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Cover image: Human osteosarcoma cells treated with HDACi ACY-1215 and stained for a marker of stress granules (green) and acetylated alpha tubulin (red). Stress granules protect tumor cells against the effects of chemo and radiotherapy and may confer resistance against some chemotherapeutic agents. They also play an important role in sarcoma metastasis, as demonstrated by Dr. Poul Sorensen’s laboratory at the BC Cancer Agency in 2015.

Photo credit: Amal M. EL-Naggar, PhD, Senior Postdoctoral Research Fellow in Dr. Sorensen’s laboratory, Molecular Oncology, BC Cancer Agency, 2015.
2015 Fast Facts
BC Cancer Agency Research

5 researchers receive
$14 Million in foundation grants from the Canadian Institutes of Health Research

$2 Million received from BC Ministry of Health for breast cancer research

More than 300 research papers published

50% of BC Cancer Agency-led research publications involved international collaboration

7 new technology licensing agreements signed

More than 500 patients enrolled in interventional cancer-related clinical trials

More than 260 patients enrolled in the Personalized Onco-Genomics (POG) program

3 researchers named among World’s Most Influential Scientific Minds

Recent publications on breast, colon, prostate and ovarian cancers ranked among top 1% most-cited in the world

Genomic profiling of 1,000 lymphoma cancers

10th Anniversary of the BC Cancer Agency Research Centre in Vancouver
Message from Dr. Malcolm Moore
President, BC Cancer Agency
Vice President, Research at BC Cancer Agency (Acting)

Cancer is a complex disease, and so cancer research is by necessity multifaceted and involves a lot of collaboration. We are fortunate in BC to have world leading investigators and exceptional research programs.

As you will see throughout this report, the BC Cancer Agency had a number of significant research achievements in 2015. A BC Cancer Agency-designed prostate cancer drug entered clinical trials. We developed a new method for single cell sequencing. Our world leading Personalized Onco-Genomics program enrolled more than 260 patients. Our scientists uncovered the role of immune suppressive cells in metastatic breast cancer. And that’s only to name a few.

Research at the BC Cancer Agency’s Cancer Research Centre has transformed treatment for patients in British Columbia and indeed, around the world. We have moved from a time where there were considered three pillars of cancer treatment – surgery, radiation, and chemotherapy – to five pillars, with the addition of immunotherapy and targeted therapy.

My hope for the future is that we will continue our advances in cancer control and treatment at the same pace as we have seen in the past five years; that we can create a system that is sustainable and make all these advances available to patients in BC. Further, we want to create a system where we learn from every patient with cancer we treat, so we can continue to make progress in the future.

Message from Carl Roy
President & Chief Executive Officer, Provincial Health Services Authority

BC plays a significant and growing role in health research in Canada. With leading research universities, a strong life science industry, and a collaborative health authority structure that has established research excellence in many areas, BC is uniquely positioned to conduct and apply research that transforms care for our patients.

PHSA is a recognized leader in academic health science, and 2015 was no exception. PHSA was ranked by Research Infosource as the largest research hospital in Canada, outside Ontario. And our talented and diverse community of researchers, including the BC Cancer Agency, is helping to directly improve health care and outcomes for patients in BC, nationally and beyond. I want to thank our BC Cancer Agency researchers and research partners, for their vital work. I hope you will be encouraged by the breadth of scientific discovery, clinical collaboration and innovation detailed in this report, and the promise it holds for all of us.
About the BC Cancer Agency

The BC Cancer Agency provides a comprehensive cancer control program for the people of British Columbia through six regional Centres that deliver assessment and diagnostic services, chemotherapy, radiation therapy, supportive care, and research.

The BC Cancer Agency’s mission is three-fold:
- To reduce the incidence of cancer
- To reduce the mortality rate of people with cancer
- To improve the quality of life of people living with cancer

This mission drives all services provided by the Agency, including cancer screening, diagnosis and care, the development of treatment standards, and research into the causes of and cures for cancer.
Research is an essential part of the BC Cancer Agency’s mission to not only find the causes of cancer, but to find better treatments for prolonged life and better quality of life.

With direct links between physicians and researchers and ongoing financial support from generous donors to the BC Cancer Foundation, new discoveries quickly translate into important clinical applications.

Research at the BC Cancer Agency is organized into nine departments across three sites. It explores all aspects of cancer, including basic biology and technology developments for cancer control, conducts clinical studies and clinical trials, examines population health and care services, and supports internationally recognized facilities and platforms in genomics, bioinformatics, molecular pathology, imaging, drug development, and tissue banking.

In October 2015, Dr. Malcolm Moore assumed the role of Vice President, Research at the BC Cancer Agency during an international search for a new candidate.

Total Funding
$75,311,803

- $59,493,701 Canadian grants and awards
- $5,811,965 International grants and awards
- $5,471,839 International industry funding
- $4,534,298 Canadian industry funding

BC Cancer Agency Research Centre in Vancouver
Four Principles of Research Excellence

People
Attract, train, and retain top calibre research personnel.
• Over the last five years, the BC Cancer Agency has managed to recruit eight new scientists, all of which have excelled in their field and have been awarded new investigator and career awards.

Platforms and Programs
Work to translate new ideas and technologies into practice through the test-bed of a living laboratory.
• The BC Cancer Agency works to create a research hospital environment that brings together and empowers British Columbia to rapidly adopt and de-risk new technologies in the prevention, screening, diagnosis, and treatment of patients with cancer, and to implement them on a population basis adding high-value jobs through the development of intellectual property.

Population
Endeavour to draw on the BC Cancer Agency population-based system to extract critical data for research.
• The BC Cancer Agency has created infrastructure that is able to integrate genomics, pathology, imaging, clinical, and outcomes data province wide, which will improve British Columbia’s capacity to evaluate risk factors, biomarkers, diagnostic tests, and treatment strategies on an on-going basis.

Partnerships
Create impactful internal and external partnerships to drive the research mandate.
• Partnerships have been created, managed, and optimized with key stakeholders both within British Columbia and beyond. Our fundraising partner, the BC Cancer Foundation, is the largest funder of cancer research in in the province, enabling donors to make contributions to leading-edge research that has a direct impact on improvements to cancer care for patients. Our academic partnerships are solid with strong affiliations with the University of British Columbia, Simon Fraser University, the University of Victoria, and the University of Northern British Columbia. We also have inter-institutional agreements with academic centres around the globe, and with 46 new industry partnerships since 2010 including, AstraZeneca, BMS, Roche, Takeda, Amgen, Roche, and Johnson & Johnson.
BC Cancer Agency Research Centre celebrates 10 years in state-of-the-art research facility

Rising from the basement of an old bakery to a state-of-the-art research facility in Vancouver, the BC Cancer Agency Research Centre celebrated its 10th anniversary in June. Bolstered with a growing number of professionals, programs, partnerships, and technology, the Centre has become a global powerhouse of scientific discovery in cancer research. Over the past decade, our researchers have redefined cancer from a biological standpoint – how it develops, how it evades treatment, and how to better attack the disease at a genetic level.

Leslie Diamond Chair in Cancer Survivorship

With advancements in early detection, diagnostics, and treatment, nearly 185,000 British Columbians are part of a growing group of cancer survivors. The Leslie Diamond Chair in Cancer Survivorship is supported with $5 million in funding from the BC Cancer Foundation and represents a significant partnership between the BC Cancer Agency and Simon Fraser University that aims to improve survivorship through research. In July, the position was awarded to Dr. Stuart Peacock to expand the scope of his research in survivorship. Dr. Peacock is leading a coordinated research effort to enhance the experience and health of individuals who are entering or transitioning out of cancer care.

Membership in the Canadian Cancer Clinical Trials Network

The Canadian Cancer Clinical Trials Network (3CTN), operated out of the Ontario Institute for Cancer Research, is a pan-Canadian initiative that aims to improve the efficiency and quality of clinical trials in Canada by investing in sustainable infrastructure at clinical trial centres across Canada. In March, the BC Cancer Agency joined 3CTN with five out of six of its regional Centres participating in the provincial roll-out. The BC Cancer Agency received a cumulative total of $47,500 in per case funding, with generous support as well from the BC Cancer Foundation toward provincial clinical trials and the BC Cancer Agency’s 3CTN efforts.
Personalized Onco-Genomics program enters Phase 2.0

In 2012, with a $12.5 million commitment from the BC Cancer Foundation, the BC Cancer Agency unleashed a world-leading clinical study known as Personalized Onco-Genomics (POG) that integrates genomic sequencing into patient care and clinical decision-making for individuals with advanced and hard-to-treat cancers. This translational research initiative, led by Drs. Janessa Laskin and Marco Marra, allows clinicians to identify clinical trials that a patient may benefit from and potentially pinpoint less toxic and more effective therapeutic options that block cancer growth. In 2015, the POG program entered the second phase of studies and enrolled more than 260 patients representing several different cancer types.

PREDICT initiative expands

The Personal Response Determinants in Cancer Therapy (PREDICT) initiative is designed to create a population-scale biobank of blood samples obtained prior to initiation of systemic therapy, with the goal of reaching 20,000 new cancer patient participants. PREDICT was launched in 2008 at BC Cancer Agency’s Trev & Joyce Deeley Research Centre at the Vancouver Island Centre in Victoria. In 2013 it was expanded to the Sindi Ahluwalia Hawkins Centre for the Southern Interior in Kelowna and in 2015 the program launched at the Abbotsford Centre.

BC Cancer Agency researchers among World’s Most Influential Scientific Minds

Three BC Cancer Agency researchers – Drs. Marco Marra, Joseph Connors, and Randy Gascoyne – were listed among Thompson Reuters’ 2015 list of the World’s Most Influential Scientific Minds. About 3,000 researchers worldwide earned this distinction by writing the greatest number of reports officially designated by Essential Science Indicators as Highly Cited Papers. These researchers rank among the top one per cent of the most cited for their subject, field, and year of publication, earning them the mark of exceptional impact.
Canadian Institutes of Health Research Foundation Scheme Grants

Five outstanding BC Cancer Agency scientists received several impressive grants totalling more than $14 million from the Canadian Institutes of Health Research (CIHR). Part of its Foundation Scheme, these CIHR grants are part of a federal health research funding initiative designed to foster a sustainable foundation of new and established health research leaders in Canada. The funds allow the investigators to build and conduct programs of cancer research for up to seven years.

Recipients and their projects at the BC Cancer Agency include:

- **Dr. Marco Marra**: Exploring the relationship between the genome and the epigenome in cancers
- **Dr. Poul Sorensen**: Targeting the tumour cell stress response in high-risk childhood cancers
- **Dr. Shoukat Dedhar**: Development of therapeutic antibodies targeting carbonic anhydrase IX (CAIX)
- **Dr. Sohrab Shah**: Clonal dynamics of ovarian cancers – phylogenetic models of chemosensitivity and resistance
- **Dr. Wan Lam**: An integrative approach to understand lung cancer development in smokers and non-smokers

$2 million for breast cancer research from BC Ministry of Health

In October, the BC Ministry of Health announced $2 million for breast cancer research at the BC Cancer Agency. Under the leadership of the BC Cancer Agency’s Dr. Samuel Aparicio, the funding will support the Breast Cancer Research Initiative with its bold goal to customize treatment for every breast cancer patient in British Columbia. The funding aims to build on several groundbreaking discoveries by Dr. Aparicio and his team over the last decade, including the world’s first sequencing of a breast cancer and metastasis, the discovery of 10 subtypes of breast cancer, and the decoding of breast cancer evolution in avatars of breast cancer.

Photo left to right: Darryl Plecas, Parliamentary Secretary to the Minister of Health for Seniors, Susan McLoughlin, Breast Cancer Survivor, Health Minister Terry Lake, Lou Del Gobbo, Interim President & CEO of BC Cancer Foundation, and Dr. Malcolm Moore, President of the BC Cancer Agency.
Technology Development Office

Technology commercialization deals with the transfer of knowledge gained from research activities to the public at large, allowing society to benefit. It can involve the development of a product, licensing of new techniques or software, or development of research partnerships that allow further study in specific areas.

The Technology Development Office (TDO) is located at the BC Cancer Agency Research Centre in Vancouver and serves researchers across the Provincial Health Services Authority (PHSA). It houses a staff of six — including two PhDs with industry experience, two members with MScs, and a Director with an MBA — who facilitate relationships between scientists, clinicians, and industry. They manage intellectual property to ensure that innovations arising from research are identified, evaluated, protected, and leveraged into working solutions that benefit patients.

TDO provides a range of services to support breakthrough technologies, including:

- Clinical trial agreements
- Intellectual property protection
- Research agreements and contracts
- Research partnering
- Start-up assistance
- Technology screening
- Technology commercialization

In fiscal 2015, the BC Cancer Agency signed seven new licensing agreements, processed 733 agreements including 18 collaborative research agreements and 21 service agreements, and processed agreements for 80 new clinical studies. There are currently 12 active start-up companies creating or producing products based upon research developed by BC Cancer Agency scientists.
Clinical Research and Clinical Trials

Clinical trials at the BC Cancer Agency support translational research initiatives and utilize expertise across platforms, reinforcing the close work between clinicians and scientists. A mixture of Phase I, II, and III clinical trials are supported by granting agencies, cooperative clinical trial groups, and consortia and are initiated by both scientific investigators and industry.

The BC Cancer Agency Clinical Research and Clinical Trials department is the largest clinical research program in the province. Over the past year alone, more than 500 patients were enrolled in interventional cancer clinical trials. While each of the BC Cancer Agency’s six Centres has an active Clinical Trials Unit, the Vancouver Centre has the largest and accrues more than 300 patients per year to systemic and radiation therapy trials combined. Since 2001, Vancouver Centre has opened more than 530 trials, accrued more than 5,500 patients to interventional Phase I to III studies, and attracted more than $51 million in research funds.

Dr. Kim Chi was appointed Director of Clinical Research in November. Clinical Trials Units also rely on the dedication and hard work of passionate investigators and staff, including Dr. Bernie Eigl, Dr. Christian Kollmannsberger, Dr. Anna Tinker, Dr. Daniel Renouf, Dr. Susan Ellard, and Dr. Joanna Vergidis.

Principle Investigators at the BC Cancer Agency are recognized as national and international leaders in cancer clinical trials, leveraging collaboration with Agency researchers and partner organizations.

BC Cancer Agency Clinical Investigators have been able to take on significant leadership roles within several important clinical trials, with genitourinary, breast, lymphoma, and gastrointestinal disease sites in particular seeing the largest successes. Significant progress has also been seen in gynecology and lung groups. These trials have led to practice-changing results and important findings published in high-impact journals.

The importance of clinical trials in facilitating translational research at the BC Cancer Agency is illustrated by several examples in 2015, including Phase I to III trials initiated from drug discovery programs in Vancouver. This has included the development of:

- **Custirsen** (OGX-011, an inhibitor of clusterin) in prostate, breast and lung cancers
- **Apatorsen** (OGX-427, an inhibitor of heat shock protein 27) in prostate, bladder, pancreatic and lung cancers
- **EPI-506** — a first-in-class inhibitor of the androgen receptor for treatment of metastatic, castration-resistant prostate cancer

Research in Focus: EPI-506

Prostate cancer is the most common form of cancer among North American men. It is estimated that more than 3,700 men in British Columbia will be diagnosed with prostate cancer this year. Metastatic castration-resistant prostate cancer (m-CRPC) is the lethal form of the disease, and is resistant to most treatments.

In December, prostate cancer drug EPI-506, developed by researchers at the BC Cancer Agency and the University of British Columbia, entered Phase I and II multi-centre human clinical trials. This was a major milestone for the BC Cancer Agency as only one out of 1,000 promising drug candidates ever make it to this stage of human trials. EPI-506 is designed to shut down m-CRPC when other treatments fail.

Designed by Dr. Marianne Sadar, Distinguished Scientist at the BC Cancer Agency, and Dr. Raymond Andersen, a professor in the department of chemistry at UBC, EPI-506 is a variant of a compound found in a type of marine sponge and is the first to target the “back end” of the androgen receptor protein, called the N-terminal domain. The androgen receptor drives growth in most prostate cancer cells and makes them sensitive to androgen hormones, such as testosterone.

Dr. Marianne Sadar
Deeley Research Centre

Opened in 2003, BC Cancer Agency’s Trev & Joyce Deeley Research Centre (DRC) was created to stimulate research and the ability to translate and implement advances in cancer care at the Vancouver Island Centre. Today, the DRC consists of 11,000 square feet of lab and office space and is involved in several major research initiatives with a primary focus on immunotherapy.

Borne from the discoveries and ambitions of the DRC and Genome Sciences Centre, the Cancer Immunotherapy Program has attracted enthusiastic participation from multiple translational and clinical research groups in Victoria and Vancouver with a goal of developing and conducting Phase I immunotherapy clinical trials for innovative T-cell therapies for cancer.

Immune Response to Ovarian Cancer began in 2007 with goal of creating a world-class biobank with serial collections of viable tumour, ascites, and blood samples for advanced immunological studies. It has resulted in dozens of publications, operating grants from multiple agencies, a Phase I trial of adoptive T-cell therapy for ovarian cancer, and an international reputation for the DRC as a leader in the ovarian cancer immunotherapy field. Based on this success, the DRC was invited by the Terry Fox Research Institute to co-lead their new pan-Canadian cancer immunotherapy network.
Immunotherapy involves the infusion of large numbers of natural or genetically engineered immune cells, together with immune stimulatory cytokines and antibodies. In the settings of leukemia and melanoma, immunotherapy is routinely achieving objective clinical responses including complete regressions in 50 to 90 per cent of cancer patients.

Money raised by two BC Cancer Foundation events, and a $2 million donation from Robert L. Conconi Foundation in October, provided funds for the construction of a clean room facility for clinical-grade T cell production at the Deeley Research Centre. The new lab will enable the production of custom immunotherapy treatments that will be used in several clinical trials with a focus on Adoptive T-cell Therapy.

Adoptive T-cell Therapy is a specific form of immunotherapy that amplifies the power of T cells — which are normally responsible for destroying viruses and tumors — extracted from an individual cancer patient. Scientists isolate, or even genetically engineer, cancer-fighting T cells and multiply them by the thousands in the lab. The end product is a supercharged batch of a patient’s own T cells that can be delivered through an IV infusion. Phase I clinical trials for ovarian, endometrial, and cervical cancer are slated to begin in early 2017. Future trials will also focus on lymphoid, pancreatic, breast, and other cancers.
Genome Sciences

Canada's Michael Smith Genome Sciences Centre (GSC) is Canada's first high-throughput gene sequencing institution dedicated to cancer research. Founded in 1999, the GSC is home to 322 faculty, staff, and trainees. Designed initially to function as a genomics technology cluster, the Centre is part of the BC Cancer Agency’s Genome Sciences Department. It also provides management support to local, national, and international projects.

The vision of the Genome Sciences Department is to transform cancer care through research and its mission is to deliver leading edge cancer research results through deployment of genome, epigenome, proteome, mechanistic, and clinical sciences. Its goals are to excel in the application of genome, proteome, and bioinformatics approaches to study problems relevant to cancer and human health; to support clinical applications of genomics and translational cancer research.

Dr. Marco Marra, Director of Canada’s Michael Smith Genome Sciences Centre
Research in Focus: Personalized Onco-genomics (POG)

The BC Cancer Agency’s Personalized Onco-Genomics (POG) program is a translational research initiative that embeds genomic sequencing into real-time treatment planning for patients with incurable cancers. Using this genomic data in clinical decision-making allows for the development of treatment strategies to block the growth of cancer and identify clinical trials that patients may benefit from, potentially identifying less toxic and more effective therapeutic options.

The timely production of genome scale data sets for individual cancer patients is something that was only theoretical a few years ago. Ground-breaking work at the BC Cancer Agency resulted in the first publication (Jones, et al; Genome Biology, 2010) in which an individual’s cancer treatment was informed by their genomic information.

Expanding collaboration over the last five years, the BC Cancer Agency’s POG program has demonstrated several important insights.

The first POG study opened in July 2012 and over two years enrolled 107 cases of advanced cancer. These first patients demonstrated the feasibility of whole genome analysis and established the POG program, bringing together a cohesive team of over 150 researchers and clinicians. A significant outcome of the pilot project has been the creation of a weekly “Clinical Genomics Tumour Board”, which is a forum that has served to expose and educate both researchers and clinicians in the interpretation and application of genome scale data sets as treatment decision aids.

To date, 62 oncologists across BC have treated more than 650 patients, representing 50 different cancer types using POG.
Molecular Oncology

Founded in 2005 by Dr. Samuel Aparicio, Canada Research Chair in Molecular Oncology, with a mission to improve the understanding of the mechanisms of cancer evolution, the Molecular Oncology Department uses genetic, genomic, and cellular methods to translate the basic mechanisms of cancer biology into clinical practice with novel diagnostic and therapeutic approaches.

Today the department consists of 12,000 square feet of laboratory space at the BC Cancer Agency Research Centre in Vancouver and houses the latest technologies to rapidly identify genes and cellular processes that are involved in the development of cancer. The department is home to 54 staff, 68 trainees, and seven research faculty members, three of which are Canada Research Chairs.

In May, Dr. Poul Sorensen and his team published an important discovery for childhood sarcomas in the journal Cell. They identified a previously unrecognized pathway involving two proteins – YB-1 and HIF1α – and found that YB-1, which is highly expressed across virtually all human sarcoma subtypes, can directly stimulate the production of HIF1α when large tumours outgrow their blood supply and become oxygen deficient. This allows oxygen deficient tumour cells to adapt to the stress of low oxygen (called hypoxia), making these adapted tumour cells more hardy and stress resistant and therefore more likely to be treatment resistant.

Dr. Sorensen and his team also published a paper in October in Cell on a novel therapeutic approach that could be applicable to several tumour types. They discovered that mosquito-borne malaria parasite produces a protein that binds to a particular type of sugar molecule found on many cancer cells. The researchers realized that this sugar molecule could be a target for anti-cancer drugs, and that the malarial protein,
called VAR2CSA, could provide the tool for carrying such drugs to tumours. The drug compound specifically targeted and killed more than 95 per cent of the cancer cell lines tested.

In October, Dr. Sohrab Shah, Canada Research Chair in Computational Cancer Genomics, and his colleagues published a new computational method to analyze both mutation and gene expression data produced by the Cancer Genome Atlas project in Nature Communications. They executed a systematic analysis of over 3,000 tumours to determine how mutations in various cancers affect gene expression and identified specific mutations that show evidence of disrupting the normal cellular processes.

Dr. François Bénard currently leads a National Sciences and Engineering Research Council of Canada / Canadian Institutes of Health Research grant on cyclotron production of 99mTc, proving that routine, high-yield production of this important medical isotope is feasible and practical, and is leading a clinical trial that should result in regulatory approval in Canada. He was awarded the prestigious Henry N. Wagner Lectureship to present this work as the opening plenary lecture at the 2015 Society of Nuclear Medicine and Molecular Imaging annual meeting — the largest meeting in this field.

Dr. Huntsman is Department co-founder and Canada Research Chair in Genomic Pathology. His research into the genetics and molecular pathology of gastric cancer has changed clinical practice guidelines. He is now using genomic data to develop novel prevention and treatment strategies for the most common types of ovarian cancer. His OvCaRe team have redefined ovarian cancer subtypes and changed treatment guidelines for prevention of serous ovarian cancers.

Dr. Kuo-Shyan Lin is a radionucleotide organic chemist, with specific expertise in fast labelling reactions for short-lived isotopes. He has developed new methods to use salt-solution targets to produce various exotic radioisotopes to improve their availability for research.

Dr. Kasmintan Schrader studies the molecular detection of known and novel cancer susceptibility. She recently discovered a novel familial leukemia susceptibility gene and is now pioneering work describing the burden of germline variation in the normal DNA of over 1500 individuals undergoing targeted tumour sequencing.

Research in Focus: Clonal evolution of solid cancers

The work of Drs. Aparicio and Shah and their teams have demonstrated the importance of understanding differences within and between tumour cells, particularly how related cells (or clones) change and evolve over time and space within an individual patient’s cancer both at the initial site of development and after metastasis.

Historically, multi-clonality has not been considered in diagnostic and therapeutic approaches to cancer. Drs. Aparicio’s and Shah’s work has shown how it could be investigated in patients and represents a significant advancement for cancer treatment. They have published several landmark papers in Nature that exemplify the importance of this work.

In 2009, Dr Aparicio’s group described the first solid primary tumour and metastasis to be sequenced with Next-Generation Sequencing methods, which paved the way for allelic prevalence measurements as a tool for understanding the evolution of cellular clones in human cancers. And, in 2012, he showed, for the first time, the clonal complexity of triple negative breast cancers at the time of diagnosis clearly revealing a wide range of genomic lesions.

This work stimulated collaborative work on new computational methods with computer science colleagues at both the BC Cancer Agency and UBC and in 2015 these methods were used to understand the evolution of breast tumour xenografts (human cells implanted in mice) resulting in the development of new methods for single cell sequencing.
Lymphoid Cancer Research

Founded in 2014 under the direction of Drs. Randy Gascoyne and Christian Steidl, Lymphoid Cancer Research is a relatively young department at the BC Cancer Agency Research Centre. The foundation of the Department was developed over the past decade as a research lab in close association with the BC Cancer Agency’s Centre for Lymphoid Cancer — a globally recognized leader in lymphoma research.

The Department has two major research directions: the discovery and detailed description of molecular processes involved in lymphoma biology and disease progression, and its translation into clinical applications. Two major cornerstone programs for research and infrastructure in the Department are the Terry Fox Research Institute Program Project Grant examining the molecular correlates of lymphoma treatment.
failure, and a large scale project on personalized treatment of lymphoid cancer using British Columbia as a model province funded by Genome BC, Genome Canada and the Canadian Institutes of Health Research.

In 2015, Department faculty authored or co-authored over 50 peer-reviewed publications, including highly cited papers in *Nature, Blood, Journal of Clinical Oncology*, and *Lancet Oncology*.

This builds upon a history of recent research achievements, including:

- genomics-based discovery, drug development, and clinical trial design (e.g., EZH2 hotspot mutations, and trials of tazemetostat for non-Hodgkin lymphoma)
- biomarker development and implementation of routine diagnostic tests, which have been included in clinical trial designs (e.g., Lymph 2Cx gene expression profiling, and biomarker companion diagnostic collaboration in the Robust Trial in diffuse large B-cell lymphoma)
- shaping of acquired immune privilege as a central concept in lymphomagenesis
- genomic sequencing of more than 1,000 lymphoid cancers

Emerging research areas include genome biology, clonal evolution, immune, and tumour microenvironment biology, as well as translational biomarker research to identify novel disease and outcome related biomarkers to enhance precision medicine in lymphoma.

Lymphoid Cancer Research has established multiple technology platforms, including a MiSeq sequencing platform, nanoString digital gene expression profiling, and a FISH microscope setup for Tissue Microarray scanning. Principal Investigators in Lymphoid Cancer Research also hold multiple patents based on genomic discoveries and the development of molecular assays, of which some are licensed to industry partners.

The Vancouver-based Department also houses a tissue biobank and clinical database for the BioLym (Biology of Lymphoid Cancers) initiative. This tissue repository program has already involved more than 30,000 participants and provides significant support to lymphoid and other cancer related research.

Research in Focus: A prognostic test for follicular lymphoma

Over 1,000 British Columbians will be diagnosed with a form of Non-Hodgkin Lymphoma this year, and approximately 300 of those will have follicular lymphoma. Follicular lymphoma is one of two main subtypes of non-Hodgkin Lymphoma, and approximately 25 per cent of those will not respond well to standard therapy. Identifying patients whose treatment is likely to fail from the outset means oncologists can plan alternate, potentially life-saving, treatment approaches.

After spending the past two years studying the genetic factors that cause treatment failure in follicular lymphoma, Dr. Gascoyne and his team published a study in September in *Lancet Oncology* that proved a test coined m7-FLIPI can identify follicular lymphoma patients at the highest risk for treatment failure. Identifying these patients up-front can be used to help determine candidates for testing novel therapies or enrollment in clinical trials.

Looking ahead, m7-FLIPI can be used in a clinical setting to test all new follicular lymphoma patients at diagnosis in order to identify the roughly 25 per cent who harbor the most aggressive disease. Traditionally, these patients would receive standard therapy, which is currently prescribed to all follicular lymphoma patients and highly effective for many, yet not potent enough for up to a quarter of people diagnosed.
The Terry Fox Laboratory fuels major improvements in cancer outcomes through basic and translational research with a focus on cancer stem cells. Its research builds on the premise that breakthroughs in clinical medicine originate from discoveries in basic research where excellence, innovation, and reproducibility are core defining principles.

Continuing a long track record of clinical translation, the Laboratory is now focussed on a research strategy based on new technology and assay developments that reflect a principle of excellence in basic science, underpinning advances in translation and clinical application providing novel insights for basic investigation.

Current initiatives include:

• testing new fluorescence-activated cell sorting (FACS) analysis programs to improve the clinical diagnosis of lympho-proliferative diseases
• development of predictive assays and testing of new therapeutic agents for improved management of tyrosine-kinase inhibitor (TKI)-resistant chronic myelogenous leukemia
• an impending trial of ex vivo expanded stem cell transplants
• Phase III clinical trials with the SHIP12 activator, AQX-1125, for chronic obstructive pulmonary disease, interstitial cystitis, and atopic dermatitis
Research in Focus: Flow Cytometry Core

Housed within the Terry Fox Laboratory, the Flow Cytometry Core facility offers the latest technology in cell and chromosome sorting as well as high-throughput multi-parameter cell analysis. The Core serves essentially all major research departments at the Cancer Research Centre and provides essential technology for the research mission of the BC Cancer Agency. The facility was established in the 1980s and has undergone continued expansion and upgrading, including a state of the art CyTOF Mass Spectrometry flow cytometer valued at over $1,000,000. Recent major enhancements in terms of equipment and capabilities have been possible through multiple competitive external awards held by multiple members of its research faculty.

Also comprised of five advanced multi-parameter cell sorters including one BD FACSAria Fusion, one BD FACSAria III, one BD FACSAria II, and two BD Influxs, two multi color BD LSRFortessas, and assorted other equipment, the facility services more than 34 faculty members and their staff and trainees, amounting to more than 140 current users. It has been crucial in attracting new recruits and highly qualified personnel over the last decade, and has allowed users to be competitive for external dollars provincially, nationally, and internationally, with more than $100 million received from external funders since its inception.

The Terry Fox Laboratory plans to continue to expand its ability to support researchers requiring multi-parameter, advanced sorting strategies, with an additional focus on CyTOF capability being the cornerstone of future plans.

In December, Dr. Connie Eaves published a high-profile study in Nature that demonstrated that a single gene inserted into a single cell isolated from normal human breast tissue can cause rapid development of breast cancer. Dr. Eaves’ team of researchers used DNA barcoding to track the growth of many different individually transformed cells transplanted into immune-deficient mice. Tumours appeared rapidly and repeatedly even when the cancer was produced from normal breast cells that had taken up a single cancer-causing gene. This disproved a longstanding assumption that the development of human breast cancer requires a long time to accumulate multiple genetic changes.

The Laboratory is fueled by 12 senior full-time faculty members with interdisciplinary interests and expertise in clinical translation and commercialization as well as a consistent publication record resulting in 2000 peer-reviewed publications to date with highly cited articles in Nature, Cell, and others.
**Cancer Control Research**

The goal of the Cancer Control Research Department at the BC Cancer Agency is to reduce cancer incidence, morbidity, and mortality in the population through innovative research projects.

The department fulfills a unique role at the BC Cancer Agency: it provides support for the planning, monitoring, and evaluation of cancer control strategies, and for identification of public health priorities related to cancer. Department faculty and...
Research in Focus: The BC Generations Project

To help scientists better understand the causes of chronic diseases such as cancers, The BC Generations Project has assembled a cohort of nearly 30,000 British Columbia residents, from all parts of the province to provide information about health, diet, lifestyle, medical and family history, various physical measurements, environmental data, and biological samples, such as DNA, blood, and urine. Over the next four decades, until 2058, the participant’s health outcomes and health care use will be tracked through follow-up questionnaires and administrative data.

From extracted DNA, researchers will be able to examine how genetic susceptibility interacts with lifestyle and environment to cause disease. Stored DNA and pre-diagnostic serum, plasma, and urine samples will accelerate the search for new disease biomarkers, facilitate clinical outcome investigations, and allow studies of the causes and prevention of today’s most troublesome chronic diseases.

The BC Generations Project is also collaborating with cohorts in four other regions across Canada as part of the Canadian Partnership for Tomorrow project. This is a national endeavour that has recruited over 300,000 Canadians, all with the same information on lifestyle, stored blood, urine samples, and physical measurements. The platform will allow large-scale studies of the causes of many chronic diseases, and facilitate identification of new early disease detection biomarkers, and markers of carcinogenic exposure by Canadian and international scientists for generations to come.
Experimental Therapeutics

Experimental Therapeutics is a translational research department at the BC Cancer Agency’s Research Centre. It provides therapeutic and diagnostic development capabilities focused on a critical need to rapidly establish therapeutic value for emerging technologies through validated assessments in preclinical models of cancer and in patients. It aspires to be one of the premiere sites in North America to evaluate therapeutic interventions designed to improve treatment outcomes in cancer patients in need of more personalized treatment options.

Its vision is to define better intervention strategies for individuals with aggressive cancers through an increased understanding of disease classification and patient selection criteria, and the development of more predictive models for targeted indications. It seeks to better understand tumour-stromal interactions and mechanistic actions of targeted therapies as well as the integration of relevant imaging tools to rapidly assess the therapeutic potential of treatments. It applies gene expression data to better understand the immediate impacts of treatment; maintains and expands needed infrastructure to develop therapeutics; and creates internationally recognized nano-medicine platforms designed to improve the therapeutic potential of cancer drugs.

The Department’s Investigational Drug Program was established to provide capabilities for bringing new treatments from the bench to the clinic. The Program’s mandate is to help research partners — academic and industry-based — develop promising anti-cancer compounds through the pharmaceutical value chain to the point that they can be tested in early-phase human clinical trials. Other initiatives include:

- **BC Pancreatic Cancer Research Net**: A partnership between clinical and basic research scientists at the BC Cancer Agency, Vancouver General Hospital, University of British Columbia, and donors focused on advancing pancreatic cancer research in the province.
- **The first Canadian clinical study of the PET imaging agent 18F-EF5**: evaluating changes in hypoxia in non-small cell lung cancer following treatment with Avastin, and supported by industry partners Roche and Varian.
- **Formal clinical development of improved formulation of irinotecan**, which includes completion of formal GLP toxicity studies and prototype GMP manufacturing.
- **Creation of the Living Tumour Laboratory**: a unique Canadian resource created to improve the predictability of pre-clinical drug efficacy evaluation of new or existing anti-cancer drugs, using patient-derived, clinically relevant cancer xenograft models.

Research in Focus: VYXEOS

In March, a drug developed by a company co-founded by the BC Cancer Agency scientist, Dr. Marcel Bally was proven effective in extending the lives of patients with an aggressive type of cancer known as acute myeloid leukemia (AML). This was a major step forward for a very difficult-to-treat patient population, and the first time in decades clinicians have been able to extend survival for patients with high-risk AML.

Celator Pharmaceuticals Inc. has now announced positive results from a Phase III clinical trial of VYXEOS Liposome for Injection (also known as CPX-351) in patients with high-risk (secondary) AML, compared to the standard regimen of cytarabine and daunorubicin, also known as 7+3. Liposomes are small structures (about 100 nanometers in diameter), which can be used to entrap single or multiple drugs inside.

Based on these results the company expects to submit a New Drug Application for VYXEOS with the U.S. Food and Drug Administration later this year and submit a Marketing Authorization Application with the European Medicines Agency in the first quarter of 2017.
Integrative Oncology

The Integrative Oncology (IO) Department is home to 14 Principal Investigators and approximately 120 researchers and trainees that cover a wide range of backgrounds — from pathology, physics, and engineering to genetics, molecular biology, bioinformatics, and statistics — focused on many different cancer sites and stages. The department has approximately $33 million in current funding and has produced over 1,200 peer-reviewed publications in high impact journals since inception.

Integrative Oncology is comprised of three principal units that work across several tumour-related programs. Radiation Biology examines the influence of the tumour microenvironment in anticancer treatment. The Imaging Unit researches the management of cancer through early detection. And the Genetics Unit deciphers genomic and epigenetic changes and signaling metabolic pathways.

The Lung Program, led by Dr. Stephen Lam, has developed a number of impactful technologies and methodologies, such as Light Induced Fluorescence Endoscopy (LIFE) that is now used at clinics around the world, and the first optical coherence tomography and auto-fluorescence imaging (OCT-ATF) catheter-based system to visualize peripheral lung nodules within patients.

The Oral Program developed Fluorescence Visualization for detection and localization of premalignant and invasive lesions, commercialized as the VELscope. A clinical study published this year in American Medical Association Otolaryngology—Head & Neck Surgery showed that VELscope guided surgery results in a reduction of oral cancer recurrence, metastasis, and mortality.

The Cervical Screening Program has invented a quantitative image cytometry platform and software for cervical screening that has been licensed to a Chinese manufacturer. Following regulatory approvals, it will now be used to clinically screen four million women annually at 25 sites throughout China.

And the Skin Cancer Program recently developed a Raman spectroscopy based system now in clinical use at several centres across Canada.

Research in Focus: The role of immune suppressive cells in metastasis

Dr. Kevin Bennewith and his team have assembled a growing body of evidence that immune suppressive cells help to create ideal conditions for the formation of metastatic tumours, specifically from breast cancers to lung tissue.

Immune suppressive cells — myeloid-derived suppressor cells, macrophages, and regulatory T cells — normally help in wound healing by turning off immune responses after an infected area is cleared. But, as Dr. Bennewith’s research into metastatic breast cancer has shown, immune suppressive cells can create “nests” in the lungs that represent fertile tissue for breast tumour metastases to grow.

His research team recently published studies in Oncotarget and Oncoimmunology that hint at two new types of cancer treatment. They suggest activation of the protein SHIP may prevent out-of-control lung inflammation and breast tumour metastasis to the lungs. They also repurposed the anti-HIV drug maraviroc to prevent regulatory T cell accumulation in the lungs and reduce metastatic breast tumour growth.
Partnerships

OVCARE

OVCARE is a multidisciplinary and multi-institutional research team dedicated to reducing death and suffering from ovarian cancer. OVCARE was formed in 2001 in order to pool resources in an attempt to improve the five-year survival rate for ovarian cancer, which is currently below 50 per cent. The OVCARE team strategy is to focus on major impediments to ovarian cancer control. The team includes Dr. David Huntsman, Distinguished Scientist at the BC Cancer Agency and Scientific Director of OVCARE, Dr. Dianne Miller, Head of the BC Gynecological Tumour Group at the BC Cancer Agency, and Dr. Blake Gilks Head of the Division of Anatomic Pathology at Vancouver General Hospital. The OVCARE team has produced a broad range of practice changing publications in leading scientific journals, including The Journal of National Cancer Institute and Nature. In 2010, OVCARE helped British Columbia become the first jurisdiction in the world to implement a comprehensive ovarian cancer prevention strategy based on high-risk screening and opportunistic salpingectomy – a term coined by Dianne Miller that refers to precancerous removal of the fallopian tubes. This practice has now been adopted across Canada.

For more information: www.ovcare.ca

Pancreas Centre BC

Despite decades of intense research, the five-year overall survival rate in pancreatic cancer is six per cent due to late detection, high recurrence rates, chemo-resistance, and lack of knowledge of clinically relevant biomarkers. Pancreas Centre BC was established in 2012 as a multicentre partnership between the BC Cancer Agency, Vancouver Coastal Health, and the University of British Columbia to support clinical and translational research excellence and optimize multidisciplinary patient care to improve outcomes from this disease. Led by Co-Directors Dr. Daniel Renouf, Medical Oncologist and clinical investigator at the BC Cancer Agency, and Dr. David Schaeffer, Gastrointestinal Pathologist and Clinician Scientist at Vancouver General Hospital (VGH), the Centre’s personnel also include a medical geneticist, two nurses, a research facilitator and scientist, a tissue microarray manager, a xenograft technician, and administrative assistants. The Centre supports pancreatic cancer research through established core resources. The prospective pancreatic biorepository and tumour registry at VGH provides high quality clinically annotated pancreatic bio-specimens for translational research. The tumour bank database integrates data from various clinical, pathological, and molecular resources into one design facilitated by a set of common data elements to create a pancreatic specific knowledge bank. Since August 2012, the database has acquired information on 1,123 prospective pancreatic cancer patients. The tumour biobank is also linked to the patient-derived murine xenograft facility, which has established over 20 xenograft lines for research. Dr. Schaeffer’s team has constructed a tumour tissue microarray of 500 patient samples with associated outcome data, encompassing tumour tissue, precursor lesions, and cancer associated stroma, which also already led to four publications and multiple conference abstracts. Pancreas Centre BC received approximately $1.6 million in major gifts in 2015 through the BC Cancer Foundation and the VGH & UBC Hospital Foundation. In addition, in 2015 over $6 million in grants were awarded to Pancreas Centre BC affiliated scientists.

For more information: www.pancreascentrebc.ca
The BC Cancer Foundation is the bridge that connects philanthropic support and research breakthroughs in cancer knowledge.

As the fundraising partner of the BC Cancer Agency and the largest funder of cancer research in British Columbia, the BC Cancer Foundation enables donors to make contributions to leading-edge research that has a direct impact on improvements to cancer care for patients in British Columbia.

As an independent charitable organization, the BC Cancer Foundation raises funds exclusively for the BC Cancer Agency that support innovative cancer research and compassionate enhancements to patient care.

**Message from Sarah Roth**

**President & CEO, BC Cancer Foundation**

This year, BC Cancer Foundation donors supported more than 400 research projects and enhancements to care at the BC Cancer Agency. This is the result of 95,000 individuals giving to advance cancer care for everyone in our province.

Working closely with clinicians and researchers to direct funds to the areas of cancer research with the greatest promise and impact, we raised $49.3 million to: advance a new prostate cancer drug into clinical trial, give more than 260 patients renewed hope as they enroll in the world-leading Personalized Onco-Genomics program, and construct a new lab to house adoptive T-cell therapy research, among other projects.

As the fundraising partner of the BC Cancer Agency and largest charitable funder of cancer research in the province, we take great pride in funding research that’s helping to forge new ground in care. Thank you for being our partners in discovery.

www.bccancerfoundation.com
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$49.3 Million raised by 95,000 donors between April 1, 2015 & March 31, 2016

More than $27 Million invested in research equipment and enhancements to cancer care

$250,000 innovation support fund provided researchers with critical lab equipment

Funding supported 800 cancer researchers in British Columbia

Donations supported more than 400 research projects and enhancements to care this year