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Photography is being used for illustrative purposes only and any person depicted in the Content is a model.
OUR MISSION

To catalyze interdisciplinary interactions among clinicians, scientists and the public that will improve the health and well being of children through the development and application of genetic knowledge and technology.
We are proud of SickKids’ 140-year history of improving the lives of the children and families we serve and want to continue our long history of pioneering research and discovery in human genetics. Here’s a look at some of the most compelling examples spanning 8 decades of genomic history at SickKids.

**1947**
**CREATION OF A DEPARTMENT**
Ontario’s first hospital to establish a department of genetics was SickKids. The creation of this service contributed to the beginning of medical genetics services in the 1950’s.

**1960**
**CONTRIBUTION TO MEDICAL GENETICS**
SickKids establishes its cytogenetics laboratory to look at chromosomal abnormalities and set up the first genetics diagnostic laboratory at SickKids following the launch of North America’s first genetics diagnostic service established one year earlier at Johns Hopkins University in Baltimore.

**1987**
**GENE DISCOVERY**
SickKids researchers contribute to the discovery of the gene that causes muscular dystrophy.

**2016**
**VERSATILITY OF CRISPR/Cas9 FOR DEVELOPING TREATMENTS FOR INHERITED DISORDERS**
Research findings established far-reaching therapeutic utility of CRISPR/Cas9, which can be tailored to target numerous inherited disorders including Duchenne muscular dystrophy.

**2014**
**NEXT GENERATION SEQUENCING GENETIC TESTING IS NOW OFFERED IN THE CLINICAL LABORATORY**
Optimizing the alignment of quality, testing capacity, and a focus on the development of practice guidelines to achieve improved patient outcomes, the evolution to provide practitioners with the knowledge and confidence they need in test identification, interpretation and related counselling has paved the way for individualized medicine at SickKids.
In the 1980’s research groups in several countries were hunting for the gene involved in cystic fibrosis. The race was won by SickKids in collaboration with the University of Michigan who used genetic markers to home in on a region of chromosome 7 and identified the gene that, when defective, is responsible for cystic fibrosis.

**THE GENETIC CODE FOR CYSTIC FIBROSIS IS CRACKED**

The Centre for Applied Genomics is founded, dedicating to conducting groundbreaking research in genomics. Today, offers a capacity of completing close to 40,000 tests annually with revenue in excess of $28 M and serves as a national and international genomic research hub.

**GROUNDBREAKING GENOMIC RESEARCH UNDER ONE ROOF**

Researchers at SickKids, with colleagues at the J. Craig Venter Institute and the University of California, publish the first-ever complete genome sequence of an individual, forever changing the future of healthcare.

**THE CENTRE FOR GENETIC MEDICINE IS LAUNCHED**

A multidisciplinary research platform is focused on treating the child’s genome as a rich source of genetic information to be repeatedly queried over time to manage the overall health of the child, rather than a one-time test performed to diagnose pre-existing disorder. The incidental and secondary variants are a major focus of study for the Genome Clinic at SickKids.

**DISRUPTIVE TECHNOLOGY TAKES A GIANT STEP FORWARD IN SEQUENCING A GENOME**

Paving the way for individualized medicine at SickKids, the Centre is positioned to play a pivotal role in elevating the ‘genetics dialogue’ with the brightest thought-leaders and community stakeholders to lead and inform change. Efforts commence to align new genomics research and next generation diagnostic testing to support translation and clinical effectiveness.
In August 2013, the Centre released its strategy map entitled, ‘A Blueprint for Change: changing the practice of medicine’, creating a 3-year roadmap of priorities intended to guide our leaders, health professionals, educators, government, and patients & families on how we can work together to make individualized medicine a reality at SickKids. As we begin to prepare for the Centre’s 5-year external review in 2016-17, we are pleased to report that significant outcomes have been achieved in all priority planning areas profilled in our Centre Blueprint.

2015-16 has been an exciting year for genomic medicine. Building on the Centre’s planning priority to focus on our understanding of disease mechanisms including diagnosis and enhancement of individualized clinical therapeutics, the Centre launched a two-year pilot project to offer exome sequencing in our clinical laboratory, Genome Diagnostics in the Department of Paediatric Laboratory Medicine. This pilot was targeted to leverage the required infrastructure and continued development of technical expertise and disease management to lead in genomic medicine outcomes. Building on the noted leadership role and expertise within SickKids in genomic diagnostics and clinical care, we will now focus our planning efforts to work towards the development of offering clinical whole genome sequencing (WGS) to change the future of paediatric medicine at SickKids and pave the way for SickKids and Toronto to become leaders in the field of paediatric individualized medicine.

“While technological advances have allowed us to make the leap from discovery to translation, there is a critical need for continued advances in our ability to determine the clinical significance and utility of this new knowledge to lead and inform change to transform children’s health through individualized medicine.” Dr. Ronald Cohn

2015-16 has also witnessed the continued acceleration of the convergence of big data in genomic medicine. With the vision to accelerate scientific discovery through the world’s largest database of sequenced genomes, The Centre for Applied Genomics (TCAG at SickKids) partnered with Autism Speaks and Google to build a computational solution for the anticipated future scale of genomic data and catalyze major discoveries of clinical value through the sharing of data through an open source. Through SickKids leadership, this project has successfully sequenced 5,000 genomes to date with a targeted volume of 10,000 by the end of the year.

Additionally, SickKids (TCAG) participated as part of a national genomic tools network initiative for transforming life science research through a $58.5M Canada Foundation for Innovation award. As one of 3 leading agencies in Canada, SickKids will now have the capability to offer up to 10,000 WGS tests per year enabling all Centre-sponsored projects as well as access for all internal SickKids researchers to take advantage of this new service immediately. Building on SickKids’ national and international reputation, SickKids was 1 of 7 top-tier institutions who profilled our genomic research and clinical care successes at North America’s largest genetic conference and meeting in 2015. A Centre for Genetic Medicine video was produced to profile our work and was showcased at the 2015 American Society of Human Genetics Annual Meeting.
While precision medicine initiatives is still in its infancy, the Centre’s Genome Clinic continued its planning efforts to evaluate the diagnostic utility and health implications of Whole Genome Sequencing (WGS) in paediatric care. In January 2016, *npj Genomic Medicine* published our research findings demonstrating WGS to expand diagnostic utility and improve clinical management. Ongoing Genome Clinic research activity continues to help us assess and determine the impact of our findings on medical management with a lens to publish these findings in 2016-17. Learnings from the Genome Clinic have influenced planning and the research design study in preparation to launch (2016) a complimentary Cardiac Genome Research Clinic funded by the Ted Rogers Centre for Heart Research initiative.

To address the education needs identified in the Centre’s multi-year education plan, the Centre launched a number of educational initiatives including a 7-part lecture series, “Conversations with Genetics: Your day to day practice”, with over 1400 participants. Additionally, the Centre hosted a fall 2015 symposium, “Individualized Medicine through Genetic Testing – Today, Tomorrow and Beyond”, with over 300 delegates in attendance. With the goal to advance genomic literacy to improve access, awareness and responsiveness to evidence-based genomic information for both care givers and families, the Centre made investments to develop a number of online educational tools that were launched in 2015 and profiled in this annual report.

To further strengthen SickKids ability to lead in genomic discovery and clinical care, the Centre’s strategy has incorporated a strategic approach to influence and inform targeted stakeholders to the many genomic policy issues that continue to attract attention. These include but are not limited to social and ethical challenges, policies to influence future funding & service delivery, and new technologies such as the new gene-editing CRISPR-Cas9.

“SickKids has long been a pioneer and innovator in human genetics. We will continue to build the required infrastructure and knowledge in bioinformatics to ensure our competitive leadership in genomic medicine.” Dr. Stephen Scherer

Specific activities supported this year include; advocacy to support adoption of genetic discrimination legislation through expert testimony to the National Senate, influencing provincial policy development for adoption of genomic medicine in Ontario, and participation at a world research policy summit on gene-editing.

The vision of individualized medicine is complex and ongoing strategies continue in the development and application of genomic knowledge and technology. We are pleased with the progress the Centre has made this year and have profiled our key outcomes and activities in our 2015-16 Centre Annual Report.

**Dr. Ronald Cohn**  
Division Chief, Clinical and Metabolic Genetics  
Centre Co-Director

**Dr. Stephen Scherer**  
Director, The Centre for Applied Genomics  
Centre Co-Director
OUR PRIORITIES

The Centre priorities focus on the themes of discovery, translation, and knowledge transfer to build on the following identified priorities:

• Improved individualized patient care throughout SickKids

• Stronger clinical/translational research in human genomic medicine

• Broader education, outreach, and commercialization activities in genetics

PRIORITY PLANNING

The Centre’s Blueprint*, identified 3-year planning priority milestones.

Targeted priorities include:

I. Accelerating Translation & Innovation Opportunities

II. Promote Provider and Public Education

III. Investment in Technology Infrastructure

IV. Investment in Health Human Resources

V. Strengthen leadership in Health System Planning

VI. Publication of Research Discoveries

* A Blueprint for Change: Changing the practice of medicine, August 2013
MEMBERSHIP in the Centre for Genetic Medicine is inclusive of all SickKids staff who are interested in advancing the Centre’s strategic goals and objectives. Targeted communiqués are directed to Centre project teams and advisors, Foundation, health centre partners, and business & industry collaborators.

EXECUTIVE COMMITTEE LEADERSHIP

Centre co-Director, (Division Chief) Clinical and Metabolic Genetics
Dr. Ronald Cohn
Centre co-Director, (Director) The Centre for Applied Genomics
Dr. Stephen Scherer
(Division Head), Genome Diagnostics – DPLM
Dr. Peter Ray
(Director) Genetic Counselling
Cheryl Shuman
(Head and Senior Scientist) Genetics & Genome Biology
Dr. Monica Justice
Department of Paediatrics – Medical Appointment
Dr. Sarah Bowdin*
Department of Surgery – Medical Appointment
vacant*
(Director of Strategy) Centre for Genetic Medicine
Chris Carew (non-voting)

Ex officio Appointments

(Clinician Scientist/Surgeon) Ophthalmology
Dr. Elise Heon**
(Vice President) Clinical Programs
Judy Van Clieaf **
(Clinician Scientist/Genetacist) Clinical and Metabolic Genetics
Dr. Stephen Meyn***

* 2-yr (voting) appointment, October 2016
** ex-officio (non-voting) 2-yr appointment based on research & clinical applications aligned to Centre’s mission, October 2016
*** ex-officio (non-voting) 1-yr appointment, December 2016

CENTRE MEMBERSHIP

Membership in the Centre for Genetic Medicine is inclusive of all SickKids staff who are interested in advancing the Centre’s strategic goals and objectives. Targeted communiqués are directed to Centre project teams and advisors, Foundation, health centre partners, and business & industry collaborators.
ACHIEVEMENTS AND INITIATIVES
**GENOME CLINIC RESEARCH PROJECT**

Following the launch of the Centre’s 5-year Genome Clinic Research project in June 2013, the SickKids Genome Clinic (project) team continued efforts to evaluate the diagnostic utility and health implications of Whole Genome Sequencing (WGS) in paediatric care. This past year,

the major focus of the genome clinic project has been to analyze Whole Genome Sequencing (WGS) data obtained on 100 patients enrolled in this research study who were also undergoing microarray analysis. The analysis focused on two types of variants:

- **Diagnostic variants** – pathogenic variants related to a phenotype for which the patient was undergoing genetic testing. The results of this analysis were published in 2016 Stavropoulos et al. *npj Genomic Medicine*, ‘Whole Genome Sequencing Expands Diagnostic Utility and Improves Clinical Management in Pediatric Medicine’ (See Appendix D for publication research results)

- **Secondary/predictive medically actionable variant** – pathogenic variants in medically actionable genes that predict risk of a disease for which the patient may not be symptomatic at the time of enrollment.

The health economics research group of the project will be conducting follow-up studies to determine the impact of these findings on medical management for the patients and their families. At present, clinical validation is being completed for all secondary variant findings and the return of results will be completed by Q1 2016/17. Published outcomes from this portion of the study will occur following the return of results to patients and families.

**WHOLE EXOME SEQUENCING (WES) PILOT PROJECT**

Leveraging the required infrastructure and continued development of technical expertise and clinical management to lead in genomic medicine outcomes, the Centre sponsored the introduction of WES to be available through a two-year funded pilot program funding 100 WES ($178K)

per year through DPLM’s Genome Diagnostics CLIA/IQMH accredited laboratory which commenced in July 2015. This newly created infrastructure includes complete sequencing workflow, data analysis using automated informatics pipelines, and WES testing for a variety of constitutional disorders. To help facilitate family and health providers’ understanding of the testing and possible risks associated prior to their consent, the Centre for Genetic Medicine produced an educational brochure, video, and a 5-part learning module, explaining the risks, benefits and limitations of this testing all aimed at helping the family make an informed decision and to facilitate the practitioners’ learning for this new clinical and diagnostic offering which are all publicly available on the newly remodeled Centre website.

**TED ROGERS CENTRE FOR HEART RESEARCH (TRCHR)**

On November 20, 2014, SickKids, UHN and the U of T launched the Ted Rogers Centre for Heart Research funded by a $130M donation from the Rogers family. Oversight and joint leadership has been provided from the Centre for Genetic Medicine (R. Cohn) and the Labatt Family Heart Centre (S. Mital).

Formal planning commenced to launch the Cardiac Genome Clinic as part of the SickKids Personalized Medicine
Research Program (Platform Development) sponsored by the Ted Rogers Centre for Heart Research. Recruitment for dedicated research (project) positions include Dr. Mohsen Hosseini (Cardiac Genomicist) and Eriskay Liston (Genetic Counsellor), supported by the scientific project co-leads Drs. Sarah Bowdin and Raymond Kim. To date the experimental research design has been completed and the team has worked closely with the SickKids cardiology group to identify high-yield families with or at risk of heart failure for whole genome sequencing. The research team has utilized a family-centered approach by working with the UHN cardiologists to ensure a seamless transition when incorporating adult family members as part of the study design. After successfully completing an Internal Scientific review, the TRCHR Cardiac Genome Clinic will commence pending Research Ethics Board approval expected by Q1 2016/17.

REALIGNMENT OF GENOME DIAGNOSTICS LABORATORIES

New genomic platforms and technology coming online will enable SickKids to take advantage of new NGS methods, maintain rigorous quality standards, and align efforts to investigate clinical validity and effectiveness. To position SickKids Genetic testing laboratories to meet future demand for testing, phase II of the capital laboratory infrastructure relocation investment (project) to streamline the current metabolic, molecular genetics, and cytogenetics laboratories was completed this fiscal 2015/16.

CLINICAL PHARMACOGENETICS (PGX) PROGRAM

Through collaborations with the Centre for Genetic Medicine, Division of Clinical and Metabolic Genetics, Department of Paediatric Laboratory Medicine, The Centre for Applied Genomics, and the Division of Pharmacology & Toxicology, Centre sponsored activities continue to build momentum with a goal to develop a fully integrated PGx program at SickKids. Specifically, a 2-year Clinical PGx Services Research Pilot Study was launched (Q4 2015/16) that will serve as a test-bed for hypotheses and strategies designed to demonstrate the medical utility and feasibility of implementing PGx approaches into routine paediatric care. Through the (research) link to the Centre’s Genome Clinic project, PGx learning’s and outcomes of the study are awaiting final confirmation for publication. The Centre continues to sponsor a salaried position [Pharmacogenetics Research Advisor position (I. Cohn)] to ensure dedicated planning continues and clinical oversight is provided by Dr. Shinya Ito in the Division of Pharmacology & Toxicology.

NATIONAL FACILITY FOR GENOME SEQUENCING AND INFORMATICS

SickKids will contribute as part of a national genomic tools network initiative for transforming life science research through an award of $58.5M funded by Canada Foundation for Innovation. As one of 3 leading agencies, SickKids [The Centre for Applied Genomics (TCAG)] will now have the capability to offer up to 10,000 WGS tests per year. Acquisition of this new technology was financed in part through the Centre for Genetic Medicine and offers SickKids the status of the only facility in Canada currently operating with this advanced technology. This new service offering in TCAG commenced in September 2015 and will allow for all Centre research projects including the Ted Rogers Centre for Heart Research as well as access to all internal SickKids researchers requiring WGS to access this service immediately which will result in an increased turn-around time, more in-depth read of the genome, and attainment of increased revenues.

LEADERSHIP IN GENETIC SERVICES PLANNING

In addition to the programmatic strengths from the Clinical Division, The Centre for Applied Genomics and Department of Paediatric Laboratory Medicine, a commitment to further position SickKids as a provincial and national leader for genetic service planning continued. Specific activities to support this objective include;

• Provincial Clinical Genetics Think Tank – hosted a provincial clinical genetics planning Think Tank for the Ontario Genetics Secretariat clinical leads in June 2015
establishing priority (provincial) planning initiatives. Provincial leadership continued this year provided by C. Carew as Secretariat Chair in addition to Drs. S. Meyn and P. Ray holding positions on the provincial executive committee.

• Utilization of Clinical Genetic Wait Time Data – Demonstrated utility of data (to the MOHLTC) resulting from a 2-year Provincial Clinical Genetics Wait Time Project led by SickKids for the Ontario Genetics Secretariat targeted to inform the hospital-based programs and the MOHLTC provincial genetic services and Laboratories Branch around future service planning and provincial policy development;

• Provincial Policy Leadership – focused efforts continued to influence provincial policies for diagnostic testing and specifically positioning hospital laboratories to acquire additional volumes through repatriating select genetic testing currently being completed in the US. SickKids was successfully awarded contracts with the MOHLTC for additional volumes in select genetic testing test offerings. Planning efforts continue both organizationally and provincially to influence provincial policy related to the service and funding model for genetic services in Ontario.

LEGISLATION AGAINST GENETIC DISCRIMINATION

As one of the only G8 countries without legislation to protect individuals against genetic discrimination, the Centre with leadership from Drs. R. Cohn and S. Scherer both testified as expert witnesses to the National Senate advocating for new legislation. It is expected that the Bill S-201 will be passed in April 2016 followed by the House of Commons in the fall of 2016. At present, the current absence of no genetic discrimination in Ontario has negatively impacted enrollment into the Centre Genome Clinic with over 42% declining participation citing genetic discrimination as a valid concern.

MEET DR. SARAH BOWDIN

Dr. Sarah Bowdin is a Clinical Geneticist with the Division of Clinical and Metabolic Genetics, and the co-director of the Centre for Genetic Medicine. Sarah was born and trained in the United Kingdom and joined SickKids in 2008.

Sarah’s contribution to genomics at SickKids started when she became involved in designing the clinical elements of the Genome Clinic, a multi-disciplinary research project which was subsequently funded by the Centre for Genetic Medicine. From the first discussions between clinical and molecular geneticists, computational medicine experts, bioinformaticians and ethicists, Sarah recognized that teamwork would be the key to maximizing the benefits of whole genome sequencing in paediatric health care.

The Genome Clinic has become a fantastic collaboration where each individual’s unique contribution ensures that the highest scientific and ethical standards are achieved, often through in-depth analysis and discussion of issues that are only obvious once this technology is used in real life situations. Sarah has enjoyed, and been stimulated by, helping families of children with rare diseases reach a diagnosis for their child, often after years of searching.

Sarah’s next aim for Genomics at SickKids is to help teach her colleagues about how to use this technology to benefit the many children who are at the beginning of their diagnostic journey.
SickKids has long been a pioneer and innovator in human genetics. This is our opportunity to align the research discoveries to patient care by ensuring we invest in the skills, processes and education initiatives to make the best use of these advances.

and Ronni Cohn, Spell Checking Nature – Interrogating CRISPR/Cas9 for the treatment of inherited disorders. The invited keynote speaker, Leslie Biesecker, Chief of the Genetic Disease Research Branch, and a Senior Investigator in the National Human Genome Research Institute at the NIH, presented; Prediction is hard, especially about the future. The overall quality of the 5 presentations was rated as ‘excellent to very good’ by an average of 71% of the respondents. The majority of the respondents indicated that the symposium would impact their work or daily practice. The 2016 Symposium is scheduled for Monday November 7. (Program outline in Appendix D)

CENTRE EDUCATIONAL LECTURE SERIES

Based on feedback from the Centre Needs Assessment survey, SickKids stakeholders revealed the necessity for better resources and easier access to new clinically relevant genetic information toward improving patient care. Toward this end, the Centre developed a Royal College accredited 7-month lecture series and concurrent webinar with interactive presentations on the advances in genetic testing and the appropriate utilization in paediatric medicine. By participating, paediatricians, nurse practitioners, nurses, surgeons and other health care providers enhanced their skills in counselling and appropriate use of clinical genetic testing, such as WGS and PGx testing. On January 28, 2015 the Centre for Genetic Medicine launched a 7-part Royal College accredited lecture series and concurrent webinar – Conversations with Genetics: You and Your Practice. The inaugural lecture, Next Gen Sequencing Results – How does it impact health and the future?, presented by Dr. Ronald Cohn, and was simultaneously web streamed by the Ontario Telemedicine Network (OTN) and the series ran for 7-months (January 2015 to July 2015). A total of 632 health care professionals and researchers registered for the 7 different lectures. A combined total of 107 evaluation surveys were completed for the entire series (17% of the registrants) of which 24 or 22% of the survey respondents indicated that they viewed the lecture via webinar. The overall feedback regarding both the activity and the quality of the presentations was positive. (Program outline in Appendix E)
ENHANCING GENOMIC KNOWLEDGE THROUGH ONLINE EDUCATIONAL TOOLS

Theme focused online educational resources continued to be a priority planning initiative for the Centre. To help patients and families make informed decisions about whole exome and whole genome testing and enhance access to education tools for all health care providers across SickKids who offer this testing can have their patients view one or more of the modules to support the consent process. These modules are one step towards enhancing efficient and effective patient care in the era of genomic medicine. (select online tools profiled in Appendix F)

Animated ‘white-board’ video – To help facilitate the understanding of Whole Exome Sequencing, the Centre for Genetic Medicine produced and launched a 6 minute animated video that is publicly available on the Centre website. The video walks the viewer through why the testing was offered, how it is done, and the possible outcomes for a fictitious young boy named Jimmy, who has development difficulties.

5-Part Genomics Education Module – A 5-part part learning tool has been developed to provide an introduction to new genetic testing technologies called exome and genome sequencing. The content has been created to be used by both health care professionals and families in preparation for or as a supplement to a face-to-face dialogue with the patient and care team.

MEET DR. SERGIO PEREIRA

Dr. Sergio Pereira is the Manager of the next generation sequencing facility at The Centre for Applied Genomics (TCAG) at SickKids. Sergio reigns from South America and obtained his BSc in Biological Sciences from the State University of Sao Paulo, and his Master and PhD degrees in Genetics from the University of Sao Paulo, Brazil. After years of working as a post-doctoral fellow in molecular genetics and evolutionary biology of vertebrates, especially birds, at the Royal Ontario Museum, he joined SickKids in 2008. He has since followed the rapid development of next generation sequencing technologies, including whole genome and whole exome sequencing, targeted resequencing, RNA-Seq, genome editing (CRISPR technologies), epigenomics, and genotyping-by-sequencing.

With an extensive network of field application specialists, sales representatives, managers and technicians in other NGS facilities across Canada and abroad, Dr. Pereira is capable of keeping the sequencing facility in the forefront of genomics through scientific and technological discussions, exchange of ideas and implementation of new methodologies and technological advances in next generation sequencing. He has been involved in technical development including the implementation of whole genome sequencing in TCAG using the latest and most-cost effective technologies available. His scientific background and years of NGS experience allows him to comfortably provide consultation and guide research designs with collaborators from around the world working on organisms as diverse as bacteria to humans, with a focus in many scientific disciplines such as medical genetics and genomics, clinical genetics, immunology, microbiology, evolutionary ecology and biology, and agriculture.
HEALTH HUMAN RESOURCES (HHR) INVESTMENT – POSITION SPONSORSHIP

The Centre has responded to strengthen targeted outcomes for identified Centre priorities through the following HHR investments:

- Educating our health professionals to champion genomic advances into everyday clinical practice is part of the Centre vision. (Adel Gilbert, Centre Education Advisor)

- Aligning Next Generation lab technology and testing to support translation and clinical effectiveness. (Dr. Christian Marshall, Associate Director, Genomic Analysis, DPLM/cross appointment to the Division of Clinical and Metabolic Genetics)

- Enhancing the effectiveness of genomic information in tailoring patient interventions. (Nasim Monfared, Research Genetic Counsellor)

- PGx testing will have profound impact on our laboratory service resulting in enhanced patient safety and clinical outcomes. Development of a hospital pharmacogenetics program (Iris Cohn, Pharmacogenetics Research Advisor)

- Demonstrating utility and strengthening health planning to lead provincial, national and international competencies to advance health policies and health economic studies in genomic research and clinical care (Dr. Robin Hayeems, Research Policy Scientist)

- Lead, advance, and inform change through the identification and execution of the most effective strategies and resources for the Centre (Chris Carew, Director of Strategy)

PATIENT VIGNETTE – GENOME CLINIC

S. and K. are parents of a 3 year old girl B. with developmental delay. The genome sequencing results in B. revealed a mutation in a newly described gene associated with intellectual disability. There is not much known about this gene, however, we could tell the family that the only body system affected by this gene seems to be brain and possibly growth restriction. The parents were relieved to hear this information; one of their main concerns had been that B. has a life-limiting condition. No secondary/predictive medically actionable findings were identified in B. and this was good news to the family. They understood that this result did not mean there was no risk of future disease, however, they found it reassuring that we didn’t find a clear risk of another disease at this time.

A few months later the parents informed us that they were expecting a child. They were referred to the prenatal genetics clinic and proceeded to receive genetic counselling regarding testing options in the new pregnancy. They underwent chorionic villus sampling (CVS) to test the fetus for the mutation found in B. The family were informed a few weeks later that the fetus was not affected.
SPONSORSHIPS AND FUNDING
• 2015 American Society of Human Genetics (ASHG) Annual Meeting and Conference, Canadian Mixer sponsorship in collaboration with CIHR and CCMG AND Staffing Bursary Travel awards for Centre Staff to attend ASHG

• 2015 ASHG Annual Meeting, $2K Travel Awards – abstracts selected for presentation: Mohammed Uddin (Scherer Lab)

• Restracomp (2015) Studentship award – 2nd year sponsorship $11K. Master’s award, Mahmoud El-Maklizi, Danska Lab, Genetics and Genome Biology R.I. Program

• Sponsorship (currently year 1 of a 3-year commitment) for the recruitment and research support for Dr. Neal Sondheimer ($50K) with research interest in Human Genetics (mitochondrial disease)

• 2015/16 Canadian Certified Medical Geneticist Fellowship Training – Centre sponsorship, Dr. Rebekah Jobling (candidate)

• Sponsorship of Post-graduate research 2015 summer project (Sean Kim) to establish policies and procedures for managing and appropriate sharing of confidential genetic information in the EMR

• 2015 ACMG Annual Clinical Genetics Meeting sponsorship, Dr. Christian Marshall, Platform Presentation

• 2015 European Society of Human Genetics Annual Meeting, Drs. Stephen Meyn and Rebekah Jobling, Platform Presentation

• CIHR STAGE International Speaker Seminar Series 2016

RESEARCH GRANTS AND AWARDS

1) 2 ($50K) Catalyst Research Grant Awards in Human Genetics: Award 1: R. Hayeems, Child Health Evaluative Sciences. Award 2: P. Kannu, Clinical & Metabolic Genetics

2) 1 ($50K) co-sponsored with the C-BMH Catalyst Research Grant in NFT1: Award K. Sinopoli, Psychology/Neurology

3) 2 co-sponsored Accelerator Grants in Genomic Research with McLaughlin Centre: Award 1: J. Stavropoulos w. Trillium Health Partners, ($24K), and Award 2: R. Hayeems, Child Health Evaluative Sciences, ($49K)

MEET DR. RAVEEN BASRAN

Dr. Basran is a director in Genome Diagnostics, located in the Department of Paediatric Laboratory Medicine at SickKids. She graduated from the University of Toronto and completed her graduate studies at the University of Oxford. She completed her Clinical Molecular Genetics Fellowship through the American Board of Genetics and Genomics at Boston University and recently became a member of the Canadian College of Medical Genetics (CCMG). SickKids Molecular Genetics Laboratory is the largest diagnostic laboratory in Canada and also serves as a CCMG training facility.

As Director of the Molecular Genetics laboratory, Raveen’s primary responsibilities include reviewing and signing the release of molecular genetic tests and providing oversight for molecular diagnostic assays run in the laboratory. As the field of diagnostic genetics is evolving, it is exciting to be part of a laboratory that is continuously implementing newly emergent genetic technologies to provide state of the art diagnostic testing for our patients and beyond.

Genome Diagnostics has recently implemented next generation sequence technology for disorders such as hearing loss and hereditary spastic paraplegia and SickKids continues to offer innovative technologies in the diagnostic genetics field to deliver the best possible patient care.
ANNUAL OBJECTIVES 2015-16

ACCELERATING TRANSLATION AND INNOVATION

1) Optimize translation opportunities through granting (focus on human genetics) opportunities across the hospital*

2) Explore co-funding opportunities with McLaughlin and other Centres – Establish ‘innovative and strategic’ Funds Grant Process*
   • 5 Grants administered (2 Centre, 1 Joint Centres (Genetics & CBMH), 2 McLaughlin co-sponsored)

3) Continue to generate activities and programs to influence the “change of practice” – Launched (pilot) to offer exome sequencing in the clinical diagnostic laboratory with practice guidelines*,***

4) Development of an ‘interventional genomic therapies research program’ in collaboration with the C-BMH. Discussion paper completed and approved through an established research and clinical advisory planning group. Centre is currently exploring funding opportunity through the Foundation.**

TECHNOLOGY INFRASTRUCTURE

8) Continued capital investment in year II to support NGS in clinical diagnostics research laboratories*,***
   • Strategically aligned to the Centre and Ted Rogers Centre for Heart Health research initiative priorities

HEALTH HUMAN RESOURCE INVESTMENT

9) Continued investment in year II for bioinformatics, human genome sciences, PGx, education, strategy***

SYSTEM PLANNING

10) Lead and influence development and funding of Genomic Medicine model (clinical and diagnostic) – preliminary planning commenced for WGS***

11) Develop benchmarks for clinical wait times and match workload data for resource alignment – data utilized by MOHLTC to influence service delivery model and policy funding efforts*

IMPACT AND EVALUATION

12) Develop new clinical pathways for optimizing efficiencies and new practices in years I, II, & III. Influence government and stakeholders through development and sharing of sustainable business models***

PROVIDER AND PUBLIC EDUCATION

5) Invest in interactive technologies to support family education*

6) Enhanced Web-based platform to support health professional education* (see website analytics)

7) Methodology for knowledge dissemination (internal & external)* & annual symposia*

*achieved objective    **work in progress or pending    ***active multi-year activity
1. Continue to refine activities and programs to influence the “change of practice” in the continuum of clinical management through genomic knowledge translation. Work efforts will include the development of clinical guidelines and therapeutic pathways, rigorous and standardized processes for clinical validity & utility, continued development of a robust bioinformatics infrastructure, and further development of supporting educational tools for clinicians and families.

2. Partner with the MOHLTC in the development of a rare disease ‘system design’ for Ontario (research to clinical care outcomes).

3. Continue to strategically invest in capital infrastructure to strategically align future requirements of the research and clinical diagnostic demands through joint investment with the TRCHR and the Centre.
4. Create opportunities to enhance research and seek additional collaborators for approaches to ‘Human Genetics’ to strengthen SickKids leadership in ‘Basic Human Genetic Science’ and secondly encourage funding collaborations with other Centres (Cancer, Brain & MH) – administer minimum of four (4) granting opportunities.

5. Execute ‘Phase II’ of the Genome Clinic Research Project with the aim to offer individualized medicine as a standard clinic and diagnostic service at SickKids, offering WES/WGS on a broader scale due to availability of expertise, untapped capacity, and organizational readiness. Specific research activities will include:
   • WGS vs. Panel Cohort Study – WGS to be completed, data analyzed and results returned for all enrolled subjects
   • Collaboration with SickKids’ Complex Care Program – targeted cases for which diagnostic uncertainty remains and potential to explore secondary variants from sequenced results. Publish data to support HTA and Health economic analysis for next generation sequencing influencing clinical care outcomes.
   • Neonatal Rapid Screening Project – customized ‘neonatal panel’ of genes for interrogation
   • Establish a Predictive Genome Clinic – designed to expand knowledge and clinical capacity to evaluate and manage secondaries for clinical or research services
   • Explore development of a ‘CLINSeq ’type project to provide WGS for a paediatric population

6. Host an international 2.5 day Workshop in Applied Genomic Medicine to profile our leadership role in genomic research and medicine supported by faculty and facilitators from Canada, the US and Ireland.

7. Influence targeted interests and promote co-funding of trainees awarded research fellowships and studentships through Restractcomp research programs – sponsorship of at least two (2) trainees and one (1) Fellow, as well as continue co-funding sponsorships, workshops, symposia and conferences to promote genomic education and collaboration.

**MEET NASIM MONFARED**

Nasim is the coordinator and genetic counsellor for the Genome Clinic for the Centre for Genetic Medicine at SickKids. Nasim was born in Iran and grew up in North Vancouver. She completed her BSc in Genetics at the University of British Columbia and joined the Canadian collaborative project on genetic susceptibility to Multiple Sclerosis as a research assistant for two years prior to pursuing the MSc program in genetic counselling at the University of British Columbia. She joined SickKids in 2013.

Nasim has a keen interest in personalized genomic medicine. She has developed expertise in the process and complexities of genomic counselling and the practical, ethical and health system implications of genomic testing in clinical and research settings.

Her primary research interest is the evaluation and return of predictive medically actionable findings and she is currently developing a clinical service focused on evaluation and reporting of such findings for patients and research participants at SickKids. Nasim is also involved in development of education strategies that will aid in implementing genomic medicine more broadly for both health professionals and for our patients and families.
SELECTED PUBLICATIONS:


Canadian Open Genetics Repository (COGR): a unified clinical genomics database as a community resource for standardising and sharing genetic interpretations. Lerner-Ellis J, Wang M, White S, Lebo MS; Canadian Open Genetics Repository Group: Ron Agatep; Peter Ainsworth;
Mohammad R. Akbari; Melyssa Aronson; Gary D. Bader; Raveen Basran; Andre Blavier; Andrea Blumenthal; Kathleen Buckley; Jodi Campbell; Philippe M Campeau; Melanie Care; Nancy Carson; Ronald Carter; George Charames; David Chitayat; George Chong; Edmond Chouinard; Kathy Chun; Ken Craddock; Rod Docking; Andrea Eisen; Hanna Faghfoury; Sandra Farrell; Harriet Feilotter; Bridget Fernandez; Cynthia Forster-Gibson; William Foulkes; Robert Hegele; Spring Holter; Sheri Horsburgh; Lauren Hughes; Stacey Hume; Franny Jewett; Rita Kandel; Aly Karsan; Sam Khalouei; Joan Knoll; Elena Kolomeit; Georges Maire; Christian Marshall; Elizabeth McCreedy; Michael Moorhouse; Chantal Morel; Tanya Nelson; Brian O’Connor; Francis Ouellette; Jillian Parboosingh; Peter Ray; Heidi Rehm; Christie Riddell; David S. Rosenblatt; Andrea Ruchon; Bekim Sadikovic; Kara Semotnik; Stephen W. Scherer; Cheryl Shuman; Josh Silver; Katherine Siminovich; Lesley Solomon-Izsak; Marsha Speevak; Elizabeth Spriggs; James Stavropoulos; Lincoln Stein; Rhonda Tannenbaum; Deborah Terespolsky; Richard F. Wintle; Beatrix Wong; Nora Wong; John S. Waye; Michael O. Woods; Philip Wyatt; Sean Young. J Med Genet. 2015 Jul;52(7):438-45. doi: 10.1136/jmedgenet-2014-102933.

The sooner the better: Genetic testing following ovarian cancer diagnosis.

NSD1 mutations generate a genome-wide DNA methylation signature.


The clinical utility of next generation sequencing for the extraction of pharmacogenetic data sets. Cohn I, Paton T, Marshall CR, Cohn R, Ito S. JAMA, under review.

2015 Canadian College of Medical Geneticists Annual Scientific Meeting. Ottawa, ON. September 2015.


Department of Molecular and Medical Genetics, Oregon Health Sciences University, Portland, OR. November 2015. Diagnostic and Predictive Uses of Whole Genome Sequencing in Children. Meyn MS.

**APPENDIX B: RESEARCH GRANTS**

**McLaughlin Centre.** Grant period 2014 – 2015. Whole exome sequencing in the NICU – Developing a rapid, specific and sensitive pipeline for the diagnosis of genetic disease in the newborn. PI: R. Cohn. **Award $20,000.**

**Complete Genomics.** Grant period 2013 – 2016. Whole Genome Sequencing for Pediatric Patients. Co-PIs: R. Cohn and S. Scherer. **Award $600,000.**


**Canada Foundation for Innovation.** Grant Period April 2015 – March 2020. Canada’s Genomics Enterprise (CGEn): A national genomic tools network infrastructure grant to build a national facility for genome sequencing and informatics for transforming life science research. PI: Jones, Co-PIs: Lathrop, Scherer. **Award $58,435,136.**

**Canadian Institutes of Health Research (Foundation Scheme).** Grant Period July 2015 – June 2022. Genomes to Outcomes in Autism Spectrum Disorders. Operating grant to identify and characterize novel ASD risk variants, and determining how to best relay whole-genome information effectively to clinicians and families. PI: S. Scherer. **Award $2,204,198.**

**Genome Canada.** Technology Development Funds for Nodes of the Genomics Innovation Network. Technology Development for Whole Genome Analysis: TCAG operating grant for technology development for whole genome analysis. PI: S. Scherer Co-PI: L. Strug. **Award $743,196.**
Excerpt from January 2016 research publication, ‘Whole Genome Sequencing Expands Diagnostic Utility and Improves Clinical Management in Pediatric Medicine’, published by the Nature Partner Journals, npj Genomic Medicine.

The standard of care for first-tier clinical investigation of the etiology of congenital malformations and neurodevelopmental disorders is chromosome microarray analysis (CMA) for copy number variations (CNVs), often followed by gene(s)-specific sequencing to identify smaller insertion-deletions (indels) and single nucleotide variant (SNV) mutations. Whole genome sequencing (WGS) has the potential to capture all classes of genetic variation but the diagnostic utility has not been well established. In a prospective study we utilized WGS and comprehensive medical annotation to assess 100 patients referred to the paediatric genetics service at SickKids and compared the diagnostic yield versus standard genetic testing. WGS identified genetic variants meeting clinical diagnostic criteria in 34% of cases, representing a 4-fold increase in diagnostic rate over CMA (8%) (p-value = 1.42e-05) alone and >2-fold increase in CMA plus targeted gene sequencing (13%) (p-value = 0.0009) (see Figure below). WGS identified all rare clinically significant CNVs that were detected by CMA. In 26 patients, WGS revealed indel and missense mutations presenting in a dominant (63%) or a recessive (37%) manner.

We found four subjects with mutations in at least two genes associated with distinct genetic disorders, including two cases harboring a pathogenic CNV and SNV. Clinical implementation of WGS as a primary test will provide a higher diagnostic yield than conventional genetic testing and potentially reduce the time required to reach a genetic diagnosis.
## Agenda

<table>
<thead>
<tr>
<th>Time</th>
<th>Session</th>
<th>Speaker</th>
<th>Institution</th>
</tr>
</thead>
<tbody>
<tr>
<td>2:30 p.m.</td>
<td>Welcome and Introduction</td>
<td>Stephen Scherer, PhD</td>
<td>GSK-CIHR Endowed Chair in Genome Sciences, SickKids and University of Toronto</td>
</tr>
<tr>
<td>2:45 p.m.</td>
<td>Paediatric Cancers: Impacting Surveillance and Treatment Through Genomic Testing</td>
<td>Adam Shlien, MD</td>
<td>Associate Director, Translational Genetics, Paediatric Laboratory Medicine, SickKids and University of Toronto</td>
</tr>
<tr>
<td>3:20 p.m.</td>
<td>Congenital Muscle Disease: New Prospectives on Gene Discovery and Therapy Development</td>
<td>James Dowling, MD, PhD</td>
<td>Associate Professor, Muscular Genetics, University of Toronto</td>
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<tr>
<td>3:55 p.m.</td>
<td>Spell-Checking Nature: Interrogating CRISPR/Cas9 for the Treatment of Inherited Disorders</td>
<td>Ronald D. Cohn, MD</td>
<td>Women's Auxiliary Chair of Clinical and Metabolic Genetics, SickKids and University of Toronto</td>
</tr>
<tr>
<td>4:30 p.m.</td>
<td>Keynote Speaker</td>
<td>Les Biesecker, MD</td>
<td>Chief, Medical Genomics and Metabolic Genetics Branch, National Human Genome Research Institute, National Institutes of Health</td>
</tr>
<tr>
<td>5:30 p.m.</td>
<td>Reception</td>
<td></td>
<td>PGCRL Gallery</td>
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</table>
APPENDIX E: 2015 CENTRE LECTURE SERIES

Conversations with Genetics: Your Day to Day Practice

This FREE lecture series offered by the Centre for Genetic Medicine will focus on the advances in genetic testing and the appropriate utilization in primary care medicine to improve patient care.

By attending this lecture series paediatricians, nurse practitioners, surgeons and other health care providers will enhance their skills in counselling and appropriate use of clinical genetic testing, such as whole exome sequencing and pharmacogenetic testing as they relate to primary care.

After this lectures series participants will:
• Assess when and how to appropriately order genetic testing in paediatric patients
• Explain the implications and complexity of next generation genetic testing to parents
• Identify pharmacogenetic testing options to improve patient outcomes
• Describe the current status of genetic non-discrimination legislation in Canada

Each of 7 sessions will be 45 minutes followed by 15 minutes of Q & A and 30 minutes of informal chat over refreshments.

Registration is required. Please visit www.cvent.com/d/n4qyx6/1Q

MONTHLY LECTURE SERIES 2015 (4th Wednesday of the Month at 4 p.m.)

<table>
<thead>
<tr>
<th>Speakers</th>
<th>Title</th>
<th>Date</th>
<th>Location</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ronald Cohn MD</td>
<td>Next gen sequencing results: How does it impact health and the future?</td>
<td>Jan 28</td>
<td>Peter Gilgan Centre for Research and Learning 2nd Floor, Event room 2a/2b</td>
</tr>
<tr>
<td>Christian Marshall MD</td>
<td>How is exome sequencing done?</td>
<td>Feb 25</td>
<td>Peter Gilgan Centre for Research and Learning 2nd Floor, Event room 2a/2b</td>
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<tr>
<td>Sarah Bowdin MD</td>
<td>Demonstrating how and when to order exome sequencing?</td>
<td>Mar 25</td>
<td>Peter Gilgan Centre for Research and Learning 2nd Floor, Event room 2a/2b</td>
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<tr>
<td>Cheryl Cytrynbaum MS, CGC</td>
<td>Whole exome sequencing in clinical care: Practical considerations for preparing patients/families</td>
<td>Apr 22</td>
<td>Daniels Hollywood Theatre, SickKids Room 1/246 Black Wing</td>
</tr>
<tr>
<td>Iris Cohn Pharm. D</td>
<td>Pharmacogenetics: A prime example of providing individualized medicine for your patient</td>
<td>May 27</td>
<td>Daniels Hollywood Theatre, SickKids Room 1/246 Black Wing</td>
</tr>
<tr>
<td>Robin Haysmann MPh</td>
<td>Day to day genetics: Ethical and policy challenges</td>
<td>June 24</td>
<td>Daniels Hollywood Theatre, SickKids Room 1/246 Black Wing</td>
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<tr>
<td>Melissa Center MS</td>
<td>Autism genetics: Where are we now?</td>
<td>July 22</td>
<td>Daniels Hollywood Theatre, SickKids Room 1/246 Black Wing</td>
</tr>
</tbody>
</table>

SickKids Centre for Genetic Medicine
APPENDIX F: ONLINE EDUCATIONAL TOOLS FOR STAFF AND FAMILIES

Exome Sequencing Animated Video
APPENDIX G: 
CENTRE SPENDING FISCAL 2014/15 
REPORTING APRIL 1, 2014 TO JANUARY 31, 2015

Centre for Genetic Medicine
F2015/16 YTD Spending (as at February 29, 2016)

Total F2015/16 Spending* = $976,026

Centre Approved Research Grant Funding (pending REB approval for release) $181,000

Financial support for the Centre is through a five-year $5M strategic priorities funding commitment (currently year 3 of 5).

*Centre 11-month expenditures (April 2015 to February 29, 2016).
A detailed statement is available upon request.
## APPENDIX H:
### CENTRE WEBSITE ANALYTICS REPORT
#### OCTOBER 2015 TO MARCH 30, 2016

### Pageviews

![Graph showing pageviews from November 2015 to March 2016.]

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<tr>
<th>Page</th>
<th>Pageviews</th>
<th>Unique Pageviews</th>
<th>Average Time on Page</th>
<th>Entrances</th>
<th>Bounce Rate</th>
<th>% Exit</th>
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<tr>
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<tr>
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<td>27.38%</td>
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The following data and statistics are based on Google Analytics from October 1, 2015 to March 30, 2016.