THE HARTWELL FOUNDATION

2023 Nominee Individual Biomedical Research Award

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Circulating Microvesicles as Biomarkers for Diagnosing Acute Food-Induced Anaphylaxis

Food allergy is disorder which disproportionately affects children and is characterized by abnormal immune responses to food(s). About 8 percent of children have food allergies and are at risk for food-induced anaphylaxis, which is a potentially life-threatening systemic allergic reaction. Accurate diagnosis of anaphylaxis is essential in both the emergency setting, when medical treatment can be lifesaving, as well as later during outpatient evaluation, when management depends on confirming the diagnosis before testing to identify the triggering food. With no reliable biomarkers of acute reactions, the diagnosis of anaphylaxis is based on symptoms, which may be problematic due to their range of variability and the overlap of allergic symptoms with other diseases. These diagnostic difficulties contribute to the misdiagnosis and mismanagement of food allergies. Currently, clinical management of an episode of ambiguous symptoms is conservative and entails food avoidance. As a result, many children in community settings may be told to avoid foods unnecessarily when they are not actually allergic to them, which can negatively affect nutrition and cause needless anxiety for the child and their family. More importantly, unnecessary avoidance can actually cause a food allergy to develop. Therefore, there is an unmet need for novel biomarkers of food-induced allergic reactions. Traditional research in the field has focused only on known substances that mast cells and basophils release when they are activated (e.g. histamine or cytokines) but these substances are not sensitive markers in patients. By contrast, extracellular vesicles are cell-specific and express surface markers unique to their cell of origin. They have been found to be extremely accurate biomarkers of many diseases, but their existence have not been explored in food allergy reactions. In preliminary experiments, using single-particle nano-flow cytometry of cell culture supernatants, I have observed that human primary skin-derived mast cells release roughly 30-fold more microvesicles after simulation as compared to basal release in vitro. I therefore hypothesize that significant increases in circulating blood mast cell-specific and basophil-specific microvesicles will be detectable in children undergoing an active food allergen challenge compared to their baseline, and that circulating mast cells and basophil microvesicles can be deployed as accurate biomarkers of food-induced anaphylaxis. I will characterize and quantify circulating microvesicles in the blood of food-allergic children before and after acute allergic reactions that may be informative of reaction mechanisms and create a biobank of patient samples to be used for measuring alternative biomarkers. If I am successful, novel biomarkers of food-induced allergic reactions will make it possible to provide pediatricians accurate diagnostic tools for rapidly assessing food allergies in the clinic or emergency room, while eliminating undesirable, protracted food avoidance testing in children.