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Memo

To: CAAIF Membership
From: Andrea Waserman, Managing Director, CAAIF
Date: October 6, 2021
Re: **2021 CAAIF Research Grants and Fellowships**

BACKGROUND:
By the end of 2021, together with our partners, CAAIF will have distributed $540,000 towards research grants and fellowships. This year will be the second and final year of the two *CIHR-ICRH/CAAIF/AstraZeneca/Allergen Emerging Researcher Awards in Allergic Asthma*. Below is a list of all Awards that have been distributed thus far.

TO BE ANNOUNCED:
The following awards are currently open for applications:

- *CAAIF-Immunodeficiency Canada Research Fellow/Early Investigator Award in Immunodeficiency*

- *CAAIF-Avir Pharma Early Investigator Research Grant in Eosinophilic Esophagitis*

CAAIF RESEARCH FELLOWSHIP IN TYPE 2 INFLAMMATION SUPPORTED BY SANOFI GENZYME CANADA

Awardee: Dr. Partho Adhikary, University of British Columbia
Project Title: *Th2 inflammation-on-a-chip: Developing an ex vivo drug discovery platform for atopic diseases.*
Amount: $75,000
Lay Abstract: Atopic diseases are common allergic diseases such as eczema, asthma or hay fever. Skin and lung cells produce a factor, thymic stromal lymphopoietin (TSLP), which is known to be a main driver of such atopic diseases as it activates immune cells that further trigger inflammation. Hence, inhibiting this factor holds a great potential to treat atopic diseases. Currently, mostly large molecules, such as antibodies against TSLP are being developed, which however must be administered by injection and cannot be applied locally, for example as a cream. Drugs which can be applied locally offer several advantages such as less side effects, being more effective, and higher acceptance rates among patients. Hence, we are currently developing effective so called 'small molecule TSLP blockers' with the goal to be able to apply them locally onto the skin without needing any needles or injections. We already have identified a few very promising candidates, yet there is no model available to test its safety and efficacy. Hence, we will develop a 'human-on-a-chip' setup which will allow us to test the promising compounds in complex and novel human-based setting without any animal models.

CAAIF RESEARCH FELLOWSHIP IN TYPE 2 INFLAMMATION SUPPORTED BY SANOFI GENZYME CANADA

Awardee: Dr. Nermin Diab, McMaster University
Project Title: *Point of care solutions to delayed Type 2-mediated drug hypersensitivies*
Amount: $75,000
Lay Abstract: Chronic cough affects approximately 10% of the general population and is one of the commonest reasons for referral to secondary care. Unfortunately, there are no

licensed treatments for this debilitating condition, which affects the social, physical and psychological well-being of patients. Asthma and Non-asthmatic Eosinophilic Bronchitis (NAEB) are known causes of chronic cough. An important feature of both these conditions is the presence of an inflammatory cell called the eosinophil which is found in the airways. The most common treatment for this is high doses of inhaled steroids, but when the cough becomes unbearable, repeated courses of oral steroids are administered. However, many patients have persistent cough despite this treatment and can develop significant steroid related side effects. Developing treatment for this condition is thus a major unmet clinical need.

Cough is a defensive reflex which is triggered by activation of nerves which are found in the airway lining. Recent evidence suggests there is a significant increase in eosinophils in the airways which sensitizes these nerves. This makes the nerves more easily activated leading to more coughing. If these eosinophils could be depleted and prevented to enter the airways then we predict that the nerves will be less sensitive and coughing will be reduced.

Mepolizumab is an injection medication, which blocks a key chemical that prevents the maturation and activation of eosinophils. It is a licensed medication which is currently used in patients with severe asthma to prevent severe asthma attacks. However, there has been no evidence to show whether this medication would improve coughing. The aim of this research project is to investigate whether mepolizumab reduces objective cough frequency in patients with eosinophilic airway diseases. The results of this study would result in a paradigm shift in the management of this challenging condition and provide patients hope of an improved quality of life.

CAAIF TOP 10 CHALLENGE FOOD ALLERGY RESEARCH GRANT

Awardee: Dr. Jennifer Protudjer, University of Manitoba
Project Title: ***NOURISH****: patie****N****t-****O****riented research to* ***U****nderstand and add****R****ess* ***I****nequities of food acces****S*** *and insecurity amongst* ***H****ouseholds managing food allergy*
Amount: $25,000
Lay Abstract: Over 3 million Canadians live with food allergy. These people must avoid the food to which they are allergic in order to prevent a potentially fatal allergic reaction. Avoidance comes at a cost, both in terms of psychosocial health, and financial costs. Before the pandemic, households managing a food allergy spent, on average, $2500 more per year on food, than households without food allergy. Preliminary data from our group suggest that these excess costs are even higher during the pandemic. At the same time, food prices have increased by almost 10% and unemployment has doubled. It is not surprising, then, that households managing food allergy report the buying foods with a "may contain" label because of a lower price point than allergy-friendly foods, and that nearly one in five households with food allergy also report food insecurity. In the proposed project, we seek to further understand and address the inequities of food access and insecurity among families with a child, with a food allergy.

ASTHMA CANADA/CAAIF GRADUATE STUDENT AWARDS

Awardee: Caren Cao, University of Toronto
Project Title*: Investigating the Effects of Rostral Fluid Shift and Obstructive Sleep Apnea on Airway Narrowing in Asthma*
Amount: $20,000
Lay Abstract: Respiratory viral infections have taken center stage as a global health emergency. As asthmatics are a vulnerable group for serious COVID-19 complications, we are reminded that non-coronavirus respiratory viruses, such as human rhinoviruses (HRV),

also pose serious health risks to asthmatics. Repeated cold virus infections during early childhood are strongly associated with wheezing illnesses and asthma development. In particular, the HRV-C genetic group of rhinoviruses are strongly linked to severe asthma outcomes and hospitalizations in children. Since all children experience numerous seasonal colds, yet not all children develop asthma, we propose that the asthmatic airways may mount a dysfunctional immune response to repeated rhinovirus infections. This may result in permanent changes in the airway cells that contribute to creating an asthmatic airway in childhood. This project investigates the phenomenon of "trained" innate immunity, in which exposure to multiple rhinovirus infections may reprogram infected airway cells to fight future infections more efficiently. Potentially, asthmatic epithelial cells may not undergo this beneficial "training" to fight repeated infections, which could explain how repeated rhinovirus infections may instigate childhood asthma development.

ASTHMA CANADA/CAAIF GRADUATE STUDENT AWARDS

Awardee: Dr. Andrew Kouri, St. Michael's Hospital, Unity Health Toronto
Project Title: *Exploring the influence and perspectives of older adults in the development and testing of mobile health interventions in airways disease*
Amount: $20,000
Lay Abstract: Mobile health (mHealth) technology using smartphones and tablets is increasingly being incorporated into the care of asthma, one of the most common chronic respiratory diseases in Canada. mHealth can facilitate asthma self-monitoring and self-management, which are essential to effective asthma care.

Given that the prevalence of asthma is growing in older populations in Canada as the population ages overall, and that older patients with asthma are disproportionally negatively affected by asthma compared to younger patients, older adults with asthma may significantly benefit from the promises of mHealth technology.

However, little is currently known about the effectiveness and acceptance of mHealth tools in older adults with asthma, and studies in other conditions like diabetes suggests that there may be important barriers that need to be overcome before mHealth tools can help older populations. My PhD thesis projects seek to determine if and how mHealth tools are currently being developed with older patients in mind, and to achieve a better understanding of the needs and perspectives of older adults with asthma in their use of mHealth technology. This understanding may hopefully be used to design and implement more effective mHealth solutions for older adults with asthma.

ASTHMA CANADA/CAAIF GRADUATE STUDENT AWARDS

Awardee: Samantha Lee, University of Manitoba
Project Title: *Investigating epigenetic changes associated with prenatal air pollution exposure in the CANDLE study.*
Amount: $20,000
Lay Abstract: Prenatal air pollution exposure is associated with an increased risk of childhood asthma. While the mechanisms underlying this association remain unclear, researchers believe that environmental exposures become biologically embedded in epigenetic patterns, specifically DNA methylation (DNAm), during critical developmental periods. These altered patterns are thought to "reprogram" cell function, and ultimately influence health outcome. This research project will identify DNAm patterns associated with prenatal air pollution exposure at birth, and examine how altered epigenetic patterns evolve through childhood. All identified DNAm changes will be correlated with childhood asthma. However, we are most interested in the association between persistent DNAms changes

and asthma, and persistent changes are more likely to influence health outcome than transient alterations. This analysis will provide insight into molecular pathways that are altered by prenatal air pollution exposure and contribute to asthma. Additionally, as we believe air pollution-induced DNAm changes arise from oxidative stress, this research will investigate if maternal diets higher in antioxidants (like vitamin C) can mitigate the effect of air pollution on child DNAm patterns. Together, this research will help clarify how prenatal air pollution exposure predisposes children to asthma, and begin identifying preventative measures.

CAAIF RESEARCH FELLOWSHIP IN IMMUNOLOGY SUPPORTED BY TAKEDA CANADA

Awardee: Dr. Daniela Stanga, CHU Sainte-Justine
Project Title: A Prime Editing-Based System for Modeling Primary Immune Disorders
Amount: $50,000
Lay Abstract: Diagnosis of inborn error of immunity (IEI) has recently seen a sharp increase, primarily due to the proliferation of genomic methods that clinicians now use to investigate their patients' genetics. The identification of an IEI as a cause of allergy, autoimmune disorder, or susceptibility to infection has a profound impact in determining the best treatment option. However, many variants identified by current genomic technology cannot be definitively linked to the pathology presented by the patient. Variants of unknown significance (VUS), thus, present a considerable challenge to making the correct diagnosis and providing effective therapy. Hence, we are currently developing a cellular model with the ability to test any genetic variant for its ability to result in an IEI using prime editing, a method to introduce small insertions, deletions, and base-swaps in DNA that has been derived from CRISPR-Cas9 systems. Using this model, we will investigate the molecular basis of the immune dysfunction associated with the mutations in RIPK1, a master regulator of cell death, and inflammation which dysfunction can provoke degenerative and inflammatory disorders.
By using prime editing to quickly re-create any given variant in a standard human cell line, validate the edit and experimentally determine the immunocompetence of the edited cells, this project will lay the groundwork for personalized medicine by providing a method that can rapidly investigate any variant identified.

CAAIF-MIRAVO HEALTHCARE RESEARCH GRANT IN ALLERGIC RHINITIS OR URTICARIA

Awardee: Dr. Anne Ellis, Queens University
Project Title: ***A****llergic* ***R****hinitis* ***M****icrobiome* ***S****tudy (****ARMS****): Investigating the nasal microbiome of allergic rhinitis using nasal allergen challenge*
Amount: $25,000
Lay Abstract: Allergic rhinitis(AR) is a disease that affects 25% of Canadians. AR is caused by an allergic reaction to airborne allergens that trigger symptoms like those seen with the common cold. Although some studies have suggested a link between allergies and the microbiome, the combined genetic material of microorganisms in an environment, there is currently little understanding of how microbiome changes can lead to disease in the nose. We have demonstrated that we can induce AR using a controlled nasal allergen challenge(NAC) model and developed methods to sample the local microbiome concurrently. This project proposes to use these tools to determine precisely how changes in the nasal microbiota affect AR via the collection of clinical and biological outcomes. Recent studies have shown that immunoglobulin(Ig)-E levels, a mediator of AR, are associated with specific microbiomes. Therefore, the total IgE levels will also be measured in this study.

Despite the therapeutics available for AR, rates of treatment dissatisfaction are high(~60%). This poor rating may because available therapies primarily treat AR symptoms and not the underlying factors driving disease progression. Our research will help clarify the role of the microbiome in AR and facilitate the development of novel treatments for this increasingly common disease.

Prepared by
Andrea Waserman
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6 October 2021