#### **CIHR Project Grant: Research Summary & PRC Justification Guidelines**

Last updated on July 10, 2023 for the Fall 2023 CIHR Project Grant competition.

## A) Research Summary

The 3,500-character (including spaces) Research Summary serves different purposes at Registration (Registration Stage Task 3: Complete Summary) and Application (Application Stage Task 3: Complete Summary), and can be revised between these two stages. As such, consider tailoring it for the intended audiences at each stage.

- 1) At the Registration stage, the Summary is a key source of information for Competition Chairs and Scientific Officers (SOs) to determine alignment with the Peer Review Committee (PRC) mandate, and for peer reviewers to assess their conflicts and ability to review the proposal. **Note:** As of the Fall 2022 competition, CIHR stipulates that, if you do not complete this section as outlined in the instructions (i.e., <u>Registration Stage Task 3: Complete Summary</u>), your Registration will be withdrawn. **Tip:** Use keywords from your chosen PRC's mandate.
- 2) At the Application stage, the Summary serves as an important introduction/overview of the Research Proposal for peer reviewers. **Tips:** (1) In addition to addressing the three <u>adjudication criteria</u>, include sex and/or gender details, as appropriate, as well as any other critical points from your 10-page Research Proposal (e.g., overview of knowledge translation (KT) plan). (2) Do not change content between Registration and Application so significantly that a reviewer mismatch results.

To clearly orient and focus the attention of: (1) Chairs and SOs to the appropriateness of your research project for their PRC (*i.e.*, so they agree to review it); and (2) the three assigned reviewers and remaining committee members, SPARC recommends a slightly different number and organization of headings than CIHR. Overall, this structure is designed to enable reviewers to more quickly and easily identify key points of interest, so as to be able to use the Summary as a useful and concise point of reference during PRC discussions.

- Goal: State overall study goal upfront to draw in reviewers
- **Significance:** Detail the reason for the study, which may include a summary of the state of the science and/or the knowledge gap addressed by the project (~2-4 lines)
- Aims (or Objectives): List 1-4 aims
- Approaches: Provide enough methodological details for reviewers to assess their ability to review
- Team: Show you have the expertise/experience needed for the work
- **KT:** Summarize your primary dissemination activities
- Impact (or Expected Outcomes): Remind reviewers of what will result at the end of the project and tie this back to the original goal

These sub-headings are particularly appropriate for Biomedical and Clinical research projects. Adjustments may be needed to tailor the Summary more appropriately for Health Services or Population Health proposals (*e.g.*, Research Questions instead of Aims, knowledge translation and engagement activities embedded throughout the application for integrated KT projects).



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## **B) Peer Review Committee Justification**

Applicants are required to select and justify – in textboxes of 750 characters (including spaces) – one or two PRCs (<u>Task 5: Complete Peer Review Administration Information</u>). **Note:** PRC selection cannot be changed at the Application stage.

**PRC Selection:** SPARC recommends **selecting only one PRC** to avoid being 'bumped' to your second choice – or another – PRC, which may result in a lower score and final ranking.

- Look through the <u>list of ~50 PRCs and their mandates</u> to identify the most appropriate expertise to assess your research project.
- Look at previously funded submissions by PRC by browsing the online <u>CIHR Funding Decisions</u> <u>Database</u>. Use the three letter PRC acronym as the keyword, then press the "Search" button. Access only Project Grants by filtering by Program. **Tip:** If the Project Title, Investigators, Keywords and Abstract/Summary are familiar to you, then you're on the right track.
- If you have not submitted an application to your selected PRC before, check the <u>list of past</u> reviewers, Chairs and SOs for this PRC, and ask any members from UBC if the committee is appropriate for your research.

**PRC Justification:** Applicants, and particularly those with an interdisciplinary project that aligns with two PRC mandates, must **clearly delineate** why the proposal should be assigned to your selected PRC(s). Include keywords/descriptors from the relevant PRC mandate(s) to build a case for your preferred PRC (*i.e.*, why it's a good fit), so that it does not end up assigned to a non-suggested PRC. For example:

- Quote the relevant part of the PRC mandate;
- Describe which types of experts (as described in the mandate) would be most appropriate to review your application; and
- State the significant and expected impact of the project.

**Reminder:** There are four PRCs with special considerations. For applicants considering applying to any of these panels, please familiarize yourself with these details:

- 1. Commercialization, CMZ
- 2. Indigenous Health Research, IHR
- 3. Randomized Control Trials, RCTs
- 4. <u>Tri-Agency Interdisciplinary, TIR</u> (new as of Fall 2021; part of the Tri-Agency Interdisciplinary Peer Review Committee)

## A Primer on the Tri-Agency Interdisciplinary Peer Review Committee Pilot

• Health-focused applications that clearly use interdisciplinary approaches (*e.g.*, represent research across disciplines and subject areas pertaining to two or more of the (1) social sciences and humanities, (2) natural sciences and engineering, and (3) health and wellness, may select the <u>TIR</u> as their first suggested PRC should they wish to be considered for review by this committee.

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- Applications submitted to the new TIR PRC will follow a specific review process with features
  that are distinct from all other Project Grant committees and will be evaluated according
  to specialized evaluation criteria.
- Justification for choosing TIR must clearly address how the proposal integrates the interdisciplinary approaches to achieve the project goals.
- **Note:** As the Tri-Agencies have not yet released an evaluation of the pilot and there are no successful TIR applications in SPARC's <u>Sample Grant Library</u> (CWL required), we are currently unable to offer concrete advice as to how to competitively pitch a proposal to the TIR criteria.

**Corresponding SPARC Service:** A discussion of the 750-character PRC justification (per committee suggestion) is the purpose of our Peer Review Committee Selection.

**Note:** The remaining pages contain examples of effective text from successful Project Grant applications generously shared by UBC researchers, both Research Summary examples and PRC Justification example. For additional ideas on how to structure this textbox and the previous section, consult SPARC's <u>Sample Grant Library</u> (CWL required).

#### Two Research Summary Examples Using SPARC's Suggested Format

# Example 1:

Goal: To inform policy for cannabis impaired driving in Canada. [Note: This statement has been moved up from the Background paragraph to align with the recommended outline.]

**Background:** Canada will introduce laws legalizing cannabis in April 2017, with legalization projected to be implemented by December 2019. Legalization may result in more cannabis-related motor vehicle crashes. The CIHR funded Cannabis and Motor Vehicle Crashes (CMVC) study investigates the association between THC (active ingredient in cannabis) and responsibility for causing the crash in injured drivers. Since 2011, this study has measured drug and alcohol levels and obtained police reports in 3000 injured drivers. The proposed research will take advantage of established CMVC procedures to evaluate the potential impact of these national policy changes on the prevalence of cannabis use in injured drivers and to provide better estimates of crash risk vs THC level.

#### **Objectives:**

Objective 1: To study changes in substance use amongst injured drivers following cannabis legalization. Objective 2: To refine estimates of the relationship between THC level and the likelihood of being responsible for a crash, with the aim of establishing an evidence-based per se THC level for driving.

**Methods:** We propose a 5 year prospective multi-centre study that will leverage existing procedures and infrastructure of the CMVC study. We will obtain excess blood remaining after clinical use from injured drivers who attend one of four trauma centres in British Columbia. Blood will be analyzed for drugs with a broad spectrum toxicology screen. Alcohol and cannabinoids will be quantified. Based on results



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from the CMVC study, we anticipate collecting a total of > 6000 blood samples from injured drivers (including >3600 samples collected as part of the CMVC study). Of these, over 1600 samples (2.5 years of data collection) will be collected after cannabis is legalized. We will obtain matching police reports and determine which drivers are responsible for the crash using a validated scoring system that we developed for this purpose.

**Analysis:** For objective 1, we will report the prevalence of cannabis and alcohol in injured drivers in the pre and post legalization periods and report the crude and adjusted prevalence ratios for cannabis and alcohol use after vs before legalization. For objective 2, we will compute the crude odds ratios for crash responsibility for different ranges of THC. We will also treat THC level as a continuous predictor of crash responsibility in a logistic regression model that is adjusted for age, sex, and presence of alcohol / other impairing substances. We will use the regression model to estimate and to plot the probability of being responsible for a crash as THC level increases.

**Expertise and Feasibility:** This project will continue using the experienced staff and proven procedures of the CMVC study. Our team includes international experts who are called on to advise Canadian policy makers on issues pertaining to impaired driving (including cannabis, alcohol, and other drugs), ensuring that our findings will be used to inform traffic policy.

**Significance:** Our findings will be relevant for road safety policy including decisions around allocating resources for impaired driving law enforcement and for introducing evidence-based per se laws for driving after using cannabis.

**Knowledge Translation:** We have engaged provincial and national road safety policy makers and will work with them to ensure that our findings inform Canadian policy around cannabis impaired driving.

## Example 2:

Stress responses protect cellular components from damage and thus ensure cell health. However, aberrant activation of stress responses allows tumors to thrive in a milieu of oxidative stress, starvation, and hypoxia. Similarly, induction of drug detoxification pathways triggers drug resistance in advanced cancers. Blocking these hyperactive pathways is thus a **promising interventional strategy** in cancer. Our **long-term goal** is to identify and characterize stress adaptive regulatory networks in order to inhibit them to combat cancer.

Stress response networks converge on evolutionarily conserved transcriptional regulators. My lab studies Mediator, a conserved multi-protein complex that is vital for gene expression. Through specific interactions with transcription factors (TFs), Mediator subunits (MEDs in mammals, MDTs in the nematode *C. elegans*) play key roles in many regulatory circuits. Critically, human MEDs are linked to cancer. For example, MED15 is upregulated in several cancers and we found that MED15 overexpression correlates with poor outcome in lung adenocarcinoma. In *C. elegans*, we found that *mdt*-

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15 (MED15's ortholog) is required for the responses to oxidative stress, starvation, and xenobiotic drugs. Thus, we hypothesize that MED15 may regulate similar responses in cancer cells.

The fact that MDT-15 regulates stress responses supports the concept that disrupting pertinent MED15-TF interactions could be a new way to treat cancers. Notably, two compounds targeting MED15-TF interactions have anti-obesity and anti-fungal activity, demonstrating MED15's drug accessibility. Alas, little is known about the mechanisms through which MDT-15/MED15 controls stress responses. Thus, our **objective** is to identify the partners of MDT-15 in stress response regulation in worms, and to study MED15 function in human cancer cells to assess the breadth of conservation. These are imperative steps towards combatting cancer by inhibiting stress responses through the MED15 entry point. We have three specific aims:

**Aim 1: Map how worm MDT-15 and human MED15 bind stress response TFs.** Our pilot studies found two conserved TFs that cooperate with *C. elegans* MDT-15 in stress responses: SKN-1/Nrf2 and NHR-49/HNF4. We will use in *vitro* protein interaction and *in vivo* genetic studies to precisely map through which domains and motifs the worm proteins bind, and test whether their human orthologs also interact (2-hybrid, GST pulldowns, *C. elegans* genetic analysis by qPCR, stress survival).

Aim 2: Identify new entry points into the MDT-15 stress response network. In worms, we will perform an RNAi screen to map the *mdt-15* network using a stress responsive gfp reporter, and genetically and pharmacologically test whether MDT-15/MED15 protein regulation by drugs is proteasome dependent. This will reveal new entry points for MED15 inhibition.

**Aim 3: Validate human MED15 as a drug detoxification factor.** In human lung cancer cell lines, we will test if MED15 is needed to express drug detoxification genes (qPCR, RNA-seq), to provide acute chemotherapy drug resistance, and adaption to prolonged drug exposure.

**Outcome:** We will gain knowledge of a stress response network, including detailed insight into MED15–TF interfaces that can be targeted for disruption by small molecules in the future. Combining studies in the rapid and tractable worm model with experiments in relevant cancer cell lines provides a powerful interdisciplinary approach towards this goal.

# Four Examples of PRC Justification Text for Projects that Align with a Single PRC

## Example 1:

"This project directly addresses the IHR mandate of research in keeping with Indigenous values and traditions [see <u>PRC Mandates for descriptors</u>] and will be most appropriately reviewed by [or, most relevant to] experts in community-based approaches, participatory action research and Indigenous methodologies [or three other key areas of expertise]."

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## Example 2:

Social Dimensions in Aging Justification: SMART is a self-management program for individuals with lower limb amputation (LLA) delivered via mobile health technologies (mHealth). On average, 7,300 Canadians have a LLA each year with increase of incidence annually (2006-2011). Social dimensions in Aging is the suitable committee for our study as the majority of people with LLA (86%) are aged>50 years. The primary cause is dysvascular complications due to diabetes. SMART, a user-centred design intervention with peer-support, will allow rehabilitation to be delivered to older adults with LLA via mHealth, and address the logistical issues related to delivering education to remote areas; and empower individuals to actively self-manage health behaviors that influence long-term outcomes.

# Example 3:

Medical Physics & Imaging Justification: This committee routinely reviews grants submitted on improving quantitative performance of medical imaging modalities, which our grant proposes, as well as application of advanced image processing and AI-based approaches to medical imaging, which again is an important part of our proposal.

#### Example 4:

Behavioural Sciences - B: Clinical Behavioural Sciences Justification: The BSB committee reviews clinical studies in neurologic populations, including stroke. Their committee membership includes individuals with the expertise to evaluate my application including brain stimulation and imaging approaches. The expertise of this committee also includes individuals with backgrounds in behavioural neurology. As such this is the ideal location for review of the proposed work.

# **Example of PRC Justification Text for an Interdisciplinary Proposal with an Ambiguous/Secondary PRC**

"This project directly addresses the CHI mandate of optimizing child development and well-being [see PRC Mandates for descriptors] with the clinical health aspects [CIA as the secondary PRC] playing a secondary [or, supportive] objective. As such, reviewers will ideally have expertise in prevention and long-term management strategies, as well as in complex family dynamics [or three other key reviewer areas of expertise] to appropriately review this proposal."

# Four Examples of PRC Justification Text for Projects that Address Two PRC Mandates

## Example 1:

Immunology & Transplantation Justification: The proposal focuses on immune response, a variety of innate lymphoid cell subsets, hematopoietic stem cell differentiation, host responses to microbes and developmental biology. I believe that this is likely the only panel that would have this range of expertise. Cell Biology – Physiology Justification: The application focuses on maternal and neonatal environmental exposures that alter stem cell behaviour and lead to altered susceptibility to allergic

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disease. Thus, it is falls within the mandate of identifying early life influences on stem cells that alter the course of disease.

#### Example 2:

Gender, Sex & Health Justification: This proposal is primarily examining the role of parity (pregnancy and motherhood) in females as they age in terms of their risk for dementia but also normal aging. As such it is appropriate for this committee.

Biological and Clinical Aspects of Aging Justification: This proposal is on how reproductive experience can change the trajectory of aging and risk for dementia and as such seems appropriate for this committee.

#### Example 3:

Gender, Sex & Health Justification: Among survivors of intimate partner violence, women are much more likely to suffer a physical injury. It is becoming increasingly apparent that the head is very often the target of the violence that occurs in abusive relationships and that traumatic brain injuries are likely to occur. Research into the impacts of these injuries and how they intersect with symptoms and neurocognitive dysfunction is sorely lacking. The proposed project will help to fill some of these knowledge gaps.

Systems & Clinical Neurosciences – A Justification: The primary measure to be used in the proposed research assesses cerebrovascular function and relates it to symptomology and neurocognitive outcome variables in an understudied population likely to be suffering from traumatic brain injury.

# Example 4:

Commercialization Justification: This grant will address topics pertaining to the commercialization of intellectual property to a state of use in the private, not for-profit, or public sector. These studies fit the mandate of the Commercialization panel.

Cancer Biology & Therapeutics Justification: Flow cytometry is the primary technology of choice for Cancer immunotherapy a target area of early adoption and a focus of this review committee.

# Example of PRC Justification Text for an RCT Submitted to a Discipline-specific PRC rather than to RC1

"This study contains an RCT and I/we am/are submitting to the discipline-specific committee, [insert PRC acronym], given that expertise in [use terms from the PRC's mandate] are required to review the proposal."