Memo

To: CAAIF Membership

From: Andrea Waserman, Managing Director, CAAIF

Date: October 1, 2020

Re: **2020 CAAIF Research Grants and Fellowships**

BACKGROUND:
By the end of 2020, together with our partners, CAAIF will have distributed $625,000 towards research grants and fellowships. Thus far, $315,000 of funding has been released. This year will be the second and final year of the *CAAIF/CSACI/AllerGen Emerging Clinician-Scientist Award*, pending approval of the progress report in October. Below is a list of all Awards that have been distributed thus far. The Awards for the CIHR-ICRH/*CAAIF/AstraZeneca/Allergen Emerging Researcher Awards* were announced last year but funding was released this year.

TO BE ANNOUNCED:
The following awards are currently undergoing adjudication:

- *CAAIF-CSACI Research Fellowships in Allergy and Clinical Immunology in "Ontario or Manitoba", "Quebec or Atlantic Canada", "British Columbia, Alberta or Saskatchewan"*
- *CAAIF/Aralez Pharmaceuticals Inc. Research Grant in Allergic Rhinitis*
- *CAAIF/Stallergenes Greer Early Investigator Award in Allergy and Clinical Immunology*

CAAIF/PEDIAPHARM, A DIVISION OF MEDEXUS PHARMACEUTICALS INC. RESEARCH GRANT IN ALLERGIC DISEASES

Awardee: Dr. Kelly McNagny, University of British Columbia
Project Title: *Prediction of childhood allergic disease from alterations in umbilical cord cell signatures*
Amount: $50,000
Lay Abstract: Food allergy is a growing health problem that affects approximately 7.5% of Canadians and can cause life-threatening systemic reactions termed anaphylaxis. Some food allergies, such as those to peanut (PN) and shellfish are typically lifelong and more often associated with anaphylaxis - PNs are the leading cause of severe food related allergic reactions and fatalities2. Without a cure for food allergy, the mainstay of therapy is allergen avoidance. There are two fundamental limitations to this approach: 1) Despite attempts at avoidance, there is a high rate of accidental ingestion (12% per year to PN), and 2) it does not address the source of the disease. Taken together, there are major challenges in the risk reduction, management, and mechanistic understanding of food

allergy. In this proposal, we aim to translate recent discoveries in PN allergy from mice, described below, to humans by embedding immunological experimentation within two key, AllerGen-funded clinical studies. In addition to the direct clinical impact of these two studies, this proposal will evaluate the utility of IgE memory B cells (MBCs) as risk stratification, response to therapy, and predictive tools for food allergy. This foundational work will also inform the candidacy of MBCs as a novel therapeutic target in allergy.

CAAIF TOP 10 CHALLENGE FOOD ALLERGY RESEARCH GRANT

Awardee: Dr. Manel Jordana, McMaster University
Project Title: *Immune re-programming in peanut allergy*
Amount: $25,000
Lay Abstract: There is no cure for peanut (PN) allergy. Current treatment consists of strict avoidance of the culprit food and rescue epinephrine following accidental exposure, neither of which address the root of the disease. A number of oral immunotherapy (OIT) clinical trials for PN have been conducted. Favorable outcomes of OIT include desensitization and sustained unresponsiveness (SU). Lack of symptoms upon exposure to the allergen, while maintaining consistent low dose consumption, is termed desensitization. SU occurs if this state persists for 1-3 months beyond cessation of OIT. The efficacy of PN-OIT is limited by its safety profile which has recently been systematically reviewed in the PACE study. Therein, it was established that OIT increased the risk of anaphylaxis, epinephrine use, and other allergic symptoms compared to the current standard of care (strict avoidance). Consequently, PN allergy in particular, and food allergy in general, is in dire need of novel, transformative therapeutic approaches

This project is an extension of the funded 2018-19 CAAIF-AAIA grant wherein we proposed to establish a human in vitro experimental system using peripheral blood mononuclear cells (PBMCs) that would be capable of evaluating both T and B cell responses, notably IgE in the case of the latter. In addition, we proposed to investigate the impact of an anti-IL-4Ra antibody treatment in PBMCs from PN allergic individuals. We have succeeded in these objectives and gone much further in that we have demonstrated that treatment with this antibody has a remarkable effect on the immune response to PN. A paper will be submitted in the coming weeks to Science Translational Medicine. However, important questions remain to be addressed.

ASTHMA CANADA/CAAIF GRADUATE STUDENT AWARDS

Awardee: Anthony Altieri, University of Manitoba
Project Title: *Regulation of Airway Inflammation: Cytokine IL-17 & Cathelicidin LL-37*
Amount: $20,000
Lay Abstract: Asthma is a heterogeneous respiratory disease characterized by airway inflammation. The severity of inflammation reflects the progression and/or onset of the disease. Individuals with late-onset, severe asthma typically have high levels of immune cells called 'neutrophils' and 'T-helper-17 lymphocytes' in the lung compared to individuals with moderate asthma. These cells produce molecules called 'Cathelicidin LL-37' and 'Interleukin-17' respectively. The interplay of these molecules enhances the severity of asthma and causes patients with severe, late-onset asthma to respond poorly to already existing therapeutics, such as inhaled corticosteriods (ICS). My project will identify how the combination of these molecules exacerbates severe, late-onset asthma. As a result,

therapeutic strategies can be created for individuals with severe asthma, who currently have limited treatment options.

Awardee: Aubrey Michi, University of Calgary
Project Title*: Evaluation of trained innate immunity to rhinovirus infections in highly-differentiated asthmatic airway epithelial cells*
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.

CIHR-ICRH/CAAIF/ASTRAZENECA/ALLERGEN EMERGING RESEARCH AWARDS IN ALLERGIC ASTHMA

Clinician-Scientist Stream Awardee: Dr. Adil Adatia, McMaster University
Project Title: *Inhibition of group 2 innate lymphoid cells as a therapeutic strategy in sever asthma*
Amount: $100,000
Lay Abstract: "Our body's immune system usually fights infections, but in many diseases it can attack the body itself, which is called autoimmunity. Autoimmunity is not well understood in asthma but appears to play a role in patients with severe asthma that involve eosinophils, a type of white blood cell. These severe asthmatics with eosinophils are treated with a drug called prednisone (corticosteroid), though it has many side effects and may not be fully effective. There is evidence of autoimmunity in the lungs of certain severe asthmatics who need prednisone chronically. They also have larger numbers of white blood cells called group 2 innate lymphoid cells (ILC2), which may play a role in their requirement for prednisone. These cells are also increased in asthma patients after they inhale a protein to which they are allergic. One of the proteins that activate ILC2 is called TL1A, and we thus propose a trial to see if blocking TL1A improves the disease control of asthmatics with eosinophils and autoimmune responses, with and without allergy.

Basic Scientist Stream Awardee: Dr. Manali Mukherjee, McMaster University
Project Title: *Investigating autoimmune responses to tailor biologic therapies in severe asthma*

Amount: $100,000
Lay Abstract: "Asthma can be very severe for approximately 10% of patients who suffer from significant symptoms, frequent hospitalizations, loss of productivity/income, and improve a significant economic burden. Severity is driven by a type of white blood cells (eosinophils) that gets recruited to the lungs as a result of allergy and other triggers and plug the airways. This is treated with glucocorticosteroids (prednisone) which causes serious side effects. Antibodies (biological) have been developed that blocks specific proteins which mediates allergy and further recruits these eosinophils to the lungs. However, for a number of reasons, they are not equally effective for all patients. Our research shows that antibodies in the airways of some patients may interfere with the action of these biological. This project will investigate how antibodies might mediate these effects and develop strategies to identify patients in whom these biological may not work.

CAAIF/CSACI/ALLERGEN EMERGING CLINICIAN-SCIENTIST AWARD

Awardee: Dr. Derek Chu, McMaster University
Project Title: *Translating Discoveries in IgE Memory to Transform Food Allergy Assessment and Management*
Amount: $125,000 (pending approval of progress report; funds to be distributed in December)
Lay Abstract: Food allergy is a growing health problem that affects approximately 7.5% of Canadians and can cause life-threatening systemic reactions termed anaphylaxis. Some food allergies, such as those to peanut (PN) and shellfish are typically lifelong and more often associated with anaphylaxis - PNs are the leading cause of severe food related allergic reactions and fatalities2. Without a cure for food allergy, the mainstay of therapy is allergen avoidance. There are two fundamental limitations to this approach: 1) Despite attempts at avoidance, there is a high rate of accidental ingestion (12% per year to PN), and 2) it does not address the source of the disease. Taken together, there are major challenges in the risk reduction, management, and mechanistic understanding of food allergy. In this proposal, we aim to translate recent discoveries in PN allergy from mice, described below, to humans by embedding immunological experimentation within two key, AllerGen-funded clinical studies. In addition to the direct clinical impact of these two studies, this proposal will evaluate the utility of IgE memory B cells (MBCs) as risk stratification, response to therapy, and predictive tools for food allergy. This foundational work will also inform the candidacy of MBCs as a novel therapeutic target in allergy.

Prepared by
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1 October 2020