



NYU



Apoptosis Inhibitor 5 (API5)-based Therapeutic for the Treatment of Inflammatory Bowel Diseases

A novel disease-modifying treatment of inflammatory bowel diseases that doesn't compromise the patient immune system.

Technology

The NYU innovators have developed a novel synthetic peptide with a differentiated mechanism of action that prevents pathological intestinal epithelium damage of various inflammatory bowel diseases (IBDs). The peptide is based on apoptosis inhibitor 5 (API5), a novel T cell effector, which the innovators demonstrated in *Matsuzawa-Ishimoto et al. Nature 2022* to be an extracellular soluble factor that masks genetic susceptibility to the major IBD, Crohn's disease. API5 is secreted by $\gamma\delta$ intraepithelial lymphocytes within the intestine and prevents cytokine-mediated Paneth cell death. In patients with Crohn's disease who carry the *ATG16L1* risk allele, inflammatory triggers lead to pathological disruption of the intestinal epithelial barrier by reducing Paneth cell viability. The NYU innovators have shown that recombinant API5 (rhAPI5) prevents Paneth cell death and promotes intestinal epithelium restitution in vivo in mice and ex vivo in human organoids with the *ATG16L1* risk allele. Further, they found rhAPI5 to reduce TNFa levels in mice and inflammatory signaling cascades in human organoids, indicating that rhAPI5 dampens the activity of harmful immune mediators associated with Crohn's disease. Altogether, these promising preliminary data suggest that recombinant administration of API5 is a differentiated disease-modifying approach for the treatment of IBD that likely carries key advantages over standard-of-care immunosuppressive therapies.

Background

There are an estimated 2.39 million people with IBD within the US as of 2023, which constitutes a 46% increase in prevalence from 15 years prior and a growing multi-billion-dollar therapeutic market. Inflammatory bowel diseases such as Crohn's disease are characterized by immune-mediated damage to the intestinal epithelium. Current therapeutic strategies for IBD primarily target immune effectors, including those blocking tumor necrosis factor alpha (TNFa) or lymphocyte migration. However, these systemic therapies often fall short in providing long-term remission, as they indiscriminately suppress both pathological and beneficial immune responses necessary for maintaining gut microbiota homeostasis. In addition, these systemic treatments can lead to serious adverse events, including an increased risk of infections, and a significant proportion of patients either do not respond or acquire resistance to these treatments over time. The API5-based innovation described here could potentially offer a more effective and safer treatment alternative, enhancing the resilience of the epithelium against immune-mediated injury without compromising the immune system.

Applications

The treatment of IBDs, including but not limited to:

Technology ID

CAD01-05

Category

Life Sciences/Biologics

Life

Sciences/Therapeutics/Inflammat
Disease

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Learn more



- Crohn's disease
- Ulcerative colitis
- Graft-versus-host disease
- Pouchitis
- Immune checkpoint inhibitor-associated colitis
- Radiation-induced gastrointestinal toxicity
- Irritable bowel syndrome

Advantages

- **Disease modifying potential:** Causes restoration of the intestinal epithelial barrier, a critical factor in maintaining long-term remission in IBD.
- **Non-immunosuppressive:** This API5-based approach selectively targets the underlying pathology in the ileum rather than systemically suppressing the patient immune response.
- **Reduced side effects:** Not expected to carry the adverse side effects common to immunosuppressive drugs (e.g., Existing biomarker: The API5-based approach would be applicable to patients carrying the *ATG16L1* risk allele or with Paneth cell abnormalities, representing more than 50% of IBD patients).
- **Monotherapy or complementary to existing treatments:** The API5-based therapeutic could be used as a monotherapy or alongside existing immunosuppressive drugs, potentially enhancing treatment efficacy.

Development Stage

The innovators are currently collaborating with NYU's internal drug development accelerator program ([Therapeutics Alliances](#)) to 1) test the efficacy of API5 across other IBD subtypes 2) develop the minimal functional fragment of API5 suitable for therapeutic development and 3) generate basic pharmacokinetic and toxicology data.

Intellectual Property

NYU has non-provisional patent applications filed in the U.S., Europe, Brazil, Canada, Mexico, Australia, Japan, Russia and China covering the composition of recombinant API5 fragments and their method of use.

References

1. Matsuzawa-Ishimoto, Y., Yao, X., Koide, A. et al. , <https://doi.org/10.1038/s41586-022-05259-y>