BC CANCER RESEARCH

Provincial Health Services Authority

2017 Research Report

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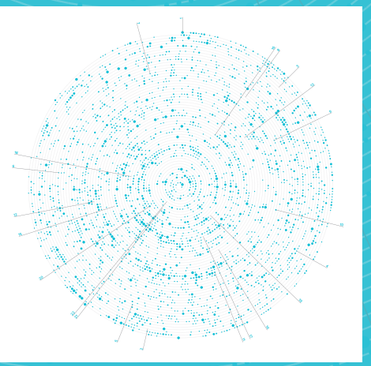
ABOUT THE COVER

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.

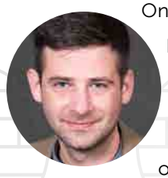
- **Dr. Connie Eaves** and BC Cancer colleagues **Drs. Martin Hirst** and **Davide Pellicani** along with scientists at UBC and the Mayo Clinic are investigating the ways that normal human breast cells turn cancerous, from changes caused by aging to the introduction of cancerous genes.

- **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.

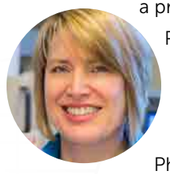
NOVEMBER

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.