Paving the Way for Individualized Medicine

The Centre for Genetic Medicine 2013-14 Annual Report
The Blueprint for action identifies approaches that will help to advance a strategy for genomics-related research, education, and clinical activities. Our new genomic knowledge and technology has the potential to bring enormous benefits to our patients: more individualized prediction of risk, more accurate diagnosis, safer use of medicines, and new treatment options to explore.

Dr. Ronald Cohn
Co-Director
Centre for Genetic Medicine
Executive Summary

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 to make individualized medicine a reality at SickKids and make the Centre accountable to achieve our intended outcomes. This Blueprint has guided the focused planning efforts identified in our 2013-14 Annual General Report.

Great efforts have been put forth this year to achieve proposed objectives that we identified in our prior Centre Annual Report, focusing on closing the current gap requiring specialized health human resource planning, further integration of NextGen sequencing technology within SickKids, and developing the world’s first paediatric clinical genome clinic.

We are pleased to report that progress has been made in closing the current gap for specialized genomic health human resource skills. Through recruitment and sponsorship of six highly specialized positions, this new genomic knowledge is being utilized to build our vision of integrating genomic knowledge across our organization. In June 2013, we launched the SickKids Genome Clinic research project with secured 5-year funding. With the end goal to transition the Genome Clinic project into a fully funded clinic in 2017, the Centre will lead important discussions with collaborators and partners to successfully integrate new genomic research and diagnostics into effective, efficient and routine clinical use for improved health outcomes.

Building on the Centre’s pillars of research, clinical care and education, the Centre released its multi-year education plan this fiscal. The development of this plan was informed through a thorough needs assessment and conversations with our partners and key stakeholders. Two of our planned public educational initiatives will be launched in June 2014, being the Centre’s first annual symposium followed by an international genetics ‘Think Tank’ in collaboration with the Children’s Hospital of Philadelphia.

To further strengthen SickKids ability to lead in discovery and genetic medicine, The Centre for Applied Genomics successfully renewed its Genome Canada Science and Technology Innovation Centre funding, with an awarded budget of $4M over two years to support its core facility operations, technology development and informatics activities. Working with key partners such as TCAG, the Centre for Genetic Medicine will continue to identify the most effective strategies and shared resources for targeted collaborations and accountabilities as the most critical accelerator to leverage change. As Centre co-leads, we will continue to review our progress annually and report our findings to the SickKids Centre review Council.

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 CENTRE’S 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.

OUR CENTRE’S DELIVERABLES

• Improved patient care throughout SickKids

• Stronger clinical/translational research in genomic medicine

• Broader education, outreach, and commercialization activities in genetics

EXECUTIVE COMMITTEE MEMBERSHIP

Representing: Centre co-Director, (Division Chief) Clinical and Metabolic Genetics

Member: Dr. Ronald Cohn

Representing: Centre co-Director, (Director) The Centre for Applied genomics

Member: Dr. Stephen Scherer

Representing: (Head) Division of Molecular Genetics – Department of Paediatric Laboratory Medicine

Member: Dr. Peter Ray

Representing: (Director) Genetic Counselling

Member: Cheryl Shuman

Representing: (Executive Director) Clinical Programs

Member: Judy Van Clieaf

Representing: (Head and Senior Scientist) Genetics & Genome Biology

Member: Dr. Monica Justice*

Representing: Department of Paediatrics – Medical Appointment

Member: Dr. Sarah Bowdin

Representing: Department of Surgery – Medical Appointment

Member: Dr. Elise Heon

Representing: Division of Clinical and Metabolic Genetics

Member: Dr. Stephen Meyn**,***

Representing: (Director of Strategy) Centre for Genetic Medicine

Member: Chris Carew

*appointed January 2014

**position expired December 2013 / ***ex-officio appointment January 2014

Members are appointed for a term of three (3) years, which shall be renewable for any number of additional two (2) year terms by major vote of the Executive Committee.

Ex Officio members may be appointed from both individuals and organizations considered to have clearly definable roles to assist the Centre achieve its objectives.
Educating our health professionals to incorporate genetic advances into everyday clinical practice is a part of our Centre vision. To embrace the evolution of genomic medicine, the Centre has made investments in unique and unconventional collaborations and partnerships this year. With a commitment to the longer term vision of ensuring our planning efforts today influence children’s health outcomes of tomorrow, the following investments this year highlight the Centre’s desire to advance genomic knowledge locally and worldwide;
Investment in Health Human Resources: Centre Education Advisor recruited, June 2013.

**Creation of a Multi-year Centre Educational Plan:**
With a goal to link genomic literacy to improve access, awareness and responsiveness to evidence-based genetic information, a genetics Needs Assessment and Environmental Scan was completed this year that informed the creation of a Multi-year Centre Education Plan. This newly developed plan has identified targeted stakeholder requirements, the needs and attitudes across the research and clinical services as well as our external stakeholders, academic partners, and our collaborators. Our education plan will direct outcomes to strengthen a learning environment for health care professionals, families, and the health service community to access emerging genomic information both within SickKids and beyond our walls. A mix of learning mediums are planned to utilize interactive online technology augmented with bi-monthly seminars entitled “Genomic Medicine for Primary Care Provider” which will include didactic lectures and case based discussions. Other proposed initiatives include the development of a one-year Bioinformatics Fellowship for Clinical Genetic Residents or Board eligible/certified Clinical Geneticists, as well as a Translational Informatics Curriculum that will be developed for a 3 month genetics resident’s rotation.

A proposed medium to longer term goal of the Centre education plan is to influence change to the medical school curricula to align to emerging genomic knowledge supported by tactical evidence. This will be achieved through collaboration established with U of T medical school and the Centre.

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**Annual Symposium:** To establish a presence within SickKids and the GTA genetics health service sector, the Centre will host its first annual Symposium in June 2014. This launch will profile the research and clinical initiatives within SickKids complimented by local and international speakers through themes addressing genomics such as societal (ethical) implications, therapeutics, diagnostics, and preparing for the next generation of genomics researchers and clinicians.
Aligning Next Generation lab technology and testing to support translation and clinical effectiveness

The demand for genetic tests has steadily grown due to the continuing translation of new technologies, disease discoveries into clinical tests and a heightened awareness of the clinical utility of these tests by physicians and patients. The Centre has responded to these needs through the following investments and planning initiatives;
**Investment in Health Human Resource:** Recruitment of an *Associate Director, Genomic Analysis.* This Department of Paediatric Laboratory Medicine position with a cross-appointment to the Division of Clinical and Metabolic Genetics will help bridge the current knowledge gap required to strengthen the translation of genetic findings into clinical laboratory testing and patient care.

**Meeting the computational challenges for Genomics:** The major bottleneck in genome sequencing is no longer data generation but rather the computational challenges supporting data analysis. To enable scientific achievement and biological applications beyond our current technology, the Centre partnered with TCAG, DPLM, Division of Clinical and Metabolic Genetics, Garron Cancer Centre, and the Centre for Computational Science Medicine to overcome these computational challenges for genomics. Bringing together expertise in biology as well as informatics, computer science, mathematics and statistics through a unique collaboration providing a solution for our bioinformatics needs. We will continue to build the required infrastructure and knowledge in bioinformatics to ensure our competitive leadership in genomic medicine.

**Capital investment in Next Generation Technology:** To continue to lead in discoveries and translation, new genomic technologies coming online requires significant investment. The Centre has responded to this need through the development and approval of a *5-year capital expenditure for key technology acquisitions.* This investment will be leveraged through partnerships with TCAG, DPLM, the Garron Cancer Centre, and key technology industry partners. This collaborative investment will support the required technology innovation agenda and aligns the HHR skill set to sustain a leadership in next generation technology.

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**We will continue to build the required infrastructure and knowledge in bioinformatics to ensure our competitive leadership in genomic medicine.**

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**Realignment of (DPLM) Genetic Diagnostic Laboratories Facilities:** The use of new genomic platforms and technologies coming online will enable SickKids to take advantage of new next generation diagnostic methods, maintain rigorous quality standards, and align efforts to investigate clinical validity and effectiveness. To position SickKids Genetic testing laboratories to meet the future demand for genetic testing, priority planning efforts resulting in a *$1.4M approved physical infrastructure relocation project to streamline the current metabolic, molecular genetics, and cytogenetics laboratories* was approved this reporting period. Completion of the relocation project is targeted for the end of calendar 2014.
The effectiveness of genomic information in tailoring interventions and, ultimately improving health outcomes for children is our greatest challenge. Demonstrating utility will be critical for widespread adoption of genomic medicine, including reimbursement by our service funders. Addressing the rapidly emerging issues will require sustained, yet agile, collaborative efforts. Since many of our healthcare infrastructures are poorly suited for the delivery of genomic medicine, the Centre for Genetic Medicine will work to develop optimal models for ensuring the best practices in genomic medicine and share these learnings broadly within the health care community and service funders.
**Investment in Health Human Resources (1):** Centre Research Genetic Counsellor recruited, February 2013.

**Investment in Health Human Resources (2):** Centre sponsored Pharmacogenetics Research Advisor recruited, September 2013.

**SickKids Genome Clinic Launches:** In June 2013, the Centre for Genetic Medicine launched SickKids Genome Clinic, a 5-year research project enrolling patients who are under investigation for a primary genetic disorder, along with their parents.

The Genome Clinic will act as a research hub for multiple projects, ranging from development of new bioinformatics tools and discovery of new genes to health policy inquiries, assessment of models of clinical care and evaluation of the medical and psychological risks and benefits of genomic medicine. The clinic is a multidisciplinary effort that will pave the way of introducing Next Generation Sequencing technology into the daily clinical care of paediatric patients for SickKids. Over 150 subjects have been enrolled to date.

As part of the Genome Clinic planning and to address the many challenging endeavors associated with genomics, the Centre for Genetic Medicine assembled a working group of individuals with expertise in clinical and molecular genetics, bioinformatics, molecular diagnostics, genetic counselling, health policy/economics and bioethics to develop the Centre’s Genome Clinic. This multidisciplinary research platform will treat the child’s genome as a rich source of genetic information to be repeatedly queried over time to manage the overall health of an individual, rather than a one-time test performed to diagnose a pre-existing disorder. As a result, incidental/secondary variants are a major focus of study rather than an inconvenient burden. For additional information, please visit the Genome Clinic website at www.sickkids.ca/Centres/Centre-Genetic-Medicine/The-Genome-Clinic/Index.html

**Genomics and Societal/Ethical Issues:** Effectively examining the societal and ethical implications of genomic research and medical advances will demand our careful attention. Supporting the Genome Clinic, a unique partnership with the Department of Bioethics to further guide and strengthen best practices, this partnership has resulted in a successful grant opportunity supported through the McLaughlin Research Institute to identify evidence based standards for informed consent and educational materials related to whole genome sequencing (WGS) for families and health care providers aimed at facilitating active engagement in the WGS testing process.

**Collaboration with Commercial Partners:** The Centre for Genetic Medicine believes targeted collaborations with industry partners and leaders will leverage the required infrastructure and knowledge for the Centre to evolve as one of the world leaders in genomic research. In 2013, the Centre 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 Whole Genome Sequencing testing to date for the clinic. Jointly through continued pursuit of collaborators, we will work in partnership to share our knowledge and findings through publications as one of the many critical accelerators for change.

**Pharmacogenetic Program Development:** The prevalence of predisposition and pharmacogenetic testing will have profound impact on our laboratory service resulting in enhanced patient safety. The Centre has partnered with TCAG, DPLM and the Division of Clinical Pharmacology and Toxicology to support a Pharmacogenetics Research Advisor to construct a pharmacogenetics program at SickKids. Continued efforts to support the development of this program have been established through a four-year commitment to fund the research position through the Centre.
Strengthen planning to lead provincial, national and international competencies to advance health policies, research and clinical care in genomics


Investment in Health Human Resources (2): Continued sponsorship (TCAG) of the Clinical Research Coordinator recruited, summer 2012.

Health Research to inform provincial health Policy: Through a unique collaboration with the Research Institute, the Institute for Clinical Evaluative Sciences, University of Toronto’s Institute for Health Policy, Management & Evaluation, and the Centre for Genetic Medicine, specialized research and knowledge dissemination expertise relating to screening policies and implications of new genetic technologies will help to inform policy recommendations for the provincial government around new genetic technologies and their broader integration into clinical care will result.

Economic Evidence to inform clinical decisions and Policy development: Through a unique collaboration with the Technology Assessment at SickKids (TASK), the role of the Clinical Research Coordinator will continue to build health technology assessment reports and health economic evaluations in genomic medicine to support the Centre’s interest in providing stakeholders and funders with high quality economic evidence for clinical and policy decision-making discussions.

Influencing Federal and Provincial Legislation against genetic discrimination – 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 a new Act.

American Society of Human Genetics Centre Sponsorship and Travel Awards – In October 2013, the Centre released its first official award competition for candidates to apply for a travel award for scientific abstracts accepted for presentation at the 2013 American Society of Human Genetics (ASHG) annual meeting and conference. We are pleased to announce that there were two successful recipients who received up to $3000 each to attend the conference. In addition, the Centre in collaboration with SickKids Research Institute and the CIHR sponsored a Canadian Mixer for ASHG delegates to profile the leadership role in genomic planning by both the Research Institute and the Centre for Genetic Medicine.

Global Alliance to Enable Sharing of Genomic and Clinical Data – In April 2013, the Centre joined an international Alliance to create a Global Alliance to enable sharing of genomic and clinical data, worldwide. This effort is a culmination of fifty leaders from eight countries proposing an idea to advance medical knowledge and improve clinical care through the widespread ability to access genomic and clinical data in a secure and trusted manner. The Alliance is proposing a ‘global alliance’ to bring together researchers, healthcare providers, funders, disease advocacy groups, life science and technology companies, and informed citizens to enable, support and promote the responsible sharing of genomic and clinical data. The first member meeting was held in March 2014 in the United Kingdom with several SickKids participants in attendance.

Genetics from a Provincial Perspective: The Centre continues to provide provincial genetics leadership through a provincial genetics network called the Ontario Genetics Secretariat. Currently, delegates from SickKids continue to assume the Chair position
and both a clinical and laboratory membership as provincial leads on the Secretariat executive committee. Hosting a joint Secretariat and Ministry of Health and Long Term Care planning retreat in November 2013, provincial planning efforts continued to support the repatriation of genetic laboratory tests back into Ontario, leveraging recommendations from the provincial genetics planning framework that was completed in 2011, and continued leadership in the development of the Provincial Clinical Genetics Wait Time Project (aimed at improving the quality and efficiency of clinical services through standardized wait time information of member institutions across the province). The Clinical Wait Time Project planning team is targeting May 2014 for a release of Ontario’s first wait time initiative for clinical genetics.

Patient Vignettes: Please refer to Appendix A for patient case vignettes.

Research Publications: Please refer to Appendix B for select Genetic/Genomic Research Publications

Research Grants: Please refer to Appendix C for select funded Research Grants

Centre Budget: Centre activities and initiatives have been generously supported by the following contributors;

- In-kind contributions from 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, Clinical Programs & Services

- Five-year Centre Operational Plan supported through Strategic Priority Funds, The Hospital for Sick Children

- Expendable Funds supported by SickKids Foundation


Centre for Genetic Medicine
The Hospital for Sick Children
555 University Avenue, Toronto, ON M5G 1X8
www.sickkids.ca/Centres/Centre-Genetic-Medicine/index.html

Phone: 416.813.7654 extension 202671
e-mail: chris.carew@sickkids.ca
APPENDIX A

PATIENT VIGNETTES:

Case Vignette 1: D. W. is a five year old boy who has recently been enrolled in SickKids Genome Clinic research study. The first time I met D. he had been admitted to SickKids for intermittent episodes of high fever and intense pain and abdominal discomfort. He was curled up in his mother’s arms and she told me this kind of episodic illness is not unusual for D. Throughout the past four years, the W. family has been a frequent visitor to SickKids and D. has been evaluated by almost all SickKids medical subspecialties. Unfortunately none of the investigations has revealed a diagnosis and his management is symptomatic at this point. His parents’ schedule revolves around D.’s episodes of pain and the parents subsequently have little interaction other than with each other due to time restrictions in caring for their child. His parents say that the greatest challenge they face is not being able to predict his health from one day to the next. And I understand the parent’s concern the next time I meet the family. I almost don’t recognize the energetic boy moving around my office chasing his toy car. They are desperate for a diagnosis, anything to explain these unpredictable episodes.

Case Vignette 2: B. H. is an adorable two year old boy, clearly unhappy to be back in the hospital. He turns his back when I try to talk to him and will only turn to take a few crackers from his dad.

B. is suspected to have a genetic metabolic condition, experiences episodic seizures, has cognitive and motor delay and is fed mainly through a G tube although he has started eating simple small meals recently. He has been followed since birth at SickKids and the family travel for several hours to SickKids for day-long appointments every few months.

None of the clinical investigations completed so far have revealed a diagnosis and B.’s parents are keen to learn of the cause and prognosis of his condition. They hope this will help guide his treatment and management for a better quality of life. The couple would also like to have other children but worry about risk of recurrence. They say they will do anything for B. and this new genomic test offering from SickKids Genome Clinic can only assist to give them more tools to help B. be as healthy as he can be.

APPENDIX B

PUBLICATIONS:

Select Genetic/Genomic themed Publications profiled by the following Divisions/Departments:

The Centre for Applied Genomics, Department of Bioethics, Division of Clinical and Metabolic Genetics, Child Health Evaluative Sciences.

*** indicates direct/indirect contribution from the Centre for Genetic Medicine

Applied Genomics


APPENDIX C

FUNDED RESEARCH GRANTS

Select Genetic/Genomic themed Research Grants profiled by the following Divisions/Departments;

The Centre for Applied Genomics, Department of Bioethics, Division of Clinical and Metabolic Genetics, Child Health Evaluative Sciences, and the Centre for Computational Science Medicine.

*** indicates direct/indirect contribution from the Centre for Genetic Medicine


2. CIHR Grant: Genetic and Epigenetic Determinants of Syndromic Intellectual Disability. PI: R. Weksberg Co-investigators: Chitayat D, Ray P, Cytrynbaum C Award: 150,080 for 5 years as of January 2013


5. CIHR Operating Grant funded through IHSPR & IG Strategic Initiative 2009–2013 “Health Services for Genetic Diseases”
Informing evidence-based policy for expanded newborn screening
Co-Principal Investigator: Miller, FA, Avard D, Carroll J

6. **McLaughlin Centre, University of Toronto 2013-2014**
Accelerator Grant in Genomic Medicine
Whole genome sequencing in pediatric care:
An informed implementation
Principal Investigator: Zlotnik-Shaul, R
Co-Investigators: Hayeems RZ, Bowdin S, Meyn S, Shuman C, Szego M, (Team members) Anderson J, Monfared N.

7. McLaughlin Centre, University of Toronto 2011-2013
Accelerator Grant in Genomic Medicine
Genomic Technologies: Impact on clinical service delivery and strategies for effective integration
Principal Investigators: Shuman C

8. Norm Saunders Complex Care Initiative 2012-2014
The Hospital for Sick Children
Joined-up government: Optimizing governance models to serve the needs of children with medical complexity
Co-Principal Investigators: Moore C and Hayeems RZ

Principal Investigators: Brudno M, Bader G
Co-Investigators: Meyn S, Ray P, Scherer S
Award: $1,093,099 Grant Period: 2013-2016
Just as important as the whole genome sequencing itself, will be learning how to organize and share the data with clinicians, all the while respecting the patient and family preferences.

Dr. Stephen Scherer
Co-Director
Centre for Genetic Medicine