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September 19th, 2016

The Honourable Kirsty Duncan
Minister of Science

Recommendations to Canada's Fundamental Science Review

Dear Minister Duncan and Members of the Review Panel:

The Canadian Association for Neuroscience welcomes this opportunity to contribute to the development and improvement of the federal government's support of science through the Science Review, launched by the Honourable Kirsty Duncan on June 13, 2016.

Executive Summary

The Canadian Association for Neuroscience (CAN) represents approximately one thousand neuroscientists dedicated to advancing brain research who are working at academic institutions across the country. In order to contribute meaningfully to the Science Review and in light of recent reforms to the funding structure of the Canadian Institutes of Health Research, we recently surveyed our membership. We have submitted those survey results for the Review Panel, and present here the major recommendations arising from that survey, with more details presented in the following pages. Specifically, CAN recommends that:

1. The Government should provide strong support for fundamental, investigator-initiated basic research.
2. The Government should increase its investment in scientific research to enable Canada to regain its position as an international leader in science and technology.
3. Government funding mechanisms should support investigator-initiated projects in a large number of diverse laboratories.
4. Government funding mechanisms should maintain and/or institute high-quality peer-review to ensure funding of the very best research.



CAN-ACN

CANADIAN ASSOCIATION FOR NEUROSCIENCE
ASSOCIATION CANADIENNE DES NEUROSCIENCES

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Who we are

The Canadian Association for Neuroscience (CAN) represents neuroscientists in Canada who are dedicated to advancing brain research. Our association is composed of approximately one thousand researchers who work at academic institutions across the country. We share the common goal of ensuring neuroscience remains one of the greatest research and innovation strengths of Canada. Our research enterprises also play a key role in training the next generation of young scientists and technical staff who will be the foundation for the knowledge and innovation economy championed by the Government of Canada.

In order to contribute meaningfully to the Science review, we have surveyed our members about recent reforms to the funding structure of the Canadian Institutes of Health Research, the funding agency that provides the widest support for neuroscience research in Canada. We have combined the results of this survey with empirical data and evidence gathered from our members to define our position.

Our Position

1. The Government of Canada should provide strong support for fundamental, investigator-initiated basic research.

Public funding of scientific research supports intellectual independence, and the investigation of fundamental research questions by many independent laboratories. Fundamental (also called basic) research is driven by questions aiming to unveil the basic building blocks of natural systems and to understand how they operate. The diversity of approaches fostered by fundamental research funding is essential to generate new and transformative ideas and discoveries that let us tackle old problems or imagine new technologies.

Most impactful scientific discoveries, including those that have enabled important applied research discoveries, have come from fundamental research. Optogenetics, for example, is a new technology that allows researchers to selectively activate or inhibit the activity of specific brain circuits with light. This very powerful technology was made possible by the discovery of light-responsive proteins in organisms living in pond scum, and it has recently allowed Canadian researchers to make fundamental discoveries about the way memories are stored in the brain (Science 353:383-387 – July 22, 2016).

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CAN-ACN

CANADIAN ASSOCIATION FOR NEUROSCIENCE
ASSOCIATION CANADIENNE DES NEUROSCIENCES

Canada has made seminal contributions to knowledge and health in this way, as evidenced by the 17 Canadian-born scientists awarded Nobel Prizes in Physiology and Medicine, Chemistry and Physics. Fundamental research as supported by CIHR is also the driver for the engine of discovery for the pharmaceutical and biotechnology industries.

Growing concern about diminishing support for fundamental research was the most prevalent concern highlighted by our members in our recent survey. In the latest CIHR funding competition, a large number of applicants received short dismissive reviews simply because they used model organisms such as fruit flies, or their work could not be immediately translated clinically. Advances in our understanding of biology and medicine come from a broad, species-diverse program of fundamental research.

Why is basic, species-diverse discovery research so important? Our fundamental understanding of how the brain works is far from complete. Knowledge generated from curiosity-driven science is the foundation on which applied research is built. Without the robust support of fundamental science, the pipeline that drives innovation dries up. Untargeted basic biological research allows for creativity and alternative solutions that will create new tools to advance research and human health, and provide critical puzzle pieces that can eventually come together to yield real scientific and clinical breakthroughs. The use of model systems from bacteria to worms to mice is valuable because these organisms contain the same fundamental materials as those used by all living things. Studying simpler organisms allows us to gain a greater, more rigorous understanding of biological events that occur in humans, and thus to advance science in unforeseeable ways.

However, the CIHR has shifted from funding this type of discovery research to translational and/or applied research. This shift is evident in the description of CIHR's strategic direction before and after CIHR reforms. Prior to the reforms, CIHR strongly and unequivocally declared its support for fundamental discovery research, as follows:

"Knowledge creation, the first tenet of CIHR's mandate, is the source of changes to our understanding of the world around us. Each new contribution to the field of health science and technology brings us one step closer to understanding the origin of disease and developing the most effective ways of delivering care and promoting health. Because all scientific progress stems from curiosity-driven questions, CIHR has always provided – and will continue to provide – strong support for discovery-based research."



CAN-ACN

CANADIAN ASSOCIATION FOR NEUROSCIENCE
ASSOCIATION CANADIENNE DES NEUROSCIENCES

However, the new strategic plan implemented with the reforms lacks a clear commitment to supporting fundamental research, as exemplified by the following excerpt:

Strategic Direction 1 focuses on promoting excellence, creativity and breadth in health research and knowledge translation. It is our intent to break down barriers to create an enabling environment that will support world-class researchers in their pursuit of innovative ideas and approaches, from discovery to application. Success demands that we achieve a broader disciplinary mix of researchers across the spectrum of health, and foster a robust culture of excellence in knowledge creation and knowledge translation. This will be achieved through the implementation of CIHR's new Open Funding Schemes and peer review processes and the consideration of diverse and evolving ethical, legal and socio-cultural issues in health research, health policy and practice.

CAN unequivocally supports the return of robust funding for basic, investigator-initiated discovery research from all of the major funding agencies, including the CIHR. In the last decade, federal funding has shifted towards translation, applied research, commercialization and industry partnerships. While these initiatives can be useful when pursued in concert with fundamental research initiatives, in Canada they were introduced at the expense of curiosity-driven basic research. Successful industry partnerships, commercialization and clinical translation only occur when they can take advantage of and build upon made-in-Canada basic research discoveries.

2. The Government should increase its investment in scientific research to enable Canada to regain its position as an international leader in science and technology.

There is an immediate need to significantly increase funding for biological research in Canada in order to reverse the effects of a decade of diminished research support. Individual investigators comprise the backbone of Canada's scientific enterprise, but the success rate for investigator-initiated projects has fallen to less than half of what it was in 2000. Our members are deeply concerned about the current funding situation and are increasingly worried about the future of their laboratories. The budget for operating grants distributed by the CIHR was effectively reduced by approximately \$150 million since 2010. These funds provide training opportunities for graduate students and postdoctoral fellows, fund international scholars and create jobs for high-level technical staff. All three groups are key pieces of the knowledge and innovation economy of the future.



CAN-ACN

CANADIAN ASSOCIATION FOR NEUROSCIENCE
ASSOCIATION CANADIENNE DES NEUROSCIENCES

The vast majority of our members operate their laboratories with funds that are provided by federal granting agencies including the Natural Sciences and Engineering Research (NSERC), the Canadian Institutes of Health Research (CIHR) and Brain Canada.

Operating funds available from the CIHR budget have not kept up with inflation. Under the current funding conditions, an increasing number of laboratories must compete for a shrinking pot of operating funds. The success rate of CIHR grant applications was 34% in 2000. This rate has steadily decreased, reaching 13% in 2016. CIHR has announced that \$138M will be available for the next round of competitions. This means that the expected success rate is ~6-7%. At this historically low funding rate, laboratories will have no choice but to let highly skilled research assistants and technicians go. Training these professionals is a lengthy process, and these people are often the 'memory' of each laboratory with regard to sophisticated experimental approaches. Sadly, this loss has already started (see the Ottawa Citizen, August 19, 2015). After a decade of decreasing success rates, this extremely low success rate will cripple our research community's ability to maintain a healthy environment where new ideas and productive researchers can flourish.

In addition, a study by the journal eLife confirmed that peer-review of grant applications reliably predicts the top 20% of applications most likely to be productive and have a scientific impact, but not those applications within the top 20%. We therefore advocate a return to the 20% success rate, a level that ensures that most of the meritorious applications and ideas can be funded, and minimizes the likelihood that the next key, transformational discovery will fail to be funded.

In this regard, we present here a number of key statistics:

- According to the latest report of the Science, Technology and Innovation Council (Advisory Council to the Government of Canada): *"Despite its priority status, however, Canada is not investing in neurosciences at a competitive scale in comparison with the United States (U.S.). Total federal funding for neuroscience research is only about 40% of that in the U.S., even after adjusting for the size of the U.S. economy which is about 11 times larger than Canada's economy."*
- Investment in research in Canada has fallen from 2 % of total GDP in 2004 to 1.6% in 2014 (<https://data.oecd.org/chart/4Cy8>). Between 2006 and 2014, Canada's rank has slipped from 16th to 24th among OECD countries (Annex 1, page 47 of the 2015 Report of the Science, Technology and Innovation Council - Advisory Council to the Government of Canada)

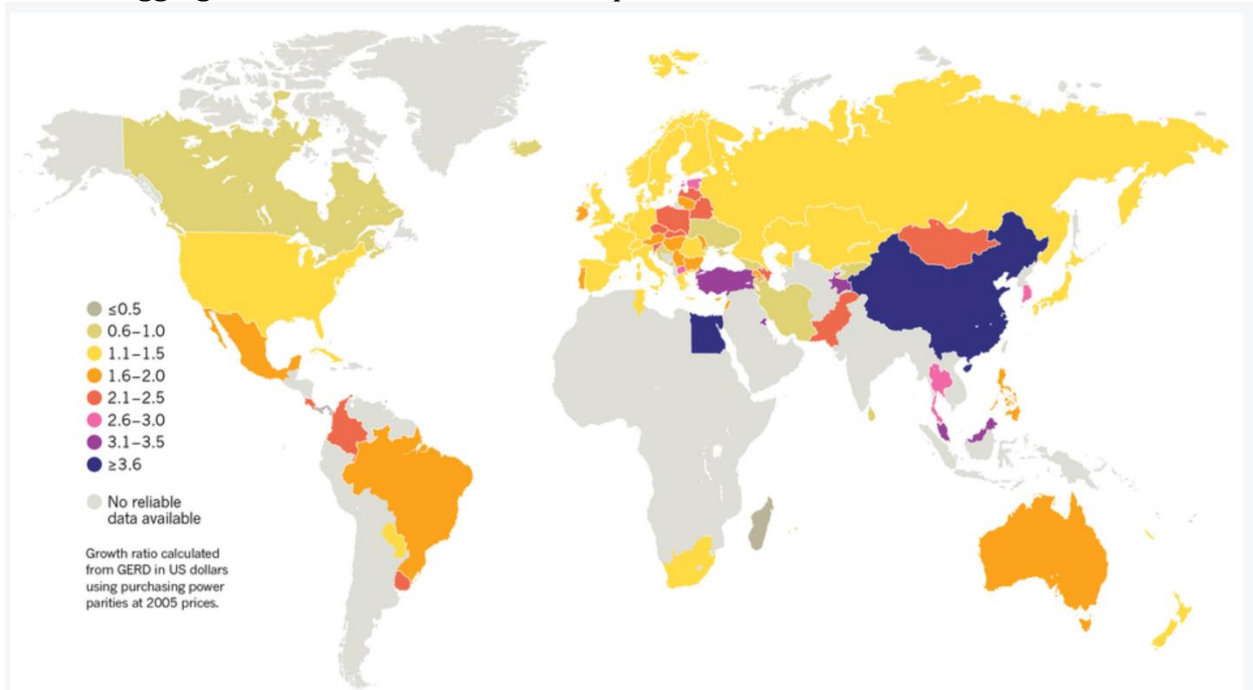


CAN-ACN

CANADIAN ASSOCIATION FOR NEUROSCIENCE
ASSOCIATION CANADIENNE DES NEUROSCIENCES

- The compound annual growth rate in biomedical R&D in Canada is currently negative, having decreased by 2.6%. (N Engl J Med 2014; 370:3-6)

In addition, a recent publication in the scientific journal Nature shows that the level of growth in gross domestic expenditures on research and development between 2003 and 2013 is lagging relative to most other developed countries.



http://www.nature.com/nature/journal/v537/n7618_supp/full/537S2a.html

As we expressed in a letter to the Honourable Bill Morneau as part of the pre-budget consultation, we strongly believe *that the CIHR budget would need an immediate injection of \$500M for 2017 to avoid high numbers of lab closures and significant brain drain*. In this letter we also highlighted *the need to double research budgets for the NSERC and CIHR* in order to reverse the trend of scientists facing increasingly limited access to operating funds.

3. Government funding mechanisms should support investigator-initiated projects in a large number of diverse laboratories.

One of the key elements of the CIHR reforms was the transition to a Foundation + Project Scheme where established researchers could apply for Foundation grants and consolidate their multiple previous grants into a single application. Recipients of a Foundation award were provided funding for 7 years. The aim of this new funding structure was to provide stable funding for highly successful laboratories. This concept



CAN-ACN

CANADIAN ASSOCIATION FOR NEUROSCIENCE
ASSOCIATION CANADIENNE DES NEUROSCIENCES

has been positively viewed by a large segment of the research community. This idea could help outstanding laboratories to focus on research instead of continuously writing grant applications. In contrast to the Foundation awards, Project awards are meant to fund single projects for 5 or fewer years.

However, this type of new funding structure and the concomitant longer-term burden on the budget could only be successfully introduced with sufficient financial support to do so. Unfortunately, this new structure was implemented without any injection of additional funds to the CIHR budget, resulting in a shift of funding to those investigators with large laboratories and multiple CIHR grants via the Foundation scheme. In particular, 45% of all operating funds have now been channelled to the Foundation Scheme leaving only 55% of the budget for the Project Scheme, in spite of the fact that the Project Scheme provides funds for the large majority of Canadian biomedical research laboratories. This shift towards larger, well-established laboratories has left smaller but equally productive laboratories grappling for very limited funds. Young investigators starting their own laboratories and mid-career researchers whose projects just started to take off were particularly hard hit by these changes. ***The Government must act to ensure equal opportunity for securing research funding across various career stages and in various types of research laboratories.*** In order to accomplish this objective, ***we suggest shifting a larger portion of the CIHR budget to the Project Scheme.*** In our survey, 93 % of our members thought that Foundation grants should receive 25% or less of the total budget allocated for operating grants.

Science funding should nourish a very large and diverse environment from where original, often unexpected discoveries can emerge. Without a strong research base pursued in a large number of well-supported, productive laboratories of all sizes and led by investigators at all career stages, we limit our chances of discovering novel molecular, cellular and network components and interactions that are essential to properly understanding the function of the healthy and diseased brain. Canada is fortunate in having many highly-talented scientists from all over the world working in our academic institutions. We should take advantage of this pool of talent by supporting their ideas and allowing their research to flourish. For these reasons, ***CAN supports robust funding for untargeted, investigator-initiated projects in diverse laboratories run by investigators at all career stages.***

4. Government funding mechanisms should maintain and/or institute high-quality peer-review to ensure funding of the very best research.

In addition to the recent switch to a Foundation + Project Scheme, the CIHR coincidentally moved to a new, largely virtual, review format. The vast majority of researchers who took our survey (80.8%) believe that this newly implemented review system is fundamentally flawed and needs to be redesigned. Our members, many of



CAN-ACN

CANADIAN ASSOCIATION FOR NEUROSCIENCE
ASSOCIATION CANADIENNE DES NEUROSCIENCES

whom acted as Chairs and Reviewers in the new system, in addition to having their own applications reviewed, have reported high number of cases where reviewers were simply unqualified to judge the applications. The new system also suffered from multiple problems stemming from an unreliable grading system and lack of reviewer accountability. Thanks to the quick intervention of the Minister of Health, the Honourable Jane Philpott, a working group has already made the first necessary steps to correct serious flaws in the peer-review system of the CIHR.

In response to this upheaval, CAN is taking a considered position on best practices for peer review. First, peer review needs to be conducted by scientists. Scientists need to be involved in all steps of the review process, including the assignment of reviewers, since only they have the necessary knowledge to determine whether grant applications have the appropriate reviewers. Second, face-to-face meetings, which were eliminated in the CIHR reforms, are the gold standard for peer-review. When reviewers meet in person, they are held accountable for their opinions. Face-to-face meetings force reviewers to express opinions that are void of bias and unjustified criticism, since these are readily detected and corrected by other committee members. Face-to-face meetings are essential to ensure that all grant applications are evaluated fairly, in a format that allows the free expression of ideas without artificial categories, thereby allowing reviewers to gain sufficient in-depth insight into the research project. In this regard, the vast majority of our members and CAN itself strong support the return of face-to-face meetings to ensure that applications are judged by experts who are fully accountable for their opinions.

The Canadian Association for Neuroscience wishes to express its gratitude toward the Government of Canada and the Honourable Kirsty Duncan for opening the dialogue between scientists and elected officials, and for its consideration of our input into this review. We are open and available to continue this dialogue, if so desired.

Sincerely yours,

Freda Miller, PhD, FRSC
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