PCTRiADD

PROSTATE CENTRE'S TRANSLATIONAL RESEARCH INITIATIVE
FOR ACCELERATED DISCOVERY AND DEVELOPMENT

TECHNOLOGY AND TALENT:
A NEW WAY FORWARD

PC-TRiADD ANNUAL REPORT 2016 - 2017

VANCOUVER
PROSTATE CENTRE
A UBC & VGH Centre of Excellence

A Message from Our Director

TECHNOLOGY AND TALENT: A NEW WAY FORWARD

PC-TRiADD is poised to capitalize on the perfect storm - a convergence of advances in genomics, structural biology, and computer sciences has enabled our group to expand our computer-aided drug design (CADD) platform and enhance our drug discovery capabilities. The early identification of drug candidates that can tackle treatment resistance in prostate cancer is now a reality and in parallel, we work to develop, validate, and commercialize our unique molecular tests as companion diagnostics to better risk-stratify cancers and support drug discovery in PC-TRiADD and globally.

The theme of this report - the technological advances that have enabled us to make these novel discoveries – is as significant as the people behind them. Our numerous publications (133 this year), conference participation (154 posters and abstracts), and 104 invited presentations speak to the knowledge translation that is taking place and the dissemination of our discoveries.

Our four core business units are maintaining their position as key support for our researchers and for external groups. Through these cores the convergence of genomics and the development of cell free DNA (cfDNA) tests to serially follow patients through treatment has led to a better understanding of the mechanisms of cancer leading to precision medicine.

In addition to supporting discovery research and product development at the Vancouver Prostate Centre (VPC), these cores provide novel resources and services that attract considerable revenue from industry and academic partners. While we focus on prostate cancer, many of our services and discoveries have utility in other cancers.

The level of funding for our research and clinical implementation is strong with some major awards this year from the Terry Fox Research Institute and Prostate Cancer Canada, as well as gifts from grateful donors. But we don't rely exclusively on grant funding or donations - our team works very hard to commercialize our discoveries, services, and products to spin-off biotechnology and attract contract research revenue from academic and industry partners. We continue to drive our discoveries and IP-protected products from the laboratory to the clinic and marketplace. Dr. Amina Zoubeidi's work, featured in her profile on page 8, is a great example of this.

Our enterprise as a whole is greater than the sum of its parts because it enables translation and commercialization of discoveries into new interventions under one cohesive team. This innovative and visionary strategy has led to major scientific, clinical, and commercial successes.

Dr. Martin Gleave

Dr. Martin Gleave,

MD, FRCSC, FACS

Executive Director,
Vancouver Prostate Centre

Chief Executive Officer, PC-TRiADD

Distinguished Professor and Head,
Department of Urologic Sciences, UBC

BC Leadership Chair
in Prostate Cancer Research

COMMERCIAL PROGRESS

We continue to move many discoveries along the pathway to commercialization. In addition to our spin-off companies, now numbering eight, we see continued success with our ongoing partnership with the BC Cancer Agency in clinical trials, where 458 patients were enrolled this year and 16 new trials were initiated.

Two therapeutics discovered at the VPC and out-licensed to OncoGenex Pharmaceuticals, custirsen and apatorsen, also reported strong results from late-stage clinical trials. Custirsen did not meet the endpoints required to move forward, but positive results with apatorsen from two randomized clinical trials were presented at the American Society of Clinical Oncology (ASCO) 2017 Genitourinary Cancers Symposium.

Positive survival results were reported for the Borealis-2™ trial of apatorsen in combination with docetaxel treatment in patients with metastatic bladder cancer who have disease progression following first-line platinum-based chemotherapy. The primary endpoint analysis met the superiority test for overall survival. The results of a Phase I safety study led by Dr. Chi demonstrated that apatorsen was tolerated at the highest dose evaluated; Phase II studies are underway.

The Pacific™ trial evaluated the ability of apatorsen, when added to Zytiga® (abiraterone acetate), to reverse or delay treatment resistance in 72 men who were experiencing a rising PSA on Zytiga alone.

The promising results for both these studies led OncoGenex to engage in partnering discussions to further explore these development opportunities.

This year Sitka Biopharma (Sitka), which Drs. Gleave and So are linked with, announced that Quark Venture made a significant seed investment in the company – a critical value-creating event that will enable Sitka to advance their lead compound for the treatment of bladder cancer into clinical trials.

Sitka remains focused on developing its breakthrough nanoparticle platform technology to increase absorption of drugs in difficult-to-penetrate tissues. Initially targeting oncology indications, Sitka is developing its lead candidate (STK-01) to address the absorption challenge of intravesical chemotherapy for bladder cancer, and later, intraperitoneal delivery for ovarian cancer. The investment from Quark enables progression through into Phase I clinical study.

The ongoing relationship with Roche Pharmaceuticals, based on the investment made into Drs. Cherkasov and Rennie's drug candidate, is moving towards its next milestone - a lead clinical compound.

The Centre's most recent spin-off company is LAST Innovations Ltd. which was formed in July 2016. LAST is currently in the process of licensing innovations discovered by Dr. Yuzhuo Wang. Preliminary work and intellectual property protection was supported in part with PC-TRiADD CECR funding.

LAST was formed to commercialize drugs to target the lactic acid transporter, MCT4. Many cancer cells rely on glycolysis to survive; by blocking the cells' ability to export lactic acid (a by-product of glycolysis), growth of the cancer cells may be suppressed. In addition, lactic acid in the tumour microenvironment creates an acidic state that may suppress local immune cells. It is theorized that reducing lactic acid in the microenvironment may lead to an immune attack on the tumour. The development of an antisense drug and a small molecule drug targeting MCT4 is well underway in Dr. Wang's lab.

Dr. Colin Collins

Dr. Mads Daugaard

BUSINESS UNITS

The ongoing investments in to our centre has helped create and operate the four key technology and service platforms: Genomics, Molecular Pathology, Preclinical Pharmacology and Clinical Trials. These business units each function as a service platform which enables researchers to discover and deliver quickly and effectively.

The Laboratory for Advanced Genome Analysis (LAGA), headed up by Drs. Collins, Wyatt and Hach, is the genomics, computer science and bioinformatics core of the VPC. LAGA provides next-generation sequencing, microarrays, RNAseq, bioinformatics, and algorithm development with project management services to academic, government, and industrial partners.

The Molecular Pathology Business Unit, led by Drs. Daugaard and Cox, has built the world's largest bank of pre- and post-treated prostate cancers with unique tissue microarrays (TMAs) of untreated and post-treated cancers linked to clinical data to study changes in gene expression associated with treatment resistance. In addition to prostate cancer, PC-TRiADD supports a diverse biorepository and pathology expertise.

The Preclinical Pharmacology Business Unit, led by Drs. Cherkasov, Guns and Zoubeidi, is integrated with target validation, molecular biology, computer-aided drug design/cheminformatics, analytical pharmacology, and preclinical pharmacology in novel models to support development of drug candidates. This unit attracts academia-partnered grant funding and contract research agreements with over 20 biotech and pharmaceutical companies.

The Clinical Trials Business Unit (CTU), led by Drs. Chi and So, conducts trials at both Vancouver General Hospital and the BC Cancer Agency. The CTU leverages national and international clinical trials networks and industry partners on a national and global scale. PC-TRiADD accelerates transfer of lab discoveries to clinical study, facilitating trials that incorporate novel correlative studies that, in turn, circle back to enhance discovery research.

This year we also entered into a collaborative research agreement with D-Wave Systems Inc. focusing on the development of quantum deep learning applications for cheminformatics including computer-aided drug design and processing 'big data'. The collaboration will explore new chemical representations within different algorithms for improved targeting of candidate drugs. D-Wave is the world's first commercial quantum computing company and the leader in the development and delivery of quantum computing systems and software.

MyPOP
MY PRECISION ONCOLOGY PROGRAM

The number of patients accrued in clinical trials and studies within the VPC's My Precision Oncology Program (MyPOP) grew exponentially in 2016. The overall goal of MyPOP is to develop a strategy for using genomic information from tumour biopsies and circulating cfDNA/RNA for diagnosis and guiding drug selection in patients with treatment resistant disease. Collectively, 'liquid biopsies' from over 400 patients (including 350 with advanced prostate cancer) have now been screened for genomic alterations as part of MyPOP. These include patients participating in an ongoing precision medicine Phase II 'umbrella trial' aimed at enrolling patients on selected targeted therapies based upon their genomic results.

Since November 2016, MyPOP has been augmented through the launch of a province-wide genitourinary (GU) liquid biobank program, so that patients with advanced GU cancers from across the province are able to provide blood samples for biobanking and/or genomic analyses.

INTERNATIONAL PROFILE & LEADERSHIP

Our team continues to maintain its profile internationally - through collaborations, publications and conference participation. This year our involvement with the Beijing Genomics Institute (BGI) was deepened as we signed an updated Memorandum of Understanding (MOU). Five leading health and research organizations in British Columbia and the world's largest genomics organization, based in China, have formed a global partnership to bring together advanced technologies and individualized therapy for cancer and other diseases.

The partnership, between BGI, Providence Health Care, St. Paul's Foundation, the VPC, Genome British Columbia (Genome BC), and Deloitte Inc., focuses on applying next generation sequencing technologies and big data to accelerate personalized medicine and improve outcomes for patients.

The collaboration aims to leverage each partner's strengths to create health centres of excellence in both Shenzhen and Vancouver. Cooperative research programs will build on BC's capability for world-class genomics research and BGI's internationally recognized expertise in 'omics' technology, data analysis and research.

In a joint news release, Dr. Colin Collins described the significance of working together to date: "The partnership has allowed scientists to develop biomarkers for identifying the most dangerous prostate tumours and to sequence a large cohort of tumours to define mechanisms of resistance to therapy."

We also renewed our commitment to the Pacific Northwest Prostate Cancer Specialized Programs of Research Excellence (SPORE). This is a group of four prominent research institutions working together toward a common goal of eradicating prostate cancer.

Our Stand Up To Cancer (SU2C) Dream Team, launched in 2012, has drawn to a close but the work is still ongoing - several high level publications have arisen from the collaboration. The team, which was looking at "Targeting Adaptive Pathways in Metastatic Treatment-Resistant Prostate Cancer" consisted of a multidisciplinary group of experts that included laboratory and clinical researchers, young investigators and senior scientists who have not worked together in the past, as well as patient advocates. An important publication in the Journal of the National Cancer Institute has led to linkages with the International Cancer Genome Consortium (ICGC), and Challenge Awards from the Prostate Cancer Foundation.

Dr. Nathan Lack

Dr. Faraz Hach

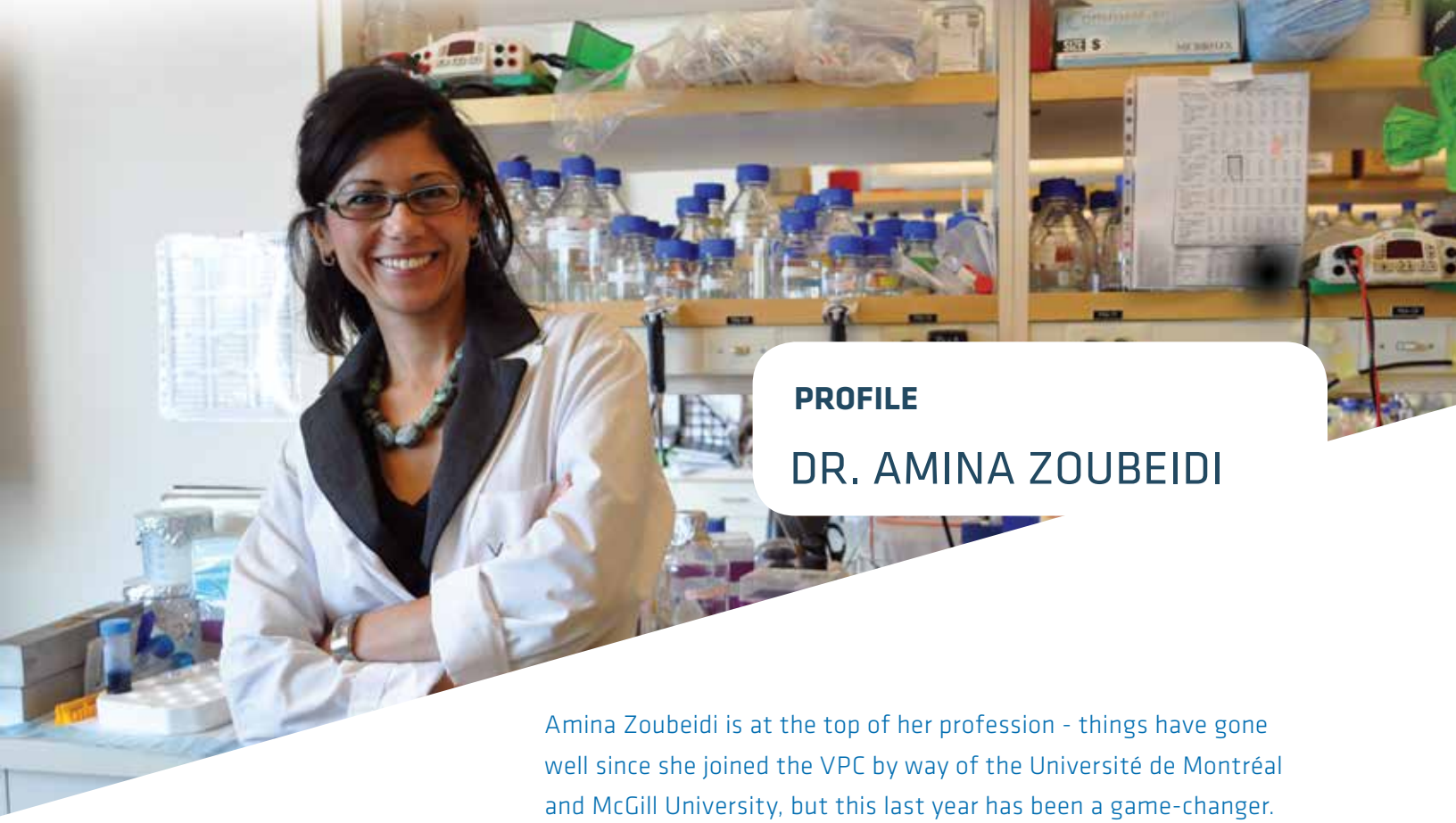
GROWING THE TEAM, GAINING RECOGNITION

Our team was enhanced this year with the addition of Dr. Nathan Lack, one of the VPC's former post-doctoral fellows, returning to his geographic and academic roots. A Vancouver Coastal Health Research Institute (VCHRI) 2011 Rising Star and a Michael Smith post-doctoral fellow, he continued to shine across the Atlantic at the exceptionally competitive and highly regarded Koç University School of Medicine in Istanbul, Turkey as an Associate Professor.

Now back in the VPC fold, Dr. Lack has the resources and drive to continue his work. He is particularly interested in better understanding the role of the Androgen Receptor (AR) in patients with aggressive or late-stage disease. Despite extensive research at the VPC and elsewhere, many questions still remain about how this important transcription factor works. Dr. Lack is determined to solve this mystery and better understand the function of the AR in order to develop more effective therapeutics to treat prostate cancer. At the VPC his knowledge and expertise in drug development is the perfect link between the computational modeling done by Dr. Artem Cherkasov and the *in vivo* pharmacology undertaken by Dr. Emma Guns.

We were also delighted to welcome Dr. Faraz Hach in his recently appointed role of Senior Research Scientist at the VPC. Dr. Hach's main focus is the field of bioinformatics, specifically computational genomics and biomolecular sequence analysis in the context of cancer research. His research involves designing unique, high performance algorithms for analyzing large amounts of data generated through sequencing of DNA. Recently, he has developed a computational tool for finding particular mutations from liquid biopsies in collaboration with Drs. Collins and Sahinalp. He is also focused on developing computational methods to better understand the progression of cancer from tissue and liquid biopsy sequencing data.

Dr. Hach's research has been internationally recognized with a number of awards and honors. These include the Ian Lawson Van Toch Memorial Award for an outstanding paper at the 20th Annual International Conference on Intelligent Systems for Molecular Biology, and the Governor General's Gold Medal for the best doctoral thesis from Simon Fraser University in 2014.



PROFILE

DR. AMINA ZOUBEIDI

Amina Zoubeidi is at the top of her profession - things have gone well since she joined the VPC by way of the Université de Montréal and McGill University, but this last year has been a game-changer.

She discovered a protein which drives the emergence of a highly aggressive form of cancer - neuroendocrine prostate cancer (NEPC) – and cutting-edge genome editing CRISPR technology enabled her to turn off the gene producing that protein. When the gene was turned off, the emergence of NEPC was prevented: this could be developed into a drug therapy could prevent this form of prostate cancer.

This groundbreaking protein discovery was validated, and published in Cancer Discovery. And, with an injection of funding of $1.5 million from Prostate Cancer Canada, Dr. Zoubeidi is well positioned to further this work. There are now novel prospects to target the resistance mechanisms with new drugs that may improve outcomes in this lethal form of the disease. Dr. Zoubeidi's ambitious plan is to have therapies in clinical trials within five years.

In addition to running a busy laboratory of three post-doctoral fellows, six graduate and three undergraduate students, Dr. Zoubeidi maintains deep international connections with others working in the field of NEPC. She has published over 200 international peer-reviewed papers and abstracts and she has been recognized as an outstanding up-and-coming scientist by the Prostate Cancer Foundation-USA (PCF). In 2010 she was awarded the prestigious PCF Young Investigator Award. Dr. Zoubeidi also holds prestigious awards from the Terry Fox Research Institute and the Michael Smith Foundations for Health Research, from which she received funding as a New Investigator and Research Scholar respectively. In 2014 she was awarded the Faculty of Medicine Distinguished Achievement Award in Overall Excellence - Early Career, University of British Columbia and Research Teaching Award for Excellence in Basic Science, Department of Urologic Sciences, Faculty of Medicine, University of British Columbia.

A dedicated mentor and community member, she serves on several grant panel review committees including Prostate Cancer Canada, the Canadian Institute of Health Research and the Prostate Cancer Foundation. Originally from Morocco, Dr. Zoubeidi has made Vancouver home since 2005 when she joined the VPC. She was promoted to Associate Professor in 2014 and keeps busy in her personal time indoor cycling and cooking with her husband, a pediatric urologist.

RESEARCH FUNDING

The team received 17 new research grants totaling $12.93 million and 16 trainee awards totaling over $1.47 million.

Some of the highlights include:

- Dr. Martin Gleave led a twenty-person program "Targeting the adaptive molecular landscape in castrate-resistant prostate cancer" and was awarded a Terry Fox Research Institute New Frontiers Program Project Grant renewal for $7.5 million of operating funds for six projects and five cores over five years. This is the longest continually funded program from the Terry Fox Foundation, 1998 to 2021, with $27.7 million awarded to date.
- Dr. Martin Gleave was also awarded a Prostate Cancer Canada Movember Translation Acceleration Grant 2016 for $1,480,000 over three years for his project "Computer-aided design of novel inhibitors of Hsp27."
- Drs. Yuzhuo Wang and Peter Black received a CIHR Operating Grant: Industry-partnered Collaborative Research award valued at $650,000 and this was matched for a total of $1.3M in support of their project "Application of antibody internalization domain to improve the efficacy and safety of Antibody Drug Conjugates".
- One of the benchmarks of scientific productivity is the number of peer-reviewed publications produced annually. Researchers at the VPC had 133 peer-reviewed publications and presented 154 posters and abstracts at national and international conferences during this fiscal year. They were also invited to give 104 presentations, 56 of these were at international sites. In fiscal year 2016-2017, 17 patents and 8 invention disclosures were filed, and 1 patent was issued.

Significant publications

- An international study led by Drs. Alex Wyatt, Colin Collins and Kim Chi demonstrated that clinically informative genomic profiling of cfDNA was feasible in nearly all patients with metastatic castration-resistant prostate cancer (mCRPC). This resulted in a publication, with first author Dr. Alex Wyatt, entitled *"Genomic Alterations in Cell-Free DNA and Enzalutamide Resistance in Castration-Resistant Prostate Cancer"* in is the definitive journal for scientists, clinicians, and trainees in the field of oncology worldwide - JAMA Oncology.
- An international study led by Drs. Kim Chi and Alex Wyatt demonstrated that metastatic castration-resistant prostate cancer patients with germline DNA repair defects respond poorly to androgen receptor-targeted therapy. Their findings were published in European Urology.
- Drs. Yuzhuo Wang and Colin Collins led a study which described the development of a certain genetic signatures that can be used to predict the metastatic potential of primary prostate cancer. Should this new prognostic tool be validated by further clinical studies, it could become a tool to strengthen decisions regarding selection of active surveillance versus surgery and/or radiation therapy for prostate cancer patients. They published their work in European Urology.

Dr. Artem Cherkasov

- Dr. Amina Zoubeidi led a study with other members of the VPC and collaborators at Weill Cornell Medicine, published in Cancer Discovery. They reported a new potential target for treating/preventing neuroendocrine differentiation in prostate tumors. This research was highlighted in the VCHRI Research Institute's newsletter, and was also featured in a Nature Reviews Urology article.
- Dr. Xuesen Dong led a publication in European Urology on the invention of a novel bioinformatics tool. The study identified a neuroendocrine prostate cancer (NEPC)-specific marker that may be a potential therapeutic target.
- Dr. Artem Cherkasov, along with his team and collaborators, developed a new chemoinformatics pipeline for predicting the activation of androgen receptor mutants, with accuracy reaching 90%. This tremendous example of computer-aided drug design was published in the Journal of Chemical Information and Modeling.

Fundraising & Community Engagement:

- The 2016 Mr. Lube Tournament for Life in support of the VPC took place on June 13, 2016 and raised over $570,000. Honorary Chair Rod Senft's family's charity, Step into Action, matched all fund-a-need donations made during the event up to $110,000. Rod's generosity along with other sponsors, donors and supporters helped to break the tournament's fundraising record. This year was the tournament's twentieth anniversary, and it has come to be one of BC's most prestigious charity golf events.
- The Terry Fox Run took place in various locations across Canada on September 18, 2016. The VPC fundraising walk/run team had a record 61 members participating at seven different sites. The team raised close to $40,000.
- The VPC's Movember team of 48 participants raised over $6,000 for Movember Canada. Dr. Michael Cox, who took part in the "My Move challenge" and cycled 1,094 km in the month, raised over one third of that.
- The VPC entered a team in the Step Up Challenge 2017 presented by Scotiabank - they climbed a total of 375 stories over five office towers on February 19.
- We received over $700,000 in support from numerous ongoing installment donations, as well as general donations and income on our endowment of $2.2 million, plus $629,726 in general donations.
- This year, the Province provided $6 million to the VGH & UBC Hospital Foundation to support the VPC in expanding its Prostate Cancer Supportive Care (PCSC) Program throughout British Columbia. Supported in part through provincial funding, the PCSC Program will now be implemented in Surrey, Prince George, Victoria and Kelowna. The provincial funding is also going towards the development of online materials to help men in communities who may not be able to physically access the PCSC Program sites.

ABOUT US

Embedded within the Vancouver Prostate Centre, The Prostate Centre's Translational Research Initiative for Accelerated Discovery and Development (PC-TRiADD) is a translational cancer research program and designated Centre of Excellence for Commercialization and Research (CECR) focused on discovering and developing new interventions to improve outcomes in prostate and other cancer.

Funded by the Government of Canada, PC-TRiADD also offers pharmaceutical and biotech companies, as well as external researchers, integrated translational research services such as gene and pathway discovery, biomarker analyses, preclinical testing, tumour biology, novel drug discovery and clinical expertise. This model enables us to attract more revenue generating contract research agreements while supporting and leveraging value-added development of our internal discoveries which creates new Intellectual Property (IP), services and products.

OUR MISSION

The mission of the PC-TRiADD Centre of Excellence for Commercialization and Research is to serve as a hybrid between academic research and the biotechnology industry, and to foster the paradigm of team-driven translational health research.

Our aim is to discover molecular mechanisms of cancer progression and therapeutic resistance and use this information to develop new services and products to improve cancer outcomes and promote regional growth of biotechnology.

PC-TRiADD HOST INSTITUTIONS ARE:

Faculty of Medicine,
The University of British Columbia

The UBC Faculty of Medicine provides innovative programs in the health and life sciences, teaching students at the undergraduate, graduate and postgraduate levels.

For more information, visit www.med.ubc.ca.

Vancouver Coastal Health Research Institute

Vancouver Coastal Health Research Institute (VCHRI), a world leader in translational health research, is the research body of Vancouver Coastal Health Authority. VCHRI includes three of BC's largest academic and teaching health sciences centres — Vancouver General Hospital, UBC Hospital, and GF Strong Rehabilitation Centre — as well as many other hospitals and public health agencies across Vancouver Coastal Health. VCHRI is academically affiliated with UBC Faculty of Medicine and is one of Canada's top funded research centres receiving between $80-100 million in research funding annually. Over 1500 personnel are engaged in a variety of research centres, programs and evolving research areas.

www.vchri.ca

BY THE NUMBERS:

2016-17

TRAINEES TRAINED:

- 13 MASTER OF SCIENCE
- 35 PHD STUDENTS
- 32 POST-DOCTORAL
- 5 CLINICAL FELLOWS
- 30 UNDERGRADS, CO-OP, SUMMER STUDENTS

16
TRAINEE'S RECEIVED AWARDS

$1.47 million
IN NEW FUNDING

4
HONOURS AND AWARDS TO PIs

RESEARCH GRANTS:

17
NEW PRECLINICAL RESEARCH GRANTS

$12.93 million
IN NEW FUNDING

16
NEW CLINICAL TRIALS STARTED

CONTRACT RESEARCH AGREEMENTS:

3
NEW CRAs WORTH $300K

4
ONGOING CRAs

INTELLECTUAL PROPERTY:

133
PEER-REVIEWED PUBLICATIONS

154
CONFERENCE ABSTRACTS/ POSTERS

104
PRESENTATIONS

8
NEW INVENTION DISCLOSURES

17
NEW PATENTS FILED

1
PATENTS ISSUED

458 PATIENTS ENROLLED IN CLINICAL TRIALS

LEADERSHIP TEAM

Our Management Team

Dr. Martin Gleave,
Chief Executive Officer
and Executive Director,
Vancouver Prostate Centre, and
Head, Department of Urologic
Sciences, UBC

Dr. Larry Goldenberg,
Vice President, Development,
Vancouver Prostate Centre

Dr. Paul Rennie,
Vice President, Laboratory Research,
Vancouver Prostate Centre

Dr. Graeme Boniface,
Chief Operating Officer,
Vancouver Prostate Centre

Dr. Kim Chi,
Associate Director, Clinical Research,
Vancouver Prostate Centre

Dr. Colin Collins,
Director, Laboratory for Advanced
Genome Analysis,
Vancouver Prostate Centre

Mr. Brian Shankaruk,
Chief Financial Officer,
Vancouver Prostate Centre

Our Business Unit Leaders

Dr. Colin Collins,
Laboratory for Advanced Genome Analysis
(LAGA)

Dr. Mads Daugaard,
Dr. Michael Cox,
Molecular Pathology and Cell Imaging

Dr. Emma Guns,
Dr. Artem Cherkasov,
Analytical Pharmacology and Drug Design

Dr. Amina Zoubeidi,
Dr. Chris Ong,
Preclinical Pharmacology

Dr. Kim Chi,
Dr. Alan So,
Clinical Trials

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Mr. Rod Senft

Dr. Ken Spencer

PARTNERSHIPS & COLLABORATIONS

Our Host Institutions

Vancouver Coastal Health Research Institute
Healthier lives through discovery

UBC FACULTY OF MEDICINE

Department of UROLOGIC SCIENCES UBC

Our Partners

BC Cancer Agency
CARE + RESEARCH
An agency of the Provincial Health Services Authority

PCF BC Prostate Cancer Foundation BC

Canadian Cancer Society / Société canadienne du cancer

Genome BritishColumbia
Leading > Investing > Connecting

GenomeCanada

Prostate Cancer Canada

Prostate Cancer Foundation

Canada Foundation for Innovation
Fondation canadienne pour l'innovation

Canada
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Networks of Centres of Excellence / Réseaux de centres d'excellence

Provincial Health Services Authority
Province-wide solutions. Better health.

Michael Smith Foundation for Health Research

A single dream. A world of hope. The Terry Fox Foundation

VGH UBC hospital foundation
ensuring excellence

SAFEWAY

MOVEMBER

CIHR IRSC

COALITION TO CURE PROSTATE CANCER

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华大科技 BGI tech