UNIVERSITY OF MANITOBA

CANADA FOUNDATION FOR INNOVATION
Innovation Fund 15-5

Notice of Intent

1. Completed NOIs must be submitted by the Associate Dean (Research)/Research Liaison Officer of the "Lead" Unit to the Office of Research Services to: Birtukan.Gebretsadik@umanitoba.ca by May 15, 2018.

Proposed name of project:	**Estimated Total Project Costs:**
Discovery Platforms for Mitochondrial Paradigms in Health and Disease	$ 3,000,000

Designated Project Leader/Faculty/Dept: **CV:** X

Lorrie Kirshenbaum/Rady Faculty of Health Sciences/Department of Physiology & Pathophysiology

List Principal Users/Faculty/Dept:

1. Lorrie Kirshenbaum	CV:	X
2. Grant Pierce	CV:	X
3. Michael Czubryt	CV:	X
4. Davinder Jassal	CV:	X
5. Amir Ravandi	CV:	X
6. Sanjiv Dhingra	CV:	X
7. Grant Hatch	CV:	X
8. Michel Aliani	CV:	X
9. Paul Fernyhough	CV:	X
10. Randy Aitken	CV:	X

'Lead' Unit ADR/RLO:

Name: Peter Nickerson, Vice-Dean Research, Rady Faculty of Health Sciences

Briefly describe (max 1 page, 12 pt. font size, 2 cm margins):

- The proposed research and how it is world-class, innovative and demonstrates clear benefits to Canada.
- The infrastructure and how it will enhance the University's existing research capacity.
- The excellence of the team, including expertise and existing collaborations necessary to conduct the proposed research.
- Plans to secure matching funds and the potential funding sources for the operation and maintenance of the infrastructure.

The proposed research and how it is world-class, innovative and demonstrates clear benefits to Canada:
Cardiovascular disease is the leading cause of morbidity and mortality and is a major financial burden to our Canadian health care system since individuals with heart disease e.g. (hypertension, diabetes, heart failure and vascular diseases) require costly long-term care. Defects in cellular metabolism, mitochondrial plasticity or both have been implicated in the pathogenesis of a variety of human diseases. At present, there remains a paucity of available information regarding the impact of mitochondrial biology in the pathogenesis of heart disease. Therefore, the CFI request is to develop a "state of the art" non-invasive *in vivo* imaging platform for studying mitochondrial plasticity, metabolism and drug discovery in models of human disease with the goal of drug discovery. We will use a highly integrated approach to study metabolic profiling by mass spectrometry, mitochondrial dynamics and cellular imaging by high resolution two photon microscopy, drug discovery by array scan VTI high content imaging, whole body *in vivo* gene expression by IVIS Lumina LT Vevo, LAZR multimodal imaging system, micro CT/PET and MRI. The infrastructure and research focus will address a specific health care need and allow for innovative leading edge health research at U of M, which does not currently exist in Canada.

The excellence of the team, including expertise and existing collaborations necessary to conduct the proposed research.
A major strength of this CFI proposal is the multidisciplinary team of basic science and clinical investigators with core expertise on understanding mechanisms that underlie mitochondrial dysfunction in ischemic heart disease, peripheral vascular disease, heart failure, extracellular matrix, diabetes, metabolism, cell regeneration, and oxidative stress. These include Drs. L. Kirshenbaum, I. Dixon, M. Czubryt, G. Pierce, A. Ravandi, P Fernyhough, M Aliani, S. Dhingra, G. Hatch, D Jassal and R. Atkin. Investigators within this group have collaborated together and have continually attracted international recognition through their research publications, innovative new technologies and international leadership in the area of cardiovascular disease. The group brings together members of the Institute of Cardiovascular Sciences, the Canadian Centre for Agrifood Medicine, Division of Neurodegenerative disease, WRHA Cardiology and U of M Lipid Atherosclerosis Research Group. Team members have ongoing collaborations with other world class institutes including Ben Gurion University (Israel) and Mayo Clinic (Rochester). For the institution to remain viably competitive, it must be equipped with specific infrastructure as requested in this proposal.

The infrastructure and how it will enhance the University's existing research capacity.
The metabolic imaging platform will add a new dimension in depth and level of scientific inquiry currently not possible with conventional imaging modalities. High-resolution biochemical and cellular analysis in living cells and animals are vital for serial studies assessing early and late disease progression; particularly involving early infarction. This CFI will bridge basic and clinical investigators, while enhancing the institution's capacity for innovative research, through enhanced training of HQPs, recruitment of faculty and development of worldwide networks with other academic centers.

Plans to secure matching funds and the potential funding sources for the operation and maintenance of the infrastructure. The infrastructure will be located in R.O. Burrell Laboratory at SBRC in a dedicated imaging suite and maintained by a cost recovery basis by veterinary staff Dr. Aitken. Matching funds will be provided by SBRC. Drs. Kirshenbaum and Pierce will be responsible for maintenance and management of infrastructure, (see equipment list on page 2).

Requested List of Equipment:

Seahorse Metabolic Analyzer XFe96 and XF Prep Station (Agilent)
Carl Zeiss two photon High Resolution microscopy
Carl Zeiss LSM880 with inverted optics and Airyscan detector for high resolution FRET analysis.
Metabolic animal cages (including respired gas analysis);indirect calorimetry
In vivo Telemetry for cardiac function and blood pressure analysis
Micro MRI for in vivo whole body and tissue imaging
Micro CT/PET Scanning for in vivo metabolic analysis at tissue level (VisualSonics: VS12239)
IVIS Lumina LT Vevo LAZR multimodal imaging system (Perkin Elmer: CLS 136331)
EnSpire multimode label-free reader (Perkin Elmer: 2300)
Exactive HF Standard MS System (ThermosFisher Scientific Ltd)