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CURED Foundation
c/o Ellyn Kodroff
PO Box 32
Lincolnshire, IL 60069

Dear Ellyn and members of the CURED Board:

I would like to thank you for your continual, extremely generous and uplifting financial contribution to the eosinophil research program at Cincinnati Children's Hospital. You keep hope alive and show the true meaning of altruism.

Over the next year, this donation will assist us with deciphering the genetic cause of eosinophilic esophagitis as we are now embarking on a large-scale genetic analysis of eosinophilic esophagitis (EE) using a multi-faceted cutting edge approach. We are also uncovering the genetic signature (genes that are turned on) in the stomach of patients with eosinophilic gastrointestinal disorders (EGID) and comparing this to the pathways that we have recently uncovered in the esophagus. Besides uncovering the steps involved in disease development and propagation, this approach provides the basis for developing drug strategies, as the molecular targets for therapy will be uncovered. We are also expecting to launch a clinical trial that is designed to test an innovative and promising strategy to medically treat eosinophilic esophagitis by blocking a pathway that was directly identified by our basic research studies. We are also analyzing the mechanism and utility of anti-IL-5 therapy as this is emerging as an effective therapy for eosinophilic esophagitis, again based on the studies that we pioneered. Additionally, we are focusing on understanding non-responsiveness to fluticasone therapy by examining the genes that are fluticasone resistant and the impact of higher doses of this medicine in a controlled clinical trial. We are also heavily invested in the development of non-invasive tests for diagnosing and monitoring eosinophil-associated gastrointestinal diseases (EGID). While we aim to provide the best care possible for each patient, we also aim to learn from each patient through medical research. Indeed, nearly all patients are being enrolled into an eosinophilic patient data bank designed to answer fundamental clinical, epidemiological, outcomes and quality of life questions concerning this debilitating disease.

The following outlines our steady progress over the past two years, all based on published studies funded in part by CURED (as acknowledged in many papers).

- Publication of ~40 articles in international medical journals.
- Identification of a novel activation pathway for eosinophils (PIR-b).
- The elucidation of a key mechanism of food allergy involving IL-9 mediated mast cell intestinal responses.

- The key positive results in an international trial designed to test the effect of anti-IL-5 therapy for hypereosinophilic syndrome (as reported in the New England Journal of Medicine).
- Mechanism of action of anti-IL-5 therapy in eosinophilic patients.
- A novel way of blocking eosinophils in vivo (anti-siglec-f antibody).
- The key role of a metabolic hormone (RELM-a) in eliciting gastrointestinal inflammation and metabolic syndrome during inflammatory responses in vivo.
- The identification of a novel pathway for eosinophil accumulation into the esophagus (involving periostin).
- Determination that the inflamed GI tissue of patients with eosinophilic gastrointestinal disorders (EGID) has active antibody production; this provides an explanation of the dissociation between skin prick testing and the effectiveness of specific food elimination diets.

While we are proud of our accomplishments, we know how much more needs to be done, especially in light of the suffering and limitations that child with EGID experience on a daily basis. Despite how close we are to further impacting eosinophilic diseases, our research is directly limited by our funds. Our primary source (the federal government via the NIH) is facing the worst funding crisis in its history. So, despite the amazing progress and the capabilities of our research to have a huge impact on eosinophilic disorders, we are now faced with an unprecedented shortage of research funding. As such, CURED's generous support is even timelier and certainly inspiration to my team and I.

Sincerely,

Marc Rothenberg, MD, PhD
Professor and Director
Division of Allergy and Immunology