Meeting the cancer challenge

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Message from the Minister of Research and Innovation

On behalf of the Government of Ontario and Ontarians everywhere, I’m pleased to thank the staff of the Ontario Institute for Cancer Research (OICR) for another successful year.

So many of us have been touched by cancer, either personally or through loved ones or friends. Your hard work and dedication brings hope to us all.

You are conducting world-class research and turning new discoveries into better prevention, more effective therapies, new technologies and better patient care.

Your accomplishments have helped make OICR a world leader in the field of cancer research. In the process, you have helped build an exceptional community of innovation and research excellence here in Ontario.

As a beacon for biomedical research you are attracting some of the world’s best scientists, both Canadians who were working abroad and scientists from around the globe.

Finally, the rapid progress you are making serves as a model of how research collaboration can result in new strengths and new opportunities to overcome disease – while helping to improve the quality of life of Ontarians through the economic opportunities that research and innovation provide.

Once again, thank you for your important work, and best wishes for your continued success.

Sincerely,

John Milloy
Minister of Research and Innovation

Science •••• Discoveries •••• Solutions

The Ontario Institute for Cancer Research is a new innovative research institute dedicated to research in the prevention, detection, early diagnosis and treatment of cancer. Its goal is to reduce the incidence, morbidity and mortality of cancer. OICR is taking on significant challenges in cancer research with multi-disciplinary, multi-institutional teams. It is strengthening Ontario’s cancer research capacity and contributing to the development of the next generation of cancer researchers.

A focus on commercialization ensures that the novel diagnostic and therapeutic discoveries resulting from its innovation programs and platforms advance towards the market, with Ontario enterprises being the primary receptors.

OICR is a not-for-profit corporation funded by the Government of Ontario through the Ministry of Research and Innovation. For more information, please visit the website at www.oicr.on.ca.
W e are pleased to present the annual report of the Ontario Institute for Cancer Research for 2008–2009. Cancer statistics underline the importance of our research. In 2009, more than 65,000 people will be diagnosed with cancer in Ontario and there will be more than 27,000 deaths. OICR’s mandate is to conduct cancer research and to innovate – to create new products or services that solve an unmet need.

Since its inception in December 2005, OICR has focused on research programs to generate new knowledge. Our research strategy, announced in early 2007 focuses on research in prevention, early detection, diagnosis and treatment of cancer. Just as important is moving discoveries from the laboratory into the clinic where patients can benefit from the research.

In the past year, OICR-funded researchers have made great strides in moving toward commercial development of their discoveries. You will read in the pages of this report about a technology to improve the diagnosis and treatment of prostate cancer, the development of a diagnostic tool and a new treatment, a new treatment for blood cancers and a new technology to identify cancer biomarkers.

The Institute has continued its rapid growth. We now occupy 55,000 sq. ft. of space in the MaRS Centre in Toronto’s Discovery District, which includes 35,000 sq. ft. of laboratory space. We have sublet part of the space to the Structural Genomics Consortium (SGC), an international consortium devoted to characterizing the three-dimensional structure of proteins that are likely to be useful in medical research, especially the development of new drugs to treat cancer. The similarity of OICR and SGC’s mandates and values means we can share some large equipment and there is great potential for a synergy created by proximity.

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OICR has recruited many talented researchers from all over the world. We are halfway to our goal of recruiting 50 principal investigators and have almost completed the recruitment of OICR program and platform leaders. In the latter group, five are Canadian scientists who had been working in the U.S. for many years before joining OICR.

We established a medicinal chemistry platform and in the past year recruited a platform leader, equipped a lab with state-of-the-art instruments, staffed the lab and have embarked on a research program to identify potential clinical candidates.

Ontario Premier Dalton McGuinty announced the formation of the International Cancer Genome Consortium (ICGC) at a news conference in April 2008. OICR will house the ICGC’s Data Coordination Centre and host the Secretariat. The participating research institutes around the world will sequence 500 samples each of the 50 most common types of cancer. This is one of the most ambitious biomedical research projects since the completion of the Human Genome Project and the Hap Map Project. Eight projects are already underway and OICR has begun work on sequencing pancreatic cancer.

We extend our special thanks to John Evans, who stepped down as Chair of the Board of Directors in January. He was the first Chair and continues to serve as a member of the Board of Directors. His leadership and sage advice were instrumental in the creation and direction of the Institute.

We also thank Jack Kitts and Terrence Sullivan, who served as members of the Board of Directors, for their guidance.

We are most grateful for the continuing strong support of the Government of Ontario. Both the Premier and the Minister of Research and Innovation are champions of research and development in Ontario, helping to establish the province as a world leader in cancer research and innovation. We congratulate Premier McGuinty on receiving the BIO 2009 Annual International Leadership Award, which provides international recognition for his impressive vision and his success in initiating that vision.

The extraordinary rapid progress we have made in the last three years is a reflection of the skills and dedication of every member of the OICR staff. Their talent, energy and commitment ensure our success. – OICR
Patents to products: Moving innovation out of the lab and into the clinic

OICR is not only innovative in the laboratory but it is also innovative in getting new discoveries out of the laboratory and into the clinic. A key element of OICR’s Strategic Research Plan is the Commercialization Group whose mandate is to foster an effective and collaborative approach to the commercialization of cancer-related innovations arising from any research, including OICR-sponsored research, in Ontario.

Thinking about commercialization starts long before the discoveries are made. When scientists apply to OICR for research grants, consideration of possible commercial applications must be an integral part of the proposal.

Scientists receive more from OICR than just funding – they get help at every step of the processes required to translate research into products or services that have commercial value. The Intellectual Property Development and Commercialization Program (IPDCP) awards funds for early stage applied research and development of inventions arising out of early discovery research. It is intended to help make the transition from academic funding to industry investment. It has created a new model of commercialization founded on collaborative working relationships among institutions, investigators, commercial partners and investors.

The Commercialization Group focuses just on cancer so it has an expertise that is not often found in many other organizations. The program provides co-management of the investments. In addition to regular meetings with the scientists, the Program has an executive-in-residence who provides strategic advice based on hands-on experience. The IPDCP reduces risk and makes the invention business ready, guiding the project through prototype testing, clinical development, manufacturing, regulatory and clinical trials, market development and growth, reimbursement approvals, and regulatory and market approvals.

Time-elapsed MRI thermometry images of a revolutionary ultrasound treatment for localized prostate cancer developed by Profound Medical Inc. OICR invested in this technology, invented by Drs. Michael Bronskill and Rajiv Chopra at Sunnybrook Health Sciences Centre, through its Intellectual Property Development and Commercialization Program.
Improving the diagnosis and treatment of prostate cancer

After years of prototypes and tests, Dr. Aaron Fenster this year saw one of his major research projects leave the lab and head into the clinical trials. Fenster, the Director of the Imaging Research Laboratories at the Robarts Research Institute in London, Ontario and Co-Director of OICR’s Imaging Pipeline Platform (IPP), has begun clinical trials using a platform of 3D ultrasound technologies to improve diagnosis and treatment of prostate cancer. OICR funded the development of these technologies through initial seed funding awarded to the IPP in 2006 and last year awarded Fenster’s lab $500,000 through the IPDCP to help accelerate the commercial development of the technology.

A biopsy is considered necessary for most doctors to make a definite diagnosis of prostate cancer, yet some prostate cancers are notoriously difficult for doctors to detect with confidence. Even when other indicators show that cancer is present, biopsies can repeatedly come back negative. If doctors can’t get an accurate sample, even after multiple biopsies some patients can remain without a conclusive diagnosis.

Fenster has developed a tool specifically for patients with suspected prostate cancer who have had negative biopsies. Fenster’s system combines magnetic resonance imaging (MRI) and 3D ultrasound technology that his lab developed so that doctors can directly biopsy to regions of the prostate identified as suspicious in an MRI, thus increasing the chances that a biopsy is taken from the suspected tumour and not from the healthy tissue that surrounds it.

Patients undergoing Fenster’s biopsy procedure first have their prostate imaged using high resolution MR technology. The MR image allows doctors to identify suspicious regions on the prostate before the biopsy begins. During the biopsy, doctors fuse the MR image and a real time 3D ultrasound image of the procedure together. The combined image shows doctors where the suspicious areas are while they are performing the biopsy procedure, helping them to take samples only from these areas and greatly increasing the chances of an accurate diagnosis.

“Cancer, especially early forms, currently can’t be seen with ultrasound imaging during the biopsy,” Fenster says. “Radiologists are often doing the biopsy without really knowing where the cancer is. The MR will tell us where it is so then we can use 3D ultrasound to guide the biopsy needle to a target identified using MR.”

Fenster with his collaborators at the University Health Network’s Princess Margaret Hospital is also testing the technology developed in his laboratory for use in a therapeutic approach for prostate focal therapy based on the MR/3D ultrasound fusion technology. The therapeutic approach uses a technique called laser ablation to burn a small cancerous region of the prostate, avoiding the need to remove the whole organ. This would allow doctors to instead treat a small region on the prostate and then monitor the patient. Focal therapy is a new approach to treating prostate cancer, especially early stage prostate cancer that hasn’t had a chance to grow or spread.

“It is essential that the doctor knows exactly where the cancer is when performing focal therapy surgery. If you are going to be burning a region, you’d better be sure it is cancer. So by integrating our system and our guidance device and 3D imaging, a doctor is able to put a needle right in the cancer and burn it away, without all the side effects of major surgery and without the risks of harming healthy tissue.”

As Co-Director of OICR’s IPP, Fenster is able to oversee the development of not just his own technologies, but also help to get other therapies into the clinic. The IPP currently funds research at four different Ontario sites: the University of Western Ontario, The Centre for Probe Development and Commercialization at McMaster University, Sunnybrook Health Sciences Centre and the University Health Network. In addition to Fenster’s work, the IPP currently funds projects based on probe translation, led by Dr. John Valliant, pathology led by Dr. Martin Yaffe, who is also Co-Director of the IPP and imaging trials led by Dr. Glenn Bauman. The IPP is using $10 million in funding from OICR to accelerate the development of new imaging tools for screening, early diagnosis of cancer, cancer therapy research and clinical trials.

“I think it is important to focus on funding at all stages of research,” Fenster says. “We can always get funding to focus on an interesting idea, but our objective with the IPP is to be able to see the path from an interesting idea all the way to commercialization and clinical translation.”

Fenster continues down that path himself with his own projects. He plans to begin clinical tests on another new technology that uses 3D ultrasound to make brachytherapy more precise. Brachytherapy involves placing small, radioactive “seeds” directly onto the prostate. By using 3D ultrasound, doctors will be able to place these seeds more precisely and help ensure better outcomes for patients.

He is also currently testing his technologies for use on breast cancer and plans to next adapt them for use in treating liver cancer.

“We, as researchers, have to do our part to give back,” Fenster says. “We are being funded with public money, so we have a responsibility to improve health care, to improve the effectiveness of therapy, and to generate economic activity in Ontario through innovation and commercialization.” – OICR
Dr. Jorge Filmus, a Senior Scientist at Sunnybrook Health Sciences Centre, has spent much of his career devoted to studying glypican-3, a protein involved in the growth of hepatocellular carcinoma (HCC), the most common form of liver cancer. Filmus is currently using glypican-3 as a diagnostic tool and as a therapeutic target in HCC.

HCC is one of the most common types of cancer in the world, yet treatment and diagnostic options for the disease remain inadequate. As a result, although there are about 600,000 cases of the disease diagnosed each year, most are diagnosed too late for treatment and the average life expectancy for patients with metastatic HCC is only six months.

In 2005, OICR awarded Filmus' lab a $297,600 grant through the Cancer Research Fund to assist in the development of a glypican-3 based therapeutic. But while working in this project, Filmus generated new antibodies against glypican-3 that are now being used to develop a blood test to detect HCC at an earlier and hopefully curable stage. In 2009 OICR's IPDCP provided $280,000 in funding to help perfect this diagnostic tool for clinical use.

“OICR is filling a vacuum ...by offering researchers support for their research even if it heads in an unexpected direction.”

Glypican-3 stimulates the growth of HCC by binding to the cell membrane. Filmus proposed that this growth could be slowed down or stopped by instead producing a mutant form of glypican-3 (soluble glypican-3) that could not attach to the surface of the cell.

“When we tried to do is block the push that this protein gives to cancer cells to grow faster,” he says. “The OICR grant really allowed us to try different approaches to see which method blocks the activity of glypican-3 best.”

When Filmus generated new glypican-3 antibodies during his studies, he soon realized that these antibodies could be used to generate a better test to detect HCC. Glypican-3 is expressed by most HCCs, but not by normal liver cells or benign lesions. This makes it extremely useful for doctors trying to diagnose the disease, allowing them to find and treat it earlier.

Currently, most doctors use the alpha-fetoprotein (AFP) blood test or ultrasound to find HCC. “Neither are very good at detecting small lesions, which are the ones that we want to detect,” Filmus says. The earlier the disease is detected, the more chance a patient has to survive.

This new method for detection of HCC will allow doctors to monitor patients at high risk of liver cancer by administering a simple blood test twice a year. The vast majority of people who develop HCC have chronic hepatitis B or C, which gives doctors a large, established target population for screening. Currently about 300 million people worldwide live with chronic hepatitis. The test could be administered almost anywhere routine lab facilities exist.

He has already produced one version of the test, currently being used in clinics worldwide, using glypican-3 to establish if tumour biopsies from the liver contain cancerous cells. Unfortunately the test often finds HCC too late for effective treatment, which is why Filmus is focusing his research on the optimization of the blood test.

Meanwhile, Filmus continues his work on the therapeutic approach for HCC that targets glypican-3. He says that while it is still very much in its early stages, initial results from in vivo experiments with mice have been quite positive. “We remain optimistic and we know we’re headed in the right direction,” he says. – OICR
Dr. Aaron Schimmer

Developing a new treatment for blood cancers

Dr. Aaron Schimmer, staff physician at the University Health Network’s Princess Margaret Hospital and researcher at the Ontario Cancer Institute, the research arm of the Hospital, is using an innovative, multi-pronged strategy to discover new cancer treatments and rapidly introduce them to the clinic.

It typically takes 10 years or more to develop a new cancer treatment. Many projects are abandoned before the compound is developed into a drug, often because of concerns over toxicity or the stability and solubility of the compound.

When Schimmer proposed to investigate new treatments for myeloma and leukemia several years ago, he looked for a strategy that would avoid some of these obstacles. He decided to screen off-patent drugs – which have already been tested and approved for use in humans for conditions other than cancer and are readily available to researchers – to see if they might have unknown cancer-fighting properties.

Schimmer was trying to find compounds that could be re-purposed as proteasome inhibitors. (The proteasome is like a disposal system for unneeded and mis-folded proteins in cells.) Inhibiting the proteasome can induce death of tumour cells, making this a promising area of cancer research.

OICR’s Cancer Research Fund supported high-throughput screening of thousands of drugs in Schimmer’s lab. Several compounds were found to kill cancer cells, but most were ruled out as useful cancer treatments for other reasons. Xinliang Mao, a research associate in Schimmer’s laboratory, proposed to do more work on a compound called Clioquinol. “It wasn’t the strongest candidate from our screen, but Dr. Mao was interested and it looked like there could be some potential,” Schimmer says.

Clioquinol is a known proteasome inhibitor, but until Schimmer’s study, scientists believed it could only inhibit the proteasome when combined with copper. Unexpectedly they also found that Clioquinol inhibits the proteasome directly and is quite active in leukemia and myeloma.

“Proteasome inhibitors are currently used to treat certain cancer patients, but Clioquinol acts differently than all other known proteasome inhibitors. This finding is significant because patients who do not respond to currently available proteasome inhibitors might respond to this new drug that acts through an alternative mechanism,” Schimmer explains.

However, the team ran into an obstacle when they tried to fully understand the copper-independent mechanism, since Clioquinol was not water-soluble enough to do detailed mechanistic studies. To solve this problem, Tabitha Wood, a postdoctoral fellow with a PhD in synthetic chemistry, identified a series of chemical derivatives of Clioquinol that were sufficiently water soluble for mechanistic studies and also more potent.

Schimmer’s group now has two avenues for getting a new proteasome inhibitor to the clinic: it could repurpose Clioquinol as a cancer treatment, or could develop the Clioquinol derivatives into new drugs. Schimmer is pursuing these options simultaneously.

Repurposing Clioquinol as a cancer treatment would be quicker than developing a new drug, but it would still require further study of optimum doses for cancer patients. Clioquinol was an effective anti-infection drug, but neuro-toxic side effects were reported in some Japanese patients between 1957 and 1970. There were similar drugs on the market and the manufacturer stopped producing the drug in the 1970s. The neuro-toxic effects were never observed elsewhere, even though hundreds of millions of doses were administered worldwide – leading some researchers to wonder whether other factors may have contributed to the side effects in Japanese patients.

Clioquinol derivatives into new drugs. Schimmer is pursuing these options simultaneously.

The research ethics board at Princess Margaret Hospital and Health Canada have approved a Phase I clinical trial of Clioquinol. Although Clioquinol tablets are no longer manufactured, the drug is produced in topical form by PharmaScience, a Montreal-based pharmaceutical company. Schimmer spoke with Tristan Booth, Vice-President, Innovative Drug Development at PharmaScience, who agreed to manufacture 50,000 tablets for the trial. This trial of Clioquinol for patients with advanced blood cancers has just opened at Princess Margaret Hospital and this is the first time this drug is being tested as a cancer treatment.

Since the Clioquinol derivatives are new compounds, moving them into the clinic would take more time and resources than repurposing Clioquinol as a cancer treatment. However, these compounds are more potent than Clioquinol and could ultimately be more effective. These derivatives are currently at a stage in which many drug-development projects stall. Funding is available to help scientists discover new compounds, but most granting agencies do not fund the follow-up pharmacokinetic and toxicology studies that show whether compounds are good drug candidates. Pharmaceutical companies are not interested in investing until this work is completed.

To bridge this gap, Schimmer received investment from OICR’s IPCDP. OICR’s investment will allow Schimmer to explore the feasibility of turning Clioquinol derivatives into a novel treatment for myeloma and leukemia.

“The grant is very important because it allows us to maintain our momentum with this promising new compound. By following up our Cancer Research Fund grant with an investment in the value-added work that could make our compound attractive to industry, OICR is ensuring we have the resources needed to bring the benefits of our research to patients.” — OICR
At age six, Dr. Scott Tanner bought his first chemistry set from his brother and by age 12 he had ruined his mom’s oven and parts of the laundry room trying to replicate Ernest Rutherford’s experiment of shooting alpha particles through gold foil. When Tanner had outgrown household experiments, he continued his scientific education earning his PhD in physical chemistry specializing in in-molecule reaction kinetics and flame-ion mass spectrometry. Today, Tanner is the president of DVS Sciences and an Associate Professor at the University of Toronto whose team has invented detection technologies for enabling patient-specific diagnosis, treatment and monitoring of diseases.

After university, Tanner joined Sciex (now MDS Sciex) where his work gained him an international reputation for his knowledge in the plasma mass spectrometry field. This attracted his future business partners and friends Vladimir Baranov and Dmitriy Bandura to form the nucleus of Tanner’s development team at Sciex. Together, the scientists proved to be dynamic in their skills and camaraderie earning them the nickname ‘the three musketeers’. After 25 years of successes at MDS Sciex, Tanner left to pursue the development of a mass spectrometer-based cytometer and was joined by his fellow musketeers. The scientists began DVS Sciences (named for the founders Dmitry, Vladimir and Scott), added Olga Ornatsky to the core of the DVS team, and joined the University of Toronto in March 2005.

Through Olga, Tanner met the internationally renowned cancer stem cell expert Dr. John Dick of the University Health Network’s Princess Margaret Hospital, who identified the potential in the chemists’ work from a biologist’s perspective. “Dr. John Dick, despite the gulf between atomic spectrometrists and cancer stem cell biologists, saw the potential in what we were trying to do,” says Tanner. Dick specializes in leukemic stem cells and agreed to collaborate to attract funding for this promising new research.

In spring 2004, Tanner co-applied for a grant from OICR’s predecessor organization, the Ontario Cancer Research Network, and was awarded $1.2 million. Dick was the principle applicant. “OICR was crucial from the early stage on. When it became apparent that we could not secure the necessary funding for the development of our technology, John Dick helped to secure a first and critical grant that spawned and earned complementary support,” says Tanner. With OICR supporting the project, a vast number of other funding agencies quickly offered support in response. Genome Canada was a large supporter of the project through the Ontario Genomics Institute.

The Mass spectrometer-based flow cytometer: methods and applications project aimed to create a technology with breakthrough quantitative and qualitative properties that would be used by researchers and clinicians to identify rare cancer stem cells in leukemia patient samples, generate large amounts of data from the cells, provide personalized diagnosis and indicate the correct therapy for patients on an individual basis.

With three years of funding, the applicants developed a prototype of the CyTOF™ Mass Cytometer. The instrument analyzes cells tagged with metal atoms instead of fluorescent dyes. The combination of metal tags and plasma mass spectrometry detection resolves the spectral overlap problems that limit the number of probes that can be used with fluorescence. The new MAXPAR™ labeling kits have the potential to allow simultaneous probing of cells with up to 100 antibodies, which is more than 10 times the coverage when using flow cytometry, the current standard. Similar to the difference between a partial and full fingerprint in forensics, the improved coverage dramatically enhances the ability to correctly and confidently identify cancer initiating cells. The CyTOF™ Mass Cytometer examines individual cells at up to 1,000 cells per second to identify rare cells, high cell variations between patients and cancer types and locate biomarkers on an individual patient basis. However promising, with the funding period completed, DVS Sciences lacked the funds to commercialize this promising new technology, John Dick helped to secure a first and critical grant that spawned and earned complementary support,” says Tanner. With OICR supporting the project, a vast number of other funding agencies quickly offered support in response. Genome Canada was a large supporter of the project through the Ontario Genomics Institute.

The IPDCP to further accelerate product development of CyTOF™. “The IPDCP brings at least as much value to the investment in the form of expert business support that it does in cash,” says Tanner. OICR provides not only funds but also critical expertise in the commercialization of the technologies.

In early 2009 DVS enhanced its corporate governance structure by establishing an independent board of directors. Frank Gleeson, OICR’s Executive in Residence, is one of the inaugural members.

“Our OICR connections have strengthened commercial development by augmenting our management team and introducing DVS to numerous international opportunities. This has accelerated our entry to the market, says Tanner. DVS Sciences is rapidly expanding and bringing its technologies to market. There are now three installations in leading research centres and orders are being accepted for commercial deliveries beginning in spring 2010.”

Dr. Scott Tanner

A new technology to identify cancer biomarkers
The mission of OICR's Medicinal Chemistry Platform is to build a drug discovery program that can efficiently translate cancer related academic discoveries into novel oncology therapies that will have a significant impact on the cancer patient population.

ICR’s Medicinal Chemistry Platform grew substantially in 2008–2009, bringing powerful new tools and world-leading expertise in drug discovery and development to Ontario. Ontario has a strong tradition of basic biological research and the province’s researchers have made substantial contributions to our understanding of cancer and other diseases. Today there are tens of thousands of academic investigators and research technicians in Ontario, including 20,000 in downtown Toronto’s Discovery District.

However, once discoveries are made, they often have to be developed into treatments by scientists elsewhere. Ontario does not have the same strengths in medicinal chemistry as it has in basic research, making it difficult for the province’s scientists to find collaborators and facilities that can do downstream work to develop new molecules into drugs. Too often, discoveries don’t make it out of the lab at all.

To respond to Ontario’s need for medicinal chemistry expertise and facilities, OICR established a Medicinal Chemistry Platform at the MaRS Centre.

Dr. Rima Al-awar, a senior chemist with industry experience, was recruited from Eli Lilly and Company in the United States as Platform Director in July 2008. Since then, Dr. Al-awar has recruited a team of 15 scientists with a mix of academic, major pharmaceutical company and biotech experience.

Dr. Al-awar and her team have already built close collaborations with the local principal investigator community and within OICR. “OICR’s Medicinal Chemistry Platform was created to design chemical probes to advance the understanding of signalling pathways and to discover new cancer therapies that can advance the translational goals of the Institute.”
The lab now has state-of-the-art analytical chemistry equipment to support medicinal chemists in evaluating newly designed and synthesized compounds. Members of Ontario’s academic community are already excited about the possibilities. “Five years ago, I was considering doing work on a new compound that seemed to have a good potential as a drug candidate, but I decided the project wasn’t feasible because we didn’t have medicinal chemistry collaborators who could help us carry the project forward to a point that we could find an industry partner and get the drug into clinical trials,” says Dr. Aaron Schimmer, a scientist at the Ontario Cancer Institute, the research arm of the University Health Network’s Princess Margaret Hospital in Toronto. “I was therefore quite impressed when I learned OICR is building a Medicinal Chemistry Platform. I recently met with some of the chemists and we’re planning to collaborate on a new drug discovery project – a project that couldn’t have been done in Ontario five years ago.”

Dr. Tom Hudson, President and Scientific Director of OICR, says inter-disciplinary collaborations such as the one between Schimmer’s laboratory and the OICR Medicinal Chemistry Platform are a step in the right direction for Ontario, and testament to the power of OICR’s collaborative model.

“We are building a Platform that is tightly integrated with the rest of the Institute and the broader scientific community in Ontario,” explains Hudson. “Our vision is to create seamless processes for taking new discoveries and translating them into applications that are useful in the clinic. By establishing a world-class Medicinal Chemistry Platform, we are making sure that Ontario’s researchers have access to the resource and expertise that will allow them to eventually licence their intellectual property to industry – and ultimately to see their research developed into treatments that help patients.” – OICR
Meeting the Cancer Challenge

The International Cancer Genome Consortium

Every tumour and every patient are different, making cancer a complex disease to treat. Understanding the specific genetic changes in a patient’s tumour as well as the patient’s individual variants will allow treatments in the future to be tailored to the patient, resulting in more successful outcomes with fewer side effects.

The Human Genome Project led the development of technologies to screen the genome, its products and molecules that interact with these products. The use of cancer genome sequencing and other high-throughput genomic techniques makes it possible to identify genes critical in the development of cancer. With this knowledge it will be possible to develop novel diagnostic tests and treatments based on the specific profile of a cancer.

With its overarching goal of analyzing the genomes of at least 500 tumours and matched normal tissue for each of 50 specific types of cancer, to date the International Cancer Genome Consortium (ICGC) is the most ambitious research collaboration stemming from the Human Genome Project. The ICGC’s long-term objective is to provide a foundation to improve our ability to diagnose, treat and prevent cancer. “Scientists around the world are contributing to the ICGC goal of characterizing the genetics of cancer. Over the next decade, this catalogue will provide the underpinning for personalized medicine and it promises to refine diagnosis, guide optimum treatment and avoid unnecessary side effects,” says Jennifer Jennings, Manager – ICGC Secretariat and Manager – Strategic Research Planning at OICR.

“Personalized medicine’s impact will continue to grow in importance as scientific breakthroughs are incorporated into targeted therapeutics – with the hope that they will prove more effective to kill stratified cancer and less likely to affect normal cells.”

As of June 2009, the ICGC has received commitments from Asia, Australia, Europe and North America. The countries participating are: Australia, Canada, China, France, India, Japan, Spain and the United Kingdom.

OICR has recruited well-known genome and informatics leaders, including Dr. John McPherson from Baylor College of Medicine (and previously Co-Director of the Genome Sequencing Center at Washington University School of Medicine), and Dr. Lincoln Stein from Cold Spring Harbor Laboratory. OICR leaders have made significant contributions to genome research, including the Human Genome Project, the International Haplotype Map Consortium and other genome projects and databases.

OICR committed $30 million to the ICGC, with a further $10 million in funding announced by Premier Dalton McGuinty on behalf of the Government of Ontario when
The International Cancer Genome Consortium

The ICGC blueprint was launched at the MaRS Centre in April 2008 in Toronto. Dr. Tom Hudson, President and Scientific Director of OICR said, “The Consortium has made substantial progress since its inception.”

At its first scientific workshop in Bethesda, Maryland in November 2008, the ICGC obtained progress reports from projects that are already underway and established scientific committees and working groups. The purpose of the workshop was to bring together some 95 participants from 13 countries to discuss and coordinate initial plans for the ICGC. The workshop agenda included presentations about existing large-scale cancer genomics projects, status reports from committed ICGC projects, and discussion about sample acquisition and stewardship, patient informed consent and bioethics, tumour genome characterization technologies, data analysis and data-sharing models.

OICR contributes to the ICGC in three ways. It hosts the ICGC Secretariat, which provides administrative support to the governance and coordination bodies of the ICGC. It houses the ICGC Data Coordination Centre (DCC), which is responsible for managing the data flow from ICGC projects and centres to the central ICGC database and public repositories, conducting quality assessment, providing data curation services, and managing data releases. OICR participates in the ICGC via its Pancreatic Cancer Genome Project. Although pancreatic cancer is a less common cancer, it has a nearly 100 per cent fatality rate, making it the fifth leading cause of cancer death in Canada.

The ICGC findings will be rapidly and freely available to all researchers working to develop better ways of diagnosing, treating and preventing cancer. – OICR
Meeting the Cancer Challenge

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.

OICR’s Commercialization Program, through the IPDCP, is co-managing investments and providing value-added services to advance products through various stages, for eventual clinical application.

**OICR Grant Supported Projects**

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<td>8</td>
<td>May 2006</td>
<td>6</td>
<td>$ 0.8</td>
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<tr>
<td>9</td>
<td>November 2006</td>
<td>15</td>
<td>$ 7.5</td>
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<tr>
<td>10</td>
<td>May 2007</td>
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<td>$ 0.8</td>
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<tr>
<td>11</td>
<td>November 2007</td>
<td>17</td>
<td>$ 8.2</td>
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<tr>
<td>12</td>
<td>November 2008</td>
<td>13</td>
<td>$ 6.4</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td><strong>139</strong></td>
<td><strong>$71.6</strong></td>
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</tbody>
</table>

Cancer type and number of projects in rounds 1–12:

- **10** All
- **32** Brain
- **10** Breast
- **29** Connective
- **19** Head and neck
- **29** Haematological
- **18** Lung
- **8** Melanoma
- **9** Multiple cancers
- **17** Other
- **9** Ovarian
- **5** Pancreatic
- **18** Prostate

*Some projects have an impact on more than one type of cancer*
Monitoring Results

**OICR GRANT SUPPORTED PROJECTS AND STRATEGIC PROGRAMS**

**Articles published in journals**

<table>
<thead>
<tr>
<th>Journal impact factor range</th>
<th>Number in range</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–10</td>
<td>56</td>
</tr>
<tr>
<td>11–20</td>
<td>6</td>
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<tr>
<td>21–30</td>
<td>6</td>
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<tr>
<td>31–60</td>
<td>0</td>
</tr>
<tr>
<td>NA*</td>
<td>13</td>
</tr>
</tbody>
</table>

**Total number of articles** 81

**OICR grant supported projects**

| 0–10 | 29 |
| 11–20 | 2 |
| 21–30 | 2 |
| 31–60 | 1 |

**Total number of articles** 34

*Unrated journals

**Highly qualified personnel working on funded projects**

- Undergraduate students: 46
- Master’s degree students: 74
- Doctoral students: 80
- Postdoctoral fellows: 150
- Researchers: 235
- Technicians: 107
- Other: 92

**Communications arising from funded projects**

- Oral presentations in Canada: 203
- Poster presentations in Canada: 41
- Oral presentations outside Canada: 248
- Poster presentations outside Canada: 61

**Source of OICR project funds** (in millions of dollars)

- Ministry of Research and Innovation: 78.3
- OICR leveraged funding: 4.9
- OICR partnered leveraged funding: 36.7
- Partner site leveraged funding: 4.9

**Commercial activity generated by funded projects**

- Patent applications: 11
- Patents pending: 5
- Patents awarded: 2
- Licences granted: 1
- Spin-off company: 2

**IPDCP investments**

Investments under co-management by OICR 10

- OICR funding in 2008–2009: $4,783,784
- Private sector funding (cash): $2,200,000
- Private sector funding (in-kind): $150,000

**Cancer type and number of investments**

- Haematological: 3
- Liver: 2
- Colorectal: 1
- Multiple: 6

**Milestones and number of investments**

- First-in-man studies commenced: 1
- Spin-off company created: 3
- Technology licensed or partnered with private sector: 2
- Products sold: 1
- Patents in-licensed: 3
- Patent applications filed: 4
- Private sector partnerships: 1

**Investment impact sector and number of investments**

- Prevention: 1
- Early detection: 2
- Diagnosis: 6
- Treatment: 2
Training the next generation of cancer researchers is part of OICR’s mandate. The Institute provides investigator awards to support high-performance investigators, both scientists with PhDs and clinician-scientists, who will play a significant role in OICR’s programs, projects or platforms. They are located in OICR laboratories or in OICR partner institutions. OICR’s program recruits and retains promising young scientists and clinical experts with leadership qualities and collaborative team-building expertise.

OICR is a great place to work in bioinformatics because the Institute is designed to promote collaboration with the many research institutes in Ontario and bioinformatics can be applied to such a wide range of different fields and locations. One of Boutros’ major ongoing projects is a partnership begun 20 years ago by Okey and two Finnish researchers, Dr. Raimo Pohjanvirta and Dr. Jouko Tuomisto, aimed at understanding and preventing cancers caused by polycyclic aromatic hydrocarbons, a class of industrial pollutants that is a major environmental cause of cancer. Okey has retired and Boutros has taken over as the Canadian principal investigator. The team has found significant differences in the response of rats and mice to these chemicals, a finding that has broad implications for cancer research. “If the two species most commonly used as models have such different responses to a common carcinogen, it shows us we need to use both models, and maybe more, to understand reliably what causes cancer in humans.”

In another prevention project, Boutros is trying to find the original site of carcinogenesis in childhood cancers that are caused by environmental toxins. This is a continuation of work started by Patricia Harper, a scientist who recently retired from The Hospital for Sick Children. “The techniques of personalized medicine are broadly applicable,” he says. “We’re confident that over the next few years, bioinformatics will contribute to a much better understanding of most human diseases.” – OICR

Paul Boutros, a highly active young investigator in the fast-emerging field of computational biology, joined OICR last year and is now applying his expertise to a range of projects spanning the cancer continuum, from prevention to treatment.”

One of Boutros’ key interests is personalized medicine – the idea that treatments can be made more effective, precise and safe if they are targeted on the molecular level to individual patients’ conditions. If scientists and doctors are to realize an era of personalized medicine for cancer, they will need biomarkers to test for the disease and develop courses of treatment tailored to specific individuals. Originally from Toronto, Boutros completed a B.Sc. in Chemistry at the University of Waterloo and developed an interest in programming and computational work during a co-op placement at Michigan State University. He worked in the laboratory of Dr. Allan Okey at the University of Toronto for two years, where he developed his own research interests and decided to pursue further studies. He completed his PhD under the supervision of Drs. Linda Penn and Igor Jurisica at the Ontario Cancer Institute, the research arm of the University Health Network’s Princess Margaret Hospital, finishing the degree in just three-and-a-half years.

While he was working on his PhD, Boutros and Dr. Ming-Sound Tsao, a clinician-scientist at Princess Margaret Hospital, identified biomarkers to predict survival in lung cancer patients. “There is a very strong variability in patient survival,” Boutros explains. “Research has shown that if two patients are given exactly the same treatment for very similar cases of lung cancer, they will not have the same outcome. The first step toward developing personalized diagnostic tools and treatments is to understand why this variability occurs.”

Boutros and Tsao tried to understand the variability by examining a lung cancer dataset involving 15,000 genes in 800 patients. However, a dataset this large presents a problem: there is so much variability that it becomes impossible to use standard tools to interpret the data. Boutros and Tsao pioneered a new non-linear analysis technique for this data and identified a six-gene signature that is effective in predicting survival.

The six-gene signature can be used to separate lung cancer patients into two groups, one predicted to have good prognosis and the other predicted to have poor prognosis. When patients were followed up over time, 40 per cent more patients predicted to have good prognosis were still alive five years after being diagnosed with cancer. The biomarker has been licensed to a company that is working toward developing it into a clinically useful application. “We think our findings could be very useful for treating patients,” Boutros says. Boutros is part of a new generation of scientists who blend biology and computation to develop powerful models for understanding disease. Unsurprisingly, this approach to research involves collaborations with colleagues in a wide range of different fields and locations.

One of Boutros’ major ongoing projects is a partnership begun 20 years ago by Okey and two Finnish researchers, Dr. Raimo Pohjanvirta and Dr. Jouko Tuomisto, aimed at understanding and preventing cancers caused by polycyclic aromatic hydrocarbons, a class of industrial pollutants that is a major environmental cause of cancer. Okey has retired and Boutros has taken over as the Canadian principal investigator. The team has found significant differences in the response of rats and mice to these chemicals, a finding that has broad implications for cancer research. “If the two species most commonly used as models have such different responses to a common carcinogen, it shows us we need to use both models, and maybe more, to understand reliably what causes cancer in humans.”

In another prevention project, Boutros is trying to find the original site of carcinogenesis in childhood cancers that are caused by environmental toxins. This is a continuation of work started by Patricia Harper, a scientist who recently retired from The Hospital for Sick Children. “OICR is a great place to work in bioinformatics because the Institute is designed to promote collaboration with the many research institutes in Ontario and bioinformatics can be applied to such a wide range of problems in research,” Boutros says. “The techniques of personalized medicine are broadly applicable,” he says. “We’re confident that over the next few years, bioinformatics will contribute to a much better understanding of most human diseases.” – OICR

Paul Boutros
Dr. Rebecca Gladdy

Dr. Rebecca Gladdy, a Canadian-trained clinician-scientist who is hoping to improve treatments for the type of cancer that Terry Fox did not survive, returned to Ontario last year and will devote part of her expertise to the Ontario node of the Terry Fox Research Institute at OICR.

Gladdy is a surgeon at Mount Sinai Hospital, a scientist at the Samuel Lunenfeld Research Institute, and an investigator with the OICR Selective Therapies Program. Before she relocated to Toronto in summer 2008, she was a fellow in Surgical Oncology at Memorial Sloan-Kettering Cancer Center in New York. Before her term in New York, Gladdy completed a postdoctoral fellowship at the Lunenfeld Institute in Toronto and her general surgery residency at the University of Toronto.

Gladdy, who holds a PhD in Biomedical Science from the University of Toronto and a medical degree from Queen’s University in Kingston, is an expert in soft tissue sarcomas. She says the collaborative spirit and opportunity to work with world leaders in cancer biology, genomics and in the dedicated sarcoma programs at Princess Margaret Hospital and Mount Sinai Hospital all factored in her decision to return to Ontario.

“There are similar job opportunities in the United States but I think the Canadian scientific community’s willingness to work together and its dedication to the open exchange of ideas is sometimes under-appreciated. For me, the excellence in the cancer research community in Ontario and OICR’s ambitious mission to bring the community even closer together made the offer to work here very attractive.”

In 2007, the Terry Fox Foundation announced a cross-Canada virtual institute composed of four nodes at research institutes and universities in Quebec, Ontario, Alberta and British Columbia. Ontario’s node is the OICR Selective Therapies Program, which is co-funded by the Terry Fox Foundation, the Government of Ontario and OICR.

Led by Dr. Robert Rottapel, a clinician-scientist at University Health Network and St. Michael’s Hospital in Toronto, the Selective Therapies Program aids in the development of novel diagnostic tests to identify the best set of agents to treat each cancer patient individually; the cancer therapies prescribed could be different for each patient to maximize the effect of treatment. The program is also identifying new clinical candidates in collaboration with OICR’s Medicinal Chemistry Platform.

Gladdy is focusing on finding selective therapies for soft tissue sarcomas, a diverse group of tumours derived from connective tissue such as muscle, fat and bone. Although progress has been made in recent years in the management of sarcoma, there is still significant work to be done to improve functional and long-term patient outcomes. Current treatments are primarily surgical procedures to remove the sarcoma, with selective use of radiation therapy and the use of conventional chemotherapy in some subtypes of the disease. Unfortunately, these treatment options are limited in their effectiveness and more than 50 per cent of patients succumb to their disease. Researchers have recognized that there is an urgent need to develop subtype-specific molecularly targeted therapeutics that can provide new treatment options unique to each histologic type of sarcoma.

Gladdy’s lab is attempting to identify therapeutic agents through the use of high-throughput screens. They are also developing novel mouse models as a tool to determine which genes are critical for sarcoma formation, and thus should be targeted in pre-clinical drug testing.

The Selective Therapies Program is hoping to take the knowledge gained from the laboratory into patient care as quickly as possible. Over the next several years their work will span from basic laboratory research to clinical trials that will deliver new therapies to Ontario cancer patients. – OICR

Dr. Brian Nieman

Mouse models of human diseases are a powerful tool in biomedical research for studying progression of illnesses and response to potential treatments. The Mouse Imaging Centre (MICe) located at the Toronto Centre for Phenogenomics continues to adapt and develop imaging techniques for noninvasive examination of mouse models. In particular, a desire to understand the role of individual cells or cell populations in disease motivates the development of cell-specific imaging methods.

Dr. Brian Nieman, an OICR supported scientist at The Hospital for Sick Children in Toronto and a researcher at MICe, aims to improve imaging capabilities to permit detection and tracking of specific cells in mouse models, particularly associated with cancer.

Nieman’s academic background offers extensive expertise on magnetic resonance physics which he has applied to biological practices. Magnetic resonance imaging (MRI) is a noninvasive technology and is used frequently in his research. MRI uses radiofrequency waves and a magnetic field to produce images of the body and detect diseased areas. Neiman uses an MRI system which generates high-resolution anatomical images in the mouse. Innovations in imaging and cell-labelling methods at MICe aim to achieve Nieman’s ultimate goal of mapping and following subpopulations of cells in vivo.

Such improvements in imaging technologies and methods align with OICR’s One Millimetre Cancer Challenge Program and the Imaging Pipeline Platform’s goal of detecting cancer in its earliest stage with detailed information about the diseased cells. The advancements that arise from Nieman’s research could also be applied to detecting and tracking rare cancer stem cells, which will aid OICR’s Cancer Stem Cells Program. Nieman received an OICR New Investigator Award in November 2008 to pursue his cancer imaging goals.

“Toronto is a great place to conduct research, especially in the discovery district with blocks of research facilities and some of the world’s best scientists in one spot. OICR’s New Investigator Award allowed me to come and participate in all of this,” says Nieman who earned his PhD at the University of Toronto and left Ontario to complete a postdoctoral fellowship at the New York University School of Medicine. “I’m not sure I would have been able to return to Toronto now if I had not received the OICR award.”

The field of biomedical imaging is quickly advancing, but many questions still remain unanswered. In the next few years, Nieman aims to answer how different cells are distributed in the body under normal and diseased circumstances and examine how changes in cellular gene expression relate to the development and progression of disease. Answering these questions will revolutionize biomedical research by providing a documented understanding of how diseases progress in the body and how a variety of cell types react to disease. Improvements in imaging technologies will also lead to useful diagnostic tools in the clinic helping to spot cancer at the earliest stage. – OICR
It’s only been about ten years since husband-and-wife researchers Shana Kelley and Ted Sargent received their PhDs, yet both already have resumes that many researchers strive their entire careers to achieve. Kelley, who was this year named one of Canada’s Top 40 Under 40, is Director, Division of Biomolecular Sciences in the Faculty of Pharmacy at the University of Toronto (U of T). Sargent, who was named “one of the world’s top young innovators” by the MIT Technology Review in 2003, is currently the Canada Research Chair in Nanotechnology, also at U of T.

Kelley and Sargent are an unconventional research team, having come together from two very different research backgrounds. But they are now collaborating on the development of the GenEplex platform, a new technology that uses inexpensive microchips to detect cancer on a molecular level. This technology will give doctors the ability to more accurately diagnose a patient’s cancer and target therapies specifically for a patient’s needs. OICR is currently funding the commercialization of the technology through the Commercialization Program.

“Microchips are usually thought of as being used to run computers,” Kelley admits, “but we have figured out how to make these microchips responsive to DNA and RNA sequences and proteins that are markers for cancer.”

Kelley and Sargent use nanotechnology to grow tiny formations called nanostructures right on the microchip itself. The structures are designed to be similar in size to DNA itself, ‘catching’ strands of DNA on the microchip. This allows the microchip to detect very small numbers of molecules and gives doctors precise information about the characteristics of the tumour.

“We now know that two people can have the same type of cancer but their cancers can be responsive to different drugs,” Kelley says. “You have to test the tumour and really understand its genetic make up to understand how to treat it. Once we get this up and running, it will help to classify what type of cancer a patient has and what therapies their physician can prescribe.”

By prescribing proper treatment, patients would not only benefit from having the best therapy to treat the disease, but could also experience reduced side effects and reduced treatment time. That’s because doctors will be able to quickly identify the exact treatment for their patient without having to try different treatments that may not work.

“The magic of what we do is all enabled by nanotechnology. You have to be probing on the right sized scale and have very fine resolution to see what we are looking for.”

The new technology could be used in a variety of places, including hospitals or even in doctors’ offices. “Because the readout is electronic,” Kelley says, “it makes for very simple analysis. You don’t need to have a PhD to read the results.” Also, because it is based on microchips that are already easy to manufacture, the new technology will be quite inexpensive to run.

“We have the technology working in the lab in a model system under very well controlled conditions. But if we can work on optimizing the chip and generating the instrumentation then we are hopeful that within the next few years we will have instruments going into hospitals and doctors offices.”

Kelley moved her research program to U of T several years ago to tap into the university’s range of strong research programs. “Since I moved here this project has absolutely taken off,” she says, adding that the institution she worked at previously was strong in her field, but not in many others. “I was starting to see that as a limitation. Toronto ended up being an ideal place for this project.”

She thinks that getting researchers from different disciplines to work together is key to the development of many new technologies, and it is something she says is a requirement on her research team. “Someone who would not stray outside of the confines of analytical chemistry could not take a project like this all the way. You would do it to a certain point, publish and then hope someone reads your paper and takes it from there. An interdisciplinary approach allows you to do a lot of things that are novel and important.

“I definitely think younger researchers are less afraid to be interdisciplinary,” she adds.

As for working side-by-side with her husband on the project, Kelley has nothing but praise for their working relationship. She says their different skill sets help to push their research farther. “Working together Ted and I are able to do things that we wouldn’t be able to do on our own,” she says. “The GenEplex platform is a great example of that.”
To the Directors of Ontario Institute for Cancer Research

We have audited the balance sheet of Ontario Institute for Cancer Research as at March 31, 2009 and the statements of operations and surplus and cash flows for the year then ended. These financial statements are the responsibility of the Institute’s management. 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 plan and perform an audit to obtain reasonable assurance whether the financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements. An audit also includes assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation.

In our opinion, these financial statements present fairly, in all material respects, the financial position of the Institute as at March 31, 2009 and the results of its operations and its cash flows for the year then ended in accordance with Canadian generally accepted accounting principles.

Licensed Public Accountants
Chartered Accountants
Toronto, Ontario
May 29, 2009

A copy of the complete audited financial statements is available upon request.
### BALANCE SHEET

**As at March 31**

<table>
<thead>
<tr>
<th>ASSETS</th>
<th>2009</th>
<th>2008</th>
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</thead>
<tbody>
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<td><strong>CURRENT ASSETS</strong></td>
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<td><strong>CURRENT LIABILITIES</strong></td>
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<td>Accounts payable and accrued liabilities</td>
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<td>Current portion of deferred gain on disposal of leasehold improvements</td>
<td>180,688</td>
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<td>Current portion of obligation under capital lease</td>
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<td>Unearned rentals</td>
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<td><strong>Deferred contributions</strong></td>
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<td>Deferred gain on disposal of leasehold improvements</td>
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<td>Obligation under capital lease</td>
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<td><strong>SURPLUS</strong></td>
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<td>Unrestricted</td>
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<tr>
<td><strong>Total</strong></td>
<td>$49,332,326</td>
<td>$34,612,193</td>
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### STATEMENT OF OPERATIONS AND SURPLUS

**Year ended March 31**

<table>
<thead>
<tr>
<th>CANCER RESEARCH PROGRAM</th>
<th>ONTARIO CANCER RESEARCH NETWORK</th>
<th>EXTERNAL GRANTS</th>
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</thead>
<tbody>
<tr>
<td><strong>REVENUE</strong></td>
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<td>Grant funding</td>
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<td>Insurance</td>
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<td>Salaries, benefits and recruiting</td>
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<td>Support service fees</td>
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<td>Support, beginning of year</td>
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<tr>
<td><strong>Surplus, end of year</strong></td>
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<td>$ -</td>
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<tr>
<td>Excess of revenues over expenses</td>
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</tr>
<tr>
<td><strong>Total</strong></td>
<td>$63,593,540</td>
<td>13,683,877</td>
</tr>
</tbody>
</table>

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OICR Annual Report 2008/09 35
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Director of Pathology Research Informatics, Director of Cancer Bioinformatics, University of Michigan

Tak Mak
Director, The Campbell Family Institute for Breast Cancer Research, Ontario Cancer Institute

Harold Moses
Hofsteter B. Ingram Professor of Molecular Oncology, Professor of Cancer Biology, Medicine and Pathology, Director Emeritus
Vanderbilt-Ingram Cancer Center

Tony Pawson
Distinguished Investigator
Samuel Lunenfeld Research Institute

Homer Pearce
Member, Board of Directors
Sunesis Pharmaceuticals, Inc.

John Potter
Member and Director, Division of Public Health Sciences, Fred Hutchinson Cancer Research Center

Charles Sawyers
Chairman, Human Oncology and Pathogenesis Program, Memorial Sloan Kettering Cancer Center

Richard Schilsky
Professor, Department of Medicine/Section of Hematology-Oncology
Associate Dean for Clinical Research, Division of Biological Sciences Biology; Director, The Cancer Research Center, University of Chicago

Jane C. Weeks
Director, Center for Outcomes and Policy Research, Dana-Farber Cancer Institute Professor of Medicine, Harvard Medical School Professor of Health Policy and Management, Harvard School of Public Health

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Vice-President, Operations

Michele Noble
Corporate Secretary

For information about the Ontario Institute for Cancer Research please contact:

Rhea Cohen
Director of Communications
rhea.cohen@oicr.on.ca
416.673.6642