THE HARTWELL FOUNDATION

2021 Individual Biomedical Research Award

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Food-Specific Memory T Cell Responses for Diagnosis and Monitoring of IgE-Independent Eosinophilic Esophagitis

Eosinophilic esophagitis (EoE) is a recently recognized type of food allergy that develops in early childhood and affects as many as 1 in 2,000 children in the US. The number of children diagnosed with EoE is increasing by 12-17% each year, making it one of the fastest growing pediatric allergies. EoE is a chronic disease in which a type of white blood cell (eosinophil) builds up in the lining of the tube (esophagus) that connects the mouth to the stomach, resulting in inflammation, tissue damage and scarring. Children with EoE experience chronic chest pain, reflux, and painful swallowing. Some children develop strictures that block food from passing from the mouth to the stomach. These symptoms can lead to severe malnutrition, requiring children be fed elemental formula diets via feeding tubes as well as secondary conditions including anxiety, sleep disturbance, and eating disorders. There is no cure for EoE, and the only definitive therapy is removal of causal foods from the diet. In that regard, routine allergy skin tests are of limited use in identification of EoE-causal foods because they rely on the presence of allergen-specific IgE antibodies, which do not cause EoE. As a result, children must undergo repeated cycles of single food elimination followed by invasive esophageal imaging (endoscopy) and biopsy. In addition to carrying some risk and considerable morbidity, this process can take months or years during which time children have chronic symptoms and are at risk for progressive disease. The heart-rending inefficiency of this approach highlights the critical need for minimally invasive allergy tests that accurately identify EoE-causal foods. Based upon my discovery that children with EoE milk allergy had milk-activated memory T cells in their blood and the fact that this T cell subtype is most indicative of persistence of an immunologic response, I hypothesize that measurement of such food-specific T cells will inform EoE diagnosis and clinical care. As a critical proof-of concept, I will seek to confirm in a prospective trial of 150 children if the presence of milk-activated memory T cells in the blood will predict clinical EoE milk allergy. I will then develop, optimize, and evaluate food-activated T cell assays for other common EoE-causal foods (soy, wheat, and egg). If I am successful in demonstrating how a minimally invasive clinical assay for food-specific T cells can efficiently identify EoE-causal foods, the clinical translation of the approach will revolutionize the diagnosis and management of this severe food allergy. Not only will such an assay reduce the need for children to undergo repeated endoscopy and biopsy, but it will also minimize the risk of serious secondary complications. In addition, rapid identification and confirmation of causal foods will contribute to reducing the time required for clinical remission, further improving the quality of life for affected children.