

2021

BC CANCER **RESEARCH** REPORT



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Table of contents

Message from the Senior Executive Director of Research, Dr. François Bénard	3
Message from BC Cancer Foundation President & CEO, Sarah Roth	4
Fast Facts	5
Awards & Funding	6
Advancements & opportunities in radiation oncology & research	11
Nursing & allied health research	20
PREDiCT Initiative begins in B.C., & is shared nationally	24
CLIC-01 Clinical Trial: Building BC Cancer’s capabilities in cutting-edge immunotherapy, genetic engineering & clinical trials	26
Celebrating the extraordinary achievements of Dr. Connie Eaves	28
Dr. Kim Chi: Improving outcomes for patients with prostate cancer in B.C. & beyond	30
New Hire Feature: Dr. Adi Steif tackles big data to better understand how cancer evolves	32
New Hire Feature: Dr. Leandro Venturutti examines B-cell lymphoma with his A-team	34
The growing importance of hereditary cancer research	36
BC Cancer melanoma immunotherapy database aims to better understand outcomes for older adults	38
Improving prostate cancer treatments	39
Clinical research & clinical trials	40

Message from the Senior Executive Director of Research, Dr. François Bénard



2021 has been a year of adaptation and adjustment. As researchers we continued to conduct our important work amidst a global pandemic and climate emergencies within the province. This has been another heavy year as British Columbians, but cancer does not stop in the wake of viruses, heat domes, and atmospheric rivers – and neither do we.

In the face of continued adversity, teams at the BC Cancer Research Institute continued to live up to our reputation as an international leader in research excellence. Our clinicians, nurses, researchers, administrators, leaders and trainees all stepped up and went above and beyond, facing challenges that no one could have predicted. As we continue to navigate the repercussions of these events, there is also time to reflect on the successes of the year and incredible achievements we’ve made to deliver a positive impact for people affected by cancer.

This year began with the launch of the Nursing and Allied Health Research and Knowledge Translation research. A first of its kind in Canada, this move cast a bold vision for BC Cancer to evolve into a vibrant, world-class leader in research across the interdisciplinary spectrum. Today, the nursing and allied health research community is more diverse than ever before, with scientific expertise across all areas of health research – from clinical research to research on health services, health and healthcare equity, and population and public health.

This year also brought incredible generosity with the world’s largest philanthropic gift to advance lung cancer research and care. The \$15.3 million dollars provided by our partners at the BC Cancer Foundation, their donors, and the Leon Judah Blackmore Foundation positions BC Cancer at the global forefront of innovation. In June, the Government of Canada and the Terry Fox Research Institute jointly signed a Contribution Agreement which opened the door for the Marathon of Hope Cancer Centres Network (MOHCCN) to begin operating. The MOHCCN brings together our national cancer centres to focus collective effort towards new precision medicine strategies for patients utilizing genomic approaches applied for our unique population here in Canada. This will mean sequencing and comprehensive genomic profiling for over 15,000 Canadians across the country in the next few years.

I’d also like to acknowledge and congratulate the researchers and trainees who continue to publish their work in the world’s most prestigious journals and receive a remarkable number of awards, acknowledgement and grants.

While there is still much work to do, what sets BC Cancer apart is our strong sense of community and a common purpose, the spirit of collaboration and our ability to come together in the face of uncertainty and press forward to achieving our vision of a world free of cancer.

Dr. François Bénard
Senior Executive Director
Research

Message from BC Cancer Foundation President & CEO, Sarah Roth



In 2021, BC Cancer Foundation donors continued to uphold our deeply shared belief that there are truly no limits to what the BC Cancer Research Institute can accomplish.

Our Foundation channeled this unabated support by funding a variety of research at BC Cancer. We were proud to help BC Cancer Clinical Fellow Louise Wade advance world-class radiation oncology for breast cancer. While also supporting radiation oncology innovation through research grants, the Dr. Peter Poon Memorial Research Awards and the Adolescent and Young Adult Clinical Research Program.

We continued to bolster the Rising Stars program, an initiative to inspire BC Cancer's women and BIPOC leaders of tomorrow, and invested \$2 million in a research sustaining grant to support programs at risk of funding gaps.

Inspired by their own cancer journeys, several Foundation donors commanded their own campaigns – not for their own personal gain, but to improve treatment for those who follow in their footsteps.

Our former Board Chair, Jess Ketchum, is zealously fundraising for head and neck cancer research, after his own squamous cell carcinoma diagnosis left him with many unanswered questions surrounding human papillomavirus (HPV)-based cancers.

He, and his wife Ramona, donated \$100,000, and have successfully raised more than \$450,000, towards a new study, Personalized Approaches in the Treatment of Head and Neck Cancers (PATH).

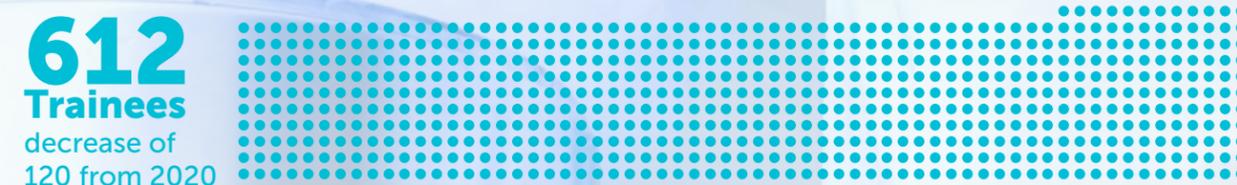
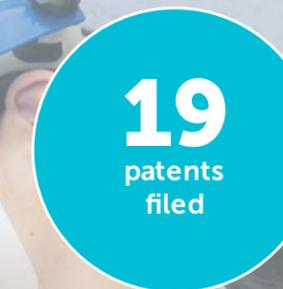
Similarly, Allan Collings and Hilary Stevens are proud to have their names on the door of Dr. Xiaoyan Jiang's lab, now known as the Collings Stevens Chronic Leukemia Research Laboratory, in recognition of their \$1 million gift to support research into chronic myeloid leukemia (CML).

Allen is in remission, thanks to a drug that was also in its own clinical trials not that long ago, and is excited to support the next big breakthrough in blood cancers that may well come out of Dr. Jiang's lab.

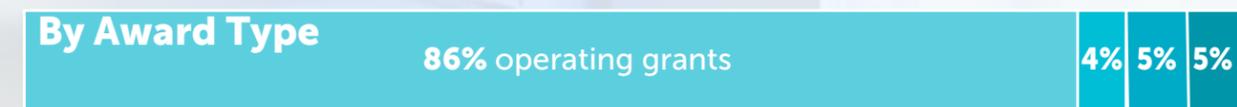
And no one has exemplified more confidence in BC Cancer's ability to advance science than the late Leon Judah Blackmore. We honoured his Foundation's decades-long relationship with BC Cancer, and incredible \$18.9 million gift, by naming the BC Cancer Research Centre after him in September.

As one grateful patient put it, "Now every person undergoing treatment at BC Cancer – Vancouver will look out their window at the L.J. Blackmore Cancer Research Centre, and not just dream of miracles, but know that inside its walls someone is working tirelessly to make them a reality."

Sarah Roth
President & CEO
BC Cancer Foundation



Funding: Total Grants Awarded: \$66 million



salary awards
infrastructure awards
other

January

Dr. Cheryl Duzenli from the Medical Physics department along with co-applicant **Dr. Robin Coope** from Canada's Michael Smith Genome Science Centre at BC Cancer (GSC) was awarded a Michael Smith Foundation for Health Research (MSFHR) Innovation to Commercialization (I2C) Grant. Dr. Duzenli and her team at BC Cancer have developed a novel device that reduces side effects and improves quality of life for breast cancer patients undergoing radiation therapy. Using advanced carbon-fibre technology, the device provides breast support that can reduce excess radiation to lung, heart, body, and skin without interfering with planned treatment. This grant will enable the team to refine the device design and manufacturing process. The award amount is \$297,249 for 2-years.



CIHR Fall 2020 Competition Results

- **Dr. Rob Holt;** co-investigators **François B nard,** **Kevin Hay,** and **Wyeth Wasserman**
Title: Lentiviral infusion as a universal approach for genetically modified immune effector cell therapies \$642,600 (4-years)
 - **Dr. Christian Steidl;** co-investigator **Shannon Healy**
Title: Somatic mutations in the JAK-STAT and IRF signalling pathways in Non-Hodgkin lymphoma \$1,120,725 (5-years)
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February

Dr. Leah Lambert from the Nursing and Allied Health Research and Knowledge Translation department was awarded funding from the Michael Smith Health Research BC Convening and Collaboration (C2) program, for the project titled "Planning to Enhance Capacity for Equity-Oriented Cancer Care in BC". The award amount is \$15,000 for 1-year.



April

Dr. Poul Sorensen and the Pediatric Cancer Dream Team were awarded the 2021 AACR Team Science award. The AACR Team Science Award acknowledges and catalyzes the growing importance of interdisciplinary teams to the understanding of cancer and the translation of research discoveries into clinical cancer applications. The Pediatric Cancer Dream Team has made incredible advancements in pediatric cancer research by developing new targeted therapies and establishing clinical trials, which offer hope to thousands of children and their families.



Dr. Kevin Hay was awarded an International Myeloma Society (IMS) and Paula and Rodger Riney Foundation Translational Research Grant for his project titled "Chimeric antigen receptor T cells secreting IL-12 and anti-IL-6 to enhance responses in multiple myeloma". The award amount is \$250,000 USD for 1-year.



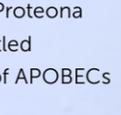
Dr. Michelle Hiltz was awarded an NSERC Discovery Grant for her project titled "The development of advanced imaging and dosimetry for permanent breast seed implant radiation therapy". The award is \$205,000 for 5-years.



Dr. Florian Kuchenbauer was awarded an International Myeloma Society (IMS) and Paula and Rodger Riney Foundation Translational Research Grant for the project titled "Exploring APOBECs as therapeutic vulnerabilities in Multiple Myeloma". The total award amount is \$220,174 USD for 1-year.



Dr. Florian Kuchenbauer was also awarded a Proteona Single Cell Multi-omics grant for the project titled "Towards a deeper understanding of the role of APOBECs in Multiple Myeloma". The award is \$50,000 USD for 1-year.



May

Canada Foundation for Innovation (CFI)

Dr. Sam Aparicio and his team were awarded CFI funding for their proposal "Cancer Single Cell Dynamic Observatory".



The project will build the Cancer Single Cell Dynamics Observatory which will innovate new single cell measurement approaches, support development and integration of patient derived tumour model systems, and define the molecular basis of drug resistance and metastasis. The observatory will benefit Canadians by providing cancer patients with improved diagnostics and therapeutic options.

The total award amount is \$5,992,026 and the funding dates are from April 1, 2021 to September 30, 2023.

Team members for the CFI application included **Drs. Alexandre Bouchard-C t ,** **Karen Cheung,** **Connie Eaves,** **David Huntsman,** **Peter Lansdorf,** **Megan Levings,** **Marco Marra,** **Josef Penninger,** and **Christian Steidl.**

Dr. Steve Jones and his team were awarded CFI funding for their proposal "CGEn – A National Platform for Genome Sequencing and Analysis"



CGEn, Canada's national platform for genome sequencing and analysis, leads the country's COVID-19 host genome sequencing initiative, which includes sequencing the genome of 10,000 Canadians to understand how the body responds to COVID-19.

Dr. Peter Stirling was awarded grant funding from the France Canada Research Fund for the project titled "Developing splice-switching oligonucleotides to rewire splicing SF3B1-mutated myelodysplastic syndromes". The award amount is \$15,000 for 2-years.



July

Dr. Sam Aparicio was awarded grant funding from Wellcome Leap Delta Tissue competition with primary applicants **Gregory Hannon** (Cambridge), **Jean Abraham** (Cambridge), and **John Marioni** (European Bioinformatics Institute) for their project titled "Predicting treatment induced state changes in triple-negative breast cancer". The total award amount for all investigators is \$4,926,445 (USD) with Dr. Aparicio receiving \$462,888 USD for 3-years.

August

Dr. Poul Sorensen was awarded the Order of British Columbia. The Order of British Columbia recognizes individuals who have served with the greatest distinction and excelled in any field of endeavour benefiting the people of British Columbia and beyond. The Order represents the highest form of recognition the Province can extend to its citizens.

Dr. Poul Sorensen also received funds from Circle of Hope. **Alex Blodgett** raised \$1.4 million for the Sorensen Lab, in a self-supported, multi-sport expedition consisting of hiking, mountain biking, mountain climbing and ocean rowing along B.C.'s coast – the Circle of Hope. The objective was to support research evaluating the efficacy of utilizing highly-targeted immune-based treatment for the most aggressive childhood cancers.

CIHR Spring Competition Results

- **Dr. Marcel Bally;** co-investigator **Dr. Dan Renouf** Title: A Novel formulation of the anticancer drug candidate CX5461 that relies on metal chemistry and liposomal nanotechnology: development for use in treatment of pancreatic cancers with BRCA deficiencies; an orphan indication \$765,000 (5-years)
 - **Dr. Kevin Bennewith;** co-investigator **Dr. Pascal Bernatchez** Title: Targeting cancer-associated fibroblasts and tumour hypoxia with angiotensin II receptor blockers \$979,200 (5-years)
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- **Dr. Will Lockwood;** co-investigators **Artem Cherkasov, Gregg Morin, and Kelsie Thu**
Title: Understanding the effects of ERK hyperactivation in cancer: implications for therapy \$956,250 (5-years)



- **Dr. Jonathan Loree** and **Christopher O'Callaghan** Circulating tumour DNA analysis informing adjuvant chemotherapy in Stage III colorectal cancer: a multicentre Phase II/III randomised controlled trial (DYNAMIC-III) \$1,426,724 (6-years)



- **Dr. Calum MacAulay;** co-investigators **Stephen Lam, Pierre Lane, and Renelle Myers**
Title: Devices for image-guided biopsy of peripheral lung nodules \$386,326 (3-years)



- **Dr. Andrew Minchinton**
Title: FLASH radiotherapy - mechanisms and translational studies \$918,000 (4-years)



- **Dr. Yemin Wang;** co-investigators **David Huntsman, Ramon Klein Geltink, and Gregg Morin**
Title: Exploit the metabolic vulnerabilities in SWI/SNF-deficient cancer \$688,501 (4-years)



- **Dr. Haishan Zeng and Dr. Catherine Poh**
Title: Autofluorescence Imaging Guided Laser Raman Spectroscopy for Non-invasive Oral Cancer Detection \$742,051 (4-years)



- **Dr. Alexander Wyatt;** co-investigators **Drs. Kim Chi and Piet Ost**
Genomic dissection of de novo metastatic prostate cancer prior to treatment \$734,400 (3-years)



Dr. Kevin Hay was awarded the Cell Therapy and Transplant Canada Hans Messner New Investigator Award for the project "Cell-free DNA: A new biomarker in CAR-T cell therapy". The award amount is \$40,000.

September

Cancer Research Society Operating Grants

Dr. Pamela Hoodless was awarded a Cancer Research Society operating grant for the project titled "Defining epigenetic alterations in liver cancer at single cell resolution". The award amount is \$120,000 for 2-years.



Gerald Krystal was awarded a grant from the Lotte & John Hecht Memorial Foundation for the project titled "Optimizing Diets during Cancer Treatment". The award amount is \$961,130 for 3-years.



Dr. Shoukat Dedhar with co-applicant **Dr. Brett Finlay** (UBC) was awarded a Cancer Research Society Operating Grant in partnership with the Canadian Institutes of Health Research - Institute of Cancer Research for the project titled "The Role of Microbiota and Immune Microenvironment in Breast Cancer Metastasis". The award amount is \$120,000 for 2 years.



Dr. Rachel Murphy was awarded a catalyst grant from the Weston Family Foundation with **Drs. Julian Lum** (BC Cancer - Victoria), **Parveen Bhatti** (CCR, BC Cancer), **Kristin Campbell** (UBC), **Jane Shearer** (University of Calgary), **Kathryn Isaac** (UBC), and **Amea Manges** (UBC and BCCDC). The award amount is for \$450,000 over 3-years, and will allow the team to study the role of the gut microbiome in the development of breast cancer.



Dr. Parveen Bhatti along with co-investigators **Drs. Rachel Murphy, Andrew Roth, and Caroline Lohrisch** received a grant from the Cancer Research Society to identify metabolomic markers to target prevention of postmenopausal breast cancer. The award amount is \$120,000 for 2-years.



Dr. Bhatti was invited to become a member of the Institute Advisory Board (IAB) for CIHR's Institute of Cancer Research (ICR). CIHR's ICR IAB advises the ICR Scientific Director on institute activities and initiatives, including setting of health research priorities. An invitation to join recognizes one's outstanding contributions to cancer research.

Dr. Poul Sorensen was awarded two NIH U54 supplement grants, the first with **Dr. Laslo Radvanyi** (Ontario Institute for Cancer Research) and **Dr. Mitchell Cairo** (New York Medical College), and the second with **Timothy Cripe** (Nationwide Children's Hospital). The total amount of the first grant was \$150,000 USD, with \$81,000 USD to BC Cancer, and the total amount of the second grant was \$150,000 USD, with \$73,440 USD to BC Cancer.

October

Dr. Andrew Roth was awarded a V scholar award from the V Science Foundation for his project titled "Predicting Follicular Lymphoma Transformation from Tumour Architecture". The award is \$200,000 for 2-years.



November

The **BASIC (BC Cancer Research Histology and Digital Imaging Core) Lab** was established in late 2020 to serve the need of the BCCRC research community for core research/translational pathology services. It became fully operationalized in 2021. The background and expertise of its directors, **Drs. David Scott, Calum MacAulay, and Stephen Yip** also highlights the collaborative nature of its mission, working with existing resources and personnel. The lab also serves as the processing hub for pathology

specimens of the Personalized OncoGenomics (POG) and Marathon of Hope (MOH) programs. The BASIC lab will undergo DAP clinical certification which will make POG/MOH a fully clinically-accredited pipeline.

Clarivate Highly Cited Researchers Announced

Dr. Marco Marra was once again listed as one of the most highly cited researchers by Clarivate, an annual list he has been on since 2014.



Dr. Amal EL-Naggar with co-investigators **Drs. David Huntsman and Poul Sorensen** were awarded an Ovarian Cancer Canada-Cancer Research Society grant for their project titled "CTH in clear cell ovarian cancer: a targetable legacy of endometriotic origins". The award amount is \$225,000 for 2-years.



Drs. Yemin Wang and Sidong Huang (McGill) with co-investigators **Drs. David Huntsman and William Foulkes** were awarded an Ovarian Cancer Canada-Cancer Research Society grant for their project titled "Developing optimal treatment combinations for small cell carcinoma of the ovary". The award amount is \$225,000 for 2-years.

Dr. Peter Stirling with co-investigators **Drs. David Huntsman, Philip Hieter** (UBC), and **Jean-Yve Masson** (Laval University) was awarded an Ovarian Cancer Canada and Cancer Research Society Strategic Partnership Grant for the project titled "Next generation DNA repair inhibitors for ovarian cancer treatment". The award amount is \$225,000 for 2-years.

Dr. Rasika Rajapakshe, a senior medical physicist at BC Cancer - Kelowna, was awarded a research contract grant for the project "Federated Learning of AI Algorithm for Breast Cancer Detection". The total award duration is 42-months and \$235,242 through a master service project agreement with Kheiron Medical Technologies Inc.



Dr. Florian Kuchenbauer received a BC Cancer Excellence Award Patient Care Champion (Patient nominated). Dr. Kuchenbauer's clinical and research work at BC Cancer focuses on acute myeloid leukemia and multiple myeloma. He is highly respected by patients, colleagues as well as students and was also nominated for the Workplace Inspiration Award. A Patient Care Champion is a physician or staff member who helps improve patients' experience, quality of life, quality of care and/or knowledge of the cancer system - either directly or indirectly. They show compassion, ingenuity and leadership, and act as a role model for others.

December

Dr. Sam Aparicio was awarded a further 5-years for UBC's Distinguished University Scholar competition. The total award amount is \$100,000.

Dr. Ly Vu received a Terry Fox Research Institute New Investigator Award for her project titled "Uncovering the role of long noncoding RNAs in myeloid leukemia stem cells". The award amount is \$450,000 over 3-years.



Dr. Florian Kuchenbauer received a Michael Smith Health Research BC Health Professional-Investigator Award for the project titled "Exploring oxidative phosphorylation as therapeutic vulnerability in high-risk acute myeloid leukemia". The total award amount is \$450,000 for 4-years.

Dr. Stuart Peacock as part of an international team, received a grant from the European Organisation for Research and Treatment of Cancer (EORTC) to develop a new quality of life measure for Adolescents and Young Adults (AYAs) who are diagnosed with cancer, since AYAs have unique psychosocial needs and outcomes. The grant is for 2021-24 and the amount is 172,187 EUR.



Trainee Awards

April

Dr. Maryam Soleimani in the department of Medical Oncology received a Canada Graduate Scholarships-Master's (CGS M) award from the Canadian Institute of Health Research (CIHR). Dr. Soleimani's work focuses on the development of biomarkers to predict response to immunotherapy in renal cell carcinoma.



June

Amber Bourgeois received a \$50,000 CIHR Health Systems Impact Doctoral Fellowship. Amber is supervised by Dr. Leah Lambert.



November

Eleah Stringer from the department of Oncology Nutrition at BC Cancer - Victoria was awarded a 5-month Patient-Oriented Research Graduate Fellowship to support her thesis research titled "Utility of Electronic Decision Support Tools for Patients with Head and Neck Cancer"



Advancements & opportunities in radiation oncology & research

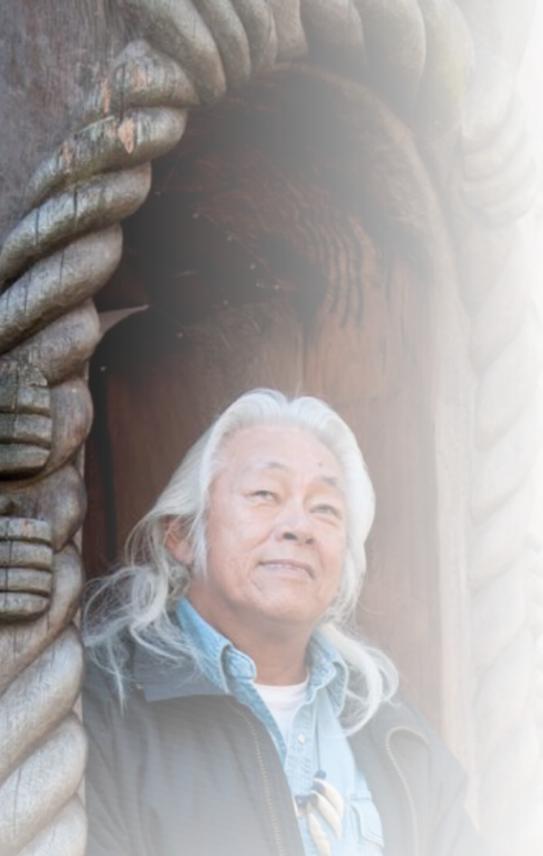
Approximately half of patients with cancer will receive radiation therapy as part of their treatment. The goal of radiation therapy is to give enough radiation to destroy the cancer cells in your body, but not enough that your normal cells cannot recover.

It works by destroying cells in the treatment area either by eradicating the cell directly or by damaging the cell's DNA so that it cannot grow anymore. Cancer cells are more sensitive to radiation than normal cells

but it is challenging to destroy cancer cells without damaging some normal cells, which is what can cause side effects.

Researchers, clinicians, physicists and trainees within the radiation program at BC Cancer have been making significant advancements in the field of radiation oncology research. Their innovation will only serve to further improve patient outcomes and lead to better techniques and technology in this field.





Small towns can have big impacts

A common misconception is that advanced research requires massive infrastructure in an urban or metropolitan core. At BC Cancer, research is conducted across the six regional centres and the L.J. Blackmore Cancer Research Centre in downtown Vancouver. Although one of the smallest centres, BC Cancer – Prince George is making a huge impact.

Dr. Rob Olson, radiation oncologist and research lead at BC Cancer – Prince George, has been leading international clinical trials on precision radiotherapy for metastatic cancer (cancer that has spread throughout the body).

“I have been honoured to lead clinical trials that showed high doses of precise radiotherapy, termed SABR, was able to improve survival outcomes for patients with metastatic cancer,” said Dr. Olson. “Moreover, this year I was able to present our latest SABR clinical trial results which demonstrated low long-term rates of serious toxicity with several safety measures in place.”



SABR technology is a highly precise form of radiotherapy where much higher doses of radiation are delivered to tumours over a shorter time period. The technology features advanced machines with built in CT scans that can sculpt the dose of radiation to tumours from multiple angles while reducing the dose to healthy normal nearby tissue. This both increases cure rates, while reducing the risk of side effects.

This work is being spearheaded in Prince George to the benefit of all British Columbians, including those in smaller northwest or southeast communities. In 2021, Dr. Olson developed a method of supporting patients participating in SABR clinical trials living in rural and remote areas around Terrace or Trail to connect with physicians closer to home for their follow-up care. This was the first clinical trial in B.C. to not require patients to travel to larger regional centres for follow-up care and high quality toxicity measurement.

“New researchers who prefer a lifestyle outside of an urban core can be well supported at BC Cancer.

World-class clinical trials can be led from anywhere in B.C. In fact, they can even be led from our smallest cancer centres, like Prince George.” The interconnectedness of the six BC Cancer regional centres is an asset.

Dr. Olson’s next areas of focus are to determine if SABR can have benefit to all cancer types, if it can be safely administered in one treatment rather than over one to two weeks, and if it can be combined with immunotherapy to increase efficacy.

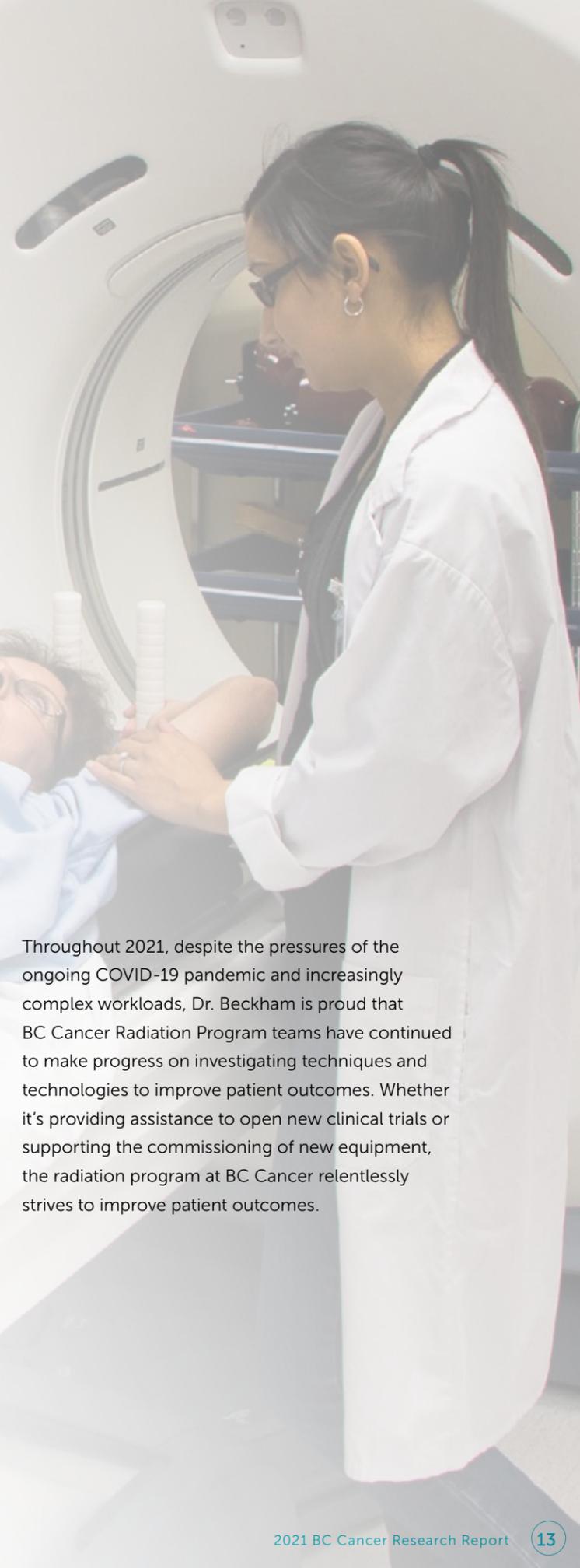
Providing support to students to facilitate learning and innovation

Ensuring that team members of the BC Cancer Radiation Program are set up for success is a core component of Dr. Wayne Beckham’s work. As the provincial professional practice leader for BC Cancer medical physics and the regional professional practice leader in medical physics at BC Cancer – Victoria, Dr. Beckham works to facilitate innovation from students and trainees to front-line health care providers.

“Most of our team members are primarily involved in clinical care delivery and new technique development,” says Dr. Beckham. “This enables BC Cancer to offer leading edge radiotherapy treatments to patients in B.C. Having caregivers involved in research that probes the efficacy of our treatment techniques and technologies makes for more informed clinical practice and can contribute to better patient care.”

Dr. Beckham supports students who are developing novel ways to use gold nanoparticles linked to tumour targeting molecules to potentially improve cancer treatment strategies. Dr. Beckham helps students design and execute experiments that involve irradiating cell systems using radiation machines at BC Cancer.

“As a provincial cancer care program, BC Cancer has a rich and comprehensive resource of centralized data. Our coordinated approach to cancer care for the entire province is truly rare in a global context and this environment provides great opportunities for population-level research and the ability to study the impacts of our cancer management strategies on the whole province.”



Throughout 2021, despite the pressures of the ongoing COVID-19 pandemic and increasingly complex workloads, Dr. Beckham is proud that BC Cancer Radiation Program teams have continued to make progress on investigating techniques and technologies to improve patient outcomes. Whether it’s providing assistance to open new clinical trials or supporting the commissioning of new equipment, the radiation program at BC Cancer relentlessly strives to improve patient outcomes.

Dr. Andrew Minchinton: radiation biology research

About half of all cancer patients receive radiation therapy as part of their treatment. Although significant improvements have been made to imaging technology and precision of radiation delivery, there are still no drugs available that specifically increase the cancer killing activity of radiation therapy. That's where Dr. Andrew Minchinton's Lab comes in.

A world leader in the field of radiation biology research, Dr. Minchinton's research focuses on the tumour microenvironments and how it can be exploited to improve treatment. For approximately seven years, Dr. Minchinton and team have been

developing a hypoxia-activated inhibitor of radiation-induced DNA damage, which would selectively increase the radiosensitivity of tumours without side effects to healthy tissue.

"Since the beginning of my career, there has been significant progress in understanding how radiotherapy-induced DNA damage can be repaired by cellular machinery," says Dr. Minchinton. "There are many excellent targets within the DNA repair pathways that could be exploited but currently only a few are being pursued in combination with radiotherapy, and those have little specificity for cancer tissue."

One target that is being pursued in the Minchinton Laboratory is an inhibitor of the DNA-PK, a key enzyme that repairs double stranded breaks in DNA, the most lethal effect of radiotherapy. Cells and tissues that lack DNA-PK are hypersensitive to radiotherapy. However, a systemic inhibitor of DNA-PK would increase the radiosensitivity of 'normal' as well as cancer cells. So Dr. Minchinton, in collaboration with Drs. Alastair Kyle and Jennifer Baker, are developing a DNA-PK inhibitor that only acts in cancers by harnessing a hypoxic-trigger mechanism.

This mechanism is the ideal target for this treatment because hypoxia occurs in cancers but rarely in normal tissues. Additionally cells with this mechanism are about three times more resistant to radiotherapy than normally oxygenated cells and are known to negatively impact the response of cancers to radiotherapy.

Targeting this mechanism is a potentially transformational concept that could increase cancer sensitivity to treatment without increasing normal tissue reactions. This research has been funded by The Wellcome Trust and LifeArc, two UK-based non-profit medicinal chemistry charities as well as the non-profit adMare Biodiscovery in Vancouver and the Canadian Institute of Health Research. The project is at the 'lead identification' phase of drug development. More funding is needed to complete the program and Dr. Minchinton is currently searching for other partners to continue the development.

The BC Cancer Research Institute is known worldwide as one of the leading radiation biology groups. Dr. Minchinton credits this reputation to his predecessors, the current facilities including TRIUMF, Canada's particle accelerator centre and the strong collaboration with scientists at BCCRI, UBC and TRIUMF that also provides young researchers a rich source of expertise in a wide variety of radiation sources including proton beams and offer exciting translational opportunities for clinical trials.



Medical physicists: Cancer care's hidden heavy-hitters

Medical physicists are critical members of cancer research and care teams, especially when it comes to radiation therapy. They work closely with radiation oncologists, specialized physicians, radiation therapists and radiation biologists and can be found working after-hours calibrating, testing and gathering data on the radiotherapy treatment machines to ensure that they are ready and safe to treat patients daily. Although their work is largely hidden from the patient experience, these dedicated professionals are involved with every single treatment plan. Each patient receiving radiation therapy has a customized plan tailored to their unique care needs, and medical physicists help to optimize each plan by contributing their unique knowledge of how radiation works. Medical physicists are heavy-hitters when it comes to patient care behind-the-scenes. From a research perspective, they are ideally positioned to develop innovative solutions to technical and radiobiological challenges and help improve patient outcomes.

This year, medical physicists at BC Cancer Research Institute developed a way for radiation beams to adjust to the movements associated with patients' breathing and heartbeats. This real-time adaptation to the patient's moving anatomy allows for more effective treatment and, importantly, less adverse effects. Research is also being done on ultra-fast treatment delivery that could be completed in less than one second. This method, known as FLASH radiotherapy, has the potential to reduce impact to normal tissue and enable a curative treatment in sites that are currently not treatable, either because of tumour resistance to radiation or close proximity to very sensitive organs like the brain, pancreas, prostate or gynecological areas.

Dr. Cheryl Duzenli, head of medical physics at BC Cancer – Vancouver.

"I am very proud of the work my colleagues and I do," says Dr. Duzenli. "We work to improve patient care by designing, building and implementing new treatment strategies and medical devices. We are continually exploring new methods for radiation treatment delivery. At BC Cancer, we have a critical-mass of multi-disciplinary research collaborators here and across the province. It's an inspirational research climate."

As part of this important work, Dr. Duzenli has developed an ultra-light carbon fibre device to support patients receiving radiation therapy for breast cancer. The device, known as CARA (Carbon-fiber Adjustable Reusable Accessory), helps position the breast to reduce acute painful skin reactions and to improve survival by reducing radiation dose in the lung. This carbon-fibre technology is transparent to radiation and is expected to find other applications in radiation therapy to improve patient care.

The value of teamwork

Radiation therapy can be used to try to cure cancer, reduce the chance of it coming back, or to help relieve symptoms. New research from Dr. Devin Schellenberg and his colleagues across the province aims to increase the impact of this treatment while minimizing adverse reactions.

"This year, significant gains were made in radiation therapy research, specifically precision radiation, which delivers high doses of radiation to small targets with the aim of sparing as much normal tissue as possible," says Dr. Schellenberg, program medical director, Provincial Radiation Therapy at BC Cancer. "Despite the impact COVID-19 and climate emergencies had on research operations, clinical trials were able to continue and make up for lost ground in 2021 thanks to dedicated teams at BC Cancer."

Each BC Cancer centre has more than just the linear accelerator machines – known as Linacs – needed to deliver targeted radiation therapy; they're also home to dedicated multidisciplinary groups of health care professionals who deliver this important therapy to roughly half of all BC Cancer patients. These teams include radiation oncologists, who see patients and determine treatment strategies, physicists who aid in the planning of radiation treatment and oversee the working and quality assurance of the Linacs, radiation therapists who run the Linacs and deliver radiation plans to patients, and specialized nurses who help patients through side-effects, and provide education and support.

At a provincial level, these teams often collaborate on new techniques and technologies and share resources, including clinical trials, leading to better



patient outcomes. Dr. Schellenberg was the lead oncologist for the national Stereotactic Radiation for OligoProgressive disease (STOP) trial which concluded this year. The trial looked at whether radiation could be used to treat metastatic sites of cancer that are no longer responding to systemic treatments or chemotherapies. In this instance, five of the six regional BC Cancer centres participated in the trial with one-third of all national participants receiving treatment in B.C. – a remarkable achievement.

In addition to supporting many trials provincially, including the SABR clinical trials led by Dr. Rob Olson in Prince George, Dr. Schellenberg is leading an early trial that would utilize magnetic resonance imaging (MRI) technology rather than traditional computed tomography (CT) to plan radiation treatments for specific cancers. Outside of cancer research, he is also looking at how to use high doses of radiation as a means to eradicate heart arrhythmias.

“The treatment is complex as the heart is beating and the lungs are filling, so the target is moving as the treatment is occurring,” says Dr. Schellenberg. “So far, we are only treating very select patients with this technique, but the lessons learned could apply to the future treatment of cancers near the heart.”

Noting the importance of teamwork and collaboration on research excellence, Dr. Schellenberg hopes to create an environment of even further collaboration between radiation oncology and research at the BC Cancer Research Institute by balancing bench to bedside research with increasing patient care needs. He hopes that the increasing clinical research outcomes achieved by BC Cancer’s radiation oncology teams will spur more multidisciplinary trials in the future.



Nursing & allied health research



A first of its kind in Canada, the Nursing and Allied Health Research and Knowledge Translation (NAHRKT) department was launched in January 2021. This move cast a bold vision for BC Cancer to evolve into a vibrant, world-class leader in research across the interdisciplinary spectrum. Comprised of nurses and allied health professionals, the NAHRKT department leverages the knowledge and expertise of these critical health care workers to deliver evidence-informed improvements in care, patient outcomes, and system performance. The team takes an equity-first approach to examine the health service needs of people diagnosed with cancer and their families, and uses a multidisciplinary approach to address gaps within the care system.

The department has a strong vision and strategic plan to advance research and knowledge mobilization initiatives that target issues at the intersection of science, policy, and practice to address what matters most. Here are the stories of some team members and trainees.

Jagbir Kaur

Jagbir Kaur is a clinical nurse specialist on the Nursing and Allied Health Research and Knowledge Translation (NAHRKT) team. Her research is broadly focussed on equity-oriented cancer research that centers the experiences of racialized and minoritized individuals and populations. Her dissertation research will examine the unmet needs of Panjabi-Sikh cancer patients during treatment to inform system level strategies to address gaps in care and fill unmet needs of one of BC's largest visible minority groups.

"Nurses and allied health professionals bring a unique perspective and curiosity informed by their clinical experiences and observations," says Kaur. "They are implored to ask particular kinds of research questions, those that often arise directly from their clinical practice. This department provides the necessary infrastructure and support to facilitate nursing and allied health clinicians to engage in research and knowledge translation activities."

Applying an equity-oriented lens to work done in the NAHRKT department is a focus for Kaur and team. The new department aims is to bring together clinicians, health system leaders, communities, and academic partners to produce—and mobilize—evidence that allows for a more equitable, diverse and inclusive cancer care system.

"Research provides the opportunity to explore those questions in a methodological way, often resulting in transferable findings and knowledge that can directly contribute to improving the care and experiences of patients and families."

Where have you seen the most significant progress in cancer research since the beginning of your career?

As a nurse, I have seen tremendous progress in research and evidence-informed approaches to managing symptoms and side effects of cancer and cancer treatments. New treatment options mean that clinicians can better support patients and their families manage the often-troubling side effects and symptoms patient's experience. I am most excited by the growing attention to equity centered research that continues to build our collective understanding about the unjust, unfair cancer-related inequities experienced by some individuals and populations. Not only does this body of research prompt critical reflection of our care and systems of care, it also creates an opportunity for research trainees like myself to engage research that centers the experiences of diverse, often underrepresented, individuals and communities within research.

Why did you choose BC Cancer for your research?

BC Cancer is internationally recognized for its research excellence and innovation. New treatments and technological advancements developed here have dramatically improved outcomes for cancer patients. However, there are still opportunities to understand and improve the patient and family experience, especially for those most impacted by structural and social determinants of health. Working on the NAHRKT team allows me to re-examine new and innovative ways in which our cancer care sector can best meet the needs of patients and their families.





Heather Kilgour

Heather Kilgour is an oncology nurse at BC Cancer – Vancouver and masters trainee who is conducting her thesis research with the Nursing and Allied Health Research and Knowledge Translation (NAHRKT) team at the BC Cancer Research Institute. Her research is focused on learning how to better support oncology nurses in engaging in meaningful advanced care planning conversations with patients. The idea for this research stemmed from her clinical practice as an oncology nurse at BC Cancer – Vancouver.

“I am grateful to be conducting my thesis research in close collaboration with BC Cancer,” says Kilgour. “Upon starting at the cancer centre, I quickly realized how much variability there is in cancer diagnoses and treatments, and how challenging navigating the cancer system can be for patients and their families. I feel lucky to be able to provide care to patients with cancer, and to act as a resource and support for those undergoing treatment for their cancer.”

For her research, Kilgour plans to interview oncology nurses across the province to better understand their perspectives and experiences related to advanced care planning, including what changes they perceive are needed to feel supported engaging in advanced care planning with their patients.

“I believe direct care nurses have unique insight into the practice environment, and when given the support and tools, may identify research priorities and determine nursing interventions with direct clinical applicability,” notes Kilgour.

Where have you seen the most significant progress in cancer research since the beginning of your career?

I’m new to cancer research so it’s hard for me to pinpoint the most significant progress; however, there has been an important shift towards nursing-led and embedded research. Nurses work so intimately with patients, and by doing so have a unique perspective about what is working in our cancer care system and what opportunities exist for improvement. BC Cancer as an organization, and patients with cancer across B.C., will only benefit from further supporting the nursing staff in identifying and addressing gaps in care through nursing-led research.

Why did you choose BC Cancer for your research?

I was working as a nurse at BC Cancer – Vancouver when I entered my graduate studies. This experience has allowed me to reflect on my clinical practice environment and identify opportunities to improve patient outcomes and nursing care. I chose to conduct my research at BC Cancer, as I was introduced to a network of nursing leaders, including Dr. Leah Lambert and her colleagues, who were passionate about nursing research at BC Cancer. It was this support that made me feel comfortable stepping into the unknown world of research here at BC Cancer.



Amber Bourgeois

Amber Bourgeois is a nurse practitioner at BC Cancer – Victoria and a second year PhD student at the University of Victoria School of Nursing. She is completing a one year Canadian Institute of Health Research (CIHR) Health System Impact fellowship within the Nursing and Allied Health Research and Knowledge Translation (NAHRKT) department working under the supervision of Dr. Leah Lambert as part of her studies.

“Nursing and allied health bring many applied disciplinary perspectives to the table in addressing gaps through observations from their direct clinical experiences,” says Bourgeois. “The NAHR department brings these perspectives one step further in building capacity for these unique perspectives to be explored in the ways research is designed, delivered, and applied.”

Her research is focused on advancing equity-oriented cancer care for structurally vulnerable populations experiencing socioeconomic disadvantage. She is especially interested in under-explored areas of study that provide an opportunity to examine social and structural contexts, which create barriers in access to cancer treatment.

Where have you seen the most significant progress in cancer research since the beginning of your career?

As a novice researcher, I have been fortunate to be part of a greater collective looking at equity- oriented research in oncology, led by Dr. Leah Lambert. There has been an overwhelming positive response to research from allied health professionals from across all disciplines within a relatively short period of time. This has given me a lot of hope for the future of cancer care.

Why did you choose BC Cancer for your research?

As a nurse practitioner at BC Cancer (and former clinical trials nurse), I have a passion for oncology, and could see no better place to situate my research.

PREDiCT initiative begins in B.C., & is shared nationally



In May 2021, BC Cancer announced a public-private partnership with Hoffmann-La Roche Limited (Roche Canada) and the Canadian Personalized Healthcare Innovation Network (CPHIN) to create a real-world evidence (RWE) framework called PREcision Oncology Evidence Development in Cancer Treatment (PREDiCT).

The PREDiCT initiative is demonstrating the possibilities of a health-care system that leverages real-world evidence and clinical trial data to provide tailored and cost-effective care options for patients.

Instead of reimbursement decisions based on static evaluations of safety and efficacy, PREDiCT envisions a health-care system that generates data and evidence to help regulators and health authorities capture insights throughout a patient's entire journey. In this way, PREDiCT proposes a learning health-care system that continuously evaluates and re-evaluates evidence and decisions as new data emerges.

"The core hope of PREDiCT is to further learning health-care systems by changing the BC Cancer health-care data ecosystem and the way real-world evidence is leveraged to make decisions about effectiveness and cost-effectiveness," says Dr. Dean Regier, senior scientist at BC Cancer and PREDiCT co-principal investigator.

In one short year, PREDiCT has profiled close to 500 patients that are outside the current indications for next-generation sequencing (NGS) at BC Cancer. This sets the stage for dynamic integration of genomic features, clinical metrics, and health economic impact.

Moreover, "PREDiCT presents a great opportunity for BC Cancer to upgrade its molecular diagnostic offering to benefit more patients with clinically actionable information," explains Dr. Stephen Yip, pathologist at BC Cancer, and PREDiCT co-principal investigator.

The investment in building the multidisciplinary team and socialization infrastructure has created a solid foundation for ongoing and future precision oncology initiatives. PREDiCT has also accelerated the integration of patient related outcomes data collection into clinics.

"The incorporation of patient reported outcomes is invaluable; it enables the health-care team focus on issues of importance to the patient and empowers the patient as a partner in their care," says Dr. Cheryl Ho, medical oncologist at BC Cancer and PREDiCT co-principal investigator.

While generating real-world evidence for decision-makers, PREDiCT has impacted the patient experience in a multitude of ways. From providing better understanding of their tumour biology to opening new communication channels with the health-care team, the initiative also has enabled access to clinical trials and more informed selection of systemic therapies for treatment.



"We've started to socialize the framework across Canada, including nationally at the Canadian Agency for Drugs and Technologies in Health, and with oncologists and decision makers in Ontario and BC," notes Dr. Regier. "BC Cancer has gone a step further by agreeing to examine life cycle assessment through the concept of a reimbursement sandbox, which is where we demonstrate to decision-makers the learnings emerging from PREDiCT."



CLIC-01 clinical trial: Building BC Cancer's capabilities in cutting-edge immunotherapy, genetic engineering & clinical trials

BC Cancer's immunotherapy team has developed the expertise and infrastructure to create genetically engineered immune cells (called CAR-T cells) for the treatment of life-threatening blood cancers. BC Cancer was the first academic group to produce and deliver CD19 CAR-T cells to cancer patients in Canada.

CAR-T cells have revolutionized the treatment of certain leukemia and lymphomas, ushering in a new era in oncology where cancer patients with advanced disease are treated with genetically engineered immune cells instead of chemotherapy and other conventional approaches. To ensure Canadian cancer patients have access to this game-changing therapy, as well as the many related innovations that promise to follow, researchers at BC Cancer developed in-house expertise and infrastructure to produce and deliver this treatment all the way from the lab bench to the patient's bedside. In October 2019, they launched a phase I/II clinical trial (called CLIC-01) which will recruit up to 60 patients with end-stage leukemia and lymphoma who have no other treatment options available to them. In April 2020, the first BC patient was treated as part of this first academic CAR-T cell therapy trial in Canada.

Drs. Kevin Hay, Rob Holt and Brad Nelson co-lead the BC Cancer Immunotherapy Program and the Conconi Family Immunotherapy Lab (CFIL) in Victoria, where the CAR-T cells are manufactured. The design and manufacturing of the DNA used for genetic engineering takes place at the Genome Sciences Centre (GSC) at the BC Cancer Research Institute in Vancouver. The GSC also supports logistics, project management, quality assurance/quality control, and regulatory functions of the program. This work

is primarily funded by the BC Cancer Foundation and Canada's Networks of Centres of Excellence (BioCanRx). The Canadian Foundation for Innovation (CFI) provided support for CFIL infrastructure.

The CLIC-01 clinical trial is a pan-Canadian effort with collaborators in Victoria, Vancouver and Ottawa working together. Dr. Hay is the lead clinical investigator in Vancouver. Over 50 patients in British Columbia and Ontario have received the therapy so far, with the trial on track to finish by the end of 2022. The availability of this therapy through the CLIC-01 trial proved especially important during the COVID-19 pandemic, when it was exceedingly difficult for patients to travel to other jurisdictions to receive this form of treatment.

How Chimeric Antigen Receptor (CAR) T-Cell therapy Works

From the patient's perspective, CAR-T cell therapy starts with a visit to the hospital to provide a large blood sample, which is then transported by volunteer couriers to BC Cancer's Deeley Research Centre in Victoria. There, white blood cells are genetically engineered to express a Chimeric Antigen Receptor (CAR), which hardwires them to recognize a protein called CD19 on cancer cells. The cell engineering process is largely automated and takes 12 days to generate a cell product that is ready for patient use. After testing for sterility and other criteria, the CAR-T cells are couriered to the Bone Marrow Transplant centre in Vancouver or Ottawa, where they are infused back into the patient's bloodstream. Once circulating in the bloodstream, the CAR-T cells are able to recognize and kill cancer cells throughout the patient's body. Patients receive only one infusion of cells, and they are then followed carefully by clinicians to manage any side effects and to record the clinical results.

Trial Outcomes

Outcomes data is available for the first 30 patients on the CLIC-01 clinical trial, with the 30th patient infused in October 2021. The clinical response rates have been very favourable so far, with several complete responses. Significantly, the BC Cancer-produced CAR-T cells appear to have a low rate of the common side effects seen with CAR-T cells.

The response from the BC Cancer community regarding the trial has been incredibly enthusiastic. Due to the positive response, and the ability of the BC Cancer team's new manufacturing capabilities, the immunotherapy team is building on the success of this first trial to develop the next generation of CAR-T cell products for leukemia, lymphomas and other cancers.



Celebrating the extraordinary achievements of Dr. Connie Eaves

This year staff at the BC Cancer Research Institute continued to prove themselves as international leaders in research excellence. Dr. Connie Eaves, distinguished scientist at BC Cancer's Terry Fox Laboratory and BC Cancer's longest serving employee, had a stand-out year achieving top honours for scientific contributions.

In 2021, Dr. Eaves was elected into the prestigious Royal Society, joining the likes of other esteemed scientists including Stephen Hawking, Albert Einstein and Charles Darwin. The Royal Society is a Fellowship of many of the world's most eminent scientists and is the oldest scientific academy in continuous existence. Dr. Eaves was also appointed to the Order of Canada in 2021. The Order of Canada is one of Canada's highest honours. Presented by the Governor General of Canada, the Order honours people making extraordinary contributions to the nation. She received the 2021 award for Outstanding Achievements in Cancer Research from the Canadian Cancer Research Alliance (CCRA) and was awarded an honorary doctorate by Acadia University and named as a Distinguished University Scholar at UBC.

In all instances, Dr. Connie Eaves has been particularly recognized for her development of robust functional methods to quantify and characterize distinct types of primitive blood and mammary cell precursors - now considered gold standards worldwide. Their use has enabled many discoveries, including Dr. Eaves' first demonstration of quiescent malignant stem cells from studies of patients with chronic myeloid leukemia. Currently, her group is exploiting new ways of prospectively analyzing the process of human leukemogenesis and breast cancer development from genetically engineered normal human cells using methods they have also pioneered in the last decade.

Dr. Eaves is already a Fellow of the Royal Societies of Canada (1994) and Edinburgh (2015), and has received many other prestigious awards over the last 3 decades including the Noble and Chew-Wei Prize for Cancer Research, the International CML Foundation Rowley Prize, and the American Society of Hematology's Stratton Lifetime Achievement and E. Donnall Thomas Awards. In 2019, she was inducted into the Canadian Medical Hall of Fame, named recipient of the 2019 of the Canada Gairdner Wightman Award and named one of Chatelaine's Women of the Year.



Dr. Kim Nguyen Chi: Improving outcomes for patients with prostate cancer in B.C. & beyond

Dr. Kim Nguyen Chi, senior research scientist, medical oncologist and chief medical officer at BC Cancer, specializes in understanding and caring for people with metastatic prostate cancer. His research focusses on clinical trials and translational research on predictive and prognostic biomarkers for patients with advanced prostate cancer. In 2021, Dr. Chi reported on results from several randomized clinical trials which involved patients with advanced prostate cancer. These studies demonstrated improved outcomes for patients and the results have helped to change and shape the way clinicians manage prostate cancer around the world.

The Phase III TITAN study, led internationally by Dr. Chi, evaluated the use of the medication apalutamide in addition to standard treatment for patients with metastatic castration sensitive prostate cancer (mCSPC). The final analysis showed a significant long-term overall survival improvement of nearly 50 per cent; establishing apalutamide as a new international standard of care.

In addition to the TITAN study, Dr. Chi reported on the final results of a Phase II clinical trial which compared chemotherapy and next generation hormone therapy in patients with mCSPC who had advanced disease and a poor prognosis. Although two active treatments are not commonly compared in clinical trials, this comparison was done in this study which was a cross-Canada trial led by Dr. Chi and funded through industry and peer-reviewed grants. Key findings revealed that there is an advantage to using chemotherapy first but that hormone therapy also had benefits. Circulating tumour DNA (ctDNA) was also evaluated as part of the TITAN study. Results also indicated that the level of ctDNA in a patient's blood was found to be highly prognostic, more than any other factor previously described.



Dr. Chi also reported on the VISION study, a trial that he helped to design and steer. BC Cancer patients were recruited through this trial, which evaluated the value of a specific type of radio-ligand therapy, a type of cancer treatment that delivers radiation to specifically targeted cancer cells, with a minimal effect on healthy cells. The treatment showed that the new radio-ligand therapy improved overall survival and patient reported quality of life. The treatment has been recently approved in the USA, and is undergoing regulatory review in Canada.

"I have patients who are still alive and doing well," says Chi. "I would not have expected this outcome had they not participated in this trial. Follow up scans showed that their cancers had regressed and had remained so over time even at their advanced stage. Overall the treatment is well tolerated and quality of life was not significantly impacted by the treatment."

When Dr. Chi first began practicing medicine, patients with mCRPC had a median survival of 10-12 months and only one treatment option. Now the median overall survival is in the range of 3 years. Advancements in precision medicine and genetic testing help cancer care teams determine the best treatment for a patient's unique cancer type and spare them from potentially ineffective treatment options as much as possible. There continue to be large efforts to develop new therapies for treatment resistant prostate cancer and to also bring new treatments into earlier disease settings where the benefits may be even greater.

Dr. Chi credits BC Cancer's critical mass of clinical, translational and laboratory-based researchers, the provincial scope and approach to patient management, and cohesive teams made of medical oncologists, radiation oncologists, pathologists, radiologists, scientists, and research staff for the research excellence that works every day to improve patient care for people in B.C. and ultimately around the world.

New hire focus:

Dr. Adi Steif tackles big data to better understand how cancer evolves

Dr. Adi Steif joined the BC Cancer Research Institute as a principal investigator in July 2021. The Steif Lab, located at Canada's Michael Smith Genome Sciences Centre, develops and applies statistical machine learning methods to characterize tumour composition and evolution. The group also collaborates with molecular biologists and engineers to advance technology for profiling the genetic material of individual cancer cells.

In the time since beginning her career, Dr. Steif notes the field of cancer genomics has seen significant progress. When she began graduate school, the first single cell genomes had only recently been sequenced. Together with colleagues at BC Cancer, she contributed to the development of new methods that allow researchers to sequence the genomes of tens of thousands of cancer cells with substantially reduced costs. This means scientists at BC Cancer and elsewhere now have the ability to examine the genetic composition of tumours in unprecedented detail, and can ask new questions about early carcinogenesis and the evolution of treatment resistance.

"I've enjoyed reconnecting with former colleagues and establishing new collaborations," says Dr. Steif, who completed her PhD at BC Cancer and returned to Vancouver following a postdoctoral fellowship at the University of Cambridge. "In addition to research I've been recruiting trainees, onboarding my group and writing funding applications."

What are your thoughts on the future of oncology?

The genetic alterations that drive cancer vary from patient to patient, and can differ between cells within an individual tumour. Due to this heterogeneity, different patients will require different treatment

approaches. To deliver on the promise of personalized medicine, researchers are working to measure genetic diversity and identify new targets for therapy. As the technology to profile tumour composition continues to advance, so does the size and complexity of datasets. Computational biology and machine learning will play an increasingly important role.

What advice would you offer to young scientists?

Research is increasingly multidisciplinary and collaborative. Find ways to reach across disciplinary boundaries and communicate your work to scientists in other fields. I was fortunate during my training to work alongside colleagues with diverse expertise, and together we were able to address challenges that we could not have tackled in isolation.

Why did you choose BC Cancer?

I had the privilege of working with incredible mentors and collaborators during my time at BC Cancer, doing research at the forefront of genomic technology and computational biology. It is great to be back and have the opportunity to build on this experience and pursue new research directions.



New hire focus:

Dr. Leandro Venturutti examines B-cell lymphoma with his A-team

Dr. Leandro Venturutti began his role as a scientist at the Terry Fox Laboratory & Centre for Lymphoid Cancer in the summer of 2021. Recruited to BC Cancer to form his own research group, Dr. Venturutti's research is focused on identifying what drives B-cell lymphomas to progress and spread, with the ultimate goal to develop less-invasive diagnostic tools and novel treatments to prevent or cure these aggressive cancers.

In his time at the BC Cancer Research Institute, Dr. Venturutti has been working on funding applications, building infrastructure in his laboratory, and recruiting members for his team. He now has a small group of highly motivated trainees who are conducting their first experiments related to their own projects, and to collaborations with other research groups in B.C. and Ontario.

"I am a strong believer that truly innovative and meaningful science requires looking at each question from multiple perspectives, and have tried to build my team accordingly," says Dr. Venturutti. "I would like to acknowledge the other groups at the Centre for Lymphoid Cancer and Terry Fox Lab, who have opened up their doors for us, making us feel part of a much larger team from the first day."

One of the topics his lab is working on is the relationship between autoimmune disorders and B-cell lymphomas.

"It has been known for some time that patients with autoimmune disorders have a higher risk of developing aggressive B-cell tumours. We are interested in understanding the extent and nature of the overlap between these diseases, as a means to identify early signs of cancerous transformation, and druggable dependencies."

Before starting at BC Cancer, Dr. Venturutti completed his post-doctoral research at the Division of Hematology and Oncology at Weill Cornell Medicine (New York, USA), studying how recurrent mutations found in often-lethal B-cell lymphomas alter the epigenome and contribute to malignant transformation.

Where have you seen the most significant progress in cancer research since the beginning of your career?

For decades, researchers have been aware that cancers are a diverse collection of diseases, something that is particularly true for lymphomas. This has a direct impact in our ability to develop tailored treatments for patients. The advent of single cell technologies in the past five years, particularly those allowing multi-parametric testing, are giving us, for the first time, the opportunity to better understand tumour variety with an unprecedented level of detail. At the same time, genetic engineering tools like CRIPR, used to edit genomes, have been a game-changer in the way we develop experimental models. These advancements continue to open new avenues to functionally test hypothesis and accelerate research.

Why did you choose to do your research at the BC Cancer Research Institute?

BC Cancer has been at the forefront of blood-borne cancer research and treatment for more than two decades. Beyond the groundbreaking contributions of excellent researchers and clinicians, BC Cancer has made it a priority to support and foster integration between basic and clinical research. This makes BC Cancer significantly stronger than the sum of its parts, and sets it in a strategic position to advance cancer care for all Canadians.



The growing importance of hereditary cancer research

Dr. Kasmintan Schrader receives Canada Research Chair in Clinical Cancer Genetics and Genomics

BC Cancer's Hereditary Cancer Program provides genetic counselling and genetic testing for B.C. and Yukon residents who may have inherited an increased risk for specific types of cancer. In 2021, Dr. Kasmintan Schrader, medical co-director of the Hereditary Cancer Program at BC Cancer and scientist in the department of Molecular Oncology at the BC Cancer Research Institute, received a Canada Research chair (CRC) in Clinical Cancer Genetics and Genomics.

"I am incredibly grateful to be awarded a Canada Research Chair as it is a recognition of the importance of hereditary cancer research and the gains that can be made from clinical translational research which will ultimately work towards improving patient and family-centered care," says Schrader. "Becoming a chairholder has also offered me new visibility and as such, has already opened the door to exciting new multidisciplinary collaborations that would not otherwise have occurred."

As part of this work, Dr. Schrader is using precision oncology to improve the use of germline variation to enhance cancer care. Germline variations, also called germline mutations, are gene changes in an egg or sperm that are incorporated into the DNA of every cell in an embryo. Variants, including those that may predispose someone to get cancer, are passed on from parents to offspring. Dr. Schrader and her research team are working to better detect hereditary cancer, differentiate hereditary from non-hereditary forms of cancer, detect cancer earlier, and uncover germline variations that may not only increase susceptibility to cancer, but provide valuable information to patients, families and caregivers.

This year Dr. Schrader also co-led the development and launch of the Hereditary Cancer Program's online portal to improve timely access to genetic testing for individuals at-risk for hereditary cancer. She notes that hundreds of patients have now gone through the portal and early examination of the patient reported outcomes show that patients feel empowered by and satisfied with the experience.

The future of research into hereditary cancer has never been brighter as new technological advances begin to open the door for clinical applications.

"I am keen for us to fundamentally change the way in which clinicians offer genetic testing and are able to assess patients and families for hereditary disease risks - in cancer and beyond," says Schrader. "In collaboration with my BC Cancer clinical and research colleagues we are improving hereditary cancer care for patients and families through the use of novel strategies and technologies to identify individuals at risk of hereditary cancer. I look forward to BC Cancer, B.C., and Canada, leading the way by real-world demonstration of the utility of these new strategies and testing approaches to the world."



BC Cancer melanoma immunotherapy database aims to better understand outcomes for older adults

In 2021, an estimated 1345 British Columbians will be newly diagnosed with melanoma. One in 52 females and one in 40 males is expected to develop the aggressive skin cancer during their lifetime. Although preventable and curable if caught early, advanced melanoma can be fatal. In 2021, Dr. Doran Ksienski, medical oncologist at BC Cancer – Victoria, created the BC Cancer Melanoma Immunotherapy Database to better understand advanced melanoma and immunotherapy treatment options after finding that many patients receiving care at BC Cancer were older, sicker, and had more comorbidities than those enrolled onto clinical trials.

“Clinical trials have clearly shown that immunotherapy improves survival for patients with advanced melanoma,” says Ksienski. “However important questions remain regarding the safety and efficacy of these medications in patients routinely seen in everyday practice. As such, I created the BC Cancer Melanoma Immunotherapy Database to better understand the incidence of adverse effects, need for treatment interruption due to side-effects, and survival outcomes for patients receiving specific combinations of anticancer treatments.”

The database includes 399 BC Cancer patients. In 2021, Dr. Ksienski published two papers on the newly created database. One paper, published in *Clinical Oncology*, was able to demonstrate that patients who experienced high grade side effects from a combination immunotherapy treatment had better survival outcomes compared to patients who did not have any side effects. Another study published in the *Journal of Geriatric Oncology* demonstrated that rates of adverse events, and treatment discontinuation due to adverse events, for patients undergoing immunotherapy treatment for advanced melanoma was similar in patients younger and older than 75 years of age.

“Immunotherapy has brought real hope to patients with advanced melanoma and some patients are able to live many years,” notes Ksienski. “I am routinely treating patients in their 80s and sometimes in their early 90s. Older patients are sometimes reluctant to undergo chemotherapy due to concerns about side effects and quality of life, however, age is not a barrier to receive immunotherapy.”

With the expansion of virtual health services due to COVID-19 concerns, Dr. Ksienski would like to see more research into whether patients followed via telemedicine are at higher risk of developing treatment side-effects than those who are seen in person.

He credits the success of the BC Cancer Melanoma Immunotherapy Database to the high level of expertise and contributions of a multidisciplinary including: medical oncologists, radiation oncologists, pathologists, internal medicine residents, and biostatisticians.

Improving prostate cancer treatments

Prostate-specific membrane antigen (PSMA) is a protein that is highly expressed on prostate cancer cells but not by normal tissues. This makes it an ideal target for developing prostate cancer treatments. Pluvicto, a new drug to treat prostate cancer, was approved by the US FDA in March 2022 to treat metastatic castration-resistant prostate cancer, an advanced and deadly form of prostate cancer. Pluvicto contains a substance that emits radiation to kill cancer cells. Although positive responses are observed from the majority of treated patients, approximately 25 per cent of patients do not respond to the treatment and the complete response rate is low. The reason for this suboptimal efficacy is because Pluvicto is quickly metabolized from the body, therefore only small amounts reach prostate cancer cells. To solve this problem, Dr. Lin and team, designed and tested Pluvicto derivatives with a built-in binder of albumin, the most abundant protein in blood plasma. Once injected, these albumin-binder-containing drugs can stay longer in blood circulation and have more chances of binding to PSMA on prostate cancer cells, leading to a higher accumulation of the drugs in cancer lesions. Compared to Pluvicto, our albumin-binder-containing drugs are expected to be more effective in treating prostate cancer. Most importantly, such design strategy



can be applied to other cancer-targeting drugs to enhance their treatment efficacies as well. “There is a critical need to improve outcomes for patients with the most advanced forms of prostate cancer,” says Dr. Kuo-Shyan Lin, senior

scientist in the Department of Molecular Oncology and head of the Radiochemistry Program at BC Cancer. “The data published this year shows that this new discovery has the potential to improve survival rates and delay the spread of the disease.”



Dr. Sara Harsini, nuclear medicine and molecular imaging physician at BC Cancer and research fellow at the BC Cancer Research Institute, also published important work this year to further develop PSMA-targeting treatment strategies for

prostate cancer. One drawback of this approach is the accumulation of the radiotracers in organs other than the prostate gland, including the salivary glands and kidneys, resulting in adverse events, such as dry mouth and damage to the kidneys. Dr. Harsini and team examined a well-known food additive, monosodium glutamate, as a potential means of reducing kidney and salivary gland radiation exposure using a PSMA-targeting radiotracer in 10 patients with prostate cancer. Their results showed that oral administration of this food additive reduced PSMA-targeting radiotracer uptake in salivary glands, kidneys, and other normal organs in patients with prostate cancer, suggesting a possible role for monosodium glutamate in normal organ protection while using PSMA-targeted radioligand therapies.

Clinical research & clinical trials



Tumour sequencing for changes of clinical significance

GSC researchers, led by distinguished scientist **Dr. Aly Karsan**, have used next generation sequencing technologies to develop a test that screens tumour tissue for variants in 45 different genes. This includes both acquired and inherited changes known to be clinically significant. In addition to providing potential treatment information to patients with advanced cancer, this new screening tool—referred to as the Oncology and Hereditary Cancer Program (OncoHCP) panel—can identify people with increased susceptibility to cancer.

Dr. Karsan's group also developed and validated a clinical transcriptome-based assay for stratification of acute myeloid leukemia (AML) — the results were published in Nature Communications.



New clinical trial for endometrial cancer

Dr. Jessica McAlpine with OVCARE and the Gynecologic Cancer Initiative opened the made-in-B.C. trial TAPER (Tailored Adjuvant Therapy in POLE-mutated and p53-wildtype Early Stage Endometrial Cancer). The trial opened across BC Cancer centres with funding from the Gynecologic Cancer Initiative-Clinical Trials Group. With CIHR funding received last year and support from the Canadian Clinical Trials Group, the trial is opening in centres nationally.



Sociodemographic characteristics of women with invasive cervical cancer in British Columbia, 2004-2013: A descriptive study

Although cancer screening has led to reductions in the incidence of invasive cervical cancer (ICC) across Canada, benefits of prevention efforts are not equitably distributed. In a large long-term study led by **Dr. Nadine Caron**, researchers investigated the sociodemographic characteristics of women with ICC in British Columbia compared with the general female population in the province. The researchers found



that women who self-identified as visible minorities, Indigenous, current smokers, non-married and from rural areas were overrepresented among women with ICC. Efforts are needed to address inequities to ensure all women benefit from cervical cancer prevention.

New test developed to diagnose aggressive childhood brain tumours

Drs. Poul Sorensen and Alberto Delaidelli developed a test that can distinguish very high-risk from lower-risk medulloblastoma cases, using an antibody-based technique, namely immunohistochemistry, widely available in clinical laboratories. Based on multiple datasets, they identified that the protein TPD52 is highly expressed in the most aggressive forms of medulloblastoma. This allows the reclassification of approximately 15 per cent of patients, who might benefit from intensified therapy. Their finding was published in Clinical Cancer Research.

Promising target identified in ewing sarcoma

Dr. Poul Sorensen screens to identify cell-surface protein IL1RAP as a key driver of metastasis in Ewing sarcoma, a highly aggressive childhood sarcoma. Expression of IL1RAP is potentially exploitable by immunotherapy. The results from the study were published in Cancer Discovery.



Impact of recurrence score (RS) on chemotherapy prescribing in breast cancer

Dr. Caroline Lohrisch and team reported real world evidence on the cost-effectiveness of a 21-gene recurrence score to guide chemotherapy use in BC Cancer patients with hormone receptor positive, HER2-negative node-negative breast cancer, and established thresholds for chemotherapy benefit in patients. Results from the trial were published in the journal Cancer.





Discoveries and progress in lymphoid cancer research

Characterization of tumour microenvironment in Hodgkin Lymphoma: Single cell approach

Data describing the intricate interactions between malignant cells of classical Hodgkin Lymphoma (cHL) and tumour microenvironment (TME) has recently emerged from projects led by **Dr. Christian Steidl** and funded by the Paul Allen Frontiers Group. To characterize the TME of lymphocyte-rich Hodgkin lymphoma (LR-HL), Dr. Steidl's group collaborated with Dr. Brad Nelson from the BC Cancer Deeley Centre. The results showed that a unique immune helper T cell subset was enriched in LR-HL compared to other subtypes. The data generated will be used towards novel immunotherapy development in Hodgkin Lymphoma; the finding was published in the Proceedings of the National Academy of Science (PNAS).



New classification of aggressive lymphoma

Drs. David Scott and Christian Steidl with the Centre for Lymphoid Cancer (CLC) have characterized a

subset of Diffuse Large B-Cell Lymphoma (DLBCL) tumours with a primary mediastinal large B-cell lymphoma (PMBL) gene expression signature. The group's studies demonstrate potential values in translating the molecular/gene expression-based assay into a routine clinical practice for accurate subtyping and to accelerate precision medicine development and improve outcomes for aggressive lymphomas. The study was published in the journal Blood.

Pediatric/AYA HL: Outcome prediction in children with Hodgkin Lymphoma

Classical Hodgkin lymphoma (cHL) is one of the most common cancers among children and adolescents. Overall survival rate for pediatric cHL has drastically improved over the past three decades, exceeding 90 per cent. However, the effective chemo or radiation therapies are often associated with long-term toxicity and morbidity, reducing quality of life of young patients, and children who experience relapse or refractory diseases have poor outcome, which remains to be the clinical unmet need. **Drs. Christian Steidl and David Scott** from BC Cancer, together with Dr. Terzah Horton (Baylor College of Medicine) developed a novel event-free survival (EFS) predictive model, 9-cellular component model (PHL-9C) for pediatric patients treated in the AHOD0031 trial. Results from this study were published in the journal Blood.

Translational Pathology: International collaborations

The CLC pathology team led by **Drs. Graham Slack and Jeffrey Craig** have contributed to discoveries in Notch signaling in splenic marginal zone lymphoma (SMZL) and immune evasion mechanism in intravascular large B-cell lymphoma. Notch signaling is important in cancer and Notch1 and Notch2 mutations have been reported in various solid and hematologic malignancies. This study was published in the journal Blood Advances.

Dr. Slack also conducted a study in collaboration with Cleveland Clinic, which investigated an immune evasion mechanism in intravascular large B-cell lymphoma, a rare and aggressive sub-type of extranodal diffuse large B-cell lymphoma. Their paper was published in the American Journal of Clinical Pathology.

Outcome of limited-stage nodular lymphocyte-predominant Hodgkin Lymphoma (NLPHL)

Dr. Kerry Savage and team conducted a large retrospective study to evaluate the long-term outcome of limited stage nodular lymphocyte-predominant Hodgkin lymphoma (NLPHL) treated with radiation (RT) or doxorubicin, bleomycin, vinblastine, dacarbazine (ABVD) chemotherapy or combination of both. This study is the largest study conducted to assess the impact of a PET-adapted approach using a real-world, population-based cohort. This study validates the PET-adapted approach in treatment of limited stage NLPHL, which minimizes radiation-related toxicity in these patients without compromising outcome. A follow-up study is needed to evaluate recurrence, the data generated from this study can contribute to standardization of the treatment policy. Results were published in the journal Blood Advances.





Genomic biology & methods

Clonal fitness inferred from single-cell sequencing of breast cancer genomes

A landmark discovery was published in the journal Nature by **Drs. Aparicio and Shah**, representing several years of work with human breast cancers that have been propagated by transplantation. Using a novel method of sequencing the genomes of single cells, they monitored the evolution of these cancers under drug treatments with platinum, a commonly used chemotherapeutic agent. They discovered that changes in gene dosage in the genome, called

copy number mutations, can contribute to platinum resistance. They also discovered that the cell state of platinum resistance has a "cost"; it makes the cells weaker than non-resistant cells when platinum is not present. This means that early platinum resistance might be reversible and suggests clinical trials to re-challenge therapy may prove worthwhile.



New molecular subgroups of pancreatic neuroendocrine neoplasms (PNETs) identified

Categorizing pancreatic neuroendocrine neoplasms (PNETs) based on molecular analysis could aid patient stratification and treatment. In a study published by **Dr. Sharon Gorski's** group in Cell Reports, four subtypes of PNETs were identified through transcriptome analysis, proteome profiling and whole-genome sequencing.

Biomarkers of response to immune checkpoint inhibitors (ICIs)

Immune checkpoint inhibitors (ICI) have revolutionized the treatment of solid tumours, however identifying patients who will respond to these drugs remains challenging. **Dr. Janessa Laskin** and colleagues with the Personalized OncoGenomics program at BC Cancer in Vancouver used whole genome and transcriptome analysis to identify multiple biomarkers that in combination may help to identify ICI responders. Results from the study were published in Clinical Cancer Research.





Straglr: a new software tool for targeted genotyping and repeat expansion detection

Several neurological diseases are characterized by abnormal accumulation of short tandem repeat (STR) sequences. Repeat sequences can be detected using short- and long-read sequencing alignments. In a study published in Genome Biology by the lab of **Dr. Inanç Birol**, distinguished scientist at the GSC, researchers have developed Straglr; a novel, robust software capable of detecting disease-causing repeats using long-read sequencing data.



Technology development

Dr. Yuzhuo Wang and his collaborators established a start-up company called "LAST innovation Ltd.". The start-up signed a license agreement with UBC UILO and has raised approximately \$2.5 million from angel investors for the development of the technology invented from Wang Lab.

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