



CHFO

RESEARCH INSTITUTE



2014
Annual
REPORT



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Vision

Discoveries today for healthier kids tomorrow.

Values

Excellence
Passion
Integrity
Creativity
Collaboration

Mission

We conduct innovative research in a dynamic learning environment and translate that knowledge into practice and policies to improve the health of children, youth and their families.

#Discoveries



A MESSAGE FROM THE CEO

Research-focused, academic hospitals like CHEO provide better health outcomes for kids. If ever there was an exemplary year, it was 2014! Over 220 researchers banded together with staff, trainees and volunteers across the hospital to make over 390 discoveries to help kids be their healthiest.

One of our core values at the CHEO Research Institute is collaboration, and it is truly inspiring to watch our researchers partner with peers both within CHEO and at other hospitals and universities across Canada and around the world. In fact, it is now the rare investigator that does not require a strong research network to solve the most important medical problems confronting our young patients. At CHEO, the scientists from our Molecular Biomedicine Program are poised to answer questions that arise from clinicians during their patient's visits. Conducting patient-relevant research that informs, improves and aids clinical care is what drives us all.

A perfect example, as highlighted in this annual report, comes from our geneticists and gastroenterologists who worked together to identify the cause for a disorder common in Inuit people, causing gastrointestinal distress and severe failure to thrive in infants. They discovered a genetic mutation that is responsible for this inherited disorder called congenital sucrase-isomaltase deficiency (CSID). As an immediate result of their findings, CSID, which was formerly diagnosed with an invasive intestinal biopsy can now be diagnosed with a simple blood test!

We have chosen to highlight a wide variety of 2014 discoveries in this report: studies which were CHEO-led (like the CSID example above), and others where we contributed to multi-site, national and international collaborations. Whether discovering a new cause of anemia, uncovering the impact of osteoporosis in childhood chronic disease, or trialing a simpler, faster, cheaper way to diagnose hearing loss, our researchers actively engaged patients and families as partners in discovery.

We also thought it would interest readers to see the many different funding sources that fuels research at CHEO, as listed in this report for the first time. That said, we would not be where we are today without the tremendous support from our community, as rallied by the CHEO Foundation.

I invite you to bookmark www.cheori.org and to follow us on Twitter @CHEOhospital to keep up to date about CHEO research and its impact. We are already off to a great start for the year ahead...

Very best wishes,

Dr. Martin Osmond
CEO and Scientific Director
CHEO Research Institute

#Collaboration

RARE DISEASE RESEARCH

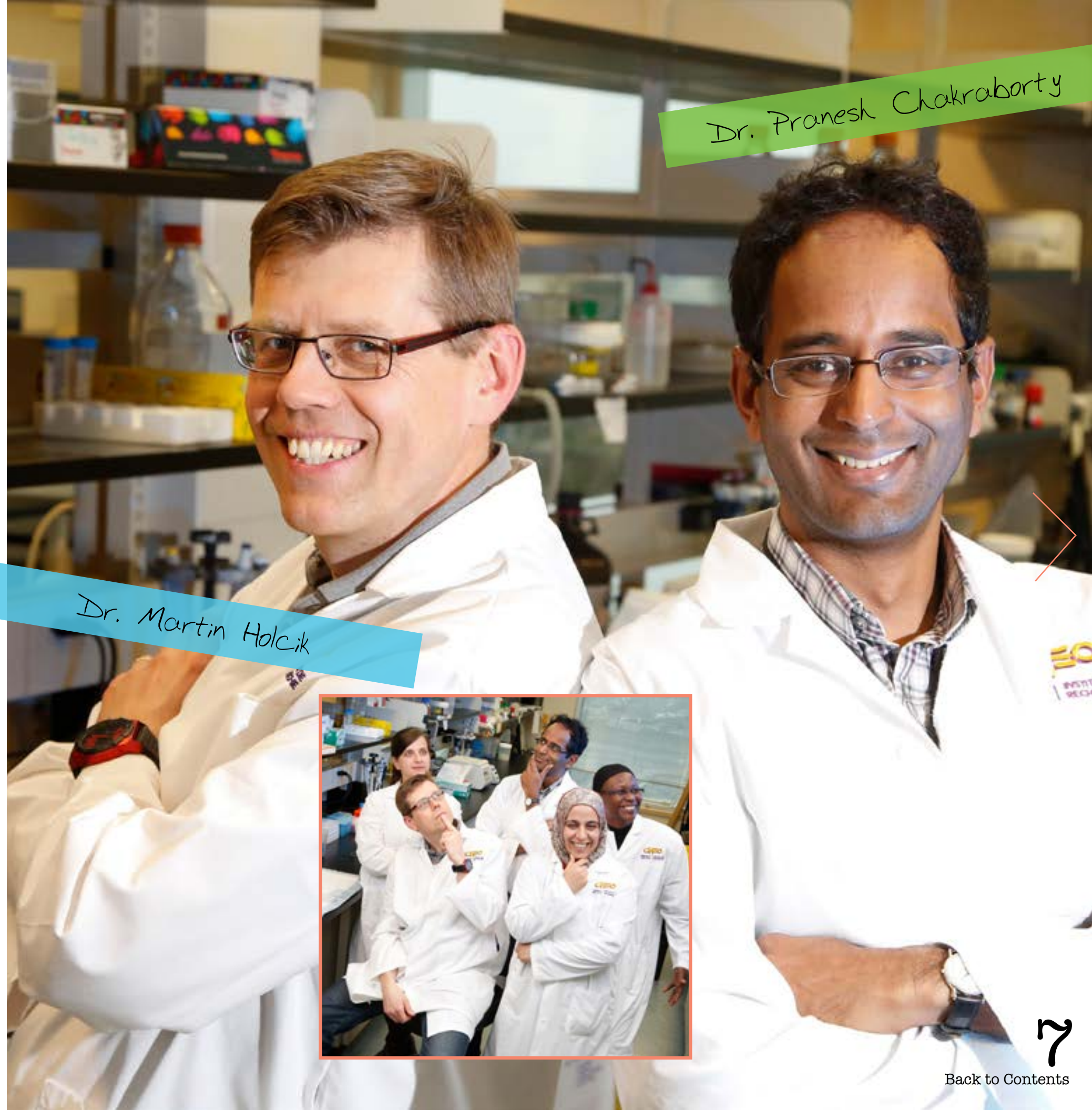
Collaboration is a core value at the CHEO Research Institute and our researchers at the bench and bedside came together for a unique project in 2014.

To set the stage, in 2013, a novel and rare disease called SIFD was clinically-described in a prestigious academic journal. SIFD (which stands for sideroblastic anemia, immunodeficiency, fever and developmental delay) was diagnosed in a small group of children, two of them from CHEO, although the genetic cause of SIFD remained unknown.

Dr. Pranesh Chakraborty, a Metabolics physician and Director of Newborn Screening Ontario, working with clinicians and researchers at CHEO, determined that mutations in a gene called TRNT1 was likely responsible for causing SIFD in one of the young patients at CHEO. TRNT1 is responsible for the maturation of tRNA in the human body, which in turn is essential for making proteins needed to support life. Realizing that more research was required to prove that TRNT1 mutations caused SIFD, Chakraborty approached Dr. Martin Holcik, a world expert on protein translation and Director of the Molecular Biomedicine Program at CHEO. Working together, they were able to rapidly kick-start the needed research – something neither could have done in isolation.

Their collaboration ultimately extended beyond CHEO's walls. The team joined forces with researchers in Boston, and clinicians around the world, who had independently identified TRNT1 as the SIFD disease gene. In addition, Dr. Paul Joyce, professor of biochemistry at Concordia, who studies the normal function of the same gene in yeast and plants; and Dr. Adam Rudner, a yeast geneticist from the University of Ottawa, joined as key members of the research team.

The collective team was successful in their quest, and in 2014 they proved that the genetic cause of SIFD is mutations in the TRNT1 gene – success made possible by a knock on a door and collaboration across projects and borders.



Dr. Pranesh Chakraborty

Dr. Martin Holcik

#Activity

OBESITY RESEARCH

Dr. Mark Tremblay wants children and youth to be more physically active because it is good for their health. The director of the Healthy Active Living and Obesity Research Group (HALO) at the CHEO Research Institute has travelled across Canada, and the world, looking at children's activity – for instance, how they play, sit and sleep. Leveraging the depth and breadth of this research portfolio, HALO has synthesized and interpreted international data, for use in informing parents, communities, and decision-makers about how active children really are, and how to get them more active.

HALO's international comparison research informed the world's first-ever Global Matrix on the Physical Activity of Children and Youth, released in Active Healthy Kids Canada's Report Card. Launched in May 2014 by HALO and Active Healthy Kids Canada in partnership with ParticipACTION, Canada was measured against 14 other countries on the levels of children's physical activity. The results were eye opening, and myth-busting. In some areas Canada performed well (Community & the Built Environment, Organized Sport Participation), and in some, not so well (Sedentary Behaviours, Overall Physical Activity). The Report Card also included a range of recommendations on how Canadians can make better choices, create better spaces and make better policy decisions to keep kids active and healthy.

Tremblay notes that the insights he gained from visiting and studying different countries were invaluable in recognizing group think trends. "We don't do that here in (country x)," was something he heard often. Interesting socioeconomic gradients emerged: he found that countries with the most developed infrastructure for supporting healthy active living received some of the lowest grades, while countries with the least infrastructure performed the best.

Achieving global reach was a significant milestone for the Physical Activity Report Card that's been released annually in Canada for the



Dr. Mark Tremblay

past 10 years. Tremblay and team HALO were instrumental in leading this charge by designing, authoring and interpreting the Global Matrix, but also acting as the scientific lead and key media spokesperson, as well as bringing together their global research partners and contacts. In the coming years, the goal is to increase the number of countries that participate, but ultimately to influence parents, communities and decision-makers to preserve and promote healthy active lifestyles for all children.



#Breakthrough

CANCER RESEARCH

Dr. Robert (Bob) Korneluk is palpably excited as he sits down with his colleagues, Drs. Eric LaCasse and Shawn Beug, to talk about the team's recent major breakthrough. Despite being a senior scientist at the CHEO Research Institute, Korneluk is almost child-like in his delight as he explains the new cancer therapy they have developed in the lab.

Their discovery is technically specific, but at the same time, surprisingly simple. His lab combined two experimental cancer treatments (each currently tested separately as part of clinical trials worldwide): one employing a class of drugs called SMAC Mimetics, which accelerate the death of cancerous cells; and the other employing viruses that infect cancer cells, known as oncolytics, that trigger a natural immune system response to kill cancer cells. In 2014, Korneluk and his team found that in combination the two treatments are up to 10,000 times more effective together, than each therapy is on its own. There is no damage to any of the surrounding healthy cells when the cancer is destroyed either.

The key component of this breakthrough is what really elevates this success story. Almost 20 years ago, in 1995, Korneluk discovered a family of proteins that control cell death, known as IAPs (Inhibitors of Apoptosis). With upwards of 70 billion cells dying each day in healthy adult human beings, Korneluk had a hunch at the time that these were very important proteins. Today, with certainty, he knows why! The SMAC Mimetics, used in the combination immunotherapy, act by targeting or removing the IAPs; Korneluk believes his team's latest breakthrough has the potential to revolutionize the way cancer is treated. This CHEO research team is laser-focused on moving it into human clinical trials for cancer within the next three years.



Dr. Robert (Bob) Korneluk

#Innovation

MOBILE HEALTH RESEARCH

Dr. Matthew Bromwich sees many children with hearing issues from Iqaluit. Only occasionally is there an audiologist that is accessible in the northern territory, so Plan B for these children is to make the trip to Ottawa. Often though, Bromwich noticed, the children's hearing was normal so he started to question the costly process. A better method had to exist, and discovering it is what spurred his research portfolio.

Bromwich and his research team developed, tested and launched a ShoeBOX Audiometer, known simply as the ShoeBOX. "Cheaper, easier, faster, better," Bromwich says when he introduces the device. It employs existing capabilities found on an iPad, a special audiological headset, and proprietary software. Following rigorous research at CHEO, the device was validated and it's now a licensed audiometer in Canada.

The innovation of the ShoeBOX though, lies in the way the hearing test works. A visually appealing game gets presented to a patient on an iPad, which then requires them to respond on the screen to what they hear on the headset. While the sounds are the beeps known to traditional audiology tests, the game itself looks like something taken out of Animal Farm, and the whole test takes no longer than 5 minutes and it can be repeated as often as needed. It is suitable for anyone from 3-103 and can be completed at home, in schools, in hospitals, or even outside. Bromwich refers to it as "Intelligent Triage" - medical testing that reaches the right people, in the right places.

Dr. Matthew Bromwich



2014 was a productive year for Bromwich and his ShoeBOX: He accepted a TELUS award for mobile health innovation at a Canadian Advanced Technology Alliance gala; he presented the ShoeBOX on Parliament Hill to members of the health research caucus; and he expanded the reach of related research projects into parts of Africa. He has new hypotheses to test in the coming year, including a goal to tailor the ShoeBOX to test the clarity of a person's hearing, not only frequency. Whatever new direction, it will be evidence-based and CHEO-led.



#Global

BONE HEALTH RESEARCH

Osteoporosis can happen to some children with chronic diseases, including leukaemia or rheumatic disorders, because of their steroid treatments. Until the internationally acclaimed research led by Dr. Leanne Ward and her colleagues at CHEO, it had been a silent phenomenon of sorts. No one understood why some kids are at more risk, or even exactly what to look for.

Ward's body of research for the past decade peaked in 2014 when her pan-Canada project entitled STOPP (Steroid-induced Osteoporosis in the Paediatric Population) amassed a total of 14 peer-reviewed publications in top journals describing the scope of the problem in kids with serious illnesses. In this large series of papers, Ward's team first showed that spine fractures are often a silent sign of osteoporosis in children and so they often go undetected. The team then went on to describe the frequency, characteristics and predictors of spine fractures and how they relate to the steroid treatment of chronic diseases.

The team poured over six years' worth of data from 11 centres across Canada, including more than 400 children afflicted with spine trouble resulting from steroid treatment. They found children's spines can be collapsed at diagnosis and then further deteriorate in the first few months after starting steroid therapy. As well, Ward's team has been able to show which children are more likely to develop spine fractures due to osteoporosis. As a result, this scientific evidence allowed the team to develop monitoring and diagnosis guidelines on this topic for the worldwide bone health community. These results also provide valuable information for designing osteoporosis treatment and prevention trials in kids.

Ward spent most of 2014 traveling the globe, speaking to peers in Australia, Europe and North America – a testament to the importance of this body of work. The next step is designing and implementing effective intervention strategies; taking those known at risk and rolling them into treatment trials. Ward has projects underway to test subcutaneous vs. intravenous treatment options in hopes to one day standardize patient care.



Dr. Leanne Ward



Dr. Eric Benchimol

#Analysis

THE ONTARIO CROHN'S AND COLITIS COHORT

Inflammatory Bowel Disease (IBD) – including ulcerative colitis and Crohn's disease – are much more common in Canada and other developed nations than in other parts of the world. Dr. Eric Benchimol conducts internationally recognized research on these illnesses.

Benchimol analyses very large health administrative databases, such as the Ontario data housed at the Institute for Clinical Evaluative Sciences (ICES), to seek trends in IBD and inform its treatment. The Ontario Crohn's and Colitis Cohort includes everyone with IBD in Ontario making it the largest IBD cohort in the world, as Ontario has one of the highest rates of the disease. One study in particular confirmed that the prevalence of IBD in Ontario has skyrocketed to 1 in every 190 people (524 per 100,000 in 2014, up from 363 in 1999), including a growing number of elderly people likely because people live longer with the disease as treatments have improved. Another noteworthy study by Benchimol last year was even more poignant. He discovered that the fastest growing group of newly-diagnosed patients with IBD is children under the age of 10. More and more children are diagnosed under 18 years old. Despite these figures, he found good news: treatments are working well, especially with the transition to new 'biologic' drugs for treatment, leading to fewer surgeries and hospital visits.

Armed with unanswered questions and a desire to find the environmental risk factors for the disease, Benchimol has three big next steps with the cohort. The first is to begin tracking changes in the rates of IBD in immigrants coming to Canada, and whether their access to healthcare differs from non-immigrants. Immigrants generally have a very low risk of contracting IBD, but this risk increases in immigrants who arrive to Canada at a younger age. In fact, the children of immigrants from some regions who are born in Ontario have similar risk of IBD as other children, indicating that early life exposure to the Canadian environment increases the risk of IBD later. In addition, he is assessing how the urban environment may increase the risk of IBD, and how the health system treats people from rural regions. The third is a study to evaluate the health system's treatment of children with IBD across Canada in an effort to improve access to care and the quality of care received by the youngest patients.

#Impact

GENETICS RESEARCH

In 2014, Dr. Matthew Lines was referred an Inuit patient by Dr. Margaret Boland, Gastroenterologist, regarding some unusual symptoms. The infant girl was failing to thrive (not gaining weight at the expected rate for a young child), and the common causes for this, such as celiac disease or dairy intolerance, had been excluded. Genetic testing confirmed that the child had Congenital Sucrase-Isomaltase Deficiency (CSID), a rare condition in which the enzyme needed to metabolize sugar (sucrose) and certain starches is not present in the intestine.

A traditional Inuit diet is low in sucrose and carbohydrates, and so it is likely that the introduction of European foods into their diet is what directly correlates to digestive problems. This is potentially a major problem for babies and infants who are not breastfed, because most formulas are high in sucrose.

Despite the fact that CSID is actually quite common in the Inuit, no one had yet identified the genetic change (“mutation”) responsible. With the help of other researchers, Lines’ group was able to demonstrate a high frequency of this same gene mutation among a group of healthy Inuit volunteers. Their research not only unveiled a significant health trend in the Inuit population, but it resulted in identifying the exact gene change that causes CSID.

There is a significant practice-changing element to this discovery! CSID, which formerly required an invasive intestinal biopsy for diagnosis, is now diagnosed with a simple blood test.

The next step in this project will be a natural history study, which will involve studying a group of patients with CSID over time to better understand how this condition manifests, and how best to manage it from a dietary standpoint.

Dr. Matthew Lines



#Data

PRIVACY RESEARCH

Dr. Khaled El Emam has spent the last 10 years developing evidence-based guidelines, models, and software to make the sharing of health data possible and in 2014, his efforts gained significant momentum. Access to integrated health data, including clinical, administrative, and genomic data, can be very beneficial for research, public health, and the commercial development of drugs and medical devices. One of challenges in doing so is addressing the privacy concerns of the patients when sharing that data especially when combining multiple pieces of information from different care settings.

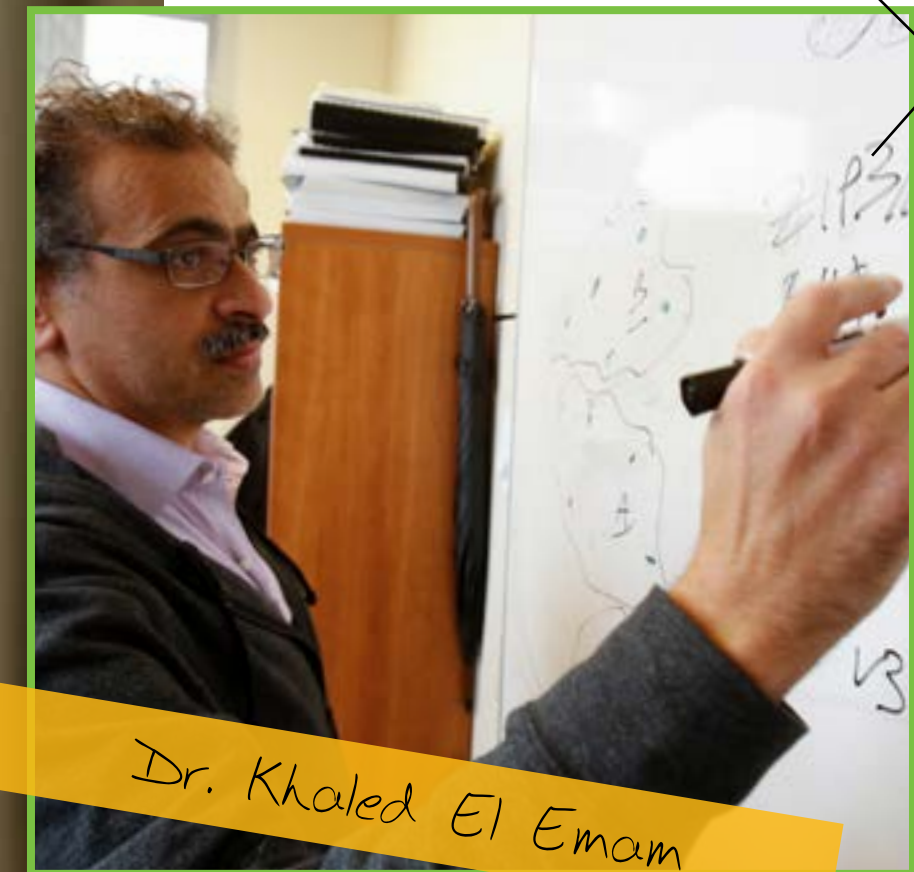
Concerns about privacy amplified over the last couple of years about how companies and governments collect and use personal information. El Emam's evidence-based work provides the mechanisms to allow health data collection, integration and sharing in a responsible way.

Over the past year, multiple important best practice standards and guidelines published based on El Emam's work on what, where, and how patient data can be shared, including those issued by: the Council of Canadian Academies, the Institute of Medicine (part of the National Academies of Science in the U.S.), the Health Information Trust Alliance (HITRUST), and PhUSE (a pharmaceutical association in Europe).

One of the key initiatives El Emam worked on in 2014 was developing methods and technologies to facilitate the responsible large-scale sharing of industry clinical trial data, amongst academic researchers. The results of this initiative mean that it will soon become easier to get access to data on thousands of historical and future clinical trials.



Privacy commissioners, the medical community and fellow researchers have all heavily scrutinized, praised or incorporated his work. Whether conducting webinars, authoring book chapters, delivering keynote presentations, or extending CHEO's reach beyond the healthcare community into high technology sectors and otherwise, one thing is consistent - El Emam has been able to translate CHEO research into practice, globally.



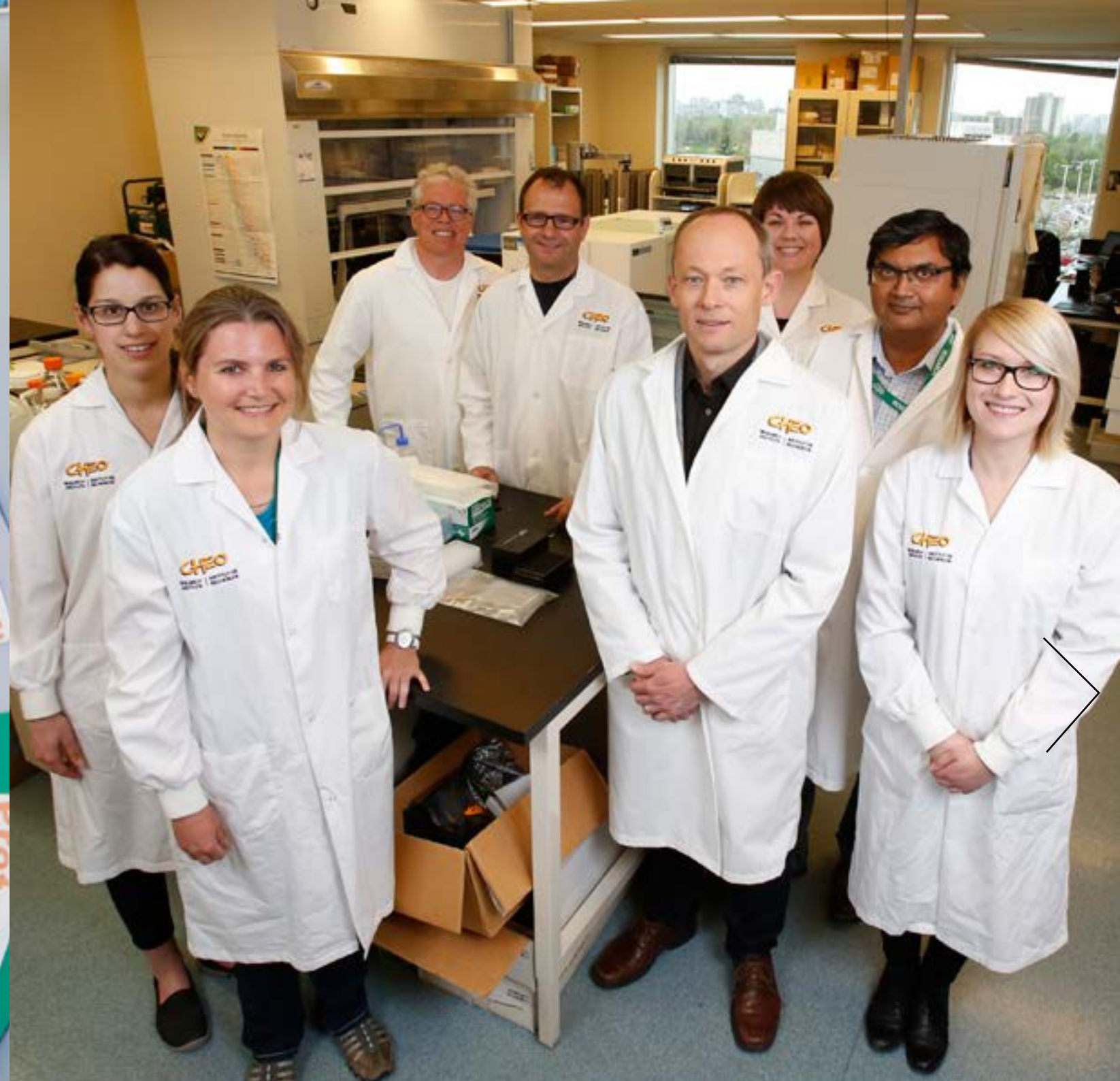
Dr. Khaled El Emam



#highlight 1

“Our team discovered that children had improved growth, felt better and had fewer complications with early introduction of some of the newest immune therapies for Crohn’s disease.”

—Dr. David Mack



#highlight 2

“Our team discovered an exciting new way of using programmable viral nanotechnology to activate a patient’s own immune response against their tumour. This is a particularly promising new approach for treating the deadly brain cancer, glioblastoma multiforme.”

—Dr. David Stojdl



#highlight 3

“Our Canada-wide team developed the first comprehensive guidelines on how to diagnose and manage concussion in children.”

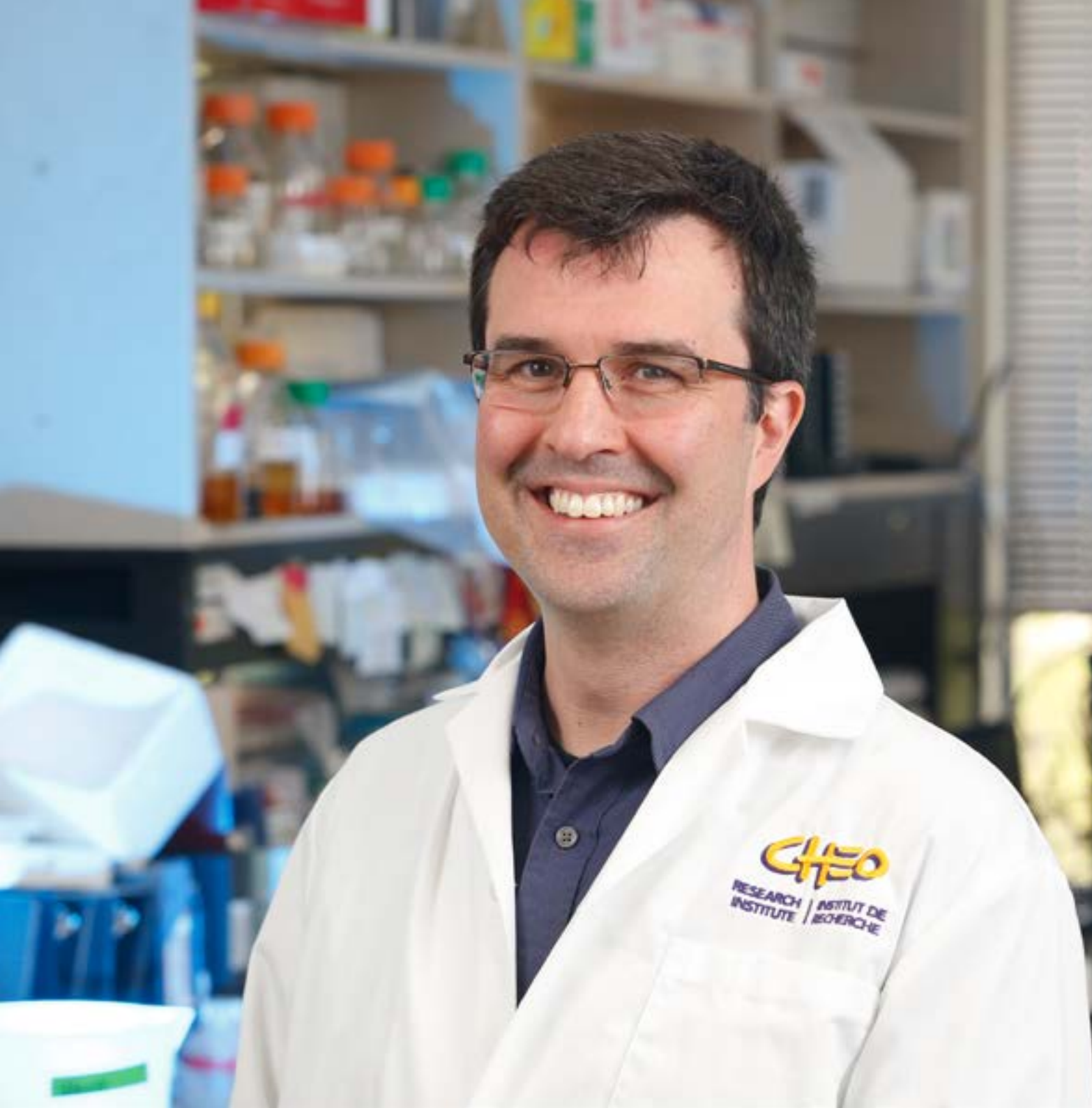
—Dr. Roger Zemek



#highlight 4

“Our team discovered blood vessel making cells that contribute to lung growth and that these cells are damaged in lung injury; conversely providing healthy cells from umbilical cord blood repaired lung injury. This could become a life-saving treatment for babies with lung diseases.”

—Dr. Bernard Thébaud



#highlight 5

“Our team has used new technologies to diagnose children with severe and rare forms of epilepsy and with this knowledge we plan to identify novel and effective treatment options.”

—Dr. David Dymant



#highlight 6

“Our team discovered neck circumference values for Canadian children, which may be applied as a screening tool for obesity-associated conditions such as obstructive sleep apnea.”

—Dr. Sherri Katz



#highlight 7

“Our researchers improved parent, caregiver and survivor’s understanding of the link between symptoms, coping strategies and quality of life in children who had completed treatment for a brain tumor.”

—Dr. Gail Macartney



#highlight 8

“Our team discovered that children born with HIV who were started on treatment right at birth have extremely small amounts of the virus hidden in memory cells in their bodies (called the HIV reservoir). Moving forward, we hope to understand how these small reservoirs impact a child’s ability to control HIV and potentially contribute to finding a cure for kids with HIV in the future.”

—Drs. Lindy Samson & Jason Brophy

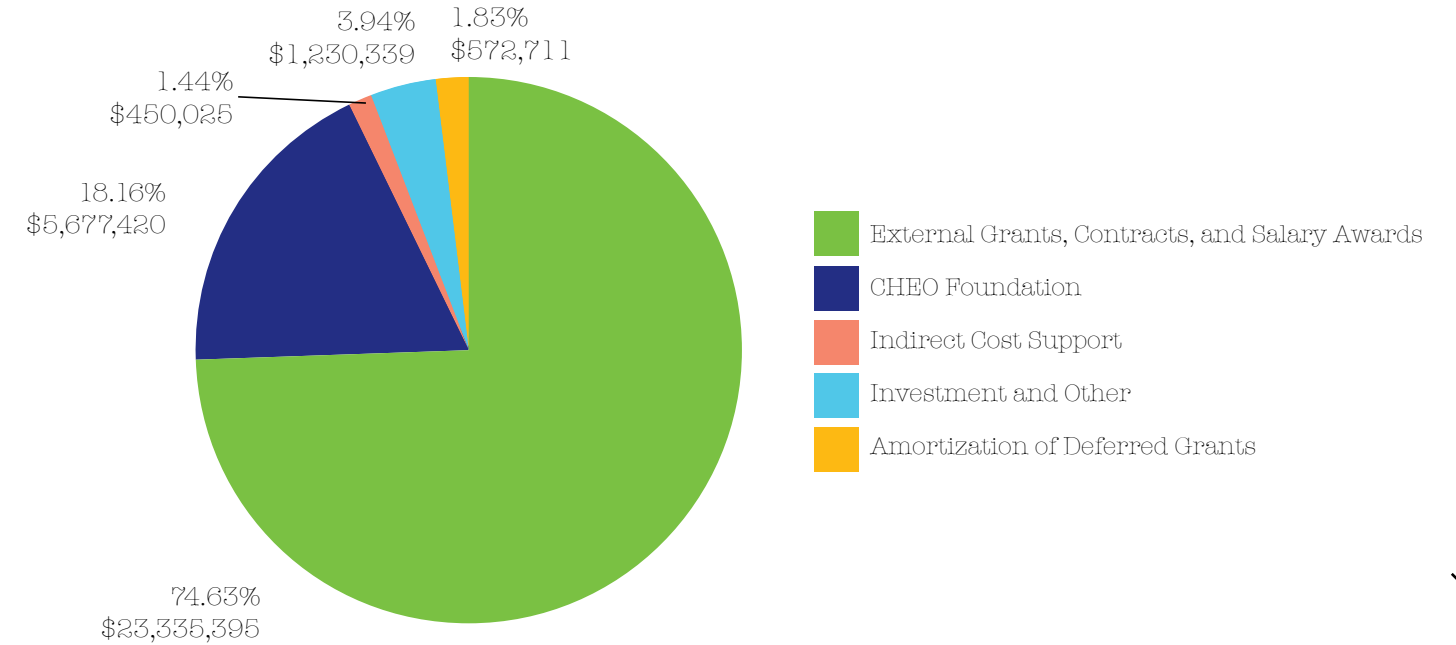
Funding agencies

| Agency | Amount |
|---|----------------|
| CHEO Foundation | \$5,677,419.90 |
| Canadian Institutes of Health Research | \$5,459,101.72 |
| CHAMO (Children's Hospital Academic Medical Organization) | \$1,000,000.00 |
| Ministry of Health and Long Term Care | \$955,405.31 |
| Juvenile Diabetes Research Foundation | \$826,374.14 |
| CHAMO (Canadian Hospital Academic Medical Organization) Innovation Fund | \$547,016.13 |
| Genome Canada | \$539,128.22 |
| Ontario Research Fund - Ministry of Economic Development and Innovation | \$470,316.84 |
| Ontario Neurotrauma Foundation | \$346,707.43 |
| Natural Sciences and Engineering Research Council | \$263,289.90 |
| Genome Quebec | \$218,757.17 |
| Canada Research Chairs | \$213,790.90 |
| Pfizer Inc. | \$211,150.32 |
| ParticipACTION | \$166,004.75 |
| Cancer Research Society | \$163,852.11 |
| Muscular Dystrophy Canada | \$153,728.63 |
| Ontario Trillium Foundation | \$138,129.20 |
| Heart and Stroke Foundation of Canada | \$135,556.20 |
| Canadian Cancer Society | \$123,546.62 |
| Canadian Diabetes Association | \$107,805.24 |
| Canadian Child Health Clinician Scientist Program | \$105,000.00 |
| The Hospital for Sick Children | \$94,764.39 |
| Canadian Pediatric Society | \$92,801.83 |
| Mach-Gaensslen Foundation of Canada | \$91,820.77 |
| Ministry of Culture, Tourism and Sport | \$91,261.96 |
| Lawson Foundation | \$82,075.82 |
| Canadian Foundation for Innovation - IOF | \$79,770.21 |
| The Michael J. Fox Foundation for Parkinson's Research | \$79,456.53 |
| Alberta Innovates Health Solutions | \$74,470.53 |
| Physicians' Services Incorporated Foundation | \$72,132.10 |
| Crohn's and Colitis Foundation of Canada | \$72,000.00 |
| Biomarin Pharmaceutical Inc. | \$70,653.20 |
| Canadian National Institute of Health | \$65,115.35 |
| MedBuy | \$59,052.45 |
| Ontario Cancer Biomarker Network | \$58,772.45 |
| Hoffman LaRoche Limited | \$56,860.77 |
| Janssen Pharmaceuticals Inc. | \$52,575.00 |
| Jesse's Journey | \$50,367.34 |
| Ontario Institute for Cancer Research | \$49,650.01 |
| Ottawa Hospital Research Institute | \$46,875.02 |
| Pennington Biomedical Research Centre | \$45,522.49 |
| Networks of Centres of Excellence of Canada | \$42,966.84 |
| Abbott Laboratories Limited | \$40,403.83 |
| University of Ottawa - Academy for Innovation in Medical Education | \$38,588.30 |
| Ataxia of Charlevoix - ^Saguenay Foundation | \$37,678.54 |
| University of Calgary | \$34,618.27 |
| Boehringer Ingelheim | \$33,408.45 |
| Mito Canada | \$33,176.48 |
| University of Ottawa | \$32,467.46 |

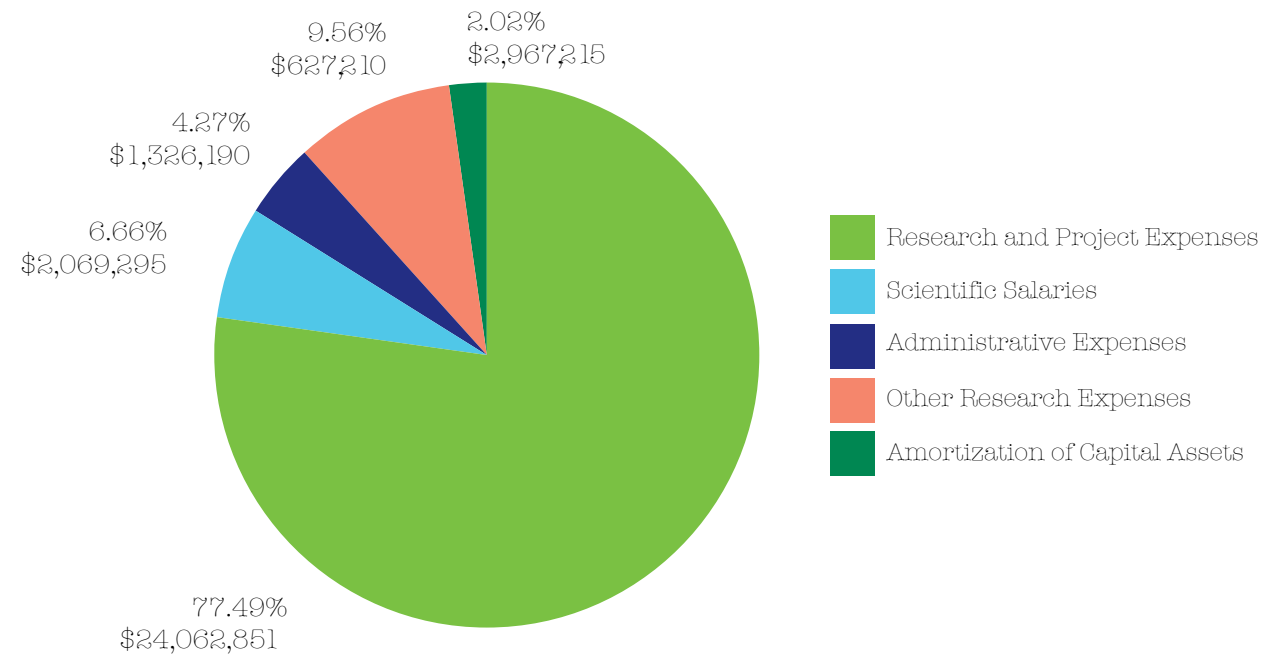
| Agency | Amount |
|---|----------------|
| Ontario Brain Institute | \$32,334.03 |
| Canadian Gene Cure Foundation | \$27,393.46 |
| Merk Canada Inc. | \$26,161.10 |
| C17 Research Network | \$25,407.54 |
| Canadian Cancer Society Research Institute | \$25,035.85 |
| Northern Ontario Academic Medicine Association | \$21,746.29 |
| Grand Challenges Canada | \$20,102.42 |
| University of Guelph | \$19,163.98 |
| Eli Lilly Canada Inc. | \$16,829.03 |
| Leukodystrophies Foundation | \$16,622.89 |
| Ontario Lung Association | \$16,045.72 |
| Mitacs Canada | \$14,226.96 |
| Population Health Research Institute | \$13,531.81 |
| Canadian Foundation for Women's Health | \$12,945.45 |
| Canadian Centre for Vaccinology | \$12,548.07 |
| Human Resources and Skills Development Canada | \$11,207.79 |
| Crohn's and Colitis Foundation of America | \$10,206.39 |
| Canadian HIV Trials Network | \$8,903.72 |
| The Champlain Local Health Integration Network | \$7,488.33 |
| The Association of Hemophilia Clinic Directors of Canada | \$7,198.99 |
| McGill University | \$6,834.28 |
| Pharmaxis Limited | \$6,567.78 |
| FightSMA | \$6,000.00 |
| CSL Behring Canada Inc. | \$5,745.41 |
| City of Hope National Medical Centre | \$5,740.77 |
| Heart and Stroke Foundation of Ontario | \$5,569.60 |
| Bayer Healthcare AG | \$5,530.00 |
| The Ottawa Hospital - Department of Pathology and Laboratory Medicine | \$5,505.19 |
| Public Health Agency of Canada | \$4,894.37 |
| Diabeters Inc. | \$4,760.39 |
| Canadian Urological Association Scholarship Foundation | \$4,240.00 |
| Novartis | \$4,194.92 |
| Ministry of Research and Innovation | \$4,157.05 |
| Alberta Children's Hospital | \$3,767.85 |
| Dystonia Medical Research Foundation | \$3,089.29 |
| Ministry of Health Promotion and Sport | \$3,048.71 |
| Canadian Association of Genetic Counsellors | \$2,880.77 |
| Health Canada | \$2,800.00 |
| Miscellaneous | \$2,413.15 |
| SANDOZ Canadian Patient Safety Institute | \$1,991.94 |
| Pediatric Oncology Group of Ontario | \$1,864.26 |
| Provincial Health Services Authority | \$1,598.63 |
| Children's Hospital of Boston | \$1,435.00 |
| Provincial Centre of Excellence for Child and Youth Mental Health | \$1,181.89 |
| Advanced Bionics Corporation | \$1,037.97 |
| Other | \$9,077,998.61 |

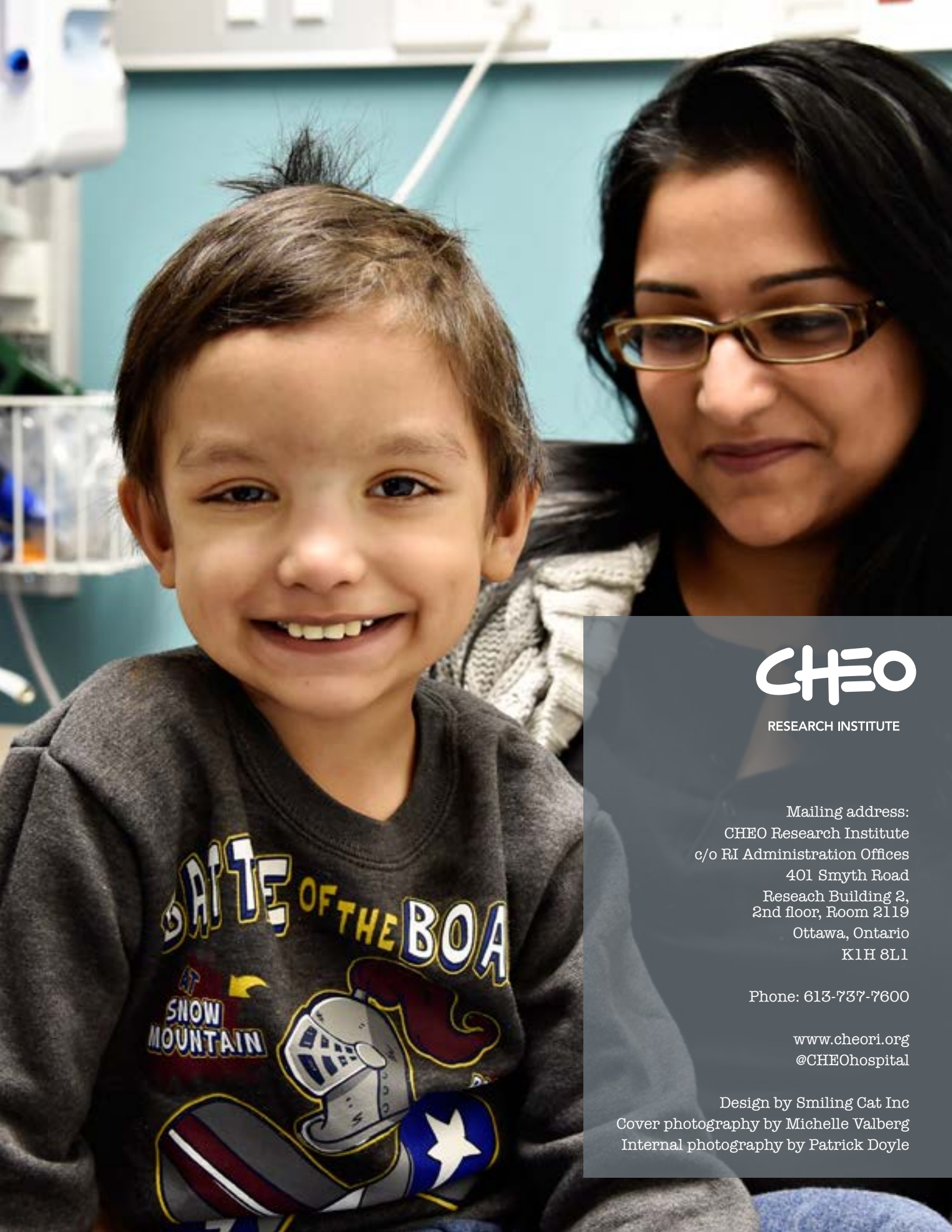
Financial Reports

Revenue Distribution 2014-2015



Expenditure Distribution 2014-2015





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