



**CANADA FOUNDATION FOR INNOVATION
Innovation Fund**

15-4

Notice of Intent

- 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: Air Pollution Simulator and Exposure Facility (AirSaFE): Deciphering Effects of Inhaled Pollution on Human Disease	Estimated Total Project Costs: \$1,700,000
Designated Project Leader/Faculty/Dept: Andrew Halayko, Tier 1 CRC, Department of Physiology and Pathophysiology, Rady Faculty of Health Sciences	CV: <input checked="" type="checkbox"/>
List Principal Users/Faculty/Dept:	
1. (co-Lead) Neeloffer Mookherjee, Rady Faculty of Health Sciences, Internal Medicine	CV: <input checked="" type="checkbox"/>
2. Hani El-Gabalawy, Rady Faculty of Health Sciences, Internal Medicine	CV: <input checked="" type="checkbox"/>
3. Meghan Jones, Rady Faculty of Health Sciences, Biochemistry & Medical Genetics	CV: <input checked="" type="checkbox"/>
4. Meghan Azad, Rady Faculty of Health Sciences, Community Health Sciences	CV: <input checked="" type="checkbox"/>
5. Madjid Birouk, Faculty of Engineering, Mechanical Engineering	CV: <input checked="" type="checkbox"/>
6. Qiang Zhang, Faculty of Engineering, Biosystems Engineering	CV: <input checked="" type="checkbox"/>
‘Lead’ Unit ADR/RLO: Dr. Peter Nickerson	
Unit Name: 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.

Proposed Research: Indoor and outdoor inhaled chemical and particulate pollutants adversely affect human health and quality of life. Acute and cumulative effects from conception throughout life in healthy and disease-vulnerable individuals can have severe health consequences. *The Lancet* 2017 Commission on Pollution and Health reports 6.5 million global deaths annually are attributable to air pollution. This links with increased rate and severity of respiratory and cardiovascular disease, lung cancer, rheumatic diseases, and other disorders. We need to understand the nature of the dysregulated biological processes caused by individual elements of diverse inhaled outdoor and indoor pollutants, including those from tobacco and cannabis smoking, and vaping and e-cigarette use, to launch effective evidence-based health and environmental policy, and to develop biofuels and environment-friendly engines with validated health-friendly emissions. *Our proposal uses an inter-disciplinary approach to enable innovation to create an internationally unique Air Pollution Simulator (APS) for the controlled generation of combustion- and aerosol-pollutants to enable us to define inhalation-to-response biological relationships in novel in vitro human cell systems, and small animal models of human disease. A key component of this initiative is that it links research to develop greenhouse-gas-limiting biofuels, engines with novel combustion strategies and air-purifying technologies to bioassay capabilities in animal models and in vitro systems that will profile whole system physiologic and biologic responses to emissions and air. We also create complementary capacity for pre-clinical assessment of preventative and therapeutic strategies for health effects of inhaled pollution.* These advances are needed to inform primary (disease onset) and secondary (disease progression) prevention strategies, and treatments for pollution-associated disease. Our work will help drive public discussion on effects of pollution and guide policymakers to enact ways to mitigate health effects. This benefits Canadians by informing the health system, and stimulating Canadian science and innovation sectors to economic advantage.

The proposed facility will produce the most detailed and comprehensive assessments of the physiological and cellular responses to diverse types of air pollution that have ever been undertaken. It is unique in enabling engineering experts to assess directly the impact of their design innovations for engines, controlling emissions, and regulating indoor air quality on human health. Based on team excellence, we will initially focus on the effects of inhaled pollutants in five disease areas that have a collective yearly healthcare burden exceeding \$5-billion in Canada: asthma, chronic obstructive lung disease, rheumatoid arthritis (**RA**), and cardiovascular complications. These diseases span the human lifecycle, and have early life origins related to environmental exposure. The detrimental impact of pollution on human health is an immediate and universal problem and our initiative will make U Manitoba and Canada leaders in the study of environmental exposures in health and disease.

Infrastructure Requested: We will establish **AirSaFE** at the U Manitoba medial school campus, within the 6th floor JBRC satellite animal facility in the Children's Hospital Research Institute of Manitoba (**CHRIM**). We are developing plans for space (three rooms) and renovations with CHRIM facility leadership. The facility will include four complementary research suites. **Suite One:** Advanced physiological assessment of small animal models, enable inhaled drug delivery, and perform exposures to tobacco and cannabis smoke and vaping exhaust. We include a Scireq flexiVENT lung function unit and inExpose compact inhalation exposure unit, an automated immune cell differential analyzer, and micro-Fluidizer unit for preparing inhalable drug formulations. **Suite Two:** Includes a culture hood and two incubators to accommodate in vitro 3D and multicellular culture models for exposure studies. We include in vitro exposure chambers from Cultex for long-term cultivation, deposition of particulate matter, and exposure to tobacco/cannabis smoke and vaping exhaust. Cryo-storage for cell banking is included. **Suite Three (APS platform):** The APS generates complex pollutants that are characterized, quantified and delivered to animal and in vitro exposure units (Suite Four) with controlled rates and duration. The APS includes an Air Pollutant Generator, Atmosphere Simulator, and Gas Sampling/Analyzing instrumentation. The APS we create will generate five common indoor and outdoor inhaled pollutants from: *fossil fuels* (diesel, gasoline, coal); *biomass* (wood pellets, straw stubble); *particle matter* (dust from mining, grain handling, animal barns); *liquid airborne aerosols* from room air samples that can contain chemical or biological agents; and, *volatile organic compounds* such as hydrocarbons and perfluorocarbons. **Suite Four (APS exposure lab):** Adjacent to the APS, pollutant delivery will be enabled with two Scireq inExpose compact inhalation exposure units (animal studies), a nano-aerosol in chamber for *in vitro* toxicology (NACIVT, Bern) and a Cultex system 3D culture models.

Excellence of the Team: Our interdisciplinary team includes international experts and new faculty from Health Sciences and Engineering, and has expertise in physiology, systems biology, immunology, clinical research, bio-aerosols and airflow systems, and combustion processes and systems. Our members have a history of productive collaboration, and capacity for integration of diverse research methods. The *de facto* co-leads are **Drs. Andrew**

Halayko and Neeloffer Mookherjee. Dr. Halayko is experienced using human lung cell culture systems and animal models of asthma and COPD. He leads multi-disciplinary national and regional research networks, including the Biology of Breathing Research Group in CHRIM. He has led, and been a co-applicant, for multiple prior successful CFI proposals, including one led by *Dr. Adrian West (Physiology)* who has established unique local 3D printing capabilities to generate human airway models. Dr. Mookherjee is a leader in studying antimicrobial host defence peptides in immune function and treatment for asthma and RA; diseases for which she uses mouse models established in collaboration with Halayko and **Dr. Hani El-Gabalawy** (Endowed Rheumatology Research Chair U Manitoba), respectively. Dr. Mookherjee has a strong record in studying traffic related air pollution in the human lung an in vitro airway models in collaboration with *Dr. Chris Carlsten (UBC)* who has established the only human controlled exposure facility (**APEL**) in North America. AirSaFE at U Manitoba will synergize with the unique capacity at APEL for human exposure studies, enabling collaborative investigation from cells to animals to humans. This includes continued collaboration involving Mookherjee and Halayko with multiple omics platforms at U Manitoba (proteomics (*Dr. J Wilkins*), lipidomics (*Dr. A Ravandi*), and metabolomics (*Dr. M Aliani*)) and RNASeq capabilities of UBC collaborator, *Dr. Robert Hancock* (Tier 1 CRC). We will enable **Dr. Meaghan Jones**, a new recruit to U Manitoba (Sept 2018) to establish a research program to study epigenetics and effects of maternal and early childhood exposure to air pollutants on lung development and risk for chronic lung disease. Our work supports **Dr. Megan Azad** (Tier 2 CRC), who leads the Manitoba node of CHILD, a prospective Canadian childhood cohort that collects home environment samples and maternal and child samples (breast milk, blood) to assay for trace pollutants that we identify, and correlate this with incidence of allergy and asthma. **Dr. Madjid Birouk** is an international leader in study of gaseous combustion processes, having developed experimental combustion chambers used around the world. His work on turbulent flow has led to dramatic improvements in combustion efficiency, reduced emissions, and improved designs for liquid-fueled combustion systems. **Dr. Qiang Zhang**, a Fellow of the Canadian Society for Bioengineering and bio-systems engineering expert for studies of aerosol formation and airflow systems in the agricultural sector and airborne transmission of disease, has made landmark contributions to Electrostatic Particle Ionization to improve air quality and the remove of bio-aerosols to reduce viral transmission in livestock. Drs. Birouk and Zhang have developed the plan for the proposed APS platform, and will lead its final design, testing, fabrication and installation with industry partners and external collaborators, including *Dr. Hongsheng Guo* at the National Research Council. We will create capacity to benefit U Manitoba researchers in developmental origins of disease (e.g. DEVOTION network, co-led by Halayko), cardiovascular sciences (*Dr. Grant Pierce*, Exec Director of Research, St. Boniface Hospital), cancer biology, Crohn's disease and colitis, and neurosciences and Alzheimer's disease.

Plans to Secure Matching Funds: We expect that the Province of Manitoba will match CFI funding. We will obtain negotiated CFI discounts from suppliers. CHRIM will be a significant matching fund contributor, up to a pre-established maximum. Support for operation and maintenance will come from the CHRIM Biology of Breathing Theme (salary for lead technical staff). AirSaFE will operate as a core on a cost recovery basis, and CHRIM will provide indirect administrative and facilities support.