“The Centre for Genetic Medicine will change the future of paediatric medicine and pave the way for SickKids and Toronto to become leaders in the field of paediatric individualized medicine.”

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At a Glance

In the ten years since the formal completion of The Human Genome Project, there has been an explosion of knowledge in human genetics and genetic diseases, as well as transformational advances in technology related to decoding DNA. These developments are fundamentally changing the way patients are diagnosed and managed, and creating opportunities for improving outcomes and reducing overall health care costs.

The dramatic advances in our knowledge of human genomics present SickKids with an opportunity to improve the health of children by introducing the concept of individualized genetic medicine. This will be achieved through the integration of new genetic knowledge across the organization to support change both within SickKids and beyond.
Despite the advances and SickKids’ long history of pioneering research and discovery in human genetics; the health system lacks the right policies and programs to translate discoveries efficiently and effectively into life-changing tests and treatments. The genetic information and genetic services available have become increasingly complex, challenging current processes to ensure we can demonstrate clinical utility and validity evidence in our patients and accurate interpretation to achieve better health outcomes. There is an urgent need for a systematic approach to translating the new genomic knowledge into daily clinical care. The Centre for Genetic Medicine will lead health professionals, researchers, policymakers, and families to understand and respond to the challenges and opportunities of genomic medicine, and its potential to transform children’s health. We will do this by focusing on discovery, translating knowledge into clinical applications and enhancing genetic education of health-care professionals and patient and families.

The Centre will promote interdisciplinary groundbreaking research in genetic medicine. This will include service and training initiatives beyond our walls. The Centre will provide opportunities for innovation in genetics that will focus on the Centre’s themes of discovery, translation, and knowledge transfer. This effort will build on the current knowledge in medical genetics, clinical services and genomics discovery underway in the SickKids Research Institute.

It is essential to identify the most effective strategies and resources to educate both health care providers and families in this rapidly developing area. Targeted collaborations will promote knowledge transfer, skill enhancement, and the integration of required skills for health care professionals to use genetic knowledge in clinical practice. Patients and families will benefit from access to high quality, timely information that will enable them to participate meaningfully in decision-making discussions and allow us as service providers to understand what their needs are and how best to present this new genomic information to the patient and family’s full advantage.

The increased use of genetic testing has created a shift in patient referral, management and testing patterns. A few years ago, most testing was ordered by doctors specializing in medical genetics; today most testing is initiated by non-genetics subspecialties such as oncology, neurology, and cardiology, all of which use genetic testing as a standard diagnostic tool for patient management. However, interpretation of next generation sequencing, which will soon take over as a common “genetic test” is still in its infancy and very complex. To support this evolution, a focused approach to provide practitioners with the knowledge and confidence they need in test interpretation and related counselling will become the norm in a cost effective way. This will be achieved through Centre priorities in research translation, investments in multi-disciplinary education, and a focus on development of practice guidelines to achieve better patient outcomes.

The Centre will play a pivotal role in elevating the ‘genetics dialogue’ with the brightest thought-leaders and community stakeholders to lead and inform change.
Due primarily to current funding mechanisms, Ontario has been slow to respond to the rapid new development in molecular testing in comparison to our U.S. and European counterparts. This has resulted in an increasing number of clinical samples being sent out-of-province through OHIP funding, challenging the ability of genetic laboratories in Ontario to offer guidance to physicians both in the appropriate choice of testing and in the interpretation of test results. The Centre will work with key partners to optimize the alignment of quality, funding and planning for new test management, investment in “system” capacity, and regulatory oversight for diagnostic genetic testing.

Lastly, we will iteratively determine the economic value of genetic analysis in the diagnosis and treatment of medical conditions and the positive impact overall on patient care and health economics. The Centre will play an important role in supporting the development of clinical practice guidelines that can direct more cost-effective, accessible, and equitable delivery of genetic services within SickKids and beyond. This will be demonstrated through targeted business case development, establishment of clinical practice guidelines to aid clinical decision making for improved patient outcomes, and attention to downstream enhancements and savings.

**Why a Blueprint for Change?**

The implementation of individualized medicine requires radical changes in the culture of healthcare delivery. The Centre for Genetic Medicine Blueprint was developed to assist in formulating and executing a strategy for the Centre and to create a roadmap that will guide our leaders, health professionals, educators, government, and patients on how to make individualized medicine a reality at SickKids.

The Blueprint is designed to assist health professionals collaborate and leverage institutional and demonstrated programmatic strengths to build system change with the longer term goal of advancing future policy development.

**Implementation Plan**

Achieving effective implementation of the Centre priorities requires a comprehensive action plan that identifies specific roles and accountabilities for each participant and stakeholder. The plan developed in this Blueprint identifies leadership, collaboration, education, and partnerships as the most critical accelerators for change.
At a Glance

Demands on the health care system are increasing at an unsustainable rate. Developments in genomic medicine will be an important mechanism for improved patient outcomes with more focused and efficient health care spending.

Ontario is not taking advantage of the rapid technological advances in genetic testing and is falling behind other jurisdictions; Ontario now only performs $\frac{2}{5}$ of the genetic tests currently available in the United States.

Rapid advances in genomics, are leading to enhanced diagnosis and individualized therapies with a significant impact on healthcare.

Four key enablers critical to fully harvest the potential of genomics and successfully integrate it into care include: 1) everyday use of (new) technologies in clinical practice, 2) strategies to determine the clinical utility, 3) strategies to determine the validity of genetic testing and the ability to interpret and communicate test results supported by targeted and individualized therapeutic approaches, and lastly 4) strategies to manage the personal, predictive, ethical, legal and associated social dimensions.
The Case for Clinical Genomics and Genetic Medicine
Genetics has already begun to have a significant impact on health care delivery. Rather than dealing with diseases after they have manifested, clinical genomics will enable clinicians to determine what diseases a person is susceptible to and which drugs and interventions hold the highest likelihood of improving the outcome. In addition, genomic medicine will also have an immediate impact on potential acute medical illness by optimizing treatment development, changing healthcare to be highly individualized and pre-emptive. The true value of genomic medicine rests in understanding and incorporating genomic information, both clinical and research outcomes, into the patient’s health management.

This type of ground-breaking work is already taking place within SickKids. This is our opportunity to align the research discoveries to patient care by ensuring that all SickKids health care providers have the skills and expertise to make the best use of these advances. SickKids has demonstrated early success in genomics research strategically designed to leverage support from key technology partners and collaborations. These partnerships have provided the essential infrastructure for SickKids to evolve as one of the world leaders in genomic research. To continue to lead in discoveries and translation, new genomic technologies coming online will require significant investment. By strategically aligning our priorities, the Centre will leverage efforts to support the genetics innovation agenda for enhanced clinical outcomes supported by downstream economic benefits. The Blueprint for Action sets out how the Centre intends to achieve its ambitious goal of leading SickKids into the new era of genomic medicine.

The steps outlined in the Centre Blueprint will:

• Identify the Centre’s immediate, medium and long term priorities to achieve its vision;
• Facilitate the required infrastructure to support enhanced integration across the organization;
• Identify steps to support the expansion of gene discovery efforts;
• Strengthen translation of genetic findings into clinical laboratory tests and patient care;
• Develop knowledge transfer opportunities for health professionals and families;
• Create processes to “institutionalize” the application of genetic and genomic medicine in patient care; and
• Strengthen planning to lead provincial, national and international collaborations, building sustainability and knowledge across the health care system.

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 educational, outreach, and commercialization activities in genetics |

What are the enablers for SickKids to harness the power of genomics/human genetics?

| Individualized Medicine and Early Diagnosis | Identifying ‘at risk’ individuals, prevention of disease, early & definitive diagnosis, and personalized treatment |
| Genomic Literacy | Improve access, awareness and responsiveness to evidence-based genetic information |
| Innovation | Maximize opportunities to create sustainable impact |
| Translation | From “bench-to-bedside” |
| Policy Leadership | Influencing policy, society, and funding streams |
Chronic disease is a major cause of world-wide death and disability\(^1\) and largely genetically determined. The adoption of genomic medicine to create individualized care and treatment for chronic disease will be a focus of the Centre with planning efforts linked to the five enablers to create sustainable change. The continued development and influence of individualized medicine will include efforts to evaluate, approve, implement and monitor activity that demonstrates immediate impact for change in managing children’s health trajectories.

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 that we have the skills, processes and expertise to make the best use of these advances.

Linking genomic literacy to improve access, awareness and responsiveness to evidence-based genetic information will be a significant driver for Centre resources and outreach planning efforts. Closely aligning responsiveness to innovation, the Centre will develop specific goals and processes to establish targeted collaborations and translational research and grant opportunities to achieve outcomes that support system capacity and innovative care delivery models.

The Centre will play a pivotal role in elevating the “genetics dialogue” with the brightest thought leaders and community stakeholders to lead and inform change. Strategic priorities will align with and leverage institutional and demonstrated programmatic strengths to build system change and advance future policy development.

Educating our health professionals to incorporate genetic advances into everyday clinical practice is our vision.

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\(^1\) OACCAC, OHA, OFCMAP, “Ideas and Opportunities for Bending the Health Care Cost Curve”, April 2010

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Laboratory Technologist preparing genomic DNA for quality check prior to clinical testing.
At a Glance

There is increasing evidence of the medical and financial benefit of integrating genomic knowledge into clinical medicine.

Evidence of clinical utility and cost-effectiveness must drive the integration of genetic testing in clinical service.

Research and development should be coordinated across specialties to prevent duplication and potential incompatibility of infrastructure and systems.

Developing capacity for molecular genetic testing must be underpinned by parallel developments in bioinformatics that will support clinical decision-analysis.

The continued drop in next generation sequencing costs will drive future clinical service development.

Pharmacogenetic applications will improve our understanding of how to optimize drug treatment and prevent adverse drug reactions.
Realizing the clinical benefits of genomic research will remain a key challenge for researchers and clinicians well into the future. The speed with which genetic discoveries are translated into better healthcare will also continue to be a challenge. New therapies and gene-based diagnostics need to be carefully examined for clinical utility and validity, cost-effectiveness, and their ability to add value to patient care and achieve improved clinical outcomes.

To provide strategic oversight in this area, the Centre for Genetic Medicine Executive, along with external advisors, will offer guidance in areas where additional focus may be required to address the current and future research and translational opportunities and challenges for SickKids, the Centre’s partners and external stakeholders.

The Centre will endeavour to support our partners with granting opportunities. Enabling the themes of innovation, translation, and strategy, the Centre will secure funding and identify processes to enhance the translation of research, support translation of knowledge to health care providers and families, and build systems for collaboration and future partnership planning.

While technological advances have led to an explosive growth in our knowledge of the human genome, there is a critical need for major advances in our ability to determine the clinical significance and utility of this new knowledge.

Recognizing the need for policy change and regulations to ensure sustainable change resulting from research translation successes, the Centre will focus efforts to support awareness, knowledge sharing and broad based discussion to stimulate SickKids’ genetics strategy and future opportunities to lead provincially, nationally and internationally.

To generate tangible health outcomes from SickKids’ Centre integration model, researchers from across different programs will want to be linked with clinical colleagues in interdisciplinary teams to accelerate translation of research. Faced with rapid technological advances and an ever changing knowledge base of human genomics, the Centre will integrate basic, translational and clinical research to execute our vision of applying genomic knowledge to improve child health through gene-based diagnostics and prognostic tests and therapies.

One of the core SickKids program supporting this innovation agenda in genomic medicine is The Centre for Applied Genomics (TCAG). Firmly established as one of the world leaders in delivering genome-based research, TCAG will continue to build immediate and long-term benefits including: novel disease-relevant variants and translation to diagnostic tests; new methodologies and algorithms for the annotation and prioritization of genetic variants; knowledge translation, public education and engagement; and collaboration with some of the world’s leading centres also engaged in research in genomic medicine.

Firmly established as one of the world leaders in delivering genome-based research, TCAG will continue to build immediate and long-term benefits.
The current approach of developing genetic tests based on traditional technologies will not be sustainable as testing demand is quickly outpacing capacity. The development of new methodologies and practices is essential.

Future genetic testing technologies will provide more accurate diagnosis, resulting in improvements in the quality of care and life of patients, enabling patients to avoid unnecessary testing & treatments, and offers potential to eliminate and/or reduce accompanying toxic pharmacological effects from medications and burden of disease.

Responding to increased demand for genetic testing, the Centre will develop strategies to increase capacity, take advantage of new technology and testing methods, maintain rigorous quality standards, and align efforts to investigate clinical validity and effectiveness.

The use of new genomic platforms and technologies coming online will require significant investment.

There is a need for a comprehensive evaluation process to review all new genetic tests, addressing clear evidence of clinical utility, laboratory capacity and alignment, and cost benefit.
Responding to the increased demand for genetic tests and improving Research and Development Opportunities:

The demand for genetic tests has steadily grown due to the continuing translation of new technologies, disease gene discoveries into clinical tests and a heightened awareness of the clinical utility of these tests by physicians and patients. The demand will continue to grow as basic science adds to our understanding of the molecular basis of diseases and gene-directed treatments are involving. Increasingly, healthcare providers from all clinical specialties are incorporating knowledge of inherited and acquired genetic disease into patient management. Developing SickKids laboratory services is a critical step to realizing our vision for the Centre.

Ontario’s first hospital to establish a department of genetics was SickKids in 1947, followed by the creation of a clinical cytogenetics laboratory in the 1960’s.

Genetic testing often provides the most accurate diagnosis, directs patient management, improves the quality of life for patients, enables patients to avoid unnecessary testing and treatment, and offers potential to reduce accompanying unnecessary toxic pharmacological effects. Genetic testing in tandem with other diagnostic tools can provide definitive answers to complex medical diagnostic dilemmas, providing improved care with a simultaneous reduction in costs. These savings can be obtained by eliminating ineffective treatment options, instituting preventative measures, improving early diagnosis through surveillance, reduced health provider workload and expenditures secondary to reduced need for diagnostic workup, and from decreased requirement for follow-up of family members. A promising application of genetic testing with potentially significant financial and medical impact is in the area of pharmacogenetics. Variations in our genes result in different individual responses to drugs. As our knowledge grows about how genes and drugs interact, patients could undergo a genetic test to predict their response and help to ensure that the medicine and dose is right the first time. This will significantly improve outcomes, avoid serious side effects, and reduce financial wastage. The Centre will continue to build on SickKids’ early successes in these areas, through the continued development of practice guidelines, translational research initiatives, cost-benefit business case development, leveraging investments through the repatriation of genetic tests to build capacity, and positioning for the adoption of new technologies and re-investment opportunities to support system change.

There is a need for a comprehensive evaluation process to review all new genetic tests addressing clear evidence of clinical utility, laboratory capacity and alignment, and cost feasibility:

Since 2005, Ontario has fallen behind other jurisdictions in genetic testing due to the elimination of a formal process for evaluating, approving and funding new genetic tests in the province. SickKids, along with other provincial regional genetic centres, has heavily relied on funding from the provincial out-of-country (OOC) Program for diagnosis, prediction of future genetic disease, prognosis and treatment. This has resulted in high volumes of genetic tests not being conducted in Ontario’s medical laboratories, and increasing expenditures within the OOC funding program.

A directed focus is required to design a comprehensive evaluation process for the review all new genetic tests, addressing the need for evidence of clinical utility, laboratory capacity and alignment, and cost feasibility. A systematic process for assessing the available evidence regarding the analytic validity, clinical validity and utility of emerging and existing genetic tests for clinical practice would help to confirm the benefits of a genetic test and distinguish tests that are safe, effective and clinically useful.

The prevalence of predisposition and pharmacogenetic testing will have a profound impact on our laboratory service. In addition, the discovery of more familial subsets in cancer and other diseases will further increase the volume of tests. As genomic testing becomes relevant for more common diseases, the number of people to be tested will become even larger. High-throughput automated testing technology will be essential to deliver quality results quickly. The Centre will prioritize future investment opportunities to align to technological innovations and support the need for changing clinical pathways.
At a Glance

Stakeholders must work in partnership to implement an effective interdisciplinary genetic strategy.

The Blueprint for action addresses the four enablers needed for change to occur:
A. Genomic Literacy;
B. Innovation;
C. Translation; and
D. Policy Leadership

The Blueprint for action suggests six overall directions to focus recommendations:
1. Link philanthropic and funding mechanisms to Centre vision;
2. Advance genomic knowledge through provider and public education initiatives;
3. Adopt new technologies as an enabler;
4. Knowledge Transfer through translation and collaboration;
5. System Planning; and
6. Demonstration of the business and public health impacts of genomic research and genetic medicine.

The human genome project has clearly shown us that people are not homogeneous populations as we carry thousands of variations in our genes, up to 1.5% of our DNA, which makes each one of us genetically different from one another.
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. The Centre will drive change through taking advantage of the safe, effective and ethical application of new genetic knowledge and technologies as they become available. Supporting and educating our health professionals to incorporate genetic advances into everyday clinical practice is our vision. To make a reality of this vision, the Blueprint sets out a detailed plan of action and targeted investment for the immediate (0-12 months), medium (12-36 months) and long-term (beyond 36 months). We will review our progress annually and report our findings to the SickKids Centre Review Council.

**Table 4.1 Blueprint Recommendations at a Glance**

<table>
<thead>
<tr>
<th>Direction</th>
<th>Strategy</th>
<th>Recommended actions</th>
</tr>
</thead>
</table>
| A. Link Philanthropic and funding mechanisms to Centre vision | Create a firm financial foundation upon which key translational and innovative opportunities can be implemented and sustained. | 1. Secure a transformational gift for Centre with a focus on integration of research activities, academic performance, and exemplary clinical care *  
2. Secure Centre endowed Chair Positions (Clinical and Translational Genomics) focusing on achieving Centre’s mission/vision **  
3. Establish Innovative Funds Grant process to support translational project activity **  
4. Establish an Innovative Therapy Funds process to support investment in new clinical treatments **  
5. Creation of CGM Professional Education Symposia Fund to support multi-disciplinary educational initiatives **  
6. Creation of a “Strategy Fund” to support activity that enables CGM strategy development and execution ** |
| B. Provider and public education | Improve access, awareness and responsiveness to evidence-based genome information for health care providers and the public. | 1. Invest in interactive technologies including “About Kids Health” and other new forms of interactive technologies to support family education **  
2. Create web-based platforms to support education initiatives in knowledge and application of genomics for health professionals **  
3. Create a systematic approach and methodology for knowledge dissemination both internally and to external stakeholders ** |
| C. Adoption of new technologies into clinical care | Facilitate scientific achievement and biological applications beyond current technology into clinical care. | 1. Introduce Next-Generation sequencing technology into clinical service */**  
2. Optimize translation opportunities to support integration of genomic medicine across SickKids and beyond ** |
| D. Advancement of genomic knowledge | Invest to support technology advances in genomic discovery. | 1. Health Human Resource investments in bioinformatics, human genome sciences, and pharmacogenetics */** |
| E. Enhance knowledge transfer through translation and collaboration | Identify targeted translation opportunities. | 1. Establish and fund innovation opportunities supporting translation of research into clinical care */**  
2. Develop process/mechanism to evaluate new genetic tests for utility, validity and effectiveness in clinical care **  
3. Encourage integration of genomic medicine across SickKids through development of a service model supporting integration into medical specialties influencing clinical practice/pathways **  
4. Creation of a Genome Clinic (combined bioinformatics/clinical) focusing on genomic variants and predictive interpretation of the risks associated with future disease ** |
| F. Lead in system planning | Identify and support provincial and system planning initiatives to achieve a sustainable service model for diagnostics and clinical service. | 1. Implement new tests and optimize efficiency to establish a sustainable funding model for genetic testing in the provincial reference centres **  
2. Lead transformation of molecular testing in Ontario for out-of-country genetic lab testing and implementation of exome/genome-based testing across the province */**  
3. Develop benchmarks for clinical wait times and match workload data for resource alignment */**  
4. Lead public discussion of medical genomics and influence health policy development for genetic medicine */** |
| G. Demonstrate the business and public health impact of medical genomics | Create formal evaluation methodologies to demonstrate the positive impact of medical genomics on public health. | 1. Influence and inform government and stakeholders through development and sharing of sustainable business models **  
2. Develop new clinical pathways for optimizing efficiencies and new practices */**  
3. Publish research, translation opportunities and successes, and demonstrated outcomes resulting from Centre’s mission and objectives ** |

**Recommended Action Timelines:** *immediate (0-12 mths), **medium (12-36 mths), *** long term (beyond 36 mths)
At a Glance

Achieving effective implementation of the Centre Blueprint priorities requires a dynamic plan that identifies the role each partner should undertake.

The plan presented in this Blueprint is a starting point and will need to be iteratively updated and refined as key parties and stakeholders assume responsibility for its implementation.

One focus of the Centre strategy involves the need for changes in provincial policy – to succeed we will need strong leadership both provincially and locally.
To embrace the evolution of genetic medicine, SickKids will need to invest in unique and unconventional collaborations and partnerships. Genomics represents cutting-edge, innovative science, and the translation of this knowledge will at times be difficult to implement. The overall lack of genomic literacy is a significant challenge to the integration of genetic knowledge to achieve successful outcomes.

The Centre’s commitment to invest in genomic literacy will result in more informed health professionals and families taking personal responsibility for creating the environment for a constructive change.

SickKids must adopt a leadership role in developing policies and boundaries that are in the interests of our patients, health professionals, ethicists, partners, stakeholders and funders. We will remain committed to the longer term vision of informing policy setting to ensure positive change into the future.

Building on the principle of leading change, the Blueprint approach is one of engagement, development, innovation and evaluation to support advancing new technology and knowledge. The ability to be an innovator in genetic medicine will rest on the execution of our planning efforts and the ability to refine our approach as the technology guides us to influence children’s health outcomes through genetic medicine.

Table 5.1 Centre for Genetic Medicine – 3 year Priority Planning Milestones

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<tr>
<th>Table 5.1 Centre for Genetic Medicine – 3 year Priority Planning Milestones</th>
<th>2013/14</th>
<th>2014/15</th>
<th>2015/16</th>
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<tbody>
<tr>
<td>Accelerating Translation &amp; Innovation</td>
<td>Secure transformation gift and endowed Chairs.</td>
<td>Establish innovative Funds Grant process.</td>
<td>Encourage integration of genomic medicine through development of a service model supporting integration into medical specialties influencing clinical pathways.</td>
</tr>
<tr>
<td></td>
<td>Establish innovative Therapy Funds Grant and process to support new clinical treatment.</td>
<td>Creation of ‘Strategy Fund’ and process to support Centre strategy execution.</td>
<td>Creation of a Genome Clinic (bioinformatics/clinical) focusing on genomic variants and predictive interpretations of the risks associated with future disease.</td>
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<tr>
<td></td>
<td>Planning &amp; implementation of a ‘Genome Clinic Research Project’ identifying targeted translation patient populations.</td>
<td>Optimize translation opportunities – genomic medicine across SickKids and beyond.</td>
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<td></td>
<td>Develop process to evaluate new genomic tests for utility, validity and effectiveness.</td>
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<tr>
<td>Provider and Public Education</td>
<td>Establish Professional Education Symposia Fund.</td>
<td>Invest in interactive technologies to support family education.</td>
<td>Continue Annual Centre Symposium.</td>
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<tr>
<td></td>
<td>Launch Annual Centre Symposium.</td>
<td>Web-based platform to support health professional education.</td>
<td>Renewal of Centre Education Plan</td>
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<td></td>
<td>Development of a 3-year Centre Education Plan</td>
<td>Methodology for knowledge dissemination (internally and to external stakeholders).</td>
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<tr>
<td>Technology Infrastructure</td>
<td>Secure next-Generation sequencing platform. Planning and Health Human Resource investment to support next-generation technology in a clinical diagnostics laboratory.</td>
<td>Continued investment in year II to support next-Generation sequencing technology in clinical diagnostics laboratory.</td>
<td>Continued investment in year III to support next-Generation sequencing technology in clinical diagnostics laboratory.</td>
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<tr>
<td>Health Human Resource Investment</td>
<td>Investment to support technology advances – bioinformatics, human genome sciences, pharmacogenetics.</td>
<td>Continued investment in year II for bioinformatics, human genome sciences, pharmacogenetics.</td>
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<td></td>
<td>Health Human Resource investments to support launch of the Genome Clinic Research Project.</td>
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<tr>
<td>System Planning</td>
<td>Lead transformation of molecular testing in Ontario for OOC testing.</td>
<td>Implementation of new tests and optimization of efficiencies.</td>
<td>Sustainable funding model for genetic testing in provincial reference centres.</td>
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<tr>
<td></td>
<td>Develop benchmarks for clinical wait times and match workload data for resource alignment.</td>
<td>Implementation of new tests and optimization of efficiencies.</td>
<td>Lead public discussion of medical genomics and influence health policy development.</td>
</tr>
<tr>
<td>Impact &amp; Evaluation</td>
<td>Develop new clinical pathways for optimizing efficiencies and new practices (yrs I/II/III).</td>
<td>Influence government and stakeholders through development and sharing of sustainable business models.</td>
<td>Publish research, translation opportunities and demonstrated successes (yrs II/III).</td>
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<tr>
<td></td>
<td></td>
<td>Continuation of new clinical pathways for optimizing efficiencies and new practices (years II/III).</td>
<td>Continuation of new clinical pathways for optimizing efficiencies and new practices.</td>
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Appendix 1: Demonstration Projects

Genome Clinic Research Project

Project Overview: The Genome Clinic Research Project will leverage whole genome sequencing (WGS) technology to build a long term multi-disciplinary clinical research project designed to test multiple hypotheses concerning the implementation of whole genome sequencing in the routine clinical care of children and their families. Project success will allow for patient stratification and outcomes analysis in both clinical utilization of WGS and discovery research care with the end goal to translate new gene discoveries into lifesaving diagnostic tests and treatments. The Genome Clinic is the first of its kind because of a combination of several unique features:

a) The project treats an individual’s genome as a source of genetic information to be repeatedly used over time to improve the overall health and well being of an individual, rather than a one-time test performed to diagnose the disorder at hand. As a result, incidental variants are an explicit focus of our project rather than an inconvenient burden.

b) The project’s scope is unusually broad – from development of new bioinformatics tools and discovery of new genes to health policy inquiries, assessment of models of clinical care and the ethics of consent.

c) The design of the project emphasizes an interactive partnership between patients, parents and health care researchers in discovering the risks and benefits of genomic medicine.

d) By focusing on pediatric patients we can offer the highest possible social and economic impact, as intervention in children leads to the greatest potential for increased quality of life years of any patient population. The broad areas of inquiry for the clinic are shown in Figure 1 which will lead clinical implementation into daily care.

Building on the Centre’s themes of discovery, translation, and knowledge transfer, this project will act as a ‘gene discovery’ resource; enabling SickKids to increase the scientific and clinical value of the data as new genes are discovered. The database will serve as a repository of value that will grow in clinical utility over time. The creation of a data base of this magnitude supports SickKids vision to transform children’s health through individualized medicine, leading to more specific disease management, directed at known mutations providing customization of treatment for improved clinical outcomes.

Opportunity: New sequencing technologies and applications are being developed at an incredibly fast rate and it is imperative that SickKids stay dedicated to this evolving environment if it is to remain a leader in pediatric medicine. These ‘next generation’ sequencing technologies permit whole genome-scale, sequence-based assays at reasonable cost and high accuracy. Similarly, the massive throughput and adaptability of the new systems opens up the possibility of genome-scale assays in clinical and other medical research, screening large numbers of samples for changes underpinning diseases and traits of interest. The shift towards genome sequencing is expected to become more valuable as scientists piece together the complex interactions of multiple genes and how they influence disease and how the body reacts to certain medications. This “systems” knowledge of clinical pathways will create medical management modalities that cannot otherwise be accomplished through the traditional route of sequencing only select genes. Effective, efficient and routine clinical use of these technologies will require fundamental changes in the practice of medicine. This effort is dependent on successfully dealing with the current uncertainties and knowledge gaps regarding the utility and impact of whole genome sequencing in clinical care. The project assumes leveraging dollars today will lead to future successes in clinical utility with anticipated downstream cost savings.
Project Goal: The genetic complexity of disease makes large-scale integrated approaches essential to provide the raw data required to provide a basis for patient diagnostic stratification, patient management and clinical research. The routine clinical use of “next generation technologies” such as whole genome sequencing offers tremendous potential benefits to the health care system, including cost effective and accurate diagnosis of genetic disorders, reductions in unnecessary testing, avoidance of adverse drug reactions, and pre-symptomatic identification of individuals at risk for both rare and common diseases who would benefit from risk reduction strategies. Enhancing our capability in genome sequencing and analysis will accelerate gene discovery, will accelerate validation and implementation of genetic biomarker diagnostics tests and will facilitate improved design for clinical trials. The clinical utility of this large-scale data repository will grow over time as the data accumulates, enabling improved diagnosis and management of both rare and common genetic disease.
Appendix 2: Centres at SickKids

Background
SickKids Centres are hospital-wide groupings that represent important areas of interdisciplinary and interprofessional activities in children’s health. Centres will bring together research, education and clinical activities to drive world leading innovation in children’s health.

Centres will emerge as groups of individuals identify unique and innovative opportunities for collaboration and integration. Centres will vary in size and scope, depending on their focus, and will respond to the emerging needs of children, youth and their families on a local, provincial, national or international level.

Strategic Goals
The creation of Centres is key to the advancement of SickKids’ strategic directions. Centres will help drive innovation across the organization, resulting in new research discoveries, strengthened system capabilities and enhancement of SickKids’ leadership position nationally and internationally. Centres also strengthen the integration of care, education and research across the organization. This will facilitate research collaborations across the Research Institute, support clinical and research training, develop best practices and policies, and translate knowledge to improve the health of children and youth.

Expected Result
Improved outcomes for children, youth and their families will be achieved through the creation of Centres that:

- Drive innovation and further development of new diagnostics, treatments and cures
- Demonstrate integration of research, clinical activities, and education
- Build on existing strengths and take advantage of opportunities as coordinated, self-organizing groups to realize new levels of excellence
- Build collaborations across disciplines, programs and services

Why develop a Centre?
Centres provide an opportunity to develop new collaborations among peers within SickKids in order to address a variety of child health issues. Centres will continue to help build SickKids’ national and international reputation for excellence and attract future talent to the organization. Centres will provide a mechanism for basic, clinical and outcomes focused researchers to work together with clinical colleagues on common problems. In some cases, Centres will also provide an opportunity to collaborate with other individuals, groups, and partnerships external to SickKids.

What advantages are there in forming a Centre?
Centres provide an opportunity to develop new collaborations among peers within SickKids – and in some cases, beyond – in order to address a variety of important child health issues. Centres will enable basic, clinical and outcomes-focused researchers to work together with clinical colleagues.

Centres provide an opportunity to develop new collaborations among peers within SickKids in order to address a variety of child health issues.
References


9. Large-Scale Genome Projects Enter the Clinic on Both Sides of the Atlantic. Tuma RS. JNCI Vol. 8 Issue 23, December 2011.


Glossary

**Bioethics**: The study of ethical problems arising in the field of biology and medicine including those arising from biological research and its applications in such medical treatments as organ transplantation and artificial insemination.

**Bioinformatics**: The application of computer and statistical techniques to the management of biological information such as DNA sequences, and the shapes of biological molecules such as proteins. Also a vital tool used in pharmacogenetics.

**Carrier**: A person who has one copy of a mutated gene causing an inherited recessive disorder. They are not affected but may pass the mutated gene onto their children.

**Cell**: The smallest unit of living organisms which, given the right conditions, can survive independently and reproduce itself. It has been estimated that the body of a human adult comprises 50 million cells.

**Chromosome**: The self-replicating genetic structures of cells containing the DNA that bears the gene sequence. Each human cell normally has 46 chromosomes. 44 chromosomes are 22 matching pairs, where one chromosome of each pair is inherited from each parent. The other two chromosomes are the X and Y sex chromosomes. Normally, females have XX and males have XY.

**Cytogenetics**: The study of the structure of chromosomes and cell division. Cytogenetic tests detect chromosomal abnormalities or abnormalities in the number of chromosomes.

**DNA (deoxyribonucleic acid) (also “Genetic code”)**: The double stranded helical chemical molecule that encodes genetic information. It is the code for life. The genetic code of nearly all living things is made of DNA.

**Gene**: The fundamental physical and functional unit of heredity. A gene is a sequence of DNA that codes for one, or more, proteins. A virus such as HIV has under a dozen genes, bacteria can have about 5000 genes, yeasts can have about 7500, and humans have around 30000 genes.

**Gene therapy**: The deliberate introduction of genetic material into a patient’s cells in order to treat or prevent a disease.

**Genetic conditions**: Conditions which are direct consequences of defects in single genes; or in whole chromosomes, parts of which may be lost, duplicated or misplaced; or due to the interaction of multiple genes and external factors. Later in life such interactions appear to be the basis of many of the common serious disorders, such as heart disease, diabetes and cancer.

**Genetic Counsellor**: A health professional providing genetic counselling in a clinical setting. Genetic counselling is a communication process between the counsellor and the individual or family which deals with the medical and other implications associated with the occurrence, or the risk of occurrence, of a genetic disorder in a family.
Genetic test: A test to detect the presence or absence of, or change in, a particular gene or chromosome. This includes indirect tests which are not based on DNA but look for a product, such as a protein, indicative of a specific gene change in a person.

Genome: A person’s genome is their total genetic information i.e. everything contained in their DNA.

Inherited dominant disorder: A disorder where, for the person to be affected, the mutated gene only has to be inherited from one parent. Dominant disorders include Huntington’s disease and familial hypercholesterolaemia.

Inherited recessive disorder: A disorder where, for a person to be affected, the mutated gene has to be inherited from both parents. Such parents are usually unaffected carriers because they only have a single copy of the affected gene. Recessive disorders include cystic fibrosis and sickle cell disease.

Mutation: The change in a gene or chromosome that can cause a disorder or the inherited susceptibility to a disorder.

Penetrance: The penetrance of a genetic mutation is the proportion of people with that mutation who develop that particular genetic condition. Penetrance is often expressed with reference to a particular age. For example, the penetrance of certain BRCA1 gene mutations (for breast/ovarian cancer) by age 70 has been estimated to be up to 85%.

Pharmacogenetics: The study of how people respond differently to drugs due to their genetic makeup, in terms of both how well the drug will work and what side effects the person might suffer.

Predictive value: The positive predictive value of a test result is the likelihood that a person with a positive result will develop the condition. The negative predictive value of a test result is the likelihood that a person with a negative result will not ever develop the condition.

Protein: A large chemical molecule composed of one or more chains of smaller molecules in a specific order; the gene coding for the protein determines the order. Proteins are required for the structure, function, and regulation of the body’s cells, tissues, and organs, and each protein has a unique function.

Glossary Reference
(Department of Health, United Kingdom, 2003)
Contributors/Acknowledgement

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While the input of many people has helped shape this Blueprint, it reflects only the views of The Centre for Genetic Medicine.

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“The Centre will position SickKids to make globally significant contributions in the field of child health genomics.”

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