SPECIAL EDITION:

Cancer Immunology and Vaccinology Research Put Dalhousie on the Global Stage

REMEDY

MAGAZINE

DALHOUSIE UNIVERSITY | FACULTY OF MEDICINE

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REMEDY

MAGAZINE

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Dalhousie University is located in Mi'kma'ki, the ancestral and unceded territory of the Mi'kmaq. We are all Treaty people.

We recognize that African Nova Scotians are a distinct people whose histories, legacies and contributions have enriched that part of Mi'kma'ki known as Nova Scotia for over 400 years.

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DALHOUSIE UNIVERSITY | FACULTY OF MEDICINE

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FEATURES & STORIES

A MESSAGE FROM THE DEAN

Dear friends,

I am honoured to share with you this special edition of REMEDY Magazine, which highlights the strength and innovation of the research teams we have built here at Dalhousie and the extraordinary strides our researchers are making in cancer immunotherapy.

Our achievements reflect the unwavering commitment of our scientists and clinicians and the vital role philanthropy plays in transforming ideas into life-saving treatments. Dalhousie has a record of success, and is home to leading research teams, and specialized infrastructure that have put us on the global stage in immunology and cancer research.

Our unique assets include the Canadian Center for Vaccinology (CCfV) and our Inflammation, Immunity, Infectious Disease, and Vaccinology (I3V) research cluster, as well as our new GMP BioLabs East. These facilities and scientists exemplify innovation and collaboration, tackling the most pressing challenges and opportunities in immunotherapy and other novel cancer treatments with groundbreaking science and a passion for improving lives.

In this special issue, you will read about our progress in harnessing the immune system to fight cancer, with a focus on meeting the distinct challenges of the people of our region. From pioneering cell-based therapies to save lives in Atlantic Canada to unlocking the potential of natural killer cells, our researchers are pushing the boundaries of possibility.

To build on this critical mass of cancer expertise and to transform health-care outcomes regionally, nationally, and globally, GMP BioLabs East is vital, and we're proud to highlight it in this issue. This critical facility for Atlantic biomedical breakthroughs will enable our researchers to advance their discoveries to clinical trials and produce immunotherapies and emerging novel treatments for people with cancer and other life-threatening illnesses.

Our mission to create healthier communities through research and education drives Dalhousie's Faculty of Medicine. This mission thrives because of the tireless efforts of our researchers and the generosity of our donors.

As you read the inspiring collection of stories in the following pages, I hope you will see the profound impact our research and philanthropists like you are making in the future of cancer prevention and treatment. Together, we can continue to advance regional discoveries and build strong national and global collaboration that will change the lives of the patients and families that cancer affects, at home and around the world.

Thank you for your continued belief in our work.

Warm regards,

David R Anderson

DR. DAVID ANDERSON
Dean, Faculty of Medicine

ADVANCING NOVEL CANCER RESEARCH AT DALHOUSIE UNIVERSITY

By Laura Eggertson & Dayna Park

Cancer is one of the most significant health challenges we face around the globe, and some of the highest rates in the country occur in Atlantic Canada. At Dalhousie University's Faculty of Medicine, our researchers are tackling this heart-breaking disease head-on.

With world-class facilities, groundbreaking clinical trials, expertise, and an unwavering commitment to innovation, Dalhousie University's Faculty of Medicine has emerged as a global leader in novel cancer immunology research, a research area allied to and benefitting from our leadership in vaccinology and our research into prevention, diagnosis and the development of novel therapeutics.

PIONEERING BREAKTHROUGHS IN CANCER IMMUNOLOGY

Our researchers are rewriting the narrative of cancer treatment by leveraging the body's immune system to fight cancer. Among the highlights of their work:

Oncolytic Viruses. Dr. Shashi Gujar's research designing cancer-killing viruses (oncolytic viruses) involves training the immune system to recognize and destroy cancer cells. His approach also aims to prevent relapses and provide long-term protection against cancer. Read more on page 8.

Natural Killer Cells. Dr. Jeanette Boudreau is studying the potential of natural killer cells to combat hard-to-treat cancers, such as pancreatic cancer. Her team's innovative research at the Beatrice Hunter Cancer Research Institute is unlocking personalized, precise cancer therapies. Learn more about Dr. Boudreau's work on page 14.

CAR-T Therapy. Dr. Mahmoud Elsawy leads Nova Scotia's CAR-T cell transplant program, providing life-saving cell transplant treatments for patients with blood cancers while addressing the therapy's impact on individuals with underlying conditions. His research involves tailoring those treatments to people with prior underlying lung, liver and kidney disease. Read about CAR-T cell therapy on page 16.

INNOVATION IN CANCER DIAGNOSTICS AND PREVENTION

The fight against cancer begins with prevention and early detection. Dalhousie researchers are also at the forefront of:

Biomarker Development. Dr. Robin Urquhart's work on biomarkers is advancing early detection methods, particularly for non-smokers at risk of lung cancer due to environmental exposures. This research will identify specific molecular markers in blood or tissue that signal the initial stages of cancer, enabling timely and potentially life-saving interventions. Read about lung cancer biomarkers on page 28.

Gene Sequencing. By analyzing the genetic profiles of patients with cancers prevalent in Atlantic Canada, our researchers are uncovering their specific mutations that drive tumour growth. This information is crucial for developing treatments tailored to an individual's unique genetic makeup, improving outcomes, and reducing unnecessary side effects.

Cancer Screening Programs. Our research teams are refining strategies to detect lung cancer at earlier, more treatable stages, through advanced imaging and risk assessment tools. These efforts are vital in Nova Scotia, which has among the highest rates of lung cancer in Canada.

Dietary Insights and Chemoresistance. Dalhousie scientists are identifying cancer-fighting compounds in common foods, such as spices and vegetables, which may enhance the efficacy of traditional treatments. Additionally, they are exploring methods to overcome resistance to chemotherapy, a major challenge in treating recurrent cancers.

Radon Exposure Studies. Recognizing that environmental factors play a significant role in cancer risk, our researchers are developing biomarkers to assess exposure to radon and other carcinogens, such as lead, elevated levels of which occur in high rates in Nova Scotia. This work informs public health initiatives to reduce exposure and prevent cancer development.

BRIDGING THE GAP BETWEEN RESEARCH AND IMPACT

Our new GMP BioLabs East facility exemplifies Dalhousie's commitment to transforming research into patient outcomes for Atlantic Canadians. This state-of-the-art centre, which adheres to Good Manufacturing Practices (GMP) and specialized lab certification, will accelerate the development of therapies from the lab to clinical trials, by creating proof-of-concept and small batches of immunotherapies as well as vaccines. This facility will enable local production of new and emerging personalized cancer treatments, ensuring that our region has access to the latest in cancer care. Read more about BioLabs East GMP facility on page 14.

GLOBAL LEADERS IN IMMUNOLOGY

Canadian Centre for Vaccinology (CCfV) and our cluster of researchers in Inflammation, Immunity, and Infectious Disease (I3V) are harnessing the power of the immune system to improve health. From advancing vaccines to developing cancer immunotherapies, these groups have earned international recognition for their contributions to science and health. Learn more about the I3V team and the CCfV on page 30.

A CALL TO ACTION

This trail-blazing research is only possible because our donors and community partners support us. Together, we can create a world where we prioritize prevention and early diagnosis, and develop more effective, less challenging treatments, so cancer is no longer a life-ending disease.

National Cancer Institute, Unsplash

COLLABORATION GENERATES BREAK-THROUGHS

DR. SHASHI GUJAR STRIKES UP GLOBAL PARTNERSHIPS IN BID TO IMPROVE CANCER CARE

By Kate Rogers

Drew Hays, Unsplash

Dr. Shashi Gujar, second from right, and his research team. Dr. Gujar is positioned to take Dalhousie from a world-class to a world-leading institute in the field of cancer immunotherapy.

Provided by Dalhousie

A Dalhousie researcher is poised to lead a revolution in cancer treatment through global partnerships.

Dr. Shashi Gujar, the executive director of Cancer Immunotherapy, Innovation and Global Partnerships in the Faculty of Medicine, is developing innovative immunotherapy options for the diagnosis, prevention, and treatment of cancers.

Cancer immunotherapies are a form of precision medicine that train our immune system to fight cancers without the usual harmful side effects of traditional treatments like chemotherapy and radiation. Dr. Gujar is developing various forms of cancer immunotherapies such as cancer vaccines, cancer-killing viruses, and light-activated anti-cancer drugs.

Through strategic international partnerships, Dr. Gujar will leverage the resources needed for his ground-breaking research enterprise to rapidly advance cancer immunotherapy discoveries in clinics and save lives sooner.

ENSURING MEDICAL DISCOVERIES REACH PATIENTS FASTER

The global COVID-19 pandemic has demonstrated that society can and must develop medical innovations more quickly than previously demonstrated.

Accelerating the discovery and development process requires prompt access to highly qualified personnel, sufficient patient populations for clinical testing, and immunotherapy manufacturing facilities, such as Dalhousie's new GMP BioLabs East facility (see story page 14). These components are limited across the country, placing Dalhousie in an excellent position to surge ahead in these advances, especially once BioLabs East is up and running.

"Cancer immunotherapies are doing wonders for many patients and creating survival stories for their loved ones," Dr. Gujar says. But for a subset of patients, immunotherapies do not work as well.

Currently, Dr. Gujar and his team are focusing on understanding why immunotherapies do not work well in aged and frail individuals. Recently, his team received a $9.1-million grant to establish advanced, first-of-its kind infrastructure in Atlantic Canada to find novel innovations promoting the efficacy of immunotherapies in the aged and frail.

Through global partnerships, Dr. Gujar is also building on Dalhousie's expertise to drive innovation and accelerate the translation of exciting medical discoveries in patients.

"We know that we need major improvements in how we diagnose, prevent and treat cancer, and more importantly, we need it faster," says Dr. Gujar. "We don't have time to wait for another 15 years for every innovation to be translated in patients, and so we are working with global partners to access the best of the best capacities in the world."

ACCESS FOR ALL

Dr. Gujar has established formal partnerships with academic, clinical and industry leaders from the United States, the United Kingdom, France, Denmark, Germany, South Korea, India, and Japan, which are facilitating an internationally collaborative and

competitive cancer immunotherapy research program he is leading from Atlantic Canada. This initiative is set to play a leading role in the rapid development of new cancer immunotherapies and make these therapies available and affordable to patients at home and around the world.

“Cancer immunotherapy is very expensive right now,” says Dr. Gujar. “We are working with true global partnerships hoping we will be able to create affordable cancer immunotherapy that will be available not only for Canadians, but to all the global citizens worldwide. We want all people to have access to these amazing therapies.”

A WORLD LEADER IN CANCER CARE

Dr. Gujar is poised to take Dalhousie from a world-class to a world-leading institute in the field of cancer immunotherapy. He would like to see this important research create opportunities to work in partnership with global organizations, including the World Health Organization (WHO) and the United Nations (UN). From a strategic perspective, this initiative will align the Faculty of Medicine’s future directions not only with Dalhousie, but with the international players who are pushing for better human health.

Though he looks forward to sharing Dalhousie’s exciting work, Dr. Gujar reiterates the importance of collaboration and contributing to the greater good.

“We know success cannot be achieved by working in silos,” he says. “But when we work together as a global community, we can do amazing things.”

The generous support of donors is critical to the success of Dr. Gujar’s mission and goals.

“Unfortunately, existing funding mechanisms available to researchers in Canada are inadequate to enable operationalization of such global initiative,” says Dr. Gujar. “This groundbreaking work is possible only through a dedicated philanthropic championship.”

“We don’t have time to wait.”

- DR. SHASHI GUJAR

HARNESSING THE POWER OF VIRUSES TO KILL CANCERS

By Alison Auld

A new paper from Dr. Shashi Gujar and research colleagues provides guidelines for the design, production and preclinical testing of viruses that infect and destroy cancer cells while also promoting protective antitumour immunity.

In the global hunt for both a cure and treatments for cancer, researchers are finding the very viruses we try to shield ourselves against hold great promise in fighting the deadly disease.

Researchers are studying pathogens—those bugs that routinely infect and sicken us, like the common cold or influenza—in labs around the world to see if they can be used safely and effectively to alert the immune system to attack and kill cancer cells. This is not a new theory, but it is showing such success that scientists are now exploring the prospect of using a range of viruses to combat cancer.

Oncolytic (or cancer-fighting) viruses are powerful tools once researchers have selected or re-engineered them to be benign. Scientists either use naturally occurring viruses or genetically engineer viruses to replicate swiftly inside cancer cells, causing them to burst and trigger an immune response within the body to rid it of any remaining cancer.

"As long as a virus is safe and not causing any disease, we can engineer it to be used as a cancer therapy," says Dr. Shashi Gujar, a cancer researcher and professor at Dalhousie who specializes in immunotherapy.

"This is an amazing technology and has so much potential," Dr. Gujar adds. "However, we need to make sure that this technology gets developed with stringent standards at the global stage. This will ensure that these amazing anti-cancer drugs are developed in a proper manner and reach cancer patients faster."

To that end, Dr. Gujar and colleagues who are driving this emerging technology created a guidebook with standards on how to develop and use these oncolytic viruses.

Dr. Gujar, along with pioneers Dr. Guido Kroemer of the Centre de Recherche des Cordeliers in Paris and Dr. John Bell of the University of Ottawa, released a paper in the journal *Nature Protocols* to guide researchers on the design, production and testing of these oncolytic viruses in cancer immunotherapy, a type of treatment that relies on using the body's own immune system to rid it of cancer.

TURNING ENEMIES INTO ALLIES

The paper describes oncolytic viruses as a novel class of cancer immunotherapy agents that infect and destroy cancer cells, while also providing a secondary benefit of promoting protective antitumour immunity.

But how does that work?

"Our immune system is designed to recognize threats in a very specific manner. When we are infected with a virus or bacteria, our immune system can immediately recognize them as 'foreign' and mount an effective immune response to eliminate them," says Dr. Gujar.

Cancers can fool the body because they have similar characteristics as healthy cells. That makes the immune system think they are not a threat, allowing the cancer to 'hide' and spread.

Decades ago, scientists began asking whether viruses, which an effective immune response eliminates, could be used to target cancer cells. They had observed that some cancer patients who developed infections reported their cancer cells decreasing or disappearing.

More recently, studies have suggested that cancer patients who developed COVID-19 saw their cancer regress following their recovery from the COVID infection.

"That's what these viruses do — they get the attention from your immune system and get them to attack the cancers," Dr. Gujar says.

"It's almost the equivalent of indirect vaccination of a person. For example, if you want to train your immune system to resist COVID, you give a COVID vaccine. Here, if you want to train your immune system to attack cancer, you use an oncolytic virus because it will train your immune system to recognize cancer as a threat."

FROM TESTING TO THERAPY

Before oncolytic viruses can be used in therapy, they need to be tested to make sure that they don't cause illness and target only cancer cells.

The United States, China, Europe, and Japan have approved oncolytic virus technology, which has been used successfully to treat several cancers, such as melanoma. The herpes simplex, reovirus, measles and adenovirus are among the viruses researchers are considering using for cancer treatment.

Canada is at the forefront of oncolytic virus research and has some of the world's largest labs focused on its development. Before Health Canada approves any oncolytic virus therapies produced here, however, researchers must create proof-of-concept formulations and then certify that they have produced the therapies according to Good Manufacturing Practices (GMP) and in GMP-certified lab facilities. They can then proceed to larger clinical trials.

Dr. John Bell, who co-authored the paper with Dr. Gujar and was one of the first scientists working on oncolytic viruses in Canada, says the paper is aimed at ensuring people who enter the field follow best practices so new knowledge meets international standards.

The paper covers everything from which viruses researchers should use and what their characteristics are, to the process of getting ready to apply for clinical trials.

"Exciting new clinical data from a number of oncolytic viruses is building excitement in the field," says Dr. Bell. "It is critical that rigorous standards are set to allow comparison of the safety and efficacy of these innovative virus products."

"As long as a virus is safe and not causing any disease, we can engineer it to be used as a cancer therapy."

- DR. SHASHI GUJAR

BRIDGING THE GAP

DALHOUSIE'S NEW BIOMANUFACTURING FACILITY ACCELERATES RESEARCH, TRIALS AND TREATMENT

By Emm Campbell

A cure for cancer. It's long been a holy grail for researchers like Dr. Jeanette Boudreau. The associate professor with Dalhousie's departments of Microbiology & Immunology and Pathology may be on the verge of better treatments using one of the most powerful weapons we have in this ongoing fight: the human immune system.

Dr. Boudreau is looking at the potential of using white blood cells, known as natural killer cells, as immunotherapies for cancer. Her research into these cells, which have proven effective in treating leukemia, shows promise. But until recently, Dr. Boudreau faced a significant challenge: a lack of publicly owned biomanufacturing facilities in Atlantic Canada to help her take this innovative idea from the lab to patients' bedsides.

"It's not just the ability to transform living organisms like white blood cells into vaccines and therapies that is missing here," Dr. Boudreau explains. "It's the ability to do what we call preclinical testing—figuring out dosing and toxicity—so these therapies are ready for prime time. Without a facility in place that can do all that, you either have to convince somebody else to pick up your discovery and run with it or you shelve it."

Thanks to Dalhousie's Faculty of Medicine, that facility is becoming a reality. Supported by the fundraising efforts of Dalhousie's Bringing Worlds Together campaign, the Faculty is collaborating with Nova Scotia Health, the IWK Health Centre, the Canadian Center for Vaccinology (CCfV), and Life Sciences Nova Scotia to bring the facility, to be called GMP BioLabs East, to life.

BioLabs East will provide researchers like Dr. Boudreau access to biomanufacturing infrastructure, processes, and personnel that will help researchers turn scientific discoveries into life-changing medicines.

"We have great discovery research taking place at Dalhousie and across Atlantic Canada," says Dr. David R. Anderson, Dean of the Faculty of Medicine. "What we have not had is a pipeline—a good manufacturing practice facility—for our researchers to translate their discoveries into drugs that can then be used in clinical trials. GMP BioLabs East fills that gap by creating an ecosystem for medical innovation in our region."

Researchers in the Faculty of Medicine, such as the Canadian Center for Vaccinology teams led by Drs. Scott Halperin and Joanne Langley (MD'84, PGM'85), first envisioned the biomanufacturing facility in 2021. In 2022, their vision came into greater focus when the Government of Canada announced $2 billion to support such infrastructure across the country.

The scarcity of this infrastructure contributed to the challenges Canada faced both in commercializing and securing vaccines during the COVID-19 pandemic. Since then, Dal researchers have been building the partnerships necessary to bring this facility to life.

"The pandemic taught us that by prioritizing collaboration, industry partnerships, specialized facilities, and skilled personnel, we could shorten the 15-year innovation pipeline significantly," Dr. Anderson says. "That's what BioLabs East is all about. It enables us to accelerate the translation of groundbreaking scientific research into health solutions that make a difference now."

The health solutions that Dalhousie Faculty of Medicine researchers envision range from vaccines that treat influenza to the development and production of novel cancer immunotherapies. But before GMP BioLabs East can run with new ideas, it will need to demonstrate that it can produce the same high-quality biomaterials that other facilities create.

Enter Dr. Mahmoud Elsawy, an assistant professor, and a hematologist with the Department of Medicine's Division of Hematology. Like Dr. Boudreau, Dr. Elsawy is interested in the potential of the immune system to cure cancer. His weapon is chimeric antigen receptor (CAR) T-cell therapy. This highly sophisticated and effective approach takes patients' white blood cells, known as T-cells, and genetically engineers them to fight blood cancer before putting them back in a patient's body.

Although he is seeing impressive outcomes among his patients, Dr. Elsawy must send their T-cells to the United States for reprogramming, which is not only costly, but also creates significant wait times in treating a disease where time is of the essence. The new facility will enable Nova Scotia to modify CAR-T cells here at home, ensuring Dr. Elsawy's patients receive this immunotherapy treatment more quickly, at a significant cost saving for the province.

"Currently, it takes about three to four weeks to get these therapies back," says Dr. Elsawy, who led the introduction of CAR T-cell therapy in Nova Scotia. "Meanwhile, those cancers are growing. With GMP BioLabs East, we could get that turnaround down to two weeks or less and a much lower cost for the health-care system. That would help make a more affordable, effective, and timely made-in-Nova-Scotia CAR T-cell therapy available. It would also create opportunities to explore how we can use CAR T-cell therapy to treat other cancers, such as solid tumours."

Once it is up to speed, GMP BioLabs East will initially focus on supporting the research of Dalhousie's Infection, Immunity, Inflammation, and Vaccinology (I3V) research team, which is making significant contributions to the prevention and treatment of infectious diseases, chronic inflammation, and cancer.

The ultimate goal is to make the facility's biomanufacturing and testing expertise available to researchers and life sciences organizations across Atlantic Canada. Sean Awalt, CEO of Life Sciences Nova Scotia, an industry association dedicated to helping startups succeed, says that will be game-changing for the industry.

"Right now, companies developing innovative biotherapeutics have to look outside the region to commercialize them," Awalt says. "They must access larger markets like Montreal or Boston to continue developing their product, which is an unfortunate loss for Nova Scotia. This facility is going to enable entrepreneurs and companies to stay here and develop their innovations. It will also create opportunities for us to develop and retain biomanufacturing talent and collaborate with global biopharmaceutical companies. That's not just going to help our life sciences sector grow, but also our economy."

Dr. Anderson agrees GMP BioLabs East is going to transform the region and patient care.

"It is really going to put Atlantic Canada on the cutting-edge in terms of making new treatments available," he says. "That means we won't have to wait in line or be dependent on another country or region to secure our share in the midst of another crisis like COVID-19. We will have those treatments available here for us when we need them."

"The pandemic taught us that by prioritizing collaboration, industry partnerships, specialized facilities, and skilled personnel, we could shorten the 15-year innovation pipeline significantly."

- DR. DAVID R. ANDERSON

NEW CELL-BASED CANCER THERAPY

SAVES LIVES IN NOVA SCOTIA

By Laura Eggertson

Charles Jesso was 57 years old when Dr. Mahmoud Elsawy called him into his office on January 6, 2022.

"The chemo isn't working," Dr. Elsawy told Mr. Jesso.

Mr. Jesso had just completed his second round of chemotherapy. The year before, he had been diagnosed with non-Hodgkins' lymphoma, the fifth most-common blood-based cancer in Canada.

If the powerful cancer-fighting drugs hadn't stopped the cancer's progression, Mr. Jesso knew he was out of conventional options.

"Basically, I had six to eight months to live," Mr. Jesso says. Then Dr. Elsawy offered a potential lifeline.

He wanted Mr. Jesso to try a new kind of cancer treatment, called chimeric antigen receptor (CAR-T) cell therapy. The process involves genetically re-engineering a patient's T-cells, programming these immune cells to recognize and destroy cancerous cells.

This new type of immunotherapy had been around to treat certain types of lymphoma and leukemia for less than five years, after conventional chemotherapy had failed. But only select cancer centres in the United States and in Ontario and British Columbia offered the treatment.

In about half the patients, CAR-T cell therapy put their cancer into complete remission: a breakthrough, considering the deadly nature of the cancers.

"When this treatment came along, it was a game-changer," says Dr. Elsawy. "It was revolutionary in changing the natural history of this disease. We have people who were destined to die within six months … and are now living for many years, cancer-free."

Dr. Elsawy, a specialist in blood diseases and cell therapies, had seen the therapy's effectiveness firsthand during his training in the United States and Canada. He brought the first CAR-T cell clinical trial to Nova Scotia, using cells re-engineered at a lab in the United States. This initial research became the basis of the program Dr. Elsawy now leads in Halifax.

Through his own research projects, Dr. Elsawy studies the quality of life of CAR-T therapy recipients, as well as the therapy outcome for patients who have prior lung, liver, or kidney disease in addition to cancer.

Dr. Elsawy thought Mr. Jesso was a good candidate for the therapy – but the Nova Scotia program was not yet quite ready to roll.

Mr. Jesso could go to Boston for CAR-T cell therapy, Dr. Elsawy told him, or wait to see if Nova Scotia Health would approve funding to deliver the therapy in Nova Scotia.

BEST CHANCE

There were no guarantees CAR-T would work, Dr. Elsawy told Mr. Jesso. But it was his best shot.

Mr. Jesso agreed to try the CAR-T cell therapy. He decided to try to wait as long as possible to go to Boston, hoping the program would start in Halifax.

"The bottom line is – was there an alternative? You're willing to do anything if you're given two options, and one is that you die," Mr. Jesso says.

Mr. Jesso began one additional short course of chemotherapy to prepare his body for the re-engineered T-cells. Then—just as he thought he would have to go to Boston, far from his family—Nova Scotia Health agreed the Nova Scotia program was ready to start. That meant he could stay close to his family while he had the therapy.

On April 4, 2022, Mr. Jesso received an infusion of his own T-cells. They had been re-engineered at a pharmaceutical facility in California and then sent back to the Queen Elizabeth II Health Centre. Nova Scotia did not have the capacity to conduct the genetic engineering itself.

The procedure itself was simple. Mr. Jesso received his own reprogrammed cells, injected into his bloodstream through a port in his chest, similar to a blood transfusion. Five minutes after it started, the treatment was over.

"You don't feel anything," he says.

For the next three weeks, Mr. Jesso stayed in hospital, cared for by a team specially trained to watch and mitigate reactions. On two occasions, Mr. Jesso suffered serious but largely reversible side-effects that sent him to the intensive care unit, the first episode just eight hours after the infusion. Unlike chemotherapy, however, the CAR-T therapy did not make Mr. Jesso feel nauseous or sick, and he had no pain.

CANCER-FREE

Over the next few months, imaging scans showed the cancer vanishing from Mr. Jesso's body. In November 2022, he walked his daughter Angela down the aisle. And in December, eight months after the treatment, he returned to work full-time.

"I'm feeling fantastic," Mr. Jesso says.

Two years later, Mr. Jesso is cancer-free. He takes no medications and does not expect to need any further treatments, since CAR-T is designed to be a "one and done" therapy.

"It's definitely a new beginning," Mr. Jesso says. "It's the Phoenix, always rising from the ashes, because when you're told you only have a couple of months to live, and you get a procedure and you live — that's a rebirth."

Since Mr. Jesso received his treatment, Dr. Elsawy and his team have treated 24 other patients with lymphoma that was not responding to chemotherapy with CAR-T cell therapy. The therapy has put more than half—57 percent—of those patients into complete remission, Dr. Elsawy says.

LIVING DRUG

"This is a living drug, meaning that with only a single infusion, the cells continue to proliferate, persist inside the body, and fight cancer," Dr. Elsawy says. "That leads to responses deepening over time until they cancer is fully eradicated."

In total, 80 per cent of the CAR-T patients Dr. Elsawy has treated were alive at their last follow-up appointment. By contrast, fewer than 20 per cent would likely have survived as long following conventional chemotherapy, he says.

Mr. Jesso believes his life-saving experience emphasizes the critical importance of research, often supported by donors who might one day need similar treatment themselves.

"You will never know when you're going to need help," he says.

He couldn't be more grateful for the care he received from Dr. Elsawy and his team, and he can't wait to make his next milestone: holding his new grandchild.

"Bottom-line is – you're speaking to someone who was supposed to be dead," Mr. Jesso says. "It's a miracle procedure."

CAR-T therapy is just the beginning of a revolutionary field of personalized, cell-based therapies to treat cancer. The therapy is also promising for other conditions, including auto-immune diseases. Without regional production capacity, however, this treatment would remain very expensive for our healthcare system, limiting its availability.

The U.S. Food and Drug Administration has just approved another type of immune cell therapy, called tumor-infiltrating lymphocytes therapy (TIL), to treat melanoma. Dr. Elsawy hopes to see TIL therapy available to Nova Scotians soon.

Dr. Mahmoud Elsawy

Facilitating CAR-T and immunotherapy research and producing this novel therapy have become top priorities for Dalhousie University. The university, along with its partners at Nova Scotia Health, the IWK Health Centre, and Life Sciences Nova Scotia, is raising money for GMP Biolabs East. This research and biomanufacturing facility will host this important work and provide Dr. Elsawy and his team with Nova Scotia's own CAR-T cell manufacturing lab.

Having an in-house lab will enable Dr. Elsawy and other clinicians to deliver the life-saving therapy to patients faster, saving them valuable weeks, while reducing the burden on our health-care system.

Together, the new facility and new cell-based therapies offer real hope to cancer patients like Mr. Jesso.

"CAR-T therapy is a lifeline for certain blood cancers," Dr. Elsawy says. "It's just a matter of time before these cell-based therapies go everywhere, beyond cancer treatment."

- DR. MAHMOUD ELSAWY

CHANNELLING THE POWER

OF NATURAL KILLER CELLS TO BEAT CANCER

By Laura Eggertson

Pancreatic cancer is one of the most difficult cancers to treat successfully, and one of the chief targets of the natural killer cell research Dr. Jeanette Boudreau and her graduate students and post-doctoral fellows pursue.

When Dr. Jeanette Boudreau envisions the future of treating pancreatic, ovarian, and colorectal and cancers that are difficult to cure, she can't contain her excitement.

Dr. Boudreau, an immunologist and the scientific director of the Beatrice Hunter Cancer Research Institute, is pinning her hope—and her knowledge—on Natural Killer (NK) cells. These white blood cells, which circulate constantly through the bloodstream and tissues, eliminate viral infections and sick cells, including cancer cells.

Dr. Boudreau's research focuses on how to aim those cells at specific types of hard-to-treat cancers, super-charging the immune system to recognize the signals these tumours emit and then destroy them." The way I see the future, there are vats of these things being made, and in the same way you (now) order up platelets or red blood cells for a transfusion, an oncologist could order up NK cells for therapy," says Boudreau, who is also an associate professor and Cameron cancer scientist at Dalhousie.

"This is obviously down the road, but that's the space I am hoping we land in."

KILLING PANCREATIC TUMOURS

Pancreatic cancer is one of the most difficult cancers to treat successfully, and one of the chief targets of the natural killer cell research Dr. Boudreau and her graduate students and post-doctoral fellows pursue.

PhD candidate Stacey Lee, who studies in Dr. Boudreau's lab, has already demonstrated that NK cells can kill pancreatic cancer tumours. She has also created a mouse model with human tumours, which she can treat with human NK cells.

Lee's work creates a living system the researchers can study. Thanks to her model, Lee has identified four proteins from pancreatic tumours she believes she can treat with NK cells — creating the foundation for more precise immunotherapy. Using donated tissue samples from patients undergoing surgery, a second PhD student, Riley Arseneau, identifies genetic mutations in the tumours removed. She's also identifying the genomic and genetic sequences of people in the Maritimes who come to Halifax for pancreatic cancer treatment.

Identifying those mutations is important. A small percentage of people with two types of gene mutations, called BRCA 1 and BRCA 2, respond better to a drug called cisplatin than they do to the usual chemotherapy cocktail for pancreatic cancer.

If Arseneau can also identify additional, rarer mutations in people's tumours, the information will help doctors plan treatments that will work better for each individual. Identifying mutations specific to the Maritime population will guide the type of precision therapy each patient would receive, Dr. Boudreau says.

Dr. Boudreau, Lee, Arseneau, and other team members are also building model systems of pancreatic tumours. They're gathering evidence to make the case that everyone diagnosed with pancreatic cancer should automatically have their tumours analyzed genetically. That analysis would help to identify the best approach to treatment, using chemotherapy that is already available here. This type of precision medicine does not require a clinical trial to implement – it could be happening now, Dr. Boudreau emphasizes.

"Our genetics aren't informing [pancreatic cancer] treatment today, but they could be tomorrow, if we can just say 'this is the difference you could make'," she says.

Once Dr. Boudreau and her colleagues understand the genetics of the Maritime population and the role NK cells can play in tackling pancreatic and other types of cancer, they can design new genetic-based therapies she says.

DEMOLISHING OVARIAN CANCER CELLS

Ovarian cancer is another focus of researchers in Dr. Boudreau's lab. PhD students Sarah Nersesian and Morgan Pugh-Toole, alongside MSc student Anna Nicolela, are determining ways to get natural killer cells to demolish ovarian cancer cells. This team shares their observations with Emily Carter, an MSc student, who is figuring out how to make large numbers of NK cells. She's using Lee's mouse model to test her hypotheses.

"A good chunk of my lab is working on NK-cell based therapies for ovarian cancer, focusing a lot on the way the NK cells direct the rest of the immune system to interact with the tumors," Dr. Boudreau says.

New therapies using NK cells are five to 10 years in the future for hard-to-treat tumours like those in ovarian cancer, Dr. Boudreau estimates. But in other diseases, like pancreatic cancer, it may be possible to help at least a proportion of patients by implementing gene sequencing right away, she says.

One of Dr. Boudreau's critical roles is to work with patient partners, oncologists and other clinicians treating patients with cancer, to bring all parties the latest developments in immunotherapy research and treatment advances.

The clinicians Dr. Boudreau works with are eager to learn about and translate the discoveries researchers have made.

"We've got some really fantastic partnerships that we have formed," Dr. Boudreau says.

Meanwhile, she focuses on making a difference in people's lives today, even as she also moves the dial on research that will deliver better outcomes tomorrow.

"I'm trying my best to do things on a scale that could be implemented, are not too expensive, and could be done with the processes that already exist, as patients are already being treated," says Dr. Boudreau.

The research Dr. Boudreau and her team is vital. Although immunotherapy is quickly becoming a mainstay of cancer treatment, it's expensive and can be challenging to deliver, she points out.

"We think with NK cells we can make a scalable, much more affordable immunotherapy, so we can treat more patients."

“A good chunk of my lab is working on NK-cell based therapies for ovarian cancer, focusing a lot on the way the NK cells direct the rest of the immune system to interact with the tumors.”

DR. JEANETTE BOUDREAU

SUPPORTING BREAK-THROUGH RESEARCH

A DONOR'S STORY

By Laura Eggertson

When doctors diagnosed Bonnie Salsman's husband Rick with pancreatic cancer, the couple searched for treatment to alleviate his suffering and prolong his life.

Bonnie and Rick Salsman

"With pancreatic cancer you struggle to find hope, because the diagnosis is so dire," Bonnie Salsman says. "There's a lot of suffering, at least there was in his case." Rick received chemotherapy at the QEII Hospital, and although the couple also travelled to Boston for advanced radiation treatment that Bonnie believes helped Rick live for nearly 18 months, his treatment did not improve his quality of life drastically.

"He didn't get a lot of really comfortable days in that period," she says.

One of the brief periods of time when Rick's pain was manageable coincided with the birth of their grandson, Théo.

"We were able to have that joy and that period of time as a family," she says.

Before Rick died at 68, he made it clear to Bonnie he wanted her to donate money to research for pancreatic cancer. So, in 2021, and again in 2023, Bonnie and her family donated to Dalhousie's Faculty of Medicine to the research Dr. Jeanette Boudreau and her team are conducting into a type of white blood cells called natural killer cells.

Natural killer cells, or NK cells, are important players in the body's immune system. They already work to kill cancerous cells, viruses, or bacteria, although sometimes cancer cells are able to evade them.

IDENTIFYING GENETIC MUTATIONS

Dr. Boudreau and her graduate students and post-doctoral fellows are developing ways to aim these impressive defenders at specific cancer cells, such as those populating pancreatic cancer tumours.

They're also analyzing samples from the tumours of people in Atlantic Canada who have had surgery for pancreatic cancer, to identify which genetic mutations exist in their cancers and match those mutations to existing drugs or new drugs in clinical trials. Making those matches could provide new treatment avenues for people with pancreatic cancer.

When deciding what type of research to support, a desire to help fund something that would make a real difference motivated Bonnie and her daughter Katherine.

"After you experience the devastation that cancer can cause, you realize how important it is to support the people who are looking for ways to help."

- BONNIE SALSMAN

Unsplash

Their first donation financed a studentship, to support one of Boudreau's graduate students, who conduct the experiments driving the advances the lab is making."Some of the most important breakthroughs in cancer have happened through the type of research Dr. Boudreau and her colleagues are doing," says Bonnie.

"They're not driven by how much money this is going to make. They're truly trying to help humanity."

Bonnie has a simple message to others who might be thinking about giving to cancer research. "After you experience the devastation that cancer can cause, you realize how important it is to support the people who are looking for ways to help."

She's thankful that Rick, a retail entrepreneur, and an adventurer who was able to retire early, had the chance to achieve one of his life-long goals. In 2007, he and Bonnie, with help from family and friends, sailed their boat Aisling 1 across the Atlantic. She hopes her family's donation will help others get the chance to achieve their goals.

"I worked in hospital pharmacy for a lot of my career, and I have had a chance to see some of the things that have been game-changers. I know it's possible," she says.

DAL ALUMNI COUPLE DONATES TO CUTTING-EDGE CANCER THERAPY

By Laura Eggertson

Dr. Mark Johnston and Dr. Ann Swain have the best reason in the world to be giving back to Dalhousie University's Faculty of Medicine: medical research saved their son Ewan's life.

It was 2017, and Ewan was just 15 years old. He was snorkeling during a family vacation when his parents—both doctors and Dal Med School Alum—noticed something odd. Ewan's snorkeling mask caught on a mole on the teenager's forehead, and the mole began bleeding.

Mark and Ann, who live in Port Williams, NS with their seven children, were worried. A week after seeing a dermatologist, the family got terrifying news: Ewan had melanoma.

Doctors immediately removed Ewan's mole and performed further testing. After a follow-up appointment, however, Mark and Ann learned the cancer had metastasized to one of his lymph nodes.

On December 21st—the longest night of the year—PET scans revealed Ewan's cancer had spread to his liver, both femurs, and spine. The family was devastated. Mark and Ann knew that cutting-edge research was their only hope.

BEATING THE ODDS

The odds were not in Ewan's favour, but he was about to beat them. Around the time of Ewan's diagnosis, a new study published in the *New England Journal of Medicine* showed the combination of two immunotherapy drugs, nivolumab and ipilimumab, were dramatically increasing the survival rates of people with this kind of advanced melanoma. Five years previously, Ewan's diagnosis carried a five per cent survival rate. Now, thanks to research, he had a fighting chance.

In January 2018, Ewan began the new cutting-edge protocol. His doctors told the family Ewan was the first person in Nova Scotia to receive the combination treatment.

By March, Ewan was cancer-free. Five years later, he remains in remission. Now, Mark and Ann want to fuel medical research right here in Nova Scotia to ensure more families get access to the groundbreaking discoveries that result in miracles, like the one they experienced.

FUELLING MEDICAL RESEARCH

Mark and Ann matched the first $50,000 made to the Molly Appeal to support the work Dr. Carman Giacomantonio is leading at Dalhousie, to investigate why immunotherapy works so well with some people—like Ewan—but is unsuccessful in beating other people's cancers.

Mark and Ann hoped their family's gift would encourage others to donate, so that together their efforts could change and save more lives. They were right, their gift did encourage others. Generous Molly donors contributed an additional $200,000 to support this immunotherapy research.

LEVERAGING IMMUNOTHERAPY

Dr. Giacomantonio's research involves finding ways to leverage immunotherapy, to make cancerous tumours more recognizable to the immune system.

He's been successfully using this strategy for years with melanoma, and is now trying to transfer what he's learned to treat prostate cancer. Mark likens the combination immunotherapy Ewan received to a fuel.

"What Carman's playing with is different kinds of sparks that might make this fuel burn even better," Mark says.

Throughout Ewan's illness and treatment, the support of the healthcare staff at the QEII, their community members, and even strangers buoyed him and his family.

Mark and Ann had put out a call on Facebook for people to share their own experiences with melanoma and with immunotherapy.

"We had hundreds and hundreds of people that sent us ideas and information and reached out to try to help," Mark says. "It was like the world's largest clinical trial."

Some information the family received was new to them, and some of it reinforced what they had already read. All of it helped them feel more active and in control as they pursued this new treatment.

They hope to extend the same approach—working together to make a difference—in garnering support for for Dalhousie's research on immunotherapy.

"What can we do to help other people out? What can we do to change things? That resonates with me," Mark Johnston says.

"Let's make it better."

Ewan Johnston and his parents

NOVA SCOTIA'S HIGH RATES OF LUNG CANCER DRIVE RESEARCH ON CAUSES, PREVENTION, AND TREATMENT

By Laura Eggertson

Stephen Sollows was an active, engaged 63-year-old who had never smoked when he became one of 1000 Nova Scotians every year who receive the devastating news that they have lung cancer.

In Mr. Sollows' case, his cancer had already spread to his spine, his pelvis, his hip, and a bone in his leg before he was diagnosed.

"I've been perfectly healthy all my life," says the retired small business owner from Yarmouth, N.S. "This just came out of the blue."

Nova Scotia has the highest rate of lung cancer in the country, and the disease costs more than 700 people their lives annually. That sobering statistic makes medical research for lung cancer vital.

One of the greatest difficulties doctors currently encounter when treating lung cancer is that doctors diagnose most people only once the disease is advanced. By the time people experience symptoms, conventional treatment is often unsuccessful.

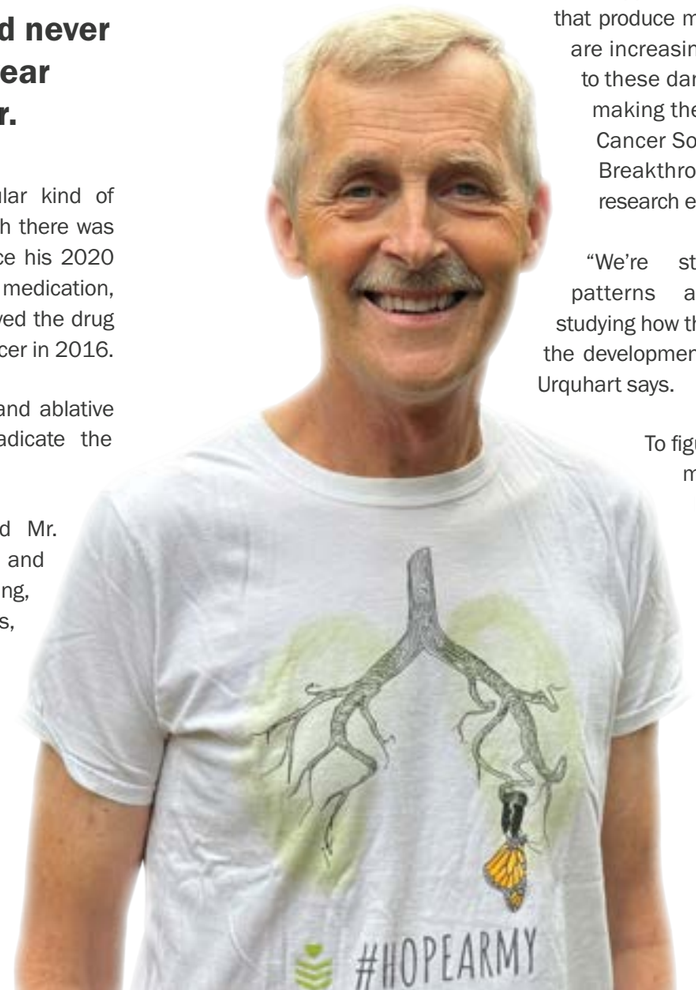
At an advanced stage, the five-year-survival rate, on average, is less than 20 per cent. Those statistics are even more dire in Nova Scotia: five-year-survival rate is 14 per cent.

Fortunately, Mr. Sollows had a particular kind of genetic mutation in his tumours for which there was a treatment. For the last four years, since his 2020 diagnosis, he has responded to a new medication, called osimertinib. Health Canada approved the drug to treat his type of non small-cell lung cancer in 2016.

He also received radiation to his spine and ablative stereotactic radiation treatment to eradicate the cancer in his lung.

Although the treatments haven't cured Mr. Sollows, they have extended his life and allowed him to continue cycling, kayaking, hiking, and the other activities he enjoys, with little to no pain.

"Without research in cancer treatments and therapies, I simply wouldn't be here," he says. "I just feel so well and have been so active. It gives you hope that you can have a future."



Stephen Sollows

Although smoking is the primary cause of lung cancer, today, as many as 30 per cent of all new lung cancer diagnoses occur in people like Mr. Sollows, who never smoked.

"We're seeing a huge increase" says Dr. Robin Urquhart, an associate professor at Dalhousie who holds the Canadian Cancer Society (Nova Scotia Division) Endowed Chair in Population Cancer Research.

Exposure to radon gas, arsenic, and air pollution are the culprits for the lung cancer diagnoses among nonsmokers, Dr. Urquhart says.

CLIMATE CHANGE RAISES RISK

Climate-driven events, such as melting permafrost that exposes more of the rocks containing radon, flooding that leaves more arsenic in drinking water supplies, and forest fires that produce more air pollution, are increasing exposure to these dangerous toxins making the Canadian Cancer Society's Breakthrough Team's research even more urgent.

"We're studying activity patterns and we're all studying how this contributes to the development of cancer," Dr. Urquhart says.

To figure out how many people here have been exposed to radon, arsenic (through well water and other drinking water) and other heavy metals via air pollution, the scientists are collecting samples of people's toenails. Toenails, it turns out, are an excellent storehouse of heavy metal exposure. They're easy to test and will ultimately enable the researchers to develop a scale, so they can advise people above a certain threshold that they are of increased risk of lung cancer and should get screened.

HOPEFUL ADVANCES

The Canadian Cancer Society study is only one of the ways Dalhousie researchers are tackling the high rates of lung cancer. Our scientists are also investigating the use of cell therapy against lung cancer.

Dr. Jeanette Boudreau and Dr. Dan Gaston are exploring the use of Natural Killer (NK) cells, which are members of the immune system, to trigger a targeted immune response to destroy lung cancer cells.

Another Dalhousie researcher, Dr. Brent Johnston, is also studying the role of NK cells in beating this disease. Dr. Mahmoud Elsawy, who runs Nova Scotia's CAR-T cell therapy, believes this therapy will also be approved in the near future to treat lung cancer in the United States and Canada. CAR-T cell therapy uses a patient's own reengineered cells to super-charge the immune system and cause it to attack cancerous cells. If current research proves successful, Dr. Elsawy is keen to see it approved here.

In all these lung cancer research projects, philanthropic donations are critical to move the generation of new knowledge forward, and to transform that knowledge into clinical practice and public policy.

"Lung cancer has been so under-funded for years and now there's an opportunity to see the growth in treatment that is saving lives, but also extending lives," says Mr. Sollows. "I'm living proof that you can live a very active healthy life at Stage 4."

"Research is absolutely life-giving."

- STEPHEN SOLLOWS

TWO POWERHOUSE MULTIDISCIPLINARY RESEARCH TEAMS,

specialized infrastructure, a pipeline of top talent trainees and years of experience have made Dalhousie the ideal environment to foster innovation in cancer immunology, vaccines and novel therapeutics.

Photo by Mulyadi on Unsplash

BREAKTHROUGH BREAKFAST

DALHOUSIE UNIVERSITY | FACULTY OF MEDICINE

BIOMANUFACTURING AND IMMUNOLOGY AT DALHOUSIE

UNDERSTANDING IMMUNE RESPONSES

By Laura Eggertson

Dalhousie researchers lead the way in investigating how older people respond to novel pathogens like COVID-19, Dr. Lisa Barrett told the Faculty of Medicine's Breakthrough Breakfast on March 26, 2024.

During the first wave of the pandemic, Dr. Barrett and her colleagues enrolled more than 350 residents of long-term care facilities in the *Long-term Care Immunity and Frailty in Elderly COVID Study*, to investigate the strength of their immune systems.

Since most research studies do not include older frail adults, public health officials had little information about how much immunity those adults could generate to withstand the SARS-CoV-2 virus, Dr. Barrett told about 150 colleagues and community members at the breakfast at Pier 21 in Halifax.

Public health officials were also uncertain how well older people would respond to the new COVID vaccines, Dr. Barrett said. They were looking for clues to prevent further deaths of long-term care residents and other seniors.

Dr. Barrett, an assistant professor and the Principal Investigator of the Senescence, Aging, Infection, and Immunity (SAIL) laboratory, was one of three researchers who described their work during TED Talk-style presentations. Dalhousie President Kim Brooks moderated and Faculty of Medicine Dean David Anderson introduced the breakfast, a quarterly event the faculty is organizing to share research insights with the community.

Although most of those who died in Nova Scotia during the first wave of COVID were long-term care residents, Dr. Barrett's study indicated many older adults can muster a strong immune response. The study also generated further questions about a potential correlation between people who had a common virus called cytomegalovirus (CMV), which may have weakened their immune cells that left them vulnerable to further infections, she said.

"There is a huge knowledge gap in older person immunity, and with those folks being the people who die the most of infections in our population, we need to reprioritize them both with funds and with education to enable that research to happen quickly," Dr. Barrett said.

The Dalhousie research study generated valuable information that is being added to Canada-wide database, she said.

She thanked the older adults who participated in the research, pointing out that every person the researchers asked agreed to join the study. She described it as the first such novel pathogen investigation involving people more than 100 years old.

“Dalhousie is leading here. Nova Scotians are leading,” Dr. Barrett said.

Dalhousie’s expertise in infectious diseases, inflammation, immunology, and vaccinology (I3V) was the centrepiece of the Breakthrough Breakfast, which also featured Dr. Scott Halperin, director of the Canadian Center for Vaccinology.

The Center is home to one of only two Human Challenge units in Canada, Dr. Halperin said. In the 10-bed unit, researchers test new treatments and vaccines on people who volunteer to be infected with viruses such as whooping cough. Doctors then treat them, under carefully controlled conditions, before the virus can progress far enough to harm them.

“Under those carefully controlled conditions we can actually determine the immune response to the bacteria,” said Dr. Halperin. “By understanding the immune response better, we can develop better vaccines.”

There are about 150 researchers, staff, and students working at the Center, where Dr. Halperin and his colleagues are developing and testing a new vaccine for whooping cough (pertussis), as well as evaluating scores of other vaccines and new therapeutics.

The I3V group is also eager to utilize the new GMP Biolabs East facility Dalhousie plans to have operating soon. The new biomanufacturing facility will allow researchers to not only develop new drugs and vaccines, but also create small batches of products manufactured under Good Manufacturing Process standards, and conduct pilot or proof-of-concept studies that could lead to larger clinical trials.

“A GMP facility has a wide variety of potential and it will put Nova Scotia on the map in terms of being able to do the type of research we need to do to have innovative therapies, treatments, and preventions,” Dr. Halperin said.

Both Dr. Brooks and Dr. Anderson emphasized the importance of having biomanufacturing capacity in order to translate the discoveries Dalhousie researchers are making into tangible health-care solutions.

“The new facility will not only fill a critical gap in the research pipeline in Atlantic Canada, it will add much-needed capacity to Canada’s entire manufacturing and life sciences sector,” said Dr. Brooks.

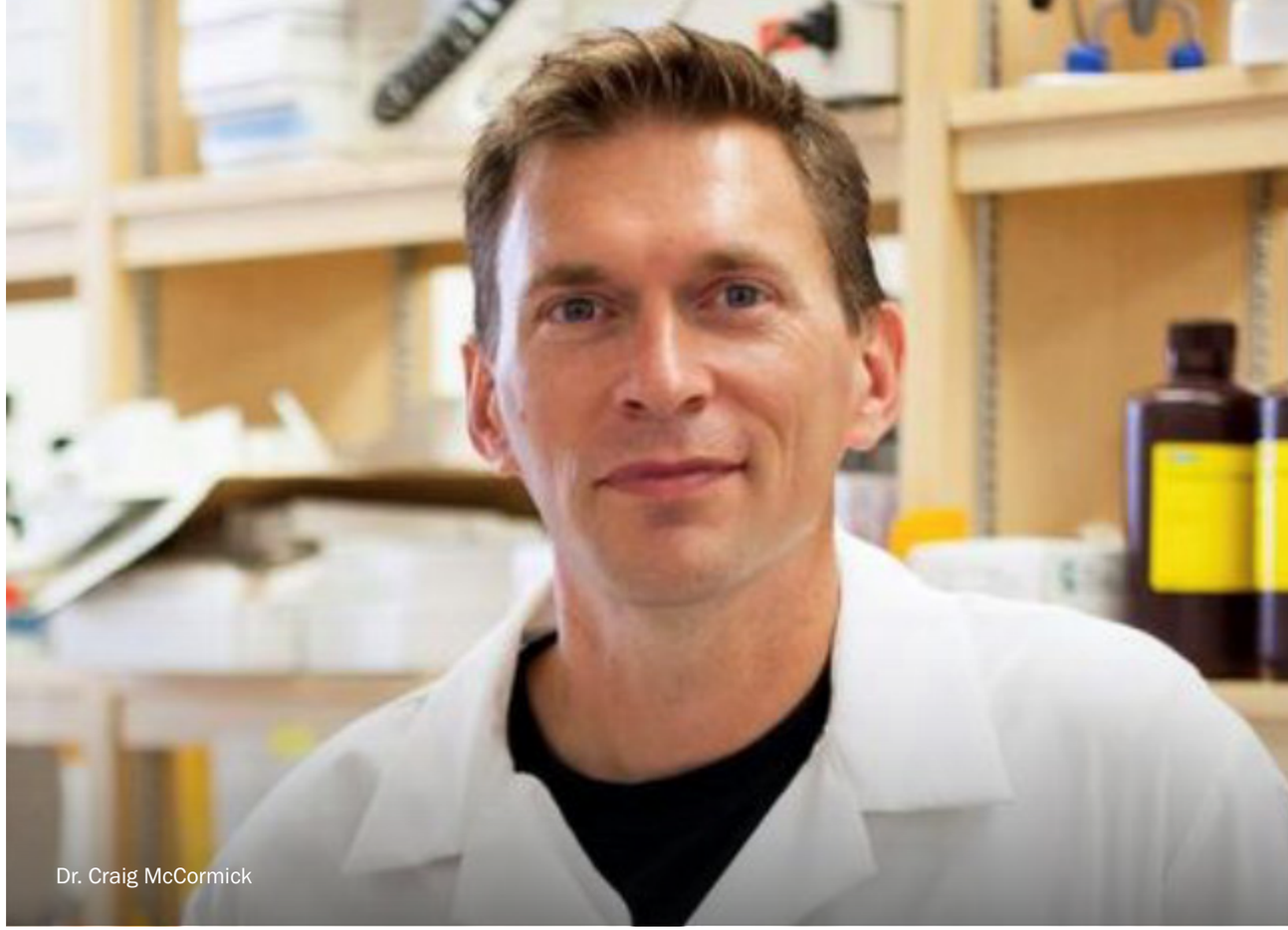
The prospect of a new manufacturing facility is enticing for research trainees, including graduate students and post-doctoral fellows working in the I3V researchers’ labs, said Dr. Craig McCormick, who investigates the way host systems respond to viruses, and how viruses evade those immune responses. His research focuses on new and emerging viruses with pandemic potential, including influenza and coronaviruses.

Research trainees in Dr. McCormick’s lab learn by deconstructing viruses to figure out how they work, he said. Among their current projects is a new antiviral drug candidate they are developing against the family of corona viruses that caused COVID-19.

“This is an incredibly exciting time for us, because there are significant investments happening in pandemic preparedness and the biomanufacturing sector,” Dr. McCormick said. “This means more jobs for our young people and I know they are excited about being able to contribute to the economy in this way.”

“This is an incredibly exciting time for us, because there are significant investments happening in pandemic preparedness and the biomanufacturing sector.”

- DR. McCORMICK



Dr. Craig McCormick

Dr. Scott Halperin

Dr. Lisa Barrett

THE BIG PICTURE

VACCINES — HOW THEY WORK, AND WHY WE STILL NEED THEM

By Michele Charlton
Photos by Danny Abriel
Originally published in DalNews in February 2020

Our world is changing, and research is changing with it. The Big Picture, a long-form Dal News series, provides an in-depth look at specific areas of research with global implications.

Between the coughing, sneezing, stuffy noses, and watery eyes, it's clear that we're in the midst of cold and flu season, which serves as an annual reminder of the critical role vaccines play in the fight against the spread of infectious disease.

Thanks to immunization, which can be considered to be one of the most important advances in the history of public health, deadly infectious diseases such as measles, polio, and chickenpox are now all preventable.

Yet, the success of those same immunization programs —estimated to have saved more lives in Canada over the past 50 years than any other health initiative—has also helped spawn one of the most divisive health-care debates today: do we still need vaccines?

"Sometimes when we see success, it's like an event," says Dr. Joanne Langley, Division Head of Infectious Diseases, and a Professor in the Faculty of Medicine. "We've hit the goal, and that's the end of it. But that's not the case with infectious diseases."

"Unless you eradicate the illness, infections are still out there and ready to come back, and the program of prevention should be continued. We know how to control diseases, but this is an effort that requires ongoing strong vaccination programs and for the public to be engaged and aware of the threat of disease if vaccination rates fall."

Dalhousie is a world-leader in vaccinology and immunology, and at the Canadian Center for Vaccinology (CCfV), our unique human challenge facility allows us to test new vaccines, host clinical trials and develop more of these key public health tools.

VACCINES: A BRIEF HISTORY

The practice of immunization dates to ancient times and coincides with the emergence of smallpox.

Smallpox is an ancient disease that a virus causes. There's evidence that it affected the ancient Egyptians, with archaeologists finding smallpox lesions on mummies. And techniques were developed in ancient China to try and stimulate the immune system, and make sure it was ready for the viral assault.

In the 18th century, English physician Dr. Edward Jenner noticed that women exposed to cowpox through their routine work milking cattle could be protected from the smallpox virus.

"Jenner stands out because he took that observation and started to perform experiments to show that if you were inoculated with cowpox, you can be protected from smallpox infection," says Dr. Alyson Kelvin, a researcher at CCfV and an Assistant Professor in the Department of Pediatrics.

Another major milestone is the development of the influenza vaccine. Influenza has been around for thousands of years, but the cause for the illness was unknown—even during the 1918 pandemic which killed an estimated 25 to 50 million people worldwide, it wasn't known if people were dying from bacteria or some other pathogen.

In 1933, the virus responsible for what we now know as influenza-like symptoms was identified, and shortly afterwards the first influenza vaccine was developed. Dr. Kelvin explains this coincided with the identification of a virus as an etiological agent and the cause of a major disease. During this time, researchers also figured out how to propagate the virus.

"If you don't know what a virus is, or you don't know where it comes from, and how it behaves, you can't grow it and make a vaccine from it," says Dr. Kelvin. "So, the researchers who figured how to isolate influenza virus were then able to take it, grow it and make a vaccine."

Researchers used these same strategies to develop the extremely successful polio vaccine, which has brought the polio virus close to eradication, saving millions of lives.

Dalhousie has its own notable spot in vaccine history. In 2014, a clinical trial for an experimental Ebola vaccine took place here, which Dr. Scott Halperin, Director of the Canadian Center for Vaccinology, and a Professor in Dal's Division of Pediatric Infectious Diseases, led.

Canadian researchers had already been studying a possible Ebola vaccine well before the pandemic occurred in West Africa, but their work was not overly visible. In response to the quickly escalating global crisis, the Public Health Agency of Canada (PHAC) and the Canadian Institutes of Health Research (CIHR) teamed up with the Canadian Immunization Research Network on a Phase 1 clinical trial of the VSV-ZEBOV vaccine on local residents. The results from this study were a key part of what led to the selection of the vaccine for a phase II-III trial.

The speed at which this vaccine was developed is considered extraordinary. Because emergency rapid response infrastructure was available, VSV-ZEBOV was available in just 12 months. Dubbed the "Canadian vaccine," it is now a highly effective tool in the fight against the Ebola virus—a Canadian, and Dalhousie, success story on the front lines of the battle against global illness.

SOURCE: CANADIAN PUBLIC HEALTH ASSOCIATION

"What you want to do is give something that gives the same immune response to protect the person as it does after natural infection—but without getting sick. So, it's understanding that pathophysiology, and that's all basic science research."

Once the researchers identify how one becomes immune, the vaccine goes into development. There are all kinds of different strategies that can be used, including purifying a protein, attenuating a virus (weakening it) so it doesn't cause disease, or making a viral-like particle.

"In the lab, researchers work to protect cell cultures from being infected by an organism, and then they look at it in multiple different animal models to test for safety," says Dr. Halperin. "Then a Phase One trial takes place, which is done with a very small group of people and with very careful monitoring."

"If it passes the Phase One study, then it goes into a Phase Two study, where one starts looking at it more towards the target population. In the Phase Three study, you're looking at if it works. You immunize a group of people with the vaccine, another group with a placebo, and then you monitor them for development of disease over time."

Dr. Halperin's own research focuses on whooping cough, which is a respiratory infection. There has been a vaccine available for over 80 years, but there has been a resurgence of the disease in the past decade.

"We've been doing a lot of research to try and figure out why that is, how the vaccine can be improved, and how we can better use the vaccine," says Dr. Halperin. "We had the idea to give the vaccine to pregnant women, which would help them develop antibodies that would be passed through the placenta to the infant. When it was implemented in the United Kingdom, it was shown to be 90 per cent effective in protecting infants in the first few months of life."

As of last spring, this immunization program became the policy across Canada. The Public Health Agency of Canada now recommends that all pregnant women receive the vaccine.

"We don't know what the uptake is yet, but some of the research we intend to do in the next year will look at that and try to see how well the program is being accepted," says Dr. Halperin, who says it's exciting that their work is now a publicly funded vaccine.

"We've been involved from the very basic design of the vaccine 20 years ago and have had the opportunity to see how it can be best be used in clinical trials, then being developed into policy. It's run the whole spectrum of taking something from the bench to policy."

EMERGING VIRUS RESEARCH

Every now and then, a new virus emerges that causes illness, dominates the news cycle and sparks a rush to create a vaccine to protect people and prevent spreading.

It was in December 2019 that the first case of the Novel Coronavirus (COVID-19) was reported in China. It's the third coronavirus to emerge in the past two decades (SARS in 2002, and MERS in 2012), and the health and economic impact it has had around the world has been significant.

According to an article co-written by Dr. Alyson Kelvin for The Conversation Canada, scientists from China were able to rapidly isolate the virus and sequence its genome using a cutting edge technology called next generation sequencing.

"Next generation sequencing allows scientists to rapidly determine the genetic code of an organism," says Dr. Kelvin. "It detects all variations or mutations in the genome, which may provide scientists with clues on mutation rates, the source of the virus and its pattern of circulation within a population."

A key part of Dr. Kelvin's work is studying emerging viruses, like COVID-19, to determine what kind of disease they cause and develop specific vaccines to keep people from getting sick.

"The sequence of the viral genome also allows scientists to begin designing and synthesizing vital

FROM THE BENCH TO MARKET

The typical vaccine can take 10–15 years to get to market. It all starts in the lab, with an understanding of the disease along with its effects and how it is transmitted.

"A key part is understanding the immunity," says Dr. Halperin. "That includes figuring out how someone becomes protected in the natural environment, what aspects of that organism causes disease, how the immune system responds to it, and determining if it is responding or protecting itself by making antibodies."

TIMELINE

1798 — Edward Jenner publishes work on smallpox vaccine, coining the term **"Vaccine"** and **"Vaccination".** By 1800, smallpox vaccination becomes commonplace.

1870s–1880s — Louis Pasteur develops first **live attenuated** viral vaccine (rabies).

1918 — Spanish influenza (flu) pandemic kills **25-50 million worldwide.**

1924 — **9,000 cases of diphtheria reported in Canada.** It was one of the most common causes of death of children from 1–5 years of age. Diphtheria toxoid is introduced two years later.

1943 — **Routine immunization against whooping cough** is approved in Canada.

1953 — **9,000 cases of polio** were reported; 12 years later, after the introduction of the polio vaccine, only 3 cases were reported.

1963 — The first measles vaccine is approved. Prior to immunization, an estimated **300,000 to 400,00** cases occurred annually.

1968 — No cases of **wild polio virus** were reported in Canada.

1969 — Rubella vaccine introduced in Canada; incidence of rubella decreased by **60,000 cases per year.**

1980 — **The global eradication of smallpox** is certified by a commission of eminent scientists and endorsed by the World Health Assembly.

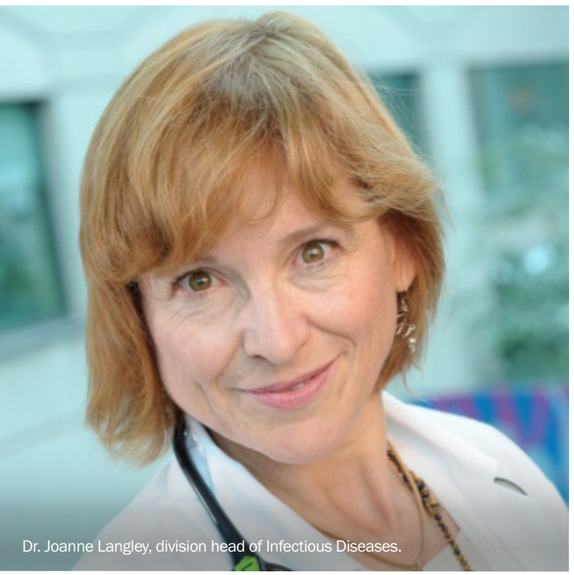
1983 — MMR (measles, mumps, rubella) immunization program introduced for all infants. Rubella cases went from **approximately 5,300/year** between 1971 and 1982 to fewer than **30 cases/year** between 1984 and 1994.

1994 — Canada is certified **polio free.**

1995 — Canada switches from live oral polio vaccine (OPV) to **inactivated polio vaccine** (IPV) to avoid further cases of vaccine associated paralytic poliomyelitis (VAPP).

2001 — **Meningococcal vaccine** against group C strains approved for use in Canada; made available in all provinces as part of routine infant immunization since 2005.


Dr. Alyson Kelvin, at work in the lab.


Dr. Joanne Langley, division head of Infectious Diseases.


Dr. Janice Graham, photographed in her office.

proteins for vaccine development. With the sequence available, a great number of researchers with a larger array of tools are able to work on vaccines and antivirals for this immediate viral threat."

STILL TOO MUCH MISINFORMATION

According to Dr. Langley, parents think critically about health care and the value of interventions, but doctors often lack the time or resources to offer the kind of collaboration and consultation needed to ensure patients fully understand the benefits of vaccines.

"The public is very science literate, and answering their questions in a way that matches with their understanding and abilities is different in 2020 than it was in 2010," says Dr. Langley. "We need to find ways to provide information that don't rely completely on spending a lot of time with health-care professionals — because they don't have that time."

To fill gaps in their knowledge, some individuals turn to the internet or media for answers.

While Dr. Langley agrees that it's wise to have lots of good sources on social media, sometimes the tenor of discussion and the discourse on social media are not conducive to making good health choices.

"We know that there's a lot of misinformation, dis-information and a lack of good information. So, how do we help people trust the sources of information, and find the good, accurate sources of information that are there?"

"People often make decisions based on how they feel —and that's invaluable. How do institutions become trustworthy? How does the health profession become trustworthy? There are so many things we need to tackle, and we're finding out more and more that if families have sources of information, and lots of chances to get their questions answered, they will decide to vaccinate."

VACCINES FROM A SOCIAL SCIENCE PERSPECTIVE

For Dr. Janice Graham, an anthropologist in the Division of Pediatric Infectious Diseases, vaccines are more than medicine—they are social products.

"Vaccines are particularly interesting because they are developed for the public's health, not simply individuals" says Dr. Graham. "This really appeals to the importance a society places on building a public foundation for universal health care, and I like to take a step back and look at the whole lifecycle production of vaccines. Who decides what vaccines for which populations, are they as safe and effective as they can be, and do all communities have equitable access to the vaccines they need? What is in the actual make-up of vaccines? What drives the need for, or hesitation in receiving, particular vaccines in particular populations?"

"The technical, political, economic and moral issues and decision-making are entangled, so I study them all together."

Her three-year, CIHR-funded anthropological study generated and analyzed accounts of Ebola interventions from community members, health-care providers (formal and informal), biomedical researchers, government officials, NGOs and multilateral organizations. Her findings are being used to create a contextually sensitive and flexible decision-making framework for national health authorities to prioritize health interventions and strengthen community health surveillance and response.

"We need better access to health care, strengthened health systems, well-trained doctors and nurses, community workers and proper clinics with medication and supplies," says Dr. Graham, who works in West Africa as well as Europe and Canada. "Low-income countries often only get offered one-off programs that target a particular disease at a particular time, usually during an outbreak. In emergency situations, urgent response is absolutely necessary, but the outbreak might never have happened if adequate health care systems and medicines and vaccines were available from the start."

In her opinion, a key part in handling these emergencies successfully is involving the people on the ground from the beginning. The Ebola crisis during 2014-2016 showed the importance of engaging with communities and working with anthropologists and other social scientists throughout epidemic response.

"Watching the sharing of local and international data and information that can take place to solve a problem, to resolve an epidemic, has been quite lovely," says Dr. Graham. "Still, I would like to see more. I think we will, it's moving that way. In the global health context, there's an increasingly awareness of the importance of building capacity for qualified health personnel and infrastructures."

"I just wish that we were doing more towards training locals and securing sustainable health-care systems so that emergency responses would be fewer, and more quickly resolved. We're making fantastic inroads in developing new vaccines for old and emerging diseases, but the ability to prevent outbreaks from happening in the first place, and responding effectively when they do occur, lies in the social determinants of health. Vaccines are one of the tools that are needed."

Learn more about the world-class work being done by researchers like Dr. Halperin, Dr. Graham, Dr. Kelvin and Dr. Langley on the Canadian Centre for Vaccinology website.

"The public is very science literate, and answering their questions in a way that matches with their understanding and abilities is different in 2020 than it was in 2010."

- DR. JOANNE LANGLEY

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