OICR Outcomes and Benefits Report
2007-2014

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A. Introduction

“The next decade or two will be the most productive and illuminating period in the entire history of biological and medical science. If Ontario launches a major initiative in cancer research, it will be close to the centre of this remarkable process, and will create new knowledge and tools that will improve the lives of millions of its citizens. While cancer provides a full and sufficient rationale for such an initiative, the benefits of engagement will be experienced in almost all aspects of health care and other aspects of our communal life and our economy.”


The Ontario Institute for Cancer Research (OICR) was formally launched on December 2, 2005 with a significant investment by the government of Ontario. Headquartered in the MaRS Centre, OICR has enhanced the provincial research capacity and is well-positioned to continue accelerating the translation of scientific discoveries and health service delivery findings into clinical applications, health practice changing guidelines and commercialization opportunities.

OICR’s two strategic plans (2007-2010 and 2010-2015) were blueprints to recruit, build infrastructure and establish partnerships in areas in which Ontario already had leadership potential. OICR’s commitment to translation has been foundational in recruiting leaders with a track record in translation and catalyzing partnerships between academics, clinical investigators, provincial and federal ministries, advocacy groups, and industry. In a short amount of time, the Institute enabled researchers across Ontario (Figure 1) to launch ambitious programs in translational research, develop new concepts and prototypes, and catalyze the formation of new companies. This report takes stock of the Institute’s achievements in order to inform internal and external stakeholders involved in generating and reviewing OICR’s strategy for the future (2016-2020).

To supplement this document, the Independent Review Panel is provided with OICR’s Progress Report for 2013-2014, (see Binder 5) which provides a more complete description of the Institute’s Programs, Translational Research Initiatives, Investigator Awards and other initiatives.

An important take-away message in this report is that OICR has developed a pipeline that is currently rich in assets (biomarkers, medical imaging devices and probes, small molecules, immunotherapeutics, and biological agents) that are moving forward towards the clinic. This rich pipeline constitutes a profound transformation of what existed in Ontario before OICR was created and provides numerous opportunities for impact.
**Figure 1:** Map of Ontario indicating cancer centres and major hubs where OICR’s research takes place.
B. Benefits to Ontario citizens, cancer patients and the economy

In its initial years, OICR’s leaders identified leading teams in the province able to accelerate the translation of innovative concepts and tools to products, guidelines and/or policies introduced in Ontario and elsewhere. The following examples illustrate OICR’s impact on the Ontario economy and health innovation, with the introduction of novel health products, technologies, services and policies.

B.1. Helping Ontario citizens live longer and healthier lives

B.1.1. Improvements in colorectal cancer screening in Ontario to reduce cancer deaths

Through partnership with Cancer Care Ontario (CCO) and the Ontario Ministry of Health and Long-Term Care (MOHLTC), OICR’s Health Services Research (HSR) Program is improving colorectal cancer (CRC) screening in the province. CRC is the second leading cause of cancer-related deaths in Canada, with an estimated 22,000 cases diagnosed in Canada in 2009, including 8,100 in Ontario. In April 2008, CCO launched Canada’s first organized province-wide screening program, Colon Cancer Check (CCC). The first OICR initiative to complement the CCC program was initiated in December 2010 and focused on increasing the uptake of CRC screening by evaluating invitation methods to increase participation. The results of this pilot study showed a 14 per cent net increase in the uptake of screening among eligible people who were overdue. This first study has already impacted approaches taken by CCO to improve its screening program. A subsequent cluster randomized controlled trial of directly-mailed fecal occult blood test (FOBT) kits to non-responders showed a further 20 per cent increase in participation if the FOBT was directly mailed to people, compared to only 10 per cent among those receiving follow-up invitations alone. Implementation of this approach is in the planning stages by MOHLTC. In the course of these studies, a surprisingly high rate of failure to follow-up participants with abnormal FOBT (25-30 per cent) was identified, a finding that has led to a new study by OICR-CCO to identify the reasons for this failure to follow-up, develop and test interventions, and ultimately ensure that evidence-based findings resulting from this work are implemented in Ontario to improve the provincial funded screening program.

B.1.2 Reduction of cancer and other tobacco-related diseases

Tobacco use is the leading cause of cancer worldwide. It is also the number one source of preventable death and disease, projected to kill an astonishing one billion people in the 21st century. In 2003 the World Health Organization responded to this global problem with the adoption of the Framework Convention on Tobacco Control (FCTC), the world’s first health treaty. The FCTC calls for policies such as pictorial warning labels, advertising restrictions, smoke-free laws and higher taxes on tobacco products.

Measuring the impact of the FCTC is the job of a team of more than 100 researchers known as the International Tobacco Control Policy Evaluation Project (ITC Project), led by Dr. Geoffrey T. Fong, Senior OICR Investigator, who is based at the University of Waterloo. Fong and his colleagues
conduct sophisticated longitudinal cohort surveys of representative samples of tobacco users and non-users in 22 countries to measure the impact of FCTC policies. These surveys allow the ITC Project team to determine whether FCTC policies are fulfilling their purpose of reducing tobacco use. In addition to measuring the success of the FCTC, the findings of the ITC Project are used to inform tobacco control policy making in Canada and elsewhere. A recent ITC study determined that the 2001 pictorial warnings in Canada were estimated to have decreased smoking rates by 12 to 20 per cent. In a subsequent eight-year study tracking the impact of warnings over time, ITC investigators found that the impact of Canada’s pictorial warning labels declined significantly over time; this ITC study led to new pictorial warnings being introduced in Canada in 2012.

B.2. Helping Ontario cancer patients access innovative medicines and tests

B.2.1. Pharmacogenetic tests in Ontario

Most novel oncology agents recently approved by Health Canada have been accompanied by a diagnostic test or the recommendation to use a pharmacogenetic test to select the patients who should be treated with that agent. For this reason, it has become essential that high-quality and scientifically sound provincial guidelines be developed in a suitable time frame to guide the use of these new agents.

In 2011, the Medical Advisory Secretariat (MAS) of the MOHLTC, CCO and OICR formed a collaboration to facilitate the development of new guidelines for personalized medicine in the province of Ontario. Initially chaired by Dr. Nicole Onetto, OICR’s Deputy Director and Chief Scientific Officer, this effort led to the development of guidelines for tests such as:

- Oncotype DX - a breast cancer diagnostic test created to help treatment decisions for patients who have been recently diagnosed with early stage, estrogen receptor-positive node negative breast cancer. In addition to the guidelines, MOHLTC funded a confirmatory field study conducted by the Ontario Clinical Oncology Group (OCOG). Recent results have confirmed that the use of Oncotype DX in Ontario was indeed influencing treatment decisions for early breast cancer and allowed 22 per cent of patients to avoid chemotherapy. In addition, OICR is supporting the comparison of assays to evaluate retrospectively the performance of more cost-effective prognostic tests than Oncotype DX in the cohort of patients enrolled in this field study;
- KRAS - a new biomarker being used to select treatment for individual CRC patients (utilisation of monoclonal antibodies directed against the Epithelial Growth Factor Receptor, EGFR MAb). The KRAS gene in a CRC tumour may be ‘wild-type’ or ‘mutant’; the form carried by a patient will help determine which treatment the patient should receive and avoid expensive and potentially toxic treatment in the KRAS mutated patients that do not benefit from EGFR MAb;
- EGFR - epidermal growth factor receptor (EGFR) for prediction of response to EGFR inhibitors in non-small cell lung cancer;
- BRAF - the BRAF test is a highly sensitive and specific mutation analysis that guides oncologists as they seek to determine whether melanoma patients should be treated with a newly approved specific BRAF inhibitor.
In addition, the collaboration team recommended that a comprehensive multiplex genomic approach, rather than specific tests, will provide the most cost-effective information for patient management in the near future.

B.2.2. Medical isotopes and novel imaging probes

The Centre for Probe Development and Commercialization (CPDC) is a not-for-profit spinoff developed out of OICR’s imaging program. The potential to capitalize on expertise and facilities at McMaster University and support Dr. John Valliant, one of Ontario’s rising stars, was recognized early. OICR supported Valliant’s grant applications in 2008 and 2013 to the highly competitive federal Centres of Excellence for Commercialization and Research (CECR) program, which leveraged over $30 million in external funds. This allowed CPDC to launch a world-class and comprehensive program that can discover, develop, translate, and manufacture new imaging probe technologies used to characterize patient tumours. CPDC’s impact can be measured in many ways:

- **High-tech job creation.** CPDC has more than 70 employees and annual revenues in excess of $5 million;
- **Health innovation.** CPDC has organized and streamlined R&D, development and manufacturing of probes, thereby increasing productivity. This has led to CPDC supplying imaging probes for more than 12 clinical trials in Canada focused on bringing new agents to Canada for improving the detection and treatment of cancer; of these, three multicentre trials conducted in Ontario are supported by OICR’s High Impact Clinical Trials Program (HICT);
- **Patient impact.** CPDC has provided doses of medical isotopes to more than 10,000 patients and is leading an initiative to address medical isotope shortages in Canada, such as the shortage that occurred when the reactor at Chalk River was temporarily decommissioned;
- **Attracting investment in Ontario.** CPDC’s high-tech manufacturing program has attracted major and long-term investments from multiple international industry partners (i.e., GE Healthcare; Progenics Pharmaceuticals Inc.);
- **Translation and commercialization.** CPDC has developed and patented a novel agent for the detection and treatment of therapy-resistant cancers. By targeting a protein that is overexpressed on the surface of cancer when a tumour is resisting treatment, CPDC’s radiolabeled antibody targeting the IGF-1R protein has shown impressive results in killing tumour cells while sparing healthy cells in preclinical studies. The current focus is to develop and commercialize this home-grown technology as a theranostic with the dual potential to diagnose and cure difficult-to-treat tumours. The probe has moved into a phase I trial at three sites in Ontario and the data will further inform on how best to develop the technology. It will form the basis for creating a new Ontario company for future development of the therapeutic agent.
B.3. Growing the Ontario economy

B.3.1. OICR as a catalyst for commercialization of Ontario discoveries

For a young organization, OICR’s commercialization record is outstanding, despite challenging economic times. OICR created a commercialization group to invest in the very best technologies arising from Ontario’s exceptional cancer research base. The Institute launched the Intellectual Property Development and Commercialization (IPDC) Fund to support cancer-related, early-stage commercialization activities including: proof-of-concept, validation, creation of standard operating procedures, market analyses, intellectual property (IP) protection and acquisition, and expert guidance and management. The commercialization team provided expert guidance and oversight to the commercial development of IPDC projects. OICR made it a priority to encourage maximum participation by Ontario organizations in the development, commercialization and use of inventions arising from OICR activities, which are core elements of OICR’s “Ontario First Policy.”

Although IPDC was the main vehicle used by OICR to launch companies, several OICR research investments led to the creation of additional companies, which together account for the following metrics:

- 20 new Ontario start-up companies created;
- $105 million in investments from the private sector (Figure 2: estimated expenditures prior to March 31, 2014);
- 7 companies have prototypes manufactured;
- 4 have products sold;
- 4 commenced first-in-man studies;
- Partnerships with a diversity of companies, including biopharmaceutical companies (Celgene, Roche Venture Fund, Pfizer Venture Investments) and venture capital firms (Genesis, 5AM Venture Management LLC, Mohr Davidow Ventures, Domain Associates, L.L.C., CTI Life Sciences Fund, Ontario Emerging Technologies Fund, BDC Capital, VanEdge Capital, etc.).

![Figure 2: Private investment in OICR supported/enabled start-up firms](image)

It has become apparent that one of the preferred models for developing partnerships with industry, including pharma, is the creation of companies (termed “Newcos”) to hold the IP. The Newco becomes the driving force for the development of products, under a unified
management team that leverages the combined expertise of academic and industry scientists who coordinate the scientific thrust of the company through joint steering committees.

Private sector financing results in the creation of new high-quality jobs in Ontario (see Table 1 and Figure 3).

<table>
<thead>
<tr>
<th>FY2010-11</th>
<th>FY2011-12</th>
<th>FY2012-13</th>
<th>FY2013-14</th>
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<tr>
<td>57</td>
<td>131</td>
<td>161</td>
<td>180</td>
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Table 1: Number of employees at all active start-up firms

Figure 3: Employees in start-up firms enabled by OICR

OICR is pleased to have contributed to the development of a revolutionary new instrument, reagents and manufacturing facility in Ontario. In 2005, OICR provided a grant to Dr. John Dick, University Health Network (UHN), Director of OICR’s Cancer Stem Cell Program, and Dr. Scott Tanner (University of Toronto), founder of DVS Sciences Inc., a University of Toronto start-up company, to enable them to build upon their prior funding to develop a disruptive analytical instrumentation platform known as CyTOF®. The CyTOF is a mass cytometer that enables the absolute quantification of multiple antigens simultaneously in single cells at high-throughput. Support for the development of a commercial prototype was provided through an additional grant from OICR’s Intellectual Property Development and Commercialization Fund (IPDC) and led to early adoption at Stanford, UHN and the National Institutes of Health (NIH). With additional funding from Genome Canada and other funding agencies, the CyTOF technology was further developed and gained global traction. In 2010, OICR brokered a USD$14.6 million series "A" financing with 5AM Ventures, Pfizer Ventures, Mohr Davidow Ventures, and Roche Ventures. This led to the opening of a global R&D and manufacturing facility in Markham, Ontario. Earlier this
year, DVS was acquired by Fluidigm (US) for $207.5 million, became Fluidigm Canada Inc., and retains its plant in Markham, Ontario (with 59+ employees).

In late 2012, OICR created a structure to further accelerate efforts in commercialization. OICR established the Fight Against Cancer Innovation Trust (FACIT) to house all the commercial assets and related commercial activities of the Institute. FACIT has become the vehicle through which OICR assets are further developed and commercialized. FACIT operates as an independent business trust with OICR as its sole beneficiary. The full transition of the OICR commercialization team to FACIT occurred on April 1, 2014.
C. The OICR Translational Research Pipeline

OICR has catalyzed the creation of a cancer innovation pipeline that will bring better approaches to control cancer that will impact patients and populations.

C.1. New cancer medicines to save lives

C.1.1. Designing oncolytic vaccines that attack cancer

Oncolytic viruses (OVs) are selected or engineered to specifically replicate in and kill tumour cells, but spare normal tissues. Dr. John Bell (Ottawa Health Research Institute - OHRI) and his colleagues in the OICR-sponsored Ontario Regional Bio-Therapeutics (ORBiT) Program are recognized internationally for their work in the development of oncolytic virus therapeutics. Building on their collective preclinical and clinical experience over the last ten years, they have designed and developed a purpose-built OV platform that directly infects and kills systemic cancers while, at the same time, acts as a vaccine to trigger potent anti-tumour immune responses. The foundation of their platform arose from work in the lab of Dr. David Stojdl (Children’s Hospital of Eastern Ontario – CHEO) who carried out “bio-prospecting” studies on a library of natural viral isolates from around the world. Stojdl found that Maraba virus, isolated from a sand fly in Brazil, had optimal therapeutic potential and he then conducted detailed genetic engineering studies to ensure its selective replication in cancer cells. In parallel, Drs. Brian Lichty and Yonghong Wan (McMaster University) unravelled the unique interactions of Maraba virus with the immune system and developed the concept of using OVs not only as tumour killers, but also as potent vaccine vectors. Now called the “oncolytic virus vaccine”, this technology became the focus of the ORBiT Program and a development plan including Good Manufacturing Practice (GMP) manufacturing, toxicity testing and assay development was put into motion. Dr. Neil Berinstein, OICR’s Director of Translational Research helped guide ORBiT’s regulatory and clinical strategy that was vital for translation into the clinic of our first Maraba product. Many positive developments have occurred over a four-year period:

- GMP facilities in Ottawa and McMaster were commissioned and have produced, vialled and released pharmaceutical grade Adenovirus and Maraba virus-based vectors to support human trials;
- Non-human primate studies were conducted demonstrating the outstanding safety profile of the ORBiT viruses and robust immune responses against a selected tumour-associated antigen;
- A Clinical Trial Application (CTA) was filed with Health Canada for a “first in man” study to be conducted at three clinical sites in Ontario. The trial sponsor is the NCIC - Clinical Trials Group (NCIC-CTG) based in Kingston;
- Broad patents have been filed globally and important claims allowed in the U.S. and Europe;
- OHRI, CHEO, McMaster University and OICR’s commercialization entity FACIT (described later) have formed a new Ontario-based company. Partnership discussions are underway.
This success story is a prime example of an Ontario discovery enabled by OICR that moved from the laboratory, through proof-of-concept testing, to manufacturing, and currently, clinical testing. This required a multi-disciplinary team of committed scientists, clinicians and entrepreneurs that is rarely seen in academia.

C.1.2. New lymphoma drug: Inhibitor of BCL6

The Drug Discovery Program at OICR has made significant progress in developing novel small molecule inhibitors of the oncogenic protein BCL6 that has been shown to drive the growth of germinal cell diffuse large B cell lymphoma (DLBCL), a common form of blood cancer with a five-year survival rate of ~50 per cent. Of interest, BCL6 seems to be a determinant activator of a specific sub-type of DLBCL, i.e., Germinal Center, which seems resistant to new agents currently developed for DLBCL.

In collaboration with Dr. Gil Privé, a structural biologist at UHN, the OICR team conducted a virtual screen on 5.2 million compounds that identified a hit with activity of around 280 μM in the primary binding assay. Although BCL6 is a transcription factor and the inhibitors target a protein-protein interaction that is difficult to drug, the medicinal chemists at OICR have been able to improve the potency of these compounds into the low nM range in both binding and cell-based luciferase assays. The team is currently optimizing the drug-like properties of the molecules in order to conduct in vivo proof of concept efficacy studies. This project is at the lead optimization stage, is attracting potential industry partners and is progressing through preclinical studies to ultimately support applications to the regulatory agencies at Health Canada and the Food and Drug Administration to allow testing in humans.

C.1.3. Stem cell therapeutic strategies:

In its first strategic plan, OICR recognized the pioneering role of Ontario scientists in cancer stem cell (CSC) research and the importance that CSCs may play in cancer initiation, tumour growth and metastasis. Dr. John Dick was asked to lead a program that would show the clinical relevance of cancer stem cells. The launch of this program catalyzed the development of new technologies to characterize CSCs (see DVS section B3), the establishment of a specialized repository of patient primary samples (live cell bank, xenografts) and strengthened basic and clinical collaborations in Ontario for cancer stem cell research among various cancer types (leukemia, brain cancer, ovarian cancer, sarcomas, and others). OICR-supported scientists have made important advances in the development of a novel preclinical drug testing paradigm using primary patient samples; drug response is measured in a surrogate human clinical trial that involves preclinical primary human leukemia xenograft models. This approach provides important information on potential efficacy to eradicate CSC and prolong survival. Advances made by CSC leukemia scientists include the identification of CSC vulnerabilities and development of new therapeutics based on these observations (i.e., targeting metabolism, mitochondria, etc.). Several of these drugs are in clinical trials after having been evaluated using the preclinical models. These approaches are being increasingly deployed in partnership with numerous pharmaceutical and biotech companies and other academic groups who see this as the future of preclinical drug development. In addition to the development of new drugs, CSC
scientists have also developed a variety of transcriptional, proteomic and genomics biomarkers that can be used as prognostic or predictive markers to guide treatment interventions. An unexpected finding arose from collaborations with the OICR genomics and informatics teams: targeted re-sequencing of cancer genes in patients with leukemia resulted in the discovery of a pre-leukemic stem cell reservoir in acute leukemia (Shlush L et al, Nature 2014). This provided new insight into the pathogenesis of human myeloid leukemia and a possible approach to eliminating pre-leukemic clones before the acquisition of additional genetic lesions engenders greater therapeutic resistance.

Ontario teams capitalized on new funding opportunities created by Canada’s Cancer Stem Cell Consortium and the California Institute for Regenerative Medicine (CIRM), which OICR was instrumental in establishing. Two Ontario-California teams (led by Dick/Dr. Dennis Carson and Dr. Tak Mak/Dr. Dennis Slamon) were awarded approximately $80 million in total to move preclinical drug candidates towards clinical trials.

Major milestones of these teams include:

- The Dick/Carson team aims to study the potential of drug candidates targeting stemness genes and pathways in various cancer stem cell models involved in different types of blood cancers (i.e., leukemias). Several of the proposed drugs were already in development by pharmaceutical companies (including Sanofi, AstraZeneca and Roche) for non-leukemia applications and one candidate drug is a novel monoclonal antibody (against ROR1) developed by members of the California team (Dr. Tom Kipp’s lab). In June 2014, a formal investigational new drug (IND) application was filed with the FDA to support a Phase I study with the ROR1 antibody. It is also anticipated that patient enrolment for a clinical trial in chronic lymphocytic leukemia will commence soon.
- The Mak/Slamon team (which leveraged resources of OICR’s CSC Program devoted to solid tumours) developed novel drug candidates to target cancer stem cells in colorectal cancer, ovarian cancer and glioblastoma. Two drug candidates developed at UHN were selected based on the observation that their respective target proteins are over-expressed in cancer stem cells and evidence that they play a role in resistance to chemo- and radiation-therapy. In 2013, a CTA submission was approved by Health Canada for a PLK4 inhibitor identified in the laboratory of Dr. Tak Mak and a clinical trial was initiated at the Princess Margaret Cancer Centre (Princess Margaret).

C.2. Better use of cancer medicines

C.2.1. Personalized biomarkers to select chemotherapy

Since its founding, OICR has recognized the importance of delivering the vision of personalized medicine, through improvements in research, therapeutics, imaging and diagnosis of cancer. Under the leadership of Dr. John Bartlett, the Transformative Pathology group has been pivotal in the establishment of two international clinical trials using diagnostic biomarkers to direct chemotherapy. The Response to Optimal Selection of neo-adjuvant Chemotherapy in Operable breast cancer (ROSCO) trial, which will open to recruitment in 2014, will test the efficacy of
biomarkers in selecting patients for either taxane- or anthracycline-based chemotherapy. The Optimal Personalized Treatment of early breast cancer using Multi-parameter Analysis (OPTIMA) trial will test the safety of multi-parameter molecular testing to select patients who can avoid aggressive chemotherapy for clinically high risk, but molecularly low risk cancers.

Novel research within the Transformative Pathology Program has led to the submission of two patent applications in 2014, underpinning the future development of molecular diagnostic panels in breast cancer. A pipeline of novel candidate biomarkers has been established with the support of local and international collaborators. Increasingly, the program will focus on the development of linked preclinical and clinical evidence for theranostic targets in drug-resistant breast cancer and seek to strengthen collaborations with the NCIC CTG and eventually other trial groups to support development of innovative clinical trials to accelerate delivery of personalized medicine.

C.2.2. Improved management of early breast and prostate cancers

OICR launched a translational research initiative (TRI) entitled Improved Management of Early Cancer or IMEC to address challenges associated with the management of patients with early breast or prostate cancer. While successful early diagnosis of these diseases certainly saves lives, it also results in the detection of small and pre-invasive cancers that may not progress during the life of the patients. This leads to significant overtreatment, increased morbidity and unnecessary healthcare costs. Developing tools to better discriminate aggressive versus indolent forms of the disease, will allow oncologists to manage patients according to specific characteristics of their disease. This will be a major advance in the personalization of cancer care. OICR has launched several projects related to this:

Breast Cancer

• The incidence of ductal carcinoma in situ (DCIS) of the breast has increased dramatically in recent years as a result of the widespread introduction of screening for breast cancer. In many cases a diagnosis of DCIS will neither be followed by a recurrence of DCIS nor by progression to invasive carcinoma even in the absence of adjuvant radiotherapy or hormonal treatment. To develop novel molecular diagnostic assays, OICR is supporting a multinational initiative linking clinicians/scientists from Ontario, Italy and Sweden to map the key molecular events driving progression from pre-invasive to invasive carcinoma through whole exome sequencing of paired primary DCIS and subsequent recurrent disease. The project will capitalize on an Ontario population-based cohort established by Dr. Eileen Rakovitch at Sunnybrook Health Sciences Centre (SHSC). The cohort includes all cases of DCIS diagnosed in Ontario from 1994 to 2003 (n=8,257) with complete data on treatment and outcomes. A tissue bank was established for cases within the provincial cohort. This will accelerate delivery of novel diagnostic approaches arising from OICR’s discovery approach into novel diagnostic tests for DCIS. OICR’s Health Services Research (HSR) Program is also involved, developing a relevant disease and economic model to ensure that any new test developed provides a cost-effective diagnostic solution that could be considered for large-scale implementation;
Prostate Cancer

- OICR supports a study led by Dr. Laurence Klotz, a leader at SHSC that is recognized for his work in active surveillance (AS) of early prostate cancer. OICR facilitated a partnership with scientists in OICR’s Imaging Translation Program (ITP) that pioneered the development of a superior biopsy system combining identification of lesions by MRI with fusion of the images with trans-rectal 3D ultrasound to guide biopsies. The Active Surveillance Magnetic Resonance Imaging Study Trial (ASIST) was launched to evaluate whether multi-parametric MRI can improve the management of prostate cancer patients on AS. This multicentre, prospective, randomized Phase III trial was started in 2011 and is enrolling patients with previously untreated favourable risk prostate cancer. As of September 1, 2014, 234 patients have been registered, 211 patients are randomized and data should start to become available for an analysis of the trial in 2014-15. Linked to this study is an invaluable sample biobank being developed for future biomarker research;

- Prostate Cancer Canada and OICR invested $15 million and $5 million, respectively, to support the Canadian Prostate Cancer Genome Network (CPC-GENE) led by Dr. Rob Bristow at UHN. CPC-GENE, which is a member project of the International Cancer Genome Consortium (ICGC), is supported by OICR’s Genome Technologies Program for sequencing whole cancer genomes from 400 intermediate risk prostate cancers. A primary objective of this project is to identify genetic signatures that differentiate intermediate risk tumours that responded well to treatment compared to those that did not. CPC-GENE is also sequencing multiple regions of prostate cancer from the same gland to determine if and how the genetic make-up of prostate cancer varies within an individual man’s prostate. This has led to the discovery and subsequent validation of several genomic biomarkers that have excellent potential for clinical translation;

- In July 2014, IMEC received an additional $5 million award from Prostate Cancer Canada and Movember for the “prostate cancer program project in rapid development of novel diagnostic markers for early prostate cancer (PRONTO)”. PRONTO is a multiphase research program linking eight Canadian research institutes and 16 investigators with the objective of developing, validating and demonstrating clinical utility for novel diagnostic approaches to early prostate cancer. PSA screening coupled with diagnostic uncertainty, relating to Gleason grading, at core biopsy results in the overtreatment of many early prostate cancers. PRONTO aims to develop novel diagnostic approaches and validate novel diagnostic assays in cohorts of 2,000 specimens of Gleason 6 and 2,000 specimens of Gleason 7 prostate cancer, each with at least ten years of clinical follow-up.

C.2.3. Big data and genomics to improve patient management

OICR has established itself as an international powerhouse in “Big Data” in genomics and health. Much of our expertise was driven by our commitment to the ICGC and OICR’s informatics team being chosen as the Data Coordination Centre of the Consortium (which currently includes 74 cancer genome projects based in 18 countries). The new ICGC Data Portal provides scientists worldwide with new powerful tools for exploring and visualizing the variants and annotations available from all ICGC projects. OICR’s data portal for the ICGC currently provides cancer
genome datasets generated by 50 cancer genome projects involving 12,232 donors (Data Release #17, Sept 2014; Figure 4).

Figure 4: ICGC Data Portal Cumulative Donor Count

The magnitude of the effort grew with the launch of the ICGC Pan-Cancer Analysis of Whole Genomes (PCAWG) project. This project aims to comprehensively catalogue patterns of cancer-related variation in the underexplored 95 per cent of the genome that contains key non-coding, regulatory and structural sites. To achieve this, the project aims to harmonize the alignment and variant calling of 2,000+ whole human genomes from ICGC projects. OICR’s software engineering team has taken on a fundamental role in this effort, which appears to be one of the largest data analysis projects of its kind. The data centres participating in the project are the Embassy Cloud at EBI (London), the Barcelona Supercomputer Center, IMSUT+RIKEN (Tokyo), ETRI (Seoul), the German Cancer Research Center (DKFZ, Heidelberg), and the University of Chicago Protected Data Cloud. Each data centre will make somatic mutations available to authorized PCAWG participants. A steering committee composed of five international superstars in cancer bioinformatics (P. Campbell/Sanger, G. Getz/Broad, J. Korbel/DKFZ, L. Stein/OICR, and J. Stuart/UCSC) are coordinating 15 working groups and 130 research subprojects relating patterns of mutation in genes and their regulatory regions, large-scale structural changes in the genome, evolution of cancer cells, and clinical outcomes, among others. The editors of Nature and Nature Genetics have offered to publish special issue(s) in 2015 to describe the findings of this massive undertaking.

In a related project, OICR investigator Paul Boutros is co-leading the ICGC-TCGA DREAM mutation-calling challenge, an international competition to develop and test algorithms for the accurate detection of cancer mutations in genomic data. This challenge has already led to significant improvements in mutation detection algorithms, standardization of mutation reporting and benchmarking technologies.
OICR’s leadership role in Big Data projects was recognized by two recent awards:

- Dr. Lincoln Stein, OICR’s Director, Informatics and Bio-Computing, led a team grant application entitled “The Cancer Genome Collaboratory” submitted to the Natural Sciences and Engineering Research Council of Canada (NSERC) for a Big Data Science Competition. Stein and his team were the only successful awardees. They will receive $7 million from NSERC and partners (Genome Canada, Canadian Institutes of Health Research (CIHR) and the Canada Foundation for Innovation (CFI));

- The OICR team supporting the ICGC Data Coordination Centre (led by Stein, Dr. Vincent Ferretti and Francis Ouellette) and the University of Chicago (BioNimbus) bid for a contract from the National Cancer Institute (NCI) to develop and maintain the NCI Cancer Genomic Data Commons. OICR and BioNimbus were the only applicants to be invited to a reverse site visit at NIH in April 2014 and subsequently, were awarded $5 million over four years for this project.

To realize the full potential of genetic and clinical research data, a group of more than 215 organizations in 28 countries, including OICR, have forged the Global Alliance for Genomics and Health (GA4GH) to establish a common international framework that will allow genetic and clinical data to be collected, managed and shared in an effective, responsible and interpretable manner. OICR was a founding partner organization in the GA4GH and is the home base of its Executive Director, Peter Goodhand.

The establishment of a big data powerhouse at OICR is an opportunity for Ontario to take centre-stage in a new era of digitized medicine in oncology and other diseases. This is an opportunity to develop software products needed for the application of personalized medicine concepts in the clinical management of cancer patients in Ontario and beyond.

C.2.4. Personalized biomarkers to select targeted therapies

OICR’s High Impact Clinical Trials, Genomics, and Informatics and Bio-computing programs collaborated with the Princess Margaret and four additional Ontario sites (in Hamilton, London, Ottawa and Thunder Bay) to conduct the Genomics Pathway Study. This was Canada’s first multicentre clinical trial evaluating clinical genomic profiling in patients with advanced cancers to identify driver mutations that may determine that a patient will respond to standard or experimental targeted agents. The trial demonstrated the feasibility of real-time next generation sequencing (NGS) profiling and developed the analytical pipeline and information tools for initial detection and identification of the clinical significance of genetic variants.

HICT and Imaging programs have collaborated on three multicentre clinical trials of novel imaging modalities to predict response to angiogenesis inhibitors, HER2 inhibitors, and therapies for castrate-resistant prostate cancer (CRPC). The program has also supported the evaluation of
three technologies for the detection and molecular analysis of circulating tumour cells as an alternative to invasive tumour biopsies in multicentre trials evaluating targeted cancer therapies.

HICT and genomics programs are collaborating with NCIC CTG on a multicentre umbrella protocol in rare tumours evaluating two targeted agents in 11 histologic and genetic cohorts to identify genomics markers of response.

OICR collaborated with Janssen on two trials: 1) Assessment of new imaging strategies for CRPC: predictive value of established ($^{18}$F-FDG PET/CT) and novel PET radiotracers ($^{18}$F-DCFBC PET/CT); 2) Assessment of CRPC response through comprehensive characterization using novel biomarkers (CTC, microparticles, $^{18}$F-FCH PET/MRI), initiated in 2014.

C.3. New medical devices to monitor and treat cancer

C.3.1 Improvements in detecting, diagnosing, monitoring, and treating cancer

OICR’s imaging programs (Smarter Imaging and Imaging Translation), under the leadership of Dr. Martin Yaffe at SHSC and Dr. Aaron Fenster at the Robarts Research Institute, Western University have generated an impressive number of medical devices, many of which are being evaluated in clinical studies to demonstrate that improved diagnosis and monitoring of treatment response of tumours can better inform clinical decisions and improve patient outcome. To augment the resources and complement the expertise required to commercialize these technologies, Drs. Yaffe and Fenster applied for and were awarded a $13.3 million CECR grant from the federal government. Tables 3 to 6 indicate promising technologies being developed by OICR’s imaging team, in partnership with other OICR programs (IMEC, Transformative Pathology, HICT, and PanCuRx) as well as the FACIT commercialization team.
Prostate Cancer

<table>
<thead>
<tr>
<th>Deliverable</th>
<th>Status (2014)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multimodality-guided biopsy to improve the management of prostate cancer</td>
<td>2 disclosures; 3 patents filed; 3D ultrasound (US) guided prostate biopsy system with magnetic resonance (MR) fusion in clinical trial in London with 13 patients enrolled; motion compensation software being evaluated in clinic; IP licensing to new start up in Toronto; and licensing discussions with another company.</td>
</tr>
<tr>
<td>MR-guided focal thermal prostate therapy hardware and software</td>
<td>2 disclosures; 2 patents filed; completed phase 1 trial (11 patients) – safety of the intervention is confirmed; In discussions with investors to spin out company.</td>
</tr>
<tr>
<td>A system for registering in vivo and pathology images for the prostate</td>
<td>Whole-mount prostate sections annotated by pathologists; registration between multi-parametric MR images and annotated prostate pathology sections completed; assessment of correlation between prostate tumour appearance and Gleason grade from pathology in progress; development of 3D pathology viewing software underway; and, discussion of licensing 3D histopathology viewing software to Canadian company underway.</td>
</tr>
</tbody>
</table>

Table 3: Medical devices developed for prostate cancer.

Breast Cancer

<table>
<thead>
<tr>
<th>Deliverable</th>
<th>Status (2014)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Microbubble contrast US and transient elastography imaging</td>
<td>The study has received Health Canada and Research Ethics Board (REB) approval; eight patients have been imaged to date; preliminary analysis of data from six patients is promising.</td>
</tr>
<tr>
<td>US methods for evaluating response to therapy in locally advanced breast cancer (LABC)</td>
<td>In a retrospective study, there is a statistically significant separation of responders from non-responders at four weeks after the start of chemotherapy, suggesting that US technology is superior to evaluate treatment response than the optical method, and more practical for patients. This could become (if validated by prospective studies) the basis for making an early treatment modification decision. A pilot prospective study has been initiated at SHSC, Princess Margaret and MD Anderson Cancer Center to demonstrate that this approach is feasible in a multicentre setting. A partnership is being established with GE and commercial development under Federal Economic Development (FedDev) funding for future product development.</td>
</tr>
<tr>
<td>New Magnetic Resonance Imaging (MRI) methods to guide changes and therapy for LABC</td>
<td>Testing of multi-stage dynamic contrast enhanced (DCE) and chemical exchange saturation transfer (CEST) sequences in a clinical environment. 15-minute protocol has been implemented in patients. CEST is being adapted for other tumours, including brain and cancer.</td>
</tr>
</tbody>
</table>

Table 4 Medical devices developed for breast cancer.
Pancreatic Cancer

<table>
<thead>
<tr>
<th>Deliverable</th>
<th>Status (2014)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MRI coil for imaging of the pancreas</td>
<td>Over 40 per cent gain in signal-to-noise-ratio; a patient controlled compression device has now been constructed and tested; patent filed; Centre for Imaging Technology Commercialization (CIMTEC) completed contract negotiations with the National Research Council (NRC) of Canada for coil design; REB application submitted for testing on human volunteers. This technology could be the basis for improved screening of high-risk patients or could be used for better staging before surgery.</td>
</tr>
</tbody>
</table>

Table 5: Medical devices developed for pancreatic cancer.

Liver Cancer

<table>
<thead>
<tr>
<th>Deliverable</th>
<th>Status (2014)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Develop multi-modality guided focal thermal liver ablation hardware and tumour segmentation software</td>
<td>Five disclosures, three patents filed; image acquisition, reconstruction and segmentation in clinical trial with 40 liver cancer patients in progress. 32 completed; image acquisition of liver cancer patients with radiofrequency applicators inserted in tumour – clinical evaluation – five patients; preclinical evaluation of 3D imaging system used for monitoring thermal ablation; and CIMTEC leading licensing discussions with company.</td>
</tr>
</tbody>
</table>

Table 6: Medical devices developed for liver cancer.

C.4. Addressing high priority issues in cancer care

OICR and CCO created a joint Health Services Research (HSR) program to provide the knowledge needed to optimize the delivery of cancer services and to ensure appropriate dissemination of health services research innovations and well-evaluated technologies. Fifteen research studies were conducted between 2010 and 2013 that spanned the continuum of cancer care, from screening to symptom management in later stages of cancer. A report of these studies prepared in 2014 is provided separately (Binder 1, Tab 2.2).

With input from OICR, CCO and the HSR Program Scientific Advisory Board, the following projects were initiated in 2014, based on the potential for clear impact by: 1) directly benefitting patients; 2) optimizing healthcare resource utilization in Ontario; and/or 3) reinforcing the infrastructure for the conduct of health services research in Ontario and elsewhere:

- Improving follow-up of abnormal gFOBT in Ontario for CRC screening;
- Improving the management of pain in cancer patients in Ontario;
- Ambulatory management of chemotherapy induced toxicity;
• Improving chronic disease outcomes in cancer survivors;
• Administrative databases for oncology case costing in Ontario;
• Knowledge translation research network: Implementation of innovations; and
• Data infrastructure.

C.5. Progress in understanding cancer

C.5.1. Pancreatic ductal adenocarcinoma

By 2030, cancer of the pancreas is projected to surpass breast, prostate, and colorectal cancers to become the second leading cause of cancer-related death in the United States (and presumably in Canada too). In order to tackle this fatal yet understudied form of cancer, OICR launched a cross-program initiative called PanCuRx, aiming at improving the effectiveness of early detection, diagnosis and treatment of Pancreatic Ductal Adenocarcinoma (PDAC) with the ultimate objective of improving the clinical outcomes of patients diagnosed with PDAC.

Ontario is particularly well positioned to address the clinical challenges associated with pancreatic cancer because of the expertise and the strengths already available. Most cases are recorded and centralized through the Ontario Pancreatic Cancer Study at Mount Sinai Hospital in Toronto. Surgical therapy is conducted at a few high-volume centres throughout the province. Multidisciplinary care is provided to patients and clinical research is part of the standard of care for patients with advanced disease. This centralized approach promotes uniform treatment practices throughout the province and OICR is capitalizing on this centralized system to have access to tumour samples well-annotated for clinical outcomes, and to enhance patients’ participation in clinical studies.

PanCuRx integrates genomic, bio-informatics, drug discovery, biology, pathology, imaging and animal model efforts, under the leadership of Dr. Steven Gallinger, Senior Investigator at the Lunenfeld-Tanenbaum Research Institute of Mount Sinai Hospital. Among the early deliverables of the program, we note the following:

• Establishment of a biobank with more than 400 tumours and matched reference material annotated with extensive clinical data;
• Advances in tumour enrichment methods through laser capture microdissection (LCM) and flow-sorting, providing enriched tumour content of 75-95 per cent to improve the quality of “omics” analysis;
• 191 exomes from primary tumours, xenografts and matched controls deposited in the ICGC database;
• Whole genome sequencing for > 100 enriched samples with matched references;
• Evaluated two candidate targets with drug discovery potential;
• Developed an MRI coil for imaging of the pancreas (described above);
• Understanding the role of hypoxia and tumour infiltrating cells: 1) Pimonidazole Trial accrued 70 patients (target = 100); 2) Imaging trial using 19F-FAZA trial in advanced pancreatic cancer patients; and investigation of a novel agent (TH-302) alone or in combination with radiotherapy to study the effect on the stem cell population.
D. Platforms to accelerate translational research

D.1. Platforms for drug discovery

D.1.1 Innovations in target validation

In recognition of the relatively low throughput and frequent challenges in understanding the biological role of novel cancer targets identified by large-scale sequencing and functional genomic screens, OICR-supported scientists launched an ambitious program to develop and deploy new technologies. Under the leadership of Dr. Robert Rottapel (UHN) and Drs. Sachdev Sidhu and Jason Moffat (University of Toronto), the Innovation in Target Validation (ITV) Program was launched to develop and deploy new technologies that will accelerate the identification and validation of candidate targets (or target classes). The Program is making significant progress in engineering new inducible, lentiviral-based shRNA libraries and inducible, CRISPR-Cas9-regulated gene editing libraries designed to improve genome-scale screening of kinases, ubiquitins and other potential drug targets. Using phage-display libraries, the Program has already developed highly selective peptide-based inhibitors directed against 44 human ubiquitin modifying enzymes that have also been identified as common essential genes in ovarian cancer using RNAi screens. Additionally, novel mass spectrometry-based methods are being used to monitor adaptive responses across the kinome to identify mechanisms of drug resistance in ovarian cancer cells. The program has enabled the development of innovative methods used to discover new cancer targets, inhibitory molecules and mechanisms of drug resistance in ovarian cancer, the 5th most common cancer for women and the most fatal women’s cancer.

Between 2008 and 2013, OICR partnered with the Terry Fox Research Institute (TFRI) in supporting the Selective Therapies Program, led by Rottapel. The Program supported the establishment of the Toronto Recombinant Antibody Centre (TRAC) led by Sidhu, recipient of an OICR Investigator Award. The TRAC is now an independent, highly successful synthetic antibody platform that relies on funding from Genome Canada, the Ontario Ministry of Research and Innovation, NIH, CIHR, and others. As a next step in the development of the TRAC capabilities, Sidhu applied to the CECR program and was recently awarded $15 million to launch the Centre for the Commercialization of Antibodies and Biologics (CCAB).

D.1.2. Medicinal chemistry and drug discovery

OICR’s Drug Discovery Program was originally established in 2008 as a Medicinal Chemistry Platform at OICR. The mission was to build a drug discovery program that could efficiently translate cancer-related academic discoveries into novel oncology therapies. Top talent with academic and industry experience was recruited and strong links with local researchers in the oncology field were forged. The platform matured into a drug discovery program, with capabilities in medicinal and synthetic chemistry, analytical chemistry and analytical method development, computational chemistry, drug delivery and formulation, biochemistry and cell biology, in vitro and in vivo ADME, early toxicity testing and efficacy studies. The group currently comprises 28 members with extensive experience in academia, pharma and biotech and has
collectively contributed to multiple Investigational New Drug (IND) submissions. The team has completed due diligence on more than 60 projects, has contributed to more than 25 projects with local researchers (e.g., by providing ADME/PK support, designing and providing tool compounds, developing assays, providing focused libraries for screening, etc.). The team has provided libraries and tool compounds to collaborators for screening, guided them in the interpretation of results and evaluation of hits from screens, and helped them generate data that have strengthened grants and enabled collaborators to obtain external funding.

Full scale drug discovery efforts on seven projects have been completed to date, with BCL6 (described previously) as the most advanced. In keeping with the philosophy of embedding medicinal chemists in academic settings, BCL6 is an example of a challenging project. The target is a protein-protein interaction. These have been traditionally difficult to drug due to challenges associated with using a small molecule to interfere with a large protein surface area. However, the team has made significant progress in identifying and optimizing small molecule inhibitors. Another notable breakthrough was the development of a proprietary nanotechnology (NanoCMC) that is being studied for delivery of anti-cancer agents. To date, the technology (Cellax) has been used to formulate Cabazitaxel, a drug approved for the treatment of prostate cancer. The new formulation has been shown to decrease the toxicity of the free drug and preliminary data suggests superior efficiency in prostate cancer animal models. The NanoCMC technology is being expanded for delivery of other anti-cancer agents that are difficult to formulate, or are too toxic in their current formulations. The Drug Discovery team works closely with FACIT, participates in due diligence and partnership meetings with industry and academia and contributes significantly to the Institute’s reputation with national and international biotechnology and pharmaceutical companies.

**D.2. Preclinical platforms for biomarker discovery**

**D.2.1. Ontario Tumor Bank**

The Ontario Tumour Bank (OTB) was created in 2004 with the goal of providing access to high quality biospecimens to academic and industry researchers across Ontario, Canada and beyond. OTB participating sites are located in Hamilton, Kingston, London, and Ottawa. OTB operates within a protected envelope within OICR and is supplemented using cost recoveries. To date, OTB has collected more than 111,000 biospecimens from more than 13,955 patients, and has fulfilled 295 requests through the release of more than 31,000 sample aliquots to researchers. In a recent comparison of OTB with five other tumour banks in Canada, OICR was the leader in regard to the number of biospecimens released per year, the number of projects supported, external revenues, and percentage of cost recovery. OTB has contributed to several projects of the NIH-sponsored The Cancer Genome Atlas (TCGA) project and was acknowledged in five TCGA-related Nature publications.
D.3. Platform for clinical research

D.3.1. Canadian Cancer Clinical Trials Network

Canada has an outstanding history of cancer clinical trials that are investigator-driven, with world-class clinical trial collaborative groups that conduct early- to late-phase trials, as well as a community of internationally-recognized cancer researchers. However, conducting clinical trials in the academic environment has become increasingly challenging due to the impact of the growing complexity of the regulatory process, trial design/objectives and the incorporation of more complex correlative studies occurring concomitantly with a long-term decline in institutional resources.

OICR inherited and continued several clinical trials support programs that were initiated by OICR’s predecessor, the Ontario Cancer Research Network. These include:

- The Ontario Cancer Research Ethics Board (OCREB): see section D.3.2.;
- The Clinical Trials Infrastructure Program and Business Development office devoted to improving clinical trials operations efficiency (standards, training, contracts, etc.) at Ontario sites. The aptitude of this team’s efforts in attracting trials to Ontario sites and increasing the number of patients in cancer trials led to the team’s selection as the national office of a Canada-wide clinical trials network described below.

In 2011 the Canadian Cancer Research Alliance (CCRA) published a report that identified many challenges associated with academic-driven clinical trials in Canada and recommended that the issues be addressed urgently. As a result of this recommendation, in 2013 the Canadian Partnership Against Cancer (CPAC) and the Canadian Cancer Research Alliance (CCRA) launched a competition for proposals to establish the Canadian Cancer Clinical Trials Network (3CTN) to strengthen academic-sponsored cancer clinical trials capacity in Canada. Under the leadership of Dr. Janet Dancey, Director of OICR’s HICT Program, OICR, in partnership with the NCIC Clinical Trials Group (NCIC-CTG) and the Network of Networks (N2) won this internationally adjudicated competition. Following this announcement in June 2013, the 3CTN Coordinating Centre was established to develop the Network’s business plan.

Over the course of nine months, the Coordinating Centre team worked with key stakeholders and collaborators within the scientific, adult and pediatric cancer research, lay, funder, and government communities from across the country to develop a successful business plan. As a result of stakeholder consultations, 3CTN’s overarching goals and objectives are as follows:

- To improve patient access to academic clinical trials;
- To improve site performance of academic trials;
- To improve the trial environment for the conduct of academic clinical trials through collaboration and facilitation of important national trial initiatives; and
- To demonstrate impact of the Network and academic trials on the Canadian health system.
In early May 2014, OICR received the following report from the Expert Panel established to review the Network’s business plan: "The Review Panel are delighted to report that after a rigorous and lengthy process, they were able to inform CPAC and the associated potential funders of the 3CTN that the business case is of very high quality. It represents the excellent product of a prolonged, thoughtful, and detailed piece of preparation and consultation carried out by Dr. Dancey, Ms. Arts, and their colleagues. We believe that, with continued support from colleagues across Canada, the business case describes an opportunity to transform clinical cancer research across Canada. This will result in benefits for Canadian cancer patients and substantially enhance the health system and the reputation of Canada as a world leader in this field. There is considerable potential for positive impact on the Canadian economy, in particular within the biotechnology and health sectors".

As of July 2014, 3CTN has secured or expects commitments for over $6 million per year from 10 cancer agencies (provincial, federal, and philanthropic charities). 3CTN represents a tremendous and unique opportunity to conduct higher-quality and more innovative academic cancer clinical trials, to increase patient participation and to create and foster multi-institutional collaborations, thereby benefiting cancer patients in the province of Ontario and in Canada.

D.3.2. Ontario Cancer Research Ethics Board

The Ontario Cancer Research Ethics Board (OCREB) provides high-quality, efficient ethics review and oversight of multi-centred cancer clinical trials in Ontario (See Figure 5). Established in 2004, OCREB serves 26 of the 27 hospitals in Ontario that conduct cancer clinical trials. OCREB supports trials sponsored by academia and industry. Once a clinical trial is up and running, OCREB continues to serve as the REB, centralizing the oversight function that would otherwise be duplicated by the local REBs. OCREB has been recognized for its efficiency and commitment to enhancing the protection of human research participants. The timing for approval for new multi-centric studies is 11.2 weeks, which is very attractive for sponsors. OCREB is at the forefront of several national and provincial initiatives that are focused on streamlining the process of REB review for all clinical trials.
Figure 5: Number of clinical trials supported by OCREB

D.4. Platforms for population and health services research

D.4.1. Ontario Health Study

The Ontario Health Study (OHS) is an innovative population-based cohort study that will serve as an integrated platform for investigating potential environmental, lifestyle and genetic causes of cancer, heart disease, diabetes, and other common chronic diseases. Using an online questionnaire, the study has already recruited more than 225,000 participants who are over 18 years of age and living in Ontario. Special efforts have been made to capture the ethnic, geographic and cultural diversity of Ontario. OHS subjects will be followed up for future diagnoses of cancer and other health endpoints through data linkage with the Ontario Cancer Registry and other health-related data collected by the province and housed at the Institute for Clinical and Evaluative Sciences (ICES). The intent is to follow participants for their entire lifespan.

The study is harmonized to a large extent with other provincial, national, and international initiatives. In particular, more than 150,000 OHS participants are in the 35 to 69 age range, contributing approximately half of the 300,000 participants recruited in a harmonized, eight-province, pan-Canadian cohort consortium called the Canadian Partnership for Tomorrow project (CPTP).

A desired goal that is behind schedule is the OHS biospecimen collection, currently at approximately 22,000 specimens. The OHS is addressing this deficit in several ways. The cohort established a contract with LifeLabs Medical Laboratory Services, which operates at more than 120 locations in Ontario, to enable the province-wide collection of blood from participants. Furthermore, OHS has developed and successfully piloted mobile assessment centres for
collecting blood samples and physical measures from existing and new study participants in communities not well serviced by LifeLabs. Lastly, the OHS is planning a new wave of recruitment emphasizing biospecimen collection as an essential part of participation.

D.4.2. cd-link

The Ontario Cancer Data Linkage Project (‘cd-link’) is an initiative of the OICR/CCO Health Services Research (HSRP) Program. Through a collaborative agreement with CCO and the Institute for Clinical Evaluative Sciences (ICES), cd-link is a data release program whereby administrative datasets relevant to cancer health services research, such as the Ontario Cancer Registry and Ontario Health Insurance Plan claims are linked, de-identified and with the protections of a comprehensive Data Use Agreement, provided directly to researchers. An innovation of the cd-link initiative is the mechanism by which the data are de-identified. All data are made anonymous by removing personal identifiers, according to Ontario (PHIPA) and U.S. (HIPAA) privacy legislation, and then further statistically de-identified. The de-identification process is conducted by a cd-link analyst in collaboration with the researcher to ensure that the final de-identified data still allow the researcher to achieve the objectives of his/her research while maximizing security of the data.

Previously, linked data from tumour registries, administrative claims, and other sources were housed internally at ICES. To access the data, a researcher had to enlist an internal ICES scientist as a co-investigator and pay for analyses to be done by ICES analysts. Through establishment of the ‘cd-link’ program, the OICR HSRP allowed for the first time de-identified data to be released directly to investigators for minimal to no cost. This model has been so successful that ICES has now created a ‘Data and Analytics Services’ platform to make all of its data available in a similar way.

D.4.3. Oncology case costing in Ontario

Given the rising cost of developing new diagnostic and therapeutic interventions (i.e., drugs, technologies, biomarkers), clinical investigators and administrators must have access to rapid and reliable cost evaluation in order to make rational investment decisions. OICR’s HSRP team has already linked a number of oncology-specific data sets from CCO with the provincial health system databases held at ICES and developed costing algorithms for a number of disease sites. These methods have been used to populate comparative economic evaluations for a variety of interventions. This platform has already demonstrated significant impact on understanding and improving resource utilization for the management of cancer patients. Currently, the team is developing “user friendly” modules for costing different types of interventions (e.g., hospitalization for febrile neutropenia, cost of adjuvant treatment) that will become readily available to healthcare professionals and provincial decision makers, and will facilitate future costing module development or enable comparative effectiveness costing studies.
E. Provincial, National and International Collaborations

OICR has been proactive in bridging collaborations within Ontario and Canada, as well as internationally (See Figure 6; specific information on named initiatives has been provided in previous sections of this document). Such networks not only contribute to the global visibility of OICR’s scientists, but more importantly, they raise the bar in regard to scientific excellence. Furthermore, by augmenting the number of patients in studies, there is increased power to detect and validate research results.

![Diagram of collaborations](image)

**Figure 6: OICR major initiatives**

According to Scimago Institutions Rankings ([www.scimagoir.com](http://www.scimagoir.com)) that are generated by Scimago Lab ([www.scimagolab.com](http://www.scimagolab.com)) and Elsevier’s ([www.elsevier.com](http://www.elsevier.com)) SCOPUS ([www.elsevier.com/online-tools/scopus](http://www.elsevier.com/online-tools/scopus)) (see *Binder 1, Tab 2.3*), OICR scientists based at the MaRS campus are ranked 3rd among 103 research institutes in Canada and 197th of > 5100 institutes worldwide for the indicator “research collaboration”. This indicator is calculated on the publication output ratio produced in collaboration with foreign institution and is independent of the size of the Institute. Both the Canadian and international ranking position indicate OICR’s effectiveness in collaborating with international scientists; this is not surprising as OICR scientists based at MaRS are involved in many consortia (i.e., International Cancer Genome Consortium).
F. External Awards received through peer-reviewed competitions

The natural growth of translational research programs that are maturing new assets towards clinical studies or commercialization outcomes requires OICR leaders to partner and raise new sources of revenue. However, OICR has been challenged by two major sources of financial strain: 1) The Ontario Ministry of Research and Innovation’s (MRI) base funding decreased from $82 million/year to $77 million/year in 2013/2014 and is scheduled to decrease (only temporarily or not at all, we hope) to $72 million/year in 2015/2016; and 2) Federal support for science and technology has declined by 14.4 per cent over the last five years. In spite of this, OICR has been proactive in seeking new sources of revenue.

Table 7 shows the leveraged funds expended by OICR-supported programs, projects and investigators in the last four fiscal years. Annual totals (from all categories) indicate growth. It should be noted that there is a steady increase in private sector funds, but that most of these funds are allocated to OICR start-ups and not to OICR’s research programs.

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Table 7: Sources of leveraged funds that support OICR’s research and investigators and OICR’s spinoffs. OICR’s program expenditures are reported annually by program directors and investigators located at Ontario-based institutions (including OICR’s headquarters at MaRS). Expenditures at start-up firms that have been created or supported by OICR (usually through the Intellectual Property Development and Commercialization Fund) are obtained from a variety of sources.

It is worth noting that 2014-2015 appears to be a boom year for both OICR’s research programs and start-up companies (now part of the FACIT portfolio, described in a separate document). More than $50 million in large grants was awarded to OICR’s program-related projects and $37 million in private investments was made to FACIT spin-off companies in the first eight months of 2014. A further $25 million in potential awards, investments and contracts is expected in the latter part of 2014.
G. Scientific Productivity and Research Excellence

Tables 8, 9 and 10 provide numerical information on OICR publications, patent applications and patents awarded between April 2010 and March 2014. More detail on the higher impact articles per OICR program is available in Binder 1, Tab 3.

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<thead>
<tr>
<th>Categories</th>
<th>FY2010-11</th>
<th>FY2011-12</th>
<th>FY2012-13</th>
<th>FY2013-14</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unrated journals</td>
<td>51</td>
<td>75</td>
<td>118</td>
<td>73</td>
<td>348</td>
</tr>
<tr>
<td>0.001-10.999</td>
<td>177</td>
<td>313</td>
<td>365</td>
<td>424</td>
<td>1,343</td>
</tr>
<tr>
<td>11.000-20.999</td>
<td>33</td>
<td>31</td>
<td>47</td>
<td>40</td>
<td>154</td>
</tr>
<tr>
<td>21.000-30.999</td>
<td>13</td>
<td>8</td>
<td>8</td>
<td>13</td>
<td>45</td>
</tr>
<tr>
<td>31.000-60.000</td>
<td>14</td>
<td>10</td>
<td>21</td>
<td>15</td>
<td>62</td>
</tr>
<tr>
<td>Total</td>
<td>288</td>
<td>437</td>
<td>559</td>
<td>565</td>
<td>1,952</td>
</tr>
</tbody>
</table>

Table 8. Number of peer reviewed publications supported by OICR funding, classified by Journal Impact Factor

<table>
<thead>
<tr>
<th>Categories</th>
<th>FY2010-11</th>
<th>FY2011-12</th>
<th>FY2012-13</th>
<th>FY2013-14</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Research Programs</td>
<td>14</td>
<td>21</td>
<td>26</td>
<td>23</td>
<td>84</td>
</tr>
<tr>
<td>IPDCP</td>
<td>10</td>
<td>1</td>
<td>3</td>
<td>4</td>
<td>18</td>
</tr>
<tr>
<td>Total</td>
<td>24</td>
<td>22</td>
<td>29</td>
<td>27</td>
<td>102</td>
</tr>
</tbody>
</table>

Table 9. Number of patent applications per year

<table>
<thead>
<tr>
<th>Categories</th>
<th>FY2010-11</th>
<th>FY2011-12</th>
<th>FY2012-13</th>
<th>FY2013-14</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Research Programs</td>
<td>7</td>
<td>7</td>
<td>0</td>
<td>9</td>
<td>23</td>
</tr>
<tr>
<td>IPDCP</td>
<td>4</td>
<td>0</td>
<td>2</td>
<td>1</td>
<td>7</td>
</tr>
<tr>
<td>Total</td>
<td>11</td>
<td>7</td>
<td>2</td>
<td>10</td>
<td>30</td>
</tr>
</tbody>
</table>

Table 10. Number of patents awarded per year
Among the goals for OICR set out by the Ministry of Research Innovation, was the development of a "critical mass" of cancer researchers located in the MaRS Discovery District to take advantage of the biomedical and life sciences branding activities of the MaRS portal and to strengthen/augment cancer research excellence at affiliated institutions across Ontario. In planning the core OICR labs at MaRS, it was deemed important to not “recreate” another silo institute and to avoid building clusters that would significantly overlap with other clusters already established in the province. This is why, for example, there are no imagers or cancer biologists. OICR’s scientists to be based at MaRS were recruited to strengthen the Ontario cancer research network’s support of the Institute’s translational mission in disciplines that were less developed than other sites in the province, e.g. cancer genomics, informatics, medicinal chemistry and molecular pathology. The publication profile of this group for the period 2010-2014 is now available as part of Scimago Institutions Rankings (described earlier), because OICR’s authors based at MaRS use the name Ontario Institute for Cancer Research as their primary affiliation. In these rankings, OICR ranks well for indicators that are size-independent (Table 11):

<table>
<thead>
<tr>
<th>Indicator</th>
<th>Indicator Description</th>
<th>OICR’s Rank in Canada n=103</th>
<th>OICR’s Rank in World n=5100+</th>
</tr>
</thead>
<tbody>
<tr>
<td>High-Quality Publications</td>
<td>Ratio of publications that an institution publishes in the most influential scholarly journals of the world, those ranked in the first quartile (25%) in their field.</td>
<td>1</td>
<td>62</td>
</tr>
<tr>
<td>Excellence Rate</td>
<td>Excellence rate indicates the amount (in per cent) of an institution’s scientific output that is included in the set of the 10 per cent of the most cited papers in their respective scientific fields. It is a measure of high-quality output of research institutions.</td>
<td>1</td>
<td>27</td>
</tr>
<tr>
<td>Normalized Impact</td>
<td>Normalized Impact of led output is computed using the methodology established by the Karolinska Institutet in Sweden where it is named &quot;Item oriented field normalized citation score average&quot;. The normalization of the citation values is done on an individual article level.</td>
<td>1</td>
<td>12</td>
</tr>
<tr>
<td>Technological Impact</td>
<td>Percentage of the scientific publication output cited in patents. Based on PATSTAT (<a href="http://www.epo.org">http://www.epo.org</a>).</td>
<td>1</td>
<td>96</td>
</tr>
</tbody>
</table>

Table 11. OICR ranks according to Scimago Institutions Rankings (www.scimagoir.com).

With respect to the above indicator, it’s important to note that there are many ways to evaluate excellence that are not captured by these indicators. OICR’s ranking is driven by its collaborations with leading groups across Ontario, Canada and worldwide.
**H. Recruitment and retention**

To meet the goal of strengthening Ontario’s cancer research capacity by attracting outstanding researchers and clinician scientists to the province, OICR established an investigator award program designed to provide stable recruitment and retention funding for investigators involved in OICR’s Programs. There are currently three categories of OICR investigators and two categories of clinician scientists (CS):

- Investigator Level I: Designates investigators in the first five years of their career as independent researchers;
- Investigator Level II: Designates investigators who have spent five to 10 years as independent researchers;
- Senior Investigator: Generally designates investigators who have spent more than 10 years as an independent investigators and who meet criteria for national/international excellence;
- Clinician Scientist I and II (CS-I and CS-II): Designates clinician scientists with 80 per cent or 50 per cent protected research time, respectively.

As of October 1, 2014 OICR Investigator and Clinician Scientist Awards were used by 13 Ontario Institutes to augment capacity through the recruitment of 32 researchers and the retention of one scientist (Geoff Fong, Waterloo and leader of the ITC project). Of the 33 investigators, 15 have a medical degree. See Table 12.

<table>
<thead>
<tr>
<th>Investigator</th>
<th>Award</th>
<th>Host</th>
<th>Previous Institution/Company</th>
</tr>
</thead>
<tbody>
<tr>
<td>Laurie Ailles, PhD</td>
<td>Investigator</td>
<td>University Health Network</td>
<td>Stanford University, California</td>
</tr>
<tr>
<td>Rima Al-awar, PhD</td>
<td>Senior</td>
<td>Ontario Institute for Cancer Research</td>
<td>Eli Lilly, Indiana</td>
</tr>
<tr>
<td>Anita Bane, MD, PhD</td>
<td>CS II</td>
<td>McMaster University</td>
<td>Mount Sinai Hospital, University of Toronto, Ontario</td>
</tr>
<tr>
<td>John Bartlett, PhD</td>
<td>Senior</td>
<td>Ontario Institute for Cancer Research</td>
<td>Edinburgh University, Scotland</td>
</tr>
<tr>
<td>Nizar Batada, PhD</td>
<td>Investigator</td>
<td>Ontario Institute for Cancer Research</td>
<td>Harvard University, Massachusetts</td>
</tr>
<tr>
<td>Paul Boutros, PhD</td>
<td>Investigator</td>
<td>Ontario Institute for Cancer Research</td>
<td>University of Toronto, Ontario</td>
</tr>
<tr>
<td>Janet Dancey, MD</td>
<td>CS I</td>
<td>Queen’s University</td>
<td>National Cancer Institute/National Institutes of Health, Maryland</td>
</tr>
<tr>
<td>Craig Earle, MD</td>
<td>CS I</td>
<td>Cancer Care Ontario/institute for Clinical Evaluative Sciences</td>
<td>Dana-Farber Cancer Institute/Harvard University, Massachusetts</td>
</tr>
<tr>
<td>Vincent Ferretti, PhD</td>
<td>Senior</td>
<td>Ontario Institute for Cancer Research</td>
<td>McGill University/Genome Quebec, Quebec</td>
</tr>
<tr>
<td>Geoffrey Fong, PhD</td>
<td>Senior</td>
<td>University of Waterloo</td>
<td>(retention)</td>
</tr>
<tr>
<td>Steven Gallinger, MD</td>
<td>CS II</td>
<td>Ontario Institute for Cancer Research</td>
<td>University Health Network, Ontario</td>
</tr>
<tr>
<td>Rebecca Gladdy, MD, PhD</td>
<td>CS I</td>
<td>Mount Sinai Hospital</td>
<td>Memorial Sloan- Kettering, New York</td>
</tr>
<tr>
<td>Eva Grunfeld, MD</td>
<td>CS I</td>
<td>University of Toronto</td>
<td>Cancer Care Nova Scotia,</td>
</tr>
<tr>
<td>Name</td>
<td>Level</td>
<td>Institution</td>
<td>Location</td>
</tr>
<tr>
<td>-----------------------</td>
<td>-------</td>
<td>-----------------------------------------------------------------------------</td>
<td>-----------------------------------------------</td>
</tr>
<tr>
<td>Masoom Haider, MD, PhD</td>
<td>CS II</td>
<td>Sunnybrook Health Sciences Centre</td>
<td>Nova Scotia</td>
</tr>
<tr>
<td>Timothy Hanna, MD</td>
<td>CS I</td>
<td>Queen’s University</td>
<td>Liverpool Hospital, Sydney, Australia</td>
</tr>
<tr>
<td>Naoto Hirano, MD, PhD</td>
<td>CS II</td>
<td>University Health Network</td>
<td>Harvard Medical School, Massachusetts</td>
</tr>
<tr>
<td>Kristin Hope, PhD</td>
<td>Investigator Level I</td>
<td>McMaster University</td>
<td>Université de Montréal, Quebec</td>
</tr>
<tr>
<td>Tom Hudson, MD</td>
<td>Senior</td>
<td>Ontario Institute for Cancer Research</td>
<td>McGill University, Quebec</td>
</tr>
<tr>
<td>Rosalyn Anne Juergens, MD, PhD</td>
<td>CS II</td>
<td>McMaster University</td>
<td>Johns Hopkins Medical Institute, Maryland</td>
</tr>
<tr>
<td>Mathieu Lupien, PhD</td>
<td>Investigator Level II</td>
<td>University Health Network</td>
<td>Dartmouth Medical School, Dartmouth, New Hampshire</td>
</tr>
<tr>
<td>John McPherson, PhD</td>
<td>Senior</td>
<td>Ontario Institute for Cancer Research</td>
<td>Baylor College of Medicine, Texas</td>
</tr>
<tr>
<td>Brian Nieman, PhD</td>
<td>Investigator Level II</td>
<td>The Hospital for Sick Children</td>
<td>New York University, New York</td>
</tr>
<tr>
<td>David Palma, MD</td>
<td>CS II</td>
<td>The Lawson Health Research Institute/The University of Western Ontario</td>
<td>VU University Medical Center, The Netherlands</td>
</tr>
<tr>
<td>Bret J. Pearson, PhD</td>
<td>Investigator Level I</td>
<td>The Hospital for Sick Children</td>
<td>Howard Hughes Medical Institute/University of Utah, Utah</td>
</tr>
<tr>
<td>Mark Purdue, PhD</td>
<td>Investigator Level II</td>
<td>Ontario Institute for Cancer Research</td>
<td>National Cancer Institute, Division of Cancer Epidemiology and Genetics, Maryland</td>
</tr>
<tr>
<td>Timothy Scholl, PhD</td>
<td>Investigator Level II</td>
<td>Robarts Research Institute</td>
<td>University of Western Ontario, Ontario</td>
</tr>
<tr>
<td>Brian Shoichet, PhD</td>
<td>Senior</td>
<td>Leslie Dan Faculty of Pharmacy, University of Toronto</td>
<td>University of California, San Francisco</td>
</tr>
<tr>
<td>Dev Sidhu, PhD</td>
<td>Senior</td>
<td>The Terrence Donnelly Centre for Cellular and Biomolecular Research, University of Toronto</td>
<td>Genentech, California</td>
</tr>
<tr>
<td>Jared Simpson, PhD</td>
<td>Investigator Level I</td>
<td>Ontario Institute for Cancer Research</td>
<td>Wellcome Trust Sanger Institute, Cambridge, UK</td>
</tr>
<tr>
<td>Lincoln Stein, MD, PhD</td>
<td>Senior</td>
<td>Ontario Institute for Cancer Research</td>
<td>Cold Spring Harbor Laboratory, New York</td>
</tr>
<tr>
<td>Rosie Thein, MD, PhD</td>
<td>Investigator Level I</td>
<td>Dallas Lana School of Public Health, University of Toronto</td>
<td>University of New South Wales, Australia</td>
</tr>
<tr>
<td>Guy Ungerechts, MD, PhD (starting 2015)</td>
<td>CS I</td>
<td>Ottawa Hospital Research Institute</td>
<td>National Center for Tumour Diseases, Heidelberg, Germany</td>
</tr>
<tr>
<td>Brad Wouters, PhD</td>
<td>Senior</td>
<td>University Health Network</td>
<td>Maastricht University, The Netherlands</td>
</tr>
</tbody>
</table>

**Table 12:** List of Investigators and Clinician-Scientists supported by OICR Investigator Awards
I. Training

OICR’s principal approach to training is by embedding undergraduate and graduate-level trainees (MDs as well as PhDs) in OICR-supported research projects (See Table 13). This exposes trainees to multidisciplinary teams.

<table>
<thead>
<tr>
<th>Categories</th>
<th>FY2010-11</th>
<th>FY2011-12</th>
<th>FY2012-13</th>
<th>FY2013-14</th>
</tr>
</thead>
<tbody>
<tr>
<td>Postdoctoral Fellows</td>
<td>159</td>
<td>202</td>
<td>166</td>
<td>161</td>
</tr>
<tr>
<td>Students (MD, PhD, M.Sc., undergraduate)</td>
<td>269</td>
<td>286</td>
<td>293</td>
<td>291</td>
</tr>
</tbody>
</table>

*Table 13:* Number of trainees participating in OICR programs and/or supervised by OICR Investigators.

In addition, OICR established numerous training initiatives to enhance skills contributing to Ontario capacity and essential areas:

- Transformative Pathology Fellowships: OICR has made available a new funding opportunity for a Research Fellowship Award in Transformative Pathology (TP). This award was created to increase the opportunities for training pathologists in the area of molecular diagnostic pathology in Ontario. OICR currently supports three fellows through this scheme;
- Canadian Bioinformatics Workshops: The OICR bioinformatics team supports a national initiative that has organized training workshops in bioinformatics that provide bioinformatics skills to more than 200 basic and clinical researchers per year;
- Biostatistics internships: To address the highest priority unmet need identified by Ontario clinical researchers, OICR/HICT, in collaboration with the University of Waterloo, created the Oncology Research and Methods Training Program (ORMTP). In total 23 M.Sc. and PhD biostatistics students were placed in eight-month internships across several Ontario cancer centres, including OICR; nine received full-time biostatistician positions upon completion; 58 peer-reviewed publications; modification to graduate biostatistics curriculum: computational statistics for high-dimensional data;
- 18 clinical oncology fellows received awards to the Methods in Clinical Cancer Workshops sponsored by ESMO-ECCO-AACR-NCI;
- OICR scientists also coordinate a variety of outreach and educational activities in cancer research that reaches high school students, undergraduate students and members of the general public.

In the last three years, OICR organized or partially funded more than 300 scientific meetings, workshops, courses, and seminars that reached more than 34,000 participants.
J. OICR’s Scientific Leadership

Building a new Institute in Ontario that has delivered a rich array of discoveries, devices, new therapeutic strategies, and guidelines that are moving towards the clinic and in some cases, have been adopted has been possible by a dedicated leadership team (Figure 7).

Figure 7: OICR leaders
K. OICR’s Scientific Advisors

OICR seeks input from national and international experts to help build its scientific strategies and to seek regular feedback on the scientific excellence of its programs. The lists of OICR Scientific Advisory Board (SAB) members and OICR Programs SABs chairs are provided below. Complete lists of all Programs SAB members and reviewers used by OICR for peer review panels are provided in Book 4, Tab 5.

K.1. OICR’s Scientific Advisory Board

Patricia Ganz, MD  
Distinguished University Professor  
Prevention & Control Research  
UCLA Fielding School of Public Health  
David Geffen School of Medicine at UCLA  
Director, Jonsson Comprehensive Cancer Center  
Los Angeles, California

Karen Gelmon, MD (Co-chair)  
Senior Scientist  
Medical Oncologist, Department of Medical Oncology, Vancouver Centre, British Columbia Cancer Agency  
Head Investigational Drug Program, Experimental Therapeutics, Department of Medical Oncology, British Columbia Cancer Agency  
Professor, Medicine, University of British Columbia  
British Columbia Cancer Agency  
Vancouver, British Columbia

Eric S. Lander, PhD (Co-chair)  
Founding Director of the Broad Institute  
Professor of Biology at MIT, Professor of Systems Biology at Harvard Medical School and Member of the Whitehead Institute for Biomedical Research  
Cambridge, Massachusetts

David Mankoff, MD, PhD  
Professor of Radiology  
Perelman School of Medicine, University of Pennsylvania Health System  
Philadelphia, Pennsylvania

Michael J. Morin, PhD  
CEO and Founder  
Supportive Therapeutics, LLC  
Cambridge, Massachusetts

Homer Pearce, PhD  
Director  
Eli Lilly and Co. (retired)  
Indianapolis, Indiana
Dennis Sgroi, MD  
Associate Pathologist  
Director of Breast Pathology  
Associate Professor of Pathology  
Massachusetts General Hospital and Harvard Medical School  
Charlestown, Massachusetts

George W. Sledge, MD  
Professor of Medicine, (Oncology)  
Stanford University School of Medicine  
Stanford, California

K.2. OICR Program SAB Chairs

**Cancer Stem Cell**  
Keith Humphries, BC Cancer Agency Research

**Drug Discovery**  
Homer Pearce, Eli Lilly and Co. (retired)

**Genome Technologies**  
Richard Wilson, The Genome Institute

**Informatics and Bio-computing**  
Gabor Marth, Eccles Institute of Human Genetics  
University of Utah School of Medicine

**High Impact Clinical Trials**  
Herbie Newell, Newcastle University

**Health Services Research**  
John Ayanian, Harvard Medical School

**Innovation in Target Validation**  
Mark A. Lemmon, University of Pennsylvania School of Medicine

**Ontario Regional Bio-Therapeutics Program**  
Nick Lemoine, Barts Cancer Institute, Queen Mary University of London

**Ontario Health Study**  
Tim Peakman, University of Manchester

**Smarter Imaging and Imaging Translation**  
Bruce Pike, Hotchkiss Brain Institute, University of Calgary

**Transformative Pathology**  
David Rimm, Yale University