men may have prostate cancer but the biopsy is negative."



Dr. Aaron Fenster Director and Scientist Imaging Research Laboratories Robarts Research Institute

could be prescribed with more certainty and, most importantly, lead to better outcomes for patients."

About 116 kilometres away in London, Dr. Aaron Fenster, Director and Scientist, Imaging Research Laboratories, Robarts Research Institute, co-leader of OICR's Imaging Pipeline Platform and co-leader of its One Millimetre Cancer Challenge Program, develops sophisticated technologies that use image guidance to accurately and non-invasively locate cancer and cardiovascular disease. "These technologies could save time, money and more lives," says Fenster.

Fenster has developed a minimally-invasive technology that uses three-dimensional (3D) ultrasound to precisely guide biopsy needles into selected targets in the prostate. This will help quickly diagnose and determine tumour aggressiveness in the individual patient.

"Prostate cancer screening can cause a significant amount of anxiety in the patient," says Fenster. "Current screening methods involve two-dimensional devices that are unreliable. More than 30 per cent of men may have prostate cancer but the biopsy is negative."

Fenster is currently focused on building technologies that can guide treatment more accurately and effectively to the tumour at its earliest stage in development. Small tumours are easier to destroy and less likely to spread. "Needles can be engineered to deliver targeted energy to the tumour site. The energy heats up and kills cancer cells," he says. "I am using this concept to design new technologies that can destroy rapidly progressing tumours in the liver."

The development of new and innovative imaging technologies will ultimately benefit cancer patients. "New imaging technologies have the potential to revolutionize health care," says Fenster. "Improvements in imaging technology coupled with advancements in cancer therapeutics are producing better outcomes for patients." •

## International Cancer Genome Consortium

ICGC IS GENERATING COMPREHENSIVE CATALOGUES OF GENOMIC ABNORMALITIES IN TUMOURS.

The International Cancer Genome Consortium (ICGC) launched in 2008 with a goal of sequencing the genomes of 50 different tumour types and making the data freely available to researchers around the world. Eventually this data will be used to help personalize treatment for cancer patients.

There are currently 40 different international ICGC projects with research underway in 13 jurisdictions, including Asia, Australia, Europe and North America.

When the ICGC was launched, it was expected such clinical application would be years, if not decades, away. The first clinical application could now appear much sooner. In February 2011, OICR and Prostate Cancer Canada launched the Canadian Prostate Cancer Genome Network (CPC-GENE), a unique, \$20 million ICGC project that will decode the prostate cancer genome while attempting to translate the results into clinical application, all within five years. The project will find better ways to personalize treatments for individual prostate cancer patients and to reduce the overtreatment of the disease. Up to \$15 million in funding will be provided by Prostate Cancer Canada and \$5 million by OICR.

Overtreatment is a significant problem because the side effects are serious and long-term. If doctors could better distinguish harmful and non-harmful forms of prostate cancer at the time of first diagnosis, many unnecessary treatments could be avoided.

"Men don't just need a diagnosis, they need to know what type of prostate cancer they have," says Dr. Robert Bristow, leader of the CPC-GENE project and Senior Scientist at the Ontario Cancer Institute, the research arm of the University Health Network's Princess Margaret Hospital. "Every patient wants to be treated as an individual, which means we must be able to recognize the cancer is unique, and we have to provide specific information and offer customized treatments. Unfortunately we can't always do that today." The CPC-GENE project differs from other ICGC projects because it uses an existing biobank of samples collected at the project's inception. The project can sequence these samples and, because they were collected over the last decade, link these genomic analyses to existing data on patient outcomes. This has given the project a five to 10 year head start on other ICGC projects.

"About a decade ago there was a proactive choice among prostate cancer researchers in Canada to collaborate rather than compete," says Bristow. "We created a unique resource in Canada that was already using the ICGC approach of whole genome sequencing to impact clinical care. We saved years of work because we already had this collaborative network in place."

CPC-GENE researchers hope to use this head start to begin finding genetic markers that may allow them to better predict how the cancer will develop. It could also help doctors better target chemotherapy in patients whose cancer may have spread, and could allow doctors to treat certain forms of cancer more aggressively with fewer side effects. Overall it would give doctors more certainty when providing a diagnosis and give many patients more peace of mind that they were choosing the right treatment option from the beginning.

"Every week patients come into the clinic asking, 'what is the best treatment for me?" Dr. Bristow says. "We know what the answer is on average if a hundred patients come through the door. But what doctors need is an individual answer to make a plan and choose an appropriate option based on the patient's genetics. As a doctor, I can't give that to them today. But I have full confidence that within five to 10 years I will be able to."

The project brings together researchers from different fields and institutions across Canada, including scientists in Vancouver, Calgary, Toronto, Kingston and Montreal. A key element of the project is that they share in a common vision.

"The project works well because each team has its own



specialty, and each team brings something unique that can't be done elsewhere," says Dr. Michael Fraser, of the University Health Network, Project Manager for CPC-GENE. "I think everyone respects everyone else's area of interest and what they are bringing to the project. And ultimately, there is a very strong commitment and shared sense of responsibility between all the project members just to do good science."

Bioinformatics plays a central role in keeping CPC-GENE research coordinated and on target. OICR's Informatics and Bio-computing team coordinates patient information from the clinical teams with genomic analyses from OICR and the University of British Columbia. Dr. Paul Boutros, a Principal Investigator at OICR and member of CPC-GENE, says CPC-GENE's unique characteristics make it more interesting from a research perspective, but also more complicated.

"The CPC-GENE project is significantly different from the other ICGC projects because of the translational focus," says Boutros. "All the ICGC projects share common challenges related to the analysis of next-generation genome sequencing data, but CPC-GENE also faces critical questions related to the application of genomic techniques to clinical questions. Our mandate is to coordinate the world-class clinical and genomic datasets and integrate them into clinical tools that can ultimately benefit patients."

In addition, CPC-GENE scientists are working in close collaboration with researchers on other ICGC prostate projects. The U.K. team is interested in the heterogeneity of the cancer, the French team is comparing the outcomes of patients from France and the French Caribbean after they have completed surgery and the team in Germany is looking at cancers in men under age 55 and whether these cancers are different than those that appear more frequently in older men.

Bristow sees all this research, together, leading to a fundamental change in how doctors and their patients talk about cancer. "What we will be giving patients is more information. Information is power, not only for the clinician, but also for the patient and his family. That will allow them to make clearer decisions about their health. This will be language that makes it onto the Internet and into the newspapers. It will be a newer type of discussion than we are having today, and I am quite confident that's going to happen."



### Ontario Health Study



Thanks to the Ontario Health Study (OHS), every adult in Ontario aged 18 or older has the opportunity to make an impact in the fight against a range of chronic illnesses like cancer, diabetes, Alzheimer's and heart disease. The OHS was launched in September 2010 following a pilot phase.

The Study will use information provided by participants to understand how factors such as environment, lifestyle, behaviour and genetics interact to cause common diseases. The findings will be used to help improve the prevention and treatment of common diseases by informing research and health policy.

More than 40,000 Ontarians have already registered online to participate. It is anticipated that several hundred thousand will join the Study in the next few years. Since the OHS is expected to continue for 20 years or more, the aim is for the number of participants to grow to more than two million. To pursue this goal, the OHS has used traditional means, such as promoting the Study on public transit and radio, reaching out to the staff and students of health care organizations, chronic disease groups and universities, and attending community events.

The Study is also one of the few large population-based cohort studies in the world to be making use of social media. Canada is one of the most "online" nations in the world, with 70 per cent of Canadians using social media. The Study's use of Facebook, Twitter and YouTube has allowed its message about volunteering to reach Ontarians across today's complex media landscape.

"In terms of participation, we needed to cast a wide net to ensure that we have enough participants to conduct the Study and that participants reflect the ethnic, geographic and culture diversity of Ontario," says Dr. Lyle Palmer, Senior Principle Investigator and Executive Scientific Director of the OHS.

The Internet also plays a central role in how the Study gathers information from participants. The OHS is the first large-scale cohort study in the world to collect baseline and



follow-up data through online questionnaires. In addition to baseline and yearly follow-up questionnaires, optional surveys will be employed to collect data on a wide range of topics, including personal and family health history, socio-demographic information, personal exposures to tobacco, alcohol and medications, residential and occupational histories, diet, physical activity and sedentary behaviour. Additional information will be obtained from a sample of volunteers through physical measures and biospecimen collection conducted at assessment centres. The intent of the Study is to follow participants for their entire lifespan.

"Having such a wide-ranging and comprehensive set of data allows us to look at the big picture of chronic disease in terms of both individual and community health. In terms of cancer specifically, scientists will be able to use the Study to increase our understanding of what causes cancer and how it can be detected earlier or prevented," says Palmer. "We will also be able to better understand chronic disease rate variation across Ontario."

The Ontario Health Study is a long-term research study initially funded by four organizations: OICR, Cancer Care Ontario, the Ontario Agency for Health Protection and Promotion, and the Canadian Partnership Against Cancer. The OHS is also part of the Canadian Partnership for Tomorrow Project, which is made up of five regional health studies across Canada.

The Study has earned the endorsement of many research institutes, hospitals and other health-related organizations.



**Dr. Lyle J. Palmer** Executive Scientific Director Ontario Health Study; Platform Leader, Genetic Epidemiology Ontario Institute for Cancer Research

### Changing clinical practice

COMMONLY DIAGNOSED CANCERS HAVE BEEN PROFILED IN DEPTH, GIVING SCIENTISTS HUGE QUANTITIES OF INFORMATION ABOUT THEIR CAUSES, DEVELOPMENT AND POTENTIAL TREATMENTS.

But other forms of cancer remain less understood – posing challenges for clinicians trying to properly diagnose and treat their patients.

Researchers studying oropharyngeal cancers (cancers of the back of the throat, including the back of the tongue and the tonsils) face a unique situation. It has become more common in the past five years and is increasing. Once associated with heavy drinking and smoking, it is now appearing in men in their mid-40s to mid-50s, about a decade younger than usually expected, and in patients who are otherwise in good health.

The observation was made in the U.S. several years ago that the human papilloma virus (HPV) may perhaps play a role in these changes. U.S. researchers began testing for the disease in patients with oropharyngeal cancers, and found that up to 70 per cent tested positive for HPV.

Funded in part by OICR in 2008, Dr. Fei-Fei Liu at the University Health Network's Princess Margaret Hospital (PMH) began to study whether this was true in Canada.

"I had initially guessed that our numbers would be less or even half of the numbers," says Liu. "But the surprising thing was that between 60 to 65 per cent of oropharyngeal cancer patients seen between 2003 and 2006 harboured the virus in their cancers. Today, that number has increased to about 70 per cent."

HPV positive forms of oropharyngeal cancers have a much better outcome than those that are HPV negative. Patients with tonsillar cancers who are HPV positive have a three-year survival rate of 90 per cent. That compares to a three-year survival of about 60-65 per cent in HPV negative patients. Somewhat counter-intuitive, it is therefore good news to have the cancer test positive for HPV.

This observation has already begun to change clinical practice. At PMH, physicians now administer simple, inexpensive HPV tests to find out if patients' oropharyngeal cancers have the HPV virus.

Using this information to improve treatment for patients

is the next step in Liu's research. The two curative treatment options for patients with oropharyngeal cancers today are surgery or radiation. Surgery can be debilitating, which means that most patients undergo both radiation therapy and chemotherapy, and endure all their side effects.

"The question now is whether we could dial back treatment for these patients to give them radiation only. We think these patients will do well but we are not 100 per cent certain. Most patients are young and healthy and they want maximal treatment to survive."

"The three-year survival is only 90 per cent for these patients. We can't identify the characteristics of the 10 per cent of 'bad' HPV positive cancers," Liu says "so we cannot risk dialing back treatment."

Currently Liu and her research team are working to better define how patients will respond to treatment to create more personalized patient profiles. Working with researchers at the Ontario Cancer Institute, the research arm of PMH, and with funds from OICR, they are using proteomic analyses on HPV positive and negative cancers to catalogue the differences in terms of protein signatures.

"With patients, you have to be 100 per cent certain that you're doing the right thing before you can really make a treatment switch with complete confidence. These protein signatures, once identified, could give us that confidence."

In the meantime Liu is hopeful that more hospitals in Ontario and across Canada will begin administering the HPV test to provide patients with a more personalized view of their cancer, and to provide more hope for those patients whose tumours test positive for HPV.



Dr. Fei-Fei Liu Head Division of Applied Molecular Oncology Ontario Cancer Institute







### 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.\*

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### **OICR Grant Supported Projects**

FUNDI	ED PROJECTS		
Round	Date	Projects funded	Funds awarded (In millions of dollars)
1	May 2002	15	\$6.9
2	November 2002	19	\$8.7
3	May 2003	9	\$4.1
4	November 2003	14	\$7.4
5	May 2004	12	\$7.0
6	May 2005	2	\$8.4
7	November 2005	11	\$5.4
8	May 2006	6	\$0.8
9	November 2006	15	\$7.1
10	May 2007	6	\$0.8
11	November 2007	17	\$8.2
12	November 2008	13	\$6.4
13	November 2009	11	\$6.0
14	November 2010	11	\$5.6
		161	\$82.8

### PROJECT TYPES 2002-2011

Tra Project Type cou	nslational grant mpetitions	Cancer Research Program	Ontario Tumour Bank	Clinical Trials Infrastruct- ure Fund	Intellectual Property Development and Commer- cialization Program
Clinical trials	28	22	-	-	-
Companion studie	es 19	-	-	-	-
Translational	113	191	-	-	-
Equipment	-	118	-	-	-
Other	1	-	5	24	15

### CANCER TYPES AND NUMBER OF PROJECTS 2002-2011

Cancer Type	Research conducted by grant recipients	Cancer Research Program	Ontario Tumour Bank	Clinical Trials Infrastruct- ure Fund	Intellectual Property Development and Commer- cialization Program
Brain	13	-	-	-	
Breast	37	1	-	-	1
Colorectal	10	1	-	-	1
Head and neck	10	-	-	-	-
Haematological	29	-	-	-	3
Lung	20	-	-	-	-
Multiple cancers	13	325	5	24	5
Melanoma	8	-	-	-	-
Other	18	-	-	-	2
Ovarian	9	-	-	-	1
Pancreatic	8	2	-	-	-
Prostate	22	2	-	-	2

### PUBLICATIONS IN JOURNALS 2010-2011

Program	Journal impact factor range	Number in range
Strategic programs	0-10	191
	11-20	32
	21-30	13
	31-60	15
	NA**	64
Grant supported programs	0-10	50
	11-20	4
	21-30	3
	31-60	1
	NA**	18

\*\* NA = unrated journals

\* Some results are cumulative since 2002 and report activities started prior to 2005 by OICR's predecessor, the Ontario Cancer Research Network.

### HIGHLY QUALIFIED PERSONNEL WORKING ON FUNDED PROJECTS 2010-2011



### COMMUNICATIONS ARISING FROM FUNDED PROJECTS 2010–2011



- 93 Poster presentations in Canada
- 86 Poster presentations outside Canada

### COMMERCIAL ACTIVITY 2010-2011

Commercial activity generated by funded projects	Cancer Research Fund	Cancer Research Program	Intellectual Property Development and Commercialization Program
Disclosures	1	9	2
Patent applications	7	13	10
Patents awarded	3	4	4
Licences granted	3	2	13
Spinoff companies	1	-	3

### SOURCE OF OICR PROJECT FUNDS 2010-2011 In millions of dollars



\* Includes \$11.6 million from industry partners.

\*\* Includes \$2.3 million from industry partners.

### Intellectual Property Development and Commercialization Program (IPDCP)

INVESTMENTS AND FUNDING FOR IPDCP	2010-2011
Investments under co-management by OICR	10
OICD funding in 2010 2011	¢1 7 million
Older funding in 2010-2011	φ1.7 minion
	A =
and provincial sources	\$5.7 million
Private sector leveraged funding	\$10.0 million

### CANCER TYPES AND NUMBER OF INVESTMENTS 2007-2011



### MILESTONES AND NUMBER OF INVESTMENTS 2007-2011

### 12 6 5 4 3 3 3 4 Companies selling product 3 First-in-man studies commenced 3 Spinoff companies created 12 Private sector partnerships 5 Technology licensed or partnered 6 Prototypes manufactured with private sector 3 Private equity investments

### INVESTMENT IMPACT SECTOR AND NUMBER OF INVESTMENTS 2007-2011





### OICR young investigator Dr. Fernando Suarez

SUAREZ IS USING THE LATEST TECHNOLOGY, INCLUDING HIGH-THROUGHPUT SCREENING AND NEXT GENERATION SEQUENCING, TO MAP THE GENES OF OVARIAN CANCER.

As a child growing up in Mexico, Dr. Fernando Suarez was always interested in science, but the exact field of study remained elusive. First, it was biological sciences. Later he became extremely interested in astronomy, which is where his passion for science was born. "I was no longer just interested in it, I needed to know more and more and more," he says.

But it was the medical sciences that ultimately appealed to him mainly because of the human interaction. After completing an internship as part of his MD, he felt there was something missing, especially in cancer. "I was treating patients during my internship and I wished I could offer them more," he says.

That was when Suarez moved to Toronto to begin graduate studies at the University Health Network's Princess Margaret Hospital. He later joined the lab of Dr. Robert Rottapel as a postdoctoral fellow in OICR's Selective Therapies Program.

Today, his team is using the latest technology, including high-throughput screening and next generation sequencing, to map the genes of ovarian cancer so researchers can develop new therapies to treat it.

The team analyzes cell lines and generates a map of the genes that cell line is sensitive to. This allows them to see what happens if they turn off that gene using RNAi. "What we're learning is that even though they have things in common, each cell line will have its own set of genes, which is different to every other cell's. That gives us insights into molecular pathways, saying that cell line A, B and C are sensitive to manipulation of one pathway, but not the others."

This information would potentially allow researchers to define groups of patients that are sensitive to manipulation of that pathway but not to others. Researchers in the Selective Therapies Program are collaborating with OICR's Medicinal Chemistry Platform so that when a target is identified it can be evaluated for development into a treatment.

"Instead of referring to ovarian cancer patients as a whole, we will one day be able to refer to different types of ovarian cancer. We are doing this already, but we could have personalized medicine. Each patient would be screened for a set of markers and given a treatment or combination of treatments based on the characteristics of their disease."

"Instead of referring to ovarian cancer patients as a whole, we will one day be able to refer to different types of ovarian cancer. We are doing this already, but we could have personalized medicine. Each patient would be screened for a set of markers and given a treatment or combination of treatments based on the characteristics of their disease."

That is still many years away, but now, Suarez's major task is to help bring together the very different – and not always easily comparable – data from the different technologies in use in their lab. This requires developing new analytical tools to make sense of all the very different datasets produced.

"Your career doesn't take you exactly where you wanted to go at the beginning, but it takes you exactly where you need to be." •



### OICR young investigator Dr. Lorraine Lipscombe

LIPSCOMBE HOPES THE APPLICATION OF PERSONALIZED MEDICINE WILL HELP PATIENTS WITH BOTH BREAST CANCER AND DIABETES.

Dr. Lorraine Lipscombe works as a research scientist at the Women's College Research Institute (WCRI) in Toronto as part of the Women's Cancer Survivorship Team. Her path to this position began when she was an undergraduate student studying psychology at Concordia University in Montreal, where she became interested in the role of reproductive hormones. After completing medical school at McGill University, Lipscombe completed two residencies, one in internal medicine and another in endocrinology.

"If we can tailor treatments to take into account a patient's diabetes we may be able to improve their prognosis."

In 2002, Lipscombe was introduced to the work of oncologist Dr. Pamela Goodwin, of the Samuel Lunenfeld Research Institute of Mount Sinai Hospital, who was studying the impact of insulin in women with breast cancer. She became very interested in the link between diabetes and breast cancer and is pursuing research into the subject. "My main research question is why do women with diabetes fare worse when diagnosed with breast cancer than those women who do not have diabetes?" says Lipscombe. Her research into this area will be funded by OICR through its Health Services Research Program.

Lipscombe hopes that the application of personalized medicine will help patients with both breast cancer and diabetes, "if we can tailor treatments to take into account a patient's diabetes we may be able to improve their prognosis," she says.



According to Lipscombe, women with diabetes may need different treatments for breast cancer due to the effects of diabetes on their hormones. She also hypothesizes that diabetes on its own could be behind the poor outcomes for women with both diseases. "Looking at what we know so far, I believe that both breast cancer and diabetes treatments may need to be modified to provide the best outcome," says Lipscombe. Another challenge facing women with diabetes is that they often experience more side effects during treatment for breast cancer than other women.

Lipscombe is also examining if women with diabetes are screened for breast cancer less often because the focus of their health is on controlling their existing condition. "If we can ensure that women with diabetes are being screened as often as other women we could diagnose breast cancer in its earlier stages, which would result in a better prognosis," says Lipscombe.

Looking at cancer in a broader sense, Lipscombe acknowledges that the treatment of cancer has advanced significantly, particularly in breast, prostate and thyroid cancers, and now "we must turn to the issue of long-term survivorship and the consequences of diagnosis experienced by patients." Lipscombe will be looking into this issue as part of a team led by Dr. Paula Rochon at WCRI conducting a breast cancer survivorship study that is funded by OICR.

The importance of health services research such as Lipscombe's is on the rise and she is thrilled to be conducting such research in Ontario. "Ontario is a highprofile and internationally respected jurisdiction in health services research. We have good access to data and great researchers to mentor new students in the field." •

### OICR young investigator Dr. Hsien Seow



SEOW CONDUCTS RESEARCH INTO THE DELIVERY OF CARE FOR SERIOUS CHRONIC DISEASES.

Majoring in biology at Yale University, Dr. Hsien Seow always had an interest in science, but experiencing cancer illness within his family is what solidified his career path in health services research, particularly palliative care. "I started asking questions about how people accessed health care, the needs of the dying, and how the organization of the health care system affected outcomes. Most importantly, I began to inquire about how the system could be improved," says Seow. Now he conducts research into the delivery of care for serious chronic diseases as a member of the department of oncology at McMaster University, where he is funded through the Cancer Care Ontario/OICR Health Services Research Program.

Seow says that although major advancements have been made in the treatment and diagnosis of chronic diseases such as cancer, the system for delivering health care is still organized for treating acute conditions. "In order to solve this problem, we need to examine the bigger picture of health care from the system level. We need to align financial incentives for providers to 'do the right thing' for the patient, within models of care that support multidisciplinary, team-based approaches to care that follow the patient across settings and providers," says Seow. Some of his interests include home and community care, particularly the impact of increasing access to homecare services, as well as evaluating innovative models to deliver care so that care is coordinated, integrated, and meets the needs of the sickest patients.

A recently conducted study showed that providing more homecare nursing hours to end-of-life cancer patients could reduce their likelihood of dying in hospital and using emergency department and hospital services at end-of-life. These results have major quality and costs implications within the health care system. Seow has set out to verify these findings using more stringent criteria and by expanding the study beyond Ontario to include Alberta, British Columbia and Nova Scotia. "What I hope to find is that the findings of the initial study are indeed true; that we can provide better care to patients with cancer and save money within the health care system through a marginal increase in the amount of homecare nursing," says Seow.

One of the main uses of health services research is to use science to inform the process of policy-making, something Seow says Ontario has a strong reputation for. "After I finished my PhD at Johns Hopkins School of Public Health in the U.S., I returned to Ontario because there is a stronger linkage and dialogue between science and policy," he says.

"What I hope to find is that the findings of the initial study are indeed true; that we can provide better care to patients with cancer and save money within the health care system through a marginal increase in the amount of homecare nursing."

According to Seow, Ontario's strong research infrastructure was another good reason to come home. "The Health Services Research Program is a great example of this infrastructure. It has brought attention to this field of research and has the people and the resources to study the entire continuum of cancer care. We are able to collaborate with an amazing group of cancer scientists, access incredibly rich data sources, and involve policy-makers in the research process. These factors together give us the potential to build the best cancer health care system in the world." •

### Independent Auditors' Report

To the Members of the Ontario Institute for Cancer Research

### Report on the financial statements

We have audited the accompanying financial statements of Ontario Institute for Cancer Research, which comprise the statement of financial position as at March 31, 2011, and the statements of operations and surplus, and cash flows for the year then ended, and a summary of significant accounting policies and other explanatory information.

### Management's responsibility for the financial statements

Management is responsible for the preparation and fair presentation of these financial statements in accordance with Canadian Generally Accepted Accounting Principles, and for such internal control as management determines is necessary to enable the preparation of financial statements that are free from material misstatement, whether due to fraud or error.

### Auditors' responsibility

Our responsibility is to express an opinion on these financial statements based on our audit. We conducted our audit in accordance with Canadian Generally Accepted Auditing Standards. Those standards require that we comply with ethical requirements and plan and perform the audit to obtain reasonable assurance about whether the financial statements are free from material misstatement.

An audit involves performing procedures to obtain audit evidence about the amounts and disclosures in the financial statements. The procedures selected depend on the auditors' judgment, including the assessment of the risks of material misstatement of the financial statements, whether due to fraud or error. In making those risk assessments, the auditors consider internal control relevant to the entity's preparation and fair presentation of the financial statements in order to design audit procedures that are appropriate in the circumstances, but not for the purpose of expressing an opinion on the effectiveness of the entity's internal control. An audit also includes evaluating the appropriateness of accounting policies used and the reasonableness of accounting estimates made by management, as well as evaluating the overall presentation of the financial statements.

We believe that the audit evidence we have obtained is sufficient and appropriate to provide a basis for our audit opinion.

### Opinion

In our opinion, the financial statements present fairly, in all material respects, the financial position of Ontario Institute for Cancer Research as at March 31, 2011, and its results of operations and cash flows for the year then ended in accordance with Canadian Generally Accepted Accounting Principles.

### Report on other legal and regulatory requirements

As required by the Canada Corporations Act, we report that, in our opinion, Canadian Generally Accepted Accounting Principles have been applied on a basis consistent with that of the preceding year.

Crost + young LIP

Chartered Accountants Licensed Public Accountants

Toronto, Canada June 22, 2011

### Statement of Financial Position

Excerpt from the audited financial statements.

At March 31	2011	2010
ASSETS		
Current		
Cash	\$ 16,466,759	\$ 12,275,907
Investments	4,275,000	10,000,000
Receivables	2,821,970	3,070,125
Supplies	359,906	525,915
Prepaid expenses	1,941,932	2,120,874
Current portion of deferred lease incentive	124,848	124,848
Total current assets	 25,990,415	28,117,669
Long-term portion of prepaid expenses	1,268,223	644,529
Deferred lease incentive	447,374	572,222
Property and equipment, net	27,289,697	25,400,320
Equipment under capital lease	—	2,286
Note receivable	478,667	451,673
	\$ 55,474,376	\$ 55,188,699

### LIABILITIES AND DEFERRED CONTRIBUTIONS

### LIABILITIES

Current		
Accounts payable and accrued liabilities	\$ 11,345,169	\$ 10,389,442
Current portion of unearned rental revenue	127,691	102,627
Current portion of deferred gain	45,172	180,689
Obligation under capital lease	—	5,425
Term loan	500,000	500,000
Total current liabilities	12,018,032	11,178,183
Unearned rental revenue	—	1,729
Deferred gain		45,172
Total liabilities	12,018,032	11,225,084
Deferred contributions	39,869,589	40,665,857
		0.007.750
Surplus	 3,586,755	3,297,758
	\$ 55,474,376	\$ 55,188,699

## Statement of Operations and Surplus

Excerpt from the audited financial statements.

Year ended March 31	Cancer Research Program	Ontario Cancer Research Network	External grants	2011	2010
REVENUE					
Grants from Ministry of					
Research and Innovation	\$ 72,734,999	\$ 10,698,670	\$ —	\$ 83,433,669	\$ 79,630,048
Other grants	8,492,157	_	7,592,692	16,084,849	8,214,595
Rent	1,411,867	_	_	1,411,867	1,258,619
Gain on sale of leasehold improvements	180,689	_	_	180,689	180,689
Fees and workshop	50,459	288,997	_	339,456	557,757
Overhead recovery and other income	121,740	—	—	121,740	53,749
	82,991,911	10,987,667	7,592,692	101,572,270	89,895,457
EXPENSES					
Amortization	8,594,275	_	277,157	8,871,432	6,600,592
Audit	69,170	_	_	69,170	67,650
Capital	26,052	_	_	26,052	31,680
Contracted services	719,498	229,143	1,078,455	2,027,096	1,570,447
Grants, Cancer Research Fund	_	7,279,498	_	7,279,498	8,707,905
Grants, Tumour Bank Operations	_	669,627	_	669,627	886,037
Honoraria	203,133	79,475	_	282,608	194,836
Information system support	1,071,617	669,576	150,399	1,891,592	1,518,121
Insurance	114,415	_	_	114,415	91,444
Investigator and research support,					
external	37,586,046	_	3,009,064	40,595,110	37,590,104
Legal	223,262	3,329	_	226,591	114,552
Marketing and communications	355,576	31,677	3,113	390,366	261,474
Maintenance, office and general	2,130,356	153,212	13,534	2,297,102	1,739,301
Rent	4,884,986	49,500	_	4,934,486	4,234,151
Research operations, internal	8,868,406	_	1,165,975	10,034,381	8,337,472
Salaries, benefits and recruiting	17,249,953	1,353,011	1,805,668	20,408,632	16,334,352
Travel	664,831	131,772	83,001	879,604	770,666
Workshops and conferences	230,335	48,850	6,326	285,511	335,892
	82,991,911	10,698,670	7,592,692	101,283,273	89,386,676
Excess of revenue over expenses	_	288,997	_	288,997	508,781
Surplus, beginning of year	—	3,297,758	—	3,297,758	2,788,977
Surplus, end of year	\$ —	\$ 3,586,755	\$ —	\$ 3,586,755	\$ 3,297,758

### Statement of Cash Flows

Excerpt from the audited financial statements.

Year ended March 31	2011	2010
OPERATING ACTIVITIES		
Excess of revenue over expenses	\$ 288,997	\$ 508,781
Add (deduct) items not involving cash		
Amortization	8,871,432	6,600,592
Gain on sale of leasehold improvements	(180,689)	(180,689)
Increase (decrease) in unearned rental revenue	23,335	(20,756)
Accretion of note receivable	(26,994)	(25,566)
Decrease in deferred lease incentive	124,848	124,849
	9,100,929	7,007,211
Net change in non-cash balances related to operations		
Receivables	248,155	(1,088,218)
Supplies	166,009	73,927
Prepaid expenses	(444,752)	(942,129)
Accounts payable and accrued liabilities	955,727	1,799,392
Deferred contributions	(796,268)	3,763,189
Cash provided by operating activities	9,229,800	10,613,372
INVESTING ACTIVITIES		
Purchase of property and equipment	(12,592,703)	(7,835,702)
Proceeds on disposal of property and equipment	1,834,180	-
Proceeds on net disposal of investments	5,725,000	-
Cash used in investing activities	(5,033,523)	(7,835,702)
FINANCING ACTIVITIES		
Payments made on capital lease obligation	(5,425)	(13,544)
Cash used in financing activities	(5,425)	(13,544)
Net increase in cash during the year	4,190,852	2,764,126
Cash, beginning of year	12,275,907	9,511,781

\$

16,466,759

Cash, end of year

\$

12,275,907

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Rhea Cohen **Director of Communications** rhea.cohen@oicr.on.ca 416-673-6642









1,291 lbs. greenhouse gases prevented

5,820 gallons wastewater flow saved

N

369 lbs. solid waste not generated

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