2022 BC CANCER RESEARCH REPORT

BC CANCER RESEARCH INSTITUTE

Provincial Health Services Authority

3 ..... MESSAGE FROM THE SENIOR EXECUTIVE DIRECTOR OF RESEARCH, DR. FRANÇOIS BÉNARD

4 ..... MESSAGE FROM BC CANCER FOUNDATION PRESIDENT & CEO, SARAH ROTH

5 ..... FAST FACTS

6 ..... AWARDS & FUNDING

11 ..... ARTIFICIAL INTELLIGENCE FEATURE

- 12..... HEAD, NECK & LYMPH NODES
- 14..... SKIN
- 16..... BREAST
- 18 ..... OVARIAN
- 20 ..... PROSTATE
- 22 ..... CELLS

24..... HARNESSING THE IMMUNE SYSTEM TO FIGHT DEADLY PEDIATRIC CANCERS

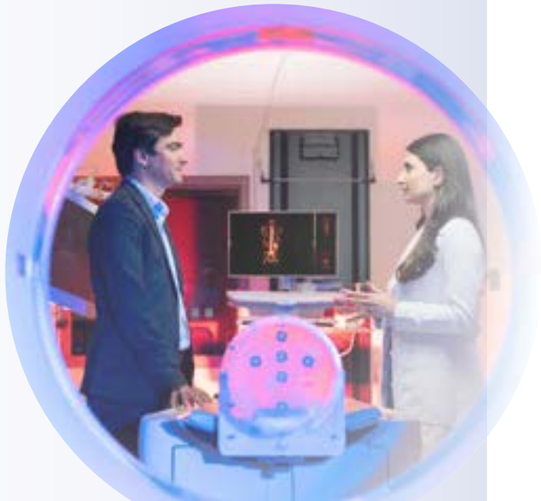
26..... ADVANCING CANCER CARE THROUGH DEDICATED CLINICAL RESEARCH

28..... BLOOD CANCERS REGRESSED TO UNDETECTABLE LEVELS IN OVER 40 PER CENT OF PARTICIPANTS IN AN EARLY-STAGE CLINICAL TRIAL

30..... ENHANCING CAPACITY FOR EQUITY-ORIENTED CANCER CARE IN B.C.

32..... NEW HIRE FEATURE: HELEN MCTAGGERT-COWAN

34..... NEW HIRE FEATURE: RAFAEL MEZA



MESSAGE FROM THE SENIOR EXECUTIVE DIRECTOR OF RESEARCH, DR. FRANÇOIS BÉNARD

Our vision of a world free from cancer inspires everything we do at BC Cancer. While this may seem ambitious, we are fortunate to have a team of world leading investigators with exceptional research programs who are motivated by this goal. This is particularly evident in our dedicated research efforts.

BC Cancer scientists, clinicians and trainees have made significant impacts in the areas of biomedical research, genomics, health services research, cancer surveillance, population health, and our goal to reduce the burden of cancer in B.C. and beyond.

In this year's report, we're focusing on the life-changing potential of our clinical research. This work takes place in centres across the province, through initial discoveries during pre-clinical trials research, the careful and conscientious design of early phase clinical trials, and the expertise and care of clinical trialists.

We are in an era of exciting discoveries. Our scientists are leveraging artificial intelligence to help us better identify cancer risk, prevent or detect cancer, and determine the best course of treatments. We are developing tools that have potential to harness the immune system to improve cancer outcomes for patients, such as those with metastatic childhood bone cancers. In 2022, we conducted more than 385 clinical trials across BC Cancer, including using genetically engineered immune cells (CAR-T cells) to treat life-threatening and treatment-resistant blood cancers. Our Nursing and Allied Health Research and Knowledge Translation (NAHRKT) department is doing foundational work in investigating strategies to enhance equity-oriented cancer care, including establishing the Cancer Health Equity Collaborative (CHEC).

We also recognize and congratulate our researchers and trainees, whose inspired, compassionate and brilliant minds continue to make outstanding contributions, publishing their work in the world's most prestigious journals and receiving numerous awards, international recognitions and grants.

While we have much work ahead of us, we are optimistic that through continued excellence, results and collaboration and with our focus on the future, we can continue to steer toward our goal.

Dr. François Bénard
Senior Executive Director
Research

MESSAGE FROM BC CANCER FOUNDATION PRESIDENT & CEO, SARAH ROTH

Research equals hope for many of our donors. Finding purpose by working towards a tangible goal to improve the cancer journey is invaluable to a community often left powerless in the face of this disease.

In 2022, BC Cancer Foundation donors continued to illuminate the path towards new treatments, improved diagnostics, and ultimately better patient outcomes, by fuelling a wide variety of projects and programs at the BC Cancer Research Institute.

Grateful for the innovations in life-saving lymphoid cancer treatment that benefitted both their children, Bob and Penny Gayton donated $500,000 to BC Cancer's Centre for Lymphoid Cancer (CLC).

Split between helping the CLC team become among the first wave of researchers in the world to acquire a CosMX SMI (Spatial Molecular Imaging) machine and the Gayton Family Endowment Fund for Lymphoid Cancer Research, this generous gift will maintain BC Cancer's lead in the race to understand a disease increasing in incidence faster than any other cancer.

Twenty years ago, Gordon Diamond donated the very land the BC Cancer Research Institute stands on. The Diamond Foundation continued their long history of supporting BC Cancer research through a $7.2-million gift that will transform hereditary cancer care and heighten discovery in familial disease through data derived from increased genetic testing.

Unfortunately, heartbreaking loss is also a catalyst to create change. Established by Laurie Rix, in honour of her late husband, the Neil Macrae Hereditary Cancer Research Fund provided $236,000 in support this year to enable BC Cancer to utilize the novel, state-of-the-art Parent-of-origin-aware genomic analysis (POAga) technology to enhance genetic assessment of male breast cancer.

Judy Hager ensured her husband Bob's legacy in creating Pancreas Centre BC continues by donating $5 million, the largest gift in B.C. history to pancreatic cancer research.

The ultimate accolade is when other scientific leaders recognize the value of our work. Dr. Thomas Madden, president and CEO of Acuitas Therapeutics, whose team enabled the development of a COVID-19 vaccine, believes in BC Cancer's ability to advance the global understanding of cancer. As evidenced by Acuitas' donation of $300,000 to be shared between the Precision Medicine for Breast Cancer Research (B-Precise) and Ovarian Cancer Research (OVCARE) programs.

While we're proud to provide hope through research, it's even more gratifying when donor investment turns that dream into a reality as it did for Noel Schacter through the Foundation's ongoing support of CAR T-cell clinical trials at the Deeley Research Centre in Victoria.

Noel says it best, "Every day I have to pinch myself and say, 'You're still here.'"

Sarah Roth
President & CEO
BC Cancer Foundation

FAST FACTS

388 active clinical trials

114 patents filed

615 journal articles

7,369 total cumulative subject enrollment in clinical trials

25 patents issued

761 total publications

15 active spin-off companies (1 new)

49 active licenses

321.5 Researchers
excluding affiliate investigators

657 Trainees
increase of 45 from 2020/21

Funding: Total Grants Awarded: $94 million

By Sector

By Award Type

AWARDS & FUNDING

2022

JANUARY

Dr. Xiaoyan Jiang was awarded CIHR Bridge funding for the project titled "A novel oncolytic virotherapy to overcome drug-resistance in acute myeloid leukemia". The award amount is $100,000 for 1-year.

CIHR FALL 2021 COMPETITION RESULTS

- **Dr. Kevin Hay** and **Dr. Natasha Kekre** with **Drs. Harold Atkins, John Bell, Rob Holt, Scott McComb,** and **Brad Nelson**

  - Title: A Phase I first-in-human trial of CLIC-2201, a VHH-CD22 CAR-T cell product for the treatment of relapsed/refractory CD22 positive B-cell non-Hodgkin lymphoma $1,667,700 (4-years)

- **Dr. David Perrin** with **Drs. François Bénard, Kuo-Shyan Lin**, and **Arman Rahmim**

  - Title: Dual Isotope Theranostics for 18F-PET Imaging and Correlated Targeted Radioligand Therapy $1,139,850 (5-years)

- **Dr. Kuo-Shyan Lin**

  - Title: PSMA/CAIX-targeting radioligands to improve the management of clear cell renal cell carcinoma $730,575 (5-years)

- **Dr. Kuo-Shyan Lin**

  - Title: Simultaneously targeting cancer cells and tumour stroma to improve detection sensitivity and therapeutic efficacy of radiopharmaceuticals $772,650 (5-years)

- **Dr. Yuzhuo Wang**

  - Title: Optimization and Validation of MCT4-targeting Small Molecule Inhibitors for Treatment of Advanced Cancers $1,147,500 (5-years)

- **Dr. Peter Stirling**

  - Title: Dominant genetics of cohesin pathway proteins to kill cancer $883,575 (5-years)

- **Dr. Kasmintan Schrader**; co-investigators **Drs. Steven Jones, Louis Lefebvre, Stephen Yip, and Peter Landsdorp**

  - Title: Parent-of-Origin-Aware Hereditary Cancer Genetic Testing $852,978 (3-years)

FEBRUARY

Dr. Yongjin Park was awarded a Cascadia Alliance grant for the project titled "Eavesdropping communications between cancer and immune cells". This grant was awarded as Azure Cloud Credits with a $169,000 USD value.

Drs. Alex Wyatt and **Kim Chi** were awarded a Canadian Cancer Society Challenge (CCS) Grant for their project titled "Accelerating clinical development of plasma ctDNA fraction as a management tool in advanced prostate cancer". The award amount is $450,000 for 3-years.

MARCH

Dr. Angie Brooks-Wilson was awarded a CIHR award for the project titled "The Genetic Architecture of Homeostasis in Health", for the CIHR Priority Announcement: Oldest Old and Centenarians. The award amount is $750,000 for 5-years.

APRIL

Dr. Poul Sorensen was awarded the Herman Suit Award for basic sarcoma research from the international Connective Tissue Oncology Society (CTOS). This award, given every year by the CTOS recognizes outstanding contributions to the basic science of sarcomas, especially research that translates into clinical benefits for patients. Sarcomas are malignant tumours of the connective tissues.

NSERC DISCOVERY GRANTS

- **Dr. Yongjin Park** was awarded a National Science and Engineering Research Council (NSERC) grant through the NSERC Discovery Grants Program, for the project titled "Statistical learning and causal inference in high dimensional genomics data across multiple information".
  The award amount is $107,500 for 5-years.

- **Dr. Andrew Roth** was also awarded the NSERC grant for his project titled, "Computational Methods for Single Cell Biology". The award amount is $157,500 for 5-years.

MAY

Dr. Poul Sorensen and co-investigator **Dr. Samuel Aparicio** are part of an international collaboration to develop treatments for osteosarcoma. The Crazy 8 Initiative will fund research into innovative and rigorous approaches that directly address the most intractable issues in pediatric cancer research today. Project teams of cross disciplinary scientists work collaboratively, accelerating the pace of new cure discovery, and each grant will provide funding for large-scale collaborative projects. The award amount is $3,100,000 USD for 4-years.

Dr. Angie Brooks-Wilson was the recipient of a competitive BC Cancer Foundation grant for "Sustaining Key Personnel for the Lymphoid Cancer Families Study". The award amount is $60,000 for 1-year.

Dr. Florian Kuchenbauer received a Pediatric Blood Cancer Research Innovation Grant from the Leukemia & Lymphoma Society of Canada (LLSC) for the project titled, "MiR-193a-based LNP drug treatment for pediatric acute myeloid leukemia". The award amount is $200,000 for 1-year.

JUNE

Dr. Brad Nelson was awarded the Bernhard Cinader Award from the Canadian Society for Immunology (CSI) for accomplishments in immunology. This annual award is the highest honour granted by the CSI, given to a Canadian scientist who exemplifies distinguished scientific leadership and accomplishments in immunology.

Dr. Poul Sorensen was awarded a Sarcoma Foundation of America (SFA) grant to examine oncofusion-driven isoforms that underpin fitness relationships essential for Ewing sarcoma tumour formation and metastasis. The goal of the SFA grant program is to encourage research that results in improved therapeutic options for sarcoma patients.
The award amount is $50,000 USD for 1-year.

AWARDS & FUNDING

2022

JULY

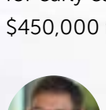
Dr. Adi Steif was the recipient of a Michael Smith Foundation for Health Research MSFHR Senior Scholar Award, which is intended to provide support for early career investigators. The award amount is $450,000 for 5-years.

Dr. Sam Aparicio was awarded a Breast Cancer Research Foundation grant renewal for his work related to patients with triple negative breast cancer (TNBC); his mission is to reduce the morbidity and mortality of TNBC patients by identifying the molecular features that distinguish one TNBC cancer from another and simultaneously suggest targets for treatment. His approach leverages new technologies such as single cell analysis, machine learning, and translational medicine to solve these challenges. The award amount is $225,000 USD for 1-year.

CIHR SPRING 2022 COMPETITION RESULTS

- **Dr. Aly Karsan**; co-investigators **Drs. Connie Eaves** and **Andrew Roth**
  - Title: Clonal interactions in myeloid malignancy $1,025,100 (5-years)

- **Dr. Laura Evgin**
  - Title: Leveraging TCR reactivity to improve CAR T therapy $745,876 (5-years)



- **Dr. Pamela Hoodless**
  - Title: Transcriptional Drivers of the Hepatic Lineage $872,100 (5-years)
- **Dr. Aly Karsan**
  - Title: Role of SASH1 in generation of hematopoietic stem cells $948,600 (5-years)

- **Dr. Inanç Birol**
  - Title: Assembly and annotation of genomes, transcriptomes, and metagenomes $753,526 (5-years)
- **Dr. François Bénard**
  - Title: Development of second-generation radiopharmaceuticals targeting the C-X-C chemokine receptor 4 for imaging and therapy of hematological cancers $860,626 (5-years)
- **Dr. Kuo-Shyan Lin**
  - Title: Next-generation GRPR-targeting radiopharmaceuticals with improved in vivo stability and minimized pancreas uptake $523,260 (3-years)

CIHR STRATEGIC OPPORTUNITY CLINICAL TRIALS OPERATING GRANT

Drs. Kevin Hay, Brad Nelson and **Robert Holt** were awarded $3.6M from CIHR for the second CLIC trial (CLIC-02) – for more information on the CLIC trial, see the full feature on page 28.

AUGUST & SEPTEMBER

Dr. Christian Steidl with **Drs. Marco Marra, Ryan Morin, Andrew Roth, Andrew Weng, David Scott, Graham Slack, Adi Steif, Laura Hilton, Connie Eaves, Kerry Savage, Jeffrey Craig,** and **Andrew Mungall** received the Terry Fox New Frontiers Program Project Grant in modeling lymphoma evolution and clinical trajectory using multiomics. The renewal program project grant is given to decipher differential histiogenic origins and modes of disease progression across a spectrum of B-cell lymphomas that are known to partially overlap in their genotypic and phenotypic features. The award amount is $6M for 5-years.

Drs. Poul Sorensen, Mitchell Cairo, and **Timothy Cripe** were awarded the National Institutes of Health (NIH) Pediatric Immunotherapy Discovery and Development Network administrative collaborative supplement. The NIH U54 collaborative supplement grant will enable the team to develop Chimeric Antigen Receptor (CAR) Natural Killer cells (NK) cells directed against IL1RAP that overcome the immunological tumour microenvironment resistance in Ewing sarcoma. The award amount is $150,000 USD for 1-year.

Dr. Aly Karsan was named a 7-year Tier 1 Canada Research Chair in Blood Cancers through the Canada Research Chairs Program with the University of British Columbia. Dr. Karsan's program focuses on acute myeloid leukemia (AML) - an aggressive blood cancer that is extremely difficult to treat and has a high fatality rate. As Canada Research Chair in Myeloid Cancers, Dr. Karsan is trying to understand how these cells resist therapy, and determine how to target them with new treatments. He and his research team are using cutting-edge genomic, epigenomic and functional techniques to examine single blood cancer cells. Dr. Karsan and his team hope to provide the knowledge needed to develop new therapies for patients who do not respond to standard treatments. The award amount is $200,000 per year.

OCTOBER

Dr. Sam Aparicio was awarded a Breast Cancer Research Foundation grant for the project titled, "Developing predictive biomarkers for genome targeting agents in TNBC, to single cell resolution". The award amount is $225,000 USD for 1-year.

NOVEMBER

Dr. Sam Aparicio was awarded a Gray Foundation grant for the project titled, "Breast Pre-cancer Atlas". The award amount is $488,950 USD for 3-years.

Dr. Sam Aparicio was renewed for a 7-year Tier 1 Canada Research Chair in Molecular Oncology and Therapeutics. Dr. Aparicio's research program aims to improve clinical outcomes for patients with cancer, building on recent insights into genomic instability and cancer evolution in triple negative breast cancers and high grade serous ovarian cancers. They will use these insights to credential new therapeutic targets and develop new single cell techniques with their Canada Foundation for Innovation (CFI) funded Cancer Single Cell Dynamics Observatory and Wellcome Trust funded Delta Tissue initiative. The award amount is $200,000 per year.

DECEMBER

Dr. Peter Lansdorp was awarded the awarded Genome Canada GAPP Grant for the project titled, "Parent-of-Origin-Aware genomic analysis". The award amount is $869,469 for 3-years.

STUDENT AWARDS

Dr. Andrew Weng was awarded the BC Cancer Foundation Research Sustainment Fund, Operating Grant for the project titled, "Epigenetic regulation of c-MYC translocation in human B-cell lymphoma". The award amount is $85,000 for 1 year (June 30, 2022 – June 29, 2023).

Dr. Andrew Weng was awarded the Leukemia and Lymphoma Society of Canada, Blood Cancer Research Jump Start Grant for the project titled, "Functional modeling of MYC translocation in follicular lymphoma". The award amount is $99,999 for 1 year (July 1, 2022 – June 30, 2023).

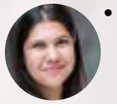
CONGRATULATIONS TO THE RECIPIENTS OF THE INAUGURAL BC CANCER RISING STARS AWARDS!

The Rising Stars program was established to celebrate **Dr. Connie Eaves'** Gairdner Wightman Award, her election to the Royal Society in the UK and her appointment to the Order of Canada. A pioneer in her field, Dr. Eaves has been a mentor to many young researchers at BC Cancer and a long-time advocate for equal opportunities in cancer research.

To honour this legacy, the awards are dedicated to the advancement of the next generation of women and BIPOC leaders in research at BC Cancer. Funding for the awards was made possible through generous donor support via the BC Cancer Foundation.

The 2022 Rising Star Recipients are:

- **Itzel Renee Astiazaran Rascon**, Molecular Oncology



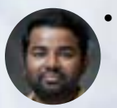
- **Sarah Dada**, Genome Sciences Centre

- **Leo Escano**, Terry Fox Lab

- **Dylan Farnsworth**, Integrative Oncology

- **Jagbir Kaur**, Nursing and Allied Health

- **Lorenzo Lindo**, Terry Fox Lab



- **Manideep Pachva**, Molecular Oncology

- **Prakruti Uday**, Terry Fox Lab

- **Elahe Shenasa**, Pathology

- **Joyce Yu-Han Zhang** , Molecular Oncology

ARTIFICIAL INTELLIGENCE IN CANCER RESEARCH: DEEP LEARNING FROM HEAD TO TOE

Researchers at the BC Cancer Research Institute are harnessing the power of artificial intelligence (AI) and deep learning to make important discoveries and advancements. From developing AI solutions to measure tumour size in various cancer types to using computational methods to understand cell interactions, BC Cancer scientists are at the forefront of cutting-edge AI applications. By applying machine learning, they aim to refine cancer diagnosis, personalize treatment selection and improve patient outcomes, advancing the fight against cancer on multiple fronts. This year, we are highlighting some of the ground breaking work carried out by BC Cancer team members who are exploring the transformative potential of AI in cancer research across the body, from head to toe.

HEAD, NECK & LYMPH NODES 12

SKIN..... 14

BREAST 16

OVARIAN.....18

PROSTATE..... 20

CELLS..... 22

HEAD, NECK & LYMPH NODES

Dr. Arman Rahmim is a provincial medical imaging physicist at BC Cancer and distinguished scientist at the BC Cancer Research Institute. His team at the Quantitative Radiomolecular Imaging & Therapy (Qurit) lab works to enhance the way medical images are generated and analyzed for clinical applications.

In 2022, Dr. Rahmim's research focused on developing AI solutions that automatically measure the tumour size or burden in PET/CT images for different types of cancers, including head and neck cancer, lymphoma and prostate cancer. By using AI techniques to reliably delineate tumour edges and extract important information such as total tumour volume, radiologists can better characterize the disease and understand the risk a patient is facing. This can improve their ability to classify patients into different treatment groups and better personalize their treatments. Members of Dr. Rahmim's team at the Qurit lab have also been working closely with AI scientists at Microsoft's AI for Health program to advance these efforts.

This past year has also been an exciting one for Dr. Rahmim and his team members, Drs. Ivan Klyuzhin and Carlos Uribe, as the group prepared to launch a BC Cancer spin-off start-up, Ascinta Technologies Inc., which provides a community and web-based hub for sharing and applying AI solutions to various clinical problems, such as cancer detection, quantification and classification. Researchers and clinicians will be able to use the Ascinta platform to share AI solutions they have developed, or search for solutions to problems they are facing, enabling other clinicians and clinical trials to benefit from each other's work.

"The reason we have created this start-up is to increase the use of AI innovation that's been happening here at BC Cancer over the past few years – both in terms of AI platform development and specific AI solutions for clinical problems – and to make it more likely for that innovation to translate to clinical usage," said Dr. Rahmim. "That's our motivation – to take it to the next level so that the rest of the world can benefit from the research and work we're doing here at BC Cancer."

SKIN

Dr. Tim Lee is a distinguished scientist and interim head in the Department of Cancer Control Research at the BC Cancer Research Institute. His work focusses on early skin cancer detection and epidemiologic research on skin cancer. In 2022, Dr. Lee's research focused on adapting deep learning to detect skin cancer from colour photographs.

Working with postdoctoral research student Dr. Yuheng Wang, Dr. Lee built a diagnostic learning system that enables physicians to submit a photograph of a skin lesion, while the learning system extracts similar-looking images from a skin image database. The system provides insight so that the physician can make a final diagnosis as to whether or not the skin lesion is malignant.

"A common drawback of using AI is that it works as a "black box"; generating predictions without explanations. To mitigate the issue, we looked for ways to include physicians into the diagnosis process, allowing them to trust the computer results," said Dr. Lee. "This type of diagnostic learning system builds trust with the users, letting them to work alongside the AI system to derive the final diagnosis."

A common issue with many AI systems is that they require huge computational costs. To address this, Drs. Lee and Wang first trained a large AI system that requires substantial resources. They then used the large system to train a smaller system and improve its detection accuracy to the point where the performance of the smaller system is on par with or better than the large system.

Since 2022, Dr. Lee has also been working to address issues around skin cancer diagnostics for people with darker skin tones. Existing image data has historically been collected from patients with fair skin tones, making skin cancer detection less accurate for patients with darker skin tones. Acquiring a sufficient number of images for patients with dark skin tones would take a long time and would be costly. To improve current diagnostic methods for people with darker skin, Dr. Lee and his research team are investigating ways to incorporate AI techniques for skin cancer detection into the workflow of physicians that will reduce the cost of applying the techniques and improve detection accuracy for patients of all skin colours across the province.

BREAST

Dr. Yongjin Park, scientist in the Department of Molecular Oncology at the BC Cancer Research Institute, focusses his work on developing a computational method that will allow learning technology to sift through the information contained in millions of cells, read their activities and organize them into common topics.

In 2022, the computational biologist turned cancer researcher, used this method to examine how breast cancer cells interact with surrounding cellular environments. He and his team discovered that the way cells communicate with each other has the potential to unlock a new avenue of research.

"A single cell is a fundamental unit of life or life-sustaining environment," said Dr. Park. "Thinking about how a potential risk factor of cancer – a bomb in the nucleus to use William Hahn's term – can work differently in different cellular environments, I started a broad hypothesis by considering the bomb may -or may not- set off depending on how we defuse the wires, or in this case, the cellular environment."

To this end, Dr. Park and his team found that gene expression patterns within cancer cells determine a substantial portion of the different types of breast cancer cells. Their machine-learning algorithms also revealed that within the same cancer cell type, there are distinct subgroups of cells that may interact differently with the surrounding environment, influenced by non-cancer cells. This means no cell acts alone, not even cancer cells. Since cancer cells lack some essential functions, Dr. Park's team believes that cancer cells borrow information they need to survive from other cells in their environment.

Dr. Park's work has also touched on pancreatic cancer. His recent work has shown that the speed and direction of how genes are expressed and regulated can be a strong clinical marker for pancreatic cancer progression. To measure this, Dr. Park and his team analyzed publicly available single-cell data from different stages of pancreatic ductal adenocarcinoma, the most common and deadly pancreatic cancer. They studied how genes in the cancer cells produced copies of their instructions, known as transcripts, and compared the number of copies before and after mRNA splicing. If a gene has more copies after splicing, it has "upward" directionality, indicating potential increased activity, and if the number of copies after splicing is lower, it has "downward" directionality, suggesting decreased activity.

"We used a machine learning algorithm to systematically detect such upward and downward patterns and organized them into dynamic topics, just as we classify an article's topic in newspapers. We then found specific combinations of genes and their directionality were significantly more prevalent in high-risk patient groups," said Dr. Park. "A traditional biomarker-based approach, including gene-based methods, often relies on the premise that gene/protein levels can be stably measured. However, we have shown that a large number of gene expressions are dynamic on the verge of either upward or downward direction."

By taking into account the dynamic information, Dr. Park and his team have uncovered a new type of gene topic linked with patients' survival risk, with potential to have a significant impact in helping clinicians monitor cancer progression in patients with deadly pancreatic cancers.

OVARIAN

Dr. Adi Steif is a scientist within the Genome Sciences Centre at the BC Cancer Research Institute. Her lab is focused on developing and applying computational methods for high-throughput genomics. This involves measuring changes in genes and their activity at scale in tumour and normal cells, and determining how these alterations impact how cancer cells develop and evolve.

In 2022, Dr. Steif's team worked with collaborators in biomedical engineering on a new platform that uses AI to improve researchers' ability to profile cancer cells for genomic analysis through neural networks; computer systems modeled on the human brain and nervous system. By combining neural networks with ink-jet printing, the platform allows rapid cell imaging and isolation, generating large datasets that can capture the diversity within tumours.

"Cells within a tumour can harbour different genetic alterations, and these differences can enable some cells to survive treatment," said Dr. Steif. "Analysing the differences between tumour cells at scale will allow us to investigate mechanisms underlying drug resistance and cancer progression."

Dr. Steif's team plans to further develop these methods as they launch a new program focused on understanding disease progression in ovarian cancer. High-grade serous ovarian cancer is very aggressive, and many patients will eventually become resistant to treatment.

However, individuals' responses to treatment vary substantially, and new technology can help shed light on why this happens and identify new strategies to improve outcomes.

"Single cell measurement technology is developing at an incredible pace, and machine learning is central to finding patterns in these large and complex datasets," said Dr. Steif. "BC Cancer has been a leader in this area, with over a million single cell genomes sequenced through our core facilities."

PROSTATE

Dr. Calum MacAulay, is the head of Integrative Oncology at BC Cancer and distinguished scientist at the BC Cancer Research Institute. During 2022, Dr. MacAulay and his team focused their research on biomedical optics and the use of AI tools in cancer imaging.

Dr. MacAulay's team developed novel deep learning tools that can accurately predict which prostate cancer patients would benefit from early treatment for prostate cancer. The AI program would look at samples taken during a biopsy to help determine the best treatment option for the patient.

"The ability, within BC Cancer of being able to work closely with my clinical colleagues and have access to patients for imaging trails has made it possible for myself and the teams I work with to develop and see implemented clinically biomedical optics / AI technologies around the world," said Dr. MacAulay. "I am very excited and optimistic that the microscopy AI based diagnostic prediction tools we have been developing over the last few years will lead to clinically implementable tests in the next few years."

The tools can accurately predict which patients would respond well to radiation treatment and which patients are likely to have recurrence even after the removal of the prostate. This information allows oncologists to identify which patients may benefit from more aggressive treatments earlier.

The tool has also been proven effective at predicting which lung or breast cancer patients have very aggressive cancer types and would benefit from aggressive new therapies delivered sooner.

Dr. MacAulay's research is also contributing to the area of early lung cancer screening that uses low dose computerized tomography (CT), a procedure that uses a computer linked to an x-ray machine to make a series of detailed pictures of areas inside the body. Along with his team, Dr. MacAulay is developing AI tools that can help to identify and differentiate early lung cancers from benign changes in CT images of a patient's lungs.

CELLS

Dr. Andrew Roth is a scientist within the Molecular Oncology department at the BC Cancer Research Institute. His lab focusses on the application of statistical machine learning to problems in cancer biology, using these tools to make sense of the thousands of measurements that come from experiments. In 2022, Dr. Roth's research focused on using new technologies to measure individual cancer cells more precisely in an effort to better understand how cancers evolve.

One aspect of this research involves trying to understand the relationship between the mutations that make a cancer cell and how it behaves. To address this, Dr. Roth's group uses statistical and deep learning AI methods to integrate multiple types of data for each cell. Another aspect of this looks at how cancer cells interact with other cells around them to understand what promotes or regulates cancer cell growth.

In 2022, Dr. Roth, together with Drs. Sam Aparicio and Alexandre Bouchard-Côté, developed an experimental and statistical approach to understand the impact different mutations have on the fitness of cancer cells. This provides a powerful approach to screen for potential therapeutic targets. Dr. Roth plans to apply this method to identify new treatment options for patients with cancers that are resistant to standard therapies.

Dr. Roth and his team also explore how single cell genome sequencing approaches can be combined with liquid biopsies, a way to monitor cancers using blood instead of tissue samples, to determine if they can measure how different populations of cancer cells fluctuate in response to treatment. Working with Dr. Jens Lagergren, Dr. Roth developed a new computational method for combining measurements of cancer DNA and RNA. This allows researchers to determine how cancer cells with different mutations in the same patient behave.

"When I started my graduate training, sequencing of tumours had just begun in research settings. We are now edging forward to sequencing of a patient's tumour at diagnosis becoming a routine part of care," said Dr. Roth. "This is one of the keys to providing more informed and personalized treatments for patients."

HARNESSING THE IMMUNE SYSTEM TO FIGHT DEADLY PEDIATRIC CANCERS

Dr. Poul Sorensen, distinguished scientist in the Department of Molecular Oncology at the BC Cancer Research Institute, has made highly significant advancements in his pediatric oncology research. In 2022, Dr. Sorensen and his team at the Sorensen Lab made exciting new discoveries that show promise in fighting pediatric cancers and beyond.

One aspect of his research built upon the knowledge that genetic alterations in childhood cancers make tumour cells more resilient, enabling them to withstand stress of the tumour microenvironment and become more aggressive. Dr. Sorensen and his team aimed to understand how tumour cells adapt to such stresses, such as reduced nutrients or oxygen levels, as this contributes to their resistance to therapy and ability to metastasize, a crucial factor in patient mortality. They discovered that many surface proteins expressed on tumour cells are important in helping tumour cells survive under stress, and that they could design an immunotherapy to target not only tumour-specific proteins, but also to target its vulnerabilities through proteins that the tumour cell needs to survive.

"By targeting these surface proteins with an immunotherapy tool, we can make tumour cells vulnerable to starvation or other stress levels," said Dr. Sorensen. "We've learned that you really have to do that in immunotherapy to have a strong chance for success, and in 2022 we've really focused on a few targets."

A key area of his research focused on immunotherapy and proteomics, discovering which proteins are expressed on the surface of tumour cells and targeting them with antibodies, and leveraging the body's immune system to fight cancer cells expressing these proteins. Dr. Sorensen and his team developed a suite of immunotherapy tools in 2022 as part of their funding from the BC Cancer Foundation, targeting surface proteins in pediatric bone cancers and in a central nervous system tumour, medulloblastoma.

Notably, this included the ability to target a protein called IL1RAP. Dr. Sorensen and his team developed CAR-T cells that bind to tumour cells that express IL1RAP, as well as antibodies carrying toxic drugs to target tumour cells expressing IL1RAP. Particularly exciting was the discovery that several adult tumours, such as melanoma, lymphoma and acute myeloid leukemia (AML) also express this surface protein, expanding the potential application of the reagents beyond pediatric cancers. This has gained interest from industry partners to collaborate on bringing the immunotherapy reagents into clinical trials.

Discretionary funding from the BC Cancer Foundation has been essential in supporting Dr. Sorensen's research, allowing his team to run programs that would not be possible with grants alone. This support has also enabled his team to be part of a global network of passionate investigators in pediatric oncology, fostering collaborations and expanding their research capabilities beyond what would be possible without the Foundation's support.

"Pediatric cancer has been instrumental in showing the world the power of immunotherapy research and targeting, and we're delighted to be part of that. The potential for clinical advancements in this field is truly remarkable," said Dr. Sorensen. "For metastatic childhood bone cancers, the survival rate is less than 20 per cent and that hasn't changed in 40 years. We need to change this outcome for patients."

Dr. Sorensen and his team are motivated to continue tackling this challenge. With the support of the BC Cancer Foundation and the global networks it has connected them to, they are excited to see that their work is contributing not only to research advancements, but also making a clinical impact for pediatric cancer patients.

ADVANCING CANCER CARE THROUGH DEDICATED CLINICAL RESEARCH

Dr. Caroline Holloway is a radiation oncologist and scientific lead of the Clinical Research unit at BC Cancer – Victoria. In addition to her medical case load, Dr. Holloway is involved in various clinical trials at BC Cancer. Clinical trials are research studies that involve patients, not just cells in a lab. Through clinical trials, doctors and researchers can discover new ways to refine treatments and improve the quality of life for people with certain diseases, including cancer. In 2022, Dr. Holloway focused her clinical research on gynecologic cancers and stewarding BC Cancer into a national collaboration for sarcoma outcomes and research, enriching our understanding of these cancers and the potential for better treatment approaches.

"As an oncologist, you understand how every change in management or technique relates to a question that was asked and answered through a clinical trial," said Dr. Holloway. "Each day in clinic, we give advice based on what we have learnt through clinical trials and how they relate to the individual patient."

To this end, Dr. Holloway and her team are participating in the Canadian Sarcoma Clinical and Research Collaboration (CanSarCC); a national initiative aimed at improving sarcoma patients' outcomes by developing a comprehensive registry that captures high-quality data from major sarcoma centres across Canada.
BC Cancer patients have already been included in abstracts and conference presentations evaluating treatments in different sarcoma patient populations.

As part of her specialty in gynecologic oncology, Dr. Holloway participated in evaluating clinical trials for vulvar, cervical and endometrial cancers. This included being part of the Taper trial for de-escalation of radiation in endometrial cancer, evaluation of the now accruing EN.10 trial in endometrial cancer and discussions on how to open BC Cancer's first surgical gynecologic oncology trial in vulvar cancer.

Additionally, her team in Victoria led a quality improvement project evaluating pathology review of endometrial cancer, which helped to support the need for pathology review of all newly diagnosed endometrial cancer patients and highlighted the need for molecular characterization of endometrial cancers. They also collaborated with colleagues at the BC Cancer Research Institute, evaluating artificial intelligence (AI) and applications in oncology imaging and outcomes for cervical cancer patients; specifically, to understand whether AI can use data from PET/CT studies to improve the prediction of outcomes for these patients.

"Working with patients is what inspires my career in clinical research," said Dr. Holloway. "Research is only possible with the support of our patients, colleagues, department, and for us, the BC Cancer Foundation, which has been instrumental in supporting my studies and the Clinical Trials unit. Whether we're opening a clinical trial or evaluating provincial outcomes, I can ensure that my patients have access to the best cancer care here in B.C."

BLOOD CANCERS REGRESSED TO UNDETECTABLE LEVELS IN OVER 40 PER CENT OF PARTICIPANTS IN AN EARLY-STAGE CLINICAL TRIAL

Directors of BC Cancer's Immunotherapy Program have seen promising results with the first 30 patients in their clinical trial using genetically engineered immune cells (CAR-T cells) to treat life-threatening relapsed and treatment-resistant blood cancers – 43 per cent of participants saw their cancer regress to undetectable levels.

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.

"When I started my career 30 years ago, the idea of treating cancer with genetically engineered immune cells was in the realm of science fiction," said Dr. Brad Nelson, scientific co-director of the Immunotherapy Program, and distinguished scientist and director with the Deeley Research Centre in Victoria. "Now we are doing exactly this, right here in B.C., and achieving impressive results for our patients."

Dr. Nelson and his Immunology Program medical co-director Dr. Kevin Hay, a clinician scientist with the Terry Fox Laboratory in Vancouver, Dr. Rob Holt, scientific co-director of the Immunotherapy Program and lead for developing this CAR-T product, together with researchers in Ottawa, are giving patients with leukemia and lymphoma an infusion of CAR-T cells that have been programmed to recognize and destroy cancer cells.

The researchers launched the first phase of the clinical trial, called CLIC-01, in October 2019. CAR-T cells are manufactured at BC Cancer in Victoria, and patients are treated at Vancouver General Hospital and The Ottawa Hospital.

CAR-T therapy worked quickly on the 30 participants who had already undergone previous cancer treatments, with significant responses seen in 77 per cent of patients at day 28 after cell infusion. The therapy was well tolerated, with only two participants (6.7 per cent) experiencing more severe toxicity, which is similar to what is seen with other CAR-T therapies.

Frontiers in Immunology (https://www.frontiersin.org/articles/10.3389/fimmu.2022.1074740/full) published the results of the trial in December 2022.

BC Cancer was the first academic group in Canada to produce CD19 CAR-T cells.

"We are doing this as cost-effectively as possible to try to ensure as many Canadian patients as possible will have continued access to this treatment," said Dr. Nelson.

Access to commercial CD19 CAR-T cells remains limited due to the logistical and financial challenges of having CAR-T cells manufactured outside of Canada.

Support from BC Cancer and BC Cancer Foundation enabled the construction of a specialized facility at BC Cancer – Victoria to manufacture clinical-grade CAR-T cell products for their patients. Funding from these sources also paid for operating expenses and patient care costs associated with this trial in B.C.

The experience of BC Cancer researchers could help others.

"Our work could guide other jurisdictions that want to create sustainable CAR-T cell programs in research settings," said Dr. Hay.

According to Dr. Nelson, the best is yet to come.

"What we're learning from treating blood cancers with CAR-T cells is now being applied to solid tumours. We are currently developing a CAR-T intervention against ovarian cancer."

ENHANCING CAPACITY FOR EQUITY-ORIENTED CANCER CARE IN B.C.

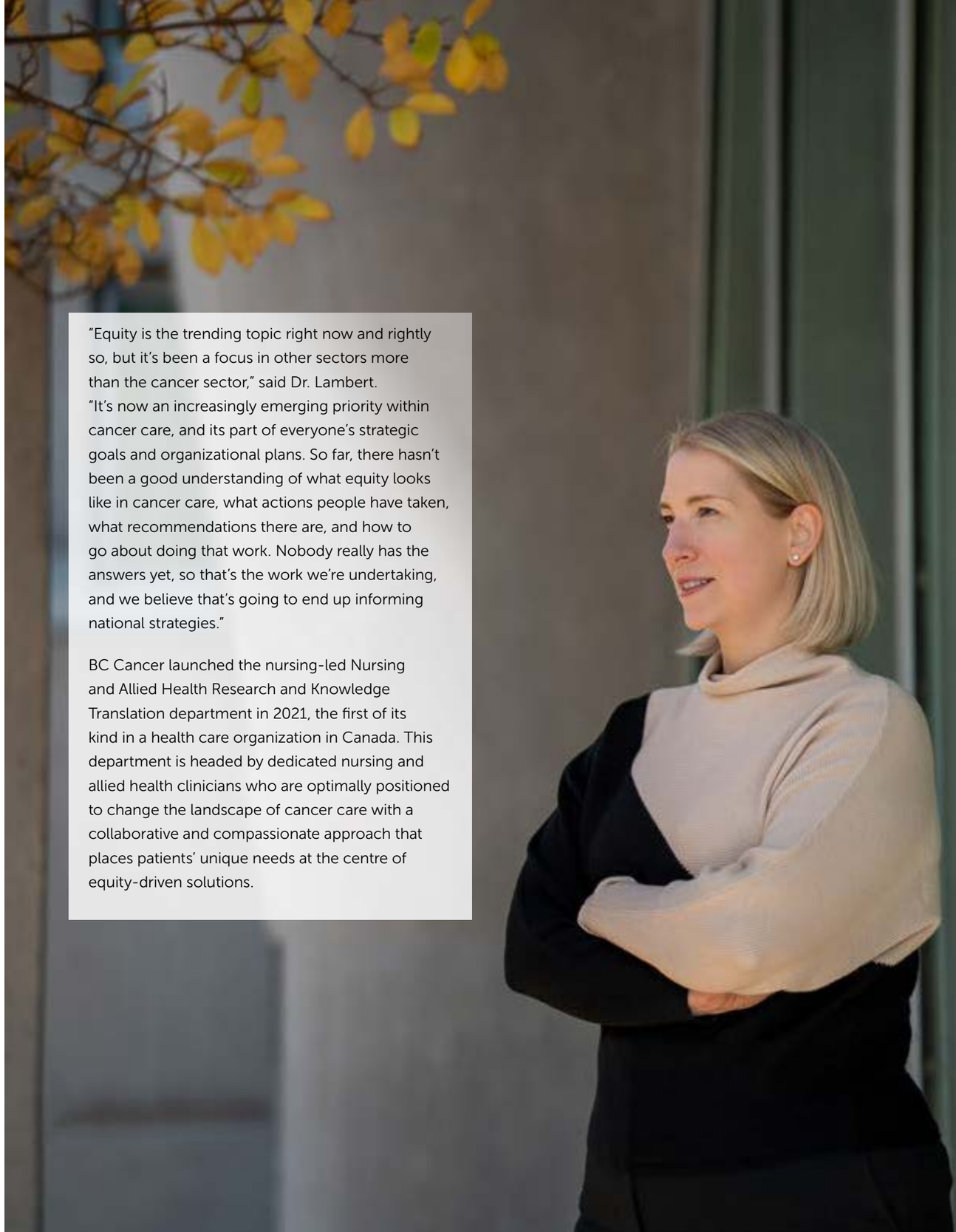
Dr. Leah Lambert, executive director and senior scientist of Nursing and Allied Health Research and Knowledge Translation at BC Cancer, is examining how cancer care practices, policies and systems are contributing to health and health care inequities. In 2022, Dr. Lambert and her team made significant progress investigating key areas of inequities in cancer care access, experience and outcomes.

The field of equity-oriented health care aims to reduce the impacts of inequities like the often-intersecting effects of poverty, discrimination and stigma that originate within the health care system itself. The cancer care system is no exception to these produced injustices. This is particularly relevant in the cancer care sector as people with lived or living experiences of inequities experience more barriers to screening, treatment, and appropriate and safe care.

To help address these discrepancies, in early 2022, Dr. Lambert led three engagement sessions to form partnerships, share knowledge and identify opportunities to advance health and health care equity in cancer care. Supported by Michael Smith Health Research BC Convening and Collaborating (C^2) funding, the sessions brought together various partners including: policy leaders from organizations such as the BC Patient Safety & Quality Council and Canadian Cancer Society, health care providers from BC Cancer centres and community partners, and members of the Senior Clinical Leadership Committee (CSLC). In collaboration with participants, Dr. Lambert and her team identified key priorities and concerns with cancer-related health equity, including how to address inequities in cancer care access, experience and outcomes at the individual and system levels.

"BC Cancer is doing foundational work with respect to health and health care equity in the cancer sector, and we are taking a leadership role that began with this C^2 = project, which has catalyzed a lot of key relationships across academia and the health system," said Dr. Lambert. "Our research team is tackling issues like how mental health and substance misuse, compounded by poverty and housing insecurity, create multiple barriers for individuals seeking or referred to cancer care."

The C^2 project sparked practical ideas, research opportunities and partnerships, leading to the formation of the Cancer Health Equity Collaborative (CHEC), one of Dr. Lambert's most significant achievements in 2022. CHEC is a team of academic and health system partners who are leading the development of new strategies to improve equity within the cancer care sector. This work aims to make equity a strategic priority through collaborating with front line community organizations and the development of organizational structures to support equity-focused care.



"Equity is the trending topic right now and rightly so, but it's been a focus in other sectors more than the cancer sector," said Dr. Lambert. "It's now an increasingly emerging priority within cancer care, and its part of everyone's strategic goals and organizational plans. So far, there hasn't been a good understanding of what equity looks like in cancer care, what actions people have taken, what recommendations there are, and how to go about doing that work. Nobody really has the answers yet, so that's the work we're undertaking, and we believe that's going to end up informing national strategies."

BC Cancer launched the nursing-led Nursing and Allied Health Research and Knowledge Translation department in 2021, the first of its kind in a health care organization in Canada. This department is headed by dedicated nursing and allied health clinicians who are optimally positioned to change the landscape of cancer care with a collaborative and compassionate approach that places patients' unique needs at the centre of equity-driven solutions.

NEW HIRE FOCUS: DR. HELEN MCTAGGART-COWAN

IS WORKING TO IMPROVE QUALITY OF LIFE ACROSS THE CANCER CARE CONTINUUM

Dr. Helen McTaggart-Cowan is a scientist at BC Cancer Research Institute with a focus on cancer survivorship research. Her research aims to improve the overall well-being of patients from the time of cancer diagnosis by maximizing their quality of life.

"Survivorship is a complex phase of care because it runs in parallel to all the other phases of the cancer care continuum; from diagnosis and treatment to end-of-life care," says Dr. McTaggart-Cowan. "With my background in health economics and patient-reported outcomes, I endeavour to address the needs of patients by implementing novel and more effective models of care. Currently, I am focused on building the survivorship work at BC Cancer in the areas of advanced and metastatic cancers."

In 2022, Dr. McTaggart-Cowan received a Michael Smith Health Research BC Convening and Collaborating grant, leading person-centred work towards identifying research priorities in the area of metastatic breast cancer to ensure meaningful work is being conducted.

"For this study, I am promoting knowledge exchange amongst patients, nurses and allied health providers, and oncologists in the province to ensure that different perspectives are heard regarding metastatic breast cancer care. The end goal is to produce a comprehensive plan of action for research, implementation, and knowledge translation for this patient population. With the goal of to improving cancer outcomes and cancer care for patients with metastatic breast cancer and their families."

One of the most significant areas of progress in cancer research that Dr. McTaggart-Cowan has seen since the beginning of her career is the engagement of patient partners in research. Patient partners ensure that their lived experiences are incorporated from the start of research design through to study completion.

"I have engaged several patient partners from BC Cancer's Patient and Family Experience on a number of different research initiatives," says Dr. McTaggart-Cowan. "In all cases, I have learned so much from them. I have been humbled by their honesty and commitment to helping to improve outcomes for others."

Dr. McTaggart-Cowan also notes that the opportunity to see the direct and meaningful impacts of her research on patients' quality of life is one of the real benefits of a research role at BC Cancer. "It is so important to treat the person as a whole. It's just as important as treating the cancer itself. Understanding the complex needs of patients during survivorship is a pressing issue that needs to be addressed, especially when it comes to improving the care of patients with advanced and metastatic cancers."

Regarding the future of oncology, Dr. McTaggart-Cowan believes that researchers and clinicians need to think beyond the classical treatment paradigms and focus on maximizing each individual's quality of life as they navigate the cancer care continuum. This may involve designing and testing models of care to enable patients to access quality cancer care in new and different ways.

She encourages young scientists to approach a career in cancer research with curiosity and determination. "I believe that constantly questioning one's own assumptions is crucial to conducting important research for both the scientific community and patients living with cancer."

NEW HIRE FOCUS: DR. RAFAEL MEZA

IS DESIGNING IMPROVEMENTS TO LUNG CANCER SCREENING & OUTCOMES

Dr. Rafael Meza, is a distinguished scientist specializing in lung cancer epidemiology, prevention, and control who recently joined the Integrative Oncology team at the BC Cancer Research Institute. His research primarily focuses on tobacco epidemiology and control and the impact of lung cancer screening.

"My goal is to characterize the impact of cancer prevention and control interventions, informing stakeholders and policy-makers on the most effective and efficient ways to reduce the burden of cancer and improve population health," says Dr. Meza. "My work at BC Cancer allows me the opportunity to have a direct impact on patients and the population at large. The cutting-edge research is designed to improve lung cancer outcomes and inform the development and implementation of lung cancer screening programs with the potential to improve health outcomes for people living in B.C. and beyond."

Dr. Meza suggests the most pressing problem facing cancer research today is the expected explosion of cancer cases in low- and middle-income countries. These countries are going through an epidemiological transition, characterized by longer life expectancies and the adoption of risky behaviors like tobacco use, which will result in increased cancer rates. Similarly, ensuring equal access to prevention and treatment options in countries like Canada to reduce cancer incidence and outcome disparities is a challenge.

The future of oncology is exciting, notes Dr. Meza, with important prevention, treatment, and care advances. "I dream of a time when lung cancer rates become much lower, and the lung cancer: tobacco epidemic is a thing of the past." Since the beginning of his career, Dr. Meza has seen significant progress in cancer research, showing that lung cancer screening works and the resulting implementation of lung cancer screening programs around the world. He also notes the improvements in lung cancer treatment, from targeted therapies to immunotherapy, have really changed the game and prolonged survival from this deadly cancer.

For young scientists pursuing a career in cancer research, Dr. Meza encourages them to consider careers in cancer prevention. "It is one of the best ways to reduce cancer's impact worldwide. Joining BC Cancer is an excellent opportunity for young scientists to learn and work with world-class cancer researchers and make a meaningful impact in cancer research."

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