

2019  
YEAR  
in  
REVIEW

Bringing Genomics to Life.™



Canada's Michael Smith Genome Sciences Centre (GSC) at BC Cancer is Bringing Genomics to Life.™ As an international leader in genomics, bioinformatics and proteomics for precision medicine research, we develop and deploy cutting-edge sequencing, computational and analytical technologies to prevent and diagnose cancers and other diseases, uncover new treatment targets and therapeutic approaches and realize the social and economic benefits of genome science.

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# PEOPLE

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## DIRECTORS

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Associate Member, Michael Smith Laboratories, UBC  
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### **ANGELA BROOKS-WILSON, PhD**

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Professor, Department of Medical Genetics, UBC

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Member, Experimental Medicine, UBC  
Founding Member, Centre for Blood Research, UBC  
Member, Stem Cell Network

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Distinguished Scientist, GSC, BC Cancer  
Professor, Department of Medical Genetics, UBC  
Associate Faculty, Department of Computer Science, UBC  
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Associate Scientist, Public Health Lab, BC Centre for Disease Control

## **MARTIN HIRST, PhD**

Head, Epigenomics, GSC, BC Cancer  
Senior Scientist, GSC, BC Cancer  
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Associate Professor, Department of Microbiology & Immunology, UBC  
Associate Director, Michael Smith Laboratories, UBC

## **RYAN MORIN, PhD**

Senior Scientist, GSC, BC Cancer  
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Associate Member, School of Computing Science, SFU

## **ISABELLA TAI, MD, PhD, FRCP(C)**

Senior Scientist, GSC, BC Cancer  
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## **NADINE CARON, MD**

Senior Scientist, GSC, BC Cancer  
General & Endocrine Surgeon, Prince George Regional Hospital  
Assistant Professor, Surgery, Northern Medical Program, UBC  
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## **MANAGEMENT & ADMINISTRATION**

### **LANCE BAILEY**

Head of IT Systems and Security

### **MARILYN GILLESPIE, CPHR, SHRM-SCP**

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Head of Project Management

### **PAUL LYTHGO, B.Sc., PMP**

Head of Laboratory Operations

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Head of Knowledge Translation

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Head of Finance

### **GEORGE YANG, B.Sc.**

Head of Sourcing and Procurement

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**ERIC CHUAH, B.Sc., Bioinformatics—Databases**

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**ANDY MUNGALL, PhD, Biospecimen & Library Cores**

**KAREN MUNGALL, B.Sc., Bioinformatics—Analysis**

**SANDRA SPENCER, PhD, Proteomics**

**RENÉ WARREN, Bioinformatics Technology Lab**

**YONGJUN ZHAO, M.Sc. BVM, Technology Development**



# 2019 IN NUMBERS

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13

PRINCIPAL  
INVESTIGATORS

239

STAFF

140

TRAINEES

11

HIGHLY CITED  
RESEARCHERS

16

VOLUNTEERS

96

PEER-REVIEWED  
PUBLICATIONS

76

PATIENTS ENROLLED  
IN POG

$4 \times 10^{14}$

BASES  
SEQUENCED

1

NEW SEQUENCER

131

STATEMENTS  
OF WORK

\$18M

COLLABORATIVE  
SERVICES

\$19.5M

GRANT  
FUNDING

# MESSAGE

## FROM THE DIRECTORS

**2019** marked a significant milestone for Canada's Michael Smith Genome Sciences Centre (GSC): our 20<sup>th</sup> anniversary.

In 1999, Drs. Don Carlow, Victor Ling and Simon Sutcliffe, leaders from BC Cancer, working with Nobel Laureate Dr. Michael Smith—with critical support from the BC Cancer Foundation, National Institutes of Health, Canada Foundation for Innovation and BC Knowledge Development Fund—created the world's first genome centre embedded within a cancer clinic, garnering fast support from important partners including the Canadian Institutes of Health Research, Genome Canada and Genome BC and Michael Smith Foundation for Health Research.

Over the last 20 years we have trained more than 2,000 highly-qualified personnel and published 1,405 peer-reviewed papers, which have attracted 173,388 citations. We have been part of 946 research projects and have contributed to thousands of national and international research

collaborations. Our 13 Principal Investigators have been leaders on projects awarded more than \$1.1 billion from more than 160 funders.

Last year alone, the GSC sequenced 391,012,881,130,938 bases of DNA, bringing its total to more than 2.74 *petabases* (2,740,000,000,000,000)—roughly equivalent to the number of base-pairs in nearly 900,000 human genomes! We were awarded \$19.5 million in funding, published 96 peer-reviewed articles and delivered \$18 million in collaborative research services. Seventy six patients were enrolled into the Personalized OncoGenomics (POG) program, including the 100<sup>th</sup> pediatric patient, bringing the total number to more than 1,000. Eleven of our researchers were named among the most highly cited in the world.

Today, the GSC is working to help BC Cancer change outcomes for people affected by cancer, in British Columbia and beyond. Working collaboratively with those who share our

vision, we have harnessed the power of genome analysis to make fundamental research discoveries and promote patient-centred care, in cancer contexts and in other important health research areas.

As we celebrated our 20<sup>th</sup> anniversary, which included an open house at our Echelon Technology Platform and with a scientific symposium, an obvious theme emerged: the value of partnership, collaboration and mentorship. We would not be where we are today—positioned to bring high-throughput sequencing technology and genome science into entire populations of patients, contributing to disease prevention and diagnosis, ready to uncover new therapeutic targets—without the contributions of our many trainees and scientific partners.

To all of you we say: thank you. We are immensely proud of what we have achieved, and of what we will continue to achieve, together.



MARCO MARRA  
PHD, FRS(C), FCAHS,



STEVEN JONES  
PHD, FRS(C), FCAHS



ROBYN ROSCOE  
B.SC., PMP

# DATA GENERATION

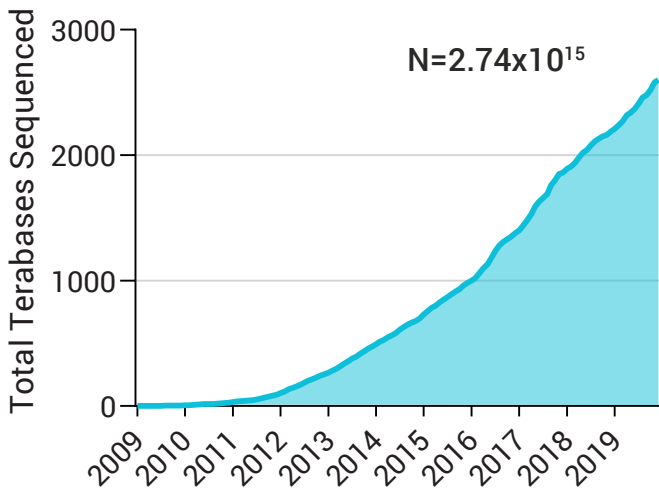
The GSC sequenced 391,012,881,130,938 bases of DNA in 2019, bringing our total to more than  $2.7 \times 10^{15}$ .

We also brought online a new state-of-the-art sequencer, the Oxford Nanopore PromethION.

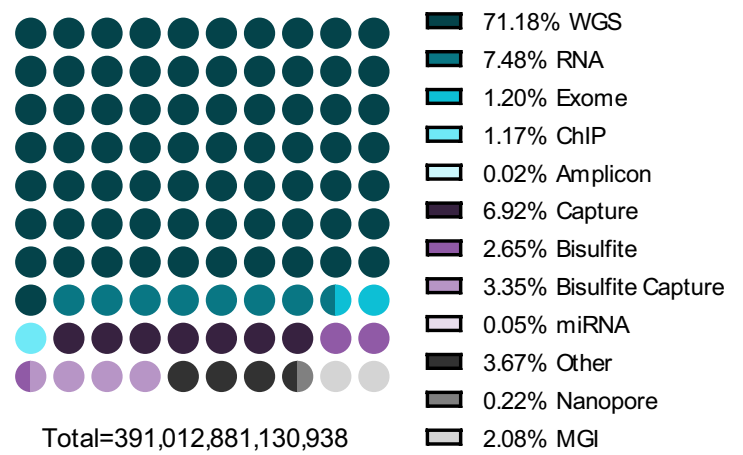
With 24 flow cells running in parallel and the ability to generate long reads of tens to hundreds of kilobases (compared to paired-end 300 base pairs for the longest read on an Illumina platform), the PromethION is enabling the GSC to more efficiently

assemble large and complex genomes, detect genomic structural rearrangements and sequence full-length RNA transcripts.

Total bases sequenced at the GSC



Bases sequenced in 2019



Each dot equals 1 per cent, equivalent to  $\sim 3.9 \times 10^{12}$  bases of DNA. WGS, whole genome sequencing; ChIP, chromatin immunoprecipitation; miRNA, micro RNA.

## SEQUENCING



## COMPUTING



## PROTEOMICS





# FUNDING

More than \$19.5 million in funding was awarded to GSC researchers in 2019, 81 per cent of which was from Canadian sources.

Major funding sources included Genome Canada (GC), BC Cancer Foundation (BCCF), Canadian Institutes of Health Research (CIHR), University of British Columbia (UBC), Simon Fraser University (SFU), National Institutes of Health (NIH), Mitacs, Leukemia & Lymphoma Society of Canada

(LLSC), Princess Margaret Cancer Centre Innovation Accelerator Fund (IAF) and American Association for Cancer Research (AACR).

GSC trainees were awarded a total of \$357,108 in scholarships, travel awards and research funding.

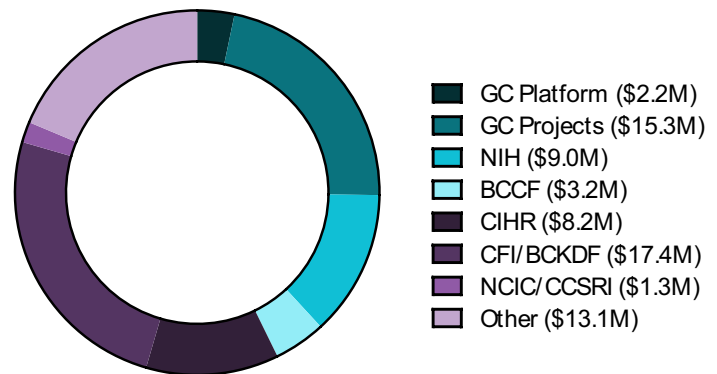
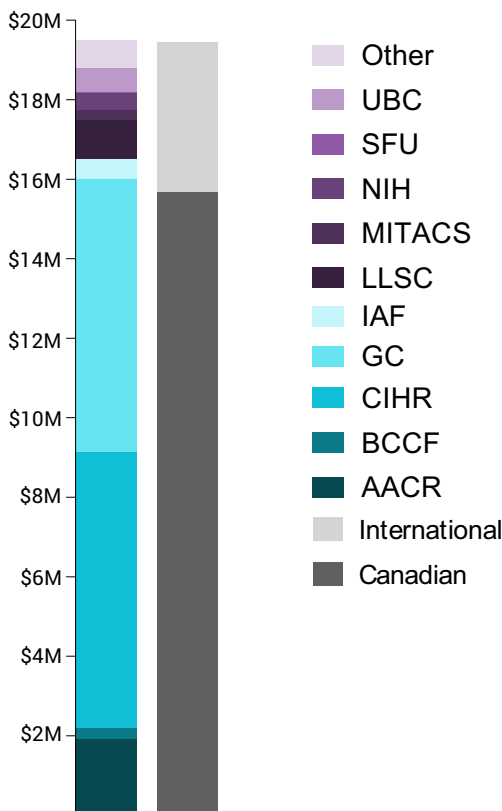
The GSC had a success rate of 45 per cent for all grant applications submitted in 2019, maintaining our consistently high success rate. (For reference, out of the thousands of CIHR project

grant applications submitted each year by researchers across Canada, only 16 per cent are successful.)

Funding currently held by GSC researchers totals \$69.8 million from GC, NIH, BCCF, CIHR, the Canadian Foundation for Innovation (CFI), the B.C. Knowledge Development Fund (BCKDF), the Canadian Cancer Society Research Institute (CCSRI); formerly the National Cancer Institute of Canada (NCIC) and many others.

Funding awarded in 2019: \$19.5 M

Current funding: \$69.8 M



# SELECT PROJECTS

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## Cancer Research UK, Grand Challenge



Cancer Research UK announced new funding for three international research teams as part of its Grand Challenge competition. Dr. Rob Holt is part of a team of 14

investigators that received up to \$25 million to examine how the microbiome can influence a person's risk of developing bowel cancer, how cancer cells and gut microbes interact, how it can influence treatment response and how it may be manipulated to treat bowel cancer. Dr. Holt's lab specifically will research new therapeutic strategies like vaccinations and antibiotics that target key organisms.

## Genome BC, LSARP grant



Dr. Inanc Birol was awarded \$6.9 million for a project that will employ genomics research to discover and develop antimicrobial peptides (AMPs) as alternatives to traditional antibiotics.

Treating and preventing bacterial infections in animals is an essential part of agriculture. However, overuse and misuse of antibiotics has led to the development of antimicrobial resistance, an issue classified by the World Health Organization as one of the most urgent global health risks facing us today. AMPs are produced by some plant and animal species and have activity against a range of bacterial pathogens, showing great potential for use in the clinic and in agriculture. Using a genomics approach will accelerate the traditionally labour-intensive process of discovering novel AMPs. Dr. Birol's team will build on their previous proof-of-concept research to scale-up their AMP discovery process. The discovery and characterization of novel AMPs by Dr. Birol's group has the potential to mitigate antimicrobial resistance issues in agriculture, among other potential therapeutic applications.

## Cancer Research Society, operating grant



Dr. Sharon Gorski was awarded \$120,000 over two years to investigate the role of the Parkinson's susceptibility gene *LRRK2* in lung cancer initiation and progression.

The Gorski laboratory has previously demonstrated that

*LRRK2* functions as a novel tumour suppressor gene in lung adenocarcinoma, and bioinformatic analyses of data from The Cancer Genome Atlas revealed that patients with low *LRRK2* expression had lower overall survival and reduced expression of immune-related pathways. Consistent with this, they demonstrated that carcinogen-driven tumours in *LRRK*-deficient mice grew more rapidly and had increased infiltration of potentially immunosuppressive cell types. The aim for this project is to elucidate immunomodulatory mechanisms in carcinogen-driven tumours in *LRRK2*-deficient mice. These studies will enhance understanding of *LRRK2* involvement in cancer and in the long term, may help inform treatment strategies for patients with lung adenocarcinoma.

## CIHR, project grant



Dr. Ryan Morin was awarded \$784,126 over five years to investigate the effect of regulatory mutations on the most prevalent form of non-Hodgkin lymphoma, known as diffuse large B-cell lymphoma (DLBCL). The goal is to identify and

characterize mutations that contribute to treatment resistance in DLBCL, with a focus on mutations that dysregulate gene expression. Mutations in genes encoding regulatory proteins can lead to widespread and extensive changes in a cell's transcriptional and proteomic profiles. Example mutations include those present in the 3' UTR of the *NFKBIZ* gene and recurrent mutations affecting the RNA-binding protein Reg1, both of which can lead to dysregulation of NF- $\kappa$ B activation and ultimately modify the transcriptome and proteome of the cell. The identification and characterization of regulatory driver mutations may lead to novel therapeutic targets for the treatment of DLBCL.

## The Leukemia & Lymphoma Society of Canada, operating grant



Dr. Aly Karsan was awarded an operating grant from The Leukemia & Lymphoma Society of Canada (LLSC) to determine if targeting the IGF1R pathway will exploit del(5q) dependencies in

lenalidomide resistant myelodysplastic syndrome (MDS). At the Toronto presentation, LLSC President Alicia Talarico also announced that Dr. Karsan was selected as the 2019 recipient of the United Food and Commercial Workers Union (UFCW Canada) Award for Leukemia Research, given annually to the LLSC's top scoring operating research grant applicant.

## CIHR funding for Canadian epigenetics research



The Canadian Epigenetics, Environment and Health Research Consortium (CEEHRC) Network, led by Dr. Martin Hirst, is a pan-Canadian network linking "nodes" of Genome Canada's Genomics

Innovation Network and other research laboratories to promote epigenomic research in the country. It also provides outreach and training resources to the broader research community. On June 25, CEEHRC received renewal funding of more than \$1 million over the next four years to carry out a variety of activities to bolster, promote and communicate epigenetics research in Canada.

## CIHR, operating grant

Dr. Aly Karsan was awarded \$910,350 over five years from CIHR to investigate the role of endothelial Meis1 in definitive hematopoiesis and vascular development, and to characterize the cellular heterogeneity within the homogenic endothelial cell population. This study will better define the transcriptional programs that drive endothelial-to-hematopoietic transdifferentiation, which has implications for optimizing the *ex vivo* production of hematopoietic stem cells, and potentially for the development of therapeutics for blood and vascular disorders.

## CIHR, project grant

Dr. Aly Karsan was awarded \$1.2 million over five years to investigate hematopoietic stem cell (HSC) aging and define the role of noncoding RNAs as determinants of aging in the hematopoietic system. Specific goals include elucidation of the mechanisms of HSC aging in response to loss of miR-146a, determination of the role of miR-146a in the aging of HSC and whether aging of HSC can be reversed.

## BC Cancer Foundation, Neil MacRae Hereditary Cancer Research Fund: Origins of male breast cancer

With new support from BC Cancer Foundation's Neil MacRae Hereditary Cancer Research Fund, three teams of BC Cancer scientists will help to shed light on the genetic origins of rare male breast cancers. Drs. **Steven Jones** (PI), Intan Schrader (co-PI), **Marco Marra**, **Aly Karsan**, Janessa Laskin, Sophie Sun, My Linh Thibodeau and Stephen Yip will use novel DNA sequencing technologies to analyze hereditary mutations associated with the disease. Drs. Connie Eaves (nominated PI) and **Martin Hirst** will design pilot studies to elucidate relevant early and targetable events in the genesis of male human breast cancer that will also set the stage for testing new therapies for patients. And Drs. Intan Schrader (nominated PI) Sophie Sun (co-PI), **Aly Karsan**, Dean Regier and MyLinh Thibodeau aim to identify inherited mutations from deceased male breast cancer patients by performing genetic testing on their cancer samples.



# AWARDS & RECOGNITION

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## Dr. Marco Marra received the LifeSciences BC Don Rix Lifetime Achievement Award

In honour of Dr. Donald Rix's memory and his many achievements, the LifeScience BC Lifetime Achievement Award recognizes exemplary leadership and determination. Dr. Marra received the award on April 4, 2019.

Dr. Marra has been instrumental in demonstrating the pivotal role of genomics in human health and disease research—through contributions to the Human Genome Project, leading the sequencing of the SARS coronavirus genome (2003) and the first proof-of-concept study demonstrating effective use of whole genome analyses in personalized cancer medicine. His research has uncovered new cancer mutations, candidate biomarkers and therapeutic targets as well as illustrating the functional interplay between the cancer genome and epigenome. Since 2014, he has been named as among the most highly cited researchers in the world.

“The major impact that Don Rix had on me and the GSC was in pushing us—and we were reluctant—into this business of personalized cancer genome medicine. Fundamentally, it was Don's belief, I think, that genome science—and cancer genome science, in particular—had a role to play in unraveling the causes of cancers, in unravelling unanticipated therapeutic opportunities to treat cancers. I think, if Don were here today, he would tell us to proceed and do so earnestly. Attack the problem and deliver solutions.” —Dr. Marco Marra



## GSC scientists among the most highly cited in the world



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 quantifies the number of citations for specific scientists in various disciplines and generates a list of Highly Cited Researchers—those who produce multiple papers ranking in the top one per cent by citations for their field. The select few that make it onto this list represent just 0.1 per cent of researchers worldwide.

For the past five years, GSC scientists have been on that list, including GSC Director Dr. Marco Marra who has been listed every year since 2014 (see this BC Cancer [video interview](#) with Drs. Marra and Steven Jones when they were listed in 2016).

In 2019, 183 researchers made the list in Canada, and eleven of them are scientists here at the GSC, including Marco Marra, Steve Jones, Martin Hirst, Rob Holt, Inanc Birol, Andy Mungall, Richard Moore, YJ Zhao, Erin Pleasance, Angela Tam and former GSC staff scientist Jacqueline Schien.

Researchers are selected for their exceptional performance in one or more of 21 fields. In 2019, 6,216 researchers were named Highly Cited Researchers—3,725 in specific fields and 2,491 for cross-field performance.

“Recognition and support of these exceptional researchers represents an important

activity for a nation or an institution’s plans for efficient and accelerated advancement,” said David Pendlebury, Senior Citation Analyst at the Institute for Scientific Information.

“The Highly Cited Researchers list contributes to the identification of that small fraction of the researcher population that contributes disproportionately to extending the frontiers of knowledge. These researchers create gains for society, innovation and knowledge that make the world healthier, richer, more sustainable and more secure.”

The continued presence of GSC researchers among the 0.1 per cent of scientists by citations since 2014 exemplifies our extraordinary cutting-edge research that is pioneering the application of genomics to precision oncology, making a difference in the lives of cancer patients here in B.C. and around the world.



## Awards & Recognition Continued:

### Dr. Martin Hirst honoured with UBC Killam Research Prize

Every year, UBC acknowledges outstanding faculty members with Faculty Research Awards, meticulously selected by a committee that spans faculties of arts and humanities, business, applied science, science and medicine. The 2018 UBC Killam Research Prize (presented in February 2019) went to **Dr. Martin Hirst**, in recognition of exceptional scholarly contributions to science. Dr. Hirst's research aims to further the understanding of the role of epigenetic dysfunction in cancer initiation and progression. He aims to translate this knowledge into improved health outcomes for Canadians and the health care system.

### Dr. Martin Hirst named member of CIHR's Institute Advisory Board

**Dr. Martin Hirst** was selected as a member of the Institute Advisory Board (IAB) for CIHR's Institute of Cancer Research (IRC). As a member of the IAB, Dr. Hirst will provide essential input and guidance to the activities of the IRC. The IRC is one of 13 "virtual" institutes operated by Canadian Institutes of Health Research. The institutes are networks of interdisciplinary researchers that are brought together to integrate their research efforts with a focus on important health problems, linking and supporting researchers, health professionals, policy-makers, provincial government agencies, industry and patient groups across the country.

### Dr. Ryan Morin received the American Society of Hematology Scholar Award

The American Society of Hematology (ASH) Scholar Award program funds hematologists in the United States and Canada who conduct basic, translational and clinical research as they transition from training programs to careers as independent investigators. **Dr. Ryan Morin** was the only Canadian recipient of the ASH Scholar Award in 2019. Each Scholar Award provides \$100,000 for fellows or \$150,000 for junior faculty over two or three years. ASH is the world's largest professional society of hematologists dedicated to furthering the understanding, diagnosis, treatment and prevention of blood disorders.

### Dr. Steven Jones appointed first Canada Research Chair in Computational Genomics

In 2019, the Government of Canada announced an investment of over \$275 million for 346 new and renewed Canada Research Chairs at 52 institutions across Canada. The Canada Foundation for Innovation also made an investment towards these Chairs of more than \$5.2 million in new funding for research infrastructure, supporting 30 Chairs at 18 institutions. **Dr. Steven Jones** was awarded the first Tier 1 Canada Research Chair in Computational Genomics.

### Dr. Nadine Caron given honorary degree from SFU



**Dr. Nadine Caron** is Anishnawbe from Sagamok First Nation, a surgeon, scientist, associate professor, an internationally renowned health advocate passionate about improving health outcomes for Indigenous peoples, and an Associate Researcher

at the GSC. Dr. Caron's main research focus involves access to equal health status and health care services for marginalized populations, including Aboriginal, northern and rural. In 2019 she was awarded an honorary Doctor of Science degree from Simon Fraser University.

### Dr. Joanne Johnson awarded Research Project Management Excellence Award



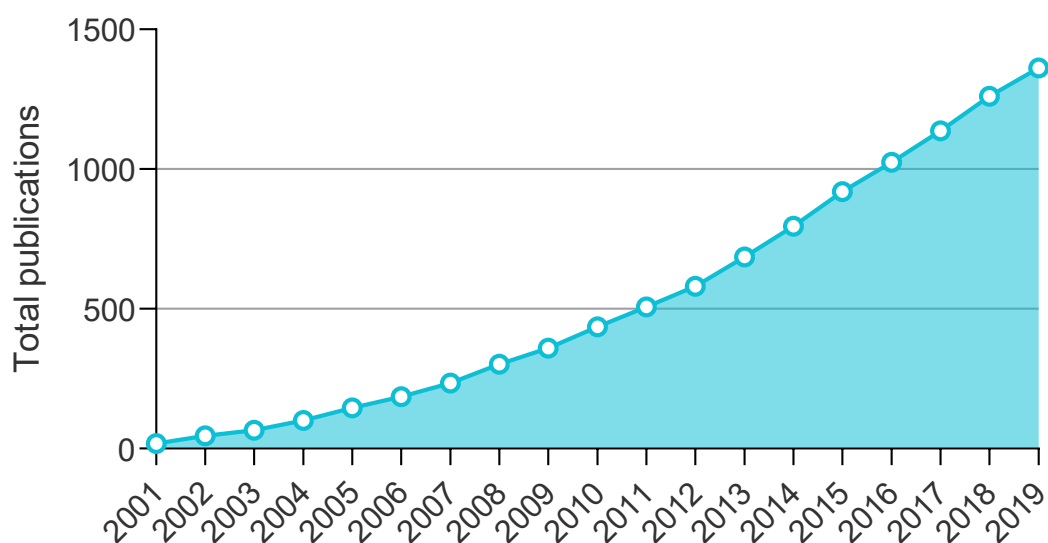
The Canadian Association of Research Administrators (CARA) Research Project Management Award is presented to an exceptional research manager who has made outstanding contributions to the profession through innovation, creativity, hard work and dedication. The

winner is determined based on voting and nominations from fellow CARA members. **Dr. Joanne Johnson**, Head of Project Management at the GSC, was recognized at the CARA 2019 Annual Conference in Montréal for her leadership of a team of about 20 project managers supporting the many research projects being carried out at the GSC.

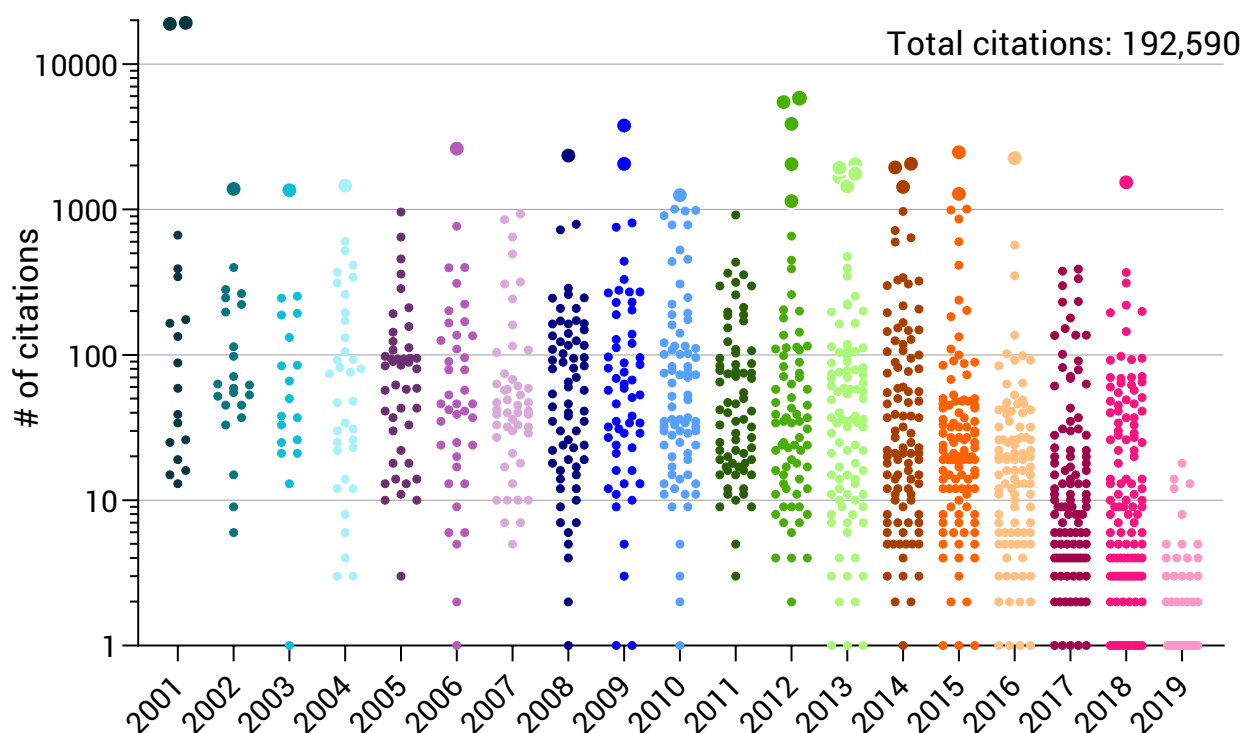
# PUBLICATIONS

The GSC published 96 peer-reviewed journal articles in 2019, 42 of which were led by GSC principal investigators. Thirty-seven per cent were published in journals with impact factors higher than 10. Since 1999, GSC authors have garnered a total of 1,406 publications with 192,590 citations, averaging 120 citations per journal article.

\*See **page 43** for the full list of 2019 GSC publications



Click on publications with >1000 citations to view.



# FEATURE PUBLICATIONS



Photo credit: Katja Schulz from Washington, D. C., USA

DR. INANC BIROL'S  
BIOINFORMATICS  
TECHNOLOGY LAB USES  
HIGH-PERFORMANCE  
COMPUTING TO BUILD  
CLINICAL PIPELINES.  
IN 2019 IT MADE A  
POWERFUL NEW  
TOOL TO HELP COMBAT  
ANTIBIOTIC RESISTANCE.

## Mining the bullfrog genome to stem the antibiotic resistance crisis

In 2016, the UN general assembly declared the most urgent global risk to human kind, and it wasn't terrorism, immigration or climate change. It was the emergence of antibiotic resistance. There are currently 1.5 million people dying worldwide annually as a result of it, and it will get worse.

According to a report commissioned by the UK government, by the year 2050 antibiotic resistance will cost US\$2.4 to 2.6 trillion per year. For comparison, Canadian GDP is estimated at US\$2.1 billion by the same time.

The UN report advises limiting access to antibiotics as an important tactic, but for much of the world access remains the more urgent problem. Curbing overuse in veterinary practice, food production and improper prescriptions is helpful, but will not be enough.

Research is ongoing for new small-molecule antibiotics, but it's becoming more difficult to find drugs with unique modes of action. Since derivatives are now only tweaks to pre-existing formulas, bacteria with resistance to substantial components of these antibiotics already exist by the time they reach the market. Another approach is needed.

Enter antimicrobial peptides (AMPs).

AMPs are naturally occurring short protein fragments (about 10 to 50 amino acids long) that are effective at killing a variety of organisms including gram-positive and gram-negative bacteria, fungi and parasites and even have anti-viral and anti-cancer properties too. Their mode of action is highly variable and under increasing investigation, but evidence indicates everything from cell membrane disruption to inhibition of DNA synthesis.

And given that AMPs are a fundamental part of the innate immune response among all classes of life, there are practically limitless naturally occurring varieties. Frogs, in particular, evolving in microbe-infested swamps, produce a plethora of them.

### Reference:

Caren C. Helbing, S. Austin Hammond, Shireen H. Jackman, Simon Houston, Rene L. Warren, Caroline E. Cameron, Inanc Birol. 2019. [Antimicrobial peptides from \*Rana \[Lithobates\] catesbeiana\*: gene structure and bioinformatic identification of novel forms from tadpoles](#). *Nature Scientific Reports*.

"I was reading an article in Nature. They were talking about frogs and AMPs and I thought, 'interesting, why not analyze our frog?'" said Dr. Inanc Birol, who leads the Bioinformatics Technology Lab comprised of about twenty researchers at the GSC.

The Lab develops novel algorithms, data structures and software designed to analyze large volumes of genome sequence data, simultaneously building data analysis pipelines for a variety of research projects and clinical purposes.

"I'm the assembly guy," he said, with a distinguished broad smile, referring to the work he has led or contributed to in assembling sequenced genomes for a multitude of species, from mycobacterium and spruce tree to the beluga whale, and bullfrog.

About two decades ago, a biologist from the University of Victoria, Prof. Caren Helbing, approached him to characterize the genome of the North American bullfrog.

"I wanted to know the genetic blueprint of the frog so that we could look at areas that are particularly affected by endocrine disrupters," said Caren on the phone from Victoria. "But metamorphosis also provided us with a brilliant opportunity to isolate AMPs, many that have yet to be discovered."

In frogs, AMPs are developmentally specific with different types occurring throughout the lifecycle of the organism from the tadpole to mature adult. The animal makes whole arsenals of AMPs, and not all at once. By having the genomic sequence in hand these scientists could theoretically look for all AMPs the animal can make throughout its lifecycle, without being limited to what was produced at one time

Generally, isolating and identifying AMPs requires taking a swab of mucous on the back of a frog or tadpole and

using analytical chemistry and proteomics. Research in this area has generated databases cataloguing a multitude of AMPs, which Birol and Helbing took advantage of to search for sequences in genome and transcriptome annotations.

"Figuring out where the active peptide starts and stops in the genomic sequence, that's the secret sauce," said Birol. "We used the wealth of information that was done the hard way and combined that with experiments that tell us what is being expressed at any one time. We put that together to develop a new computational method that ultimately will be able to find many new candidate AMPs rapidly."

*"Figuring out where the active peptide starts and stops in the genomic sequence, that's the secret sauce."  
—Dr. Inanc Birol*

Birol and Helbing started with the genome, identified sequences they thought might be AMPs, cleaved them and estimated protein confirmation in silico, and, if they liked what they saw, they sent it to be produced in protein

from component amino acids, then testing them on bacteria in a lab.

"And it worked!" he said, beaming more than usual. "It was quite something to go from a bunch of As, Gs, Cs, and Ts, to real biological function. It was exciting!"

Birol's and Helbing's study, published in [Nature Scientific Reports](#) in February 2019, shows the first real proof of concept for a bioinformatics driven AMP production pipeline. Now it can be applied to other genomes. They're now writing proposals to test their AMPs on multidrug resistant strains of bacteria in the proper containment facilities.

Will this new approach change the outcome from antibiotic resistance?

"Many high hopes get crushed," says Birol, smiling. "But it just may."





COMBINING PATIENTS' GENE EXPRESSION DATA AND A MACHINE LEARNING TECHNIQUE, GSC SCIENTISTS HAVE SHOWN THAT COMPUTERS CAN ACCURATELY DIAGNOSE CANCER, EVEN IN CASES THAT FAIL HUMAN ASSESSMENT.

## Provided with whole genome sequencing data, computers can make accurate cancer diagnoses

In order to diagnose a cancer, pathologists use a variety of techniques to analyze the features of a tissue biopsy. This works best when the specimen being analyzed is of high quality, contains many cells and has clearly identifiable features. Unfortunately, this is not always the case, and rare cancers are especially difficult to diagnose using traditional diagnostic methods.

Cancers are diseases of the genome. Imagine if, armed with the genetic data from the genes of tens of thousands of other consenting cancer patients, we could train computers to provide fast and accurate diagnoses?

[A study](#) led by GSC scientists and published in the Journal of the American Medical Association (JAMA) Network Open demonstrates how novel use of whole genome sequencing and machine learning techniques—specifically, measuring expression of all of the genes in the genome—can provide cancer diagnoses with quantifiable confidence, including for cases that had previously failed human assessment.

“Our analysis highlights the progress machine learning approaches have made in fields previously considered to be the domain of highly skilled human expertise,” says Dr. Steven Jones, GSC Director, Head of Bioinformatics and principal investigator for the study. “It also demonstrates where computational approaches can not only augment but improve upon clinical decision making.”

In this study, scientists trained computers to look across 17,688 genes in the human genome and generate a diagnosis, with a confidence score, out of a set of 40 different cancer types. They found that the method had approximately 99 per cent accuracy in identifying cancers with mixed tissue types, and had a success rate of 80 to 86 per cent in the most challenging cases—advanced cancers and those of unknown origin—that had failed human assessment or were extremely difficult for human experts to diagnose.

### Reference:

Jasleen K. Grewal, Basile Tessier-Cloutier, Martin Jones, Sitanshu Gakkhar, Yussanne Ma, Richard Moore, Andrew J. Mungall, Yongjun Zhao, Michael D. Taylor, Karen Gelmon, Howard Lim, Daniel Renouf, Janessa Laskin, Marco Marra, Stephen Yip, Steven J.M. Jones. 2019. [Application of a neural network whole transcriptome-based pan-cancer method for diagnosis of primary and metastatic cancers](#). *Oncology*. 2(4):e192597.



While gene panels looking across smaller gene subsets are already available to help pathologists make more accurate cancer diagnoses, their application is restricted to commonly occurring cancers. Rarer cancers, metastatic cancers, and cancers of unknown origin are all challenging to diagnose using traditional pathology and through gene panels.

“This illustrates that there is huge potential to develop interpretable machine-learning methods using the entirety of sequencing data,” says **Jasleen Grewal**, lead author on the study and a graduate student in Dr. Jones’ lab. “Algorithms that incorporate this high-resolution data as a whole to provide insights into cancers can serve as a powerful means of analysis and decision-making.”

*“Our analysis highlights the progress machine learning approaches have made in fields previously considered to be the domain of highly skilled human expertise.”  
—Dr. Steven Jones*

Machine learning methods are only as good as the data they have to train on. Efforts are needed to properly curate and sequence rare and advanced cancers so that scientists can better incorporate and improve pathologist’s ability to diagnose them. Future research will examine the ability to leverage genomic data for other manually-driven cancer analysis tasks, such as alignment with appropriate therapies.

“For me, the most interesting finding will be when we start to dig into what these algorithms are learning about cancer,” says Grewal. “I’m interested to learn whether machine learning at this scale can be used to uncover subtleties and facets about cancer that have so far been eluding us.”



THE REFERENCE GENOME  
MAY ASSIST IN BETTER  
UNDERSTANDING THE  
SPECIES, GENETIC  
EFFECTS OF ITS  
POPULATION DECLINE  
AND IN EVOLUTIONARY  
STUDIES, BUT ALSO  
KNOWLEDGE OF  
PROCESSES IN CANCER.

## Steller sea lion genome sequenced

Scientists at the GSC have helped to add yet another species to the world's repertoire of reference genomes: the Steller sea lion.

The resulting reference genome is highly complete, with a total length of 2.4 billion base pairs of DNA in 18 chromosomes. Annotation of the genome identified 19,668 protein coding genes. For comparison, humans have 3.2 billion base pairs of DNA in 23 chromosomes.

The assembled Steller sea lion genome sequence and data can be found at the National Center for Biotechnology Information (NCBI) under the BioProject accession number PRJNA475770. The results of the study were published in the journal [Genes](#).

"The genome of the Steller sea lion assembly not only provides insights into the genetics of species that we share our environment with but also improves our own ability to understand human cancer," said Dr. Steven Jones, Director & Head of Bioinformatics at the GSC and principal investigator for the study.

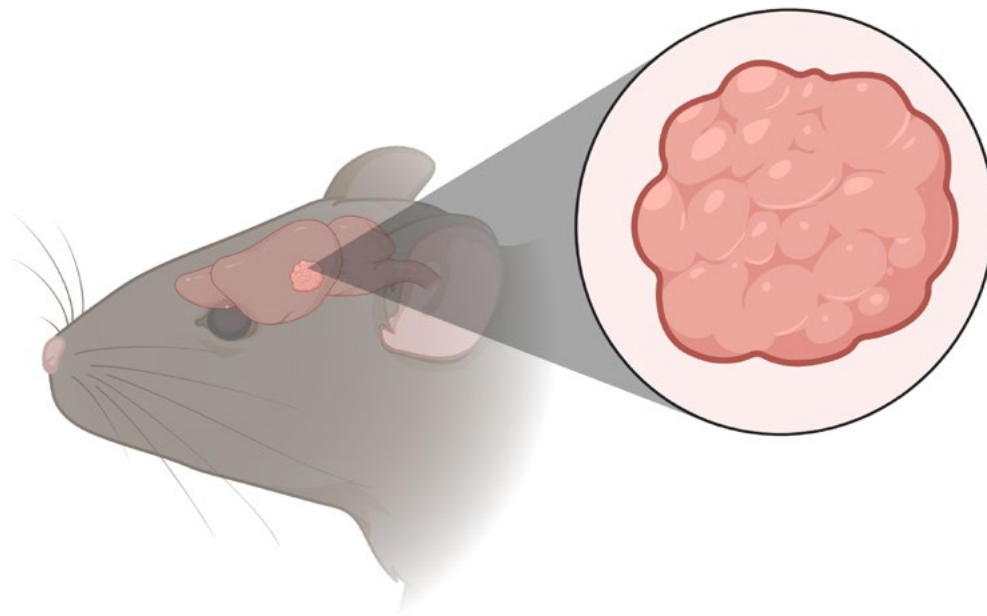
"Cataloguing the diversity between similar genes across different mammals allows us to understand what genetic changes are tolerable, and which likely adversely affect function—important for us to know when trying to interpret the effect of mutations observed in the genes of tumours."

A reference Steller sea lion genome may also assist the understanding of the genetic effects of its population decline, and ultimately aid in the conservation process. Additionally, the genome, alongside the California sea lion reference genome, can serve as a strong starting point for evolutionary studies regarding the divergence of sea lions from other pinnipeds. It also aids in enhancing understanding of genomic and bioinformatic techniques.

The study also showed that the use of microfluidic portioned libraries greatly improves our ability to produce high-quality genomes and that additional information from the newly developed Nanopore sequencers can improve the assembly even further.

### Reference:

Harwood H. Kwan, Luka Culibrk, Gregory A. Taylor, Sreeja Leelakumari, Ryan Tan, Shaun D. Jackman, Kane Tse, Tina MacLeod, Dean Cheng, Eric Chuah, Heather Kirk, Pawan Pandoh, Rebecca Carlsen, Yongjun Zhao, Andrew J. Mungall, Richard Moore, Inanc Birol, Marco A. Marra, David A.S. Rosen, Martin Haulena and Steven J.M. Jones. 2019. [The Genome of the Steller Sea Lion \(\*Eumetopias jubatus\*\)](#). *Genes*. 10(7):486.



GENOME AND  
TRANSCRIPTOME  
PROFILING OF HUMAN  
TUMOURS GROWN IN  
MICE SHOWS PROMISE  
FOR A MORE ACCURATE  
INTERPRETATION OF  
GLIOBLASTOMA  
MULTIFORME RESEARCH.

## Improving a crucial research tool for deadliest form of brain cancer

Despite decades of research and countless clinical trials, a diagnosis with glioblastoma multiforme (GBM) essentially remains a death sentence. Even with surgical removal of tumours followed by radiation and chemotherapy, 90 per cent of patients succumb to the disease within five years.

Compiled by GSC scientists and published in [PNAS](#), an extensive catalogue is now available of genome and transcriptome data comparing GBM tumours from humans as well as those grown in a dish or in mice. This will ultimately enable improved approaches for drug screening, contributing to the search for effective treatments for people with this devastating disease.

The lack of effective treatment is a reflection of the complexity of this disease. Like all types of cancer, every case of GBM is different. Each tumour possesses a different set of mutations, epigenetic modifications, gene expression profiles and metabolic alterations. The diffuse nature of GBM tumours limits surgical interventions while the inherent ability of this cancer to become resistant to conventional therapies thwarts attempts of oncologists to manage the disease.

The limited success in drug development can partly be attributed to the lack of accurate and predictive pre-clinical cancer models. GBM research in the past has relied heavily on cell-based models. Brain tumour-initiating cells (BTICs) can be isolated from primary tumours and used to investigate GBM pathogenesis in the laboratory, but they have limited utility when it comes to drug discovery—it is difficult to test novel compounds without a more physiologically relevant setting, like an animal model.

This is why the recently developed mouse xenograft model of GBM is of paramount importance to researchers in the field. Cancer cells are taken from patients, allowed to multiply in the laboratory and are then transplanted into mice to produce what is called a xenograft. While this method is crucial for the study of GBM, it is important to keep in mind that humans and mice differ in their biology. What cures GBM in a mouse may not work in a human.

“A significant limitation to drug discovery for GBM is that compounds that

### Reference:

Yaoqing Shen, Cameron J. Grisdale, Sumaiya A. Islam, Pinaki Bose, Jake Lever, Eric Y. Zhao, Natalie Grinshtein, Yussanne Ma, Andrew J. Mungall, Richard A. Moore, Xueqing Lun, Donna L. Senger, Stephen M. Robbins, Alice Yijun Wang, Julia L. MacIsaac, Michael S. Kobor, H. Artee Luchman, Samuel Weiss, Jennifer A. Chan, Michael D. Blough, David R. Kaplan, J. Gregory Cairncross, Marco A. Marra and Steven J.M. Jones. 2019. [Comprehensive genomic profiling of glioblastoma tumors, BTICs, and xenografts reveals stability and adaptation to growth environments](#). *PNAS*. 116(38):19098-19108.

seem to work well in cell lines, don't always work when we then try them in mouse xenograft studies," said Dr. Steven Jones, "or worse, when compounds work in mouse studies but do not work in studies with human patients."

To avoid these disappointing outcomes, scientists need a clear picture of the similarities and differences between GBM cells in patients, in a dish and in a mouse.

In collaboration with scientists at the University of Calgary, the Hospital for Sick Kids, the University of British Columbia, and the University of Toronto, GSC researchers employed their expertise in DNA sequencing and analysis to characterize genomes and transcriptomes of tumour cells in patients, in the laboratory and in mice.

Their findings demonstrated that while the GBM xenograft model resembles the human disease and may provide valuable insights into GBM, variations in how the cancer cells behave in the human, laboratory and mouse settings do exist. Genomic aberrations were well conserved in matched tumours, cell-lines and xenografts. But gene expression and methylation diverged, likely due to the different growth environments.

The group also identified a potential mechanism that allows GBM tumours to evade drug treatment. Previously, the ability of GBM to become drug resistant has been attributed to the tumours acquiring a hypermutated phenotype following treatment with

the drug temozolomide (TMZ). But in this study, the group found that five out of the 14 TMZ-resistant GBM samples did not show this hypermutated phenotype, leading them to hypothesize that another mechanism of resistance was at play, revealed by genome and transcriptome analyses: increased expression of a gene

encoding a DNA repair protein (MGMT). These findings may help guide treatment strategies in patients with recurrent GBM.

The wealth of information provided by this research is extremely valuable for the future study of GBM, particularly in the accurate interpretation of studies relying on this disease model and understanding its limitations. The in-

depth comparison of human, laboratory and mouse GBM cells will enable researchers to avoid biases introduced by the experimental conditions

"It will help with determining what are the druggable pathways that behave similarly between the human disease and the models, and which ones don't," said Dr. Jones. The findings will further enable improved approaches for drug screening, thus contributing to the search for effective treatments for this devastating disease.

"It is crucial for drugs to be tested in animal xenograft models before embarking on painstaking and time-consuming patient studies," said Dr. Jones. "Without xenograft models drug development for cancer would likely grind to a halt".

*"It is crucial for drugs to be tested in animal xenograft models before embarking on painstaking and time-consuming patient studies. Without xenograft models drug development for cancer would likely grind to a halt"*  
—Dr. Steven Jones





SOME PATIENTS WITH  
NON-HODGKIN  
LYMPHOMA RESPOND  
POORLY TO STANDARD  
TREATMENT. THANKS TO  
DNA SEQUENCING,  
SCIENTISTS NOW  
KNOW WHY.

## A genetic explanation for lymphoma patients that can't be cured by standard treatment

The most common form of non-Hodgkin lymphoma, known as Diffuse Large B-cell Lymphoma (DLBCL), is considered a curable disease with the exception of a subset of patients for whom the standard treatment is not effective. But scientists at the GSC have uncovered a genetic explanation for why some patients have poor prognosis.

Like all forms of cancer, DLBCL is the result of DNA mutations. And these patients have particularly damaging ones termed “double hit”. Unfortunately, some patients test negative for double hit mutations using a standard laboratory test called fluorescent in-situ hybridization (or FISH) yet still respond poorly to standard treatment. This means they may not receive the intensive treatment they require.

In a study published in [Blood](#), Dr. Ryan Morin, Senior Scientist at the GSC and associate professor at SFU, and his team employed DNA sequencing to shed light on these discrepancies. Their results revealed the presence of double hit mutations in samples that had tested negative by FISH. The study demonstrated that testing by FISH may miss up to 19 per cent of patients with double hit mutations.

“We are systematically under-identifying patients that have the genetic event that predicts poor outcomes,” said Dr. Laura Hilton, a post-doctoral fellow in Dr. Morin’s group and lead author on the study. “Our findings reveal why.”

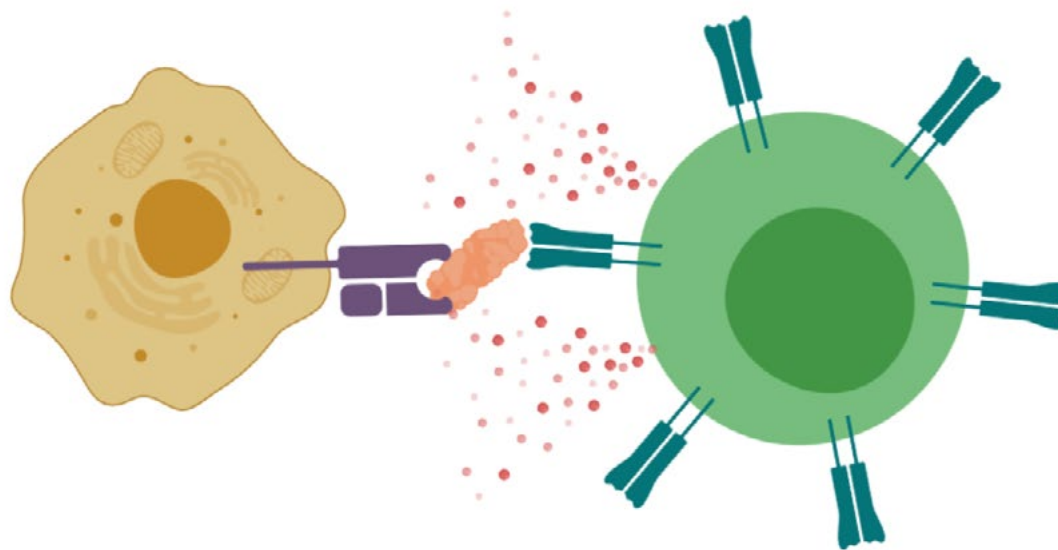
The group found that these patients can more reliably be identified by looking for a particular cellular signature. Fortunately, there is a laboratory test called a NanoString that can be used to identify the signature, allowing clinicians to more accurately determine which patients may need more aggressive treatments.

Exactly what those treatments should be remains a current area of research, but clinical trials show that a more intensive drug regimen may be effective. By identifying more of these cases, further clinical trials will be made possible.

### Reference:

Laura K. Hilton, Jeffery Tang, Susana Ben-Neriah, Miguel Alcaide, Aixiang Jiang, Bruno M. Grande, Christopher K. Rushton, Merrill Boyle, Barbara Meissner, David W. Scott and Ryan D. Morin. 2019. [The double-hit signature identifies double-hit diffuse large B-cell lymphoma with genetic events cryptic to FISH.](#) *Blood*. 134(18):1528-1532.





HARNESSING THE POWER OF OUR OWN IMMUNE SYSTEMS CAN HELP FIGHT OFF CANCER. GSC SCIENTISTS HAVE DEVELOPED A METHOD TO TELL IMMUNE CELLS EXACTLY WHAT TO LOOK FOR.

## Scientists develop a new method for finding cancer-killing cells

Lying in wait within our immune systems are specialized cells called cytotoxic T cells (or CTLs), searching for and eliminating diseased cells. Scientists have shown that we can harness the search-and-destroy functions of CTLs to help our bodies fight off cancer, but its like searching for a needle in a haystack. A new method developed in the laboratory of Dr. Rob Holt, Distinguished Scientist at the GSC, has made it a lot easier.

“CTLs are these natural micro-machines that we have in our bodies to fight disease,” said Dr. Govinda Sharma, a post-doctoral fellow in Dr. Holt’s lab and lead author of the study. “There are a lot of people working to leverage them for therapeutics but we don’t really understand their language.”

This language is mediated by chemical signals displayed on cell surfaces, called antigens, which tell CTLs whether or not disease is present. If a cell is infected with a virus or has gone rogue and become cancerous, they display antigens that signal disease. Once a CTL finds and recognizes a disease signal, it releases proteins called perforin which act as molecular bullets, forming holes in the diseased cell, and granzymes which enter the holes and destroy the target cell from the inside out.

Their ability to destroy cancer cells is what makes them so attractive as a therapeutic strategy. Scientists can take CTLs from a patient, allow them to multiply in the laboratory to create an army of cancer-fighting cells, inject them back into the patient and let them do their job.

To make use of CTLs, scientists need to know exactly which antigens the cancer cells are displaying. Every patient and every tumour can display a different set of antigens and figuring out what they are has been a bottleneck for CTL-mediated therapy to date.

**Reference:**  
Govinda Sharma, Craig M. Rive and Robert A. Holt. 2019. [Rapid selection and identification of functional CD8+ T cell epitopes from large peptide-coding libraries.](#) *Nature Communications*. 10:4553.

“The method we developed allows us to rapidly and comprehensively survey the interactions between CTLs and their targets,” said Dr. Holt. “This is a major improvement over the conventional methods we had to work with previously; we can now screen hundreds to thousands of times more potential antigens in parallel.”

The method takes advantage of the CTLs' granzyme-mediated cell killing to identify disease antigens. To do this, the scientists generate a library of cells, each displaying a different antigen. Only a small fraction of these antigens will signal disease, and the goal is to find them. They mix the cell library together with CTLs and wait. Within a couple of hours, the CTLs will have found their targets and will have released their arsenal of perforin and granzymes. Once the target cells have been invaded by granzymes, they light up in a way that can be detected by specialized laboratory instruments. Then, using DNA sequencing, the team can determine precisely which antigens signaled the presence of disease.

CTL-mediated immunotherapy is a promising avenue for novel cancer treatment. But it is not without risk. It is possible that the disease signals being displayed

by cancer cells may also be present elsewhere in the body. Injecting an army of CTLs all searching for these antigens can lead to unintended consequences. But the method developed by Drs. Holt and Sharma can

help prevent these undesired effects.

*“This is a major improvement over the conventional methods we had to work with previously; we can now screen hundreds to thousands of times more potential antigens in parallel.”*

*—Dr. Rob Holt*

“Our screen will have the potential to identify and avoid some really severe off-target activities, which may eventually save lives,” said Dr. Sharma.

Dr. Sharma plans to take the method he developed during his graduate work, which was published in the journal [Nature Communications](#), to start a biotech company. Offering this method to cancer researchers and industry scientists will greatly enhance our ability to rapidly identify target antigens, helping pave the way towards safe and effective CTL-mediated immunotherapies and cancer vaccines.



Artwork by lead author Elizabeth Chun, appearing on the cover of volume 29, issue 8 of *Cell Reports*.

GSC SCIENTISTS FOUND  
THE UNEXPECTED  
PRESENCE OF IMMUNE  
CELLS THAT SUGGEST A  
POTENTIAL THERAPEUTIC  
STRATEGY FOR  
RHABDOID TUMOURS.

## Scientists identify a possible treatment strategy for a deadly childhood cancer

Rhabdoid tumours (RTs) are rare and highly aggressive pediatric cancers typically diagnosed before the age of two. These invasive tumours spread rapidly throughout the infant's body, and even with surgical interventions and aggressive chemotherapy, the outcome is often devastating. With a four-year survival rate of just over 20 per cent, novel therapies are urgently needed to help save the lives of children with RTs.

Using the power of genomics to decode the biology of RTs, scientists at the GSC have potentially identified a novel therapeutic strategy. In a study published in [Cell Reports](#), researchers conducted an extensive analysis of RTs from different anatomical locations, allowing them to classify all RTs into five distinct subgroups. And some patients falling into one of these groups may be candidates for a new treatment method.

While nearly all RTs are caused by loss of a protein called SMARCB1, they often show diverse clinical and biological characteristics, including multiple organ sites in which they occur. So far, RTs have been broadly classified into brain and non-brain types. In 2016, scientists at the GSC employed genomics technologies to extensively study non-brain RTs from the Children's Oncology Group in the U.S., while researchers at the German Cancer Research Center (DKFZ) in Heidelberg carried out a similar study of brain RTs. The two groups independently showed that RTs, even within one anatomical location, are diverse, implying that classifying RTs based on anatomical location alone was likely not accurate or useful.

To better understand biological relationships among RTs from multiple anatomical locations, researchers at the GSC and the DKFZ joined forces, working together to combine and analyze their data, studying the largest cohort of RTs to date. The study was co-led by Dr. Marco Marra, Distinguished Scientist and Director of the GSC and by Dr. Marcel Kool, a Senior Researcher at DKFZ. Their collaboration proved to be a fruitful one, leading to discoveries with direct implications for a novel treatment strategy.

### Reference:

Hye-Jung E. Chun, Pascal D. Johann, Katy Milne, Marc Zapatka, Annette Buellesbach, Naveed Ishaque, Murat Iskar, Serap Erkek, Lisa Wei, Basile Tessier-Cloutier, Jake Lever, Emma Titmuss, James T. Topham, Reanne Bowlby, Eric Chuah, Karen L. Mungall, Yussanne Ma, Andrew J. Mungall, Richard Moore, Michael D. Taylor, Daniela S. Gerhard, Steven J.M. Jones, Andrey Korshunov, Manfred Gessler, Kornelius Kerl, Martin Hasselblatt, Michael C. Fruwald, Elizabeth J. Perlman, Brad H. Nelson, Stefan M. Pfister, Marco A. Marra and Marcel Kool. 2019. [Identification and analyses of extra-cranial rhabdoid tumor molecular subgroups reveal tumours with cytotoxic T cell infiltration](#). *Cell Reports*. 29(8):2338-2354.e7



By profiling the genomes, epigenomes and transcriptomes from 301 RTs from multiple anatomical locations, their work revealed that not only were tumours from the same anatomical location diverse, but in some cases, brain RTs were actually more similar to tumours in distant locations than they were to other RTs in the brain. Digging deeper, the team identified five distinct subgroups. Being able to classify tumours into distinct subgroups is important – the more we learn about each subgroup, the better we can tailor cancer treatment based on key tumour characteristics.

Upon further examination of the RT subgroups, the team discovered that some RTs appeared to be interacting extensively with the immune system. Within the tumour tissues, they observed the presence of immune cells, called cytotoxic T cells, which play an important role in eliminating cancer cells. The team further corroborated their findings based on genomic data with extensive validation experiments. Because these traits have been seen in other cancer types that respond well to a particular type of immune-based treatments called immune checkpoint inhibitors, this discovery has raised a hypothesis that immune checkpoint inhibitors may be of utility for a subset of RT patients.

“This study underscores the importance of studying rare pediatric cancers, which, as in our case, can integrate research and clinical data from other cancers to reveal new insights,” said Dr. Marco Marra.

The unique setting of the GSC embedded within a cancer clinic allows for meaningful collaborations between scientists and clinicians. The hypothesis raised in

*“This study underscores the importance of studying rare pediatric cancers, which, as in our case, can integrate research and clinical data from other cancers to reveal new insights.”*

*—Dr. Marco Marra*

this study needs to be tested through such collaborations. And the search for improved cancer therapeutics is already underway. The work has been presented to oncologists in the Children’s Oncology

Group in the US and at the Terry Fox PROFYLE (PRrecision Oncology For Young peopLE) Initiative.

While this study provides the groundwork for further validation, research and identification of potential therapeutics for different RT subgroups, there are many remaining questions that dedicated researchers are striving to solve.



RESEARCHERS AT THE GSC DEVELOPED AN ELEGANT METHOD FOR TRACKING TISSUE SAMPLES THROUGH COMPLEX LABORATORY PROCESSES USING UNIQUE DNA IDENTIFIERS.

## A new DNA-based method for tracking samples through the lab

As precision medicine for the treatment of cancer and other diseases becomes a reality, there is increased demand for DNA sequencing. With the high volumes of samples now being sent for analysis, Scientists at the GSC have created streamlined, tightly regulated processes that minimize errors and ensure production of high quality data.

In a study published in the [Journal of Molecular Diagnostics](#), GSC researchers describe a new method for keeping track of the thousands of samples sent to the Centre using DNA itself.

Every sample received by the GSC is processed through a series of steps, which together compose a “pipeline”. With up to 15 different pipelines running at any one time, and each consisting of many intricate steps, keeping track of samples as they move in parallel through these complex processes is no small feat.

“If we didn’t track our samples effectively, we wouldn’t be able to find or do anything,” said Dr. Richard Moore, Sequencing Group Leader at the GSC and lead author on the study. “It is essential that we track each sample through whichever pipeline they enter.”

### Through the pipeline

From the time a sample is received by the GSC to the time it is loaded onto a sequencer, it will have passed through several instruments and the hands of multiple laboratory technicians. High confidence in sample identity at each step—especially when processing clinical samples—is of utmost importance; multiple levels of control are in place to ensure that the data produced at the end of a pipeline correspond to the correct input sample.

As soon as samples enter the doors of the GSC, they are provided with an optical barcode, allowing samples to be tracked using a Laboratory Information Management System, or LIMS. Every processing step and storage location is logged in the LIMS so that scientists know where each sample is at all times and what has been done to it.

Other tracking controls include having one technician observe another as samples are transferred between tubes and plates, checking specific regions

### Reference:

Richard A. Moore, Thomas Zeng, T. Roderick Docking, Ian Bosdet, Yaron S. Butterfield, Sarah Munro, Irene Li, Lucas Swanson, Elizabeth R. Starks, Kane Tse, Andrew J. Mungall, Robert A. Holt, Aly Karsan. 2019. [Sample Tracking Using Unique Sequence Controls](#). *Journal of Molecular Diagnostics*. 22(2):141-146.



of the DNA sequence called SNPs (single-nucleotide polymorphisms; pronounced “snips”) before and after samples have moved through the pipeline, and fusing unique DNA sequences onto the sample DNA before it is loaded onto the sequencers.

### Ensuring quality

While these controls are very effective when used in combination, none can be used to definitively confirm sample identity at every stage of the pipeline, or be used to distinguish between multiple samples from the same patient.

“For some samples, even more controls are needed to ensure data quality,” said Dr. Moore. “For example, if you had multiple samples from the same person, or you are running twin studies, you can’t check which is which by doing SNP concordance assays.”

The novel method developed by Dr. Moore and scientists at the GSC relies on circular pieces of DNA called plasmids. Each of the approximately 5,000 different plasmids created at the GSC have a known, unique DNA sequence. As soon as a sample is received, before the tissues have even been broken open for DNA purification, a control plasmid is added.

As the sample proceeds through all of the processing steps of the pipeline, the control plasmid goes along

with it. Once the sequencing data has been produced, technicians can ensure that the DNA sequence of the control matches the plasmid that was added at the beginning of the pipeline.

“The beauty of using plasmid DNA is that we can use bacteria to produce the plasmid again and again, so we have a never-ending supply of the same thing without needing to re-order more,” said Dr. Moore.

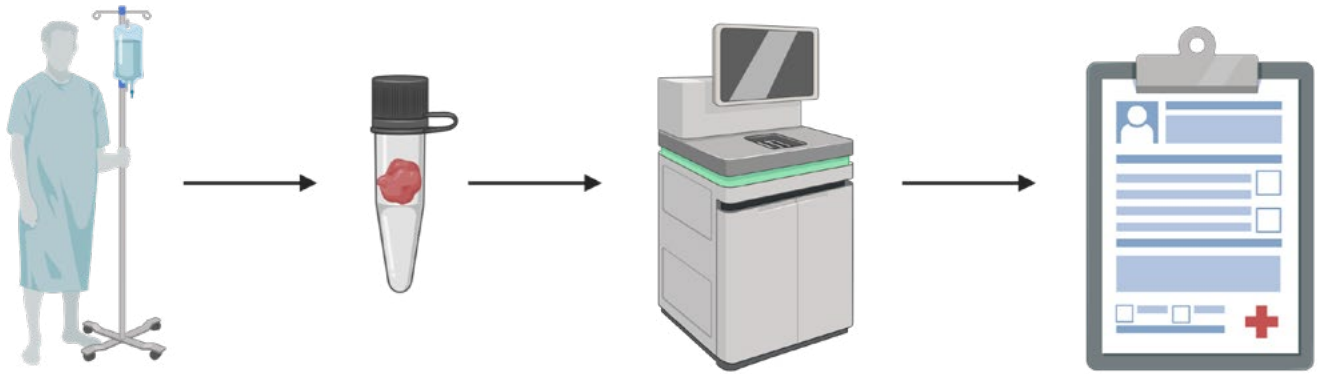
*“If we didn’t track our samples effectively, we wouldn’t be able to find or do anything. It is essential that we track each sample through whichever pipeline they enter.”*

*—Dr. Richard Moore*

With so many levels of control, pipeline errors are extremely rare, but occasionally the DNA sequence produced does not match what researchers expected. This method can be used to distinguish between a sample swap that may have happened somewhere along the pipeline, cross-

contamination between samples run in parallel or an incorrect sample sent to the GSC from collaborators.

As we move closer to precision medicine through genome sequencing becoming the norm, the demand for parallel processing of large numbers of samples within high-throughput laboratories will continue to increase. Controls such as the one developed at the GSC will be essential to ensure the highest level of data quality and accuracy, providing patients and clinicians with high confidence diagnostics for personalized treatment planning.



5-FU IS A DRUG USED TO TREAT MULTIPLE CANCER TYPES, BUT FOR SOME PATIENTS IT CAN BE TOXIC. THROUGH WHOLE GENOME SEQUENCING, GSC SCIENTISTS HAVE SHOWN 5-FU MAY BE A POTENT DOUBLE-EDGED SWORD FOR THE TREATMENT OF CANCER.

## Genome sequencing helps prioritize cancer treatment options

Every tumour is as unique as the patient from which it came. Everyone carries genes inherited from their parents—the “normal” or inherited genome. Mutations to the inherited genome can influence cancer development, progression and response to treatment. Cancer cells in turn develop additional mutations, with implications for the prognosis and treatment of the disease. Cancer genomics aims to decode each patient’s normal and cancer genomes to enable clinicians to determine the best course of treatment for each individual.

This is the approach taken by the Personalized OncoGenomics (POG) program at BC Cancer, led by Medical Oncologist Dr. Janessa Laskin and GSC Director Dr. Marco Marra. POG employs whole genome sequencing to analyze both the inherited and the cancer genomes of individual patients. In a study published in [Cold Spring Harbor Molecular Case Studies](#), the POG team has again demonstrated the power of this approach to inform personalized cancer treatment planning.

“This case really highlighted the strength of the POG program,” said Dr. Kathleen Wee, a research associate at the GSC and an author on the study. “POG is identifying new mutations that can be harnessed to target a patient’s cancer in a way that is really personalized.”

### A double-edged sword

Cancer patients who have a mutation in a gene called DPYD in their normal, inherited genomes will experience dangerous toxicity when exposed to the cancer drug 5-FU; however, patients without an inherited mutation in the same gene can be safely treated with this type of chemotherapy.

In this study, which analyzed the genome of one patient enrolled in the POG program, scientists identified a DPYD mutation present in the patient’s tumour but not in their normal, inherited genome. These findings indicated that the patient could be safely treated with 5-FU without the risk of toxicity, but that the drug could act both as an anti-cancer agent while also causing toxicity to the tumour itself.

### Reference:

Elisa Majounie, Kathleen Wee, Laura M. Williamson, Martin R. Jones, Erin Pleasance, Howard J. Lim, Cheryl Ho, Daniel J. Renouf, Stephen Yip, Steven J.M. Jones, Marco A. Marra, Janessa Laskin. 2019. [Fluorouracil sensitivity in a head and neck squamous cell carcinoma with a somatic DPYD structural variant](#). *CSH Molecular Case Studies*. 6: a004713.

"5-FU was actually a standard therapy in this case," said Dr. Laskin, "but it only would have been chosen as a third-line drug. After the POG findings, it was bumped up as the next therapy to try."

A third-line treatment is given when both an initial (first-line) and subsequent treatment (second-line) treatment don't work, or stop working. In this case, following whole genome sequencing, clinicians realized that a drug normally reserved for later stage treatment could be immediately effective, and was applied to the patient as a second-line treatment.

This reveals the importance of screening patients early for DPYD mutations not only in their normal genomes to prevent toxicity, but also within their tumours to identify patients that are ideal candidates for 5-FU therapy.

### The value of whole genome sequencing

This study demonstrates the immense potential of integrating whole genome sequencing into cancer treatment planning. Standard genetic testing, which involves sequencing only a subset of genes within a tumour, would not have detected the DPYD mutation.

*"Standard genetic testing would not have picked up this mutation of interest and we would not have been able to recommend 5-FU as a therapy. Whole genome sequencing was key."  
—Dr. Kathleen Wee*

Whole genome sequencing allowed for the identification of a mutation that could be exploited, allowing the team to prioritize treatment with 5-FU over other treatment strategies.

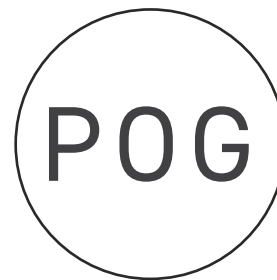
"Standard genetic testing would not have picked up this mutation of interest and we would not have been able to recommend 5-FU as a therapy," said Dr. Wee. "Whole genome sequencing was key."

# EVENTS & MILESTONES



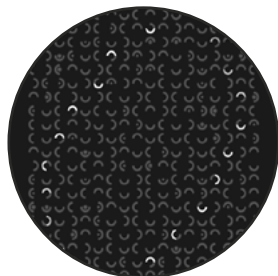
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KNOWLEDGE  
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PLATFORM  
TOURS

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# 20<sup>TH</sup> ANNIVERSARY

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On November 15, 2019 the GSC turned 20. Collaborators, partners, family members and friends joined us in celebration at our Echelon site, home of our technology platforms. Guests

learned about genomics and bioinformatics during facility tours led by Marco Marra, Steven Jones, Robyn Roscoe, Andy Mungall, Richard Moore, Robin Coope and Lance Bailey.

In the evening, all three floors were open to guests for live music and science-inspired cocktails. With over 500 in attendance, it was a event to remember.

## CANADA'S MICHAEL SMITH GENOME SCIENCES CENTER 20TH ANNIVERSARY CELEBRATION



*An invitation to the GSC's Open House 20th Anniversary Celebration on November 15, 2019, created by Martin Krzywinski by solving the "Travelling Salesman Problem" through a 29,751-point SARS-coronavirus genome, drawing the number 20.*





*From left to right: The family of the late Dr. Michael Smith and other GSC founders, former BC Cancer President, Dr. Don Carlow, and former BC Cancer VP of Research, Dr. Victor Ling, with GSC Director, Dr. Marco Marra.*



*Clockwise from left: Dr. Steven Jones, GSC Co-Director, Robyn Roscoe, Director of Management and Administration, Lance Bailey, Head of IT Systems & Security, and Leader of Biospecimen & Library Cores, Dr. Andy Mungall, give tours of the GSC's Echelon site, home of our sequencing & IT platforms.*



*Left to right: Drs. Jones and Marra deliver speeches reflecting on the GSC's 20 year history to an over-flowing crowd in the lobby of Echelon. A proclamation from the government of British Columbia hangs beside Marco, declaring November 15, 2019 as "20th Anniversary of Canada's Michael Smith Genome Sciences Centre at BC Cancer Day" (seen in full on the adjacent page).*





**Canada**  
**Province of British Columbia**  
**A Proclamation**

ELIZABETH THE SECOND, by the Grace of God, of the United Kingdom,  
Canada and Her other Realms and Territories, Queen, Head of the  
Commonwealth, Defender of the Faith

**To all to whom these presents shall come – Greeting**

WHEREAS November 15, 2019, marks the 20th anniversary of Canada's Michael Smith Genome Sciences Centre at BC Cancer (GSC), established with support from Canadian Nobel Laureate, Dr. Michael Smith, and

WHEREAS the GSC is a world leader in sequencing and analyzing DNA and RNA, and was Canada's first serious capacity in genome science, allowing British Columbia to emerge as an international leader in genomics and bioinformatics, and

WHEREAS the GSC, in partnership with BC Cancer and the Provincial Health Services Authority, is helping to reduce the burden of cancer and other diseases by using genome science to develop new precision-medicine based approaches to the prevention, diagnosis, treatment and care of cancer and other diseases, and

WHEREAS the GSC has made significant contributions to life science, genomics and bioinformatics through training of thousands of highly qualified personnel, through hundreds of local, national and international research collaborations, and through thousands of scientific publications in leading peer-reviewed scientific journals, and

WHEREAS the GSC is helping British Columbia to realize the social and economic benefits of genome science, not only for cancer research and care but also in the prevention and treatment of other diseases, and other life sciences and resource sectors, including agriculture, forestry, fisheries, environmental studies and engineering;

NOW KNOW YE THAT We do by these presents proclaim and declare that November 15, 2019, shall be known as

**"20th Anniversary of Canada's  
Michael Smith Genome Sciences Centre at BC Cancer Day"**

in the Province of British Columbia.

IN TESTIMONY WHEREOF, We have caused these Our Letters to be made Patent and the Great Seal of Our Province of British Columbia to be hereunto affixed.

WITNESS, The Honourable Janet Austin, Lieutenant Governor of Our Province of British Columbia, in Our City of Victoria, in Our Province, this fourth day of November, two thousand nineteen and in the sixty-eighth year of Our Reign.

BY COMMAND.



\_\_\_\_\_  
Attorney General  
(counter signature for the Great Seal)



\_\_\_\_\_  
Lieutenant Governor

# CELEBRATING WITH SCIENCE

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On November 21, the first day of the 2019 BC Cancer Summit, the GSC hosted a scientific symposium at the Sheraton Wall Centre in Vancouver. Sixteen researchers, partners and leaders in the field of genomics, including some former trainees, gave presentations, highlighting

the technological advances, scientific investigations and groundbreaking discoveries that have propelled the field of genomics to where it is today. The event brought together current GSC scientists and staff, colleagues, alumni, collaborators and friends, all sharing a passion for

employing genomics to improve human lives. A touching presentation from a patient about her experience with the Personalized OncoGenomics program—many of the scientists and clinicians were in the room—reminded us all of why we do what we do.



*Symposium Speakers, from left to right: Victor Ling, Martin Hirst, Rodrigo Goya, Trevor Pugh, Janessa Laskin, Ryan Morin, Steven Jones, Athanasios Zovoilis, Robert Waterston, Obi Griffith, Elaine Mardis, Malachi Griffith, Pinaki Bose, Stephen Montgomery, Martin Krzywinski, Samuel Aparicio, James Kronstad and Marco Marra.*





Marco

People and the importance of Mentorship

Importance of trainees

Decoding DNA

# Opening Remarks

Victor Ling, Steven Jones, Marco Marra

Understanding the basis of cancer

Vancouver



Changing how we treat cancer



Steve

The frontiers of genomics



Reflecting on our Past



Debra Sparrow

Indigenous Welcome

Knowledge is a gift  
Remember who we are

Improving patients lives



@ATJGagan

*"This is a great event because it celebrates all of the work you have done over the past 20 years to make the GSC what it is today. The work at the GSC matters. It changes the way we care for cancer patients in British Columbia."*

Dr. François Bénard, Senior Executive Director, Research, BC Cancer

*"We had a vision of a genome centre inside a cancer clinic. None of us knew what was going to happen. We were guided by risk taking and dreaming big. Cancer is a big problem that requires big thinking."*

Dr. Victor Ling, President and Scientific Director, Terry Fox Research Institute, former VP Research at BC Cancer and GSC co-founder

*"I look back and see that we have had a fantastic run. I am hoping that our endeavors will continue to increase exponentially in the years to come."*

Dr. Steven Jones, Director and Head of Bioinformatics, GSC

*"The single most important ingredient that has knit us together is people and the importance of mentorship. I have been blessed to have access to incredible mentorship."*

Dr. Marco Marra, Director, GSC



[GSC20 in Review](#) commemorates our 20<sup>th</sup> anniversary with memorabilia, summaries of symposium presentations, photos, videos and more.

# PERSONALIZED ONCOGENOMICS

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The Personalized OncoGenomics (POG) Program, co-led by Dr. Marco Marra, Director of Canada's Michael Smith Genome Sciences Centre at BC Cancer and BC Cancer Medical Oncologist Dr. Janessa Laskin, is a patient-centric research initiative, consisting of oncologists, pathologists and other clinical, research and technical personnel that aims to study the impact of embedding whole genome and transcriptome analysis into treatment planning for British Columbian cancer patients with otherwise incurable metastatic cancers.

A key research objective for the POG program is to identify and better understand the genomic alterations that drive cancer and its progression, metastasis and response to therapies. One of the aims of the program is to use genomic data to rationally align patients to treatment options, identifying potential therapeutic targets for individual cancer patients. Another aim is to understand genomic correlates of treatment resistance.

In 2019, the POG team enrolled 76 more patients into the program, including the 100<sup>th</sup> pediatric POG patient, bringing the total number of patients enrolled since 2012 to more than 1,100.

In a landmark study published in the May 2019 *Clinical Cancer Research* journal, POG researchers discovered three patients, from a set of 47 advanced pancreatic cancers, who had tumours with characteristics indicating that they might be sensitive to a targeted therapy typically used to treat lung cancer.

Two patients were treated with this therapy, and showed a remarkable and rapid response.

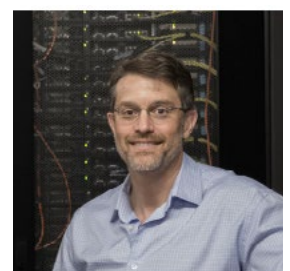
In response to this study, Andrew J. Aguirre of the Dana-Farber Cancer Institute wrote an editorial in the journal of *Clinical Cancer Research*, saying:

*"Deep genomic and transcriptomic analyses—preferably utilizing whole genome and whole transcriptome approaches to identify fusion events—should be pursued for KRAS wildtype [pancreatic] tumors in a prospective manner to discover targetable events early in a patient's disease course."*

Two unpublished POG successes included:

- The identification of a gene amplification for a teen patient with Alveolar Rhabdomyosarcoma. The POG team was successful in treating the patient with a drug class called cell cycle inhibitors, that otherwise would not have been used. The patient is doing well with controlled disease.
- A young woman with metastatic breast cancer was found to have a 'BRCA-like' tumour by POG experts. This resulted in genetic testing that identified hereditary cancer that would not have otherwise been found and also led to new targeted treatment options.

*"The POG Program has started something that goes beyond our own scientific discoveries. It has started a revolution."  
—Dr. Marco Marra*



76

PATIENTS ENROLLED IN POG IN 2019

1,161

TOTAL NUMBER OF PATIENTS CONSENTED TO DATE

83

PERCENTAGE OF ALL CASES TO DATE THAT HAVE YIELDED ACTIONABLE RESULTS

~200

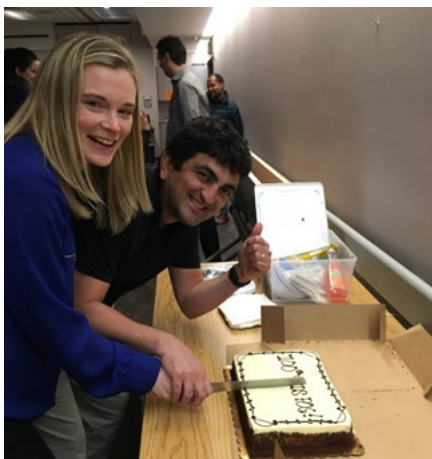
NUMBER OF SCIENTISTS, CLINICIANS AND OTHER POG TEAM MEMBERS

36

PEER-REVIEWED POG PAPERS PUBLISHED

500+

TERABYTES OF POG DATA GENERATED



Celebrating the 100<sup>th</sup> pediatric POG patient. Left: Cake was served to celebrate the 100<sup>th</sup> pediatric patient, and the “100” slice was given to the patient. Pediatric POG leaders Drs. Rod Rassekh and Rebbecca Deyell cut the cake. Right: Drs. Rassekh and Deyell pose for a picture with POG leaders Drs. Marco Marra and Janessa Laskin.



Some members of the Personalized OncoGenomics team.



# KNOWLEDGE TRANSLATION

The GSC is of interest to diverse audiences: clinicians, fellow scientists, educators, media outlets, patients, their families, donors, the public and more. The GSC's Knowledge Translation team, established in November 2018, strives to not only accurately and effectively disseminate exciting and impactful research discoveries but also to enhance awareness of the GSC and its work as a whole.

Kevin Sauvé is Head of Knowledge Translation. With a Bachelor's in biology, a Master's in science journalism and experience in both the newsroom and as a communications strategist, he has a unique ability to effectively distill complex information for

broad audiences. At the GSC he's working to develop a KT and communications strategy, provides project-specific KT and communications planning and support.

KTaC doubled in August 2019 with the addition of a Science & Technical Writer, **Kirstin Brown**. Kirstin provides writing and editing support and manages publications for the GSC. She completed her PhD in Microbiology and Immunology at UBC, is experienced in grant and manuscript writing, editing and typesetting, was senior editor for an undergraduate research journal, and has graduate training in science journalism.



Kevin Sauvé and Kirstin Brown, GSC Knowledge Translation and Communications (KTaC)

## Canada's Michael Smith Genome Sciences Centre

### Fresh face, same domain: we have a new website!

After more than two years of collaboration with many stakeholders at BC Cancer and its research departments, we were proud to launch the new GSC website in December, 2019!

The GSC's website endeavours to showcase our research, clinical programs, our technology platform

[bcgsc.ca](http://bcgsc.ca)

and certificates, and provide more ease of use for scientific partners and collaborators, including a detailed Collaborative Services section and a new Software Centre.

Along with the website, the GSC now has a social media presence with a new Twitter account. Find us [@BCCancer\\_GSC](https://twitter.com/BCCancer_GSC).







THERE ARE SOME NEW SHAPES ON THE STREETS OF VANCOUVER. THE DNA ON 10<sup>TH</sup> WAY-FINDING SIGNS, DESIGNED BY GSC STAFF SCIENTIST MARTIN KRZYWINSKI, MARK THE ENTRANCE TO THE CITY'S HEALTH CARE CORRIDOR AND THEIR INTRICATE DETAILS ARE BASED ON SEQUENCE DATA FROM POG.



Martin Krzywinski, Staff Scientist  
[www.mkweb.bcgsc.ca](http://www.mkweb.bcgsc.ca)

## Where are the signs?

On the east side of the intersection of 10<sup>th</sup> Avenue and Oak Street.

## What do they show?

Each shape on the signs represents a nucleotide base and each row represents a gene sequence. The shapes of complementary bases are vertical (A/T) or horizontal (C/G) reflections. Circles inside the shape indicate where a base repeats twice (small circle) or three times (large circle). These shapes are part of the DNA ON 10<sup>TH</sup> font designed for the sign. Bright bases signal a gene mutation and form a double helix—the 3-dimensional shape of DNA. The sequence along the helix is part of the *TP53* gene—an important tumour suppressor and regulator of cell division. There are several puzzles and “Easter eggs” built into the signs.

## Where did the data come from?

The data represent DNA from cancer patients sequenced at Canada's Michael Smith Genome Sciences Centre at BC Cancer. Each unique row of shapes is a real gene sequence implicated in cancer. Modern breakthroughs in cancer treatment have been made possible by genomics, the study of DNA and its role in heredity, health and disease. In our Personalized OncoGenomics program (POG), we compare patients' tumour and normal DNA to find the best targeted therapies.

## How are they different?

Sequences in rows that intersect with the 5' helix (the one that starts on the bottom row) are oriented in the direction of the sign. The helix shape on the north sign is as the helix on the south sign would appear if you were to look at it from the back.

## How are they different in the day compared to at night?

The signs are dimly backlit, giving them different day and night personalities. As the night ascends, the mysteries of the cell are revealed—the background sequence forming the double helix becomes distinguishable.

Learn more: <http://mkweb.bcgsc.ca/dnaon10th/>



# PLATFORM TOURS

As a publicly funded science, technology and research centre that also receives philanthropic support from generous BC Cancer Foundation donors, the GSC frequently offers tours of its genomics and bioinformatics technology platform at its Echelon site, located at 570 West 7th Avenue in Vancouver, B.C. **In 2019, the GSC provided tours for more than 240 people in more than 30 different tour groups**, including one for the Premier of British Columbia and another for the Member of Parliament for Vancouver Granville, Ms. Jody Wilson-Raybould.

## THE HONOURABLE JODY WILSON-RAYBOULD

**O**n March 14, 2019 the GSC hosted the Honourable Jody Wilson-Raybould, Member of Parliament for Vancouver Granville, former crown prosecutor, treaty commissioner and BC Association of First Nations regional chief. While reaching out to people and organizations in her constituency, Ms. Wilson-Raybould became aware of the GSC after Dr. Inanc Birol was awarded funding from Genome Canada, with which he is developing new ways to better annotate and visualize genome and transcriptome data.



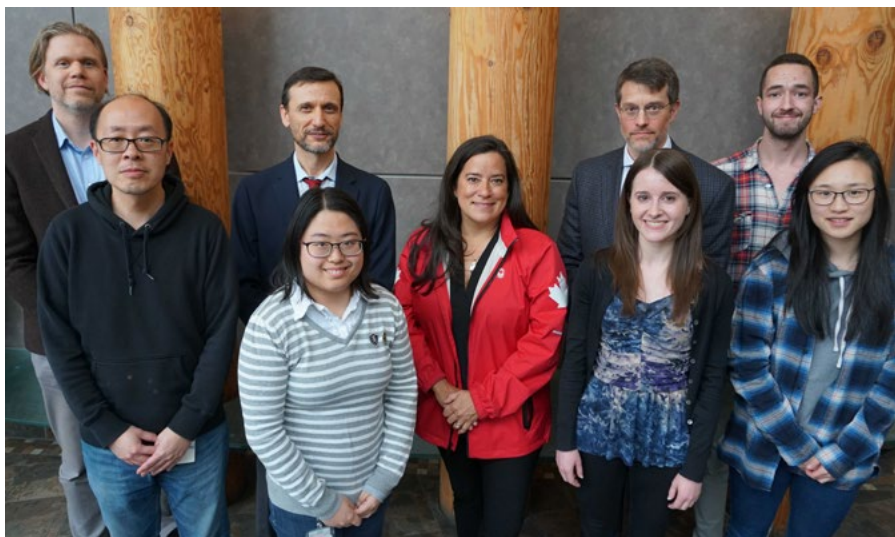
*Robyn Roscoe giving Ms. Wilson-Raybould an overview of GSC sequencing data and statistics.*



*Ms. Wilson-Raybould receiving a crash-course in genomics and bioinformatics from Dr. Birol.*



*Dr. Inanc Birol, Ms. Wilson-Raybould and Dr. Marco Marra.*



*Ms. Wilson-Raybould with Dr. Marra and members of the Birol laboratory.*

## THE HONOURABLE PREMIER JOHN HORGAN

On September 20, 2019 the GSC had the pleasure of hosting the Premier of British Columbia. The Honourable John Horgan received a hands-on, personal tour of our DNA sequencing and bioinformatics technology platform from Director, Dr. Marco Marra.

The Premier prepared DNA for extraction in a liquid handling robot, experienced different types of DNA sequencing technology, saw live normal and cancerous pancreas cells in culture, explored single-cell extraction and sequencing, toured

through the GSC's computer server room and learned of the different types of data with which the GSC's bioinformaticians work.

"Cancer touches us all. About half of us can expect to receive a cancer diagnosis in our lifetime. That's why the work of [the GSC] is so important," [said the Premier in a tweet](#) following the tour. "What I saw yesterday, and the people I met, gives me confidence that we can beat this disease. Thank you for having me."



*Dr. Marco Marra and Premier Horgan on a tour of the GSC, in the server room (left) and in the lab (right).*



*Left to right: PHSA Executive VP for Clinical Delivery, Susan Wannamaker; BC Cancer Chief Medical Officer, Dr. Kim Nguyen Chi; BC Cancer Chief Operations Officer, Heather Findlay; BC Cancer Foundation President and CEO, Sarah Roth; B.C. Premier John Horgan; GSC Director, Dr. Marco Marra; and BC Cancer Senior Executive Director, Research, Dr. François Bénard.*



# APPENDIX

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## All 2019 publications, listed chronologically.

1. Schuetz J.M., Grundy A., Lee D.G., Lai A.S., Kobayashi L.C., Richardson H., Long J., Zheng W., Aronson K.J., Spinelli J.J., **Brooks-Wilson A.R.** [Genetic variants in genes related to inflammation, apoptosis and autophagy in breast cancer risk](#). 2019. *PLoS One*.
2. Ramos-Miguel A., Barakauskas V., Alamri J., Miyauchi M., Barr A.M., Beasley C.L., Rosoklija G., Mann J.J., Dwork A.J., Moradian A., **Morin G.B.**, Honer W.G. [The SNAP25 interactome in ventromedial caudate in schizophrenia includes the mitochondrial protein ARF1](#). 2019. *Neuroscience*.
3. Mavaddat N., et al. (incl. **Brooks-Wilson A.R.**). [Polygenic risk scores for prediction of breast cancer and breast cancer subtypes](#). 2019. *American Journal of Human Genetics*.
4. Grande B.M., et al. (incl. **Jones S., Ma Y., Mungall A.J., Novik K., Zhao E.Y., Marra M.A., Morin R.D.**). [Genome-wide discovery of somatic coding and non-coding mutations in pediatric endemic and sporadic Burkitt lymphoma](#). 2019. *Blood*.
5. Haase D., et al. (incl. **Karsan A.**). [TP53 mutation status divides myelodysplastic syndromes with complex karyotypes into distinct prognostic subgroups](#). 2019. *Leukemia*.
6. Yasin H., Gibson W.T., Langlois S., Stowe R.M., Tsang E.S., Lee L., Poon J., Tran G., Tyson C., Wong C.K., **Marra M.A.**, Friedman J.M., Zahir F.R. [A distinct neurodevelopmental syndrome with intellectual disability, autism spectrum disorder, characteristic facies, and macrocephaly is caused by defect in CHD8](#). 2019. *Journal of Human Genetics*.
7. Rothe K., **Porter V.**, Jiang X. [Current Outlook on Autophagy in Human Leukemia: Foe in Cancer Stem Cells and Drug Resistance, Friend in New Therapeutic Interventions](#). 2019. *International Journal of Molecular Sciences*.
8. Ennishi D., Takata K., Beguelin W., Duns G., Mottok A., Farinha P., Bashashati A., Saberi S., Boyle M., Meissner B., Ben-Neriah S., Woolcock B.W., Telenius A., Lai D., Teater M., Kridel R., Savage K.J., Sehn L.H., **Morin R.D., Marra M.A.**, Shah S.P., Connors J.M., Gascoyne R.D., Scott D.W., Melnick A.M., Steidl C. [Molecular and Genetic Characterization of MHC Deficiency Identifies EZH2 as Therapeutic Target for Enhancing Immune Recognition](#). 2019. *Cancer Discovery*.
9. Guest W., Forbes D., **Schlosser C.**, Yip S., **Coope R.**, Chew J. [Imaging-based 3-dimensional printing for improved maxillofacial presurgical planning: a single center case series](#). 2019. *Canadian Association of Radiologists Journal*.
10. Saleh A., Cheng H., Martin S.E., Si H., Ormanaglu P., Carlson S.G., Clavijo P.E., Yang X., Das R., Cornelius S., Coupar J., Chepeha D.B., Danilova L., Harris T.M., Prystowsky M.B., Childs G., Smith R.V., **Robertson G., Jones S.J.M.**, Cherniack A.D., Kim S.S., Rait A., Pirolo K.F., Chang E.H., Chen Z., Van Waes C. [Integrated genomic and functional microRNA analysis identifies miR-30-5p as a tumor suppressor and potential therapeutic nanomedicine in head and neck cancer](#). 2019. *Clinical Cancer Research*.
11. Helbing C.C., **Hammond S.A., Jackman S.H.**, Houston S., **Warren R.L.**, Cameron C.E., **Birol I.** Antimicrobial peptides from *Rana [Lithobates] catesbeiana*: [Gene structure and bioinformatic identification of novel forms from tadpoles](#). 2019. *Scientific Reports*.



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13. Korecki A.J., Hickmott J.W., Lam S.L., Dreolini L., Mathelier A., Baker O., Kuehne C., Bonaguro R.J., Smith J., Tan C.V., Zhou M., Goldowitz D., Deussing J.M., Stewart A.F., Wasserman W.W., Holt R.A., Simpson E.M. [Twenty-seven Tamoxifen-inducible iCre-driver mouse strains for eye and brain; including seventeen carrying a new inducible-first constitutive-ready allele](#). 2019. *Genetics*.
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21. Levine A.B., Schlosser C., Grewal J., Coope R., Jones S.J.M., Yip S. [Rise of the Machines: Advances in Deep Learning for Cancer Diagnosis](#). 2019. *Trends in Cancer*.
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