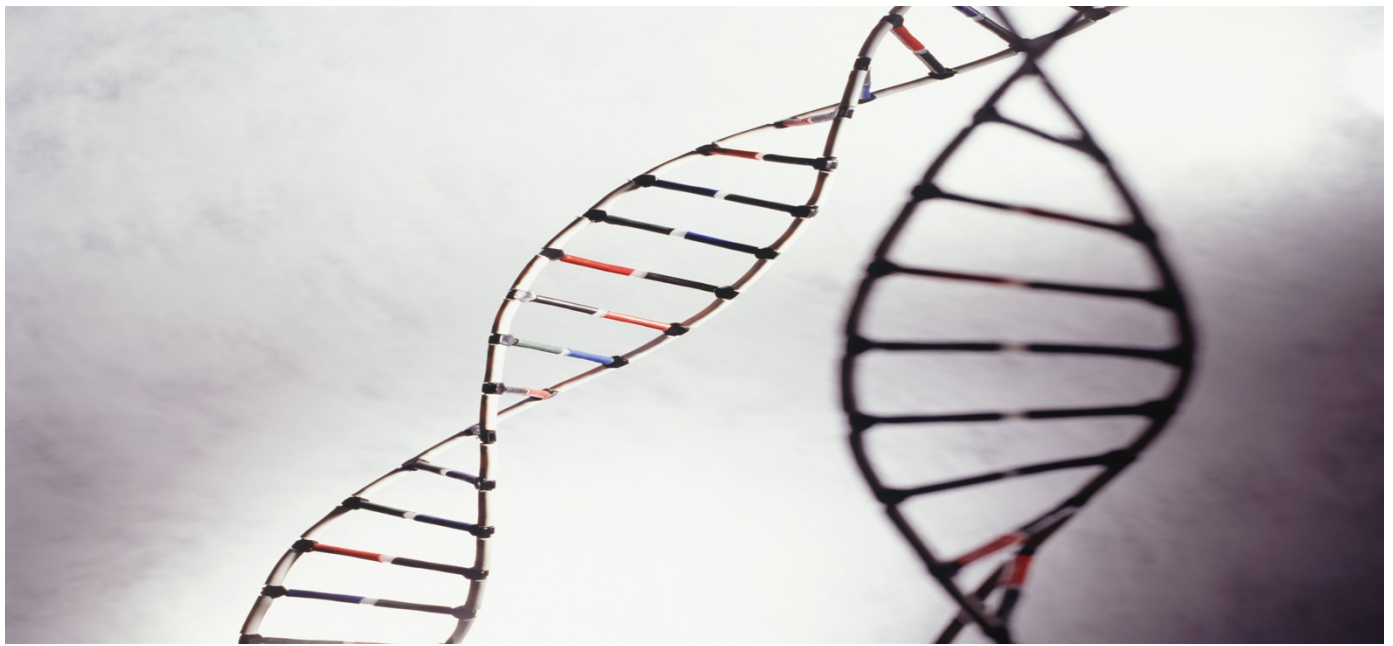




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Discoveries for Life



Review of the Institute of Genetics (IG)

Report of the IG Review Panel

February 2018



Canadian Institutes of Health Research Instituts de recherche en santé du Canada

Canada

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I. Executive Summary

The review of the Institute of Genetics (IG) was undertaken by the Canadian Institutes of Health Research (CIHR) as part of the review of the mandate and performance of CIHR Institutes by CIHR's Governing Council (GC) outlined in the CIHR Act. The review assessed the relevance and performance of IG to inform decisions regarding the role and functioning of the Institute. The review was conducted by the CIHR Evaluation Unit and overseen by a panel of experts in IG's mandate areas who reviewed and interpreted the findings and made the final recommendations. The recommendations and observations of the Panel are summarized below in relation to the two broad issues addressed by the review.

Are changes needed within the current IG mandate in order to address emerging areas of research?

The Panel concludes that IG's mandate is appropriate given the fundamental and central role of genetics in biology and medicine. The Panel recommends that the Institute continue with its current mandate.

The Panel recommends that the next SD direct more attention to computational biology and computational medicine as these areas will revolutionize medicine. It is advisable that these areas be stressed as priorities under the next Institute Strategic Plan. It is imperative that the new SD is able to shape IG's priorities in the early part of his/her mandate.

Furthermore, given the breadth of the IG's mandate and the limited resources currently available, more discretion should be granted to the Institute to select and focus on certain aspects of the current mandate. The Panel

recommends that CIHR commit an additional \$4 M per year to support new investments in areas of strategic priority given the breadth of IG's mandate and available Institute resources.

Observations and Recommendations for the Next Scientific Director

As the current SD of IG will complete his second and final term in June 2018, the Panel provides advice to GC and CIHR to inform the transition of the Institute and the work of the next SD. The current IG SD has demonstrated strong skills in engaging the research community and is well-regarded by both researchers and stakeholders.

The Panel feels strongly that the next SD should be an active and respected scientist. The Panel agrees that the next SD needs to have the ability to manoeuvre and quickly respond to emerging areas within the Institute's mandate and this would be facilitated by the establishment of the proposed innovation fund. The Panel recommends that the next SD, in consultation with the IAB, develop a strategy to assess the ongoing research priorities in order to ensure that emerging areas under the IG mandate can be prioritized. Additionally, the next SD will need to access a broad domain of expertise across IG's mandate as well as in the areas of new and early-career investigators, and training of scientists and clinicians. The Panel recommends that the next SD develops an effective communication strategy about the mandate and funding opportunities sponsored by IG with a particular emphasis on early career investigators. The Panel recommends that the IG explores ways to increase involvement of early career investigators in their funding opportunities.

II. Overview of the Review

A. Institute of Genetics: Background

As one of the 13 CIHR Institutes, the IG has a vision to maximize the health opportunities offered by genetic, basic biochemistry and cell biology research to the benefit of Canadians and the global community by advocating for and supporting the Canadian genetic community both nationally and internationally¹.

IG's mandate is to support research on the human and model genomes and on all aspects of genetics, basic biochemistry and cell biology related to health and disease, including the translation of knowledge into health policy and practice and the societal implications of genetic discoveries. Within its mandate, IG supports capacity building in addition to emphasizing knowledge translation and exchange into health policy and practice, and developing a comprehensive understanding of the societal implications of genetic discoveries.

B. Review Objectives

The review of the IG was conducted by CIHR as part of the ongoing assessment of the mandate and performance of the 13 CIHR Institutes. The review assessed the relevance of the mandate of IG and the performance of the Institute in order to inform decisions regarding the role and functioning of the Institute and the transition of the Institute to the next SD. The aim of the review is to provide the GC with valid and reliable findings to inform decisions regarding:

1. Whether changes are needed to the current IG mandate in order to address emerging areas of research; and,
2. Observations and considerations for the Institute transition and next SD.

The review was overseen by the IG Review Panel (hereafter referred to as the Panel) comprised of experts in the IG mandate areas and conducted by the CIHR Evaluation Unit. The names and affiliations of the Panel members are listed in [Appendix 1](#).

The review covered the period 2000-2016, with a focus on the period under the leadership of the current SD, Dr. Paul Lasko, from 2009 and 2016². The review was informed by a review of documents and data, interviews with the IG stakeholders, and a bibliometric study of the publications of Canadian researchers within the field of genetics. The methods and data sources used are outlined in [Appendix 2](#) and key figures are presented in [Appendix 3](#). While each line of evidence has limitations, there is convergence among them so as to produce key findings for the review.

¹ CIHR Institute of Genetics Strategic Plan, 2012 – 2017. Retrieved from: <http://www.cihr-irsc.gc.ca/e/46326.html>

² Dr. Lasko assumed the position of Scientific Director of the Canadian Institutes of Health Research (CIHR) Institute of Genetics in 2009.

III. Observations and Recommendations

A. Are changes needed within the current IG mandate to address emerging areas of research?

1. Context

As outlined in the *CIHR Act*, the objective of the CIHR is:

*“to excel, according to internationally accepted standards of scientific excellence, in the creation of new knowledge and its translation into improved health for Canadians, more effective health services and products and a strengthened Canadian health care system...”*³

Among the many activities to achieve its objective, CIHR is responsible for “encouraging innovation, facilitating the commercialization of health research in Canada and promoting economic development through health research in Canada.” And, as divisions within CIHR, the Institutes are expected to contribute to the achievement of CIHR’s overall objective within their mandate through a number of activities, including: “work in collaboration with the provinces to advance health research and to promote the dissemination and application of new research knowledge to improve health and health services.”

The Panel agrees that the IG’s mandate is appropriate given the fundamental and central role of genetics in biology and medicine, and the clear progression from discovery to translation. However, IG is challenged by an expansive mandate relative to the size of its budget. The SD is required to balance his emphasis, timing and evaluation in consideration with the current scientific context and the funding

pressure. In addition, partnership with the private sector and commercialization is a challenge for IG as well as for the other CIHR Institutes more broadly. One particular factor which clearly hampers commercialization efforts for IG is the absence of an orphan drug regulation in Canada, in contrast to the large majority of developed countries, which clearly stifles rare disease drug discovery and development, an area championed by IG.

IG’s current SD has demonstrated success, particularly in the area of rare diseases, where Canada is now recognized as an international leader working to catalyze and partner with the research and stakeholder community. IG co-leads the Personalized Medicine Initiative in conjunction with the Institute of Cancer Research (ICR) and Institute of Health System and Policy Research (IHSPR)⁴, which includes major partnerships with the Cancer Stem Cell Consortium and Genome Canada. In 2012, CIHR, in partnership with Genome Canada, invested in the Large-Scale Applied Research Project (LSARP), which aimed to fund research projects focusing on the application of genomics in the area of precision health.⁵ In addition, IG also co-leads the Canadian Epigenetics, Environment and Health Consortium (CEERHC), with the Institute of Neurosciences, Mental Health and Addiction (INMHA) and ICR. The Initiative aims to position Canada for the rapid translation of epigenetic discoveries into practical health benefits.

⁴ IG also co-leads Personalized Health initiative which is a phase II of personalized Medicine with the same CIHR Institutes plus the Institute of Aging and the Institute of Gender and Health.

⁵ CIHR’s contribution to LSARP was made available by the following Institutes (IG, ICR, ICRH, INMHA, III, INMD & IHSPR) & Initiatives (HIV/AIDS & Breast Cancer)

³ CIHR Act Available at:

<http://laws.justice.gc.ca/PDF/C-18.1.pdf>

Moreover, IG is committed to and supports capacity building through partnerships with other health organizations and professional associations, as well as by providing support to new investigators via holding an Annual New Principal Investigator (NPI) Meeting.

2. Scientific and Funding Landscape

The era of personalized and genomic medicine is upon us⁶. Sequencing provides a diagnostic tool that allows for individualized treatment strategies. Indeed, the development and approval in the US of agents such as ivacaftor (Kalydeco) to treat cystic fibrosis and, more recently, luxturna (*RPE65* gene therapy) to treat Leber congenital amaurosis mark important milestones in realizing the promise of genetics research for the treatment of diseases since these therapies target, in different ways, specific genetic defects. A similar drive towards personalized, genomics-based management of multiple other diseases is gaining pace, with oncology leading the way⁷.

A varied, bench-to-bedside, portfolio of research is necessary for the development of personalized therapies. The examples of ivacaftor and luxturna's development are telling. From the initial identification of mutations in the *CFTR* and *RPE65* genes, the development of these therapies necessitated a deep understanding of the molecular and cell biology of their gene products, research in chemistry, in virology, the development of models and then translation into products. The development cycle of personalized medicine dovetails remarkably well with the broad mandate of

IG, which is to support research on the human and model genomes and on all aspects of genetics, basic biochemistry and cell biology related to health and disease, including the translation of knowledge into health policy and practice and the societal implications of genetic discoveries. Since personalized and genomic medicine has deep implications for the diagnosis, management and treatment of diseases that are the focus of most of the other CIHR institutes (diabetes, neuromuscular disorders, cancer, etc.). The IG should continue to take a leadership role, as it has taken with the Personalized Medicine/Health Initiative at CIHR.

The emergence of genomic data and other massive-scale "omics" approaches provides both opportunities and challenges for the biology and medicine of the future. How can one extract meaningful information from these multidimensional datasets, how can these datasets be readily accessible to a wide range of researchers, and what are the best practices to store this data? These issues are especially acute with respect to clinical and patient-derived data with their associated legal and ethical concerns. We encourage the IG to develop a broad-based strategy to ensure the continued development of the computational biology and medicine communities. It is advisable that these areas be stressed as priorities under the next Institute Strategic Plan.

The Institute is uniquely qualified to contribute to the development of health care policies and practices that will potentially improve the health of all Canadians. IG-supported research is wide ranging, complex and innovative. Due to the growing importance of genetics in all branches of health research, IG facilitates and supports the genetic, biochemical and cell biology research initiatives of each of CIHR's other 12 institutes. IG also organized the "DNA on Loan: Exploring Biobanking with Indigenous Values" forum to explore the issues surrounding long term storage of biological samples when research involves

⁶ The new science of personalized medicine: Translating the promise into practice, <http://www.ucd.ie/t4cms/Personalized-medicine-pwc%20Article.pdf>

⁷ Patient-centric trials for therapeutic development in precision oncology, <https://www.ncbi.nlm.nih.gov/pubmed/26469047>

the Indigenous Peoples of Canada. The objectives were to provide national and international views on good practice and policy in this area and encourage dialogue that would provide background for enhancing current Canadian policy.

With respect to funding, the Canadian landscape of public funding of research under the IG mandate is dominated by CIHR investments in the investigator-initiated operating grant competition⁸ and by investments from Genome Canada, a non-profit corporation dedicated to harness the power of genomics for the benefit of Canadians⁹. With a comparably smaller budget, the IG needs to play a role of catalyst with strategically placed investments. The panel welcomed the level of cooperation between the IG leadership and Genome Canada in order to develop a strategic vision around genomics research.

3. Panel Observations

Achieving its mandate

CIHR's budget has been effectively flat for approximately the last 10 years, and therefore it is declining substantially in real terms, greatly affecting the ability of researchers to sustain competitive research programs.

The Government of Canada's 2017 Budget did not provide new, untargeted funding for the three federal research funding agencies: CIHR, the Natural Sciences and Engineering Research Council of Canada (NSERC) and the Social Sciences and Humanities Research Council of Canada

(SSHRC).¹⁰ The 2017 Budget established the position of Chief Science Advisor and related secretariat, funded the creation of approximately 25 Canada 150 Research Chairs and a number of investments to simplify and target support to Canadian innovators, including: Innovation Clusters and Networks, Impact Canada Fund, Strategic Innovation Fund, Venture Capital Catalyst Initiative, and Innovation Canada.

In terms of funding for CIHR, the 2017 Budget proposed funds for Health Canada, the Public Health Agency of Canada and CIHR to support measures associated with the Canadian Drugs and Substance Strategy (\$100M over five years) and National Action Plan on Climate Change Adaptation (\$47M over five years).

The final report of Canada's Fundamental Science Review, released on April 10, 2017, stresses that significant reinvestment in the federal research ecosystem needed over a more predictable and better planned multi-year horizon as well as improved coordination and collaborations between the three federal granting agencies (CIHR, NSERC and SSHRC) and the Canada Foundation for Innovation (CFI).¹¹ The panel supports Canada's Fundamental Science Review recommendations and their implementation would have a positive impact on the ability of IG to support its mandate. The 2017 Budget document indicates that the federal government will finalize its response to the advisory panel's recommendations before making any new investments in the federal granting agencies, which could mean Budget 2018.

⁸ Over the past 16 years, the average annual percentage of CIHR investment in IG's mandate was 32% of CIHR's annual investment.

⁹ As of 2015-16 Genome Canada's contribution in Health was \$ 57 M.

¹⁰ Budget 2017: Building a Strong Middle Class. Available at: <http://www.budget.gc.ca/2017/home-accueil-en.html>

¹¹ Investing in Canada's Future: Strengthening the Foundations of Canadian Research. Canada's Fundamental Science Review (2017). Available at: <http://www.sciencereview.ca/eic/site/059.nsf/eng/home>

Until 2014-15, each of the 13 CIHR Institutes received a strategic research budget of \$8.6 M per year. As a result of the Institute Modernization, in 2015-16, half of each Institutes' strategic research budgets (\$4.3 M per year) was invested in CIHR's Roadmap Accelerator Fund (RAF) to support multi-Institute and multidisciplinary initiatives align with CIHR's research priorities patterned along the lines of CIHR's existing signature and strategic Initiatives. The remaining half of the budget remained under the control of Institutes to direct toward Institute-specific initiatives.¹² As of 2017-18, Institutes returned to a strategic research budget of \$8.6 M; however, the investments of funds in multi-Institute and multidisciplinary initiatives are guided by the same "spirit" and principles as RAF. In the case of IG, the return to an \$8.6 M strategic research budget will have limited impact on the available research for the next SD due to forward commitments to CIHR and Institute initiatives. For example, based on the current budget and commitments, the next IG SD will have a limited available research budget for much of their first four-year term: 2018-19 (\$128.8 K), 2019-20 (\$454 K); 2020-21 (\$1.4 M); and 2021-22 (\$2.1 M)¹³. The lack of funds available for the next IG SD may hamper his/her ability to shape the IG's priorities for many years of his/her mandate.

In addition to the IG budget, the total CIHR investment in the IG mandate research area (e.g. originating from investigator-led operating grants competitions) increased steadily between 2000-01 and 2007-08, from \$118 M to \$298 M, during a period when CIHR's overall budget increased steadily, then decreased slightly until 2009-10 before it increased over the following six years to reach \$385 M in 2015-16. For more information about CIHR

¹² Given that many collaborative initiatives were pursued and initiated by IG since this structural change, the changes were not viewed by the current scientific director as an impediment.

¹³ As per December 2017 data

investments in IG's mandate by research areas,¹⁴ see [Figure A](#) (Appendix 3).

In light of this, the Panel noted that offering each of the 13 CIHR Institutes a limited yet equal budget is not reflective of the reality of the scientific opportunity and importance of genetics to the domain of health research, nor does it reflect the broad mandate of the IG. As a consequence, the panel concludes that IG receives insufficient funding to effectively meet its mandate to support priority driven research and its translation. The Panel remarked that given the emergence of "big data" in every aspect of genetics, genetic medicine and health, this will be an important area of partnership for IG with Genome Canada, academic institutions, international organizations, patient groups and commercial partners. These areas also flag the need to focus on computational medicine and biology as priority areas under the Institute's new strategic plan, given the limited resources.

Another upcoming challenge for IG is the SD transition. In particular, the change in staff allocation from Ottawa-based Institute staff (OBIS), who were personnel at CIHR's central office dedicated to provide service to IG, to Integrated Institute Teams (IIT), who are providing support across all 13 Institutes undermines the ability of building the IG corporate memory, continuity and staff loyalty.

Furthermore, the Panel noted challenges with the assessment of IG's performance in terms of knowledge translation and commercialization given it is a broader CIHR objective.

¹⁴ IG mandate research areas include: Computational & Systems Biology, Health Services, Policy & ELSI, Models & Mechanisms to Therapies, Strengthening the IG Research Community.

4. Recommendations

Recommendation 1: The Panel recommends that IG continue with the current mandate.

Recommendation 2a: The Panel recommends that the next SD direct more attention to computational biology and computational medicine as these areas will revolutionize medicine.

Recommendation 2b: The Panel recommends that CIHR commit an additional \$4 M per year to support new investments in areas of strategic priority given the breadth of IG's mandate and available Institute resources.

5. Strategic Considerations

The Panel supports CIHR's recent move to return to the 13 Institute-specific IAB model from the five IAB model aligned with the strategic directions and research priorities of CIHR's five-year strategic plan, Health Research Roadmap II. The model is perceived to have diluted the domain expertise required by the SDs. The Panel advises that the new advisory board should include members with experience and knowledge of the international know-how. It should also be forward looking, diverse and covering all aspects of the IG mandate.

Moving forward, the Panel sees the need for a periodic assessment of the Institute's strategic initiatives in order to ensure their success and their relevance and effectiveness and that they are meeting the needs of the research community.

B. Observations for the Next Scientific Director

1. Context

There is widespread appreciation for the current SD in the IG research and stakeholder community. IG's current SD has been a tireless advocate and champion of rare disease and epigenetics research that led Canada playing a leadership role in these two areas. In addition, the current SD has been active building the networks (e.g. rare disease models) and developing collaborative initiatives. He also actively took on the responsibility of ensuring that the Institute is providing opportunities for the mentorship of new investigators. Furthermore, the current SD brought the Institute to the forefront in the patient networks. Throughout the SD's term, the profile of the Institute has been brought to the forefront internationally.

The Panel expresses a need that the new IG leader be an active and well respected researcher with the following characteristics:

- Understanding of basic science;
- Understanding of the opportunities and challenges of translating science into clinical practice;
- Motivated toward translation and the application of research; and
- Strong communication and collaborative skills to be able to foster and maintain partnerships with other institutes, nationally and internationally.

The next SD should be able to elaborate an effective outreach and communication strategy that reaches the full spectrum of researchers working under the broad IG mandate. This strategy should pay particular attention to new investigators and early career scientists. Furthermore, the Panel

agrees that the next SD needs to have the ability to both “step back” and set a clear strategic path for the Institute and be able manoeuvre and quickly to respond to emerging areas and opportunities. For example, areas such as genome editing, cryoelectron microscopy or single-cell biology/genetics are revolutionizing research areas under the IG mandate. The Institute-specific IAB will be important for the next SD to help ensure he/she has the domain expertise required to develop and focus on the strategic priorities, and to obtain advice from and communicate with their Institutes’ research community.

Recommendation 3: The Panel recommends that the next SD, in consultation with the IAB, develop a strategy to assess the ongoing research priorities in order to ensure that emerging areas under the IG mandate can be prioritized.

Recommendation 4a: The Panel recommends that the next SD develops an effective communication strategy about the mandate and funding opportunities sponsored by IG with a particular emphasis on early career investigators.

Recommendation 4b: The Panel recommends that the IG explores ways to increase involvement of early career investigators in their funding opportunities. As one example, the IG could require the presence of early career investigators in team grants.

2. Panel Observations

The appointment of the IG’s next SD is crucial, since genetics and genomics is central to so many disciplines. After considering the activities, dedication and accomplishments of the IG’s current SD and the context within which the Institute is operating, the Panel concluded that the next SD should have the aforementioned characteristics.

IV. Review Key Findings

A. Review Objectives

The review of the IG was conducted by CIHR as part of the rolling review of all CIHR Institutes. The aims of the review are to:

1. Provide CIHR management with valid, insightful, and useful findings regarding the ongoing institute relevance and performance; and
2. Inform decisions regarding the transition of the Institute and the next SD.

Using a common framework of analysis, the review drew on multiple lines of evidence, including qualitative and quantitative data sources (Appendix 2). It uses administrative data on expenditures related to the IG mandates, bibliometric analysis on the ranking of Canada compared to the top active countries in the field of genetics research in IG's priority areas, interviews with a number of IG stakeholders and Panel deliberations. While each line of evidence has limitations, there is convergence among them so as to produce key findings. Overall, we are reasonably confident that the results presented provide an accurate portrait of the relevance of IG's mandate and the Institute's performance.

The review was conducted by the CIHR Evaluation Unit and overseen by the Panel members who reviewed and interpreted the findings and made the final recommendations.

1. Relevance

Ongoing relevance of the IG mandate

The expanded areas of research that have emerged in the wider environment include an increased focus on Models & Mechanisms to Therapies, advances in Computational & Systems Biology, Strengthening the IG Research Community and significant Health Services as well as Policy & Ethics, Legal and Social issues.

The bibliometric analysis results showed how Canada ranks regarding IG's priority research areas, namely computational biology, rare disease, precision medicine, Genetics-Ethical, Legal and Social Issues (GELS), epigenetics and genetics, when compared to the top 10 most productive countries in these research areas. The results provide a background concerning whether or not more investment is required in these areas moving forward to boost Canada's position internationally. These results could also be of help to the next scientific director while developing and defining the Institute's new strategic priorities.

Between 2011 and 2016, Canada's ranking improved from the 7th to 6th concerning the number of publications¹⁵ in the six priority areas accounting for an average of 5% of the world's total annual publication. Results show that Canadian researchers are publishing in journals that are cited more

¹⁵ The number of publications per country is calculated as: The number of scientific articles, review notes and review papers with authors from a country, as found in authors' addresses. These numbers of publications are also compiled for Canadian institutions and sectors (university, hospitals, industries, federal government, provincial government and others).

often than the world average. This is more so for computational biology, genetics and epigenetics compared to the other areas. Between 2011 and 2016, the specialized index (SI)¹⁶ shows that Canada is more specialized in the 6 priority areas compared to the world average. However, countries like UK, US and the Netherlands have consistently had higher SI than Canada over time.

There is a need for an institute that supports research on all aspects of genetics related to health and disease including the translation of knowledge into health policy and practice and the societal implications of genetic discoveries.

IG has been playing an integral role in developing, promoting and maintaining a research environment that addresses issues related to Genetics. Genetics research priorities are supported financially by CIHR more broadly and by IG specifically. From 2000-01 to 2015-16, the average annual percentage of CIHR investment in IG's mandate was 32% of total annual CIHR investment. [Figure A](#) (Appendix 3) depicts CIHR's investment in IG mandate by the Institute's research priority areas, defined in its 2012-17 Strategic Plan. [Figure A](#) (Appendix 3) shows that from 2011-12 to 2015-16, the amount invested by CIHR in the "From Models & Mechanisms to Therapies" priority represents an annual average of 26% of total CIHR investment in IG mandate, compared to 7% in Computational & Systems Biology; 3% in Strengthening the IG Research Community; and 2% in Health Services, Policy & ELSI. From 2011-12 to 2014-15, CIHR's annual investment in Models & Mechanisms to Therapies increased gradually and was always the highest compared to investment in the other research priorities.

¹⁶ Specialization index is an indicator of the relative intensity of publications of a country in the priority areas relative to the intensity of the world's publications in the same areas.

When asked how effectively the Institute has met its mandate and current strategic priorities, the majority of the IG stakeholders interviewed highlighted that the Institute's mandate covers important areas in the context of health of Canadians and the current SD has been striving diligently to support the research community under these areas of priority. Three of the interviewees were not sure what the mandate of the institute was, however.

Most of the stakeholders interviewed flagged that the IG mandate is very broad and while this important to make sure it covers important areas of genetics, the breadth of the mandate poses a challenge to the SD, given the limited resources at his/her discretion. As result the stakeholders interviewed see that there is a need for additional resources to address emerging areas of research in the field of genetics, most notably computational biology and medicine, precision health and precision medicine, and GELS, which the stakeholders deem as important and still need more attention from IG.

While the majority agrees that IG should invest more in funding basic science and research few highlighted that it would be better in the future to see that patient-engagement is made explicit in IG's mandate.

2. Impact

Support to Innovative Research and Advancing Knowledge

The IG is committed to supporting innovative research and advancing knowledge. The SD is supportive of transformative research and is open to innovations, engages various stakeholders, is committed to client oriented research, and is an active researcher himself.

IG supported the integration of physical scientists and engineers into biomedical research. Between 2002 and 2011, IG

invested nearly \$20 M in biomedical research. The Institute co-led the Regenerative Medicine and Nanomedicine Initiative (RMNI), offered annual funding opportunities to foster the development of tools, techniques and devices, and organized several workshops. In addition it provided support to expand the GE3LS (Genomics and its ethical, environmental, economic, legal and social) research (basic & applied) community.

Moreover, IG has contributed to the 2012 Large-Scale Applied Research Project Competition (LSARP), which is one of the most significant public sector investments in Personalized Medicine. The outcomes of LSARP include: identifying recurrent driver mutations affecting DNA structure, now part of WHO test recommendations, developing an oncology panel which is now used in clinical trials and is certified by Clinical Laboratory Improvement Amendments (CLIA). Moreover, LSARP resulted in studying 845 different rare diseases, provided a diagnosis to over 1000 patients, identified 131 novel rare disease genes, developed three experimental therapies and contributed to international data sharing standards.

Contributions to Building Capacity of the Health Research Enterprise

IG engages in a number of capacity building activities, including Institute-facilitated capacity building events and other investments to maintain and strengthen research capacity in mandate areas. This is in part fostered by the SD, who is viewed as supportive of young investigators and invested in ensuring they have the proper mentorship and training to help them become independent investigators.

From 2009 to 2014, IG spent an annual average of 13% of its budget on capacity building, including investments in catalyst/pilot programs, training grants and

awards, and development grants (Figure B, Appendix 3). As of 2015-16, 33% of total CIHR funded direct trainees¹⁷ (Figure C, Appendix 3) and 45% of indirect trainees¹⁸ (Figure D, Appendix 3) were funded under the IG mandate.

Between 2012 and 2016, IG has invested around \$ 1 M in postdoctoral fellowships under the Canadian Epigenetics, Environment and Health Research Consortium (CEEHRC).

IG dedicated substantial resources to capacity building, through the New Principal Investigator (NPI) Meetings, awards, and Strategic Training Initiative in Health Research (STIHR) grants, which sought to build capacity within Canada's health research community through training and developing researchers, fostering and supporting their careers.

IG's stakeholders commended the effort made by the SD regarding raising the capacity of the research community; however, they flagged that the phasing out of the Clinical Investigator Program (CIP) was unfortunate as it left a gap in clinical fellowship. A few stakeholders mentioned that more investment needs to be made, moving forward, in raising the capacity of the new, early, and mid-career investigators. The stakeholders were concerned that the shortage of funding directed to those levels of researchers could ultimately lead to a

¹⁷ Direct Trainees = Bachelors, Masters, Doctoral, or Post-Doctoral students/fellows who received/are receiving a training award through a CIHR-funded program within the Institute's mandate. A direct trainee is counted as funded within a specific Institute's mandate can also be counted as a direct trainee funded under another institute's mandate if the award this person receives is also relevant to the other institute.

¹⁸ Indirect Trainees = The Full Time Equivalent (FTE) of Bachelors, Masters, Doctoral or Post-Doctoral students/fellows who received/are receiving a stipend paid through researcher grants within the Institute's mandate.

brain drain. Although IG's stakeholders praised the NPI, they highlighted that more work still need to be done to improve communications with the new investigators especially to increase their awareness of and access to funding opportunities of IG and within IG's mandate.

3. Convener and Catalyst

Contribution of Scientific Leadership to the Convener-Catalyst Role

There was a consensus amongst the stakeholder interviewed that IG's SD was very active in building and maintaining partnerships and collaborations. He has engaged in a variety of activities to identify, connect and engage with multiple organizations, and has participated in events (i.e., workshops, meetings and conferences) where he spoke to IG's strategic priorities and to those of CIHR more generally.

The IG's SD is regarded by stakeholders as a leading source of information in the Institute's mandate areas and that he is well respected in the wider community, both nationally and internationally. He is also seen by stakeholders to be adding credibility to the Institute and defers to experts when relevant.

Under the current SD leadership, IG convened a "Best Brains Exchange" with Health Canada in 2013, to explore the possibility of integrating epigenetic effects of food and environmental contaminants into risk assessments. In 2016, IG also collaborated with the Institute of Aboriginal Health (IAPH) and INMD to organize a 'DNA on Loan' conference, which discussed best practices for genetic and biomedical researchers in order to facilitate interaction with Indigenous communities.

Public outreach has been one of IG's main priorities under the current SD. IG has supported between 10 and 20 national

meetings per year. IG organized numerous *Café Scientifiques*, which provide insight into health-related issues of popular interest. For the past 3 years, *Café Scientifiques* organized by IG were aired through a partnership with Canal Savoir.

IG also collaborated with CIHR's Marketing and Communications Branch to co-host the first-ever CIHR Science Writers Workshop, which brought together the Canadian VHO community's top medical reporters, communicators and genetics researchers.

At the international level, in 2012, IG announced the creation of Orphanet-Canada, the Canadian branch of Orphanet, the world's online reference portal for rare diseases and orphan drugs, which includes 37 countries. In addition, IG supports the International Rare Diseases Research Consortium (IRDiRC), a global collaborative effort involving over 18 countries established in 2011. IG's current SD chaired the IRDiRC Executive Committee for three years until December 31, 2015.

Since 2012, IG facilitated Canadian participation in 5 joint transnational calls of E-Rare-3 ERA-NET consortium, which is a key international research partnership that coordinates research activities carried out at the national or regional level in member states.

Partnering to Achieve CIHR and Institute Objectives

Under the leadership of the current SD, IG fosters effective partnerships with all stakeholder groups via reliable collaboration, scientific integrity, and research excellence. The institute has been actively seeking out partnership opportunities and reaching out to various organizations. Partner organizations include other CIHR Institutes, government agencies and departments, and not-for-profit organizations (e.g. health charities). Partnerships are primarily with national organizations, with some

collaboration at the international level. A sample of the IG's partners is found in Appendix 4.

IG's partnerships and collaborations with other entities took several forms, such as collaborating and convening to enable knowledge exchange and networks of researchers and practitioners, raising more research funding as well as increasing the capacity within specific research areas.

Partnerships have proven to be a significant contributor to funding research under IG mandate over time as depicted in [Figure E](#) (Appendix 3). The annual partner contributions to funding opportunities under IG mandate had an overall increasing trend from \$3.7 M to \$37 M between 2001-02 and 2015-16. Between 2010 and 2015, contributions from federal partners (29%) and international organizations (29%) comprised the largest shares of the partners' contribution to IG mandate. Collaborating with the Government of Canada, IG invested \$2.3 M in "Rare Diseases: Models and Mechanisms (RDMM)", a project supported by the Rare Diseases Research Catalyst Network and facilitates collaboration between basic and clinical scientists in functional studies of novel rare disease genes. Also the CIHR-Genome Canada partnership is one of the most significant public sector investments in personalized medicine. As of 2012, the partnership's cumulative investments surpassed \$165 M, including a combined total of \$68.8 M from CIHR, IG, ICR, INMHA, III, INMD and IHSPR.

Contributions from other partners involved, IG co-funding with the Canadian Gene Cure Foundation (CGCF) the "\$90,000 Champions of Genetics: Building the Next Generation Grant" in order to enable young scientists advance their genetic research while mentoring the next generation of scientists. Moreover, IG in collaboration with ICR, Genome Canada, the Canadian Agency for Drugs and Technologies in

Health (CADTH) and the Axe éthique et santé des populations, sponsored the Canadian GE3LS and Health Services & Policy Research Conference, which examined the integration of new genomic technologies into the healthcare system, at the level of practice and policy. The conference also considered the implications for patients and their families, as well as clinicians, health care systems and society at-large.

4. Operational Effectiveness

Overall, IG is viewed as operating effectively, while wider reforms^{19,20} at CIHR are viewed less favorably in terms of the resulting impacts.

The Institute is recognized as fostering successful working relationships and the levels of effectiveness, training, and organization are viewed positively. However, additional support and targeted funding was identified as potentially useful. Despite budgetary constraint, IG's pursuit of its strategic and operational plans has led to progress and the implementation of initiatives in various areas. In contrast, the implementation of reforms at CIHR are perceived as having been undertaken in a sub-optimal manner and are viewed as not particularly beneficial or useful to the Institutes. Additionally, the reforms are seen as resulting in reduced resources, such as funding.

The Institution within which IG operates receives \$1 M annually from CIHR as an Institute Support Grant (ISG). An annual average of 54% of the funds was spent on Institute Operations and the remainder was used for Institute Strategic Development. Because IG does not spend all of its ISG funding annually, the balance is transferred to the next fiscal year and therefore the total annual funds available for ISG exceed the

¹⁹ <http://www.cihr-irsc.gc.ca/e/47656.html>

²⁰ <http://www.cihr-irsc.gc.ca/e/50183.html>

\$1M allotment to the Institute every year
(Figure F, Appendix 3).

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VI. Appendices

Appendix 1: IG Review Panel Members' Affiliations and Conflict of Interest Declaration

Chair:

- **Daniel Durocher**, Senior Investigator, Lunenfeld-Tanenbaum Research Institute

Panel Members:

- **Bartha Knoppers**, Professor and Director, Centre of Genomics and Policy, McGill University, Canada
- **Monica Justice**, Professor of Molecular Genetics, Program Head and Senior Scientist, University of Toronto, Canada
- **Durhane Wong Rieger**, President and CEO of the Canadian Organization for Rare Disorders, Canada
- **Han Brunner**, Professor and Head of Clinical Genetics, Maastricht UMC+, Netherlands
- **David Valle**, Director, Institute of Genetic Medicine, Johns Hopkins University, US

Panel Member	Conflict of Interest Declaration
Daniel Durocher	Confirmed no real, apparent or potential conflict(s) of interest with respect to his involvement with the Review Panel
Bartha Knoppers	Confirmed no real, apparent or potential conflict(s) of interest with respect to his involvement with the Review Panel
Monica Justice	Confirmed no real, apparent or potential conflict(s) of interest with respect to his involvement with the Review Panel
Durhane Wong Rieger	Confirmed no real, apparent or potential conflict(s) of interest with respect to his involvement with the Review Panel
Han Brunner	Confirmed no real, apparent or potential conflict(s) of interest with respect to his involvement with the Review Panel
David Valle	Confirmed no real, apparent or potential conflict(s) of interest with respect to his involvement with the Review Panel

Appendix 2: Overview of Data Sources and Methods

Data source	Description
Situational Analysis (SA)	<ul style="list-style-type: none"> • Analysis of secondary data and documents, which aims to: <ul style="list-style-type: none"> - Present an overview of the evolution and current status of IG investments and activities, mapped against the four quadrants highlighted under CIHR’s Institute Review design. - Provide IG’s context and background within which the data collected from other lines of evidence (primary data collection methods) could be interpreted. • The SA covers the period from 2000-01 to 2015-16 and analyzes data from: <ul style="list-style-type: none"> - CIHR Electronic Information System (EIS) - Financial data for IG’s Institute Support Grant (ISG) - IG-related documents such as Strategic Plans, reports to the Governing Council, Internal Assessment Reports, and Website
Key informant interviews	<ul style="list-style-type: none"> • 30 min telephone interviews with 10 members of IG research communities who have worked with and/or are knowledgeable about IG, to gain informed perspectives on Institute relevance and performance. • Interviewees identified by Institute and vetted by the Panel Chair • Interviews conducted by the panel members and Chair during the 2 day face-to-face panel workshop or, in the case of a few interviews, by CIHR evaluation staff prior to or following the workshop.
Bibliometric Analysis	<ul style="list-style-type: none"> • Illustrate the position of Canada compared to the 10 most active countries in publications related to the Institute’s priority areas of: computational biology, precision medicine, epigenetics, rare diseases, genetics-ethical, legal and social issues, and genetics. • Provide information about the power of citation of Canadian publications, their number and the extent of international collaboration in publications within the Institute’s priority areas. • The bibliometric analysis was conducted by the Observatoire des sciences et des technologies, Centre interuniversitaire de recherche sur la science et la technologie.

Appendix 3: Key Figures and Tables

Figure A : CIHR Investment in IG Mandate by 2012-17 Research Priorities

Figure B: Investment in Capacity Building out of IG Budget

Figure C: Percentage of Direct Trainees Funded under IG Mandate

Figure D: Percentage of Indirect Trainees Supported under IG Mandate

Figure E: Leverage Ratio of Partnership to CIHR Investment in IG Mandate

Figure F: Utilization of Institute Support Grant (ISG) Budget

Figure A: CIHR Investment in IG Mandate by 2012-17 Research Priorities

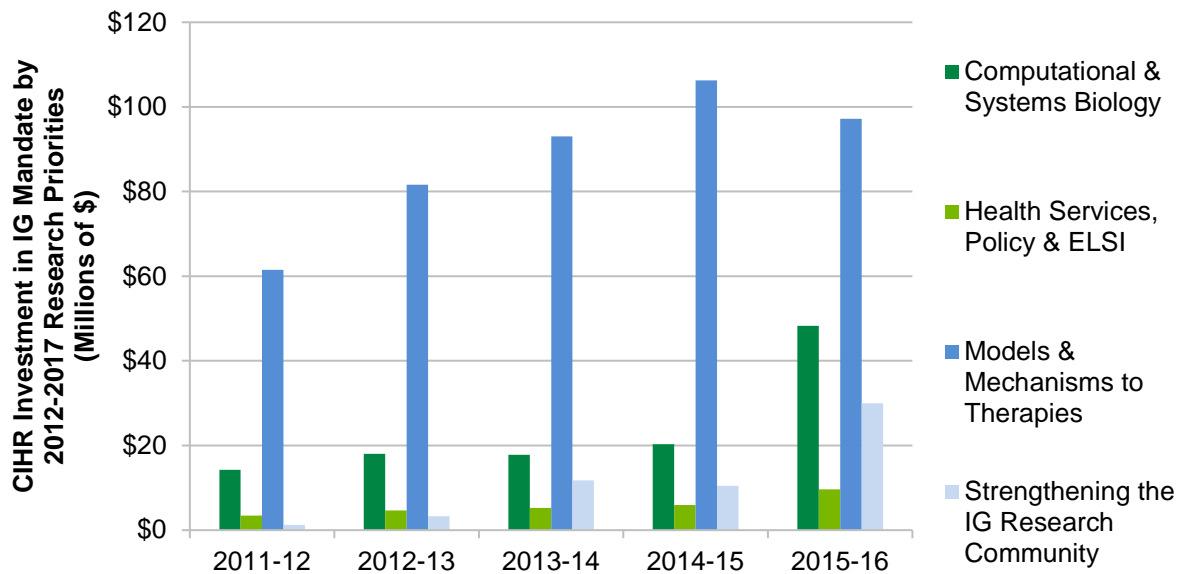
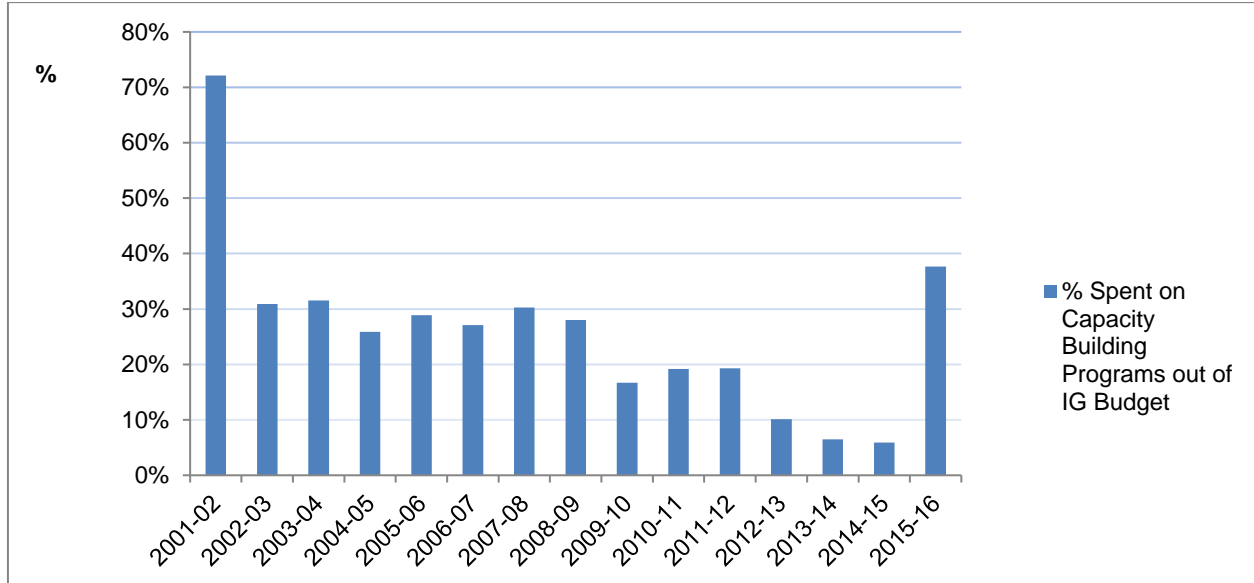
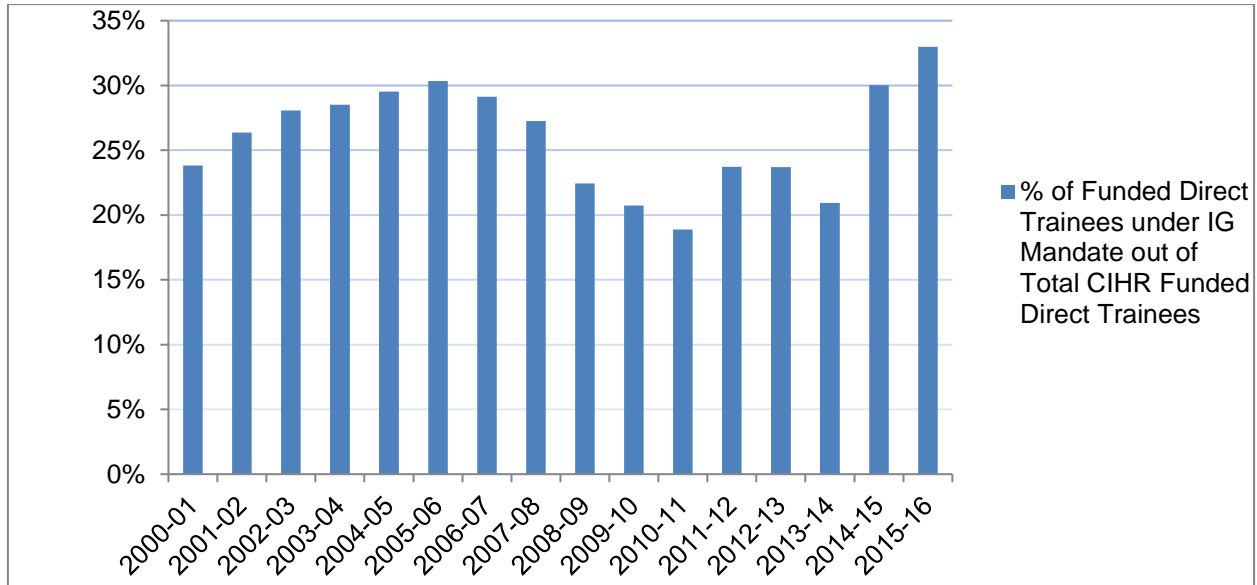


Figure B: Investment in Capacity Building out of IG Budget



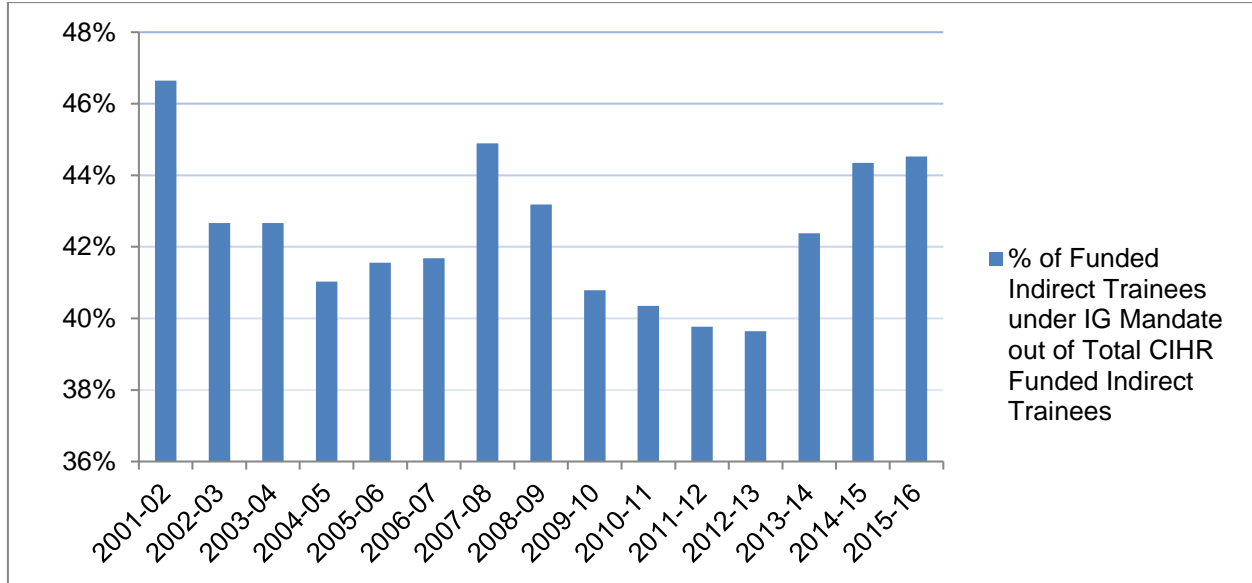
- IG's spending on Capacity building programs as a percentage of IG's annual budget had an overall decreasing trend (decreasing from 72% in 2001-2002 to 6% in 2014-15).
- It is worth noting that the percentage invested in capacity building in 2015-16 is high not due to an actual increase in the money spent but due to a drop in the institute Strategic budget to \$1 M because of commitments to the RAF.

Figure C: Percentage of Direct Trainees Funded under IG Mandate



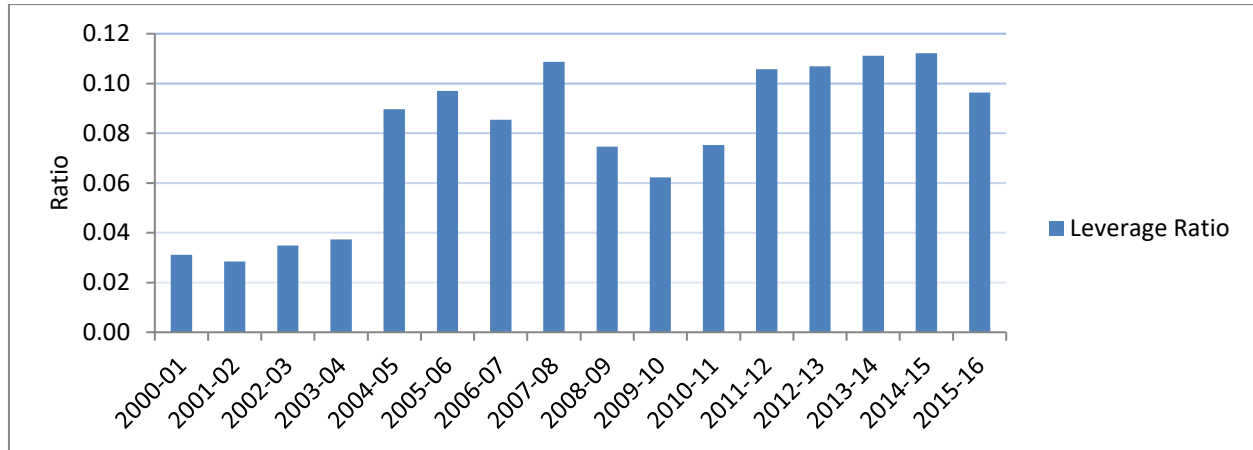
- The annual number of Direct Trainees funded under IG’s mandate expanded from 370 in 2000-01 to approximately 600 in 2006-07. The figure surpassed 730 in 2014-15 and 2015-16.
- The number of Direct Trainees funded under IG’s mandate, as a proportion of the total CIHR-funded direct trainees, ranged from 24% to 30% between 2000-01 and 2007-08. The minimum share (19%) was reached in 2010-11, while the maximum (33%) was achieved in 2015-16.

Figure D: Percentage of Indirect Trainees Supported under IG Mandate



- The number of Indirect Trainees funded under IG's mandate increased from 2001-02's 1,142 to 2,632 in 2006-07. The figure fell to roughly 2,600 during the next couple of years, and then experienced an uptick, ultimately reaching its maximum of 3,151 in 2013-14 before it fell again in 2015-16.
- The average annual percentage of the Indirect Trainees funded under IG's mandate out of the total number of those funded by CIHR was 42% over the past 15 years.

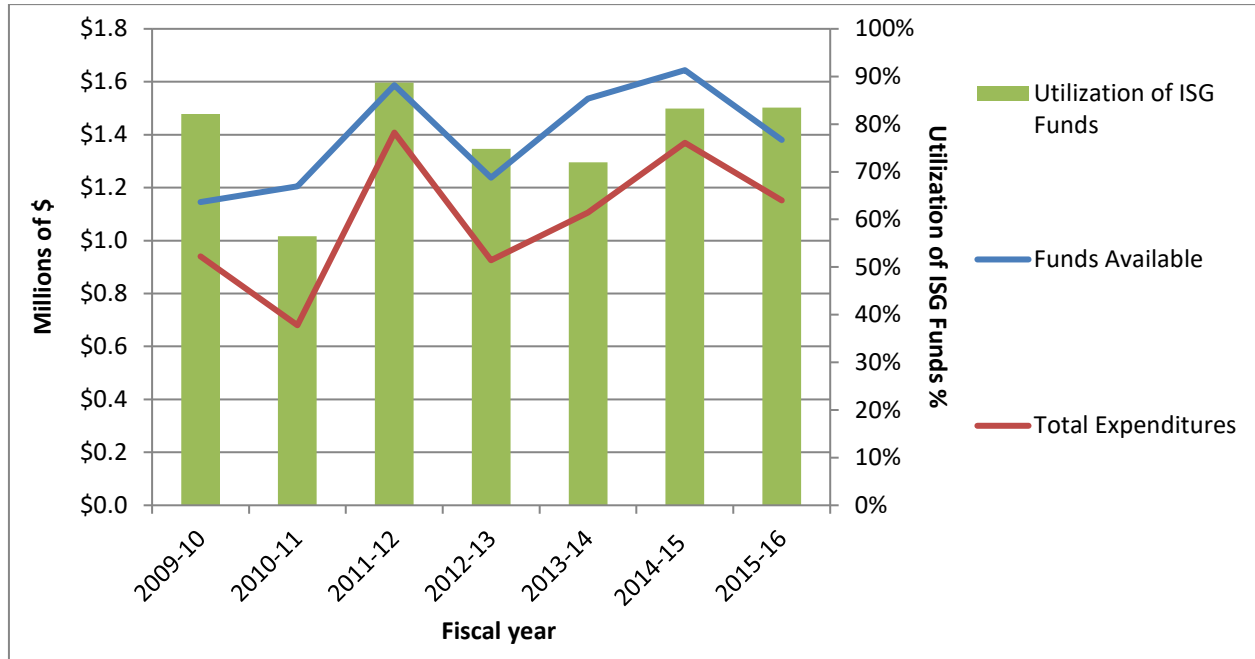
Figure E: Leverage Ratio of Partnership to CIHR Investment in IG Mandate



$$\text{Leverage ratio of Partnership} = \frac{\text{Partners' contributions to Institute's Mandate}}{\text{CIHR Investment in Institute's Mandate}}$$

- The leverage ratio of partnership to CIHR investment shows how much was invested in IG mandate through partner contributions for every dollar of CIHR investment in the IG's mandate areas. This ratio had an overall increasing trend from 0.03 to 0.11 (between 2000-01 and 2007-08). The ratio then dropped until it reached 0.08 in 2010-11 after which it rose to 0.11 and was maintained to 2014-15 before it slightly decreased to 0.10 in 2015-16.

Figure F: Utilization of Institute Support Grant (ISG) Budget



- The unspent portion of the annual Institute Support Grant (ISG) is transferred to the next fiscal year’s budget. Consequently, as the above chart indicates, the “Funds Available in \$M” exceeds the \$1M of ISG funds provided by CIHR each year.
- From 2009-10 to 2015-16, IG annually spent as little as 57% (2010-11) and as much as 88% (2011-12) of the ISG funds at its disposal.
- Given its sound management of its funds, IG will be able to ensure a 6-months period with the Montréal staff assisting the establishment of the new team and their introduction in the various networks developed under Paul’s current mandate. Expected balance at the end of this period is of \$20,000, which represents 0.25% of the overall \$8M budget managed over 8 years.

Appendix 4: Sample list of Partners

- National Research Council (NRC);
- Natural Sciences and Engineering Research Council (NSERC);
- Genome Canada;
- Health Canada;
- CIHR Institutes;
- Heart & Stroke Foundation;
- Cystic Fibrosis Foundation of Canada;
- Muscular Dystrophy Canada;
- Fonds de recherche du Québec;
- Kidney Foundation of Canada;
- Canadian Gene Cure Foundation (CGCF);
- Maternal Infant Child & Youth Research Network (MICYRN);
- Ataxia of Charlevoix-Saguenay Foundation;
- University of Toronto;
- Mount Sinai Hospital's Lunenfeld-Tanenbaum Research Institute;
- Canadian Agency for Drugs and Technologies in Health (CADTH);
- Axe éthique et santé des populations;
- Canadian Agency for Drugs and Technologies in Health (CADTH);
- Japan Science and Technology Agency (JST);
- French National Research Agency (ANR);
- German Federal Ministry of Education and Research (BMBF);
- European Commission;
- International Rare Diseases Research Consortium (IRDiRC);
- International Human Epigenome Consortium (IHEC);
- Structural Genomics Consortium (SGC);
- Autism Genome Project.