Anti-Bin1 to Treat Inflammatory Bowel Disease

Technology Readiness Level 6: Demonstrated in Relevant Environment

Lead Investigators

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Unmet Need

Inflammatory bowel disease (IBD), which includes ulcerative colitis (UC) and Crohn's disease, is a debilitating autoimmune condition that is clinically challenging to manage effectively. In the U.S., the CDC estimates that 1.3% of adults (about 3 million) have been diagnosed with IBD. Many IBD patients are diagnosed early in life. As a result of chronic gut inflammation, they experience a higher incidence of colorectal cancer. Available treatments tend to generally suppress natural immunity or inflammatory signals, leading to many side-effects and elevated risks of infection and cancer. At present, there are still no therapies that can treat or prevent IBD flare-ups in a disease-selective manner, without damaging in parallel normal immune or inflammatory processes that are limit infections and cancer risks.

Opportunity

In developed countries, the incidence of autoimmune diseases including IBD is skyrocketing. As newly industrialized countries become more Westernized IBD incidence rises, extending the global reach of this disease. The global market for gastrointestinal autoimmune disease therapeutics is expected to grow from US $51.9B in 2016 to US $65.1 by 2025, according to the business intelligence provider Grand View Research.[1]

Unique Attributes

Building on their expertise in tissue barrier functions of the gastrointestinal tract, LIMR scientists developed an approach that broadly tames chronic inflammatory and autoimmune cells. This approach focuses on antibody-mediated inactivation of the inflammatory modifier protein Bin1, a membrane-associated molecule that promotes gastrointestinal inflammation in the setting of IBD. LIMR's therapeutic technology is based on a novel MOA to tighten the leaky gut-barrier function that occurs in all IBD patients, thereby attenuating multiple sources of inflammation that are associated with a leaky gut-barrier at once.

The scaffold and signaling molecule Bin1 modifies stress and inflammatory responses of cells under stress. In genetic studies in mice, LIMR scientists discovered that Bin1 ablation dramatically attenuated colonic inflammation and risks of colon carcinogenesis. In exploring therapeutic directions to mimic this effect, they discovered a cell-permeable anti-Bin1 antibody that is safe and effective when delivered systemically in preclinical models of IBD. Human colon tissue studies confirm observations that antibody uptake is sufficient to tighten barrier function, as measured physiologically or molecularly at the

[1] Grand View Research, San Francisco. March 2018.

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level of tight junction protein expression. Accordingly, anti-Bin1 acts to tighten colon barrier function, coordinately reducing mucosal lesions, crypt loss, lymphoid follicle rupture, and infiltration of neutrophils and lymphocytes into mucosal and submucosal areas of the colon.

Clinical Applications

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The LIMR mAb-based strategy offers potential uses to treat multiple types of IBD by the unique mechanism of action of tightening gut barrier function.

Stage of Development

Current work is at a preclinical stage of development, including antibody humanization and ongoing mechanism of action and pharmacology studies.

Intellectual Property

U.S. Patent 10,494,424, issued 3 December 2019. "Methods and Compositions for the Treatment of Diseases and Disorders." Also protected in EP and Japan.

Collaboration Opportunity

Optimization and humanization of murine anti-Bin1 mAb 99D that alleviates IBD in preclinical models and represents a lead for clinical development.

Published References

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