Gene Therapy for Eosinophilic Disorders

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Technology description

This invention allows for the treatment of eosinophilic disorders by administration of an adeno-associated virus (AAV) expressing the genetic sequence for an anti-eosinophil monoclonal antibody.

Technology Overview

Eosinophils are highly specialized, bone-marrow derived, granulocytic effector cells (white blood cells) that store and release several highly active mediators. They have been implicated in a variety of chronic allergic disorders, including asthma, eosinophilic esophagitis as well as certain types of cancers and are characterized by persistent blood eosinophilia and infiltration of eosinophils into the diseased organ, wherein they release cellular mediators involved in disease pathogenesis.

Eosinophilic disorders have largely been treated with chronic administration of corticosteroids; while often effective, chronic corticosteroid therapy is commonly linked to numerous adverse effects. Monoclonal therapeutics have also been developed to: (1) reduce bone marrow eosinophil production by targeting eosinophil receptors; (2) induce eosinophil apoptosis; and (3) modulate eosinophil function.

While there has been some success with anti-IL5 and anti-IL4/anti-ILI3 receptor monoclonals, this approach suppresses only production, with no effect on tissue eosinophil accumulation secondary to local signals in the diseased tissues. In contrast, while far less attention has been paid to antibodies that induce eosinophil apoptosis, there is compelling experimental animal data to demonstrate that anti-eosinophil antibodies not only reduce the numbers of blood eosinophils, but also the numbers of bone marrow and tissue eosinophils.

The inventors have disclosed a technology for the development of a therapeutic that induces apoptosis of eosinophils. However, rather than using an anti-eosinophil monoclonal antibody which requires repeated parenteral administration to maintain anti-eosinophil efficacy, they disclose a novel gene therapy-based platform in which an AAV expressing the genetic sequence for an anti-eosinophil monoclonal can be used to genetically modify liver hepatocytes to express and secrete an anti-eosinophil monoclonal which will function to induce apoptosis of bone marrow, blood and tissue eosinophils.

Application area

Thisin vivogene therapy can be used to treat diseases with no known cures, such as chronic eosinophilic leukemia-not otherwise specified (CEL-NOS).

Advantages

This technology is designed as a one-time therapy to suppress total body eosinophils in atopic individuals and will provide sustained, long-term therapeutic benefit for the treatment of eosinophilic disorders.

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