

TECHNICAL FIELD

Therapeutic: CCR3 Regulation (1999-0210)

BACKGROUND

Eosinophils are a type of granulocyte (white blood cell) that normally appears in peripheral blood at a concentration of ~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, 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.



TECHNOLOGY

CC chemokine receptor-3 (CCR3) is the major chemokine receptor on eosinophils and represents a potential target for intervention in allergic illnesses and other eosinophil-related diseases. Expression and modulation of CCR3 is therefore a useful tool in assessing eosinophil targeting and in regulating eosinophil-related inflammatory processes. Drs. Marc Rothenberg and Nives Zimmermann of the Cincinnati Children's Research Foundation have discovered methods for regulating the expression of CCR3. One such method involves the regulation of expression at the level of untranslated exon 1 of a CCR3 gene or messenger RNA. Another approach utilizes the regulation of expression of CCR3 at the level of the CCR3 promoter.

These methods represent a distinct advantage over other approaches to eosinophil regulation by providing the ability to selectively regulate CCR3 expression in eosinophils and not in other cell types. Such selectivity is highly desirable for markedly reducing deleterious side effects of a pharmacologic treatment embodied in these methods. These methods likewise represent a platform technology because of the wide variety of diseases that potentially can be effectively treated.

APPLICATIONS

- 1. Therapeutic for Eosinophilic-related diseases and other allergic and inflammatory disorders**
- 2. Research tool**

ADVANTAGES

- Increase therapy effectiveness**
- Potential direct therapeutic for eosinophilic diseases and other inflammatory disorders, providing multiple market opportunities**

INVESTIGATORS

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STATUS

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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.

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Hematology / Oncology, Children's Hospital and Dana Farber Cancer
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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;
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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.