BC CANCER RESEARCH

Provincial Health Services Authority

2017 Research Report

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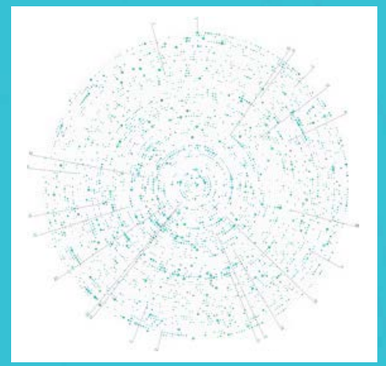
ABOUT THE COVER

Genes that make us sick by Martin Krzywinski

The human genome is shown as a spiral, starting at the top with chromosome 1 and proceeding clockwise. The spiral is formed by 10,087 segments that correspond to 286,000 bases each. Segments that contain genes implicated in disease are indicated by dots, sized by the number of genes. Chromosomes X and Y are not shown.

Martin also contributed other data visualization and graphic art seen throughout this report. *See a feature about his work on page 24.*



MESSAGE FROM THE VICE PRESIDENT OF RESEARCH, DR. FRANÇOIS BÉNARD

Everything we do at BC Cancer is driven by our vision of a world free from cancer. We know that's ambitious. We know some think it's impossible. But to the inspired, compassionate and brilliant minds that fill our halls, it's a raison d'etre. Nowhere is this more evident than in our research.

As you can see in this year's Research Report, our scientists, clinicians and trainees continue to deliver results. Whether *New England Journal of Medicine* or *Nature*, their ground breaking publications appear in the world's highest-impact journals. Whether named members of the Royal Society of Canada or listed among the World's Most Influential Scientific Minds, they're recognized by their peers for unparalleled contributions to the field. From granting agencies, foundations and industries both at home and abroad, they continue to secure promising funds for the future.

Of course, none of this would be possible without our partners. We continue to build, develop and cherish the work we do with institutions here in British Columbia, across Canada and around the world, at universities, hospitals and other institutions. As well as with our most valuable partners: our patients.

At BC Cancer we know that we must focus on our future and our students and trainees are our most valuable assets. This year, we had more than 550 trainees involved in important research projects. From uncovering new genetic subtypes of ovarian cancer, to identifying treatment targets for childhood neuroblastoma and developing new approaches to lung cancer screening, among many others, BC Cancer trainees continue to make significant contributions to cancer research.

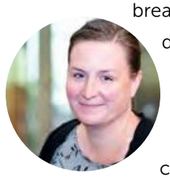
There is no question we have a difficult road ahead, but through continued excellence, results and collaboration, with our eyes fixed on the future, we will continue to steer toward our vision.

AWARDS & GRANTS

JANUARY

Each year, the **Canadian Cancer Society** and **Canadian Institutes of Health Research (CIHR) Institute of Cancer Research** partner to provide funds for innovative cancer research. In 2017, three BC Cancer scientists were each awarded $196,000 over two years from these **Innovation Grants**.

- **Dr. Xiaoyan Jiang** is leading a team in the development of new combination treatments to tackle slow-growing leukemic stem cells that escape treatment and result in cancer relapse. They are combining standard treatment with a chemical that blocks PAK6, a protein that is known to be abnormal in drug-resistant leukemic stem cells.



- **Drs. Andrew Minchinton** and **Jennifer Baker** are examining the distribution of Herceptin, a targeted breast and gastric cancer drug that distributes heterogeneously in cancer tissue — a phenomenon that could impact its activity. Conjugating Herceptin with a carrier protein that more ubiquitously crosses blood vessel barriers aims to improve the distribution and therefore activity of monoclonal antibody drugs like Herceptin.

- **Dr. Christian Steidl** and his team are exploring the ways that cancer cells communicate with each other and other normal cells that are closely situated in classical Hodgkin lymphoma (HL). They will use two novel technologies to study the immune cells in the microenvironment around tumour cells to learn whether the cancer actively manipulates its surroundings. While many HL patients can be cured with chemotherapy, about 30 per cent currently cannot.

FEBRUARY

In 2017, the **BC Cancer Foundation** initiated a new program, the **Strategic Priority Fund Awards**, providing $1.5 million to seven BC Cancer projects focused on cancer detection and treatment.

- **Dr. Connie Eaves** and BC Cancer colleagues **Drs. Martin Hirst** and **Davide Pellicani** along with scientists at UBC and the Mayo Clinic are investigating the ways that normal human breast cells turn cancerous, from changes caused by aging to the introduction of cancerous genes.

- **Dr. David Huntsman** and team, with support from the Vancouver General Hospital and UBC Hospital Foundation, are analyzing protein expression of 20 different ovarian tumour types that are currently difficult to distinguish yet require different treatments, with the aim to discover, develop and implement a suite of new biomarkers to aid in the diagnosis and management of ovarian cancer subtypes.

- **Dr. Pierre Lane** and his team together with Simon Fraser University's School of Engineering and UBC's Biomedical Engineering Program are developing novel image guided biopsy devices for difficult to sample peripheral lung nodules; they are developing a tool to safely and accurately sample suspicious nodules in the small airways of the lungs, designed to complement existing three-dimensional optical imaging probes.

- **Dr. Peter Lansdorp's** research team, working with colleague **Dr. Kasmintan Schrader**, in close collaboration with the European Research Institute for the Biology of Aging in Groningen, Netherlands, are exploring structural variations in the genome as a source of familial cancer predisposition using a unique single cell genome sequencing approach to find causes of inherited cancers that are difficult to identify using conventional techniques.

- **Dr. Dirk van Niekerk** is testing the feasibility of expanding a highly successful online sexually transmitted infection-testing platform to include self-collected cervical cancer screening samples. Participants who test positive for high-risk strains of human papillomavirus (HPV) will be contacted and referred for further testing and care. This approach is designed to improve access and acceptability of screening to prevent cervical cancer among high-risk women.

- **Dr. Dean Regier** is embarking on a research project to better understand the resource and health impacts of BC Cancer's Personalized OncoGenomics program. (POG; see page 22). Regier's team will ask POG patients about the value they attach to genomic knowledge and combine this with cost and health outcome information.

- **Dr. Haishan Zeng** is developing a technology called Laser Raman Spectroscopy for improving lung cancer detection, with the intent to develop it into a new clinical tool for improving periphery lung cancer detection. If lung cancer can be detected early, in the pre-invasive stage, five-year survival is greater than 90 per cent.

MARCH

In 2017, **CIHR** awarded six **Project Grants** to principal investigators with appointments at BC Cancer:

- **Dr. Marcel Bally** is receiving $489,000 over four years to investigate the development of novel copper-based drug complexes for treatment of cancers that are insensitive to platinum.

- **Dr. Pamela Hoodless** is receiving $960,000 over five years to study how liver cells grow and differentiate. The aim is to improve methods of growing liver cells from human pluripotent stem cells for treatment via transplant of liver diseases such as cancer.

- **Drs. Pierre Lane** and **Calum MacAulay** are receiving $378,675 over three years, and $638,776 over four years, respectively, to evaluate high resolution multimodal optical camera imaging for the development of screening methods for gynecologic cancers.

- **Dr. W. James Morris** is receiving $1.1 million over six years to elaborate upon a successful randomized clinical trial known as ASCENDE-RT (Androgen Suppression Combined with Elective Nodal and Dose Escalated Radiation Therapy). The new protocol, dubbed OPTIMAL (Optimizing Prostate cancer Treatment in Men with Advanced Local disease) uses advanced imaging technology to reduce and better redistribute radiation directly to prostate tumours.

- **Dr. Yuzhuo Wang** is receiving $765,000 over five years to study the function of the gene HP1a in neuroendocrine prostate cancer and produce potential therapeutics designed to target HP1a.

Dr. Dean Regier, a scientist in the department of Cancer Control Research at BC Cancer, was nominated as Canadian Representative for **PopSeq International Health Economics Leadership Council**. This leadership council is international in scope, supported by **Illumina**, with an aim to develop economic frameworks for the sustainable adoption of precision medicine in health care.

Daniel Kwon, a graduate student working with Dr. François Bénard, was a recipient of **Radiological Society of North America's Research Medical Student Grant** of $6,000 to conduct research into the development of novel radioactive compounds for non-invasive, accurate and early imaging of cancer using positron emission tomography (PET).

APRIL

BC Cancer start-up company, Cuprous Pharmaceuticals, initiated by **Dr. Marcel Bally** and colleagues, received **Industrial Research Assistance Program (IRAP)** funding from the **National Research Council of Canada** for the development of therapeutically active copper complexes. This work will develop a new class of drugs useful in the treatment of cancer as well as bacterial infections.

MAY

Cancer Research UK named **Dr. Samuel Aparicio** as a member of one of its first global research teams to be part of its **Grand Challenge**.

The Grand Challenge aims to solve some of the biggest obstacles facing cancer research today by equipping multidisciplinary international teams with funding and cutting edge technology. Armed with more than $35 million and the latest virtual reality system, Dr. Aparicio is part of a team led by Dr. Greg Hannon of the University of Cambridge, with collaborators from Switzerland, Ireland, Canada, USA and UK, that is developing an entirely new way for scientists and physicians to understand cancer and predict its clinical behaviour. The integrated approach will produce three-dimensional representations of tumours and their host environments, wherein each cell is identified, molecularly annotated and presented in an interactive, virtual reality framework. This approach will be applicable to virtually all tumour types but the team will begin with breast cancer.

Dr. Santa Ono, President, University of British Columbia, exploring virtual tumour cells while Dr. Aparicio looks on during a recent tour of the BC Cancer Research Centre in Vancouver.

The **Michael Smith Foundation for Health Research (MSFHR) Health Professional-Investigator Awards** support professionals in the application of research relevant to health and the health care system. Each award recipient receives a salary contribution to help them protect time for research for up to five years, or to support research personnel directly associated with their work. In its inaugural year, MSFHR announced 11 recipients, including BC Cancer's **Drs. Robert Olson** and **Daniel Renouf**.

- **Dr. Robert Olson's** research team has shown that it is feasible to collect and use Patient Reported Outcomes (PROs) on a population scale in British Columbia. PROs are any report of the status of a patient's health condition that comes directly from the patient, without interpretation by a clinician or anyone else. Using PROs Dr. Olson has shown that reported pain improvement for patients with bone metastases is similar when treated with single fraction radiation therapy (SFRT) compared to longer and more complex radiation therapy courses. This has resulted in an increased prescription of SFRT across all six of BC Cancer's regional centres and an invitation from the Canadian Partnership for Quality Radiotherapy to lead PRO collection across the Canadian radiation therapy community. With the MSFHR Award, Dr. Olson's research team is leveraging national partnerships to build a more robust population-level evidence base to support increased use of SFRT for bone metastases.

- **Dr. Daniel Renouf's** research focus is pancreatic cancer, a disease in which 90 per cent of diagnosed patients are not expected to survive five years; it claims the lives of approximately 5,000 Canadians every year. Advances in understanding various cancer subtypes have revolutionized treatment of multiple cancers, but clinically meaningful pancreatic cancer subtypes have not yet been uncovered. Using funds from the MSFHR Award, Dr. Renouf's research team is performing detailed genetic and molecular analyses of patient tumour samples to investigate their distinct molecular characteristics. Patients are enrolled in a clinical trial at BC Cancer and are provided with detailed information about their cancer to help guide treatment decisions.

JUNE

Dr. Sharon Gorski was awarded the US$250,000 **Neuroendocrine Tumour Research Foundation – American Association for Cancer Research Grant.** With these funds, Gorski and her team will research the molecular subclasses of pancreatic neuroendocrine tumours using innovative, first-of-its kind protein and genomic analyses to help guide treatment decisions and the development of novel therapies for these understudied tumours.

Dr. Marcel Bally was honoured with a **Canadian Society of Pharmaceutical Sciences Award of Leadership** for advancing pharmaceutical research and development in Canada. The award was presented at the Society's 20th Annual Symposium in Montreal.

Dr. Kevin Bennewith received a **UBC Distinguished Achievement Award** for **Excellence in Basic Science Research in Pathology and Laboratory Medicine**.

JULY

Each year, the **Canadian Organization of Medical Physics** holds research **Poster Awards**, judged on both scientific merit and communication. **Dr. Cheryl Duzenli**, department head of medical physics at BC Cancer – Vancouver, received first place for her presentation of "Recommendations for Dosimetric Commissioning of Proton Therapy for Iris Melanoma", highlighting collaborative work between BC Cancer, University of Victoria, University of British Columbia and TRIUMF.

Canada's Advanced Research and Innovation Network, CANARIE, has awarded **Dr. Sohrab Shah's** bioinformatics research team a new research project. Its **Research Software Program** champions the development of software tools that accelerate discovery by simplifying access to digital infrastructure to support software development for single cell sequencing at scale. Dr. Shah's team is developing new software they are calling *Montage* that aims to encapsulate a number of pre-existing software packages for use in cancer genomics analysis in the form of a unified web application. All tools developed in this program will be available openly online to allow other researchers to leverage the digital infrastructure developed. Cancer Research UK is using the software developed as part of its Grand Challenge project.

Dr. Marco Marra received the **Outstanding Achievements in Cancer Research** award from the **Canadian Cancer Research Alliance** for fundamental contributions to understanding the role of genetic alterations in promoting cancer progression and translating these insights for the benefit of patients. His research uses massively parallel genomic sequencing technologies and bioinformatics tools to characterize tumours from patients, leading to the discovery of new cancer associated mutations, biomarkers and therapeutic targets.

Dr. Marra holding his Outstanding Achievements Award from CCRA. Photo credit Jon Benjamin Photography.

AUGUST

Drs. Calum MacAulay and **Andrew Minchinton** were among 11 recipients for the inaugural **Innovation to Commercialization (I2C) Awards** from the **Michael Smith Foundation for Health Research**. The I2C Program is designed to help researchers advance discoveries or inventions towards commercialization by supporting commercialization activities that strengthen the value of their intellectual property, facilitate collaboration, and attract future investment.

- **Dr. MacAulay's** research team is commercializing new imaging tools to assist with the active surveillance of prostate cancer. This technology uses measurements of genomic organization at large in individual cells along with tumour cell position within the patient's tissue to predict aggressive behaviour in prostate cancers with greater than 80 per cent accuracy.
- A new class of drugs known as DNA-PK inhibitors developed by **Dr. Minchinton's** lab show promise in treating radiation-resistant oxygen deficient (hypoxic) tumour cells. With the I2C grant, they will improve these small molecule inhibitors by developing therapeutic regimens to optimize their use for maximum anti-cancer benefit.

CIHR awarded **Dr. David Huntsman** a **Foundation Grant** of $2.7 million over seven years for his research on the pathogenesis of ovarian cancer. The overarching goal of Dr. Huntsman's research is to decrease death and suffering from ovarian cancers, by improving the way they are diagnosed, prevented and treated.

The 2017 **Pancreas Centre BC IDEAS Grant** was awarded to **Drs. Kuo-Shyan Lin, Donald Yapp** and **François Bénard** for development of new positron emission tomography (PET) tracers for early detection of pancreatic cancer. If successful, their research will greatly provide a convenient, sensitive and non-invasive method for early diagnosis and characterization of pancreatic cancer.

SEPTEMBER

CIHR awarded **Dr. Stuart Peacock** two **Cancer Partnerships for Health System Improvements Grants**. Dr. Peacock, along with fellow Principal Investigators, Kelvin Chan with the Odette Cancer Centre, Michael Sherar, President and CEO of Cancer Care Ontario and Wanrudee Isaranuwatchai with the Institute of Health Policy at the University of Toronto, received $970,640 to investigate the development of a framework for the incorporation of real world evidence into cancer drug funding decision-making in Canada. Dr. Peacock, along with fellow Principal Investigators, Michael Sherar, and Michael Burgess, Research Chair in Biomedical Ethics at UBC, also received $775,000 to investigate the role of deliberative public engagement in informing cancer control decision-making in Canada.

OCTOBER

Dr. Marcel Bally, also a member of the Centre for Blood Research, Professor of Pathology and Laboratory Medicine and Adjunct Professor in Pharmaceutical Sciences at the **University of British Columbia**, was honoured with a **Distinguished Achievement Award** from the **Faculty of Medicine**.

Dr. Aly Karsan and scientists from BC Cancer's Terry Fox Laboratory and Genome Science Centre received nearly $7.5 million over five years from the **Terry Fox Research Institute's New Frontier Program Project Grant (PPG)** for their research exploring pathogenic mechanisms in acute leukemia for clinical translation. This award represents another successful renewal of the long-standing PPG originally awarded to TFL investigators in 1981, making the Terry Fox Lab at BC Cancer the longest (1981-2022) continuously funded PPG in Canada by TFRI. Team members include: **Drs. Keith Humphries, Connie Eaves, Andrew Weng, Martin Hirst, Peter Lansdorp, Gregg Morin** and **Raewyn Broady**.

The **Canadian Foundation for Innovation** announced more than $550 million in funding, with matching contributions from the BC Knowledge Development Fund (BCKDF), for 117 new infrastructure projects at 61 universities, colleges and research hospitals across the country. BC Cancer recipients included **Drs. François Bénard, Brad Nelson** and—through a project led by Dr. Artem Cherkasov from Vancouver Prostate Centre and Dr. Natalie Strynadka from the University of British Columbia — **Marcel Bally**. Dr. Bénard's work in the production of rare isotopes for cancer therapy received $7.9 million, Dr. Nelson's research engineering precision immunotherapies for cancer (EPIC) received $8 million and Dr. Cherkasov's work with Dr. Bally in drug discovery using clinical translation received $18 million.

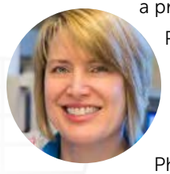
- **Engineering Precision Immunotherapies for Cancer (EPIC):** Through the collaborative efforts of the Deeley Research Centre, led by **Dr. Brad Nelson** in Victoria, and the Genome Sciences Centre, led by **Dr. Rob Holt** in Vancouver, and equipped with the new Conconi Family Immunotherapy Lab, the Immunotherapy Program will initiate cutting edge clinical trials to treat gynaecological cancers (i.e. ovarian, cervical and endometrial cancers) and blood cancers (i.e. leukemia and lymphoma). More than $2.8 million was also awarded to the Immunotherapy Program by **BioCanRx**, with matching funds from the **BC Cancer Foundation** and the **Canadian Cancer Society Research Institute**, to develop these clinical trials. As the program grows, it intends to develop clinical trial protocols for other cancers in need of new treatment approaches.

NOVEMBER

Dr. François Bénard honoured with **Western Region Society of Nuclear Medicine Distinguished Scientist Award**.
Dr. François Bénard is the Vice President, Research and a Distinguished Scientist at BC Cancer as well as Associate Dean for Research and Professor in the Department of Radiology at UBC. In addition, he holds the BC Leadership Chair in Functional Cancer Imaging. As a clinician scientist, his research interests are in positron emission tomography (PET), nuclear medicine, cancer imaging and targeted radionuclide therapy. His research team has developed several new radiopharmaceuticals targeting tumour receptors, and he initiated the program that developed cyclotron production of Technetium (99mTc) at BC Cancer – Vancouver.

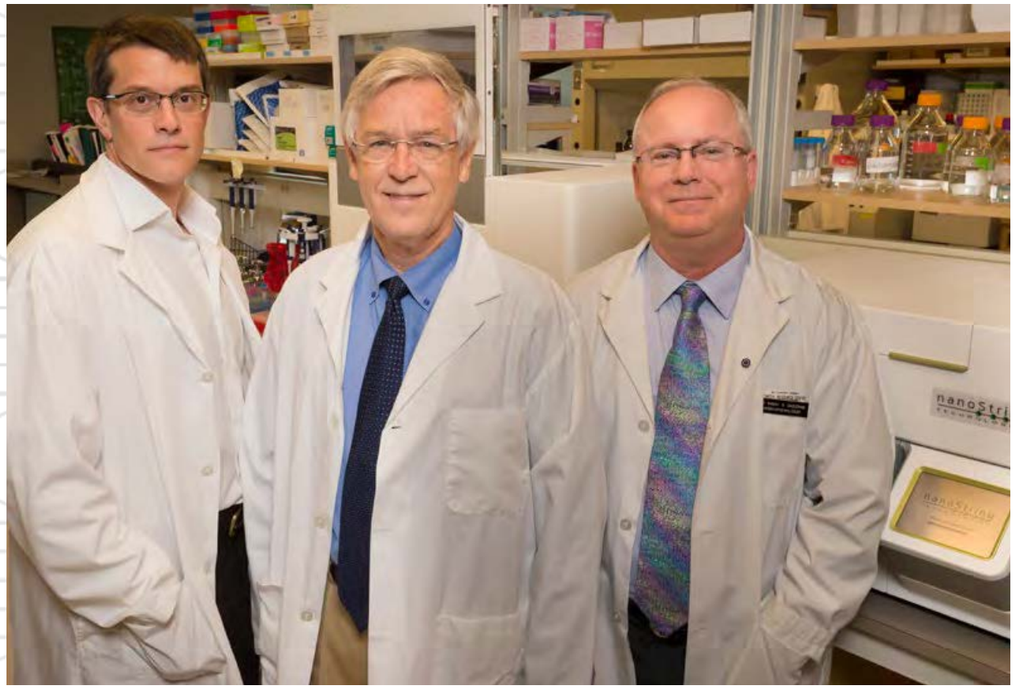
Dr. Christian Steidl named a member to the **Royal Society of Canada**.
Dr. Christian Steidl, Department Head for Lymphoid Cancer Research at BC Cancer and world leader in lymphoma research has been recognized by the Royal Society of Canada as a Member of the College of New Scholars, Artists and Scientists. Dr. Steidl holds an MD from the University of Muenster, Germany, and a PhD-equivalent degree from the University of Witten-Herdecke, Germany. He has expertise in clinical malignant hematology, cytogenetics, molecular genetics, next generation sequencing and functional genomics and is most known for his work on biomarkers in Hodgkin lymphoma and the discovery of novel gene fusions in B cell lymphomas. He serves as a member of the Lymphoma Research Foundation's Panel of Scientific Advisors and on the Cancer Research Society's Medical Expert Committee.

Dr. Marianne Sadar was appointed to a four-year term with the Board of Trustees for the **Canada Science and Technology Museum**. Dr. Marianne Sadar is a Distinguished Scientist with BC Cancer's Genome Sciences Centre, a professor in the Department of Pathology and Laboratory Medicine at UBC and a co-founder and Chief Scientific Officer of the biotechnology company Essa Pharma Inc. She has over 20 years of experience in developing treatments specifically for prostate cancer. The Canada Science and Technology Museum is one of the three museums comprising the Canada Science and Technology Museums Corporation, which is responsible for preserving and protecting Canada's scientific and technological heritage and promoting and sharing knowledge about it.



DECEMBER

Every year, scientists and scholars worldwide publish their findings in academic journals and proceedings, producing papers estimated in the range of more than two million. How does the research community determine the papers with the most value? Citations are one way, and a paper that other scientific authors have frequently cited has arguably proved itself to be highly significant. This is the approach taken by **Clarivate Analytics** (which in 2016 purchased the scientific properties of Thomson Reuters, including the Web of Science). For the past several years, they have been quantifying the number of citations for specific scientists in various disciplines and generating a list of **Highly Cited Researchers**, or what they call, **The World's Most Influential Scientific Minds**. Four BC Cancer scientists are recognized as having peer-reviewed papers that rank in the top one per cent by citations from publications in their field, including veteran Highly Cited Researchers, **Drs. Randy Gascoyne, Joseph Connors** and **Marco Marra**, and newly listed BC Cancer Medical Oncologist, **Dr. Karen Gelmon**.



From left to right: Drs. Marra, Connors and Gascoyne.

AMONG THE WORLD'S MOST INFLUENTIAL SCIENTIFIC MINDS: AN INTERVIEW WITH DR. KAREN GELMON

> *"The most significant progress has been made in understanding cancer as multiple diseases, not just one disease."*

What does it mean to you to be listed among the World's Most Influential Scientific Minds?

When I started my training I had this fear of things not changing, of rolling over one day many years later and realizing that I was treating cancer in the same way that I had for years, that there were not any improvements in cancer outcome. This led me to want to participate in research, to be part of the work that could improve the outcomes of persons with cancer. Fortunately, since the time I started my career, there have been significant improvements in cancer treatments and outcomes and it's been a very exciting time. Having said that, we haven't improved enough, more research is very necessary. Being part of this list is an honour, and it's rewarding in that it suggests that my attempts to do research that has impact has been noticed, and it certainly inspires me to do more research. I think getting cited is also important for people to really realize the importance of cancer research.

What is the focus of your research?

I've done research in clinical medicine in a number of different areas. Most of my work has been research in the area of clinical trials, ranging from Phase I to III, trying to develop new and promising drugs as well as comparing new agents to standard therapies. I've also participated in translational research of prognostic and predictive factors to try to figure out how to treat specific cancers and which tumours have a higher risk of relapse. This has included outcomes research looking at our patient population. And finally I've also done research in supportive care and survivorship issues. I've always felt it important to look at the whole focus of cancer care and where it can improve.

What's the most pressing problem you're facing in your research now?

We're zooming ahead with what we know in the lab and we're really progressing in terms of understanding molecular and genomic targets as well as hereditary factors of disease, but we're behind in getting patients into clinical trials or translating our findings into standard clinical care. We're limited in the number of clinical trials that we can open and the number of patients we can accrue to them. We're also limited in funding for clinical trials compared to a number of years ago when investigator led research was easier to develop and fund. We have really great people doing clinical research, but it needs to be more integrated into care across the province.

Where have you seen the most significant progress in your field of research?

The most significant progress has been made in understanding cancer as multiple diseases, not just one disease. And it's also been in the area of understanding both risk and responsiveness; risk relates to what is the risk of this cancer recurring, and responsiveness is how the disease will respond to certain treatments. With the success of some treatments and more understanding of the tumours, we are now asking whether we can decrease treatment in persons who have a very good chance of a good response, versus how we can escalate treatments in those persons that have worse prognoses and are not responding to treatment. These studies are important for quality of life and our guidelines but are difficult to do.

Where is this research leading you next?

It's leading us to do some interesting trials on decreasing the duration of hormone therapy in very low risk patients. It's leading us to talking about how long we really need to continue some targeted therapies. And it's increasing our interest in doing targeted therapies in combination and avoiding classic chemotherapy in some malignancies.

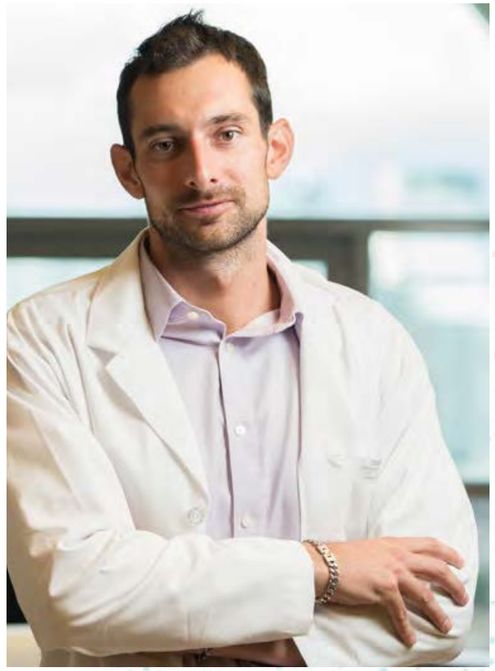
What kind of advice would you offer to budding clinical scientists?

Stay curious and passionate about what you do. Get a really good grounding in laboratory and/or statistical methodology so that you can be highly competitive in being successful with funding and grants. Look for institutional organizations that support research. Love what you do, and find a really good faculty who you love working with. Have fun with your work.

OUTSTANDING TRAINEE PUBLICATIONS

The Office of the VP, Research held a Publication Awards competition for papers of outstanding scientific merit first-authored by BC Cancer Students, Residents, Post-doctoral Fellows or Graduate Students. Awards were given in the categories of Basic and Translational, Clinical and Translational and Cancer Control and Health Services Research.

In the category of **Basic and Translational** research, **first place** was awarded to **Dr. Yikan Wang**, a Post-doctoral Fellow supervised by Dr. Sohrab Shah in the Department of Molecular Oncology, for the paper "Genomic consequences of aberrant DNA repair mechanisms stratify ovarian cancer histotypes" published in *Nature Genetics*. Dr. Wang and colleagues examined the global genomic patterns of 133 ovarian cancer patients and identified different patient subgroups.



Second place in the category of **Basic and Translational** research was awarded to Graduate Student **Dr. Alberto Delaidelli**, supervised by Dr. Poul Sorensen in the Department of Molecular Oncology, for the paper "MYCN amplified neuroblastoma requires the mRNA translation regulator eEF2 kinase to adapt to nutrient deprivation" published in *Cell Death & Differentiation*. Dr. Delaidelli and colleagues identified eEF2K as a pivotal mediator of the adaptive response of tumour cells to nutrient deprivation in childhood neuroblastoma with MYCN amplification, a pediatric cancer associated with aggressive disease and high mortality.

The award for the best **Clinical and Translational** paper was given to **Hanna McGregor**, a PhD student supervised by Dr. Haishan Zeng from the department of Integrative Oncology for the paper "Real-time endoscopic Raman spectroscopy for in vivo early lung cancer detection" published in the *Journal of Biophotonics*. McGregor and colleagues present the use of a real-time endoscopy Raman spectroscopy as an improvement over standard imaging techniques, to improve the specificity for localizing lung cancers in central airways.

In the category of **Cancer Control Research and Health Services Research** related to cancer (including Health Economics), the award was presented to **Deirdre Weymann**, a health economist with Dr. Dean Regier in the department of Cancer Control Research for the paper "The cost and cost trajectory of whole-genome analysis guiding treatment of patients with advanced cancers" published in *Molecular Genetics & Genomic Medicine*. Dr. Weymann and colleagues estimated the costs of applying whole-genome analysis to guide treatments for patients with advanced cancers, and characterized how costs evolve over time for BC Cancer's Personalized OncoGenomics program.

SCREENING & DIAGNOSIS

International collaboration leads to new genetic markers for breast-cancer risk

An international research project involving BC Cancer scientists, **Drs. John Spinelli** and **Angela Brooks-Wilson**, has identified new genetic markers associated with the risk of breast cancer. The findings, published in two separate studies in the journals *Nature* and *Nature Genetics*, reveal 72 new genetic variants that predispose women to breast cancer. Previously about 107 were known, including well-known mutations of the BRCA1 and BRCA2 genes, which occur in less than one per cent of women. Some of the newly identified genetic markers are much more common and, although each variant only increases the risk of cancer modestly, when combined the risks are multiplied. The project involved about 550 scientists around the world and was carried out by the OncoArray Consortium. The two studies, funded primarily by Genome Canada and the Canadian Institutes of Health Research, involved analyzing the genetic data of about 275,000 women, including 146,000 who had been diagnosed with breast cancer. BC Cancer provided data and DNA samples from approximately 1,200 breast cancer cases and an equal number of cancer-free controls identified through its breast screening program.

Advances in lymphoma and leukemia screening and diagnosis

A research team led by **Dr. Christian Steidl** in the Lymphoid Cancer Research (LCR) department has developed a novel prognostic model for classical Hodgkin lymphoma (cHL), called RHL30. Currently cHL patients with refractory or relapsed lymphoma receive salvage chemotherapy followed by high-dose chemotherapy and autologous stem-cell transplantation (ASCT), which has a success rate of about 50 per cent. Dr. Steidl and his team used the NanoString digital gene expression profiling platform to develop RHL 30, a more reproducible biomarker assay for post ASCT outcome prediction, which can guide treatment decisions at the time of relapse. The results of the study have been reported in the *Journal of Clinical Oncology*.

Dr. Christian Steidl

Dr. David Scott

Dr. David Scott of the LCR department led the development of the MCL35 assay through a Lymphoma/Leukemia Molecular Profiling Project (LLMPP) consortium collaboration. This assay translates a previously described gene expression-based signature for proliferation in mantle cell lymphoma into an assay that can be applied to routine biopsies using the NanoString technology platform. The assay will allow the development of trials that will match treatment regimens to the risk of relapse of the patient. A patent has been filed on this assay, which was described in a paper published in the *Journal of Clinical Oncology* this year. In collaboration with several European groups, the assay has been applied to four clinical trials, demonstrating that it is prognostic for outcome and that intensive treatments improve outcomes in selected risk groups, suggesting that the assay will be useful in treatment planning.

Using MicroRNA to identify pediatric patients at risk of treatment failure or relapse

Children with acute myeloid leukemia (AML) whose disease is unresponsive to standard chemotherapy therapy or who experience relapse after initial response have dismal outcomes. A Canadian and American research team led by **Dr. Marco Marra**, Distinguished Scientist and Co-Director of the Genome Sciences Centre at BC Cancer, sought to comprehensively profile pediatric AML microRNA (miRNA) samples to identify dysregulated genes and assess the utility of miRNAs for improved outcome prediction. In a study published in the *Journal of Clinical Oncology* they identified 36 miRNAs where expression levels at diagnosis were highly associated with event-free survival. They then used the combined expression of these 36 miRNAs to create a novel miRNA-based risk classification scheme called AMLmiR36 to help identify patients who are at high risk of experiencing treatment failure.

Implementation of a novel molecular barcoding strategy for ctDNA sequencing

Genetic material from tumours is commonly present at low levels in the bloodstream of cancer patients. The use of this circulating tumour DNA (ctDNA) as a source of genetic material from tumours is rapidly being adopted as a non-invasive approach for studying changes in a tumour over time. **Dr. Ryan Morin**, Senior Scientist with BC Cancer's Genome Sciences Centre, has implemented a new molecular barcoding technique that allows for unprecedented sensitivity in the detection of mutations from ctDNA. This research, published in *Scientific Reports*, demonstrates the method can reveal changes in tumour burden over time, and that these changes are relevant to a patient's clinical response and have the ability to provide a signal for a possible relapse. The research team has developed customized assays for a variety of cancer types including some paediatric cancers.

New test identifies the risk of breast cancer reoccurrence

Molecular research has identified several distinct types of breast cancer, which have different risks of spreading and therefore warrant different treatment. Research performed by **Dr. Torsten Nielsen** at BC Cancer in collaboration with colleagues from the USA generated a test originally called PAM50 that identifies the major molecular types of breast cancer and assigns a risk score. Through BC Cancer's Technology Development Office, this new test has been commercialized in partnership with Seattle-based NanoString technologies and renamed Prosigna. Prosigna is used to identify a patients' 10-year risk of distant breast cancer recurrence and provides guidance as to the benefit of hormonal therapy and chemotherapy for an individual patient. The test was approved by FDA and Health Canada, and is now recommended in several independent international guidelines and health care assessments. In 2017, Prosigna became available as a test run in Vancouver for the benefit of women in British Columbia, while also being used in 13 countries around the world.

Origins of endometriosis and of clear cell and endometrioid carcinomas of the ovary and uterus

Dr. David Huntsman, and researchers at UBC and Johns Hopkins University, published a study in the *New England Journal of Medicine* that examined tissues from women with endometriosis and found non-hereditary gene changes. They discovered that endometriosis, until now viewed mostly as a hormonal and inflammatory disorder, contains genetic changes found in some cancers that likely cause the gynecological condition and could lead to more personalized treatments. Although these mutations are also found in some cancers, they do not indicate risk of developing cancer in most cases of endometriosis.

Endometrial epithelium is also the presumed tissue of origin for both eutopic and endometriosis-derived clear cell and endometrioid carcinomas; however, no single class of mutations has been found exclusively in either histotype. Dr. David Huntsman and his team identified the protein cystathionine γ-lyase (CTH) as a lineage-specific marker for clear cell carcinoma, as it is expressed at high levels in clear cell carcinomas of the ovary and endometrium. The results of this study were published in the *Journal of Pathology*.

Dr. David Huntsman

TREATMENT

Seven new subtypes of ovarian cancer identified

BC Cancer research led by **Drs. Sohrab Shah** and **David Huntsman** has uncovered seven new subtypes of ovarian cancer, which could result in new treatment strategies for some ovarian cancer patients including those that do not respond well to chemotherapy. The discovery, published in *Nature Genetics*, analyzed the genetic information of more than 100 ovarian cancer patients in order to identify abnormalities in the DNA of ovarian cancer cells. Two of the new genetic subtypes uncovered belong to a very common and deadly form of ovarian cancer called high grade serous carcinoma (HGSC). Scientists believe they have found a structural change in the DNA of one subtype that can identify HGSC patients that will not respond to chemotherapy and who may instead benefit from new classes of treatments. The other five subtypes uncovered were found by analyzing clear cell, endometrioid and adult granulosa cell ovarian cancers. The results from this work suggest that some of these subtypes may be susceptible to existing treatments, but clinical trials are needed to test and confirm this hypothesis. This information may be used to develop tests that can direct patients toward new investigational treatments.

Approach to treatment for small cell carcinomas of the ovary, hypercalcaemic type

Small cell carcinoma of the ovary, hypercalcaemic type (SCCOHT), is a rare but aggressive and untreatable malignancy affecting young women. **Dr. David Huntsman's** research group, in collaboration with the Translational Genomics Research Institute (TGen) at the University of North Carolina recently discovered that SMARCA4 is the only gene recurrently mutated in the majority of SCCOHT cases. As recently published in the *Journal of Pathology*, they discovered that loss of SMARCA4/SMARCA2 caused a dependency of SCCOHT cells to the enzymatic activity of a protein called EZH2. Based on this discovery and a similar independent discovery by Epizyme Pharmaceutics, clinical trials are now underway to evaluate the efficacy of EZH2 inhibitors in SCCOHT patients.

Dr. Sohrab Shah

New radio-ligands ready for clinical trials

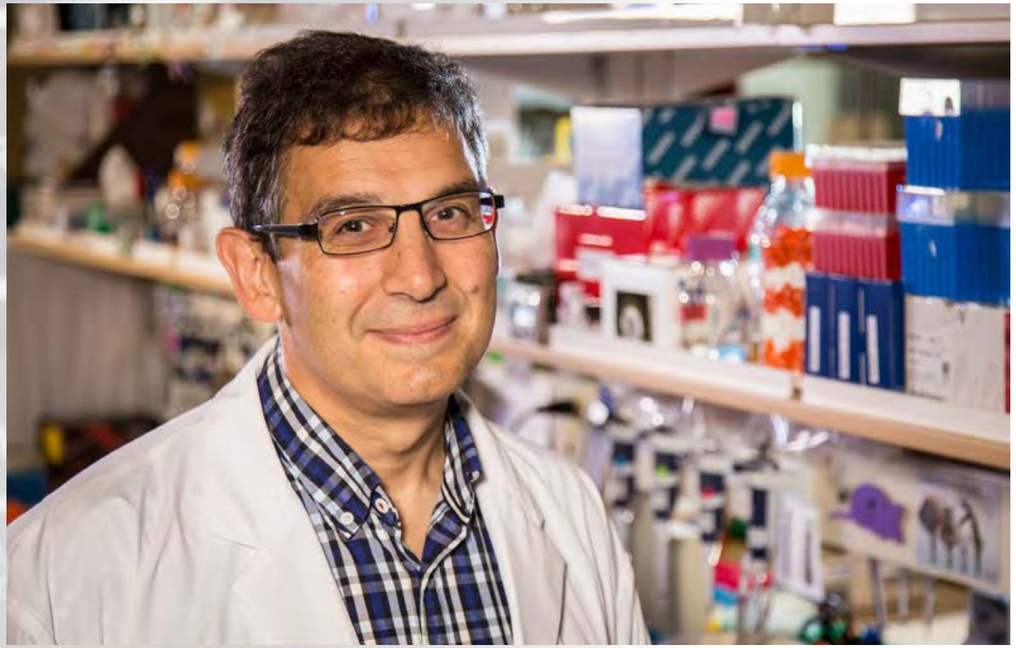
The bradykinin B1 receptor is overexpressed in many cancers. A team led by **Drs. François Bénard** and **Kuo-Shyan Lin** have developed a large number of improved radioactive ligands (molecules that bind to proteins in the body) targeting the bradykinin B1 receptor. Starting in 2015, using relatively unstable compounds, they have now developed, studied and identified many candidate compounds to be tested in clinical trials. As published in the journals *Molecular Pharmaceutics* and *Bioorganic and Medicinal Chemistry,* these new radiopharmaceuticals are very potent and stable and show very high accumulation in cancer cells, and also atherosclerotic plaques, that express the bradykinin B1 protein. This opens up the possibility for new therapeutic and cancer imaging options, using radiation that specifically targets cancer cells while reducing the amount of radiation exposure in healthy tissue.

Dr. Kuo-Shyan Lin

Radiopharmaceuticals are also promising for imaging and the treatment of metastatic melanoma.
A research team led by Dr. Bénard has developed highly promising radiopharmaceuticals for melanoma imaging and radionuclide therapy. This was based on a known molecule that binds to a receptor known as melanocortin 1 that is overexpressed in melanoma. By modifying a link between the radioactive tag and the molecule, they were able to significantly enhance tumour retention and decrease the accumulation of the compound in the kidneys. These new radiopharmaceuticals have high potential to improve the imaging and treatment of metastatic melanoma.

Caspase protein helps cancer cells resist treatment by proteasome inhibitors

The maintenance of protein homeostasis is important for normal physiology and good health. There are two main degradative pathways in cells that contribute to this process, known as proteostasis.
How these two pathways are coordinated is not well understood. In a study using the fruit fly model organism published in the journal *Autophagy,* **Dr. Sharon Gorski** and colleagues identified a molecule called a caspase that links the two pathways under conditions of cell stress. They showed that when one of the degradative pathways (called the proteasome) is inhibited, the caspase is essential for activating the other pathway to enable cell survival. As the proteasome is a target for cancer treatment, this discovery reveals a potential way that cancer cells may avoid being killed by the effects of proteasome inhibitor drugs, such as bortezomib in the treatment of multiple myeloma and mantle cell lymphoma.



Dr. Samuel Aparicio

Two new breast cancer drug discoveries

As published in *Nature Communications*, **Dr. Samuel Aparicio** has discovered that the drug CX-5461, originally developed for cancers of the blood and lymph system, can be repurposed as a treatment for breast cancer. Still early in development, Dr. Aparicio has shown that CX-5461 can bind to the DNA of certain regions of the genome causing it to fold up and interrupt the DNA copying process. The compound is selectively active in tumours from patients with mutations in the BRCA1/2 genes, known to cause a strong familial predisposition to breast cancer, and account for approximately 15 per cent of the population with the disease. The study is currently in Phase I of a multi-centre clinical trial that began in June 2016. Phase II will accept even more patients, to determine whether the activity found through preclinical studies is reflected in responses in patients.

In addition, a second paper also published in *Nature Communications* by Dr. Aparicio highlights the discovery of a different prototype drug, called 'T3', engineered to alter the way that cells translate DNA through splicing of RNA into proteins. This small yet highly-potent drug-like molecule is currently in lab-testing and is being used to understand how different breast cancer cells might be susceptible to having RNA splicing interrupted. The drug molecule interferes with the molecular machinery that stiches gene sequences together to make fully functional proteins. Mutations in RNA splicing genes and defects in splicing have been found in diverse cancers, including breast cancer. The prototype drug molecules are allowing Dr. Aparicio and his team to seek out situations where cancer cells are uniquely susceptible to interference with RNA splicing.

FIVE YEARS OF PERSONALIZED ONCOGENOMICS (POG)

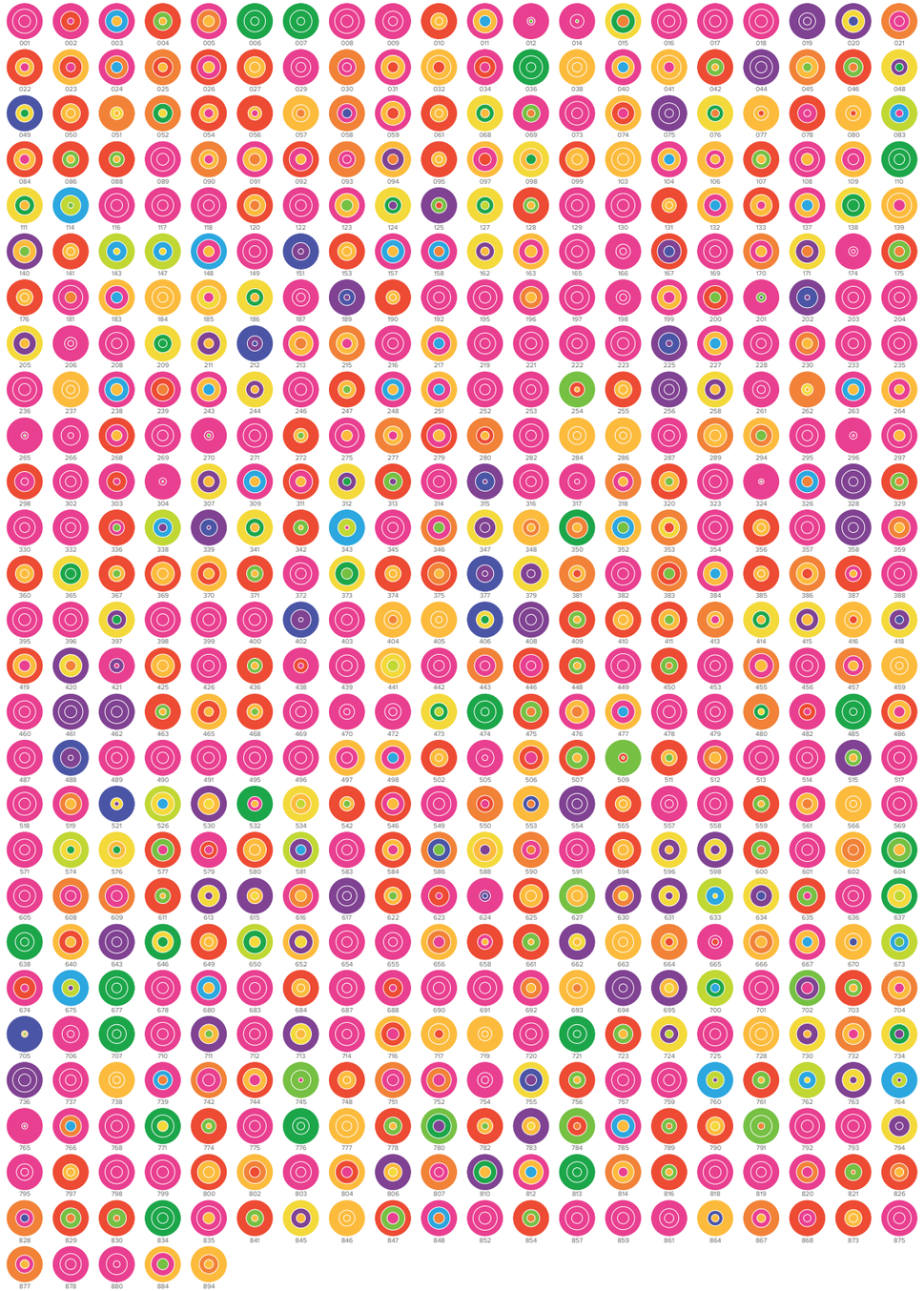
The **BC Cancer Personalized OncoGenomics (POG)** program is a clinical research initiative studying the impact of embedding whole genome sequencing into real-time treatment planning for British Columbian patients with metastatic cancers. It is a collaborative research study including many BC Cancer oncologists, pathologists, other clinical staff, researchers and technical personnel.

Since the launch of the program in 2012, POG has successfully recruited 1,000 patients with metastatic cancer and completed sequencing and analysis on more than 600. For those 600 patients and their clinicians, they had access to additional personalized information to inform their treatment decision options. BC Cancer is the only centre in the world conducting a study on the scope and scale of POG.

The majority of the funding for the direct cost of POG comes from the BC Cancer Foundation. That funding has been leveraged to obtain additional support for advanced research equipment, trainees, and related research programs such as the Terry Fox Research Institute's Canadian Comprehensive Cancer Centre Network and a new pan-Canadian clinical trial called CAPTUR, which will further align patients in POG with targeted treatments.

In 2017, POG research resulted in eight publications in peer-reviewed journals, from studies identifying genomic signatures that can predict responses to some treatments for breast cancer patients and the molecular characterization of metastatic pancreatic tumours to analyzing the cost-trajectory of using whole-genome analysis to guide treatment decisions. Ten presentations were delivered at high profile clinical or scientific events and several news stories were published about POG, including an award-winning documentary on CBC's *Nature of Things* called *Cracking Cancer*.

Over the past five years, the POG team has grown to include more than 200 people from across BC Cancer, including at all its regional centres. The impact and momentum of the resulting collaborations will continue to foster research studies and advances in clinical translation and outcomes for the foreseeable future.



MAKING ART WITH SCIENCE: INTERVIEW WITH MARTIN KRZYWINSKI

> *"We've been training to spot patterns ever since life began on Earth."*

Cancer is complicated. Decades of painstaking experiments, meticulous measurements and reams of computer code have resulted in a dizzying array of data about the disease that even the most mathematically inclined minds find boggling.

At BC Cancer's Genome Sciences Centre (GSC), scientists use this data to crack cancer's code, running DNA sequencing machines 24 hours a day, seven days a week, analyzing the three billion base pairs that make up approximately 30,000 genes within the 23 chromosomes of the human genome; errors in the code, known as mutations, result in the plethora of cancers we know too well. To date, the GSC has sequenced more than two petabases of DNA, or about the same as 66,000 whole human genomes.

How to make sense of all of these numbers? Enter Martin Krzywinski, staff scientist with the GSC. He makes art from it. From popularizing science to facilitating dialogue between disciplines and inspiring ideas for research, his data visualizations and illustrations aren't just pretty; they're helping to uncover clues about cancer.

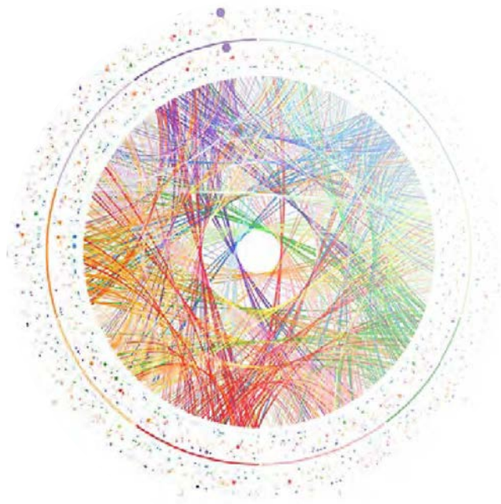
Popularizing science

In 2003, Martin did something simple, yet elegant, that made his colleagues, and the world, take notice.

"I looked at the way that people would traditionally represent chromosomes as horizontal lines, using diagonal lines to connect genes to represent relationships. I thought: turn the chromosomes into a circle. Put connecting lines on the inside."

Making a horizontal chart into a circle turned out to be really useful in showing similarity or dissimilarity between regions in a genome, for comparing genetic information between species or analyzing differences between cancer and normal DNA, for example. It's also a useful "stopgap measure," Martin says, a way to make-up for what's missing. "Visualization can indicate where to look when we don't really know yet."

He called the design Circos, and before he knew it, it was everywhere. After appearing in the *Catalogue of Somatic Mutations*, Martin began to see it in all sorts of peer-reviewed publications. But it wasn't just interesting to scientists. It appeared in the *New York Times* and on the back of a coffee table book by David Cronenberg. *Wired Magazine* asked him to make a version depicting the relationship between the characters on the popular television series, Lost. Circos wasn't just useful, it was beautiful.



"I think the reason why visualization of complex data works so well, is because we've been training to spot patterns ever since life began on Earth. We've had solid schooling in finding patterns, because we wanted to avoid predators. We aren't trained in mathematics in the same way. You can't fall back on natural faculties for it like you can for shapes."

Facilitating dialogue

Martin's work has been useful in BC Cancer's Personalized OncoGenomics (POG) program where whole genomes of cancer patients are sequenced and compared to DNA from their cancer. Visualizations can communicate this information quickly. It can also cut across specializations, which is important to POG's multidisciplinary teams.

To celebrate POG's fifth anniversary in July 2017, Martin made a graphic of all the individual POG patients that had been sequenced. He represented each patient as a circle with three concentric rings, shaded with 12 different colours representing different tumour types (see page 23). What you see in a circle is the three most similar tumour types, based on the genetic information of the patient's tumour sample, to their cancer. For example, despite a diagnosis of breast cancer, the mutations in a patient's cancer may be similar to a patient with colorectal cancer or quite different to another with breast cancer.

"Between the fundamental aspects to the overwhelming aspects of cancer, is where this art comes into play. Does it tell a story? Does it look like something you could understand even if you don't know what it is? In this example, the colours obviously mean something. The circles do too. So, now I can tell you a story about cancer."

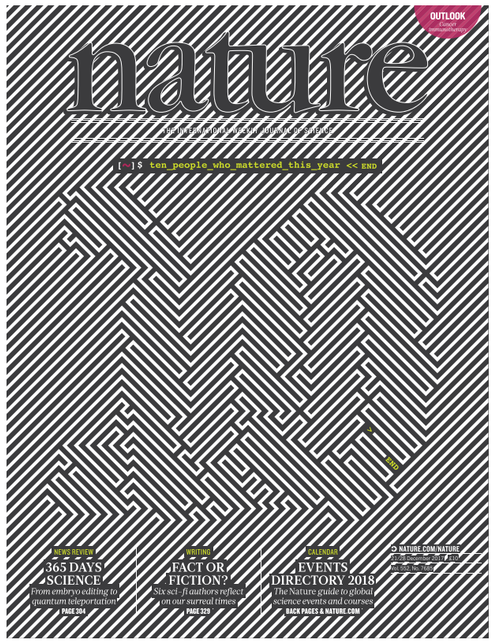
Insights and inspiration

Every December, *Nature* publishes its "10" issue highlighting 10 science stories that had a big impact in the past year. In 2017, the themes included quantum entanglement and artificial intelligence. Generally the number 10 appears somewhere on the cover and the publication solicits for art. Martin took up the challenge.

"I only make 2D flat stuff, so I thought of the Traveling Salesman Problem."

The Travelling Salesman Problem (TSP) is all about finding the shortest route through a number of points without crossing the same point twice, and it's inspired a genre of art. TSP art are black and white images represented by dots that the artist tries to find the shortest path through without doubling back. The final product is zebra-like, full of dense lines where it is black, less dense where it is grey and no lines where it's white. Depending on the solution, the image could be compelling or just a bunch of lines. Martin did this with the number 10.

"You have to throw an algorithm at TSP art. There's the artificial intelligence angle. And it looks kind of tangled too, right? So I ran it and *Nature* ended up using it. It's striking. It's jarring. I like it. It fits my personality.

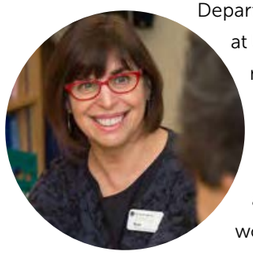


"A lot of the stuff that I make is not useful in the way that a hammer is useful. It's not a tool for getting something done. But hopefully it's inspiring. I think it gives people ideas. Or, perhaps, it helps to relieve the crushing burden of trying to understand science. I hope it puts people in a better mood; a mood that helps to maintain focus on science but provides relief in the form of a pleasant pattern. Maintain focus on science but provides relief in the form of a pleasant pattern. Maybe it even gives a scientist hope that their data has a pleasant pattern too. They just haven't found it yet."

PAIN & SYMPTOM MANAGEMENT

The role of nutrition and exercise during cancer treatment

Exercise and healthy eating programs have been shown in research studies to improve the health and well-being of women receiving chemotherapy for breast cancer. However, access to such programs is currently not a common part of cancer care. A project led by the BC Cancer Nutrition and Rehabilitation program, in collaboration with the Department of Physical Therapy at UBC, has examined how many physicians would refer patients to such a program, how many women would attend and what the benefits would be. As published in *The Oncologist* and *Medicine & Science in Sports & Exercise*, the researchers found that physicians liked having a pathway to refer women to a program they trusted. Women enjoyed the program and had improvements in fitness.



Now the team, co-led by **Drs. Ryna Levy-Milne,** Provincial Director for Therapeutic Oncology Services, and **Kristin Campbell,** Affiliate Scientist in Cancer Control Research, has received an **MSFHR Reach Award** to investigate the development of an exercise guidance program specific to cancer survivors in British Columbia. The Reach Program provides funding to support teams to co-develop activities that inform or improve further health research practice or policy-making. Previous research by Drs. Levy-Milne and Campbell has established that structured exercise after a cancer diagnosis is effective in managing symptoms, improving health and returning to normal life.

Post-operative pain control for breast surgeries using breast block technique

Pectoral nerve block (aka, breast block) is a relatively new technique for providing surgical anaesthesia and postoperative analgesia during breast surgery that relies upon the placement of local anaesthetic between the thoracic wall muscles. It allows local anesthesia for up to 36 hours postoperatively, and is even safe for patients who cannot receive general anesthesia. At the BC Cancer Surgical Retreat, **Drs. Sara Gough** and **Frances Chow** presented the results of retroactive analysis of 200 breast cancer surgeries using breast blocks. They found that providing breast blocks gave superior pain control and fewer post-anesthetic complications of drowsiness, nausea and vomiting. Breast blocks may also be correlated with reduced metastasis, which the researchers intend to explore through future research.

BIOLOGY & GENETICS

Spatial heterogeneity in medulloblastoma

Tumour heterogeneity poses a major challenge for the development of targeted therapies that will be effective against an entire tumour. A research team led by Dr. Michael Taylor at the Hospital for Sick Children and **Dr. Marco Marra** at BC Cancer analyzed spatial heterogeneity of genomic profiles, showing medulloblastomas, but not high-grade gliomas, have spatially homogeneous transcriptomes, which allowed for accurate subgrouping of tumours from a single biopsy. Conversely, suitable mutant candidate genes for targeted therapy showed high levels of spatial heterogeneity in medulloblastoma, malignant glioma and renal cell carcinoma, which brings the efficacy of monotherapies against a single target into question. Clinical trials of targeted therapies for medullo-blastoma should first ensure the spatially ubiquitous nature of the target mutation.

A review of the MYC family of cancer genes and the protective effects of gene eEF2K

Distinguished Scientist, **Dr. Poul Sorensen** and colleagues summarized a review of research on the MYC family of cancer genes in *Cell Cycle*, which contributes to more than 50 per cent of all human cancer types. Sorensen's team has found that inhibition of the gene eEF2K can significantly decrease survival of pediatric neuroblastoma tumours that have amplified expression of the gene MYCN under caloric restriction. In their review, they suggest that eEF2K may also have relevance for other tumour types that overexpress MYC genes.

Translational control of aberrant stress responses as a novel hallmark of cancer

Under stress, cells block global protein synthesis to preserve energy while maintaining selective synthesis of proteins that support cell survival. One highly conserved mechanism to regulate protein synthesis under cell stress is to sequester messenger RNA (mRNAs) into stress granules, where their translation is silenced. Stress granules confer survival advantages and chemotherapy resistance to tumour cells under stress. Recently, it has been shown that genetically blocking stress granule formation dramatically reduces tumour invasive and metastatic capacity *in vivo*. In a review prepared for *The Journal of Pathology*, **Drs. Poul Sorensen** and **Amal M. El-Naggar** explain how deciphering mechanisms of selective mRNA translation under cell stress holds great promise for the identification of new targets in the treatment of cancer.

New Developments in Single Cell Genomics

Single-cell genomics is critical for understanding cellular heterogeneity in cancer. To enhance single cell whole genome sequencing, the labs of **Drs. Sohrab Shah, Samuel Aparicio** and **Carl Hansen** (UBC) collaborated to develop and patent a new technique to prepare Illumina libraries for sequencing. The results were published in *Nature Methods*. This technique has the capacity to routinely sequence 3000 cells at a time and represents the highest throughput and most unbiased method of whole genome sequencing of single cells in the field to date.

In 2017, **Dr. Sohrab Shah's** lab made several advances in computational methods for single-cell genomics. Published in *Genome Biology*, his team developed and released software, called ddClone – they showed this approach improves detection accuracy of cell populations present in a tumour, providing a tool for richer insight into how cancers evolve and ultimately acquire resistance to treatment. Also published in Genome Biology, Dr. Shah's team also developed a novel whole genome sequencing analysis method called ReMixt that can infer structural variations from cancer genomes, and developed a new data visualization software framework (E-scape tool suite) tailored for interactive browser-based data visualization of cancer evolution data, published in *Nature Methods*.

Installation of a new **Single Cell Genomics Suite** at BC Cancer was completed in December last year. This suite houses cutting edge sequencing and ancillary equipment in a clean environment. It is accessible to all researchers throughout the Centre. The Department of Lymphoid Cancer Research, in collaboration with the Genome Sciences Centre at BC Cancer, aims to define comprehensive mutational landscapes of refractory and relapsed lymphoid cancers at the single cell level. The fully characterized genomic information extracted from clinically relevant cell populations will give insights into treatment resistance and lead to identification of potential therapeutic targets.

FUNCTIONAL IMAGING

Development of a novel tracer for imaging tumour perfusion with positron emission tomography

Solid tumour perfusion is a proven variable of interest for predicting cancer aggression and response to therapy. Current methods for noninvasively imaging tumour perfusion with positron emission tomography (PET) are limited by restricted accessibility and short half-lives of perfusion radiotracers. As published in the *Journal of Nuclear Medicine*, a team led by BC Cancer's **Drs. Kuo-Shyan Lin, François Bénard**, and **Kevin Bennewith** has developed and verified the compound 2-18F-fluoroethanol (2-18F-FEtOH) can act as a "perfusion reporter" that can now help investigators distinguish between tumours of varying perfusion, and screen the efficacy of blood flow-modifying drugs for use as enhancements to existing cancer therapies.

POPULATION ONCOLOGY

Anne (Syexwaliya) Whonnock, Squamish Elder

Comparison of cancer incidence and survival between First Nations and non-First Nations people in BC

The first study ever to compare cancer development and survival between First Nations and non-First Nations people in BC shows an overall lower incidence of the disease for First Nations people, but also indicates lower survival rates for most cancers. The study was conducted jointly by BC Cancer and First Nations Health Authority and published in the journal *Cancer Causes & Control*. The 1993 to 2010 data set includes "Status Indian" peoples only and is not inclusive of all First Nations, Métis or Inuit peoples in BC.

The results indicate that both First Nations men and women in BC experience a higher incidence of colorectal cancer, with a 22 per cent higher age-standardized incidence rate for women and 39 per cent for men. There also appears to be a trend towards increasing incidence of colorectal cancer for both sexes. A 92 per cent higher incidence rate of cervical cancer was observed among BC First Nations women. Incidence rates of almost all other cancers were generally similar or lower in First Nations populations compared to non-First Nation populations. Trends in incidence rates over time were also similar, with the exception of lung cancer, which is increasing at a rate among First Nations people that may soon overtake declining rates in non-First Nations people. More research is needed to understand the specific reasons for these cancer rates among BC First Nations people.

First Nations people are also less likely to survive a cancer diagnosis compared to non-First Nations people in BC. Overall, poorer survival was seen in the First Nation population in 10 of the 15 cancer types examined in women and 10 of the 12 cancer sites examined in men. Lower survival rates could be influenced by a number of factors including challenges in access to high quality, timely, appropriate and effective cancer treatment, especially in rural and remote areas. Lower diagnosis may be impacted by limited access to screening programs.

The findings in this study suggest a complex basis for these disparities in cancer incidence and survival, and further studies along the entire spectrum of cancer care are required. It also affirms the need for a system-wide response to improve cancer diagnosis and care for First Nations people in BC. For many First Nations peoples, their cancer journey is negatively impacted through the experience of racism in health and social support settings. Culturally safe health and social services reduce barriers to accessing care and detecting cancer early. First Nations people are more likely to access care that is appropriate to their wellness beliefs, goals and needs.

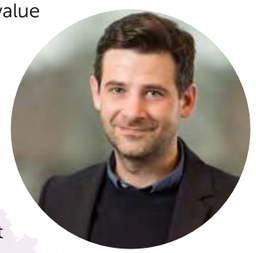
To address these disparities in cancer incidence and survival, BC Cancer, First Nations Health Authority, BC Association of Aboriginal Friendship Centres and Métis Nation BC developed an Indigenous Cancer Strategy for the province that was launched in December, informed by research and extensive engagement with BC Indigenous communities, patients, survivors and their families.

Improving quality of community care for women with breast cancer across the care continuum

BC Cancer is committed to quality care for cancer patients throughout British Columbia. This involves not only treatment, but also community care for early diagnosis, patient support and care of comorbidities during treatment, and post-treatment care to minimize ongoing and late-occurring impacts of cancer. A research team led by **Mary McBride** identified factors leading to a higher (pre-existing disease) or lower (living in remote locations, or neighbourhoods with many immigrants) chance of being diagnosed through screening, and subgroups (immigrants) with longer time to diagnosis. They found that those living in different health regions or in lower income neighbourhoods had variable access to chemotherapy and a significant level of non-compliance with breast cancer follow-up guidelines, pointing to gaps in care that can affect survival. This research was part of a multi-province initiative — Canadian Team to Improve community-based cancer care coordination along the continuum of care (CanIMPACT) — to identify gaps in community care for breast cancer patients across Canada, funded by the Canadian Institutes of Health Research. As well as generating several publications in 2017, including in the *Journal of Family Practice Oncology, Current Oncology, International Journal of Population Data* and *Osteoporosis International*, the results from these studies have been shared with oncology practitioners, family physicians and screening programs throughout BC and Canada.

The cost and cost-trajectory of whole-genome analysis guiding treatment of patients with advanced cancers

Research exploring costs and benefits of whole-genome analysis-guided cancer care are crucial to guide health policy, yet limited data exist on the real-world costs of applying whole-genome analysis in a clinical setting. BC Cancer research led by economist **Dr. Dean Regier** and published in the journal of *Molecular Genetics & Genome Medicine* estimated the costs of applying whole-genome analysis to guide treatments for patients with advanced cancers. It characterized how costs would evolve over time, using the Personalized OncoGenomics program as a case study. Over time, the total costs decreased, driven by a reduction in costs of sequencing, though costs of some of the other components increased; expenditures needed to truly realize whole-genome analysis-guided cancer care remain significant. Dr. Dean Regier was invited to give a talk on a value framework approach to disclosing secondary findings from colorectal cancer screening based on his research into cost and cost-trajectory of whole-genome analysis at The Roundtable on Genomics and Precision Health of the National Academies of Sciences, Engineering and Medicine in Washington DC.



BC as a model province for personalized treatment of Lymphoid cancer

To date, genomic personalization of cancer treatment has only been applied in research settings, not day-to-day medical care, and has not been widely available to patients especially when they live at a distance from research centres. A research project led by the Centre for Lymphoid Cancer at BC Cancer has demonstrated that inclusion of cutting edge research can be provided for patients all across British Columbia in a practical way that rapidly and cost-effectively enables local cancer specialists to use genomic sequencing information to identify different and more effective treatments than would otherwise be offered.

Core components of this project have been the careful analysis of all the costs and cost savings that result from personalized lymphoid cancer care and development of economic analytic tools that enable health care planners to assess the economic impact when similar techniques are applied to treating other cancers and other diseases. This project used BC as a real world laboratory to show that genomic analysis will be able to cost-effectively cure more cancer patients in a way that can readily be duplicated elsewhere around the world.

Establishment of the BioCancer Initiative

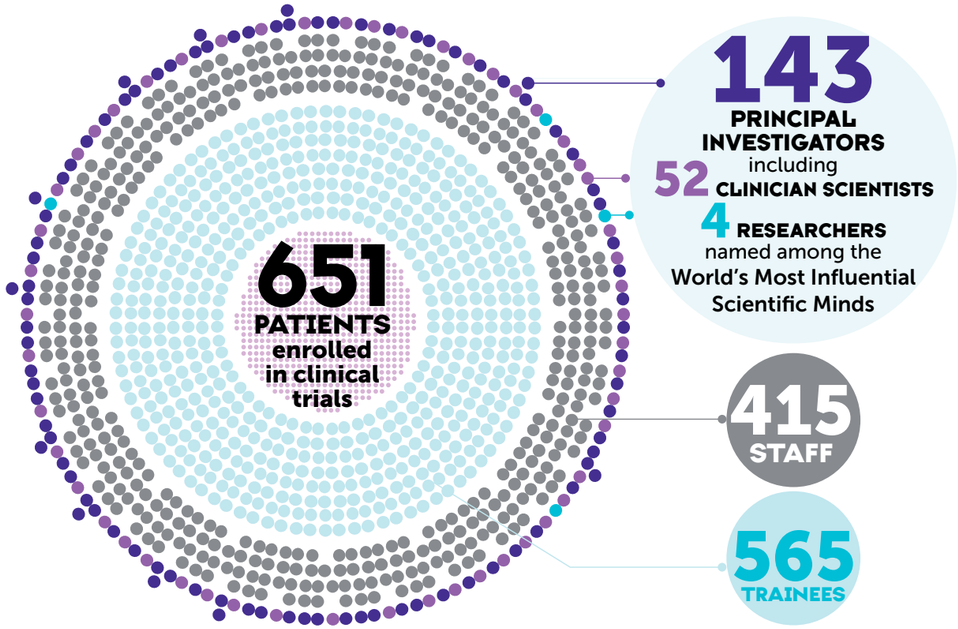
Dr. Christian Steidl from the Centre for Lymphoid Cancer at BC Cancer has recently joined forces with the breast and prostate tumour groups at BC Cancer led by **Drs. Stephen Chia, Samuel Aparicio and Dr. Kim Chi**, respectively, to create a province-wide system for patient consent of biospecimen collection for translational research, and to build comprehensive research and clinical databases housing clinical outcome and analysis data for each tumour type. Called the BioCancer initiative, an integrated system of BC Cancer's six regional centers allows recruitment of cancer patients and specimen acquisition from all across the province for translational research, overcoming under-representation of the patient population from remote areas such as the Northern region. This multi-disciplinary collaboration among the lymphoma, breast and prostate groups will be extended to other tumour groups within BC Cancer.

PATIENT & FAMILY COUNSELLING

Web-based advance care planning resources for cancer patients

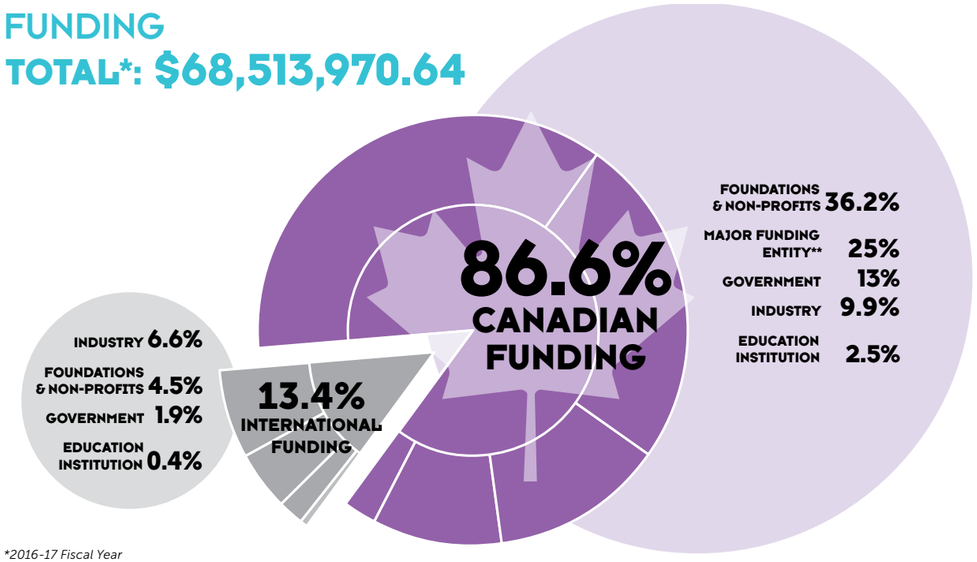
Advance care planning is the process of thinking about and writing down your wishes or instructions for present or future health care treatment in the event that you become incapable of deciding for yourself. It involves having conversations that are difficult for patients, physicians and care providers, but are very beneficial in supporting treatment and end-of-life decisions consistent with what patients want. **Martha Cresswell**, a Master's student and nurse at BC Cancer – Kelowna, in collaboration with researchers at BC Cancer and UBC, examined the use of software called PREPARE — a web-based advance care planning resource (www.prepareforyourcare.org) — for use within cancer care. Funded by the BC Cancer Foundation and published in the journal *Supportive Care in Cancer*, the study found that overall cancer patient participants found PREPARE to be acceptable, applicable, and understandable for advance care planning. It engaged them in personal reflection, helping to clarify their beliefs and values, though some had difficulty with the end-of-life language. Follow-up research is needed to determine whether some of the terminology it uses causes distress or disengagement with the planning process, but overall the web-based resource appears to be a good first step toward easing into difficult conversations associated with advanced care planning.

2017 FAST FACTS



604	335	62	47	9
UNIQUE STUDIES IN PROGRESS	RESEARCH PUBLICATIONS	ACTIVE CLINICAL TRIALS	INVENTION DISCLOSURES	PATENT APPLICATIONS

FUNDING
TOTAL*: $68,513,970.64



*2016-17 Fiscal Year

**Includes The Canadian Institutes of Health Research (CIHR) and its institutes, Genome Canada and provincial Genome agencies, Michael Smith Foundation for Health Research (MSFHR), Natural Sciences & Engineering Research Council (NSERC) and the Social Sciences & Humanities Research Council (SSHRC)

MESSAGE FROM THE PRESIDENT & CEO, BC CANCER FOUNDATION, SARAH ROTH

BC Cancer Foundation donors are vital partners in changing the outcome for British Columbians facing cancer. With 90,000 donors investing in the scientists and clinicians at BC Cancer, this translates into more than $55 million raised to advance life-saving work.

A former patient and one of BC Cancer's steadfast supporters Robert Conconi says: "I owe my life to cancer research and believe BC Cancer is leading the world in personalized cancer treatments for future generations."

Robert Conconi and his son

With one in two of us expected to be diagnosed with cancer in our lifetime, the cause is not only urgent, it's personal. And it's the work of BC Cancer that's going to bring new prevention strategies, new diagnostics and more effective treatments to patients.

For the 77,000 people undergoing cancer treatment today, they have reason to hope for new treatment solutions around the corner. This is in thanks to our generous donors who believe that BC can personalize treatments for every patient and that together, we can provide the best outcomes in the world.

The progress is real and the BC Cancer Foundation is committed to growing support and arming our innovative leaders with the resources to break down cancer.

Sarah Roth, President & CEO
BC Cancer Foundation

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