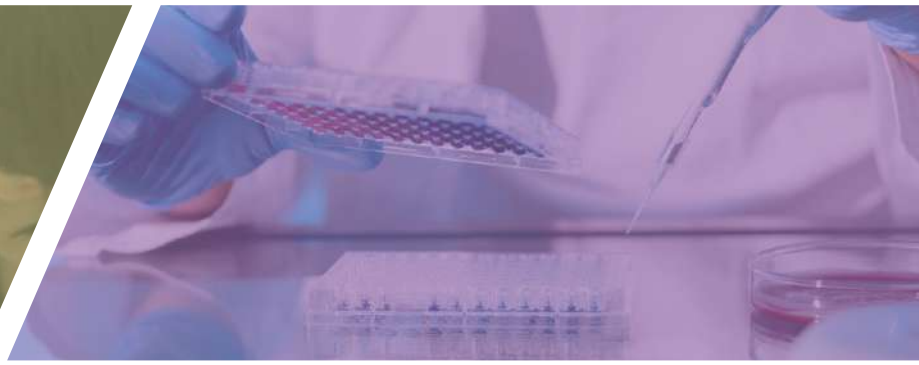
GlycoNet



TRANSLATING RESEARCH FOR HEALTHIER COMMUNITIES

CANADIAN GLYCOMICS NETWORK

2019 ANNUAL REPORT

SUPPORT

GlycoNet is made possible with support from the Government of Canada through the Networks of Centres of Excellence program, a joint initiative of the Natural Sciences and Engineering Research Council, the Canadian Institutes of Health Research and the Social Sciences and Humanities Research Council.

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CANADIAN GLYCOMICS NETWORK

2019 ANNUAL REPORT

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INTRODUCTION

VISION

Delivering solutions to important health issues and improving the quality of life of Canadians through glycomics.

MISSION

1. Ensure that the Network and Canada are internationally recognized as leaders in glycomics research
2. Deliver exceptional training in glycomics research and entrepreneurship
3. Bridge the translation gap between glycoscience research and industry
4. Translate research advances into tangible benefits for Canadians

WHAT IS GLYCOMICS?

Glycomics is the study of carbohydrates (sugars) in biological systems. Carbohydrate chains, or glycans, are found in the cell membrane of every living cell and are key to almost every biological process. The field is experiencing an explosion of activity with the recognition that there are many ways scientists can exploit biological processes involving carbohydrates to improve human health.

WHAT DOES GLYCONET DO?

- Invests in innovative, multi-disciplinary research in glycomics, with an emphasis on projects that benefit human and animal health
- Fosters translational research by creating an innovative environment and providing strategies for commercialization of Network research
- Creates strategic partnerships with government agencies, industry, non-profits and research institutions in Canada and worldwide
- Trains the next generation of glycomics scientists, providing them with the skills for future careers in academia or in the biotech and pharmaceutical industries
- Provides leadership and coordination of glycomics research in Canada by promoting collaboration and networking within the glycomics community

MESSAGE FROM THE BOARD CHAIR AND NETWORK DIRECTORS

The 2018-2019 fiscal year was one of delivering on the promise for GlycoNet as we met many milestones and gained more recognition as a leader in glycomics research at home and abroad. Our theme this year, *Translating research for healthier communities*, summarizes key achievements emanating from Network research projects and new partnerships.

Our Network Investigators and trainees made significant strides towards research translation and commercialization, showcasing research outcomes in over 250 publications to date and filing nine new patent applications this year, bringing the total to 34. It was also a busy year for Network-affiliated start-ups GlyCa Biosciences, PanTHERA Cryosolutions, and 48Hour Discovery. They aim to improve Canadian healthcare through the development of innovative and cost-effective products and research tools. These include a blood test allowing for early diagnosis of prostate cancer, a mechanism to ensure long-term preservation of stem cells for transplants, and a platform to accelerate drug discovery. All have roots in GlycoNet-funded research projects; the Network provides expertise and in-kind support to ensure their development and commercial success. Furthermore, in the past year, we established multiple industrial partnerships with biotechnology and pharmaceutical companies through our Strategic Initiatives program. These partnerships have enabled us to accelerate research translation and address the needs of the industry.

In addition to supporting research and development, GlycoNet provides training to the next generation of glycomics researchers to help develop highly qualified personnel (HQP); more than 370 trainees benefitted from GlycoNet training over the last four years. This number includes students at all stages of academia from undergraduate students to post-doctoral fellows, as well as research assistants and technicians. HQP training is centered on developing technical and transferable skills required by many careers. For example, our Advanced Training Opportunity Program is designed for senior students or post-doctoral fellows. It provides an opportunity to sharpen the leadership skills necessary to supervise and mentor junior students. Last year, the Network launched an online platform to enable HQP to share advice and tips with fellow community members. Every month, a trainee or a trainee-invited guest blogger highlights a subject of interest to the community. Topics ranged from professional etiquette to transitioning into industry and more.

Our outreach activities, carried out in partnership with the Centre for Math, Science, and Technology Education (CMASTE), went upstream this year to offer professional development workshops to large groups of high school teachers. These events, which were enthusiastically received by the participants, provided the teachers with hands-on activities

and lessons on glycomics. Taking carbohydrate science back to their classrooms, they will be able to give students a glimpse into one of the fastest growing research fields in Canada.

We continue to promote Canadian leadership in glycomics research internationally. This year, more than 13 Network Investigators and HQP put the Network's leadership on display, giving more than 24 presentations in 10 different countries around the world. The fourth Canadian Glycomics Symposium attracted over 200 researchers and industry leaders, including many from Australia, Taiwan, and the United States. GlycoNet scientists also met for a two-day workshop in Toronto with their counterparts from the United Kingdom to share knowledge and identify strategic opportunities for collaboration in research relevant to the biopharmaceutical and bioenergy industries. The event was sponsored by GlycoNet and the Biotechnology and Biological Sciences Research Council, the largest public funder of bioscience research in the United Kingdom.

At GlycoNet, we believe that diversity is essential to the advancement of science, better decision-making and the fulfillment of our mission. Following broad input of voices and perspectives, we are finalizing the establishment of an Equity, Diversity and Inclusion (EDI) committee to advise and guide GlycoNet's inclusivity efforts. We are already committed to integrating EDI principles into GlycoNet's operations and have enshrined that all funded projects have to meet certain EDI criteria. This includes a mandatory EDI statement in all Network project proposals, in which applicants explain their approach to EDI in all aspects pertaining to their projects. Over the next year, we plan to continue to identify inequities and representation gaps which we will address by implementing concrete measures to encourage full participation of diverse individuals in all Network activities. We have already begun developing workshops and offering webinars to start the culture change needed to integrate EDI into our work.

GlycoNet relies on continuously refreshing the leadership of its Board and Committees with new individuals representing diverse perspectives and skills. This year, Ms. Norma Sebestyen, Dr. Lynne Howell, and Dr. Matthias Ruth joined our Board of Director. Dr. Warren Wakarchuk was appointed as Associate Scientific Director. In addition, we are pleased to announce the recent international recruitment of Dr. Lara Mahal, the new Canada Excellence Research Chair in Glycomics at the University of Alberta. Dr. Mahal has already started discussions with fellow Network Investigators to identify avenues of collaboration. More importantly, Dr. Mahal will serve as the GlycoNet Associate Director for Clinical Partnerships, a newly created position designed to deepen outreach to and involvement of clinicians in our research programs.

We continue to expand the Network and support translational research that will benefit Canadians. In the last year, GlycoNet welcomed 14 new Network Investigators, bringing the number of investigators to 154. Many of our investigators received prestigious awards and research grants. For instance, Dr. Matthew Macauley and Dr. Karla Williams were respectively named Tier 2 Canada Research Chair in Chemical Glycoimmunology and Tier 2 Canada Research Chair in Oncology. These recognitions are given to exceptional emerging researchers and acknowledge their potential to become world leaders in their fields. Since its creation, GlycoNet has funded 93 projects. It now involves the participation of 239 organizations from our members nationwide and internationally, including research institutions, industries, and federal and provincial agencies.

The Network continues to focus resources from the federal government and partner organizations to answer some of Canada's most critical health challenges. Looking to the 2019–2020 fiscal year, we will strive to strengthen our efforts to bridge the gap between glycoscience research and industry by building and enhancing partnerships at home and abroad. Our investigators will continue to display Canada's leadership in glycomics research internationally. The Network and its partners will endeavor to find concrete solutions to the pressing health needs of Canadians. The research we do today will translate into healthier communities tomorrow.

Sincerely,

Mr. Frank Gleeson
Chair, Board of Directors

Dr. Todd Lowary
Scientific Director

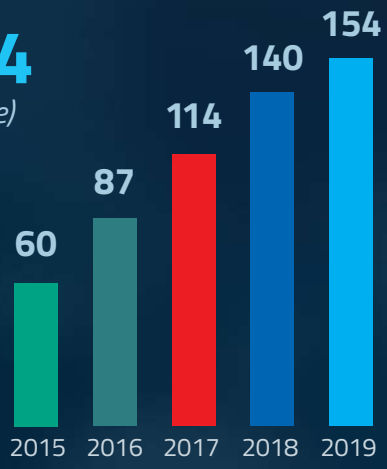
Dr. Warren Wakarchuk
Associate Scientific Director

Dr. Elizabeth Nanak
Executive Director

BY THE NUMBERS

NETWORK INVESTIGATORS

154
(to date)



WHO IS GYLCONET?

To date, we have...

154 researchers from across Canada

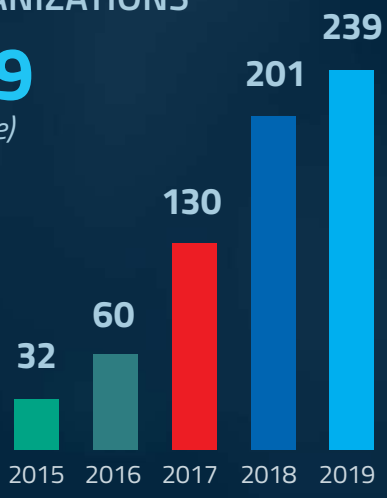
239 participating organizations

379 highly qualified personnel (HQP)

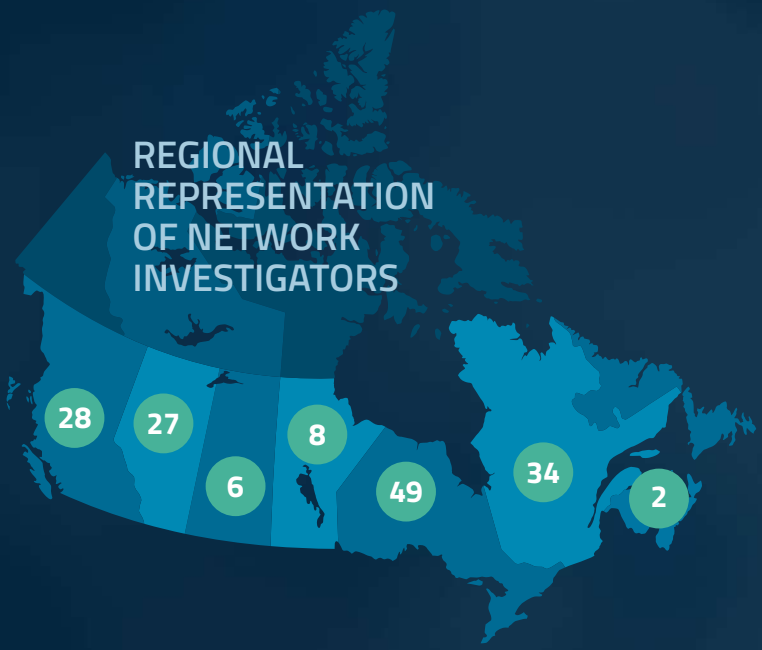
33 member organizations

PARTICIPATING ORGANIZATIONS

239
(to date)



REGIONAL REPRESENTATION OF NETWORK INVESTIGATORS



FUNDING

93 research projects *(to date)*

$20.2M research funds distributed and committed *(to date)*

$14.3M cash and in-kind partner contributions *(to date)*

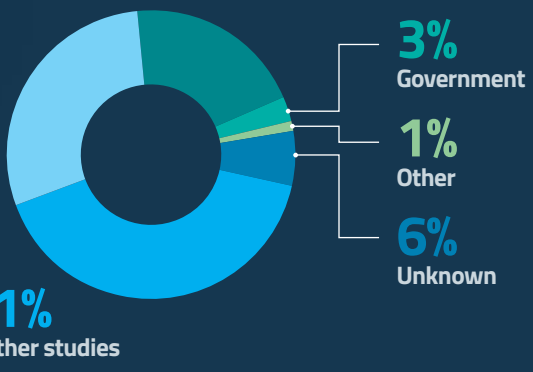
NETWORK HQP

379 *(to date)*

- **68** Undergraduate students
- **47** Master's students
- **76** PhD students
- **82** Postdoctoral fellows
- **59** Technicians
- **47** Research Associates

GLYCONET HQP TRANSITIONING TO WORKFORCE

from **173** *former HQP*



COMMUNICATIONS

970 Twitter followers

348 LinkedIn followers

623 GlycoNet newsletter subscribers

6,700 YouTube video views

RESEARCH HIGHLIGHTS

Glycomics is a broad and fast-growing scientific discipline focused on defining the structures and functional roles of glycans, or carbohydrates, in biological systems. GlycoNet's research efforts focus on providing solutions to human and animal health issues through the study of glycomics. Working at 33 institutions across Canada, our research teams collaborate with industrial partners to move research from the bench to the bedside.

93
RESEARCH PROJECTS
(to date)

$20.2M
RESEARCH FUNDS
distributed and committed
(to date)

253
PEER-REVIEWED PUBLICATIONS
(to date)

$14.3M
CASH AND IN-KIND PARTNER CONTRIBUTIONS
(to date)

5 THEMES:
antimicrobials, rare genetic diseases, diabetes and obesity, chronic disease, and therapeutic proteins and vaccines

BETTER TREATMENT FOR RARE DISEASES

Protein engineering unlocks the potential of enzyme replacement therapy for metabolic disorders

PROJECT INVESTIGATORS: DR. BRIAN MARK, DR. BARBARA TRIGGS-RAINE, DR. HÉLÈNE PERREAULT

One in every 5,000 Canadian newborns will develop a lysosomal storage disorder (LSD), a type of metabolic disease caused by genetic mutations. Tay-Sachs and Sandhoff diseases are amongst the most severe LSDs. Children suffering from these diseases lack an enzyme that can recycle used lipids (gangliosides) in their neurons. Eventually, the un-recycled gangliosides accumulate in the brain, interfering with normal biological processes and leading to brain damage. This is fatal in many cases and there are no known cures for Tay-Sachs or Sandhoff diseases.

For some LSDs, patients can receive intravenous infusion of solutions containing the enzymes they are missing, a procedure called enzyme replacement therapy (ERT). ERT can be compared to patching potholes on the road: the infused, healthy enzymes fill in the gap left by the deficient enzymes. Although effective, there are challenges to this procedure. The infused enzymes have to be stable enough to circulate in the blood stream before reaching the targeted neurons. They also have to cross the blood-brain barrier—a highly-selective border that separates the blood and biomolecules from the brain—to arrive at the neurons. Neither of these challenges have been met clinically for Tay-Sachs and Sandhoff diseases.

For years, researchers have been trying to design the "perfect" enzyme, one that can sail steadily through the blood vessels and across the blood-brain barrier. But much like developing a type of asphalt strong enough to withstand Canadian winters, the elusive search for this perfect enzyme continues. However, GlycoNet researchers are working on a uniquely promising approach.

Drs. Brian Mark, Barbara Triggs-Raine and Hélène Perreault from the University of Manitoba are forging ahead, determined to find that elusive, perfect enzyme. The team has recently been awarded a CIHR grant to evaluate a stable hybrid enzyme that can be used in ERT for children with Tay-Sachs and Sandhoff diseases.

"The defective enzyme that causes Tay-Sachs and Sandhoff diseases is a relatively large protein encoded by two separate genes," says Mark. "In order to make enough functional enzyme for ERT, we extracted the important features of both genes to make a new hybrid gene. I did this in collaboration with Dr. Don Mahuran (Toronto Hospital for Sick Children, retired). The enzyme encoded by the hybrid gene is now much easier to produce, and more stable than the natural enzyme."

Mark and his team have moved the goal post ahead several steps by visualizing the enzyme responsible for Tay-Sachs and Sandhoff diseases at a very high resolution. "This gave us insight into how the enzyme clears the metabolites in the brain and how other proteins are involved in the clearing process," he says. "All this information lays a solid foundation for developing the enzyme for use in clinical testing for ERT."

> ***By combining different skills from collaborators, we created a team with the necessary breadth of knowledge and experience to maximize our potential.***
>
> **Dr. Brian Mark**

Dr. Brian Mark (R) is finding a better way to treat rare genetic diseases. Photo by Kira Koop.

However, one main roadblock remains: after infusion into the blood, the enzyme has to pass through the blood-brain barrier to reach the brain and carry out the desired therapeutic function.

To find the solution, Mark's team is exploring different "Trojan horse" molecules that are recognized by the barrier and trigger it to transport cargo through. Think of going through a gate to enter a national park. The blood-brain barrier is the mechanical arm stopping you from entering. The "Trojan horse" molecule is the car displaying a park pass. The hybrid enzyme is the passengers in the car. In the case of Mark's research, the fusion of Trojan horse molecules with hybrid enzyme is like a car with a pass in which there are passengers—the vehicle and its occupants can get through the gate and head to their intended destination (i.e. the brain).

Yet, a successful passage through the blood-brain barrier does not guarantee an uptake of the enzyme by neurons. It needs to be decorated with phosphate groups, the amount and pattern of which dictate the efficiency of the uptake by the cells. To solve this problem, Mark is working with Perreault, a mass spectrometrist, to monitor the enzyme, making sure it has the optimal presentation and attachment of phosphate groups. Triggs-Raine, an expert in CRISPR gene editing technology, is generating a mouse model of the disease. It will allow the team to validate if the recombinant enzyme could alleviate the symptoms of the disease.

Mark thinks this research could also help advance another type of treatment—gene therapy. Unlike ERT, which uses a healthy enzyme to replace a mutated one, gene therapy is a technique that supplements mutated gene (DNA) with healthy DNA. Given the remarkable advances in virus-mediated gene delivery, this healthy DNA could potentially be delivered to patients' brains to produce functional enzyme within their neurons.

"One technical hurdle of gene therapy is that there is a limited capacity of genetic material that can be packaged into a virus for delivery," says Mark. "By reducing the size of two genes to a compact hybrid, the DNA material is now small enough to address this issue."

From protein engineering to mass spectrometry and gene editing, Mark and his collaborators are determined to find solutions to treat LSDs. "To answer complex questions for diseases like LSDs, a single laboratory simply does not have the capacity or the tools to fully explore the problem," says Mark. "By combining different skills from collaborators, we created a team with the necessary breadth of knowledge and experience to maximize our potential. Our project contributes to a strategy—crossing the blood-brain barrier—that could be coupled to a whole range of different therapeutics. We hope that the project will serve as a springboard for designing effective therapeutics and drug delivery systems to the brain for a wide range of diseases." ▪

NON-OPIOID PAIN RELIEF

A gel-based drug delivery system with massive potential?

PROJECT INVESTIGATOR: DR. MOLLY SHOICHET

Dr. Molly Shoichet, a Professor of Chemical Engineering & Applied Chemistry and Biomaterials & Biomedical Engineering at the University of Toronto, developed a safer way to deliver pain killers for patients who undergo surgeries. This new biomaterial can deliver anesthetics to surgical sites without causing side effects typical of opioids, such as addiction.

"There is a big unmet clinical and societal need," says Shoichet. "When most people undergo surgeries, they are treated with common anesthetics that don't last very long. Typically, these patients will then leave the hospital with prescribed opioids."

In collaboration with AmacaThera Inc.—a company born from the work done in the Shoichet Lab—Shoichet and her team are developing a drug delivery system that could eliminate the need to prescribe powerful opioids to patients after surgery. This gel-based drug is easy to store and to inject, says Shoichet. It can target specific surgical sites and the effects can last up to three days. Common local anesthetics typically wear off four to 12 hours after being administered. The long-lasting effect of this new gel-based drug can be traced back to its composition.

"The gel-based drug comprises a hydrogel and a bioactive molecule. By formulating the drug this way, we can achieve sustained release and thereby keep the bioactive molecule longer at the site to relieve pain," says Shoichet.

Shoichet uses an analogy to explain how the formulation works. "Imagine injecting a drop of dye into a bowl of water. The dye will diffuse quickly. However, if the dye is mixed together within a gel medium, a drop of the gel-dye mixture will diffuse slower in the bowl." In Shoichet's case, the dye is the bioactive molecule that relieves pain, and the gel medium is the proprietary hydrogel.

Another huge advantage of using the gel-based drug is that it is not addictive. Unlike opioids, which block pain signals sent from the brain to the body while releasing large amounts of dopamine—a substance that gives pleasure—local anesthetics obstruct the nerve transmitting signals to the brain without changes in awareness and sense perception in other areas. The gel developed by Shoichet achieves local delivery.

The gel-based drug has also been shown to be safe and efficacious through animal testing.

Yet, several steps still need to occur before the product can be commercialized. The team's next challenge will be to scale up the production of the gel-based drugs to make it possible to test them in clinical trials. Shoichet remarks that this is the hardest step so far, but remains focused, knowing that when commercialized, the technology will alleviate at least some of the heavy medical burden stemming from the opioid crisis.

Dr. Molly Shoichet (R). Photo courtesy of Roberta Baker.

Other than post-surgical pain relief, Shoichet mentions that this breakthrough can also be applied to tissue engineering and regeneration. In particular, the hydrogel serves as a carrier for cells and proteins, which can be delivered to sites to treat stroke, traumatic spinal cord injury, and blindness.

"Other than delivering pain killers, we are also using the hydrogel delivery system to carry biologic or small molecule therapeutics to the brain and the spinal cord to promote tissue repair and regeneration. We are also investigating different formulations of the hydrogel to carry cells to the retina and replace those cells that have died due to blindness. This could stop retinal degeneration, and even restore vision," she says.

The versatile technology platform, as Shoichet describes, is analogous to the "Fedex of drug and cell delivery."

"Our lab works on the packaging of the drug; we try to figure out how to deliver molecules, where they need to be, and for how long they need to be there," says Shoichet. "Like Fedex, we don't invent the contents of the package; rather, we ensure that the drugs and cells are delivered in the most efficient way." ▪

AN ANTI-INFLAMMATORY DIET

Restoring the ecosystem in the gut

PROJECT INVESTIGATOR: DR. BASTIEN CASTAGNER

Dr. Bastien Castagner

Keeping the gut microbiota in perfect balance in our intestines is important in preventing disease.

A GlycoNet-funded project is looking at using glycans (sugars) to restore an imbalance that occurs in patients suffering from inflammatory bowel disease (IBD). The chronic digestive disease, which includes Crohn's disease and ulcerative colitis, affects more than 200,000 Canadians.

"The gut microbiota is an ecosystem, much like a forest, and if there is any imbalance, the host or in this case, the person, suffers," says Dr. Bastien Castagner, a GlycoNet Network Investigator and Assistant Professor at McGill University. "This imbalance can contribute to inflammation, obesity, or in the case of our study, IBD."

"Together with McGill University microbiologist Dr. Corinne Maurice, our team is researching the metabolism of the gut bacteria to understand what they eat," he says. "Once we know that, we can suggest dietary glycans to change or modulate the gut microbiota to bring it back into balance in patients that suffer from IBD."

Castagner says people who suffer from IBD are missing key bacteria from their gut. Glycans can offer a solution to help restore a healthy balance. His research looks to identify the right food to sustain and promote key bacteria in patients' guts.

"Dietary glycans are a very important source of food for, and one of the main determinants of, the composition of gut microbiota," he says. "The key goal is to alter the composition of the gut microbiota using these glycans to get it to a healthier state."

The gut microbiota is an ecosystem, much like a forest, and if there is any imbalance, the host or in this case, the person, suffers.

Dr. Bastien Castagner

Castagner says the idea of using glycans to alter the composition of the gut microbiota is not new. In fact, human milk includes oligosaccharides, sugars that help maintain a healthy composition of bacteria in breastfeeding infants.

To collect data and develop a proof of principle, Castagner works with a bioengineer who created a completely automated artificial gut. "The reactor mimics a large intestine and will help us validate our hypotheses on a complex community of micro-organisms," he says.

GlycoNet's one-year catalyst grant provided Castagner's lab with the resources to hire a graduate student and a research associate to conduct the research.

"GlycoNet's funding was crucial because we could gather data to create a proof of principle," says Castagner.

Alongside his colleagues at McGill and other Network Investigators across Canada, Castagner is testing different glycans in the artificial gut to determine which ones bring the gut microbiota back to a healthy balance.

"We are also able to collaborate with other GlycoNet Investigators, and meet other experts in their respective fields of discipline, which is really helpful," he says.

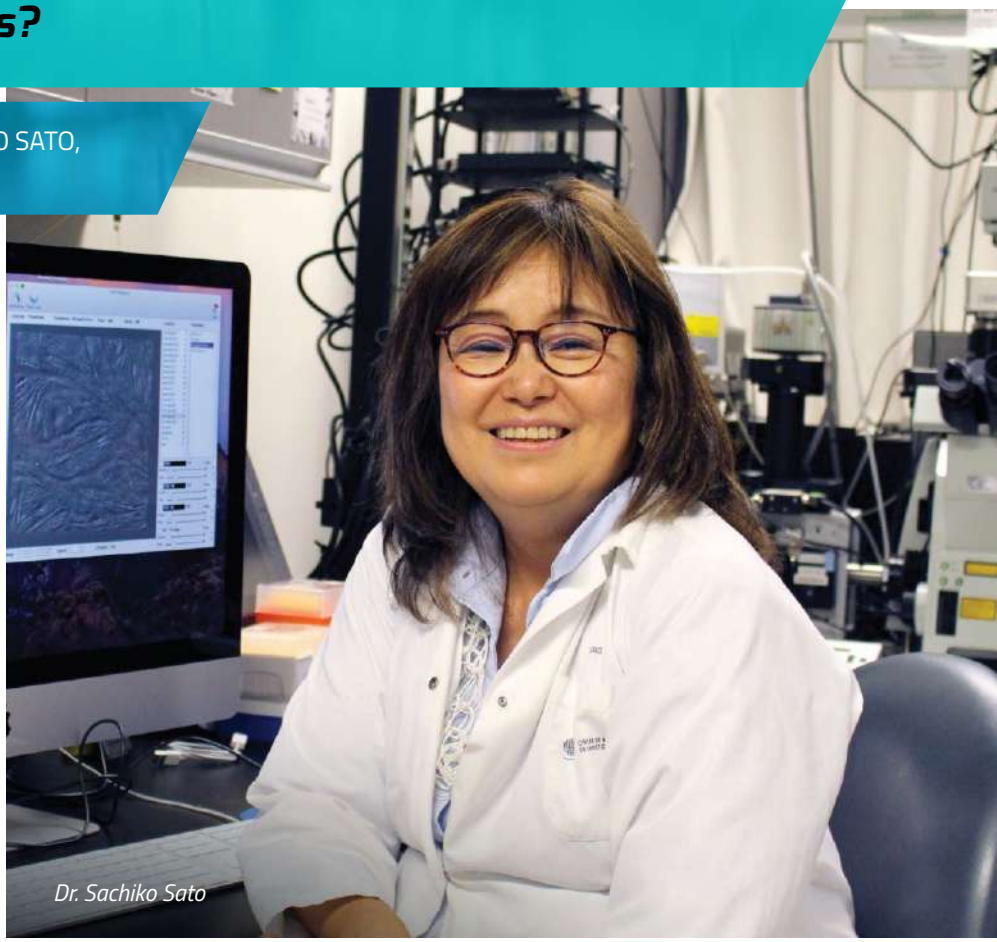
This strategy would also be applicable to other diseases, but before that can happen, Castagner says the strategy has to be tested in clinical trials on patients. ▪

TUG-OF-WAR IN YOUR IMMUNE SYSTEM

How does a carbohydrate-binding protein help battle fungal pathogens?

PROJECT INVESTIGATORS: DR. SACHIKO SATO, DR. DON SHEPPARD, DR. JAMES RINI

In a world where drug-resistant pathogens are more and more common, *Aspergillus* is having a field day. We breathe in the spores of this airborne fungus every day. Most people won't get sick from it. People with weakened immune systems, however, are at higher risks of developing health problems from breathing in these spores. As a result, they may experience symptoms including allergic reactions and pneumonia. To some, this may even be fatal.



Dr. Sachiko Sato

If we breathe the same air, why is the risk of illnesses higher for those who are immunocompromised? It turns out there is a constant tug-of-war between pathogens and immune cells within our immune system. In healthy individuals, white blood cells called "neutrophils" patrol the body looking for spores, which they then consume and kill. In immunocompromised patients—patients undergoing cancer therapies, transplant recipients or those with diabetes and HIV/AIDS—neutrophils become relatively inactive, allowing pathogens to kill healthy cells. Every year, over 1.5 million people fall ill because invasive fungi win the battle against neutrophils.

GlycoNet Investigators Dr. Sachiko Sato from Université Laval, Dr. James Rini from the University of Toronto, and Dr. Don Sheppard from McGill University are looking for ways to defeat these fungal pathogens. Instead of developing anti-fungal agents that may be quickly outrun by the pathogen's evolving drug-resistance, they are using a natural agent present in human beings to boost the ability of neutrophils to do their job.

This natural agent is a carbohydrate-binding protein called galectin-3.

"When we breathe pathogens (into our lungs), our bodies sense foreign matters and release galectin-3; this protein is known to be involved in the signaling pathways to tell the body to prepare for a series of immune responses," says Sato.

One of these responses consists of the body sending a signal to prompt neutrophils to go to the infected site. After the signal is sent, galectin-3 facilitates the migration.

However, their preliminary results suggest that some immunocompromised patients may not have the capacity to produce enough galectin-3. Moreover, these patients' bodies are under immunosuppressive conditions that reduce the ability of neutrophils to migrate to the lungs.

Sato and her team found that, from animal model studies, the lack of galectin-3 prevents neutrophils from being directed to the infection site. This finding may indicate the reason why immunocompromised patients are more susceptible to airborne fungal infections. To improve this situation, Sato and her team proposed developing galectin-3 into an aerosol drug, and to deliver it to patients' lungs to boost their immune systems. "The increased concentration of galectin-3 in the lungs may be able to signal to the neutrophils to migrate over and destroy pathogens," explains Sato.

Typically, the research process begins with *in vitro* experiments (experiments performed in a place outside a living organism) and later on moves to *in vivo* testing—Sato explains this project started directly at the *in vivo* stage with mouse models. The team was able to accelerate the normal process because of the breadth of the collaboration.

"Dr. Don Sheppard is playing a key role in the success of the project," says Sato. "He is an expert when it comes to fungal infections in the lungs. His lab plays a critical part in all the *in vivo* experiments. Our lab, on the other hand, supports from the point of view of glycobiology, where we accumulated knowledge of galectin-3, neutrophils, as well as deep understanding of host-pathogen interactions. In addition, some detailed biochemical approaches are performed in collaboration with Dr. James Rini."

Sato points out that the project is not only leading to the development of a natural boosting agent to enable the immune system to fight off fungal pathogens. It also inspired her to investigate other uses for galectin-3.

> ***The increased concentration of galectin-3 in the lungs may be able to signal to the neutrophils to migrate over and destroy pathogens.***
>
> **Dr. Sachiko Sato**

"We found that galectin-3 is also heavily involved in the generation of muscle fibres (myogenesis), and this gives us ideas for leveraging this protein to treat patients suffering from Duchenne muscular dystrophy," says Sato.

Duchenne muscular dystrophy is a genetic disorder characterized by progressive muscle degeneration and weakness. Sato thinks that augmenting the signaling of galectin-3 in the body may be a possible way to treat these patients and make them generate muscles.

"But I'm not talking about directly injecting galectin-3 into the patients," says Sato. "Since 40% of our body mass is muscle, if we inject an equivalent amount of galectin-3 as the treatment, it would be very pricy." She is working on an alternative solution.

"Similar to the idea of using a carbohydrate-binding protein (galectin-3) to boost the immune system, we decided to deliver a natural compound, which serves to increase the production of a sugar molecule in the body. This sugar molecule will then in turn incentivize the activity of galectin-3 in patients with muscular dystrophy." she says.

From restoring immune balance to boosting the body's power to fight off pathogens, Sato and her team are making significant headways to solve the issue of antimicrobial resistance. Their next step, says Sato, is to investigate the formulation of the aerosol so that it can efficiently be delivered to patients' lungs. They hope that the completed, formulated aerosol drug will benefit hospitalized patients as their bodies fight invasive fungi. ▪

TRACING THE PATH OF PARKINSON'S DISEASE

Like a GPS, this tracer could identify and monitor the disease progression

PROJECT INVESTIGATORS: DR. CHRISTOPHER PHENIX, DR. REBECCA DAVIS, DR. JUSTIN HICKS, DR. DARRELL MOUSSEAU, DR. DAVID PALMER

When we think we are healthy, we may overlook minute symptoms like anxiety or light-headedness. But those can in fact be symptoms of Parkinson's disease (PD). While Parkinson's disease is more commonly associated with motor symptoms like tremor, in many cases, and often prior to a diagnosis, patients may experience non-motor symptoms such as mood or cognitive disorders. Some people might think they have mood swings because they are experiencing stress at work, for example. Since some of these issues are not automatically associated with more severe health problems, they can easily be written off, which can get in the way of a timely PD diagnosis.

What if there was a real-time tracking system that could monitor for early onset of aggressive disease, even before severe symptoms appeared? A team of GlycoNet Investigators comprising Drs. Christopher Phenix, Rebecca Davis, Justin Hicks, Darrell Mousseau, and David Palmer are looking to develop just that.

Specifically, the team is working on an injectable tracking device—a positron emission tomography (PET) tracer—that can tell in real-time if a patient is at risk for early onset of PD. PET requires the injection of small amounts of a radioactive tracer to create pictures that measure biochemical activity in the living brain. Due to its unrivaled power to image brain activity, PET is already used in clinics to reveal various neurological disorders.

While the causes for PD are not yet fully understood, one of the earliest changes in the brain is the aggregation of insoluble proteins. This accumulation is heavily correlated with the dysfunction of an enzyme—β-glucocerebrosidase (GCase).

"Patients who have Parkinson's disease are known to have lower activities of GCase in the brain," says Phenix. "This enzyme normally functions by recycling cell wastes and metabolites through removal of sugars from fats found in cell membranes. If there is an insufficient amount of GCase, wastes would build up and eventually damage brain cells, resulting in more severe symptoms of Parkinson's disease earlier on. We are designing a PET tracer to monitor this enzyme's activity."

Unlike other PET tracers for PD, which give a snapshot of glucose (sugar) metabolism or dopamine receptor activity in the brain, the version proposed by the GlycoNet researchers would track the activity of GCase. This could give a better indication of early biochemical changes in the brain of PD patients.

"Existing diagnostic PET tracers that monitor dopamine receptors show the areas where brain neurons are dead. At this stage, there is already irreversible damage to those areas of the brain," explains Phenix. "Whereas tracing GCase would produce a PET image showing the extent of GCase dysfunction. Recent evidence suggests that this phenomenon occurs at a much earlier stage in Parkinson's disease."

In medicine, earlier is always better. Early diagnoses enable patients to receive appropriate care and treatment sooner.

However, designing a radioactive tracer that can image GCase is no easy task. It involves several complex steps. First, investigators need to design, synthesize, and optimize radio-labeled molecules that bind to GCase—usually this step involves multiple iterations of improvement to tease out a set of best candidate molecules. Second, the team conducts exhaustive testing in neuronal cells and animal models before the molecules can be put through clinical trials in humans. Prior to moving into a full scale clinical trial, in-patient studies are necessary to confirm that the tracer can image GCase in humans. The team needs to be made up of experts from different fields in order for the process to move along seamlessly.

"It is much more efficient to have various experts working within a collaborative team throughout the project," says Phenix. "Dr. Rebecca Davis (University of Manitoba), for example, uses computers to identify lead compounds that will bind to GCase; she looks at the enzyme's structure in 3D and helps us optimize the affinity of the compound to our target. Based on her advice, we then prepare the compounds she has identified and test them in the lab."

Phenix is also collaborating with two other Investigators from the University of Saskatchewan and one from the Lawson Health Research Institute in Ontario. Dr. Palmer (University of Saskatchewan) is helping the team synthesize and identify new compounds that efficiently target GCase. Dr. Mousseau (University of Saskatchewan) provides expertise in neurobiology to evaluate the radiotracers in cells and animals, while Dr. Hicks (Lawson Health Research Institute) leverages his knowledge of radiotracers in the brain to inform the team's next steps.

At this stage, the multidisciplinary team has developed synthetic routes to efficiently prepare a variety of radio-labeled derivatives and have identified promising compounds based on experiments using neuronal cells. The group is moving towards preclinical studies to ensure that the radioactive compounds can trace GCase in living animals properly. "Selectivity," or the act of binding only to the target enzyme, will be validated in living animals during this phase of the research process.

Dr. Christopher Phenix in his lab. Photo courtesy of Saskatchewan Health Research Fund.

"Selectivity of the tracer is absolutely critical," says Phenix, "there are over ten thousand other proteins in the body, and there are three other enzymes that are very similar to GCase. We need to make sure our tracer only binds to GCase, so that the PET image would show the accurate trace."

In addition to being used as a diagnostic aid for PD, the PET tracer could potentially facilitate the development of new PD therapeutics. "There are several companies developing therapeutics that aim to increase GCase activity. Our tracer could help guide their development—by tracing GCase, we can tell which drug candidates are most effective in increasing the enzyme's activity," says Phenix.

If Phenix and his collaborators are successful in developing a PET tracer, the team believes it can benefit neurologists, researchers, and patients by using the tracer as a tool to understand the biology of PD and potentially as a diagnostic aid.

"There are certainly examples where it can be difficult to distinguish Parkinson's disease from related disease, such as dementia with Lewy bodies (aggregation of insoluble proteins). We hope that our tracer could become a diagnostic aid to confirm and identify the disease earlier, improving patients' quality of life," says Phenix. ▪

DECIPHERING ALZHEIMER'S DISEASE

Carbohydrate-binding protein in the brain may correlate with disease protection

PROJECT INVESTIGATOR: DR. MATT MACAULEY

Dr. Matt Macauley. Photo courtesy of John Ulan.

Matthew Macauley, GlycoNet Investigator and professor in the Department of Chemistry at the University of Alberta, was recently named a Tier 2 Canada Research Chair in Chemical Glycoimmunology. Early this year, he was awarded a major five-year grant from the Canadian Institutes of Health Research (CIHR). This project builds upon work previously funded by GlycoNet. The project aims to clarify the role of CD33, a sugar-binding protein on white blood cells in the brain (microglia).

"To use a very simple metaphor, microglia are like the janitorial staff of the brain. Among the many important things they do, they help prevent accumulation of unwanted material, such as proteins. They play a role in pathogenesis of Alzheimer's disease. Accumulation of amyloid-beta, in particular, can lead to the formation of neurodegenerative plaques in the brain. This is one of the reasons microglia are increasingly being viewed as important in preventing this accumulation under healthy conditions" says Macauley.

Studies have shown that two different versions of CD33 are found in the human population. In previous studies, individuals who have a version of CD33 that does not bind its sugars were shown to be highly correlative with protection from Alzheimer's disease.

> ***Current studies point to the need to prevent the accumulation of plaques in the first place. That is why it is so important we understand how CD33 regulates the process of plaque accumulation.***
>
> **Dr. Matthew Macauley**

Using a mouse model, Macauley and his team are looking at the cause-effect relationship between the different versions of CD33 and microglia's ability to dispose of cellular debris. Macauley explains that once these proteins aggregate, there appears to be no turning back. This type of plaque (aggregated proteins) has been found in all people who develop Alzheimer's disease. This key trigger eventually leads to the devastating loss of brain function.

"Current studies point to the need to prevent the accumulation of plaques in the first place. That is why it is so important we understand how CD33 regulates the process of plaque accumulation," he adds. The Alzheimer Society of Canada reports that 747,000 Canadians are living with Alzheimer's or another dementia. By 2031, it is estimated that 1.4 million Canadians will suffer from Alzheimer's or another dementia. Women are disproportionately affected, representing 72% of cases.

Macauley, who trained as an immunologist during his postdoctoral studies, believes that his laboratory's interdisciplinary approach to research provides a unique opportunity to tackle an issue that is central to human health. His ultimate goal is to perform research that will impact people's lives. He hopes his research will lead to tangible benefits for people at home and worldwide. ▪

FIGHTING ANTIBIOTIC RESISTANCE

GlycoNet researchers identify a possible target in the prevention and treatment of bacterial infections

Originally published by the Canadian Light Source, June 27, 2019

PROJECT INVESTIGATORS: DR. CHRIS WHITFIELD, DR. TODD LOWARY, DR. MATTHEW KIMBER

The fight against infectious disease urgently requires new targets and treatments. The World Health Organization calls antibiotic resistance one of the biggest threats to global health, food security, and development. It is crucial to find new ways of tackling infections and to gain a deeper understanding of bacteria themselves.

GlycoNet Investigators Drs. Chris Whitfield and Matthew Kimber, from the University of Guelph, together with Todd Lowary from the University of Alberta have made great strides in understanding a critical component of bacterial capsules by using the Canadian Light Source (CLS) at the University of Saskatchewan. The capsules act as armour to shield the microbes from our immune system defenses. The results were published in Nature Chemical Biology.

While these capsules play a role in protecting pathogens like *Neisseria meningitidis*—the bacteria responsible for meningococcal disease—they are also a good target for therapeutics like small molecule inhibitors and vaccines.

If you get rid of the capsule, then the bacteria become very susceptible to attacks by the immune system, helping patients to get the upper hand during infections.

"The idea is that you identify molecules that inhibit one of the early enzymes. This prevents bacteria from making their capsule coats and renders them susceptible to normal host defenses," Whitfield said.

> ***The idea is that you identify molecules that inhibit one of the early enzymes. This prevents bacteria from making their capsule coats and renders them susceptible to normal host defenses.***
>
> **Dr. Chris Whitfield**

"This is an approach called 'anti-virulence'— the compounds don't kill the bacteria, but they eliminate a key component required for survival and virulence in the host."

The enzymes that Whitfield, Kimber, and their team investigated are commonly found amongst a range of pathogens, making it a great target for different therapeutic techniques.

Drs. Chris Whitfield, Todd Lowary and Matthew Kimber

Whitfield's group has been working to understand the details and mechanisms behind the assembly and export of these surface molecules for decades. While there have been clues in the scientific literature for years, more pieces of the puzzle are finally now coming together, offering a more detailed view of these processes.

The Canadian Macromolecular Crystallography Facility (CMCF) beamline at the CLS helped the researchers understand the structure of one of the enzymes, KpsC, through X-ray diffraction techniques.

"The CLS was critical for this work as all the structural data sets used were collected there," Kimber said. "CLS is our preferred venue as it bypasses all of the uncertainty and complexity of shipping crystals internationally. It is very easy to use, is generally available on a reasonable time scale, has great support staff, and has world-class technical capabilities."

Isolating a target is a huge step towards the creation of clinical applications, but it is still a long journey to a tailored-fit therapy. Whitfield would like to get as far as possible so that pharmaceutical companies can use this target in drug development.

He emphasized the importance of funders like the Canadian Institutes of Health Research, Natural Sciences and Engineering Research Council, and Canadian Glycomics Network.

Both Kimber and Whitfield stressed the importance of understanding the intricacies of bacterial systems. The researchers hope to better understand how enzymes interact with the cellular machinery inside different bacteria species and to keep people healthier in the process. ▪

PREVENTING A COMEBACK

GlycoNet researchers work to limit the spread of tuberculosis

PROJECT INVESTIGATOR: DR. LORI BURROWS (PROJECT LEAD: DR. ANNE VILLELA)

Most people in North America may be under the illusion that tuberculosis (TB) is an antiquated disease belonging to Victorian times. But TB is alive and well and ravaging many regions of the world. In 2017, a quarter of the world's population was reported to be infected with *Mycobacterium tuberculosis*. The disease was responsible for 1.6 million deaths in 2017 alone.

The multifaceted problem of TB has led the medical and research communities to sound the alarm. Many are working to find ways to prevent and treat this contagious disease. BCG (Bacillus Calmette–Guérin), the only approved vaccine to protect against TB, is not effective in adults. TB outcomes also worsen in people suffering from illnesses that affect the immune system, such as HIV.

Dr. Anne Villela, a post-doctoral fellow in Network Investigator Dr. Lori Burrows' lab at McMaster University, is among those who have made it their mission to identify effective ways to prevent TB. Along with Burrows and a team of GlycoNet researchers, including Dr. Zhou Xing, Villela is investigating the use of glycosylated pilins as a vaccine candidate for tuberculosis.

"I like that this project can make a tangible difference," says Villela, who is conscious that she has her work cut out for her. "It can take around 10 years for a vaccine to go from preclinical trials to the market," she adds. Villela is not in it for the short term. She does hope that a concrete solution to this health crisis will be uncovered sooner rather than later.

Burrows, Xing and Villela and their team are making headways towards preventing TB. They are evaluating type IV pili found in *Pseudomonas aeruginosa* as a vaccine against TB. Some type IV pili from *P. aeruginosa* are modified with a glycan found in the bacterium that causes TB. Since *P. aeruginosa* is a fast-growing bacterium and pili is highly expressed on the bacterium's surface, the necessary quantity of this protein can be easily isolated through shearing and formulated into a vaccine. Mouse studies are underway to evaluate the protective efficacy and immunogenicity of the pilin-based vaccine. They hope that immunization using glycosylated pilins will enhance anti-TB immunity by stimulating the production of antibodies against the bacterium that causes TB. In the near future, Villela and her colleagues are looking to combine the pilin-based vaccine with Ad-Hu5Ag85A - an adenoviral-based vaccine developed by the Xing lab at McMaster University that is currently in clinical trials - to elicit both humoral and cellular immune responses, as both are important to control TB.

Dr. Lori Burrows

Dr. Anne Villela

Originally from Brazil, Villela's passion for research was ignited in 2004, when one of her former molecular biology professors, invited her to come work at his biopharmaceutical company. She enjoyed working with biopharmaceutical research and development and pursued a Master's degree in this field. Villela's increasing interest in tuberculosis and infectious diseases led her to pursue a PhD in biochemical characterization and genetic studies of an enzyme as a drug target for tuberculosis in Dr. Diogenes S. Santos's lab (CPBMF, PUCRS, Brazil). Looking for new challenges and to further her knowledge in tuberculosis and infectious diseases, she connected with Burrows and Xing who had received funding from GlycoNet to study the pilin from *P. aeruginosa* as a vaccine candidate for TB. This funding was instrumental to Villela finding her way to the Burrows's lab.

Villela understands the important interdependency of industry and academia. She has dabbled in both and is keen to conduct research that addresses major health issues head-on. Before leaving Brazil, she contributed to many projects in the field of tuberculosis research. "I'm glad that I was able to implement new techniques, train people and contribute to research in Brazil," she says. "The sense of achievement made it easier to leave the country, looking for new challenges."

> ***I'm glad that I was able to implement new techniques, train people and contribute to research in Brazil. The sense of achievement made it easier to leave the country, looking for new challenges.***
>
> **Dr. Anne Villela**

Asked if she would once again leave her home to come to Canada, Villela has a clear and inspiring message for young researchers who are contemplating a move: "Leave. Do something else. Learn new things. It was challenging but it was one of the best things I have ever done. I look forward to continue working towards the development of a vaccine that might be approved for the prevention of TB, impacting the life of thousands of people across the globe." ▪

NETWORKING AND PARTNERSHIPS

GlycoNet favors a multidisciplinary approach. Its researchers harness the power of glycomics and uncover concrete solutions to pressing health needs. Building a sense of community, facilitating the exchange of information and ideas, and creating strategic partnerships with industries and funding agencies are important to the success of the Network.

33

NETWORK MEMBERS
(to date)

239

PARTICIPATING ORGANIZATIONS
(to date)

144
Universities and research institutes

45
Industry partners

16
Other (investment firm, law firm, etc.)

34
Federal or provincial departments and agencies

Forging global partnerships

GlycoNet continues to work with industry partners and other members of the scientific community. Over the past year, GlycoNet increased partner engagement and support through knowledge exchange, strategic partnerships and international collaborations.

Strengthening glycomics research in Alberta

The Alberta Partnership Program (APP) was created following the integration of the Alberta Glycomics Centre into GlycoNet. This program is funded with support from Alberta Innovates. It fosters translational human and animal health research in the field of glycomics, helps bolster Alberta's leadership in the field, and leverages the province's dynamic research environment to generate economic opportunities for Albertans. In 2019, five projects were funded through this program, focusing on:

- Developing a new drug to treat gastrointestinal inflammation in humans and livestock;
- Leveraging mass spectrometry to prevent Alzheimer's disease;
- Analyzing how carbohydrates can be used to stop neurodegeneration;
- Improving diagnosis and treatment of cancer;
- Designing a test to determine organ transplant compatibility when the donor and recipient have different blood types.

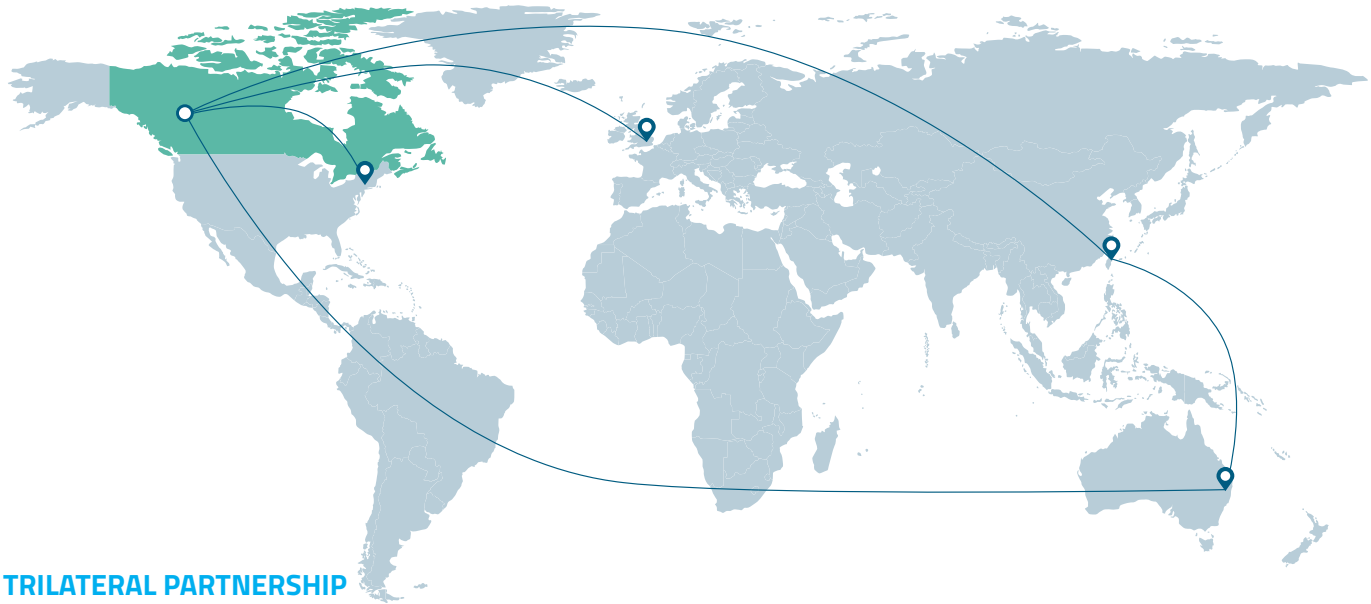
Strategic initiatives targeting unmet healthcare needs

GlycoNet's Strategic Initiatives (SI) Program is reserved for large-scale, multidisciplinary projects that need Network support to increase their likelihood of moving towards commercialization. This program requires that funded projects secure matching funds from sources other than GlycoNet. Under the SI Program, GlycoNet seeks out industrial partners and connects them with the appropriate researchers. Network partners include:

- **Appili Therapeutics Inc.:** to improve therapies for infectious diseases by developing new classes of anti-infectives.
- **Zucara Therapeutics Inc.:** to determine if its lead drug candidate "ZT-01" for type 1 diabetes can also benefit patients with type 2 diabetes
- **Merck:** to develop novel synthetic chemistry routes to improve the efficiency of drug development
- **Centre for Drug Research and Development:** to develop and evaluate a treatment for bacterial infections from *Pseudomonas aeruginosa*, including patients who have cystic fibrosis
- **National Research Council:** to improve cryopreservation processes that are essential for regenerative medicine and immune cell therapies
- **Ovensa:** to develop therapeutics for patients with Alzheimer's disease by using TRIOZAN™-based nanoparticles
- **Roche:** to identify potential therapeutic gene targets for Parkinson's disease.
- **Wellesley Therapeutics:** to develop a therapy for Duchenne muscular dystrophy with a carbohydrate-derived molecule

BRIDGING RESEARCH FRONTIERS

In an effort to strengthen connections with the international glycomics research community, GlycoNet initiated partnerships in North America, Asia, Australia, and Europe.



TRILATERAL PARTNERSHIP

The trilateral partnership between Canada, Taiwan, and Australia started with a focus on knowledge exchange. In February 2019, five GlycoNet Investigators travelled to Taiwan for a weeklong meeting hosted by Academia Sinica. The seminars created a space for researchers to share ideas about the latest developments in carbohydrate research and emerging pharmaceutical technologies. The collaboration continued and expanded in May 2019 as GlycoNet held its fourth Canadian Glycomics Symposium, inviting speakers from the Institute for Glycomics in Australia and Academia Sinica in Taiwan.

"The research expertise on both sides is complementary," says Dr. Hans Chun-Hung Lin, Associate Director at the Institute of Biological Chemistry in Academia Sinica. "Partnering with GlycoNet definitely facilitates bilateral collaboration, which helps scientists to tackle longstanding challenges and reach global excellence in research."

The Lin lab has been working with Network Investigators Drs. Ratmir Derda and Todd Lowary from the University of Alberta. Their collaborative projects range from designing small molecule inhibitors for proteins responsible for tumor progressions to screening arrays of carbohydrates to optimize tuberculosis diagnosis.

"These meetings help strengthen the research community and foster ongoing conversations that can be hugely beneficial in speeding up advancements in glycoscience," says Dr. Todd Lowary, Scientific Director at GlycoNet.

CANADA-UK CLUSTER COLLABORATION

GlycoNet and its partner Plantform joined the Biotechnology and Biological Sciences Research Council—the largest UK public funder of bioscience research—along with four other institutions from the UK at a two-day workshop. Researchers from different sectors were brought together to identify opportunities and technological barriers in biopharmaceutical and bioenergy research. Participants included leading experts in renewable feedstocks, metabolomics, glycoscience, cell biology, and biopharmaceutical productions.

ACCELERATING IMPACT THROUGH SYNERGIZED EFFORTS

GlycoNet actively seeks potential synergies with various organizations to advance research. In particular, GlycoNet has formalized partnerships with MaRS Innovation and CQDM, not-for-profit organizations that support the development of emerging technologies and help to get them to market. Current collaborations with CQDM include a project that aims to develop immuno-oncology therapeutics. MaRS Innovation is supporting a research project that is looking to develop a novel class of antifungal agents for point-of-care testing.

FOSTERING CANADIAN LEADERSHIP GLOBALLY

A pan-Canadian network, GlycoNet is also working to foster Canadian translational research leadership abroad. At the 2019 BIO International Convention, GlycoNet met with 23 biotechnology firms, accelerator/incubator funding groups, and pharmaceutical partners to showcase the breadth of research projects being carried out by Network investigators. Discussions with industry leaders led to the renewal of funding commitments as well as to the emergence of new sources of funding.

Highlights from the 2019 Canadian Glycomics Symposium

Putting Canadian leadership in translational glycomics research on display

Two hundred and twenty scientists, industry partners, and international experts in glycomics research gathered in Banff on May 15–17 for the 4th edition of the Canadian Glycomics Conference, which is organized by GlycoNet.

Train

The next generation of glycomics researchers, including undergraduate and graduate students, postdoctoral researchers, research associates, and technicians, engaged in peer learning about various disciplines related to glycoscience.

In addition, three workshops were offered exclusively to trainees the day before the Symposium. These workshops allowed trainees to build capacity and develop transferable skills that are important when pursuing a career in research, academia, and elsewhere. Topics included leveraging social media to promote your research activities, persuasion and negotiation strategies, and the R programming language.

This meeting is a unique opportunity for the Canadian and international glycomics communities to learn about advancements in the field. Together, researchers and industry leaders are finding inspiration in the work of others and creating collaborations to deliver concrete health solutions.

Dr. Elizabeth Nanak, Executive Director, GlycoNet

Inspire

CBC Radio One columnist Dr. Torah Kachur kicked off the event with a keynote address encouraging researchers to put themselves, and their research, out into the public sphere. Kachur challenged attendees to find their voice and use it to promote their work with audiences outside of the scientific community. In an ultra-connected world, where people have information at their finger-tips, scientists have an important role to play in popularizing science by providing real expertise, and information.

"Are we learning science from the Big Bang Theory? No! But what the show does is demystify science," said Kachur, who invited scientists present to, like the popular show, become advocates for science and research. She reminded those present that although the science is awesome and needs to be at the center, the story behind it, the why, the researchers' motivations, are often what will resonate most with the public.

Over the course of the three-day event, Canadian, Australian, and Taiwanese experts provided insights into groundbreaking glycomics research being done around the globe, particularly in Canada.

Discover

Attendees had a chance to hear newly-named Canada Excellence Research Chair (CERC) in glycomics Dr. Lara Mahal for the first time. She will be joining the University of Alberta in September 2019. Mahal set out an ambitious agenda for her lab. She touched on her collaborative vision for the CERC, reminding her colleagues that collaboration is key to advance Canadian leadership in glycomics research and deliver positive health outcomes for patients in need.

As glycans cover every cell in our bodies, glycomics is gaining attention and recognition as a field of research that is central to a better understanding of human health and a motor for uncovering concrete solutions to a wide-range of health issues. Attendees had a chance to learn more about glycomics research being done by fellow scientists around the globe. Talks covered a wide range of topics including:

- Using sugars to develop vaccines for infections like flu and tuberculosis
- Developing characterization technologies to understand the glycome
- Building glycans on the cell surface to study sugars and their roles in disease mitigation
- How degradation of sugars in the lungs is linked to pneumonia
- The role of glycomics research in uncovering treatments for common and complex health issues in a post-antibiotic era
- Unmasking the functions of sugars in the onset of genetic diseases and cancer

And the list goes on.

Six out of 25 trainees were selected by the Symposium organizing committee through a comprehensive screening process to give lightning talks—presenting their current research projects in three minutes using only three slides.

Over 90 scientists put their communications to the test by designing posters that detailed their latest research projects. From increasing the concentration of proteins known to stimulate brain development in children in formula, to gum health and its importance to overall human health, and intestinal health in chickens, this cutting-edge science fair gave attendees a chance to discover how others are harnessing the power of glycomics.

QUICK OVERVIEW OF THE CANADIAN GLYCOMICS SYMPOSIUM

222
TOTAL ATTENDEES

108
HQP ATTENDEES

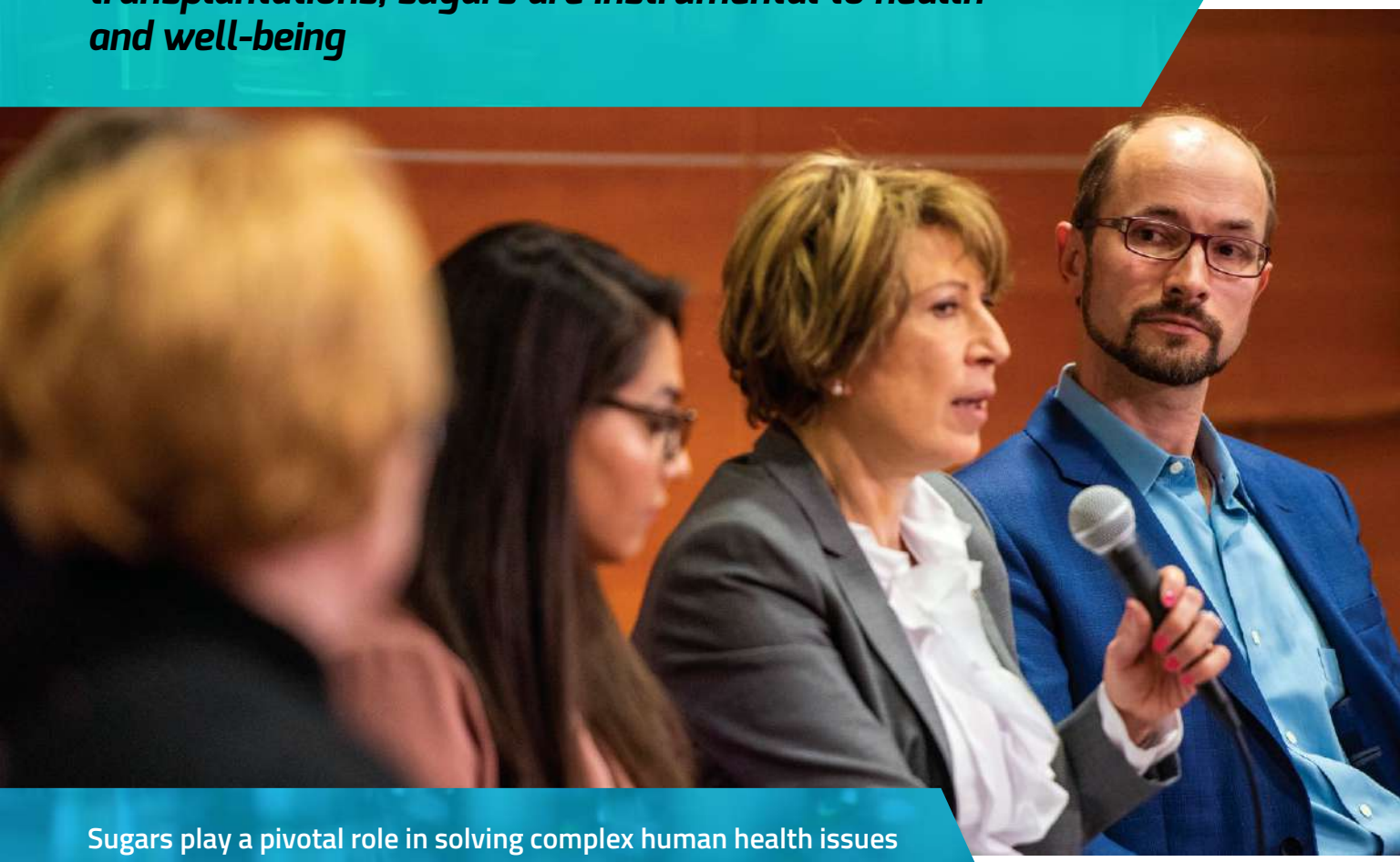
28
SPEAKERS

92
SCIENTIFIC POSTERS

21
INDUSTRY ATTENDEES

PUBLIC FORUM: WHY SUGARS MATTER

From fine-tuning the immune system to life-saving transplantations, sugars are instrumental to health and well-being



Sugars play a pivotal role in solving complex human health issues including heart, infectious, and neurodegenerative diseases.

That was the consensus among a panel of carbohydrate experts at a public forum on November 1, 2018 in Edmonton, hosted by GlycoNet. The panel discussion, Why Sugars Matter in Fighting Disease, explored the role and significance of carbohydrates in fighting disease.

Panel members included experts from cardiac medicine, chemistry, oncology, infectious diseases, carbohydrate synthesis, and cell and tissue transplantation. Author and former Daily Planet host Mr. Jay Ingram was the master of ceremonies and moderated the event.

"Sugars are essential building blocks of every living cell in our body," says Dr. Todd Lowary, GlycoNet Scientific Director. "They can regulate the way cells communicate with one another and the more we know about how they interact in our body, the better we can treat diseases. This has critical implications in the biotechnology industry."

"Sugars are the first point of contact with other cells, the first line of defense against bacterial infections, they help tune the immune system, and they define the outward facing parts of cells," adds Ingram.

Ingram noted that many functions of carbohydrates are still largely unknown and that any changes in those molecules have consequences for human health.

Dr. Lori West, a GlycoNet Investigator and Director of the Canadian National Transplant Research Program, explained that carbohydrates play a significant role in the success of organ and tissue transplantation.

"All cells are coated with carbohydrates that determine the blood type of an individual. Dogma tells us that the donor and recipient must be matched for successful transplant outcomes. However, we found that this is not true for infants," says West. "Over the past several years we've been digging into the science behind our findings, supported by GlycoNet and others, and are using that knowledge to develop better tools to inform and follow incompatible transplants."

Another area where carbohydrates can make a significant impact is in infectious diseases. As the number of infectious disease outbreaks and rates of antibiotic resistance rise worldwide, researchers are looking for ways to improve the effectiveness of antibiotics.

"In nature, bacteria preferably congregate and form a biofilm. A biofilm is a community of bacteria in a self-produced slime-like substance. A major component of biofilm are sugars the bacteria make. Bacteria in biofilms are up to a thousand times more tolerant to antibiotics," explains Ms. Erum Razvi, a GlycoNet trainee and PhD candidate at The Hospital for Sick Children in Toronto.

Razvi's research is investigating how bacteria make sugars and identifying a molecule that prevents these sugars from being released outside of bacterial cells, thereby preventing biofilm formation and making antibiotics more effective.

Canada's Chief Science Advisor, Dr. Mona Nemer, brought a national perspective to the discussion by encouraging bioscience organizations to focus on taking their basic research all the way to commercialization.

"GlycoNet is a great platform to bring scientists together to focus on a specific area of research," says Nemer, also a GlycoNet Investigator. "We need to capitalize on our strengths in bioscience, including glycomics. We need to make sure bioscience is a source of great national pride in Canada in the years to come – to put us in the top five nations in the word in this area. We need to ensure we have the capacity building, the infrastructure, and that we attract investments from around the world."

> ***GlycoNet is a great platform to bring scientists together to focus on a specific area of research. We need to capitalize on our strengths in bioscience, including glycomics. We need to make sure bioscience is a source of great national pride in Canada in the years to come – to put us in the top five nations in the word in this area. We need to ensure we have the capacity building, the infrastructure, and that we attract investments from around the world.***
>
> **Dr. Mona Nemer**

GlyCa BioSciences, a start-up company based on GlycoNet-funded technology, is an example of a company translating a technology that bridges oncology and glycomics for new cancer diagnostics. The company uses carbohydrates as a cancer biomarker to detect and/or predict high-risk prostate cancer with a simple blood test.

"We know that all cells are coated in sugars but that cancer cells are coated in different sugars," says GlyCa BioSciences co-founder and GlycoNet Investigator, Dr. Karla Williams. "By knowing what they are, we can find them in the blood of patients who are at risk of specific cancers. Looking at sugars in the blood can tell us a lot about someone's state of health."

While still a developing field of study, glycomics-based research has led to the development of commercial drugs such as Tamiflu, an antiviral medication used to treat and prevent seasonal flu, and Precose, a drug to treat diabetes.

"This public forum was a great celebration of GlycoNet successes that educated people about the role of sugars in developing new drugs and diagnostics, and making clear the commercial potential of glycomics research," concludes Mr. Frank Gleeson, Chair, GlycoNet Board of Directors. ▪

KNOWLEDGE TRANSLATION

Through its knowledge translation initiatives, GlycoNet provides tools to ensure that glycomics research moves from bench to bedside. GlycoNet's knowledge translations goals include:

- Facilitating the commercialization of promising technologies
- Creating an innovative culture that promotes and supports entrepreneurial activities derived from research
- Providing assistance for patent applications, IP recognition and licensing

34

PATENT APPLICATIONS FILED
(to date)

42

INDUSTRIAL PARTNERS INVOLVED IN GLYCONET PROJECTS
(to date)

$14.3M

CASH AND IN-KIND PARTNER CONTRIBUTIONS
(to date)

3

START-UP COMPANIES

GlycoNet focuses on four substantial pillars to achieve its knowledge translation goals:

PILLAR ONE

Research

To date, the Network has funded 93 research projects, 87 of which are multidisciplinary or translational. Other than funding, projects are also supported through core services and access to high-throughput screening facilities to help accelerate research outcomes.

A rigorous project management process allows for early identification of promising technologies and IP. To date, 34 patent applications were filed and several research projects have led to the development of technologies or products that have been or are on their way to being commercialized.

PILLAR TWO

Talent

GlycoNet has held several professional development workshops for investigators and HQP. Topics included entrepreneurship, intellectual property rights, project management, communications, and more.

In 2018-2019, two selected Network Investigators took part in a certification program from the Institute for Biomedical Entrepreneurship. The program fosters research translation by teaching attendees to take a project from idea to maturity. It helped the investigators understand how to move their research from the bench to the bedside.

PILLAR THREE

Linkages

GlycoNet believes that collaboration is key to research translation. It focuses on developing meaningful partnerships by:

1. Raising the Network profile and addressing industry needs through strategic partnership with research institutes, biotechnology, and pharmaceutical companies.
2. Leveraging international meetings, such as the BIO Convention, to connect potential partners with researchers working on projects that show commercialization potential.
3. Partnering with NCE-funded or Tri-Council funded Centres, and other national research networks to advance projects of joint interest.

PILLAR FOUR

Capital

From proof-of-concept studies to pre-clinical trials, GlycoNet programs aim to bridge the gap between academia and industry. The Network provides translational and start-up grants, as well as funding for IP protection. GlycoNet also provides other forms of commercialization support by helping researchers start their businesses derived from technologies that came about thanks to Network funded research. The Network also helps minimize risks of third party investment losses by helping researchers secure patents or other intellectual property recognition.

Commercialization stories

Scaling ideas into new business and proliferating technologies

An essential part of GlycoNet's mandate is to bolster Network-generated technology and speed up the delivery of commercial outcomes. Since its foundation, GlycoNet contributed to the creation of three start-ups—PanTHERA CryoSolutions, 48HourDiscovery and GlyCa BioSciences Inc. All entities were created to commercialize technologies derived from GlycoNet-funded research projects. In addition, SP Nutraceuticals, AmacaThera and Bright Angel Therapeutics leveraged GlycoNet funding to further develop and improve their existing core technologies.

PanTHERA CryoSolutions

Revolutionizing regenerative medicine through cell cryopreservation

A collaboration between Drs. Robert Ben and Jason Acker led to the creation of PanTHERA CryoSolutions. The company is improving long-term cryopreservation of cells so that they can retain their potential for clinical use. Working closely with GlycoNet, it uses a patented technology to create more hospitable environments for cells by minimizing damages caused by fast thawing and freezing. GlycoNet has provided commercialization support through every stage of the process, including funding a proof-of-concept study and scaling up manufacturing of the product. PanTHERA CryoSolutions was one the first Alberta-based companies to join the University of Alberta Health Accelerator. Learn more about PanTHERA CryoSolutions: pantheracryo.com

48Hour Discovery

Speeding up drug discovery with a molecular warehouse and a search engine

48Hour Discovery strives to accelerate drug discovery. Founded by Network Investigator Dr. Ratmir Derda, the company developed a series of modular platforms, including technologies to produce billions of bioactive molecules on demand, a screening system to identify active compounds, and a search engine that sorts, stores, and ranks identified active compounds. These three platforms were developed to help researchers conveniently and quickly find the best drug candidates for a given disease. GlycoNet has helped the company secure IP rights and has supported the commercialization of the technology. Learn more about 48Hour Discovery: 48hourdiscovery.com

GLYCA BIOSCIENCES

Non-invasive detection of prostate cancer

GlyCa BioSciences is working to enable doctors to determine if a patient has an aggressive form of prostate cancer using only a few drops of blood. After developing a nano-scale flow cytometry method that can detect the presence of a carbohydrate derivative associated with prostate cancer in the bloodstream, Drs. Karla Williams and Hon Leong founded the company. GlycoNet worked with the founders to advance the research and patent the technology, known as a liquid biopsy. It offers a less invasive alternative than other tests to determine the risks of prostate cancer. It also provides quick and accurate results, which can help with deciding who needs treatment. In the fiscal year 2019, GlyCa BioSciences has secured IP rights and is raising capital to make the tool available to doctors and patients.

SP NUTRACEUTICALS
Scientifically Proven. Naturally Derived.

Scientifically Proven. Naturally Derived.

SP Nutraceuticals is converting scientific discoveries into medicinal products to tackle diseases for which there are few treatment options. The company was co-founded by Dr. Paul Spagnuolo in 2016 after he and his team developed a plant-derived compound capable of breaking down kidney stones. GlycoNet continues to support the company's research and development efforts. In the 2018–2019 fiscal year, the company started recruiting patients in preparation for clinical trials that will start in September 2019. These trials are a major step in the product's go-to-market journey. Learn more about SP Nutraceuticals: www.spnutra.com

Dr. Paul Spagnuolo

AmacaThera

Redefining how therapeutics are delivered

AmacaThera's star product is a glycan gel-based drug delivery system that extends the life of anesthetics at surgical sites without the need for potentially addictive opioid painkillers. Through its Strategic Initiatives Program, GlycoNet has helped the company with corporate development and research funding. AmacaThera recently closed its Series A by securing $3.25M in seed financing from Sprout BioVentures, Viva Biotech, and Grey Sky Venture Partners. This funding will enable the gel-based delivery system to proceed to Phase I clinical trials. Learn more about AmacaThera: www.amacathera.ca

BRIGHT ANGEL THERAPEUTICS

Targeting antifungal resistance

Bright Angel Therapeutics is a pre-clinical stage biotechnology company focused on developing novel therapeutics for the treatment of drug-resistant and life-threatening fungal infections. Fungi infect billions and kill ~1.5M people per year, causing illnesses such as tuberculosis or malaria, yet only three major classes of antifungal drugs have been approved to treat systemic infections to date. Resistance to all three classes has been seen in the clinic and is now a major impediment to treatment. The company was co-founded by Network Investigator Dr. Leah Cowen following the discovery that intact fungal stress responses are needed for the emergence and maintenance of antifungal drug resistance. The company is targeting key regulatory proteins involved in the antifungal stress response. Learn more about Bright Angel Therapeutics: www.brightangeltherapeutics.com

KNOCKING OUT HEARTACHES

GlycoNet researchers win championship at AmorChem KNOCK OUT competition

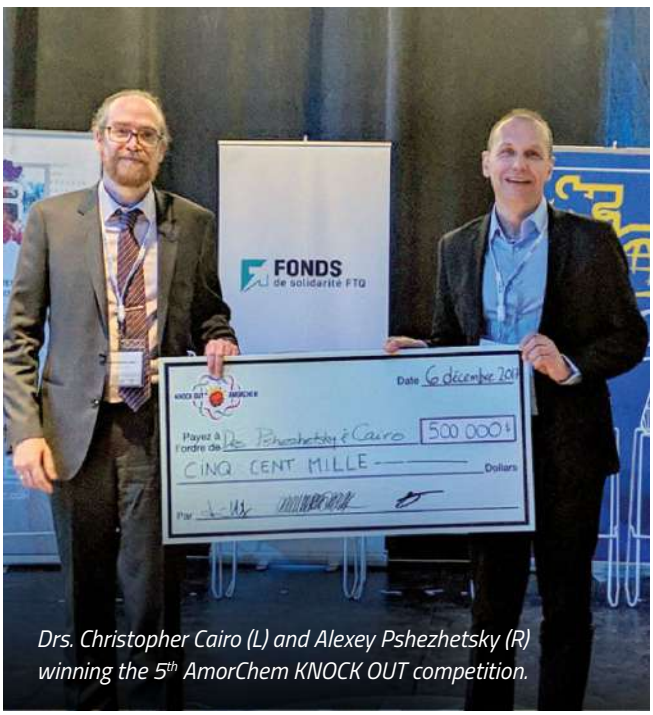
Issued by AmorChem on AmorChem, April 26, 2019

The Contenders of the fifth AmorChem KNOCK OUT™ Event valiantly climbed into the ring and duked it out against a panel of Heavyweight Champions for a chance of winning a coveted $500,000 financing from AmorChem.

All the Contenders displayed remarkable courage and agility in the ring, yet only one team could stand victorious. The winners of the 2019 KNOCK OUT Event are:

- **Dr. Alexey V. Pshezhetsky**, Sainte-Justine University Hospital Research Center & University of Montreal
- **Dr. Christopher Cairo**, University of Alberta

Subject of financed program: Human neuraminidase inhibitors for the treatment of cardiovascular and autoimmune diseases.



Drs. Christopher Cairo (L) and Alexey Pshezhetsky (R) winning the 5th AmorChem KNOCK OUT competition.

"The 5th Edition of AmorChem's KNOCK OUT was a great success," says Inès Holzbaur, Founder and managing partner at AmorChem. "We created this KNOCK OUT to increase the research community's awareness of our fund and to encourage its members to promote the commercial potential of their work. This team jumped at the opportunity and we are very excited to start working with researchers collaborating with GlycoNet, one of the Networks of Centres of Excellence of Canada."

"The Heavyweights had a tough job deciding on a winner among our high-quality Contenders," comments Elizabeth Douville, Founder and managing partner at AmorChem. "We would like to thank the Contenders for rolling with the punches, our Heavyweights for bringing their individual expertise into the ring today and Christopher Hall for successfully keeping everyone battling within the rules."

This KNOCK OUT was part of Effervescence, a scientific and business beehive event in the area of life sciences held on April 24–25 in Montreal. The AmorChem team warmly thanks its proud sponsors: Fonds de solidarité FTQ, Merck, Robic, and RBC Ryoal Bank. ▪

KNOCK OUT™ AMORCHEM

AMORCHEM

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VIDEO
SLO-MO

TRAINING AND EDUCATION

Training the next generation of glycomics scientists is vital to GlycoNet's mission and vision. GlycoNet HQP include undergraduate students, master's students, PhD candidates, postdoctoral fellows, technicians and research associates who work in various fields including chemistry, biology, microbiology, medicine, and immunology.

GlycoNet offers workshops, webinars, industrial internships, and other training activities to help young researchers develop technical and transferable skills important to career success in academia and industry. Every year, GlycoNet's Canadian Glycomics Symposium provides trainees with opportunities to present their work to colleagues, researchers, and industry partners.

379
NETWORK HQP
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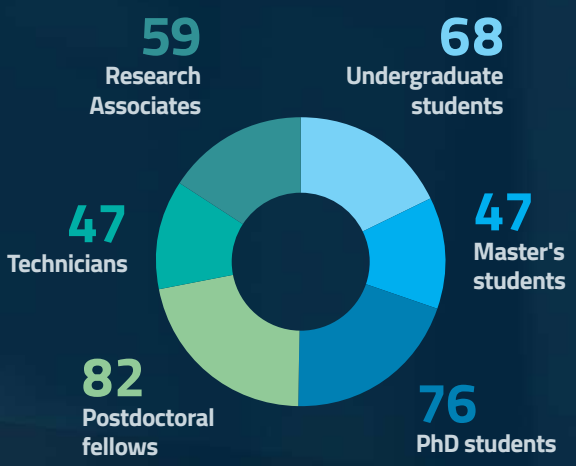

Training

HQP play a vital role in the design of GlycoNet's training programs. Represented by the GlycoNet Trainee Association Executive Committee (GTA–EC), HQP weigh in on what kind of training they require to further their careers or advance their current research projects. The GTA–EC meets regularly to discuss ideas and issues that matter to the next generation of Canadian glycomics scientists. It helps ensure that all GlycoNet trainees have access to diverse opportunities during their time with the Network.

GlycoNet training programs

Research Exchange Program

GlycoNet leverages its partnerships with universities nationwide and internationally to provide HQP with opportunities to work in different labs and develop technical and transferable skills. Through the Research Exchange Program, HQP learn new research techniques to advance their current research projects. Trainees learn to network and develop other skills that enable them to increase their contribution to their home lab once they return.

Advanced Training Opportunity Program (ATOP)

This program allows senior HQP, such as postdoctoral fellows or senior graduate students, to apply for funding to support a project of their own design. From these funds, the applicant can hire and supervise an undergraduate student. Through the ATOP, senior HQP gain experience in grantsmanship, project management, and mentorship, all of which are important skills for any number of future careers.

Mitacs Accelerate Internship Program

GlycoNet and Mitacs have joined together to create stronger connections between academia and industry. Accelerate internships allows HQP to intern with a Canadian company currently working on an eligible research project. Through this type of placement, trainees develop strong analytic and communication skills, learn to manage industrial projects, and gain a better understanding of industry realities. The experience provides the intern with important insights into what is needed to succeed in today's global market.

Undergraduate Summer Awards

Undergraduate students get a chance to conduct summer research projects. They are supervised and receive coaching from Network Investigators. To date, 33 recipients have received funding. These awards have also enabled Network Investigators to identify and recruit emerging glycomics research talent.

Professional Development and Technical Workshops

Each year, the GTA–EC works with the broader HQP community to determine topics of interest for professional development workshops. Past workshop topics ranged from transitioning to non-academic careers, presentation skills, building your professional online presence, career insight panel discussions, project management, entrepreneurship, and more. These workshops help trainees become aware of the specific skills they need to advance their careers in and outside the lab.

"Industry is very different from academia. As an industrial intern, I acquired the necessary tools to transition into industry after I graduate. I also learned that I don't have to stay in academia to work in research. In fact, from the internship, I found that working in the industry might be better suited for me because it's faster-paced and more structured."

Katarina Mandic, MSc student, Mitacs Intern at Mirexus Inc.

"My research project has focused on chemical syntheses. I make complex carbohydrates and study their structures, but I never see what happens after I make them. I usually just send them to my collaborator for downstream "biological experiments." But while on exchange at the Whitfield lab, I actually learned to conduct these experiments. It has given me a new perspective, helping me understand the big picture. With experience in synthetic chemistry, and now with molecular biology, I was able to boost my knowledge and apply for a post-doctoral fellowship in neuroscience."

Bo-Shun Huang, PhD candidate, Research Exchange Program participant

"How does one get creative in academic-based social media? The workshop opened my eyes. I have been missing out on a lot of networking opportunities because I didn't have a professional online presence. With all I learned from the workshop, I updated my LinkedIn profile and am looking into creating other academic platforms to track any publications of interest to my work."

Jennifer Crha, Master's student, "Cultivating your Online Presence" workshop attendee

CuriOSEity blog

In June 2018, supported by the Network's leadership, the GTA–EC launched CuriOSEity—a blog and online forum that tackles questions surrounding professional development. It highlights activities available to the HQP community, encourages discussion and interaction on glycomics-related topics, and offers peer advice on career development and advancement. Trainees learn to communicate their thoughts through creative writing, promote their research, and connect with other Network HQP. To date, 17 blog posts have been published, each tackling a topic related to the challenges and triumphs of the everyday life of scientists.

Learn more: canadianglycomics.ca/curioseity

"This was my first lab experience with organic synthesis. My supervisor (Alena) was an excellent mentor. I learned to take on responsibilities and solve problems independently. Alena and I communicated a lot; we discussed project planning and execution throughout the program. Self-motivation, patience, and a great mentor made this project a success."

Edward Schmidt, undergraduate student, junior mentee from ATOP

"I learned to encourage my team and became more organized. Research is not only about successes, but also about all the failures that contribute to new discoveries. Being positive and being able to deal with unexpected results while maintaining the right attitude is important. The project I started with Eddie is still ongoing, but I am proud of what we have accomplished in just one year."

Alena Pratasouskaya, Master's student, senior mentor from ATOP

Mentoring

Indigenous scientists in research

Dr. Jöerg Bohlmann and his mentee Olivia Baptiste bring inclusiveness to the forefront

As a member of the Soda Creek Indian Band in British Columbia, Olivia Baptiste was an athlete. She learned about science in high school, but never pictured herself setting foot in a lab. But in 2015, her passion for scientific research was ignited.

In grade 10, Baptiste participated in the Verna J. Kirkness Science and Engineering Education Program. She had the chance to live on the University of British Columbia (UBC) campus for a week while shadowing a scientist from the Faculty of Forestry. Throughout the week, Baptiste completed mini projects using wood products and learned to identify different types of trees from a lab field trip. Since then, she has been determined to pursue a career in research.

Baptiste, now a second-year undergraduate student at UBC, is conducting research under the supervision of GlycoNet Investigator Dr. Jöerg Bohlmann from the Michael Smith Laboratories. Her project, in collaboration with a postdoctoral fellow in the Withers lab, focuses on the production of a carbohydrate-decorated plant metabolite, which is being studied as a potential drug candidate to treat diabetes.

From forestry to carbohydrate biochemistry, Baptiste's journey to research may seem smooth. However, as an Indigenous student, the first of her family to attend university, and as a first-generation university student, she recalls several roadblocks when she first thought about a career in research.

Olivia Baptiste (L) and Dr. Jöerg Bohlmann (R)

The underlying challenge

"Growing up, there hasn't been much encouragement nor awareness for scientific research in my community," says Baptiste. "At the university, I started noticing the lack of diversity in science. I haven't met many Indigenous students in research, and it was intimidating to step into research on my own without a role model to look up to."

In 2016, Indigenous people represent 4.9 per cent of the Canadian population. Only 7 per cent pursue a post-secondary degree in science and technology. Beyond post-secondary education, even fewer were employed in professional, scientific, and technical services.

More diversity in science

As Baptiste's mentor, Bohlmann is aware of the underrepresentation of Indigenous students and the need to increase diversity in science. From a researcher's perspective, he stresses that this issue, if not properly addressed, may limit the scientific community's ability to drive innovation.

"Scientific research generates knowledge that improves our society," says Bohlmann. "But when we exclude contributions from certain parts of the community, it pushes us further away from improving society because none of the fractions can assume the voices of others completely."

Mentoring with listening ear and guiding hand

The two main reasons why Indigenous students are a minority in science are a lack of awareness about opportunities and difficulties in identifying role models. For Baptiste, working with Bohlmann has been rewarding, and his mentorship positively impacted her overall experience in research. With support and guidance, Baptiste's confidence has increased significantly. "As a minority group member, I wouldn't be able to commit to research if I didn't have my mentor (Bohlmann)," says Baptiste.

Baptiste initially came to the Bohlmann lab through the UBC Indigenous Undergraduate Research Mentorship Program, and subsequently received an NSERC USRA award to spend four months in his lab. For the past four years, the Bohlmann lab has been working with Indigenous youth, teaching them about science through mentorship programs and outreach activities. Every year, two Indigenous high school students spend a week in Bohlmann's lab to dig deeper into the biochemistry of forest trees and medicinal plants.

"Early exposure to laboratory research will help high school students explore the option of post-secondary education, as well as creates awareness of possible career directions," explains Bohlmann.

Embracing diversity with an open mind

Increasing diversity in science requires educating the scientific community about the challenges that certain groups of researchers are currently facing.

> ***Scientific research generates knowledge that improves our society. But when we exclude contributions from certain parts of the community, it pushes us further away from improving society because none of the fractions can assume the voices of others completely.***
>
> **Dr. Jöerg Bohlmann**

"A common mistake for scientists is that we may assume there is only one way of generating knowledge—through modern scientific method," says Bohlmann. "We forget that some of the present power of science builds upon a foundation of traditional knowledge."

While some people perceive Western practice and traditional knowledge as two non-converging schools of thoughts, Baptiste and Bohlmann say that the synergy between both knowledge systems adds immense value and helps advance science and society. The integration of one knowledge source with the other brings together varied technical and transferable skills sets and allows individuals with unique problem-solving capabilities to contribute to the success of a project.

Baptiste, when reflecting on her path to research, admits that it was bumpy. It took her a long time to find confidence to pursue research because she was intimidated by the underrepresentation of Indigenous students in science. Now, as a biology major, her passion and perseverance have made her a role model for future generations of Indigenous scientists. Back in the Soda Creek Indian Band, Baptiste continues to share stories with her community, hoping to make connections and inspire more Indigenous youth to leap into the wonderful world of science. ▪

Three scientists on the frontline of change

Advice and inspiration to encourage women in science

Three scientists from GlycoNet, working on different projects across Canada, share a determination for improving Canadian healthcare. We spoke with them as these three women of science shared their experiences with mentoring and training, talked about some of the challenges they face as women in scientific fields, and discussed their perspective on the value of bridging geography through networking in order to advance scientific research.

In her lab in Edmonton, Alberta, Dr. Lori West is overseeing the analysis of biological samples from pediatric heart transplant patients and preparing to send the results to a team of collaborators. They are carbohydrate chemists, and they create and modify tools to better understand the structure of blood type-related sugars. These sugars hold the answers to important questions, among them how infants can survive after receiving an incompatible organ transplant—a procedure that involves the recipient and donor having different blood types.

In another room in the West lab, Morgan Sosniuk, a fourth-year undergraduate student, is pacing back and forth, anxiously waiting for the results from the flow cytometer, an instrument that she uses to measure blood group-related antibodies. Unlike the conventional assay to detect blood group antibodies, which only identifies the main A, B, and O blood groups, Sosniuk's method will identify antibodies to the more intricate subtypes within each blood group. This will allow her to monitor patients' blood group antibody changes after an incompatible organ transplantation. Since high school, she has been focusing on developing this high-precision medical test. The test's simplicity will facilitate its integration into the already complex transplantation pipeline.

A few provinces to the east in Toronto, Ontario, Natalie Bamford, a doctoral student, is also hard at work. In Dr. Lynne Howell's lab at SickKids Hospital. Bamford sits steadily in front of a polarized light microscope with a 48-well plate, each well containing different chemical solutions. Patiently checking each plate through the lens, she is trying to see if a specific protein from a fungal pathogen has formed a crystal in any of the wells. If it has, it will significantly help the scientific community understand the structure and the properties of the protein, which could lead to it being used as a therapeutic agent against fungal infections.

> ***We need to encourage girls and women to be confident. If girls and women are interested in science, we need to support their growth, enthusiasm, and their participation in science. It is especially important to be confident about what you know and what you do, while acknowledging what you don't know and remaining open to continuous learning.***
>
> **Dr. Lori West**

Curiosity is genderless

When speaking about what motivated them to pursue careers in science, they all point to one common denominator: curiosity.

As a child, West, who has been an investigator with GlycoNet since 2015, remembers pondering questions about the nature of science and wanting to understand how things worked. This curiosity led her to pediatrics. It was the same tireless, inquisitive mind that later made her a pioneer in her field when she proposed a dramatic change in transplantation procedures, which successfully led to heart transplants being performed in infants from mismatched donors. This allowed a much higher likelihood that a donor could be found for these highly vulnerable babies. Previously, the mismatched heart transplant procedure had not been considered a viable option, since having a mismatched donor and recipient increases the risk of the rapid organ rejection that could lead to death. Thinking back on her accomplishments, West suggests that if you want to find solutions that can improve patients' quality of life, sometimes "you have to challenge the way things are taught to you, and establish new paradigms."

Mentored by West, Sosniuk joined GlycoNet's trainee program a year ago. As soon as she started her current research project, she knew the road ahead would be filled with its share of obstacles. Sosniuk is challenging the way clinicians traditionally identify blood type-related antibodies. Detecting and identifying these antibodies is required prior to any transplant surgery to ensure the best donor-recipient matching or, in the case of mismatched transplants, to allow accurate monitoring and guide effective interventions if required. However, at a time when medical science is leveraging technology to reinvent how things are done, the method currently used to identify these antibodies is the same as the one used since the early 1900s. Sosniuk is working to bring this process into the 21st century, aiming to make the procedure more accurate while modernizing it. She recalls that her main motivation has always been being able to address questions that no one has been able to answer yet. "I'm not only trying to solve puzzles, but as a scientist, I am also privileged to be asking questions people haven't asked before," says Sosniuk, who knows that answers to those questions could improve the lives of many.

> ***If you're willing to push yourself, be open-minded, and find positive support, you can really do more than you think you can.***
> **Natalie Banford**

More mentors, role models, and sponsors for women

Bamford recalls her experience as a first-year undergraduate student; she, like most newcomers to university, found herself in an introductory class of more than a thousand students. "We were all told that we were one in a thousand," she chuckles. "Did that imply a low chance of success?" she wonders.

Two years later, Bamford started thinking about doing research during the summer. With the "0.1% success theory" lingering in her mind, she emailed five professors she wanted to work for, presuming they would not reply. After all, they probably got at least 999 other emails from students who also wanted to get their first experience in a lab. Why would they pick her? To her surprise, she received four responses.

"If you're willing to push yourself, be open-minded, and find positive support, you can really do more than you think you can." Bamford says. Now working in Howell's lab, she is surrounded by successful female role-models who are not only her supervisors, but have become her peers.

While Bamford was finishing her undergraduate studies, Sosniuk was still in high school. The two, who were years away from meeting, shared a curiosity that would ultimately lead them to a career in science. Sosniuk always knew she wanted to be a scientist and do research. Her young age did not temper her ambition. However, the fact that she did not encounter or even see many women in the positions she aspired to holding, was a concern.

Be passionate about what you're doing, and find something where the passion is natural.
Morgan Sosniuk

Reflecting back, Sosniuk explains that her own experience helped her see the need to have female representation at every stage of a career path in research. Making women role models visible is critical. If young women do not see themselves reflected in the field, they may abandon the pursuit of a career in research at a time when equity, diversity and inclusion are more important than ever.

Interestingly, during the conversation, West, the most experienced scientist in the group, brought up the need for women to find not only mentors, but also sponsors. What's the difference you ask? Sponsors do not only coach and guide the way mentors do. Their job is to open doors, advocate for someone they believe in, and provide that person with opportunities.

Showing how diversity is a game-changer

Diversity is emerging into public dialogue at many levels. This topic seems to be on everybody's mind and lips. The scientific community is no exception.

"I'm glad to see that Canada is leading the way when it comes to equity, diversity and inclusion (EDI) by including new policies in the system, from government regulations to granting agencies' funding strategies" West says. To raise public awareness of the importance of EDI, the scientific community must lead by example.

Publicly acknowledging the successes of a diverse group of individuals can also lead to a better understanding of why diversity matters. Bamford explains that "Role models already exist, but they need to be highlighted more. Having more diverse people shown in public outlets and invited to talk at conferences are critical steps to raise awareness of EDI. It will also increase diversity over time."

West gives an example of a successful conference that welcomed women bringing their children along, and provided appropriate facilities and arrangements, as opposed to them having to secure childcare. This is a good example of a simple action all conference organizers can take to remove a systemic barrier for many women and empower them to attend these events, which are important networking and learning opportunities.

One last piece of advice

As the conversation draws to an end, West shares one final bit of advice: "We need to encourage girls and women to be confident. If girls and women are interested in science, we need to support their growth, enthusiasm, and their participation in science. It is especially important to be confident about what you know and what you do, while acknowledging what you don't know and remaining open to continuous learning."

Sosniuk's parting words are focused on passion. "My advice is to be passionate about what you're doing, and to find something where the passion is natural. If you're falling in love with the type of research you're doing and with the environment you're a part of, everything else falls into place more naturally, and you'll want to put in the hard work. It will be very rewarding because it's something you love."

Last but not least, Bamford speaks in a fearless and determined tone. "Coming this long way, my advice is to simply go for the things you want to pursue. Push past your boundaries, and remember, if you immerse yourself in a supportive environment, you will succeed."

As we finished the conversation, these three scientists will go back to their lab benches, microscopes and data. From Newfoundland to British Columbia, other women just like them will continue to move beyond working in the shadows to advance medical research. If we ask you what advice you would give to young women who are considering pursuing a career in research, what would you tell them? ▪

Shedding light on the wonders of glycomics

Indigenous high school students take part in weeklong research seminar thanks to GlycoNet

GlycoNet is proud to promote inclusion and diversity in science by giving Indigenous youth a chance to experience life in the lab first-hand.

Two Indigenous high school students from Glaslyn High School in Saskatchewan, along with their science teacher, attended the 17th annual Apprentis en biosciences thanks to GlycoNet's sponsorship. Network Investigator Dr. Christopher Phenix (University of Saskatchewan) helped in the recruitment of the two students, while Dr. Yves St-Pierre (Institut National de la Recherche Scientifique) organized the week-long event in Quebec. High school students team up with a graduate student and perform mini-experiments in the lab. The event was a wonderful opportunity for students to travel out of province, network, and see how their unique background allows them to make meaningful contributions in a research lab environment. It is necessary to offer a variety of experiences to Indigenous students to ignite their passion for science, while creating an opportunity to learn from the students and leaders in their communities.

Phenix, an Assistant Professor of Chemistry at the University of Saskatchewan, says that university outreach programs can do just that. They give young Indigenous students early exposure to cutting-edge science. Phenix, who is of Métis ancestry, is involved in numerous outreach activities to engage Indigenous youth in hands-on activities that promote an interest in science. Last year, he and other faculty at the University of Saskatchewan organized the first ever "Indigenization and Reconciliation in Chemistry Education" symposium during the 101st Canadian Chemical Conference and Exhibition. The event aimed to understand how education is key to reconciliation, attract more young Indigenous students to study chemistry and discuss traditional ways of discovery and knowing in order to improve success in chemistry courses.

Phenix sees tremendous value in participating in outreach programs. "One thing we can do as faculty is to work alongside teachers and leaders in First Nations communities, helping them develop curriculum to capture the interest of youth at an early age," he says. "Together we are coming up with strategies and ways to be more inclusive, ensuring success when Indigenous students pursue science."

For more about the program, visit www.apprentisinrs.ca. ▪

Carb loading: high school teachers taking new skills back to classrooms

High school teachers were on the other side of the classroom at the University of Alberta with the chance to play with the research on carbohydrates being done in their own backyard.

Originally published in The Edmonton Journal, December 1, 2018

About 40 Edmonton-area teachers took part in the daylong program offering 42 hands-on activities and lessons created by local teachers and researchers on glycomics, the study of carbohydrates in humans.

The workshop was hosted by GlycoNet, a Canadian research network focused on supporting the study and teachings of glycomics, and the university's Centre for Mathematics, Science and Technology Education (CMASTE), with the aim of helping local teachers bring carbohydrate science into their classroom through a local lens.

"We wanted to break down the barriers between what teachers are expected to teach and some of the research that's going on in Edmonton and in Alberta," GlycoNet Training and Project Management Coordinator Ryan Snitynsky said. "Today we're highlighting people and projects that are happening right down the road from where many of these teachers teach."

Snitynsky said GlycoNet hopes this Alberta pilot project will provide role models for students and help develop an interest in the study of carbohydrates.

"We don't expect that they'll all be carbohydrate scientists, but through this experience as voters, citizens and taxpayers, they'll be able to have a deeper appreciation of the science that's going on in their communities and be able to critically analyze issues that society faces," he said.

The pupil teachers learned about research being done at the university looking for treatments for tuberculosis and Alzheimer's disease through the study of glycomics as sugars are the first point of contact for diseases in cells, Snitynsky explained.

"If we can understand those types of interactions, we can use that information to develop new treatments and new drugs," he said.

After completing a hands-on activity to build a protein structure, Grade 11 and 12 biology teacher Katie Teeuwsen said she hopes to bring the practical implications of carbohydrates in the body, such as blood typing and immune response, back to the classroom.

"It makes kids care more because it actually does impact them in some way," she said of the day's workshop created by fellow teachers who spent three summers with researchers at six universities across the country. "There's more understanding of what you can actually use in the classroom because it's developed by former teachers."

GlycoNet, which is headquartered at the U of A and now has researchers in 31 institutions across the country, is hoping to expand the workshop program to other provinces and further help translate carbohydrate science to high school students. ▪

About us
Funding mechanisms

HQP alumni perspectives

Dr. Samy Cecioni on developing tools for chemical glycomics

HQP alumnus shares how the Network helped him reach where he is at today

In 2012, Dr. Samy Cecioni left France, where he completed all his education, and decided to move to Canada for a post-doctoral position.

Dr. Cecioni became a GlycoNet HQP when the Network was in its infancy. He joined a team of six scientists for a project in Dr. David Vocadlo's group at Simon Fraser University.

Fast-forward to this February, Samy Cecioni was appointed Assistant Professor at l'Université de Montréal and established his research lab. Reflecting on his career path, Prof. Cecioni knows he has made the right decision. "The extraordinary support that I have received from my mentors and the scientific community in Canada has really been instrumental in my desire to start my independent career here," he says.

We asked him to walk us through his journey and tell us more about what keeps him going.

What are you working on?

We are developing chemical tools and molecular probes that allow us to image the biology of glycans in live cells. When it comes to sugars, the cell is a busy and crowded environment—the assembly and recycling of complex glycans by enzymes but also transient interactions between proteins and carbohydrates are all continuously happening to maintain a healthy cell. We want to design the next generation of molecules that could enable us, and others, to take snapshots of these events, and ultimately to monitor in real time what's going on in live cells.

What problem does it solve?

The balance between the assembly and breakdown of glycans is an important determinant for health. When this subtle balance is disrupted, cells end up with altered glycan structures at their surface which can perturb cellular function. We now know that this is a hallmark of diseases such as cancer. For example, cancer cells can hijack the glycan machinery to alter glycan recognition and evade our natural defenses. So, this is a very promising area for developing therapeutics, but these processes are very complex and not easy to study using current approaches. That is why it would be extremely valuable to design molecular probes that enable us to image what is happening in the true physiological environment of the cell. Novel strategies would also help to streamline the development of glycomimetic molecules that can directly perturb these processes, restoring the proper balance of glycome dynamics and providing therapeutic benefits.

What inspired you to pursue work in this field?

My background is in organic chemistry and, early on, I became very interested in the specificities of carbohydrate chemistry. Joining graduate school, I started reading the glycobiology literature and I recognized that this was a field of underappreciated potential. For my PhD studies, I split two thirds of my time performing syntheses in an organic chemistry lab and one third of my time in a glycobiology lab. I knew this field would emerge and would require expertise from different disciplines to advance.

Then, it boiled down to meeting supportive mentors and I have been particularly lucky on that front. On my first day meeting with my post-doctoral supervisor, David Vocadlo, we sat down and talked about challenges in the fields and ways to address them. It was very exciting to sketch potential chemical designs that could be efficient probes for imaging glycosidase activity in live cells. This project needed both synthetic skills and an ability to work with enzymes and live cells. His mentoring is one of the main reasons why I am where I am today.

Was there a challenge shifting from organic chemistry to glycobiology?

No, I wouldn't say it's a shift. This is all science and, with the emergence of fields such as glycomics and deep changes in the industry, we must recognize that it is important to complement our primary skills with the techniques and expertise that are necessary for our research. In that respect, the way GlycoNet is bringing scientists together is a great catalyst. The projects I worked on were highly multidisciplinary and in my lab, we are now starting projects from organic synthesis all the way to their use in cells.

How has your previous work shaped where you are today?

To me, the academic trajectory is very appealing in the sense that, at every stage (undergraduate, graduate student, postdoc, principal investigator), you come in as a beginner and acquire new skills and knowledge, taking on more and more roles. For example, as a HQP, I became involved in project management and training of younger colleagues; as a new professor, I am now learning to finance our research and to take responsibility not just for the projects but for the team. It is important to remind ourselves what the end goal is to train scientists and to do science that could improve people's lives. This is both humbling and extremely motivating.

Scientifically, my previous work has really convinced me of the importance of comprehensive chemical biology approaches for the field of glycomics. But our experience also shapes what kind of mentor and colleague we aim to become. Mentoring students is a privilege but also a big responsibility when it comes to preparing students for the job market and making sure that funds are available for them to carry the research that will advance their career ambitions.

Like other GlycoNet HQP, Prof. Cecioni credits the mentoring he received for helping him gain the confidence he needed to tackle each step of his career. "Having great mentors in my career motivates me to become a good mentor myself," concludes Cecioni. It is this pay it forward mentality that helps the next generation of scientists to excel. ▪

Other HQP Alumni say:

"Being a trainee with GlycoNet has given me the exposure I need—not just to the field of research I'm in, but beyond that. This is especially true during the annual Symposium; not only the professors but the students were given a chance to share the stage with world-renowned researchers. Throughout my three years in GlycoNet, I networked whenever I could and the connections I built have successfully helped me build a career in research."

Radhika Chakraberty, '18, Analyst, Labs-Mart Inc.

"I was equipped with the skill set to excel in my current position in the biotherapeutics industry. Through my experience with the Network, I understood the rigor for conducting high-level research and gained the confidence to go into industry. Being an executive member of the GTA–EC was particularly impactful because it allowed me to get a more diverse perspective outside of just chemistry. I was able to see problems from different viewpoints and work with 'non-chemist scientists' to create innovative solutions that address unmet medical needs."

Jose Mendez Campos, '18, Intern, Zymeworks

Dr. Warren Wakarchuk named new GlycoNet Associate Scientific Director

GlycoNet is pleased to announce the appointment of Dr. Warren Wakarchuk as the Network's new Associate Scientific Director, effective November 2, 2018.

Dr. Wakarchuk is a Network Investigator and Professor of Biochemistry in the Department of Biological Sciences at the University of Alberta in Edmonton. He was recruited to the University of Alberta from Ryerson University in Toronto. He received his PhD degree in microbiology from the University of British Columbia. He was a Research Officer at the National Research Council Canada for 19 years, before taking his current position at Ryerson in 2012. He has an outstanding international reputation within the glycomics community, and he has an extensive track record in research partnerships with industry.

"I am very excited to be taking on this new position as part of the GlycoNet executive team," says Dr. Wakarchuk. "I am looking forward to working with everyone to shape the direction of the Network as we head toward the Cycle II call for proposals."

Research in the Wakarchuk lab is centred on the structure and function of the enzymes involved in making various glycoconjugates. Major areas of research include the determination of glycosyltransferase enzyme donor/acceptor specificity and enzyme engineering for improved activity and 3-dimensional structure determination. The lab has invested in producing these enzymes in sufficient quantities to make possible the enzymatic synthesis of authentic glycans and modified derivatives. The application of these enzymes to the synthesis of bioactive glycoconjugates in vitro and in vivo for health and wellness is the goal of its research.

GlycoNet would like to extend its sincere appreciation to Network Investigator Dr. Stephen Withers for his service as Associate Scientific Director for the past four years.

"Steve provided critical leadership throughout the first four years of the Network," says GlycoNet Scientific Director Todd Lowary. "We look forward to continuing to work with him as a Network Investigator and are excited about working with Warren in his new role." ▪

$20M in government funding brings new talent in glycomics research to Canada and the U of A

Glycomics researcher Lara Mahal announced as Canada Excellence Research Chair.

Originally published in folio, April 17, 2019

A world-renowned chemist is bringing her expertise to the University of Alberta to further her work in understanding how sugars interact with human health and disease, thanks to $10 million in federal funding over the next seven years through the Canada Excellence Research Chairs program. The funds will be matched by the Government of Alberta.

"Glycans, the sugars on proteins and lipids, are involved in the development of every major disease—and yet they are one of the least studied and least understood classes of biomolecules," said Lara Mahal, currently a professor at New York University.

She will join fellow leading experts in glycomics at GlycoNet, a pan-Canadian Network of Centres of Excellence of more than 140 researchers headquartered at the U of A.

"Canada, and the University of Alberta in particular, have a rich history of supporting research into carbohydrates—including federal support for GlycoNet," said Mahal. "As a result of that investment, Canadian glyco-science research is well known internationally, making it a welcoming place for my science and for us to continue to advance this field at a world-class stage."

Mahal said her work at the U of A will focus on identifying sugars involved in diseases critical to human health, from pancreatic cancer to HIV, and exploring offshoots of her earlier work—which may hold the key to more rapid discovery of targets for new drugs to treat the diseases.

She said the CERC funding will enable her to expand her studies in glycosylation to encompass more clinical collaboration.

"The U of A is known for its concentration of carbohydrate researchers. There's an exciting group of researchers at this institution in this field, including Matthew Macauley, Lisa Willis, Chris Cairo, Ratmir Derda, John Klassen, Warren Wakarchuk and Todd Lowary," said Mahal.

"I'm looking forward to working with them. I think that this will open up great new opportunities for synergy to help advance this important field."

The CERC program awards universities funding to support world renowned researchers and their teams to establish ambitious research programs at Canadian universities.

Mahal follows the university's three previous CERCs, Graham Pearson (Arctic resources research), Thomas Thundat (oilsands molecular engineering research) and Michael Houghton (virology). ▪

AWARDS

Lara Mahal, University of Alberta, was named Canada Excellence Research Chair in Glycomics, which brings $20 million in funding to support research teams and programs at the University of Alberta.

Mona Nemer, University of Ottawa, received the CSMB Arthur Wynne Gold Medal from the Canadian Society for Molecular Biosciences. The award honors a scientist who has made a major contribution to molecular biosciences in Canada.

Molly Shoichet, University of Toronto, was elected as a Fellow of the Royal Society, the U.K.'s national academy of sciences.

Todd Lowary, University of Alberta, was named a recipient of Alfred Bader Award from the Canadian Society for Chemistry. The award is presented as a mark of distinction for excellence in research in organic chemistry.

David Vocadlo, Simon Fraser University, won the Bernard Belleau Award from Canadian Society of Chemistry, for his distinguished contribution to developing chemical biology tools for studying glycoconjugates.

Rebecca Davis, University of Manitoba, won the Pilot and Feasibility Award from the American Cystic Fibrosis Foundation and Cystic Fibrosis Canada.

Ratmir Derda, University of Alberta, received the Faculty of Science Research Award and Science Commercialization Fellowship from the University of Alberta.

Matthew Macauley, University of Alberta, was named a Tier 2 Canada Research Chair in Chemical Glycoimmunology.

Karla Williams, University of British Columbia, was named a Tier 2 Canada Research Chair in Oncology, and received the Michael Smith Foundation for Health Research (MSFHR) Scholar Award.

Robert Britton, Simon Fraser University, was chosen to receive the Biological and Medicinal Chemistry Lectureship Award from the Canadian Society for Chemistry to recognize his contribution to the field of biological or medicinal chemistry.

David Lillicrap, Queen's University, received the Erasmus Hematology Award from the Erasmus University Medical Center. This award is given once every two years to honor a distinguished scientist who has made pivotal contributions to the area of hematology.

Marcelo Gottschalk, Université de Montréal, was awarded Honoris Causa (honorary doctorate) from the University of Ghent, Belgium for his outstanding achievements in veterinary bacteriology.

Ziv Gan-Or, McGill University, received Pedaling for Parkinson Canada's New Investigator Award for his project on *genetic variance and the progression from REM sleep behavior disorder to Parkinson disease*.

Lori Burrows, McMaster University, received the McMaster University Faculty Association Award for Outstanding Service. This award recognizes individuals who have made outstanding contribution to the mission of the University through the provision of exceptional service to faculty, staff, and students.

Mark Taylor, University of Toronto, was named a recipient of the Dean's Outstanding Teaching Award from the University of Toronto to recognize his teaching excellence in undergraduate and graduate education, with a focus on classroom instruction and course design, and curriculum development.

APPENDICES

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CANADIAN GLYCOMICS NETWORK

STATEMENT OF FINANCIAL POSITION

As at March 31, 2019

	2019 $	2018 $
Assets		
Current assets		
Cash and cash equivalents (note 5)	739,233	1,116,946
Accounts receivable	5,000	10,909
GST receivable	6,645	2,579
Prepaid expenses	310,647	27,704
Due from Network Host (note 4)	4,762,421	4,389,176
	5,823,946	5,547,314
Liabilities		
Current liabilities		
Accounts payable and accrued liabilities	57,000	55,632
Deferred revenue (note 5)	5,355,526	5,239,539
	5,412,526	5,295,171
Net Assets		
Unrestricted net assets	411,420	252,143
	5,823,946	5,547,314

Going concern (note 1)

Approved by the Board of Directors

_____ Director

_____ Director

The accompanying notes are an integral part of these financial statements.

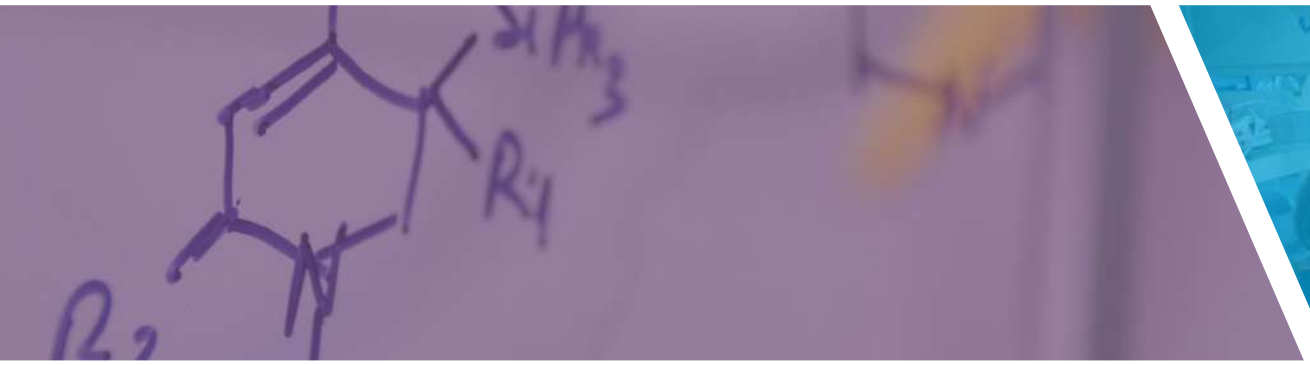
CANADIAN GLYCOMICS NETWORK

STATEMENT OF OPERATIONS

For the year ended March 31, 2019

	2019 $	2018 $
Revenues		
Grants (note 5)	6,521,510	8,144,771
Contributed services (note 6)	172,401	252,614
Symposium	111,490	62,430
Services	73,671	55,617
Interest income	11,689	4,939
	6,890,761	8,520,371
Expenditures		
Research project funding	4,758,203	6,745,432
Salaries and employee benefits	870,572	714,009
Symposium	373,302	346,081
Other	178,044	85,853
Travel	143,505	125,841
Communications	136,370	126,737
Consulting fees	70,085	31,291
Training programs	63,327	62,747
Patent costs	46,792	49,480
Professional fees	36,865	53,240
Seminars, workshops and networking	27,942	42,065
Office	15,989	22,668
Insurance	10,099	10,099
Equipment	389	3,660
	6,731,484	8,419,203
Excess of revenues over expenditures for the year	159,277	101,168

Please contact glyconet@ualberta.ca for the entire audited financial statements.



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