Weill Cornell Medicine

Vectorized Anti-Eosinophil Antibodies for Treatment of Eosinophilic Leukemias and Inflammatory Disorders

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Vectorized Anti-Eosinophil Antibodies for Treatment of Eosinophilic Leukemias and Inflammatory Disorders

Background & Unmet Need

- Eosinophils are highly specialized, bone-marrow derived, granulocytic effector cells (white blood cells) that store and release several highly active mediators
- Eosinophils are implicated in a variety of chronic allergic disorders, including asthma and eosinophilic esophagitis (EoE), as well as certain cancers (e.g., chronic eosinophilic leukemia-not otherwise specified (CEL-NOS))
- Eosinophilic disorders have largely been treated with chronic administration of corticosteroids, which are commonly linked to numerous adverse effects
- Antibody therapeutics are effective for many patients, but must be repeatedly administered for continuous efficacy
- **Unmet Need:** Therapeutics for eosinophilic disorders which address eosinophil accumulation and provide sustained, long-term benefits for patients

Technology Overview

- **The Technology:** AAV gene therapy that provides sustained *in situ* expression of an anti-eosinophil monoclonal antibody for eosinophilic disorders
- Various anti-eosinophil antibodies for targets such as Siglec-8 or IL-5 may be incorporated in the vector
- AAVrh.10mAnti-Eos is an rh.10 AAV vector encoding antibody Siglec F, which induces eosinophil apoptosis
- **PoC Data:** A single dose of AAVrh.10mAnti-Eos resulted in high, persistent serum levels of Siglec-F
- In a mouse model of CEL-NOS, a single dose of AAVrh.10mAnti-Eos provided long-term suppression of eosinophils in blood and increased survival
- In a mouse model of EoE, AAVrh.10mAnti-Eos administration reduced blood and esophageal eosinophil numbers ($P < 0.02$ and $P < 0.002$, respectively), protected from esophageal tissue remodeling, and minimized food impaction

Inventors:
Ronald G. Crystal
Odelya Pagovich
Katie Stiles

Patents:
US Application Filed
EP Application Filed
Additional Applications Filed in AU, BR, CA, CN, IL

Publications:
Pagovich et al. *Leukemia*. 2022.
Camilleri et al. *Allergy*. 2021.

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Cornell Reference:
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CEL-NOS: Chronic Eosinophilic Leukemia-not otherwise specified
EoE: Eosinophilic Esophagitis

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Technology Applications

- Treatment of CEL-NOS and other leukemias where eosinophils play a prominent role
- Treatment of EoE and related eosinophilic gastric disorders
- Treatment of other disorders in which eosinophils are elevated, including allergic and endocrine disorders

Technology Advantages

- A single dose may be sufficient for sustained therapeutic effect
- Provides a platform for expression of various anti-eosinophil antibodies, such as Siglec-8 or IL-5

Supporting Data / Figures

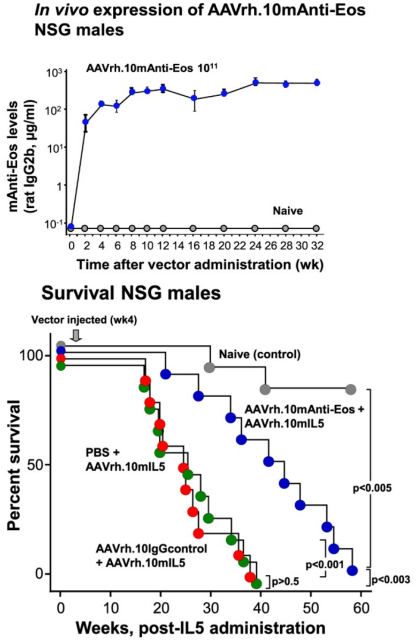

Figure 1: Top: Mice administered intravenous AAVrh.10mAnti-Eos demonstrate high levels of murine anti-Siglec-F monoclonal antibody levels over time. **Bottom:** Mice administered with AAVrh.10mAnti-Eos demonstrate improved overall survival in a model of CEL-NOS (AAVrh.10mIL5).

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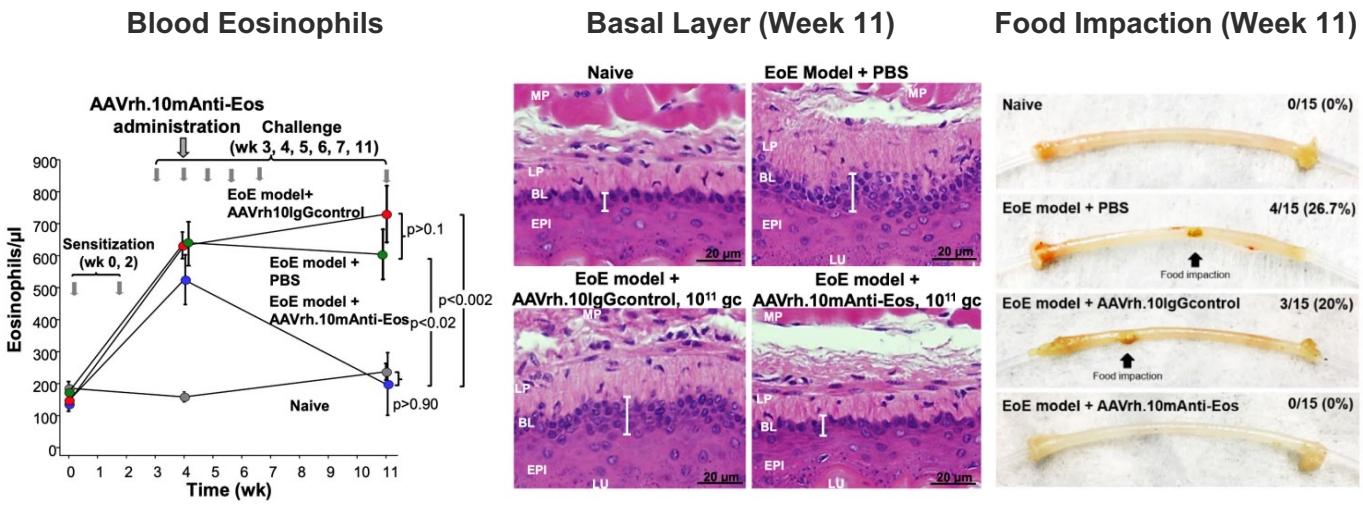

Figure 2: Left: Eosinophil numbers in blood of EoE mice treated with AAVrh.10mAnti-Eos were reduced compared to controls **Middle:** Tissue remodeling, as demonstrated by increase in area of basal lamina (white bar), was decreased in mice treated with AAVrh.10mAnti-Eos in a murine model of EoE **Right:** Food impaction in esophagus over 11 weeks decreased with administration of AAVrh.10mAnti-Eos.

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