PAVING THE WAY FOR INDIVIDUALIZED MEDICINE
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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.
EXECUTIVE SUMMARY

The Centre for Genetic Medicine continues to play a pivotal role in elevating the ‘genetics dialogue’ both within SickKids and with key stakeholders to lead and inform change in research, clinical care & discovery, and education. To address the changing environment of clinical genetics, SickKids partnered with the Children’s Hospital of Philadelphia this year to lead an international Think-Tank with (genetic) leaders from across Canada and the United States to lead and inform change on best practices and shared these findings through a published paper. To embrace the necessity to link genomic literacy to improve access, awareness and responsiveness to evidence-based genomic information within the hospital and beyond, the Centre created a multi-year education plan in early 2014 and launched a number of educational initiatives including a 7-part lecture series, “Conversations with Genetics: Your day to day practice”, which launched in January 2015. Additionally, the Centre hosted a spring education symposium, “Genetic Medicine: Advancing Family Health Care”, with over 200 health care and research delegates in attendance.

Significant efforts continued to position SickKids (genetic) diagnostic laboratories (renamed Genome Diagnostics) to meet future demand for Next Generation Sequence testing. This included a $1.4M infrastructure relocation project, investment in the development and launch of a clinical whole exome sequencing pilot project, continued support in the development of a SickKids pharmacogenetics program, and the successful $2M award of repatriated genetic testing from the Ministry of Health and Long Term Care for genetic testing. Financial support and planning has continued this year to bridge the current gap for specialized health human resource positions, advance further integration of Next Generation sequencing technology, and continued development of the world’s first paediatric clinical genome clinic, all contributing to concerted efforts to publish our research discoveries in high-end research journals (see appendix A). To further strengthen SickKids ability to lead in discovery and genomic medicine, the Centre for Applied Genomics (TCAG) was successful in securing a $2M Genome Canada infrastructure grant (TCAG: Genomic Innovation Network), supporting critical operations, technology development, and informatics activities. In addition, TCAG launched a ground-breaking collaboration with SickKids, Google and Autism Speaks US to create the world’s largest genomic data base (on autism) through cloud technology paving a roadmap for future genomic ‘Big Data’ research.

The Centre also led a number of provincial planning initiatives with a lens to influence provincial policy development targeting ‘key’ components required for a provincial genetic services model and associated funding. Specifically, SickKids led the development of a Provincial Clinical Genetics Wait Time Project resulting in the completion of Ontario’s first provincial standardized wait times report released in January 2015 as well as leading a provincial genetics Think Tank & Consultation with the MOHLTC on provincial genetic services planning strategy. From a national perspective, the Centre provided planning to support the McLaughlin sponsored ‘Canadian Prenatal Genomic Microarray and Sequencing Symposium’, held at
SickKids in the fall of 2014. This national forum brought global leaders together to discuss and build consensus related to policy, clinical utility & validity, test interpretation and related reporting and patient counselling issues in the application of new genomic testing for prenatal care and screening.

In February 2015, Dr. Stephen Scherer was appointed the Editor in Chief, for a unique partnership with the Nature Publishing Group and the Centre of Excellence in Genomic Medicine Research, King Abdulaziz University in Saudi Arabia to publish npj Genomic Medicine. The new journal will be published via open access, meaning that all research will be freely available upon publication, aiming to publish the very best papers in genomic medicine from around the world.

Ongoing Centre leadership combined with broad strategic planning efforts came to fruition in the fall of 2014 to form the creation of the Ted Rogers Centre for Heart Research (TRCHR), a unique partnership between SickKids, The University of Toronto, University Health Network. To provide leadership and scientific direction for this new initiative, the Centre for Genetic Medicine formed a partnership with the Labatt Family Heart Centre (R. Cohn and S. Mital as scientific co-leads) and collaborated in the development of key project deliverables supporting SickKids’ identified role to lead in the genomic science of heart research through the creation of a Precision Medicine Research Program aligned with the development of a Genome Clinic Research Platform.

As one of the only G8 countries without legislation to protect individuals against genetic discrimination, the Centre has publicly advocated with federal and provincial government leaders to influence content and adoption of legislation.

Learning’s and data as a result of the Centre’s Genome Clinic has armed the hospital with quantitative data profiling the profound impact on families and patients when making decisions related to genomic testing.

As profiled in our 2014/15 Annual Report, the Centre for Genetic Medicine continues to identify and implement the most effective strategies and shared resources for targeted collaborations as the most critical accelerator to leverage change to achieve the Centre’s vision. On behalf of the Centre executive committee, we are pleased to share summary outcomes and activities in our 2014/15 Centre Annual Report.

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

Dr. Stephen Scherer  
Centre Co-Director  
Director, The Centre for Applied Genomics
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 genomic medicine
• Broader education, outreach, and commercialization activities in genetics

Riyana Babul-Hirji,
Genetic Counsellor,
Clinical and Metabolic Genetics
The implementation of individualized medicine requires radical changes in the culture of healthcare delivery.

With the dramatic advances in our knowledge of human genomics, this presented SickKids with an opportunity to improve the health of children by introducing the concept of individualized genomic medicine. To achieve integrating the new genomic knowledge across the organization, the Centre’s Blueprint (A Blueprint for Change: Changing the practice of medicine, August 2013), identified 3-year planning priority milestones. Highlights of the 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

The Blueprint was designed to assist healthcare professionals collaborate and leverage institutional and programmatic strengths to build system change with the longer term goal of advancing future policy development.
CENTRE GOVERNANCE – 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*

(Program 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

Ex officio Appointments

(Clinician Scientist/Surgeon) Ophthalmology
Dr. Elise Heon**

(Vice President) Clinical Programs
Judy Van Cleaf**

(Clinician Scientist/Geneticist) Clinical and Metabolic Genetics
Dr. Stephen Meyn***

* 2-yr (voting) reappointment, October 2014
** ex-officio (non-voting) 2-yr appointment based on research & clinical applications aligned to Centre’s mission, October 2014
*** ex-officio (non-voting) 1-yr appointment, September 2014
CENTRE MEMBERSHIP

Membership in the Centre for Genetic Medicine is inclusive of all SickKids staff who is 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.

Jennifer Orr,
Laboratory Technician,
Genome Diagnostics,
DPLM
Hosted International Think-Tank ‘The Future of Clinical Genetics’: Collaboration with Children’s Hospital of Philadelphia

To address the changing nature of the medical genetics practice in the era of exome and genome sequencing, with a goal to produce a publishable document (white paper) to lead and inform of changes in the evolving role of the clinical geneticist, SickKids partnered with the Children’s Hospital of Philadelphia (CHOP) to
The power to access and analyze enormous (genomic) data sets can improve our ability to foresee and treat disease – this will only be achieved through the creation of unconventional partnerships and educating our health care providers and families.

co-lead two international Think-Tanks held on June 2, 2014, at SickKids and a follow up Think Tank on September 29, 2014 at CHOP. Invited participants included 35 geneticists, bioinformatics/translational leaders, and genetic counselors from all over North America including participation from five families. The lead organizers, Drs. Sarah Bowdin (SickKids), and Ian Krantz (CHOP) will lead the completion of the academic paper identifying the ‘best practice’ to the overall process of integrating genomic sequencing into clinical care.

**Genome Clinic Research Project** Following the launch of the Centre’s 5-year Genome Clinic Research project in June 2013, the SickKids Genome clinic has enrolled 183 children with a variety of genetic conditions in the project evaluating the diagnostic utility and health implications of Whole Genome Sequencing (WGS) in paediatric care. The research study participants have been referred by SickKids specialist clinicians (ophthalmology, cardiology, neurology, endocrinology, rheumatology, clinical and metabolic genetics). Based on preliminary analysis of WGS data on a subpopulation of this study, the diagnostic yield of WGS is similar to that of clinical microarray plus WGS. A major focus of the genome clinic project is to evaluate the clinical and psychosocial implications of identifying secondary (incidental) medically-actionable variants in 2800+ disease genes listed in the National Institutes of Health Clinical Genomic Database. Each participant is given the option of learning about secondary Medically Actionable Variants and carrier status at the time of consent. Depending on participant and family choice, these results are returned to them and placed on their medical records. The Centre has collaborated with Complete Genomics, a commercial diagnostic leader to optimize the alignment of quality, funding and coordinated planning for new test management. Through this collaboration, Complete Genomics has funded all WGS testing to date for the clinic. Three manuscripts are in final preparation for submission to high-end journals (1. diagnostics, 2. secondary findings, and 3. pharmacogenetics). See Appendix G for research project highlights.
E. is intelligent and self-reliant. She asks that we discuss any results with her before involving her parents because she does not want them to worry about things that are out of their control. It is inspiring to hear her communicate her wishes and plans.

**Whole Exome Sequencing Pilot Project**

Sponsorship Leveraging the required infrastructure and continued development of technical expertise is critical to ensure SickKids remains competitive to lead in genomic medicine outcomes. Aligned to the vision of offering individualized medicine as a standard clinical and diagnostic service, the Department of Paediatric Laboratory Medicine’s Genome Diagnostics has created the infrastructure to commence offering Next Generation Sequencing tests in a Clinical Laboratory Improvement Amendments certification (CLIA) approved setting. This testing will be clinically available in the spring of 2015 through a two-year Centre sponsorship. This newly created infrastructure includes complete sequencing workflow, data analysis using automated informatic pipelines, and WES testing for a variety of constitutional disorders. To help facilitate parents and health providers understanding of the testing and possible risks associated, prior to their consent, the Centre for Genetic Medicine produced an educational brochure, explaining the risks, benefits and limitations of this testing that can be used in combination with genetic counseling. In addition this resource is available on the Centre’s web page for free access (see brochure in Appendix E). Web-based tutorials and videos are currently being developed to augment the need for additional education.

**Ted Rogers Centre for Heart Research**

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. Joint leadership from the Centre for Genetic Medicine (R. Cohn) and the Labatt Family Heart Centre (S. Mital) as scientific co-leads, collaborated to identify SickKids contribution and develop a plan to harness the power of genomic science to decode the genetic foundations of cardiac disease, enable better predictors of health disease, and support development of individualized therapies for children and adults, based on the unique genome of each patient. Progress to date for the Ted Rogers Centre for
Next Generation testing technologies will provide more accurate diagnosis, resulting in improvement in the quality of care and life of our patients, enabling patients to avoid unnecessary testing and treatments, and offers potential to eliminate and or reduce accompanying toxic pharmacological effects from medications and burden of disease.

Heart Research can be viewed in the ‘100-Day Progress Report’ in Appendix I.

(Department of Paediatric Laboratory Medicine) Genome Diagnostics Laboratory Development To position SickKids Genetic testing laboratories to meet future demand for testing, priority planning efforts from the Centre in developing planning requirements resulted in the approval for a large capital laboratory infrastructure relocation investment (project) to streamline the current metabolic, molecular genetics, and cytogenetics laboratories this fiscal year. Phase I of a two stage redevelopment project is now complete with a completion date targeting summer of 2015. The structure of the new laboratories will enable SickKids to take advantage of new generation diagnostic methods, maintain rigorous quality standards, and align effort to investigate clinical validity and effectiveness.

Development of a Clinical Pharmacogenetics Program Through collaborations with the Centre for Genetic Medicine, Division of Clinical and Metabolic Genetics, DPLM, TCAG, and the Division of Pharmacology & Toxicology, planning efforts have been underway throughout fiscal 2014/15 to develop a fully integrated pharmacogenetics program at SickKids. Although SickKids has not received funding to implement this program, we have decided to continue planning efforts to continue to build a program and commence implementation in next fiscal year. A business case is currently being developed to solicit internal support as well as comprehensive business plan submitted to the MOHLTC. The Centre continues to sponsor a salaried position (Pharmacogenetics Research Advisor (I. Cohn)) to ensure dedicated planning efforts and tie-in to the genomic data from the Centre’s Genome Clinic Research Project. Clinical oversight is provided by Dr. Shinya Ito in the Division of Pharmacology & Toxicology.

Interventional Genomic Therapies Program Through a joint collaboration with the Centre for Genetic Medicine and Centre for Brain and Mental Health, select clinical and research leaders convened to identify opportunities and targeted outcomes for the development of a discussion paper profiling the opportunity to develop a SickKids ‘Interventional Genomic Therapies Program’. Specific outcomes would include; development of robust pipeline to advance CRISPR based therapies, proof of concept studies in small and large animals (to establish safety and efficacy) for at least 3-5 different genetic disorders, novel vehicles for the in vivo delivery of CRISPR constructs such as exomes (that are immunologically inert), clinical trials, and targeted commercialization of delivery methods, therapies, and treatment protocols. Next steps are to present the idea...
to Chiefs of Research and Paediatrics as well as exploring funding opportunities to commence start-up following project approval.

Provincial, National and International Leadership in Genetic Services Planning In addition to the programmatic strengths from the Clinical Division, TCAG and DPLM, a commitment to position SickKids as provincial and national leaders for genetic service planning continues. Specific activities to support this objective include:

- Led development of a 2-year Provincial Clinical Genetics Wait Time Project – completing Ontario’s first provincial standardized wait times report in October 2014 – influencing MOHLTC’s provincial genetic services and policy planning;

- Provincial Think Tank – hosted an annual provincial genetics planning Think Tank and MOHLTC Consultation for the Ontario Genetics Secretariat in January 2015. Provincial leadership provided by C. Carew as Secretariat Chair in addition to Drs. S. Meyn and P. Ray holding positions on the provincial executive committee.

- 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 (~$2M annually) for additional volumes. Planning efforts continue both
organizationally and provincially to influence provincial policy related to the service and funding model for genetic services.

- Global Alliance to Enable Sharing of Genomic and Clinical Data – since joining the international Alliance of over eight countries, SickKids continues to advance the idea of widespread ability to access genomic data in a secure and trusted manner. Attendance at two international meetings in 2014 with membership on multiple planning and advisory efforts will culminate the current gap in sharing medical knowledge and improve clinical care.

**Advocacy to influence Federal and Provincial Legislation against genetic discrimination.**
As one of the only G8 countries without legislation to protect individuals against genetic discrimination, the Centre with leadership from Dr. R. Cohn, has publicly advocated with federal and provincial government leaders to influence content and adoption of a new Act. Learning’s and data resulting from the Centre’s Genome Clinic Research Project has armed the hospital with quantitative data to share profiling the profound impact on families and patients when making decisions related to genomic testing.
EDUCATION INITIATIVES AND SPONSORSHIPS (SELECTED)

The Centre for Genetic Medicine is committed to continuing education and training of scientists and health care professionals through a broad spectrum of activities including workshops, seminars and symposia leading to enhanced research collaborations.

Centre for Genetic Medicine Symposium – Advancing Family Health Care – June 18, 2014

The Centre hosted an Inaugural Symposium, Advancing Family Health Care, attended by over 200 health care professionals and researchers.
Educating our healthcare professionals to incorporate genetic advances into everyday clinical practice is part of our Centre vision.

from SickKids, U of T, Mt. Sinai and UHN. The symposium hosted international and local speakers addressing the themes of advancing genomic medicine from a research, clinical, ethical and political perspective. Presentations were given by Steve Scherer, Cheryl Shuman, and Adalsteinn Brown, from the University of Toronto. The invited keynote speaker, Dr. Han Brunner, from Radboud University Nijmegen Medical Centre in the Netherlands, Professor of medical genetics and Head of the Department of Human Genetics, discussed the profound impact the recent ground breaking discoveries in diagnosis of rare genetic disorders can have on families, patient communities and treatment options. The overall success of the symposium was rated as excellent to very good by 85% of the respondents of the post feedback survey.

Centre Educational Lecture Series ‘Conversations with Genetics: You and Your Practice’, January 2015 through July 2015 Based on feedback from the 2014 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 will enhance their skills in counselling and appropriate use of clinical genetic testing, such as whole exome sequencing and pharmacogenetic testing. 78 health care providers registered for the launch lecture by Dr. Ronald Cohn, held on January 28, ‘Next Gen Testing (NGT) Results-How does it impact health and the future?’. Based on his personal experience, Dr. Cohn discussed how the results of Next Generation Technology can (or cannot) directly impact one’s health management and lifestyle decision-making. 80% and 92% of the post activity survey respondents felt the quality of the activity and Dr. Cohn’s presentation, respectively, were very-good to excellent. Each of the upcoming sessions has between 70-80 registrants to date.

CRISPR Lunch & Learn Networking Workshop – collaboration with the Garron Family Cancer Centre Joint Centre collaboration to profile the current research (at SickKids) using the CRISPR technology targeting research trainees was profiled in February 2015. Presentations were given by representatives from the Cohn, Derry, Irwin, and Yu laboratories with over 75 attendees.

Research and Educational Sponsorship The Centre provided partial salary support and sponsorship for the following research and education initiatives:

· Restracomp (2014) Studentship award – 2-year $22K. Master’s award, Mahmoud El-Maklizi, Danska Lab, Genetics and Genome Biology R.I. Program
• Co-sponsorship, Social Paediatrics Research Summer Studentship (SPReSS), Student Maragarita Komarova – 8 week studentship, Dr. Eyal Cohen, P.I.

• 2015 Canadian Certified Medical Geneticist Training candidate – approved for Centre sponsorship, Dr. Rebekah Jobling

• Bioinformatics Research Student, Stephanie Bacopulos – Collaboration with Division of Pharmacology & Toxicology supporting development of a clinical pharmacogenetics program

Health Human Resources (HHR) Investment – Position sponsorship The Centre has responded to the requirement to help bridge the current knowledge gap required to strengthen the translation of genetic findings into influencing clinical care practice and research. The following investments in HHR have been supported;

• Educating our health professionals to incorporate 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)

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

• The prevalence of predisposition and pharmacogenetic testing will have profound impact on our laboratory service resulting in enhanced patient safety and clinical outcomes. Closely linked to the Genome Clinic project, the Centre collaborates with TCAG, DPLM, Division of Pharmacology &

The Centre for Genetic Medicine is committed to continuing education and training of scientists and health care professionals through a broad spectrum of activities including workshops, seminars and symposia leading to enhanced research collaborations.
Toxicology to support development of a hospital pharmacogenetics program (Iris Cohn, Pharmacogenetics Research Advisor)

- Strengthening planning to lead provincial, national and international competencies to advance health policies, research and clinical care in genomics (Dr. Robin Hayeems, Research Policy Scientist)
CENTRE SPONSORSHIPS
AND FUNDING ACTIVITIES

- 2014 Genome Canada ‘Genomics: the Power & the Promise’ conference co-sponsorship with the Research Institute and Centre

- 2014 American Society of Human Genetics Annual Meeting and Conference, Canadian Mixer sponsorship in collaboration with CIHR and CCMG

- 2014 American Society of Human Genetics Annual Meeting, $2K Travel Awards – abstracts selected for presentation: Stephanie Kyle (Justice Lab), Sanaa Choufani (Weksberg lab), Mohammed Uddin (Scherer Lab), and Mehdi Zarrei (Scherer Lab)

- 2014 Canadian Association of Genetic Counsellors Annual Meeting, Travel Awards – selected abstracts presentation: J. Anderson, N. Monfared

- Contributed funding to support additional genomic patient data collection for a cerebellar atrophy (PMPCA mutations) research study to bolster research data for publication. Manuscript accepted for publication in Brain (2015).
ANNUAL OBJECTIVES
2014-15

Accelerating Translation & Innovation
1) Optimize translation opportunities (genomic medicine) opportunities across the hospital*
2) Establish ‘innovative and strategic’ Funds Grant Process** (*pending – to be administered in fiscal 2015/16)

Provider and Public Education
3) Invest in interactive technologies to support family education***
4) Web-based platform to support health professional education*
5) Methodology for knowledge dissemination (internal & external)* & annual symposia*

Technology Infrastructure
6) Continued investment in year II to support NGS in clinical diagnostics laboratory***

Health Human Resource Investment
7) Continued investment in year II for bioinformatics, human genome sciences, pharmacogenetics, education, strategy***

System Planning
8) Led transformation of molecular testing in Ontario for ‘out-of-country’ testing*
9) Develop benchmarks for clinical wait times and match workload data for resource alignment*

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

* achieved objective
** work in progress or pending
*** active multi-year activity
PROPOSED CENTRE OBJECTIVES 2015-16

1. Establish ‘Basic Science Research Grant’ opportunities in addition to targeted research funding opportunities to encourage collaboration with other Centres (Cancer, Brain & MH) – administer minimum of four (4) granting opportunities.

2. Continue co-funding of trainees awarded research fellowships and studentships through Restracomp including summer 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 – as per Centre plan

3. ‘Refresh’ Genome Clinic Research Project (targeted outcomes) AND seek opportunities for alignment with the launch of the Cardiac Genome Clinic and Genomic Platform in 2015/16 – establish development of business funding case for the MOHLTC using genome clinic data including supporting business case from data resulting from the first targeted clinical exomes sponsored by the Centre

4. Co-lead with the Centre for Brain and MH in development of an ‘interventional genomic therapies research program’ at SickKids

5. Launch the (pilot) to offer exome sequencing in the clinical diagnostic laboratory – launch targeted spring 2015.

6. Continue to generate activities and programs to influence the “change of practice” at SickKids – development of clinical guidelines to support next generation/genomic medicine discoveries, optimizing efficiencies and education

7. Strategically invest in capital infrastructure (diagnostic) required to best position SickKids – strategically aligning future requirements of the research and clinical diagnostic demands through joint investment with the TRCHR and the Centre
Financial support for the Centre is through a five-year strategic priorities funding commitment (currently year 2 of 5). In-kind contributions from the Department of Paediatric Laboratory Medicine, The Centre for Applied Genomics, Division of Clinical and Metabolic Genetics, Genetics and Genome Biology Research Program, Corporate Strategy, Performance & Communications, and Clinical Programs and Services.

Centre 9-month expenditures (April 2014 to January 31, 2015) is $742,896. A breakdown of Centre spending is available in Appendix I.

APPENDIX A: SELECT PUBLICATIONS


Disruption of the ASTN2 / TRIM32 locus at 9q33.1 is a risk factor in males for Autism Spectrum Disorders, ADHD and other neurodevelopmental phenotypes. Lionel AC, Tamimies K, Vaags AK, Rosenfeld JA, Ahn JW, Merico D, Noor A, Runek CK, Pillalamarri VK,


APPENDIX B: INVITED/PLATFORM/POSTER PRESENTATIONS

Invited Presentations:


May 2014, R Cohn. Rationale microarray genetic testing, follow-up and counseling, and future genetic testing. Annual Pediatric Update. Toronto Region Board of Trade. Toronto, ON, Canada.

May 2014, R Cohn. Genetic and genomic medicine: THE best example of a paradigm shifting subspecialty. IBD Cross-Talks Session. Inflammatory Bowel Disease Cross-talk seminar. The Hospital for Sick Children. Toronto, ON, Canada.

May 2014, R Cohn. Is genetics reshaping the Health Care Provider duty to patients. Bioethics Grand Rounds. The Hospital for Sick Children. Toronto, ON, Canada.


September 2014, R Cohn. Bridging clinical and basic science in genetics and genomics. Genetics Grand Rounds. The Hospital for Sick Children. Toronto, ON, Canada.


January 2015, MS Meyn. Biomedical Center, University of Iceland, Reykjavík, Iceland. Diagnostic and Predictive Uses of Whole Genome Sequencing in Paediatrics.
Platform Presentations:


**52nd annual Great Lakes Chromosome Conference**, Toronto, ON, Canada. May 2014. C. Marshall, Discovery of novel CNVs with clinical significance in a research setting.


**Frontiers in Laboratory Medicine**, Birmingham, UK, January 2015. J. Stavropoulos. Next generation sequencing – why whole genome sequencing is poised to provide new diagnostic tools for laboratories.


Poster Presentations:


**Bridging Research & Care, Celebrating Education**, The Hospital for Sick Children. Gilbert A. e-Poster showcasing The Centre for Genetic Medicine’s Education Plan for 2014/15.

APPENDIX C: GRANTS

APPENDIX D: 2014 CENTRE SYMPOSIUM

Centre for Genetic Medicine Inaugural Symposium
Genetic Medicine: Advancing Family Health Care
June 18, 2014
Peter Gilgan Centre for Research and Learning (PGCL) Auditorium
Register at www.sickkids.ca/Centre/Centre-Genetic-Medicine/

Participants will:
- Understand the role of whole genome sequencing in daily patient care
- Become familiar with the national conversations on ethical issues associated with genomic medicine

AGENDA
1:00 p.m. Welcome and Introduction
Ronald D. G劳, MD, FACP
Women's Auxiliary Chair of Clinical and Metabolic Genetics,
The Hospital for Sick Children and University of Toronto

1:30 p.m. Genomics: The Medium for 21st Century Biology
Stephen Scherer, Ph.D.
GSK-CGRI Endowed Chair in Genomic Sciences at The Hospital for Sick Children and University of Toronto

2:00 p.m. Translating Genetic Information for Families: Tales from the Frontline
Cheryl Shuman, MS
Director, Genetic Counseling, The Hospital for Sick Children

2:55 p.m. Genetic Medicine: Critical Issues in Policy
Adolfo Barra, M.D., M.H.S.
Director, Institute of Health Policy, Management, and Evaluation, Faculty of Medicine
Dalla Lana Chair and Division Head in Public Health Policy, Dalla Lana School of Public Health, University of Toronto

1:30-3:45 p.m. Coffee Break

3:45-4:30 p.m. Poster Session
How Genomics Changes Medicine
Harm Bunnik, M.D., Ph.D.
Professor of Human Genetics, University Hospital St Radboud in Nijmegen, Netherlands

4:35 p.m. Speaker Panel Question Period
Moderator: Ronald Cohn, MD

5:30 p.m. Reception
PGCL Gala

SickKids Centre for Genetic Medicine
# 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 lecture 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.event.com/6/60483/0](http://www.event.com/6/60483/0)

Information regarding web streaming option provided through registration process. The lectures series is a self-approved group learning activity (Section 1) as defined by the Maintenance of Certification program of the Royal College of Physicians and Surgeons of Canada.

### 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 Cappello</td>
<td>Next gen sequencing results: How does it impact health and the future?</td>
<td>Jan 28</td>
<td>Peter Gigan Centre for Research and Learning, 2nd Floor, Event room 2e/2b</td>
</tr>
<tr>
<td>Christian Marshall</td>
<td>Is exome sequencing done?</td>
<td>Feb 25</td>
<td>Peter Gigan Centre for Research and Learning, 2nd Floor, Event room 2e/2b</td>
</tr>
<tr>
<td>Sarah Bowdin</td>
<td>Demystifying how and when to order exome sequencing</td>
<td>Mar 25</td>
<td>Peter Gigan Centre for Research and Learning, 2nd Floor, Event room 2e/2b</td>
</tr>
<tr>
<td>Cheryl Cysteinem</td>
<td>Whole exome sequencing in clinical care: Practical considerations for preparing patients/families</td>
<td>Apr 22</td>
<td>Peter Gigan Centre for Research and Learning, 2nd Floor, Event room 2e/2b</td>
</tr>
<tr>
<td>Dr. Cuthbert, D.</td>
<td>Pharmacogenetics: A prime example of proving individualized medicine for your patient</td>
<td>May 27</td>
<td>Daniels Hollywood Theatre, SickKids, Room 1246 Blackwing</td>
</tr>
<tr>
<td>Ron Haynes</td>
<td>Easy-to-day genetics: Ethical and policy challenges</td>
<td>June 24</td>
<td>Daniels Hollywood Theatre, SickKids, Room 1246 Blackwing</td>
</tr>
<tr>
<td>Melissa Carter</td>
<td>Autism genetics: Where are we now?</td>
<td>July 30</td>
<td>Daniels Hollywood Theatre, SickKids, Room 1246 Blackwing</td>
</tr>
</tbody>
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32 The Hospital for Sick Children
APPENDIX F: WHOLE EXOME SEQUENCING EDUCATION BROCHURE

Whole Exome Sequencing

Cells and DNA
Our bodies are made up of cells, which contain our DNA. DNA is like a recipe book for how we are made. Changes in our DNA can lead to health problems or increase the chance of having a health problem. We do not always know why these changes occur, sometimes the change is passed down in a family, sometimes the gene change just happens by chance.

Whole Exome Sequencing Results
Testing may take several weeks to complete. Your doctor or genetic counselor will report the results to you. There are four possible result outcomes:
1. Positive result
2. Negative result
3. Results of unclear significance
4. Additional findings

Possible Risks
WES may show changes in a gene that produces a risk for a person to develop another genetic condition. This is called an additional finding. These findings are unexplained and not related to any previous testing that was done in the first place. If an additional finding is discovered, other family members may need to be informed and offered testing. It is therefore best to consult with a healthcare professional to learn about these additional findings.

Results of WES testing will be shared with your doctor, and you will be informed of any significant findings.

Samples
A small blood sample (1-2 teaspoons) is needed to perform the testing.

Whole Exome Sequencing Possible Results

Testing Information

Centres for Genetic Medicine, SickKids
Tel: 416-813-1654, ext. 22025
email: geneticmedicine@sickkids.ca
www.sickkids.ca/centres/centres/genetics-medicine
APPENDIX G: GENOME CLINIC ACTIVITIES

SickKids Genome Clinic: Recruiting update (Dec 2014)

Families:
336 approached
181 Enrolled (54%)
142 Declined (42%)
13 Undecided (4%)

Enrolled patients:
79 female (44%) mean age (6 y 9 m)
97 male (56%) age range (newborn to 18 y)

Average time to obtain consent – 8.7 days after first contact and receipt of consent forms
F/U counselling discussions typically occur by phone or via e-mail
Average time: ~ 90 minutes spread over 2 encounters for participants
~120 minutes spread over 3 encounters for non-participants

SickKids Genome Clinic Activity

Work in Progress:
• Validation of initial secondaries underway
• Accrual of additional gene panel patients
• Complete analysis of secondaries and select additional candidates for validation
• REB protocol amended to include NICU WES cohort
• Coordination with Bioethics working group to complete WGS impact study

Next Steps:
• Return secondary results to patients & families
• Standardize protocol for collecting data for health economic data
• Secondary variant manuscript
• Continue to develop long term strategic goals and new projects
APPENDIX H:  
100-DAY REPORT –  
TED ROGERS PERSONALIZED MEDICINE PROGRAM FOR CARDIAC DISEASE

100-Day Report (March 2015)

Ted Rogers Personalized Medicine Program for Cardiac Disease (SickKids)

The Ted Rogers Personalized Medicine Program will harness the power of genomic science to decode the genetic foundations of cardiac disease. This will lead to the prediction of heart disease before it occurs and enable individualized therapies for children and adults, based on the unique genome of each patient.

The overall goal of the Program is to identify the genomic basis of heart failure and to use this genomic knowledge to develop targeted therapies to personalize the care of affected individuals. The specific objectives are to (i) Identify susceptibility genes for heart failure in at risk populations including congenital heart disease and cardiomyopathies; (ii) Identify genetic predictors of response to therapies to help individualize the type and timing of intervention; (iii) Identify the molecular signature of various types of heart failure unique to a pediatric population through the study of myocardial expression patterns, and behavior of cardiac cells derived from patient induced pluripotent stem (iPS) cells; (iv) Identify potentially “druggable” targets and perform drug screens in patient iPS cells and model organisms to develop targeted drug therapies; (v) Perform pilot clinical trials to test safety and preliminary efficacy of new and repurposed drugs and of regenerative therapies in target populations. New genetic diagnostics and personalized therapeutics will permit early detection of at-risk patients and early interventions to improve survival and quality of life, and reduce heart failure related death and hospitalization. The genomic and functional data will support integration with the Translational biology and engineering program of the University of Toronto and the Comprehensive Cardiac Function Program at UHN.

SickKids has two unique resources to help achieve these goals. The Heart Centre Biobank Registry is an Ontario province-wide Biobank that has enrolled over 5,000 children and adults with/at risk for heart failure (congenital heart disease, cardiomyopathy, arrhythmias, acquired heart disease) with DNA, myocardial and skin samples for reprogramming available in affected individuals. The SickKids Genome Clinic is a multidisciplinary clinic led by the Centre for Genetic Medicine
that harnesses the power of whole genome sequencing in affected families to identify novel genes associated with genetic disorders. There are strong linkages between the Heart and Genetic Centres and we will leverage these two resources to achieve the goals of the program. As a first step, an Open Forum was co-hosted by the SickKids Scientific Leads (Cohn, Mital) in February to inform the community and seek input regarding research, innovation and education opportunities in the program. The forum was also attended by the (interim) Executive Director (Husain) and by the SickKids Executive Sponsors (Rossant, Caldarone). Research Advisory groups are being formed to initiate implementation of program goals.

Precision Cardiac Medicine: The focus in year 1 is to initiate large scale whole exome sequencing of target populations at risk for heart failure available through the Heart Centre Biobank in order to identify heart failure susceptibility genes. We will also reprogram patient skin fibroblasts to generate iPS cells and cardiac lineages for drug screens. The team includes researchers from various disciplines from SickKids and partner institutions with expertise in paediatric and adult cardiology, surgery, cardiac imaging, genomics, stem cells, model organisms, bioengineering, big data, and bioinformatics. Year 1 deliverables include:

**Next Generation sequencing based diagnostics:**

- Sequence 500-1000 exomes from patients with cardiomyopathy or congenital heart disease in the Heart Centre Biobank Registry to identify heart failure susceptibility genes enriched for pathogenic mutations.
- Hire 2-3 new staff

**Cardiac phenotyping and genotype-phenotype associations:**

- Reprogram and differentiate 5-10 iPS cells from patients harbouring pathogenic mutations for modeling disease “in a dish” and for high-throughput drug screens
- Assess gene and protein expression patterns in myocardium from patients harbouring pathogenic mutations to identify the molecular signature of myocardial dysfunction
- Develop a data platform to host large scale phenomic, genomic, transcriptomic and proteomic data
- Hire 1-3 new staff

**Cardiac Biobanking**

- Sustain Heart Centre Biobank Registry operations which include participant recruitment, clinical data collection and analysis, and sample collection, processing, storage and distribution.
- Expand operations by recruiting additional target populations in year 1

**Cardiac Genome Clinic:** This initiative will establish strong links between scientists, pharmacologists and other research programs worldwide caring for children and adults seen at SickKids and our UHN partner sites. Clinical uptake and application of genome-guided diagnostics and therapeutics will be facilitated by establishing a robust sequencing pipeline, a strong bioinformatics core, strengthening genetic counseling services, and exploring health economic and ethical implications of genomic medicine. The focus in year 1 is to
launch and expand the operations of the Cardiac Genome Clinic (CGC) to prospectively enroll 200 affected children and adults with cardiomyopathy, structural heart disease, and/or arrhythmias. Planning for the CGC has commenced and will build on the experience gained from the current SickKids Genome Clinic launched in June 2013. An important goal of the CGC is to find disease causing genes in children and adults at risk for heart failure by harnessing the power of whole genome sequencing, and use this knowledge to develop new genomic diagnostics. New genomic targets identified through this effort will not only guide new diagnostic testing but will also align with the Precision Medicine Program and drug screening pipeline described above to further develop new genome-guided therapeutics.

Drs. Raymond Kim and Sarah Bowdin recently confirmed their role as co-leads for the CGC supported by Dr. Ronni Cohn as project sponsor. A Scientific Advisory Committee is currently under review intended to provide advice and direction for the clinic. A detailed project plan that will define the exact patient populations for the first year will be developed over the next 30 days and targeted recruitment is underway to support the start-up of the clinic. Planning is currently underway for a CGC REB submission in fiscal Q1 2015/16. Targeted collaborations are under review but it is expected that the CGC co-leads will partner with the model organism community to develop one or more rapid-throughput models for defining pathogenic variants versus rare polymorphisms and secondly partner with a population geneticist in an effort to maximize the potential use of the genome to determine disease modifying genes as an important outcome of the clinic.

**Endowed Research Chairs:** To advance the program’s vision and build on existing strengths in genetics and systems biology, we propose to recruit two strategic chairs in the following areas. We anticipate commencing an external search in the summer of 2015. The process for the selection of chair positions will be completed in Q2 2015/16.

The **Ted Rogers Chair in Cardiac Genetics** will direct research that is designed to increase understanding of the linkage between specific genes and the development of heart disease. By studying the genomes of patients at UHN and SickKids, we will be able to identify people at risk for heart disease before the disease ever develops.

The **Ted Rogers Chair in Translational Genomics** will translate genome information into a mechanistic understanding of gene defects and lead the development of new cell or developmental-based screens for novel therapeutic interventions in heart disease.
APPENDIX I: CENTRE SPENDING FISCAL 2014/15 (REPORTING APRIL 1, 2014 TO JANUARY 31, 2015)

Centre for Genetic Medicine
F2014/15 YTD Spending (as at January 31, 2015)

![Pie chart showing spending distribution]

Genome Clinic Research
Education, Events, Travel & Admin
Accelerating Research & Innovation
One-time Expenditures

Total 2014/15 Spending = $742,896 (10 mths)