2019

Annual Newsletter for the Department of Urologic Sciences

Message from the Chairman

The Department of Urologic Sciences had an exceptional year of talent building and major research advancements, highlighted by recruitment of two new full-time faculty supported by major salary awards.

We are also fortunate to have an opportunity to recruit a Canada Excellence Research Chair (CERC) that would add to the environment supporting Precision Cancer at the Vancouver Prostate Centre (VPC) that promises to revolutionize the way we discover novel anti-cancer drugs. Our scientists, and their collaborators across other UBC departments, have made world-leading discoveries in cancer genomics and biology, and expanded the repertoire of putative drug targets driving cancer treatment resistance that emerge as a function of clonal evolution. These novel targets are often not amendable to traditional drug screening, and there is an unmet need and unique opportunity for the CERC to rapidly resolve protein structure and link this to computer-assisted discovery of drug inhibitors.

Recent innovations at UBC in structural biology and cheminformatics, in particular those supported by Dr. Cherkasov's 2017 $24M CFI award, facilitate characterization of surface-exposed, protein-protein and protein-DNA interaction sites to enable computer-augmented drug design (CADD). The PCDD will integrate UBC's world-leading genomics, structural biology, translational cancer research and CADD expertise to accelerate discovery of cancer drugs and predictive biomarkers to more precisely treat specific subsets of patients with novel drivers of cancer treatment resistance. The PCDD will accelerate breakthroughs in understanding disease progression, discovery of new drugs to control treatment resistance and enhance translation of new drugs in early phase clinical trials across Canada, all key to nurture progress in precision oncology and growth in Canada's biotechnology sector.

Dr. Ryan Flannigan was recruited back to our departments as an Assistant Professor with the help of a prestigious Translational Medicine and Innovation award from the Faculty of Medicine. The Faculty of Medicine launched the call for proposals for a faculty renewal initiative in early 2018.

Department of UROLOGIC SCIENCES UBC

Department of Urologic Sciences

Faculty of Medicine

The Translational Medicine and Innovation Faculty Renewal in the area of translational medicine recruits interdisciplinary, highly collaborative researchers who have experience and interest in development of new educational programs.

Dr. Sriram Subramaniam, a global authority on cryo electron microscopy (EM), was recruited to Department of Urologic Sciences and the Department of Biochemistry and Molecular Biology as the Khorana Chair in Cancer Drug Design.

In addition to these major steps, even more of our other big highlights this year came from our people:

- Dr. Andrew MacNeily (Professor) is the President Elect for the Canadian Urological Association. He will take up the appointment officially from June 2019 - June 2020.
- Dr. Lynn Stothers (Professor) has been elected to UBC Senate for term 2017-2020.

New full - time academic appointments included:

- Ryan Flannigan – Assistant Professor
- Henry Tran – Assistant Professor
- Sriram Subramanaim – Professor

Clinical appointments were:

- Herman Kwan to Clinical Instructor
- Chris Zappavigna to Clinical Instructor

Clinical Promotions:

- Michael Eng – promotion to Clinical Assistant Professor
- Zeid Mohammedali – promotion to Clinical Assistant Professor

And while all of this was happening, we managed to have some fun as well! In June of 2018 our golf tournament raised more than $645,000, with a big thank you to Rod Senft and our partners at the UBC and VGH Foundation. Also, in June we held our departmental Research Day. Highlights included a keynote lecture from Dr. Robert Reiter, Bing Professor of Urology and Molecular Biology and Director of Prostate Cancer Treatment and Research Program at the David Geffen School of Medicine at UCLA. Endourology Fellow, Kymora Scotland, was recipient of the Best Clinical Paper presentation and Jake Noble, MSc student (supervisor Dr. Michael Cox) won the Basic Science Research Prize.

This year has been one of the record books. I am so proud to be leading this group of dedicated, talented scientists. And I am looking forward to another exceptional year.

Sincerely,

Martin Gleave, CM, MD, FRCSC, FACS

British Columbia Leadership Chair
Distinguished Professor and Head,
Department of Urologic Sciences, UBC
Director, Vancouver Prostate Centre

Highlights

Vancouver Prostate Centre and
Department of Urologic Sciences

24
New grants valued at over
$11.5M

$18M
A major philanthropic investment: Khorani Chair

$20M
Canada Excellence Research Chair (CERC) in Precision Cancer Drug Design (PCDD)

185
Peer-reviewed publications

>50
Filed or issued patents

4
New drug products and two biomarker assays

29	Full Time Faculty
55	Clinical Faculty
4	Research scientists
1	Part Time Faculty
18	Research Associate
3	Visiting Faculty
2	Adjunct Professors
4	Honourary Faculty
34	Postdoctoral Research Fellows
5	Clinical Fellows
49	Staff
43	Laboratory Assistants

This year we welcomed three exceptional new faculty members:

Dr. Ryan Flannigan completed his fellowship training in Male Reproduction, Microsurgery and Sexual Medicine at the world-renowned Weill Cornell Medicine and Memorial Sloan Kettering Center in New York, NY.

Clinically, Dr. Flannigan is specialized in male infertility and sexual medicine. Dr. Flannigan evaluates men with all presentations of infertility, manages men both medically and surgically. His research program is focused on evaluating genetic and molecular mechanisms contributing to non-obstructive azoospermia (NOA), using precision single-cell strategies and in vitro methods.

Beyond bench science, Dr. Flannigan is involved in numerous clinical trials and is actively involved in research related to preventative health and health promotion jointly with the Canadian Men's Health Foundation.

Dr. Henry Tran is a graduate from the UBC Urology Residency program in 2016. He was born and raised in Vancouver, BC and completed his undergraduate degree program in Computer Engineering from UBC. He currently practices urology at Providence Health Care at St. Paul's Hospital and Mount St. Joseph's Hospital in Vancouver.

He completed a fellowship in Female Pelvic Medicine, Dysfunctional Voiding and Reconstructive Urology at Columbia University Medical Center in New York in 2016-2017. He has research interests in technological applications in urology, and has presented at numerous Canadian and American conferences. He was awarded the Canadian Urology Association Pfizer Incontinence fellowship award in 2016. Dr. Tran's areas of interests include:

- treatment of male and female incontinence (slings, neurostimulation, Botox injections, artificial urinary sphincters)
- surgical management of pelvic floor disorders including pelvic organ prolapse (vaginal surgery, laparoscopic and robotic sacrocolpopexy)
- complex neurourology and videourodynamicsy

Dr. Sriram Subramaniam is a global authority on cryo electron microscopy (EM) and joins the UBC Faculty of Medicine as a Professor in the Department of Urologic Sciences and the Department of Biochemistry and Molecular Biology. Dr. Subramaniam also holds the Khorana Chair in Cancer Drug Design and is the Associate Director of Laboratory Research at the Vancouver Prostate Centre. Dr. Subramaniam's pioneering work in structural biology will play a key role in UBC's effort to harness the latest advances in imaging - particularly cryo-EM - to transform drug discovery in the treatment of cancer, neurological disorders and infectious diseases.

Dr. Subramaniam received his Ph.D. in Physical Chemistry from Stanford University and completed postdoctoral training in the Departments of Chemistry and Biology at the Massachusetts Institute of Technology with Nobel Laureate Har Gobind Khorana, who began his academic career at UBC. Before joining the National Cancer Institute, he was an Assistant Professor and Associate Professor at The Johns Hopkins School of Medicine, and a Visiting Member of the MRC Laboratory of Molecular Biology in the U.K., where he worked with Nobel Laureate Richard Henderson, one of the pioneers of cryo-EM. His publications have been cited over 6,400 times.

Our new clinical fellows this year were a talented and diverse group:

Dr. Phyllis Kisa was born and raised in Uganda (East Africa). She completed medical school at Makerere University, Kampala, Uganda. She then worked as an intern doctor and as a medical officer (general doctor) in the surgical department at St. Mary's Hospital in Lacor, Uganda. Phyllis had always intended to become a pediatrician, but along the way, her interest switched to surgery. She worked with several great surgeons during this time and they were a great support for her in the pursuit of this new path. She was always inclined towards pediatrics and reconstructive surgery of some kind.

Following this, Phyllis got her MMED in General surgery from Makerere University and soon after started a pediatric surgical fellowship with the College of Surgeons of East Central and Southern Africa (COSECSA). As part of this training, she spent 18 months (2014-mid-2015) at the BC Children's Hospital in general surgery and pediatric urology.

Phyllis returned home to Uganda where she has been working as a pediatric surgeon and urologist for the last three years. She has returned to the BC Children's Hospital as a pediatric urology fellow for more training after an initial six months back home in Uganda.

Dr. Simon Ouellet was born and raised in Rimouski, in the eastern part of Québec. He attended medical school at University of Sherbrooke, where he developed a strong interest in urology and research. Dr. Ouellet started his residency program in urology in Sherbrooke and completed his training at McGill University, in Montréal, where he also gained further research and clinical experience in urology oncology, convincing him to pursue a career in this subspecialty.

Dr. Ouellet is excited about the opportunity to be working with, and learning from, a great team at the Department of Urologic Sciences at UBC and the Vancouver Prostate Centre. Upon completion of his fellowship in uro-oncology, he will return home to Québec , but in the meantime, he is looking to make the most of this beautiful city of Vancouver.

Dr. Bhavish B. Kowlessur was born on the beautiful paradise Island of Mauritius where he also spent his formative years. He subsequently moved to South Africa where he started training in General Surgery at the University of Natal in Durban but soon developed a keen interest in Urology which led him to migrate to the University of Cape Town which is the premier training institution in the country to pursue his residency in Urology. During residency, he developed a particular interest in Urologic Oncology which led him to look for fellowship training positions in this subspeciality. The Department of Urologic Sciences at UBC is world renowned in this field and he is excited about the opportunity to be working with and learning from great mentors and world leaders.

New Residents:

Mark Dawidek was born and raised in London, Ontario, where he completed an undergraduate in electrical engineering and medical school at Western University. He was introduced to urology early during medical school and was initially captured by the technical aspect of the specialty. He is grateful to wonderful mentors at Western who further developed and encouraged my interest. He had an excellent experience during my elective at VGH and was impressed with the residents' proficiency and teamwork. He was thrilled to have matched here and am excited to begin my training and contribute to the team. When outside the hospital, he enjoy rowing, cycling, and hiking and am keen to explore the unparalleled British Columbia outdoors.

New Residents:

Cyrus Chehroudi was born and raised in Vancouver and did his undergraduate studies at UBC prior to moving to Ottawa for medical school. He gained a keen interest in Urology through shadowing and by getting involved in Pediatric Urology and Urologic Oncology research. He was drawn towards the wide variety of surgery Urologists perform and ability to use these different approaches to individualize patient care. Cyrus is beyond excited continue the next phase of his journey here in Vancouver with the opportunity to train alongside world experts and to give back to his community. Outside of work, he enjoy playing tennis, cooking, and is an amateur runner with the hopes of doing the Sun Run this year.

Davide Cina grew up in Toronto, and completed his undergraduate studies at McMaster University with an Honors Bachelor of Arts and Science in interdisciplinary studies. While he got the chance to try many different disciplines during this time he became really hooked on the kidney and kidney research, and decided to pursue an MD-PhD at the University of Toronto. There, under the supervision of Dr. Sue Quaggin he studied the genes that regulate how the kidney filtration system works . When Dr. Quaggin was recruited to Northwestern University in Chicago to chair their department of nephrology, he decided to follow her there to complete both my PhD work and the remainder of my MD.

While the kidney was his first love, during clerkship he was completely taken in by the excitement and pace of surgical specialties and Urology was the perfect way to bring both these interests together! Of course he wanted to come back home to Canada, and when it came time for choosing where to go, the program here at UBC seemed to be a perfect fit with a strong emphasis on excellent surgical training backed up by a world renowned research center. Outside of work he enjoys distance paddle board racing, hiking, making sourdough bread, brewing beer and of course going on adventures with his dog Finnegan! Davide is very excited to be here in Vancouver for the next stage of his training!

Feature Postdoctoral fellows/trainee:

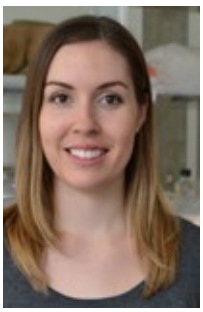
Alistair Davies grew up in Calgary, and completed his undergraduate degree in Biomedical Sciences at the University of Calgary. Through his summer research he developed a strong interest in stem cell biology and knew he wanted to pursue a career in research to unlock the potential of these enigmatic cells. So, he traded his winter jacket for yoga pants and moved to Vancouver to begin his PhD at the University of British Columbia studying how breast cancer cells hijack stem cell processes to evade targeted therapy. Now, as a post-doctoral fellow in the Zoubeidi lab at the Vancouver Prostate Centre, he has led the charge on understanding how prostate cancer cells "change their identity" to mask themselves from treatment. Alistair has had the honour to be selected as an AACR Scholar-in-Training and was invited to deliver a podium presentation at the AACR Annual Meeting in both 2017 and 2018, as well as the 2017 AACR Prostate Meeting. His forward-thinking research, which is supported by the Canadian Institutes of Health Research and a Prostate Cancer Foundation Young Investigator award, is leading to more and better weapons to outwit cancer and defeat it at last.

Outside of the lab, you will find Alistair exploring the many great restaurants and breweries that Vancouver has to offer. He is also an avid traveler with the goal of visiting every country in the world (only 155 more to go!).

Feature Postdoctoral fellows/trainee:

Morgan Roberts is a postdoctoral fellow in the labs of Drs. Peter Black and Mads Daugaard at the Vancouver Prostate Centre. She is originally from Montreal, Canada and completed her undergraduate degree in Microbiology and Immunology at McGill University. After spending a year in Seoul, South Korea teaching English to kindergarten students, she moved to Vancouver to purse a PhD in Microbiology and Immunology. During her PhD she investigated how regulating signalling thresholds in innate immune cells affects intestinal immune responses and host-microbiota interactions. As a graduate student, Morgan was awarded a CIHR Master's Award and a CIHR Training Program in Transplantation Award.

Looking to gain expertise in urologic oncology and industry experience, Morgan joined the Vancouver Prostate Centre in early 2016 as a Mitacs Elevate Fellow shared by Dr. Peter Black and iProgen Biotech. During this fellowship she investigated the efficacy of improved antibody-drug conjugates in models of bladder cancer. Her passion for immunology and basic science led her to change her research focus, and in July 2017 Morgan started a full-time academic position as a postdoctoral fellow in Dr. Black's lab, shared with Dr. Mads Daugaard. She now investigates mechanisms of immune evasion in muscle-invasive bladder cancer, through projects that include the characterization of immune cells in muscle-invasive bladder tumours by mass cytometry, and through a supporting role in immuno-oncology projects in both labs.



Gillian Vandekerkhove is a PhD student in Dr. Alexander Wyatt's laboratory at the Vancouver Prostate Centre. She was raised on Vancouver Island, where she completed my BSc in biology at the University of Victoria before attending the University of Toronto to study human evolutionary genetics during her MSc. Missing the West Coast, Gillian returned to BC after completion of her MSc and joined Dr. Wyatt's laboratory as a research assistant. Her role in the laboratory evolved as my interest in cancer genomics grew, providing a perfect transition into a PhD. Gillian applied to the Experimental Medicine program at UBC, and began as a PhD student in September 2017. Her research focuses on the genomics of advanced genitourinary cancers, and utilizing standard blood draws to profile patient's circulating tumor DNA. In May 2018, Gillian was awarded a CIHR Doctoral Research Award to continue her investigation of circulating tumor DNA as a predictive biomarker in metastatic bladder cancer. She has also been funded through a four year fellowship from UBC, a Vancouver Coastal Health Research Institute Rising Star Travel Award and a UBC Faculty of Medicine Graduate Award.

Funding and Awards

Martin Gleave

Order of Canada,
Faculty of Medicine;

Martin Gleave

Dr. Chew Wei Memorial Prize in Cancer Research;

Martin Gleave

Huggins Medal from the Society of Urologic Oncology

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MSFHR Innovation to Commercialization

Chris Ong

MSFHR Innovation to Commercialization

Her Excellency the Right Honourable Julie Payette, Governor General of Canada, invested Dr. Martin Gleave as a Member of the Order of Canada on Thursday, September 6, 2018, at Rideau Hall.

Elspeth McDougall

Endourological Society Karl Storz Life Time Achievement award

Ben Chew

Endo Society: Industry award for Innovations in Endourological Instrumentation

Peter Black

MSFHR Health Professional Investigator award

Peter Black

European Urology – Platinum award for excellence in peer review

Amina Zoubeidi

FoM Distinguished Achievement Award – Excellence in Basic Science

Ryan Flannigan

VCHRI Mentored Clinician Scientist award

Ryan Flannigan

Canadian Urological Association SF award

Alex Kavanagh

Canadian Urological Association SF award (renewal)

Larry Goldenberg

Long Service Award (25 years)
Vancouver Coastal Health

Mads Dauguard and Dirk Lange

MSFHR Innovation to Commercialization Award

Of 185 publication this year the following were very noteworthy:

Genomics and Treatment Resistance

Wyatt AW, Annala M, Aggarwal R, Beja K, Feng F, Youngren J, Foye A, Lloyd P, Nykter M, Beer TM, Alumkal JJ, Thomas GV, Reiter RE, Rettig MB, Evans CP, Gao AC, Chi KN, Small EJ, Gleave ME. Concordance of Circulating Tumor DNA and Matched Metastatic Tissue Biopsy in Prostate Cancer. J Natl Cancer Inst. 2017 Dec 1;109(12). doi:10.1093/jnci/djx118. PMID: 29206995 *IF: 13.525*

Quigley DA, Dang HX, Zhao SG, Lloyd P, Aggarwal R, Alumkal JJ, Foye A, Kothari V, Perry MD, Bailey AM, Playdle D, Barnard TJ, Zhang L, Zhang J, Youngren JF, Cieslik MP, Parolia A, Beer TM, Thomas G, Chi KN, Gleave M, Lack NA, Zoubeidi A, Reiter RE, Rettig MB, Witte O, Ryan CJ, Fong L, Kim W, Friedlander T, Chou J, Li H, Das R, Li H, Moussavi-Baygi R, Goodarzi H, Gilbert LA, Lara PN Jr, Evans CP, Goldstein TC, Stuart JM, Tomlins SA, Spratt DE, Cheetham RK, Cheng DT, Farh K, Gehring JS, Hakenberg J, Liao A, Febbo PG, Shon J, Sickler B, Batzoglou S, Knudsen KE, He HH, Huang J, Wyatt AW, Dehm SM, Ashworth A, Chinnaiyan AM, Maher CA, Small EJ, Feng FY. Genomic Hallmarks and Structural Variation in Metastatic Prostate Cancer. Cell. 2018 Oct 18;175(3):889. doi: 10.1016/j.cell.2018.10.019.

Seiler R, Ashab HA, Erho N, Van Rhijn BW, Winters B, Douglas J, Van Kessel KE, Fransen Van De Putte EE, Sommerlad M, Wang NQ, Choeurng V, Gibb EA, Palmer-Aronsten B, Lam LL, Buerki C, Davicioni E, Sjödahl G, Kardos J, Hoadley KA, Lerner SP, Mcconkey DJ, Choi W, Kim WY, Kiss B, Thalmann GN, Todenhöfer T, Crabb SJ, North S, Zwarthoff EC, Boormans JL, Wright J, Dall'era M, Van Der Heijden MS, Black PC. Impact of molecular subtypes in bladder cancer on outcome and response to neoadjuvant chemotherapy. *Eur Urol.* 2017 Oct;72(4):544-554. doi: 10.1016/j.eururo.2017.03.030. Epub 2017 Apr 5.2017 Apr 5. PMID: 28390739. *IF: 16.265*

Aggarwal R, Huang J, Alumkal JJ, Zhang L, Feng FY, Thomas GV, Weinstein AS, Friedl V, Zhang C, Witte ON, Lloyd P, Gleave M, Evans CP, Youngren J, Beer TM, Rettig M, Wong CK, True L, Foye A, Playdle D, Ryan CJ, Lara P, Chi KN, Uzunangelov V, Sokolov A, Newton Y, Beltran H, Demichelis F, Rubin MA, Stuart JM, Small EJ. Clinical and Genomic Characterization of Treatment-Emergent Small-Cell Neuroendocrine Prostate Cancer: A Multi-institutional Prospective Study. J Clin Oncol. 2018 Aug 20;36(24):2492-2503. doi: 10.1200/JCO.2017.77.6880. Epub 2018 Jul 9.

The long noncoding RNA landscape of neuroendocrine prostate cancer and its clinical implications. Ramnarine VR, Alshalalfa M, Mo F, Nabavi N, Erho N, Takhar M, Shukin R, Brahmbhatt S, Gawronski A, Kobelev M, Nouri M, Lin D, Tsai H, Lotan TL, Karnes RJ, Rubin MA, Zoubeidi A, Gleave ME, Sahinalp C, Wyatt AW, Volik SV, Beltran H, Davicioni E, Wang Y, Collins CC. Gigascience. 2018 Jun 1;7(6). doi: 10.1093/gigascience/giy050. PMID:29757368

Bishop JL, Thaper D, Vahid S, Davies A, Ketola K, Kuruma H, Jama R, Nip KM, Angeles A, Johnson F, Wyatt AW, Fazli L, Gleave ME, Lin D, Rubin MA, Collins CC, Wang Y, Beltran H, Zoubeidi A. The Master Neural Transcription Factor BRN2 is an Androgen Receptor Suppressed Driver of Neuroendocrine Differentiation in Prostate Cancer. Cancer Discov. 2017 Jan; 7(1):54-71. doi: 10.1158/2159-8290.CD-15-1263 pii: CD-15-1263. PMID: 27784708 *IF: 19.78*

Ci X, Hao J, Dong X, Choi SY, Xue H, Wu R, Qu S, Gout PW, Zhang F, Haegert AM, Fazli L, Crea F, Ong CJ, Zoubeidi A, He HH, Gleave ME, Collins CC, Lin D, Wang Y. Heterochromatin Protein 1a Mediates Development and Aggressiveness of Neuroendocrine Prostate Cancer. Cancer Res. 2018 May 15;78(10):2691-2704. doi: 10.1158/0008-5472.CAN-17-3677. Epub 2018 Feb 27. PMID: 29487201

Drug Development

SEMA3C drives cancer growth by transactivating multiple receptor tyrosine kinases via Plexin B1. Peacock JW, Takeuchi A, Hayashi N, Liu L, Tam KJ, Al Nakouzi N, Khazamipour N, Tombe T, Dejima T, Lee KC, Shiota M, Thaper D, Lee WC, Hui DH, Kuruma H, Ivanova L, Yenki P, Jiao IZ, Khosravi S, Mui AL, Fazli L, Zoubeidi A, Daugaard M, Gleave ME, Ong CJ. EMBO Mol Med. 2018 Feb;10(2):219-238. doi: 10.15252/emmm.201707689.

Discovery and characterization of small molecules targeting the DNA-binding ETS domain of ERG in prostate cancer. Butler MS, Roshan-Moniri M, Hsing M, Lau D, Kim A, Yen P, Mroczek M, Nouri M, Lien S, Axerio-Cilies P, Dalal K, Yau C, Ghaidi F, Guo Y, Yamazaki T, Lawn S, Gleave ME, Gregory-Evans CY, McIntosh LP, Cox ME, Rennie PS, Cherkasov A. Oncotarget. 2017 Jun 27;8(26):42438-42454. doi: 10.18632/oncotarget.17124.

Choi SYC, Ettinger SL, Lin D, Xue H, Ci X, Nabavi N, Bell RH, Mo F, Gout PW, Fleshner NE, Gleave ME, Collins CC, Wang Y. Targeting MCT4 to reduce lactic acid secretion and glycolysis for treatment of neuroendocrine prostate cancer. Cancer Med. 2018 Jun 14. doi: 10.1002/cam4.1587.

Carabet LA, Lallous N, Leblanc E, Ban F, Morin H, Lawn S, Ghaidi F, Lee J, Mills IG, Gleave ME, Rennie PS, Cherkasov A. Computer-aided drug discovery of Myc-Max inhibitors as potential therapeutics for prostate cancer. Eur J Med Chem. 2018 Dec 5;160:108-119. doi: 10.1016/j.ejmech.2018.09.023. Epub 2018 Sep 11.PMID: 30326371

A randomized phase 2 study of a HSP27 targeting antisense, apatorsen with prednisone versus prednisone alone, in patients with metastatic castration resistant prostate cancer. Yu EY, Ellard SL, Hotte SJ, Gingerich JR, Joshua AM, Gleave ME, Chi KN. Invest New Drugs. 2018 Apr;36(2):278-287.

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