

PCTriADD

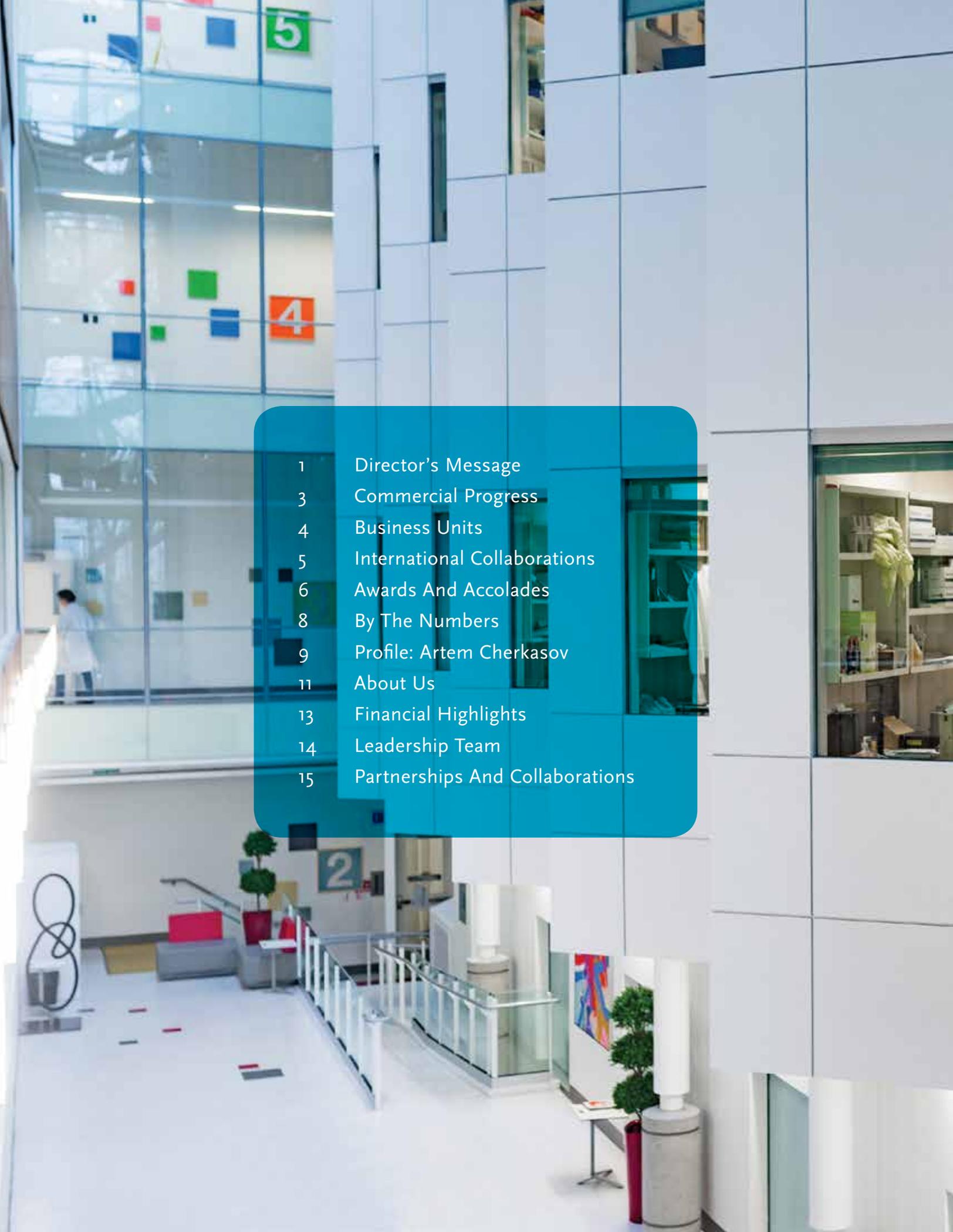
PROSTATE CENTRE'S TRANSLATIONAL RESEARCH INITIATIVE
FOR ACCELERATED DISCOVERY AND DEVELOPMENT



PC-TRIADD ANNUAL REPORT 2015-2016



VANCOUVER
PROSTATE CENTRE
A UBC & VGH Centre of Excellence



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A MESSAGE FROM OUR DIRECTOR

SETTING RECORDS AND LEADING THE WAY

This has been an incredible year, the pinnacle of which has been the largest out-licensing deal on record by the University of British Columbia (UBC) as a result of work by our own Drs. Artem Cherkasov and Paul Rennie. The new drug, currently in pre-clinical development, could one day be used to treat advanced prostate cancers that have become resistant to existing treatments by targeting a unique part of the androgen receptor, its DNA binding domain.

The goal is to have a simple pill that prostate cancer patients can take daily when their cancers have become resistant to first and second line hormone therapies. The licensing agreement was reached in December of 2015 and stipulates that research will continue in collaboration with the Vancouver Prostate Centre and PC-TRIADD.

Commercialization efforts continue to grow for all Principal Investigators as we filed 13 more patents this year bringing the total since 2008 to 259. One of our most notable numbers came in our clinical trials groups, where we enrolled a record 325 patients bringing the total to 1,721. Our clinical trials

launched to date now numbers 109. We also signed three new Contract Research Agreements valued at over \$220,000.

Our team continues to advance prostate cancer research and disseminate the knowledge with publications (132) and conference presentations / posters (141). Our Principal Investigators were also honoured this past year with prestigious accolades - 13 in total. The next generation of the best and brightest, our post-doctoral fellows, accumulated 19 such distinctions.

One of the staples of our Centre is leadership matched by an equal strength in mentorship which is reflected in the numerous awards received by our trainees. Some other highlights from the year included the ongoing recognition of our up and coming stars. Dr. Alex Wyatt, working with Drs. Kim Chi and Colin Collins, published several seminal papers leading the field in the role of plasma cell-free DNA in prognostic and predictive biomarkers for advanced prostate cancer. Dr. Alastair Davies, a post-doctoral fellow, was a very worthy recipient of a three-year CIHR fellowship.



PC-TRIADD has also become involved with a proposed new hub for global innovation, the Pacific Health Innovation eXchange (PHIX). PHIX will enable researchers, clinicians, health administrators, industry and the public to work together, in both real and virtual worlds, to advance innovations, drive economic development and contribute to the overall health of people in British Columbia and around the world. PHIX has the potential to become a source of national pride and a centre of production for cutting edge health care technology on the global stage. We are working in close collaboration with the institutions involved on the implementation of their vision which is a similar model to ours. This speaks well to PC-TRIADD as an innovator and successful business model, and we are well represented with myself taking on the role of Chief Scientific Officer

This past year we have been fortunate in attracting two large philanthropic donations, \$7.5M and \$1.2M, to support the My

Precision Oncology Program (MyPOP). We have partnered with Dr. Marco Marra at the BC Cancer Agency's Genome Sciences Centre to form a Translational Cancer Genomics Institute, selected by UBC as its only candidate for a \$150M proposal to the Canada First Research Excellence Fund, again to catapult our integrated research and clinical care programs forward towards the future of precision oncology.

It is my honour to thank the efforts of our senior leadership and management team. There is little doubt that without them we would be much less successful. I also thank the Board of Directors, particularly our Chair Mr. Conrad Pinette, for their efforts in this exceptional year. The faculty, staff and trainees are essential to our mission and I thank them for their continued dedication. With this group and our current trajectory, I foresee another gratifying year of leadership and making a mark on prostate cancer research and patient care.

Dr. Martin Gleave

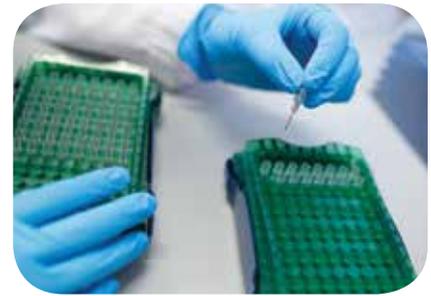
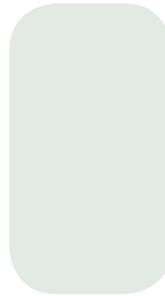
MD, FRCSC, FACS

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

ENTERING THE NEXT PHASE

Initial collaborations and investments in Aquinox Pharmaceuticals (Aquinox) continue to reap rewards. This past year saw a large investment into Aquinox and they advanced their portfolio products towards Phase 3 trials with the SHIP1 inhibitor, AQX-1125. Aquinox's public offering on the NASDAQ stock exchange netted proceeds of USD \$98 million. Aquinox is using this funding towards further clinical research of development of AQX-1125 in bladder pain syndrome/interstitial cystitis (BPS/IC) and potentially other inflammatory and immune-oncology indications, as well as funding the submission of regulatory filings and preparation of commercial activities for AQX-1125.

OncoGenex Pharmaceuticals has advanced to Phase 3 studies in advanced prostate and non-small cell lung cancer with more than 2000 men treated with a new cancer-fighting drug (Custirsen) which has been shown in an earlier study to prolong the life of patients with advanced prostate

cancer. More than 600 men have been enrolled in this study to date. PC-TRIADD provided critical pre-clinical development of this drug as well as access to a national clinical trials network.

Drs. Martin Gleave and Alan So continue to share their expertise with Sitka Pharmaceuticals to develop a drug delivery method to overcome the challenges associated with treating non-muscle invasive bladder cancer, with potentially far-reaching implications. At present, the most immediate benefit of the research being conducted is the hyperbranched polyglycerol (HPG) polymer's potential for increasing drug uptake in tissues where there are problems associated with conventional delivery. Beyond this technology, the team forged a path that could lead to extremely positive consequences for the treatment of bladder cancer as well as the treatment of other cancers and potentially even other diseases.

KEY OUTCOMES 2008-16: COMMERCIALIZATION

Negotiation of 44 new CRA's with Pharmaceutical/Biotech Companies worth \$18.7 million

Intellectual Property Activities

259 patent filed/issued
9 Licensing Agreements of IP with Industry (8 drug, 1 Biomarker)
DBD Ligand binding technology licensed to Roche in 2015 -
Largest out-licensing deal ever from UBC

4 Companies spun out of PC-TRIADD

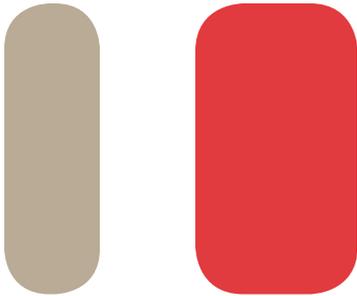
OncoGenex

OGX-011: in advanced Phase III studies
OGX-427: in multiple Phase II studies
Over \$100M reinvestment back to Canada clinical trials networks

Aquinox - novel AR ligands

Sitka - Formulation of Paclitaxel for bladder cancer

Andronex - AR binding drugs



BUSINESS UNITS

SUPPORTING PC-TRIADD AS A GLOBAL LEADER

Our Centre continues to integrate commercialization as a key part of translating our discoveries as per our mandate as a Centre for Excellence in Commercialization and Research (CECR). A key aspect of our work as a CECR is clinical trials, and our Clinical Trials Unit has had an exceptional year. Our ability to offer new potential therapies to patients and services to major companies is growing annually, with 14 new clinical trials started and 325 new patients enrolled this year.

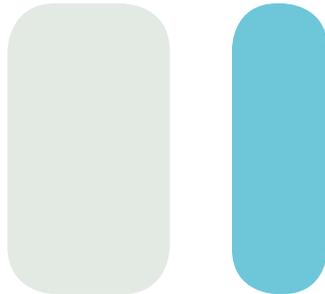
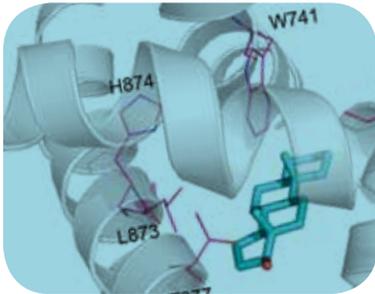
The diversity and scope of our trials is supported by our Clinical Assay Laboratory, which is CLIA (Clinical Laboratory Improvement Amendments) certified and CAP (College of American Pathologists) accredited. Last year the laboratory passed assessments by both organizations and continues to hold its accreditation. This year the group

undertook projects with Oncogenex, SignalChem Lifesciences Corporation and Welichem offering ELISA (Enzyme-linked immunosorbent assay) services. This past year we increased throughput for diagnostic clinical samples and increased the number of processed samples by 67%.

Of note, our Clinical Assay Laboratory Manager, Jenny Bazov, was appointed to be a Canadian representative in the revision of the Quality Management Systems for laboratories. It is a very prestigious nomination from the Clinical Laboratory Standard Institute located in the USA. The impact of this is that in the future all laboratory audits will use this new revision.

Our other business units continue to flourish. The Pre-Clinical Pharmacology Platform remains seamlessly integrated with other platforms and offers a

unique ability to researchers to do work on-site instead of shipping it out. The Laboratory for Advanced Genome Analysis (LAGA) continues to be a beacon nationally and internationally for the acquisition, processing, statistical analysis, integration, and visualization of high-density sequencing and microarray data. Along with the Beijing Genomics Institute (BGI) there is a continued investment into LAGA of sequencers to further the collaboration and training efforts. The Molecular Pathology Unit continues to offer clinical grade, high throughput analytical services with fast turnaround times. Our access to recently resected human tumour tissues enables research including the identification of new tumour targets, validation of function, and development of tumour models.



INTERNATIONAL COLLABORATIONS

MAKING WAVES ABROAD

As always, international relations continue to be a key facet of PC-TRIADD's success. Our ongoing relationship with the Beijing Genomics Institute has expanded and we are yielding positive results including mutually beneficial training in bioinformatics and data analysis.

The Stand Up to Cancer Dream Team 2, of which Dr. Martin Gleave is a Principal, continues to make advances. The "Targeting Adaptive Pathways in Metastatic Treatment-Resistant Prostate Cancer" Dream Team consists of a multidisciplinary group of experts that includes laboratory and clinical researchers, young investigators and senior scientists who have not worked together in the past, as well as patient advocates. We look forward to continuing to participate in this international endeavour.

In October 2015, Drs. Mads Dugaard and Poul Sorensen had a major international collaboration come to fruition. With their teams in Vancouver and Copenhagen, they published the result of their ground-breaking work identifying that a specific sugar molecule could be a target for anti-cancer drugs, and that the malarial protein, called VAR2CSA, could provide the tool for carrying such drugs to tumours. Two companies, Vancouver-based Kairos Therapeutics and Copenhagen-based VAR2 Pharmaceuticals, are developing the compound for clinical trials in humans. The hope is that clinical trials will take place within three years.

AWARDS AND ACCOLADES

WORKING AS A TEAM AND REAPING THE BENEFITS

PC-TRIADD continues to succeed and we know that this is a direct reflection of the talented people who work towards research, translation and application on a daily basis. Our team brought in thirty new research grants totaling \$13.95 million this year. This includes a \$5.7 million investment from the Canadian Foundation for Innovation (CFI) and the BC Knowledge Development Fund, for a program led by Dr. Collins; this will provide infrastructure to expand research capabilities, particularly in MyPOP. MyPOP was further enriched with a \$1.25 million annual donation, for five years, from a private donor.



Dr. Colin Collins

The Centre raised \$15.27 million from local fundraising and philanthropy, notably \$7.5 million for the MyPop Program and \$3 million for the Khosrowshahi Bladder Cancer Chair. This year the Mr. Lube Golf Tournament for Life raised over \$520,000 and another \$323,000 was received from directed donations. In addition to these fundraising endeavors, our faculty, staff and trainees frequently enter joint teams in local fundraising initiatives for charities such as Prostate Cancer Canada, Prostate Cancer Foundation - BC, the Terry Fox Foundation and Movember Canada.



Dr. Peter Black

Senior staff at the Centre were well recognized by peers this year. 13 honours and awards went to our Principal Investigators including:

- UBC's Goldenberg Chair in Urologic Sciences to Dr. Martin Gleave
- The Silver Medal of Service from the Doctors of BC to Dr. Larry Goldenberg
- American Urologic Association Honorary Membership to Dr. Martin Gleave
- The Teaching Excellence Award in UBC's Department of Urologic Sciences to Dr. Yuzhuo Wang who was also promoted to the rank of Professor
- Prostate Cancer Canada's Movember Rising Star Award to Dr. Alex Wyatt
- The Canadian Cancer Society's Robert L. Noble Prize for outstanding achievements in basic biomedical cancer research to Dr. Poul Sorensen
- Best Reviewer for the Journal of Urology; First Prize for Physician Essay from the American Urologic Association; and, European Association of Urology best poster and best paper in clinical research to Dr. Peter Black

Dr. Black not only received many nods from his international colleagues, in January of 2016 he and Dr. Wang were award a five-year Canadian Institutes of Health Research (CIHR) Collaborative Research Grant for their project "Application of antibody internalization domain to improve the efficacy and safety of Antibody Drug Conjugates" in partnership with iProgen Biotech Inc. of Richmond, BC.

Not to be outshone by their senior colleagues, our trainees again this year advanced themselves through major funding successes. Salem Malikic, a PhD student at our Centre co-supervised by Drs. Cenk Sahinalp and Colin Collins, was awarded a prestigious Vanier Canada Graduate Scholarship (NSERC) valued at \$50,000 per year for three years. The Government of Canada launched the Vanier Canada Graduate Scholarships (Vanier CGS) program in 2008 to strengthen Canada's ability to attract and retain world-class doctoral

Peer recognition was again an area of strength for our team this year with 132 peer-reviewed publications and 141 conference presentations and posters.

Drs. Shusuke Akamatsu, Alex Wyatt, Martin Gleave and Colin Collins and their team at our Centre published the result of their ground-breaking work identifying a gene called PEG10 as a novel and highly-specific therapeutic target for neuroendocrine prostate cancer (NEPC), "The placental gene PEG10 promotes progression of neuroendocrine prostate cancer", in Cell Reports.

Dr. Artem Cherkasov along with other team members published "Functional analysis of androgen receptor mutations that confer anti-androgen resistance identified in circulating cell-free DNA from prostate cancer patients" in Genome Biology.



Dr. Amina Zoubeidi

students and establish Canada as a global centre of excellence in research and higher learning.

Nineteen of the 44 national and international post-doctoral associates (post-docs) at our Centre received awards and honours. Of these, 10 were salary awards totaling \$550,000. This past year we hired 10 new post-docs. We also support 111 graduate and summer students as a continued investment into our legacy of mentoring and great research.

Some other highlights from our trainees include Dr. Alastair Davies's three-year Fellowship from the CIHR for his project "A Cancer Stem Cell-Directed Therapy for Enzalutamide-Resistant Prostate Cancer." Dr. Davies is a postdoctoral fellow in Dr. Amina Zoubeidi's lab.



Dr. Alex Wyatt

In the Journal of American Medicinal Association Oncology, Dr. Alex Wyatt was first author and Dr. Kim Chi senior author on a breakthrough paper for precision and personalized therapies for different cancers. In "Genomic Alterations in Cell-Free DNA and Enzalutamide Resistance in Castration-Resistant Prostate Cancer" it was explained that researchers have discovered a method for testing prostate cancer DNA from a small blood sample, making it possible to retrieve exact information about how the cancer is genetically changing and helping determine the type of treatment best suited to treat it at that moment.



Dr. Mads Daugaard

In Cancer Cell, Drs. Mads Daugaard and Poul Sorensen led the publication "Targeting Human Cancer by a Glycosaminoglycan Binding Malaria Protein".

In addition to academic prowess, our team has also advanced two previous staff members on to industry positions. Dr. Anna Lapuk is now a key member of the team at Contextual Genomics and Dr. Jennifer Bishop has taken up a position at Zymeworks. These highly skilled and innovative scientists with solid backgrounds in translational research are an asset to industry, promoting the commercialization aspects of our mandate.

BY THE NUMBERS: 2015-16

RAISED
\$15.3 M
FROM LOCAL FUNDRAISING/
PHILANTHROPY

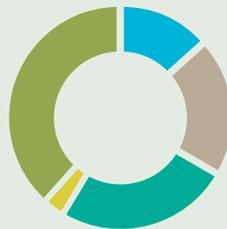
- \$520K MR LUBE TOURNAMENT FOR LIFE
- \$3 MILLION GOLDENBERG CHAIR
- \$3 MILLION FOR BLADDER CANCER CHAIR
- \$7.5 MILLION AND \$1.2 MILLION DONATED FOR MYPOP FUND
- \$323K GENERAL DONATIONS
- \$1.3 MILLION IN INVESTMENT INCOME FROM ENDOWMENTS

14
NEW CLINICAL TRIALS
STARTED

 **132**
PEER-REVIEWED PUBLICATIONS

 **141**
CONFERENCE PRESENTATIONS/
POSTERS

30
NEW RESEARCH GRANTS
TOTALING
\$13.95M



- 21 MASTER OF SCIENCE
- 31 PHD STUDENTS
- 39 POST-DOCTORAL
- 5 CLINICAL FELLOWS
- 59 UNDERGRADS, CO-OP, SUMMER STUDENTS

INTELLECTUAL PROPERTY:

LICENSING OF AR DBD TECHNOLOGY TO ROCHE - LARGEST OUT-LICENSING DEAL EVER FROM THE UNIVERSITY OF BRITISH COLUMBIA (OR FROM A CANADIAN UNIVERSITY)

3 NEW CONTRACT RESEARCH AGREEMENTS WITH PHARMACEUTICAL/ BIOTECH COMPANIES TOTALING \$225K

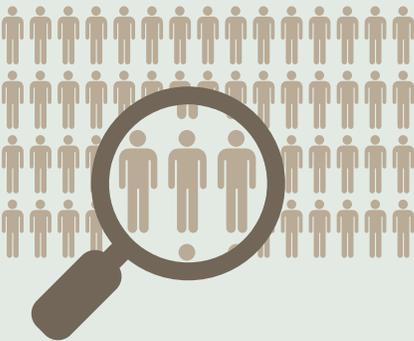
13 PATENT FILINGS

 **3** PATENTS ISSUED

3 NEW IP PRODUCTS

 **5** NEW INVENTION DISCLOSURES

325 PATIENTS ENROLLED IN CLINICAL TRIALS



GGTACCATACATT ACGGACATTTTAA GATACCATAACATT ACGGACATTAC GATACCATACATT ACGGACATTTTAG PUZZLE MASTER

It has been fifteen years since Dr. Artem Cherkasov arrived in Vancouver. Prior to that he likens himself to an NHL player with different postings in Europe and Canada after receiving his PhD from Kazan University in Russia.

Today Dr. Cherkasov is a Professor in UBC's Department of Urologic Sciences and Senior Research Scientist and Head, Chemoinformatic Drug Design at the Vancouver Prostate Centre. After years of effort, this past year has been his most impactful - Dr. Cherkasov's work is at the crux of a promising new treatment for drug-resistant prostate cancer.

Dr. Cherkasov, in collaboration with Dr. Paul Rennie and with support from UBC's University Industry Liaison Office (UILO) and PC-TRIADD's Chief Operating Officer Dr. Graeme Boniface, has licensed a targeted therapy to the pharmaceutical company Roche for more than \$140 million USD. Using Dr. Cherkasov's three-dimensional modeling techniques to identify their target location on a cancer-causing protein, the duo was able to isolate a small-molecule inhibitor which will shut the protein down.

Using Dr. Cherkasov's three-dimensional modeling techniques to identify their target location on a cancer-causing protein, the duo was able to isolate a small-molecule inhibitor which will shut the protein down.

The origin behind this design was using *in silico* modeling of a protein called the Androgen Receptor (AR). The structural information on AR existed, and was used in Dr. Cherkasov's drug design pipeline to link its protein structure to potential small molecule therapies.

In an interview with the Vancouver Sun in December 2015, Dr. Cherkasov explained: "Drugs and proteins work like a key in a lock, so we have to find the perfect key for the existing lock. Using computer simulations, we sometimes go through 50 million compounds to find a molecule that will seat in a precise and accurate way."

However, reliable structural information is not always available for potential cancer drug targets. To bridge that gap and to repeat the success of the 'AR story' on other cancer targets, Dr. Cherkasov focused his attention on the second piece of the puzzle – the identification and purification of novel target proteins and the use of cryoEM (Electron Microscopy) which helps to visualize the proteins' three dimensional structure.

With such reliable structural data on novel targets, the team can rapidly plug in *in silico* drug discovery. Dr. Cherkasov predicts that the field of drug discovery will soon produce an abundance of promising candidates because of this work.



Dr. Artem Cherkasov

The ability to blend together breakthrough *in silico* technologies with powerful platform technologies allows the capability to see molecules interact, which means that the modeling informs the choice of potential activators/inhibitors that interact with the target protein. Once potential activators/inhibitors are selected *in silico*, they can be tested for functional verification in the wet lab; the most promising are then advanced to pre-clinical studies. This acceleration of the drug discovery pipeline is truly revolutionary.

In order to fit the final pieces together, Dr. Cherkasov is leading a major funding application to expand the drug discovery and development platform with added infrastructure, focusing primarily on hardware and software for protein production and structural elucidation. For Dr. Cherkasov the puzzle is well on its way to completion.



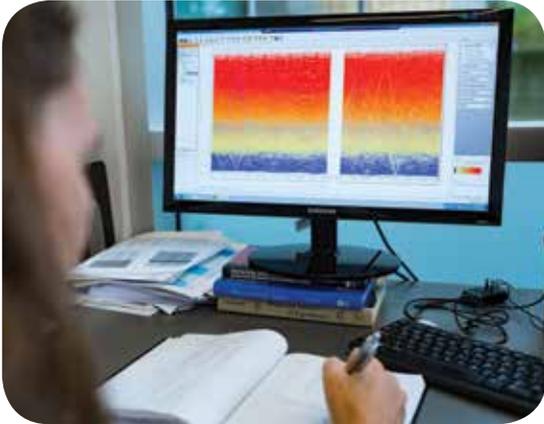
Dr. Paul Rennie



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.



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. Its faculty members received over \$305 million in research funds, 57 percent of UBC's total research revenues, in 2014-15.

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 the 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 internationally renowned research centres, programs and evolving research areas. The research focus is on innovation and discoveries that improve patient health, transform health systems, create technology transfer jobs, and foster a new generation of knowledge and innovation leaders.

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,
Director, Development,
Vancouver Prostate Centre

Dr. Paul Rennie,
Director, Laboratory Research,
Vancouver Prostate Centre

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

Dr. Kim Chi,
Head, Clinical Trials Unit,
Vancouver Prostate Centre

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

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

Our Business Unit Leaders

Dr. Colin Collins,
Head, Laboratory for Advanced
Genome Analysis

Dr. Mads Daugaard
Head, Molecular Pathology

Dr. Emma Tomlinson Guns,
Head, Analytical Pharmacology

Dr. Artem Cherkasov,
Head, Chemoinformatic Drug Design

Dr. Kim Chi,
Medical Director,
Genitourinary Clinical Trials Unit,
BC Cancer Agency

Dr. Alan So,
Clinical Trials Unit,
Vancouver Prostate Centre

Our Board of Directors

Mr. Conrad Pinette, Chair

Mr. John Blunt

Dr. Graeme Boniface

Mr. Scott Cormack

Ms. Karimah Es Sabar

Dr. Martin Gleave

Dr. Larry Goldenberg

Dr. Robert McMaster

Mr. Dennis Parolin

Mr. Rod Senft

Dr. Ken Spencer

PARTNERSHIPS & COLLABORATIONS

Our Host Institutions



Our Partners



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.



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



**VANCOUVER
PROSTATE CENTRE**
A UBC & VGH Centre of Excellence

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