

BC Children's Hospital furthering development of immunotherapy treatments for kids

BC Children's Hospital has joined CureWorks, an international collaborative of leading academic children's hospitals focused on improving care for children with hard-to-treat cancers by expanding clinical trials and accelerating the development of leading-edge immunotherapy treatments.

Every year in BC, approximately 150 kids are diagnosed with cancer. Thanks to rapid and significant advances in cancer treatments, 80% of kids are now expected to survive. For the remaining 20%, who have cancers that are difficult to treat with traditional therapies, immunotherapy provides new hope.

Working with the newly formed Seattle Children's Hospital-based CureWorks, researchers at BC Children's will further the science of a promising type of immunotherapy called "chimeric antigen receptor (CAR) T-cell therapy," add to the body of knowledge around this innovative treatment, and develop expertise within the research institute and the hospital.

The first CAR T-cell clinical trials will launch this fall at BC Children's and will initially be available to children with certain types of leukemia who are no longer responding to conventional treatment.

Immune-resistant HIV mutations in Saskatchewan

The BC Centre for Excellence in HIV/AIDS (BC-CfE) and Simon Fraser University conducted research in response to reports in Saskatchewan of unusually rapid progression of HIV to AIDS-defining illnesses in the absence of treatment—revealing genetic mutations in HIV strains in that province.

The study, presented at the 2018 AIDS Conference in Amsterdam and published in the scientific journal *AIDS*, shows that HIV strains circulating in Saskatchewan have adapted to evade host immune responses. These HIV strains are being commonly transmitted and, if the resulting HIV infections are left untreated, rapid progress to AIDS-related illnesses may happen.

Researchers on the study—from the BC-CfE, SFU, and the Public Health Agency of Canada, in partnership with Saskatchewan physician-researchers and with funding from the Canadian Institutes of Health Research—were startled at the prevalence of immune resistance mutations. One key mutation was found in more than 80% of Saskatchewan HIV strains, compared with only about 25% of HIV strains found elsewhere in North America. The pervasiveness of such mutations is increasing over time. More than 98% of the HIV sequences collected in Saskatchewan most recently (2015 and 2016) harbored at least one major immune resistance mutation. HIV antiretroviral treatment, however, works equally effectively against immune-resistant HIV strains.

The multi-year analysis compared more than 2300 anonymized HIV sequences from Saskatchewan with data sets from sites across the United States and Canada. Genetic analyses of HIV strains in Saskatchewan showed high levels of clustering—indicating that viruses with similar mutations are being frequently and widely transmitted.

This study is significant as HIV incidence rates in Saskatchewan are among the highest in North America, with 2016 rates in some regions more than 10 times the national average. Saskatchewan's HIV epidemic is also unique in that nearly 80% of infected

persons self-identify as having Indigenous ancestry.

"Smart stent" detects narrowing of arteries

For every three individuals who have had a stent implanted to keep clogged arteries open and prevent a heart attack, at least one will experience restenosis—the renewed narrowing of the artery due to plaque buildup or scarring—which can lead to additional complications.

A team led by UBC electrical and computer engineering professor Kenichi Takahata has developed a "smart stent" that monitors even subtle changes in the flow of blood through the artery, detecting the narrowing in its earliest stages and making early diagnosis and treatment possible. The device uses medical-grade stainless steel and looks similar to most commercial stents. Researchers say it's the first angioplasty-ready smart stent.

Research collaborator Dr York Hsiang, a UBC professor of surgery and a vascular surgeon at Vancouver General Hospital, noted that monitoring for restenosis is critical in managing heart disease.

The device prototype was successfully tested in the lab and in a swine model. The research team is planning to establish industry partnerships to further refine the device, put it through clinical trials, and eventually commercialize it.

The research is described in the May issue of *Advanced Science*.

Matchmaking service combats antibiotic-resistant infections

UBC researchers have matched peptides with antibiotics so they can work together to combat hard-to-treat infections that don't respond well to drugs on their own. The study builds

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on previous research that showed that the peptides are key to making harmful bacteria more responsive to drugs.

The study aimed to find new treatments for infections caused by antimicrobial-resistant bacteria including *Escherichia coli* and the so-called ESKAPE pathogens, a group named from the first-letter of six bacteria species: *Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa* and *Enterobacter*. These infections collectively account for more than 60% of all hospital infections, manifesting as abscesses in the skin or infections in internal tissues like the lungs or urinary tract.

Most antibiotics are designed to work on bacteria that are swimming freely in the body. However, in the majority of infections, bacteria grow together on body surfaces in massive communities known as biofilms, shielded by a protective structure. Together, biofilm bacteria adapt to stress by learning to resist the immune system and chemicals, making them extremely resistant to antibiotics and difficult to treat.

The peptides help several antibiotics to work by removing the bacteria's ability to respond to stress and form these resistant communities. To find the best combination of peptide and drug, the researchers tested different options in a laboratory setting. Once they identified possible mixtures, they tested them in mice with abscesses on their skin. In total, they found seven combinations that worked better than antibiotics on their own.

When the peptides worked in combination with the drugs, the researchers observed a reduction in the size of the abscess in mice and the number of bacteria in the infection area. The combinations offered up to 100-fold improvement.

The results are particularly important for patients with cystic fibrosis

who often deal with dense, chronic infections in the lungs. The disease causes mucus to build up around tissues, creating an ideal environment for bacteria to form biofilms and thrive.

Researchers are hoping to commercialize this treatment and have licensed the peptides to ABT Innovations, a UBC spinoff company owned by Dr Bob Hancock.

The research was funded by Cystic Fibrosis Canada, a Canadian Institutes of Health Research Foundation grant, the Canada Research Chair program, and the Alexander von Humboldt Foundation. The study was published in *PLOS Pathogens*.

Novel therapy offers hope for social anxiety

People with social anxiety disorder benefit from group therapy that targets the negative mental images they have of themselves and others, according to a study at the University of Waterloo. Called "imagery-enhanced" cognitive behavioral therapy (CBT), the new group treatment helps relieve symptoms including social performance and interaction anxiety, depression, and stress.

More than 4 million Canadians will develop social anxiety disorder at some point in their lives. Without treatment, the disorder can impair people's functioning at school, work, and relationships.

The 13-session treatment used specialized exercises including video feedback and imagery rescripting, where patients are guided to reimagine the outcomes of past negative experiences and to challenge distorted images of themselves and others. The goal was to see if the successes achieved in a pilot and open trial could be replicated in a different setting, without input from the treatment developers. The results were strikingly similar in treatment retention and symptom improvement, strongly suggesting that imagery-enhanced group CBT is effective.

The study suggests that this new group therapy may work as well as individual therapy, but at half the cost per patient.

The study, "Transportability of imagery-enhanced CBT for social anxiety disorder," appears in *Behaviour Research and Therapy*.

Anger overlooked as feature of postnatal mood disorders

Women in the postpartum period should be screened for anger in addition to depression and anxiety, new research from the University of British Columbia suggests.

Although anger has been recognized as an element of postpartum mood problems for some women, it has not been well studied and is not included in the Edinburgh Postnatal Depression Scale screening tool. In a review of existing research, UBC nursing PhD student Christine Ou found anger to be a significant feature in postpartum mood disturbances.

Ou's analysis, recently published in *Birth*, also found that feelings of powerlessness, a mismatch between reality and expectations of motherhood, and unmet expectations of support contributed to anger in the context of postpartum depression.

Fifteen minutes of exercise creates optimal brain state for mastering new motor skills

A recent study in *NeuroImage* demonstrates that exercise performed immediately after practising a new motor skill improves its long-term retention. The research shows, for the first time, that as little as a single 15-minute bout of cardiovascular exercise increases brain connectivity and efficiency. It's a discovery that could accelerate recovery of motor skills in patients who have suffered a stroke or who face mobility problems following an injury.

To find out what was going on in the brain as the mind and the muscles

interacted, the research team asked study participants to perform two different tasks. The first, known as a pinch task, consists of gripping an object akin to a gamer's joystick (and known as a "dynamometer") and using varying degrees of force to move a cursor up and down to connect red rectangles on a computer screen as quickly as possible. The task was chosen because it involved participants in motor learning as they sought to modulate the force with which they gripped the dynamometer to move the cursor around the screen. This was then followed by 15 minutes of exercise or rest.

Participants were then asked to repeat an abridged version of this task, known as a handgrip task, at intervals of 30, 60, and 90 minutes, after exercise or rest, while the researchers assessed their level of brain activity. This task involved participants simply repeatedly gripping the dynamometer for a few seconds with a similar degree of force to what they used to reach some of the target rectangles in the pinch task. The final step in the study involved participants in both groups repeating the pinch task 8 and then 24 hours after initially performing it, allowing the researchers to capture and compare brain activity and connectivity as the motor memories were consolidated.

Researchers discovered that those who had exercised were consistently able to repeat the pinch task, connecting different areas of the brain more efficiently and with less brain activity than those who hadn't exercised. The reduction of brain activity in the exercise group was also correlated with a better retention of the motor skill 24 hours after motor practice. This suggests that even a short bout of intense exercise can create an optimal brain state during the consolidation of motor memory, which improves the retention of motor skills.

When they looked more spe-

cifically at what was going on, the researchers discovered that, after exercise, there was less brain activity, most likely because the neural connections both between and within the brain hemispheres had become more efficient.

What researchers found especially intriguing was that when they tested participants at the 8-hour mark, there was little difference between groups in skill retention. Both groups were less able to retain the skills they had newly acquired than they were at the 24-hour mark, when the difference between the two groups was once more apparent.

This suggests that sleep can interact with exercise to optimize the consolidation of motor memories.

To learn more about the research, read "Acute cardiovascular exercise promotes functional changes in cortico-motor networks during the early stages of motor memory consolidation" by Fabien Dal Maso and colleagues in the 1 July 2018 issue of *NeuroImage*.

Breakthrough discovery will change treatment for COPD patients

Permanent lung damage caused by chronic obstructive pulmonary disease (COPD) starts much earlier than previously thought, even before patients are showing symptoms.

These are the findings of a study published in *The Lancet Respiratory Medicine*. The discovery, led by Dr Tillie-Louise Hackett, associate professor in the University of British Columbia's Faculty of Medicine, will dramatically change how patients are treated for COPD, the leading cause of hospital admissions in BC and Canada.

Hackett, who is also a principal investigator at St. Paul's Hospital Centre for Heart Lung Innovation (HLI), and her research team found that even patients diagnosed with mild COPD have already lost a significant por-

tion of their small airways (more than 40%) on average.

Currently, patients with mild COPD, as determined by a lung function test, are given minimal or no treatment.

The new findings also suggest previous large clinical trials testing new COPD treatments may have failed because patients already had substantial lung damage.

Lung samples from 34 patients were analyzed using an ultra-high resolution microCT scanner, one of three scanners of this kind in the country. Though the HLI Lung Tissue Registry Biobank at St. Paul's has been collecting specimens for more than 30 years, the recent addition of the microCT scanner made it possible to image samples that are embedded in paraffin in extreme detail.

It is estimated approximately 1 in 10 people over the age of 40 may suffer from COPD. Dr Don Sin, the Canada Research Chair in COPD and a St. Paul's respirologist, said the findings have significant implications. By 2020, COPD is expected to be the third leading cause of death worldwide.

BCEHS Action Plan transforming emergency health services in BC

BC Emergency Health Services (BCEHS) has made significant progress in the first year of implementing the 3-year BCEHS Action Plan.

The bold plan focuses on improving ambulance response times for life-threatening and time-critical 9-1-1 calls, and enhancing services for patients who don't require ambulance transport to hospital.

A newly released progress report on the BCEHS Action Plan describes many of the changes that have already taken place in year 1 of the 3-year plan. Progress includes adding 127 paramedic positions, 20 dispatch

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positions, and 45 ambulance vehicles, as well as other investments to ensure high-quality, sustainable services.

BCEHS has also introduced innovations in its dispatch centres to improve clinical oversight and enhance the patient experience for those who have nonurgent medical issues.

The first year of implementation of the BCEHS Action Plan lays the groundwork for more service improvements in years 2 and 3. As part of year 2, BCEHS has implemented a new clinical response model and will introduce more pathways for patients to be treated in their homes and communities.

BCEHS is responsible for the delivery and governance of pre-hospital emergency medical care and interfacility patient transfer services through the BC Ambulance Service and the BC Patient Transfer Network. BCEHS is supported by the Provin-

cial Health Services Authority. For more information, visit www.bcehs.ca.

University of Winnipeg research aims to identify resistance to breast cancer treatment

A simple test could improve the treatment odds of patients diagnosed with breast cancer, thanks to new research at the University of Winnipeg.

The drug Tamoxifen, used to treat the majority of breast cancer cases, is ineffective in approximately half of all patients who receive it. Dean Reddick, a graduate student in the Master of Science in Bioscience, Technology and Public Policy program, is researching a way to identify these patients before treatment starts.

The research impacts the treatment of estrogen receptor positive (ER+) breast cancer, which accounts for approximately 70% of all breast cancer

cases, and is characterized by estrogen binding to an abnormal number of receptors. Doctors typically prescribe Tamoxifen at the start of any ER+ treatment, thanks to its success rate in patients who are responsive to it.

Key to solving the issue is a protein within cancer cells known as N-Mycristoyltransferase (NMT), which the lab has already discovered activates with increased estrogen receptor activity. Since last September, Reddick has produced 14 different variants of breast cancer cells, each with different localizations of the protein. The plan is now to treat each one and monitor their responses. Although the lab still has further testing to do, Reddick believes the protein is an indicator of responsive cells. Once the indicators are identified, Reddick says within 3 to 4 years a biopsy could be used to determine a patient's resistance level and prescribe appropriate treatment.



Elders of Northern Secwepemc: Clara Camille, Jean William, and Cecelia de Rose



Medication use in Indigenous communities

An Indigenous storytelling project called Coyote's Food Medicines was launched in front of an audience of 4000 Elders at the BC Elders Gathering in July to encourage conversations about wellness and how to manage medications for a healthy life. Secwepemc Elders created the *Coyote's Food Medicines* story using a traditional approach to share knowledge and humor to raise awareness of the issue of multiple medications and their potential impact on health.

Shared Care's Polypharmacy Risk Reduction Initiative (a partnership of Doctors of BC and the BC government), the First Nations Health Authority, and Interior Health worked with Elders, initiating conversations that led to the creation of the Coyote story. In describing the challenges concerning medication use in First Nations communities, Elder Jean William said, "In the past, our Elders didn't take lots of medication, mostly just Aspirin. But now, cupboards look like pharmacy shelves."

The Coyote's Food Medicines project promotes healthy conversations between patients and providers, such as doctors, nurses, and pharmacists, in an effort to prevent side effects and adverse events, such as falls and injuries, from polypharmacy.

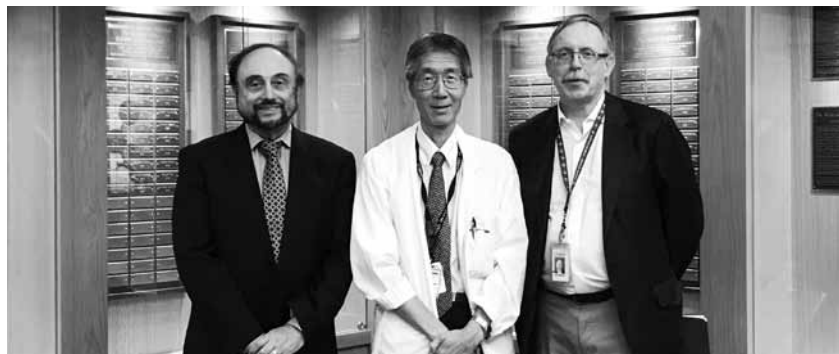
Dr Keith White, physician lead for the Polypharmacy Risk Reduction Initiative, says, "We feel this story can provide a platform for discussions among First Nations families and their health care providers, to help initiate regular medication reviews and find options that optimize health and minimize risks of multiple medications."

Copies of the book are available online at www.coyotestory.ca, along with materials to help track medications, and tips on how to talk about medications with health providers.

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The Vancouver Medical Staff Hall of Honour (VCH): Remember the heroes of the past



Photograph by Jennifer Laxamana

[L-R] Drs Simon Rabkin, Eric Yoshida, and Stephen Nantel inside the VCH Hall of Honour.

The Vancouver Medical Staff Hall of Honour of Vancouver Coastal Health was created, with the approval of the hospital administration, to commemorate both the 110th anniversary of the Vancouver General Hospital (2016), and the 150th anniversary of Canada's Confederation (2017). Although it is appreciated that all health care professionals at VGH and its allied institutions have provided outstanding service since 1906, the intention of the Vancouver Community of Care Medical, Dental, and Allied Staff Association (VMDAS) is to recognize and honor those who have provided exceptional leadership and dedicated clinical/academic service that has profoundly benefited the residents of BC as well as advanced the practice of medicine/surgery in this province. In doing so, the Hall's inductees have brought great distinction and honor to VGH and its allied institutions.

In the inaugural induction ceremony, held at VGH in February 2018, the inaugural members of the Hall were:

Dr Wallace B. Chung, CM, OBC – Professor emeritus of Surgery, UBC, former head of General and Vascular Surgery, UBC Hospital.

Dr Felix Durity, OBC – Professor emeritus of Neurosurgery, UBC, former head of Neurosurgery, VGH.

Dr Robert E. McKechnie, CBE – acclaimed pioneering surgeon, VGH, and longest-serving UBC chancellor.

Dr Sheldon (Shelly) Naiman (1937–2016) – BC's first clinical hematologist and first head of Hematology, VGH.

Dr George Fredrick (Fritz) Strong (1897–1957) – former chief of medicine, VGH, and creator of the G.F. Strong Rehabilitation Hospital.

Dr Donald Paty, MSM (civil division) (1936–2004) – pioneer in multiple sclerosis and former head of Neurology, UBC.

The VCH Hall of Honour is physically located on the main floor of the Jim Pattison Pavilion, VGH, and was unveiled prior to the annual VMDAS awards ceremony at the end of June 2018. The Hall is the first of its kind in Western Canada and, along with the Canadian Medical Hall of Fame in London, Ontario, is one of the few of its kind in the country. It is hoped that the Hall and its inducted members will be a source of inspiration to physicians, surgeons, and allied health care professionals in the years to come.

—Eric M. Yoshida,
OBC, MD, FRCPC

Hall of Honour Committee Chair
—Marshall Dahl, MD, PhD, FRCPC
Past Chair VMDAS

—Stephen Nantel, MD, FRCPC
Hall of Honour Committee Member
—Jennifer Laxamana

Administrative Assistant, VMDAS
—Simon W. Rabkin, MD, FRCPC
Chair VMDAS

BC Medical Journal Writing Prizes



J.H. MacDermot Writing Award

The *BCMJ* invites writing submissions from student authors, and each year awards a prize of \$1000 for the best medical student submission accepted for print and online publication. Students are encouraged to submit full-length scientific articles and essay pieces for consideration.

The J.H. MacDermot Writing Award, sponsored by Doctors of BC, honors John Henry MacDermot, who served as editor for 34 years (1932–1968), overseeing the publication's transition from the *Vancouver Medical Association Bulletin* to the *BCMJ* in 1959. Dr MacDermot also served as BCMA president in 1926.

BCMJ Blog Writing Prize

To encourage med students to take their first foray into medical writing, the *BCMJ* awards an additional writing prize of \$250 twice per year for the best 200- to 400-word blog submission accepted for online publication.

For submission guidelines and contest deadlines, please visit www.bcmj.org/jh-macdermot-writing-awards.