

April 23rd, 2012

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CIHR Science Council
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Dear Dr. Beaudet, Dr. Aubin and Dr. Lasko,

As faculty of the biomedical research community at the Université de Montréal, we wish to thank CIHR for the opportunity to provide feedback on the proposed reforms to the operating grants competition and peer review process. This letter and its recommendations are supported unanimously by 79 principal investigators who are members of different Departments (Biochemistry, Chemistry, Informatics, Medicine, Microbiology and Immunology, Ophthalmology, Pathology and Cell Biology, Pharmacology, Physiology, Stomatology), Research Institutes (Institute for Research in Immunology and Cancer - IRIC, Institut de Recherches Cliniques de Montréal - IRCM, CHUM Research Centre, Montreal Heart Institute, Maisonneuve-Rosemont Research Centre, Sacré-Cœur Hospital Research Centre, Ste.-Justine Research Center) and Faculties (Medicine, Pharmacy, Arts and Sciences, Dentistry) at our institution.

The cosignatories of this letter represent a spectrum of junior to senior CIHR-funded investigators, with extensive experience as peer reviewers for the CIHR as well as for many other national and international agencies including CFI, CCSRI, NSERC, FRSQ, FQRNT, NIH, NSF, LLS, Pew Foundation, the Wellcome Trust, CRUK, BBSRC, MRC, the European Commission, ERC, ANR, HFSP, SNF, and ISF. Based on our collective expertise and experience in competitive research funding and peer review, we would like to unequivocally state three primary concerns:

- The fundamental problem faced by the biomedical research community is a shortfall in the open operating grant envelope and historically low funding success rates, and not a problem with either the peer review process or the structure of the open operating grant scheme.
- A radical revision of the CIHR peer review system is not justified and, if undertaken, would seriously exacerbate the problems already caused by low funding success rates
- A two-tier operating grant system of "foundational" and "project" grants will stifle innovation and competitiveness, with potential long term negative effects on biomedical research in Canada

The basis for these concerns and the ramifications for Canadian biomedical research are described below. We follow this analysis by what we hope is a set of constructive suggestions as to how the current system can be improved through cost-effective and non-disruptive adjustments.

1. Is there an actual case for radical overhaul of the CIHR system? Cause versus effect.

The CIHR discussion document of February 8th is framed by numerous claims of "barriers" to success and the overarching assertion that "The time has come to re-design the existing system" (p14). We see no basis in fact for these claims. The only dominant barriers to success - as articulated in the International Review Panel (IRP) report of 2011 - are the now chronic shortfalls of open operating funds and the multiplicity of often ineffective strategic initiatives. The funding shortfall has been brought on in part on the well known mismatch between increased investments in researcher recruitment (CRC and CERC) and infrastructure renewal (CFI) on the one hand, versus the flat number of total operating grants awarded on the other. As CIHR statistics show (<http://www.cihr-irsc.gc.ca/e/44063.html#fig9>), the total number of awards funded per year was unchanged over the period 2000/2001 (801 awards) – 2009/2010 (797 awards) but overall success rates dropped from 33.7% to 21.7% over this same period due to markedly increased application pressure. We note that these annual success rates are artificially inflated by the inclusion of small bridging and priority announcement grants. In the Fall 2011 competition 401 of 2294 applications were funded, for a real success rate of 17.4% (<http://www.cihr-irsc.gc.ca/e/44779.html>). At the same time, the fraction of total CIHR budget designated as "strategic" increased from 10% in 2000/2001 to 33% in 2009/2010. These problems will be exacerbated by the additional fiscal pressures facing CIHR in the 2012 Federal budget. The IRP report clearly identifies underfunding of operating grants and the proliferation of programs as primary issues of concern, but does not find any fault with the review process itself. While the IRP openly commented that larger grants would help improve the competitiveness of Canada's leading researchers, a two-tier funding system was not advocated.

The CIHR cites informal internal surveys and general dissatisfaction with the grant award process as the prima facie reason that the entire system must be redesigned. The one certain correlation that can be drawn is that dissatisfaction has grown in direct proportion to the drop in funding success rates. Instead however, CIHR reaches the overarching conclusion that panel-based peer review has failed and that it should be replaced with a virtual review process based on a large "college" of reviewers. A valid concern raised by CIHR is that the strongest investigators have disengaged from the review process, in large part because their time is consumed by cycles of writing many small grants with low funding success rates. This concern does not, however, mean that the peer review system is fundamentally flawed. No review system can solve the problem of arbitrary funding decisions when cutoffs are determined by second decimal fluctuations in scores. We strongly contend that there is no rational case for disassembling the panel-based review system, much less for replacing it with a less rigorous virtual review mechanism.

2. Panel-based review meetings versus internet-based virtual review.

The claimed advantages of anonymous internet-based "college of reviewers" over face-to-face panel-based review do not bear scrutiny.

(i) Reviewer integrity and accountability. There is no substitute for the accountability that comes from the knowledge that a reviewer will have to defend his/her evaluation in person before a panel of experts. In contrast, virtual reviewers have no such accountability and this opens the door to biased review. The arbitrariness of virtual grant review will be magnified greatly by the all-or-none consequences of funding decisions on a research program.

(ii) Reviewer efficiency and workload. The argument that a virtual review process will allow more efficient use of reviewer time is not supported by the facts. First, the vast majority of time spent in review of a grant application is in the careful reading of the proposal, investigation of the literature to understand background knowledge and evaluate significance, and consideration of the applicant's track record and scientific impact. For robust analysis, all of this must be undertaken regardless of whether the review is presented at a panel or electronically. Second, if as proposed

more reviewers are to be engaged (e.g., 5-8 reviewers per grant), the reviewer load will greatly increase on a per grant basis. According to CIHR estimates, the college of reviewers will require evaluation of 15-20 applications per reviewer over two different stages, compared to the current number of 9 or 10 applications assigned to each reviewer on an average panel. The solution to the futile grant cycle problem is not an increased number of shallow reviews. In our collective experience, there is not a single example world-wide of a successful, large open operating grant competition that functions through virtual review. In contrast, we can cite many examples of flawed outcomes based on different incarnations of virtual review, including the European Commission, the UK research councils, and the recently terminated NIH Eureka program.

(iii) Score variation. The problem of reviewer score variation in internet-based review is well documented, both internally in CIHR fellowship programs and externally in the UK and Europe. This problem cannot be solved by even large numbers of virtual reviewers, especially when funding pay-lines are tight and miniscule variation determines whether an application is funded or not. This problem is exacerbated by the fact that in virtual review no single set of reviewers is assigned to more than one grant, i.e., a relative ranking of applications is impossible. In contrast, panel-based review provides a clear mechanism to establish a relative ranking of all grants based on a full panel discussion of each application. The cited literature that claims bias in NIH peer review (Johnston PNAS 2008; Kaplan et al PLoS ONE 2008; Kaplan FASEB J 2007) is based on flawed assumptions (e.g., see comments at <http://www.nature.com/news/2008/080728/full/news.2008.988.html>). A recent analysis of NIH scores suggests that panel-based discussions play an important role for determining the final scores for a significant fraction of applications (Martin et al PLoS ONE 2010). Expert decision-making at the leading edge of knowledge cannot be achieved by any amount of training, structured forms or multi-staged review. Further, on-line live discussions of review panels have been trialed by NIH (e.g., in the EUREKA program) and rejected as a means of engendering fair review.

(iv) Triage at the LOI stage. This approach combines the flaws of virtual review with an initial application that contains minimal information. LOIs provide essentially no basis for meaningful evaluation as they relate neither scientific details of the proposal nor the track record of the investigator, both of which are key determinants of research success and impact. Moreover, given the minimal effort needed to write an LOI, it can be expected that the number of LOIs will greatly exceed the current application rates, which will increase reviewer burden and add considerable noise to the go-forward decision. In contrast, with full applications, panels are able to effectively triage the weakest proposals on the basis of all parameters, and provide valuable critical feedback to applicants. A triage stage based on LOIs will only exacerbate the funding crisis by making initial decisions more arbitrary and less accountable.

(v) Virtual review followed by a general panel. This system is essentially followed in the UK, where random assortments of 8 or 9 virtual reviews of highly variable depth and quality are used to numerically rank application and then assessed by a general oversight panel that typically gives applications no more than a cursory read. A general panel is in no position to evaluate the details of the science, particularly for large numbers of applications. If, on the other hand, such panels were structured to possess the requisite expertise and depth of coverage, then there would literally be no need for virtual reviewers.

In summary, a panel of critical, broadly knowledgeable and experienced scientists that engage through transparent and unbiased discussions is the only proven mechanism for fair and open review. This mechanism has been used in Canada and the US for decades, and has underpinned the many fundamental discoveries that have fostered innumerable biomedical breakthroughs as well as the entire biotechnology sector in the US. The claim that this system has failed is simply unsupported. There is an unquestionable desire in the Canadian community to strengthen panel composition. Below we offer simple, low-cost suggestion to immediately improve the quality of peer review (see section 4).

3. Unintended consequences of a two-tier funding system.

As is widely acknowledged, and cited by the 2011 IRP report, the CIHR system has entered into an increasingly futile state wherein more and more grants are written and success rates are lower and lower. This problem could, in the first instance, be alleviated by an increase in the size of each individual award, thereby reducing the number of grants that need to be written and reviewed. Several parameters bear on the optimal grant size but in general the level of support should be for a credible team of 4-6 individuals in any given research area. The NIH system, which has been well honed over time, supports about this number of individuals per R01 grant, which is now at an average of \$350K per year, after subtraction of indirect costs. The average size of a CIHR grant, currently \$123K per year, has always been too small to build a critical team mass on a single grant. While sound arguments can be made to increase the average grant size, these arguments cannot be taken to justify a two tier system based on a limited number of larger "foundational" grants and a pool of smaller "project" grants. The two-tier system as proposed by CIHR raises myriad conceptual and logistical concerns.

(i) Assessment based on ideas versus track record. The claim "Around the world, two main funding approaches have been found to be successful in enabling innovation and supporting research excellence" (p13) is an oversimplification that represents two extremes. These crucial assessment parameters should never be segregated. Scientific excellence is best evaluated according to a combination of parameters - concepts and ideas, feasibility and technical knowhow, investigator track record and research environment - all of which are taken into account by expert panel-based review, as in the current NIH and CIHR systems.

(ii) A two-tier culture. The arbitrary distinction between the award of foundational and project grants will lead to a culture in which most researchers are restricted to small, short term operating grants, while a select few have the luxury of higher level support for long periods of time. The transition between these extremes is intrinsically difficult to manage and will lead to a host of operational issues, including the complexity of evaluation of two distinct streams of applications.

(iii) Small short term grants are inimical to sustainable and innovative science. Project grants will be intrinsically difficult to renew, both because it will be problematic to build critical research mass with short time frames and because of increased competition for a more limited pool of grants. In the UK, small project grants tend to fund science of very limited scope and negligible impact, which is carried out in tiny groups that are unable to build research momentum. The two-tier system will create a large underclass of researchers who will have little prospect of building a sustainable research program.

(iv) Bias against early stage investigators. The proposed project grant scheme would selectively disfavour the career development of new investigators. These small grants will be of insufficient scale or term to build a competitive program, such that junior investigators will face an extreme uphill climb at the outset of their careers, with poor prospects of transitioning to the limited pool of foundational awards. A new investigator sub-stream of the foundational grants will not solve the essence of the problem since the decision to fund at a high initial level would then become essentially arbitrary. If the career progression of new investigators is further compromised, the long term excellence of Canadian science will be irretrievably eroded, and the substantial start-up investments made in new investigators will be lost.

(v) Single large program grants may suppress innovative science. The larger foundational grants may engender a limited class of moderately well-funded researchers, but will unfortunately not stimulate excellence. These single awards, under which additional applications to support new directions or ideas will be forbidden, may have the unintended effect of stifling innovation by Canada's best researchers. That is, the natural tendency will be to focus on safe science with the primary goal of obtaining renewal funding as to do otherwise would risk the researcher's entire program through catastrophic loss of all funding. In the direct experience of some of our faculty, this pattern is evident for holders of single large program grants in the UK.

(vi) A two-tier system is intrinsically non-adaptive and non-scalable. A key underappreciated feature of the current operating grant system is its scalability. This feature is critical both to fund innovation through new grants, and to match the variability in the natural career progression of all investigators. Ambitious new investigators with good ideas and a strong early track record can apply for additional grants. Senior researchers with a high risk potentially

transformative idea can similarly compete for new funding, without jeopardizing their existing core research programs. Conversely, if an aspect of a research program underperforms and a particular grant is not renewed, the entire research program is not lost. Importantly, the absence of any intrinsic cap in the current operating grant system provides incentive for Canada's best researchers to build strong, sustainable and well-funded programs based on multiple CIHR grants that cover several avenues of enquiry. This feature has likewise served the NIH extremely well. The locked-in single program grant model removes this competitive incentive. In the UK, the transition of the Wellcome Trust to an HHMI-like investigator program model, in which very few researchers will be funded, is decimating many strong research groups that fail to make the transition to the investigator-level award.

(vii) Recruitment and retention. We believe there is a serious risk that the above issues will rapidly impair Canada's ability to attract and/or retain both outstanding junior and senior investigators. The capture of top scientific talent in the face of international competition depends on the fairness of review, access to adequate grant support, and an open-ended potential to support innovative science.

To summarize, in the best case scenario, the proposed two-tier system will offer no advantage and will sow confusion and complexity. In the worst case scenario, it will achieve precisely the opposite of the desired goal of research excellence. A two tier system will very likely undermine the career progression of new investigators, and cripple the long term potential of Canadian biomedical research.

4. Recommendations from the researcher's perspective.

The root problem of the current crisis will ultimately only be solved by re-normalizing funding success rates to a historically productive level of at least 25%, not including bridging or priority announcement grants. Radical changes to the review and funding systems will not solve this problem, and will instead only exacerbate the stress on the research community. To ensure that Canada's research investments are dedicated to the best possible science, we would like to table the following 5 suggestions for low-cost and non-disruptive improvements to the existing CIHR framework.

(i) Allocate strategic funding to the open operating grant competition. The ostensible 70:30 ratio of operating to strategic funds is in fact an exaggeration of the funds that are directed to open grant competitions, which by CIHR's own statistics are currently at 43.5% of total budget for panel-based competitions. Moreover, the 70:30 split is an arbitrary ratio established by unexplained criteria at the outset of CIHR. Strategic initiatives often take too long to implement, typically exclude the majority of the research community, are typically less competitive, and are non-sustainable. A reduction in excessive strategic initiatives in favour of open operating grants was a specific recommendation in the IRP report. We concur with the IRP that Canadian biomedical science would be well served by re-invigorating the open competition by re-allocating funds from the enshrined strategic initiative envelope. This solution could be achieved in the first instance without any net increase in the overall CIHR budget.

(ii) Improved scientific excellence of panels. The quality of peer review panels has gradually eroded, in part due to the lack of participation of Canada's scientific leaders, but is by no means irretrievably lost. The reasons for the lack of engagement on panels are complex. We believe that participation rates could be improved by giving more power to panel chairs to aid in the selection process and to actively recruit senior researchers with strong track records. It is essential that all reviewer credentials are vetted by more than just keywords in a CIHR database: Does he/she have a strong track record in funding? An established international reputation? Publication in high impact journals? A record of transformative and/or highly cited publications in the appropriate fields? The current administratively-driven selection process encumbers panels with members who have not published significant research for many years and/or who have not held relevant peer-reviewed funding. Such reviewers in fact account for much of the score variation. These stringent selection criteria should also be applied to panel chairs given their critical role. Most importantly, each panel chair should be an undisputed leader in the relevant field for the panel.

(iii) Re-normalization of the CIHR panel portfolio. As emphasized by the IRP report, CIHR has a profusion of panels, including a number with closely overlapping mandates. Despite the increase in funding pressure, the expansion of panels at CIHR has meant that the number of grants reviewed per panels has in fact declined. Many

panels review less than 40 grants and, in the extreme, some panels only award 1 or 2 grants per competition. As a consequence, the arbitrary decision as to which panel a grant is reviewed at can have a disproportionate impact on the chances of success, due to random partitioning effects. We recommend that related panels be merged to allow more grants to be reviewed per panel. As at NIH, and previously in Canada, an average of 70 applications per panel, with about 12 applications per reviewer, is a reasonable scale. An advantage of consolidated panels is that fewer total reviewers are needed. In addition, more consistency and fairer relative ranking will result because the grant pool per panel is larger.

(iv) Panel concordance with research trends. We are concerned that the historical panel structure may not adapt well to rapidly changing trends in research. For example, computational biology is of burgeoning importance, yet has been notoriously difficult to fund at CIHR because of the limited mandate of the genomics panel. Systems biology and most recently synthetic biology have befallen the same fate. The solution we propose is not to create more panels or to disperse review to random collections of reviewers, but rather to ensure that panel expertise accurately reflects these research trends. Larger panels with a broader mandate, and a greater depth of expertise and scientific acumen, would ensure fair and flexible review of leading applications in new fields. For example, a genomics-based panel should easily be able to review grants on computational, systems and synthetic biology. The arguments concerning reviewer specialization made by CIHR fail to take into account an important trend, namely the growing multidisciplinary nature of many individual researchers. Only in rare cases where application pressure warrants, should new panels be created.

(v) Optimal grant size. As argued by the IRP report, the average size of CIHR grants should be increased to allow a single grant to support a dedicated avenue of investigation, with the expectation that the bar for award of multiple grants be raised concomitantly higher. This would eliminate the problem of researchers applying for multiple closely related grants in order to support a single research activity. To put this in perspective, the current average CIHR grant is \$123K. In contrast, the average for an R01-type NIH grant is \$350K (\$450K less the average of 28.5% in indirect costs), which substantially exceeds the CIHR average, even after principal investigator salary is deducted. It is no wonder Canadian scientists must resort to writing multiple grants. In place of the proposed two-tier system, the efforts of Canada's best researchers could be directly stimulated by a merit award-type supplement added to the top 5-10% of grants, as determined by panel ranking.

To summarize our two main concerns with the proposed reforms: 1) We believe that CIHR should not replace a proven and fundamentally sound peer review system with one in which accountability, open critical discussion, and in-depth review are disbanded. 2) We believe that a two-tier funding system has the potential to do rapid, deep and long-term harm to Canadian biomedical science. As the great majority of the CIHR research community is opposed to the fundamental features of the proposed reforms we do not see how CIHR can proceed without substantial further consultation and a true mandate from the community. We respectfully propose that the reform process be advised by a panel of Canadian scientific leaders who directly reflect the interests of the research community.

In closing, we would like to express our appreciation to CIHR for engaging in this consultative process, which we hope will ultimately be manifest as cost-effective and non-disruptive improvements to the funding and review systems.

All of the cosignatories on the attached list have agreed to the content of this letter.

Sincerely,



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