

Diagnostics and Therapeutic Targets for Eosinophilic Esophagitis



Center for Technology Commercialization

TECHNICAL FIELD

Therapeutic, Diagnostic, Research Tool: Eotaxin-3/CCR3 (2004-1003, 2005-0401)

BACKGROUND

Eosinophils are one type of granulocyte (white blood cell) that normally appear in peripheral blood at a concentration of about 1-3% of total leukocytes. Normally, their presence in tissue is primarily restricted to the mucosa. However, in various disease states, such as eosinophilic esophagitis (EE), eosinophils appear in increased numbers in peripheral blood and/or tissues, a condition known as eosinophilia. Tissue accumulation of eosinophils may cause potent pro-inflammatory effects as seen in various disorders such as asthma, chronic inflammatory disorders, parasitic infections and certain types of malignancies.

Numerous pharmacologic agents such as glucocorticoids, very-late-antigen 4, and inhibitors of IL-5 are used, or are proposed, to treat a variety of eosinophil-related diseases; however none are specifically targeted to eosinophils. Therefore, there exists a need to identify and develop an effective therapy to treat eosinophilic diseases.

Also of importance is the development of reliable, noninvasive diagnostic tests for eosinophilic diseases. Currently, diagnosis is made by using costly endoscopic procedures and subjective microscope analysis of biopsy samples.



TECHNOLOGY

Research in Dr. Rothenberg's laboratory has identified eotaxin-3 as a critical molecule in the pathogenesis of eosinophilic esophagitis. Studies have shown that the gene for eotaxin-3 is induced nearly 100-fold in patients with EE compared to normal controls. Further, studies identified that eotaxin-3 is elevated in the plasma of patients with EE and that the level of this protein may serve as a diagnostic marker for the disorder.

To validate findings, an animal model was developed and used to analyze the role of the eotaxin-3 receptor (CCR3) in the disease and have been able to show that the mice deficient in CCR3 are protected from the disease. There is indication that a blocker of the eotaxin-3 and/or its receptor will be of clinical benefit to patients suffering from this poorly treated disease.

Dr. Rothenberg has also identified diagnostic criteria for eosinophilic esophagitis, allowing physicians to distinguish EE from chronic esophagitis typical of gastroesophageal reflux disease (GERD) and normal individuals. These biomarkers can also be used as indicators of therapeutic effectiveness.

We are currently seeking partners to develop Dr. Rothenberg's findings into beneficial therapeutics and diagnostics for patients with eosinophilic esophagitis.

APPLICATIONS

1. Therapeutic target and diagnostic for eosinophilic esophagitis disease
2. Criteria for distinguishing EE from GERD and normal individuals
3. Biomarker for monitoring therapeutic effectiveness
4. Murine model
5. Research tool

ADVANTAGES

- Non-invasive, less expensive method of diagnosis
- Distinguish between types of esophagitis
- Biomarker of therapeutic effectiveness

INVESTIGATORS

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STATUS

Patent applications pending.

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THE INVENTOR

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BACKGROUND

MD, PhD: Harvard Medical School, Cambridge, MA, 1990.

Residency: Pediatrics, Children's Hospital, Boston, MA, 1991-1992.

Fellowship: Immunology / Allergy, Children's Hospital, Boston, MA, 1992-1994;
Hematology / Oncology, Children's Hospital and Dana Farber
Cancer Institute, Boston, MA, 1992-1995.

Certification: National Board of Medical Examiners, 1991;
Board of Registration in Medicine, MA, 1992;
American Board of Pediatrics, 1995, 2001;
Ohio State Medical Board, 1997;
American Board of Allergy and Immunology, 1997;
American Board of Pediatrics recertification, 2000.



Dr. Rothenberg investigates the mechanisms of allergic responses especially in mucosal tissues with a primary focus on the gastrointestinal tract. The goal of the research is to develop the best treatment strategy for allergic disorders (especially eosinophilic gastrointestinal disorders (EGIDs) based on mechanism-driven research.

He uses multiple approaches involving analysis of the cellular and molecular processes in vitro and in vivo, often utilizing genetically engineered mice. In addition, several novel models of antigen-driven allergic gastrointestinal disorders have been developed and these provide the experimental framework for identifying mechanisms of disease.

Furthermore, translational research involving several aspects of patient-based research including innovative drug intervention clinical trials, genome wide expression profiling of intestinal tissue, and genetic analysis using candidate gene approaches are underway. For example, early results with humanized anti-IL-5 therapy in patients with EGIDS have revealed a promising role for this new biological modifier, prompting an ongoing placebo-controlled clinical trial.