UNIVERSITY OF MANITOBA

CANADA FOUNDATION FOR INNOVATION
Innovation Fund

15-7

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: SUper Resolution Facility (SURF)	**Estimated Total Project Costs:** **$5.2M**

Designated Project Leader/Faculty/Dept: Sabine Mai/Rady Faculty of Health Sciences/Physiology and Pathophysiology **CV:** x

List Principal Users/Faculty/Dept:

1.	Kathleen Gough/Science/Chemistry//& Engineering/Biomedical Engineering aka BME	CV: x
2.	Zahra Moussavi/ Engineering/Electrical Engineering//Director BME	CV: x
3.	Benedict Albensi/Max Rady College of Medicine/Pharmacology// & BME	CV: x
4.	Malcolm Xing/Engineering/Mechanical Engineering// & BME	CV: x
5.	Kirk McManus/Rady Faculty of Health Sciences/Biochem & Medical Genetics	CV: x
6.	Ian Dixon/Rady Faculty of Health Sciences/Physiology and Pathophysiology	CV: x

'Lead' Unit ADR/RLO:

Name: **Kevin Coombs/ Rady Faculty of Health Sciences**

Briefly describe (max 2 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, how it is world-class, innovative & demonstrates clear benefits to Canada. Critical biochemical interactions occur at the nanoscale. We propose to acquire the most advanced infrastructure for super-resolution, single molecule fluorescent imaging and infrared imaging at the 20 nm length scale. Exploration of single cells at the molecular level is the key to understanding disease processes, whether general or unique to an individual's genetic makeup. Such knowledge will enable selection of appropriate and optimal therapies, and personalized medical treatment. These tools will enable us to identify new biomarkers for both diseases and through knowledge translation and implementation, result in innovative changes to health care for the benefit of Canadians.

Specifically, super resolution (SR) fluorescence imaging and near-field infrared (NFIR) imaging of cells and nuclei and their 3-D nano-structure will be used to understand mechanisms of cancer cell generation/evolution and AD neurodegeneration, to identify structural biomarkers and prognostic tools. This request for such instrumentation to focus on these research problems is a first in Canada. World-class research is summarized below by areas and expertise of the team:

SM: Conventional and super-resolution fluorescent imaging of nuclear architecture and 3D genome organization in cancer and AD; Director, GCCRD; Director, Founder of 3D Signatures

KG: Infrared spectrochemical imaging of biological materials, including AD brain tissue, normal and cancerous cells and nuclei; Far-field IR and NFIR imaging

BA: Synaptic Plasticity and Cellular Memory Dysfunction Lab; Mitochondria and disease; Manitoba Dementia Research Chair

KM: Mechanisms of Chromosomal instability (CIN) and CIN-targeting treatments; Senior Scientist, Research Institute in Oncology and Hematology.

MX: Design of nanoparticles for tumor therapy; development of nanotechnology and biomaterials for tissue engineering; CFI-funded Biomaterials and Nanomedicine Laboratory (2017).

ID: Autophagy events that contribute to cell differentiation, wound healing, stem cell proliferation and cancer progression; Heart disease and cellular mechanisms underlying cardiac fibrosis

ZM: Brain health and neurodegenerative diseases; clinical trials of a new treatment for Alzheimer's disease; Canada Research Chair in Biomedical Engineering, Tier II

Benefits to Canada will occur at multiple levels. The need for innovative therapies and their implementation in both cancer and Alzheimer's Disease (AD) is crucial in the Canadian health care system: 30% of all deaths in Canada are cancer-related; 1 in 2 Canadians are expected to get cancer. 1.1 million Canadians are directly affected by dementia, primarily AD. Combined costs exceed $20B.

HQPs with new skills will be trained in the facility and will be Canada's future innovators. Canada will emerge as a leader in SR and IR imaging, with a strong focus on personalized medicine solutions, which will lead to significant health care savings and better patient outcomes. Spin off companies will result, and these innovative technologies can be exported globally.

The infrastructure and how it will enhance the University's existing research capacity. The proposed infrastructure builds on and enhances four previous CFI investments ($13.7M) into the Genomic Centre for Cancer Research and Diagnosis (GCCRD) and CFI investments in PI labs (eg: Xing, $340,000, Biomaterials & Nanomedicine Laboratory, 2017). In addition to its other multifaceted capabilities, the GCCRD became the 3D Imaging Node for Canada in 2004, and has gained an international reputation for excellence, as evidenced by the caliber of its facilities and the many collaborations with top international researchers in the field.

SR -summary: The facility will acquire two conventional 3D imaging fluorescent microscopes (**AxioImager Z1) ($0.310M**) to examine the 3D structures of cells at a maximum resolution of 200nm. The fluorescent super resolution equipment will include a novel ELYRA system that has new laser capabilities for **single molecule localization microscopy (SMLM**) **($0.311M).** These

lasers are 300mW (561nm), 300mW (488nm) and 500mW (642nm) and can be added to the existing CFI-funded ELYRA system, making it the only one in Canada with SMLM capabilities (≤ 20 nm resolution). The same ELYRA system will house the **airyscan ($0.137M)**, which enhances the resolution of the existing ELYRA confocal imaging module by a factor of 2.4 (120nm in *x,y* and 350nm in *z*). Next generation SR developments by Zeiss will add 4D super resolution capabilities and combine conventional and super resolution in two complementary instruments **($3.1M**). Long term 4D measurements of live samples will be a first in Canada, making SURF the only 3D SR facility in the country with these capabilities, and the only one focused on cancer and AD.
IR – summary: 1. **s-SNOM Near-field IR platform, $1M**: Groundbreaking apertureless near-field microscopes (known as scattering-type Scanning Near-field Optical Microscopy, s-SNOM) combine Atomic Force Microscopy (AFM) with optical imaging and spectroscopy at the nanoscale. An AFM tip is illuminated with either a tunable wavelength Quantum Cascade Laser or a broad-band infrared laser. The optical amplitude and phase of the elastically-backscattered light are detected simultaneously, and processed to yield spectra that match far-field infrared spectra, at 20 nm, i. e. $(1/500)^{th}$ of the Abbe diffraction limit. Single cell spectrochemical analyses complementary to fluorescent imaging will provide insight into cell biochemistry at the same length scale as SR fluorescence. **2. Conventional Far-field imaging microscope, $0.350M** with high magnification optics and Focal Plane Array detector will provide conventional imaging at 1 to 5 μm spatial resolution, for development of rapid, clinically relevant, translational screening methodologies.
The excellence of the team, including expertise and existing collaborations necessary to conduct the proposed research. The core team includes established and emerging leaders in the fields of imaging, cancer and Alzheimer's disease. The team members have ongoing collaborations, publications and mentor trainees together. Each team member brings his/her national and international networks of clinical and basic research excellence to this proposal. SM is part of the Canadian Telomere Network, The Myeloma Canada Research Network, The Canadian 3D Molecular Cytogenetics Imaging Node, and the Terry Fox Research Institute –funded Myeloma Project (T. Reiman, PI). KG, with two colleagues in Biosystems Engineering, established the Spectromicroscopy Imaging Laboratory, located in the Faculty of Engineering. She is a leader in spectrochemical and NFIR imaging of biomaterials, and a founding member of CLIRSPEC, the Society for Clinical Infrared and Raman Spectroscopy. BA is engaged in MitoCanada, MitoNet and the AD Society of Canada. ID organized the MatriNet (Matrix and Tissue Remodeling Network) Excellence of Research Program that focuses on fibrosis and matrix remodeling. ZM is involved in five clinical trials related to brain health and AD, including a major clinical trial funded by the Weston Brain Institute. MX is an emerging leader in biomedical engineering and nanomedicine; he is now building the Biomaterials and Nanomedicine Laboratory at the University of Manitoba. Every member of the team has national and international collaborations that will be enhanced by this novel equipment. National and international team members will be included to the application (this NOI allows only 6).
Plans to secure matching funds and the potential funding sources for the operation and maintenance of the infrastructure. Once NOI is approved by U of M, a financial contribution is expected from CCMB, which has always supported CFI applications, and supports the operations in the GCCRD with ~$200k/yr. This includes supplies and two salaries: Project Manager (Dr. Klewes) and IT specialist (D. Lichtensztejn). Vendors provide a 20% discount on equipment. Service contracts (4 years each) will be included in the application. IOF funds will be used to hire 2 technicians (1 for fluorescent and 1 for near field IR). User fees will cover partial costs, currently $50/hr academics, and $200/hr for industry. A GCCRD user committee (Drs. Mai, Davie, Mowat, Murphy, McManus, Gibson and Johnston) oversees facility operations. Dr. Gough will be added to represent IR knowledge.