

# Novel Therapeutic for Eosinophilic-related Diseases



Center for Technology Commercialization

## TECHNICAL FIELD

Therapeutic: Mig, Eosinophilic Diseases (2002-0924)

## BACKGROUND

Eosinophils are granulocytic leukocytes (white blood cells) normally present in low numbers in peripheral blood and their presence in tissues is normally restricted to gastrointestinal mucosa. The primary function of eosinophils is to defend against invading organisms. Several disease states including allergic disorders, asthma, eosinophilic gastroenteritis and hypereosinophilic syndrome are associated with increased numbers of eosinophils in blood and/or tissues. Th2 cytokines, especially IL-5, control the proliferation and differentiation of eosinophils. Eosinophil accumulation is controlled by a variety of chemokines, including the eotaxins which interact with the eosinophil-specific CCR3 receptor. Activated eosinophils release toxic enzymes and induce the synthesis of inflammatory mediators, killing invading organisms but also resulting in local tissue damage. In eosinophilic diseases, increased numbers of eosinophils cause tissue damage and disease progression.

Methods to control the proliferation and/or trafficking of eosinophils in these diseases would provide therapeutic value.



## TECHNOLOGY

Dr. Marc Rothenberg and colleagues at Cincinnati Children's Research Foundation discovered that Mig (monokine induced by interferon), a chemokine induced by Th1 cells, inhibited both eosinophil recruitment and effector function in a mouse model of lung allergy<sup>1</sup>. Intravenous administration of microgram levels of Mig prior to IL-13 or allergen stimulation inhibited eosinophil migration to lung tissue. Pretreatment of mice with Mig inhibited eotaxin induced eosinophil migration to the lung, demonstrating that Mig specifically interferes with CCR3 ligand induced functions. Pretreatment with Mig also inhibited eotaxin-induced mobilization of eosinophils to blood. In isolated eosinophils, Mig caused decreased superoxide production in response to eotaxin, demonstrating that Mig regulates eosinophil effector function. Mig inhibits eosinophil responses to both CCR3 and non-CCR3 ligands through negative signaling via the CCR3 receptor.

Its ability to regulate both eosinophil recruitment and effector function suggests novel therapeutic applications of Mig in a variety of eosinophil mediated diseases including asthma, allergy and eosinophilic syndromes.

<sup>1</sup>Fulkerson PC et al, Proc. Natl. Acad. Sci. 101:1987-92 (2004).

## APPLICATIONS

**1. Therapeutic for Eosinophilic-related disorders, such as asthma and allergies**

**2. Research tool**

## ADVANTAGES

- **Non-invasive therapy**
- **Avoid potential tears in esophagus caused by 'gentle esophageal dilation' therapy**
- **Avoid long term effects from steroid therapy**
- **Multiple disease states and potentially large therapeutic markets**

## INVESTIGATOR

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Professor and Division Head  
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## STATUS

Patent applications pending.

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# Novel Therapeutic for Eosinophilic-related Diseases

## THE INVENTOR

Marc E. Rothenberg, MD, PhD  
Director, Allergy and Immunology

## 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.