Lunenfeld-Tanenbaum Research Institute
Sinai Health System

TECHNOLOGY TRANSFER & INDUSTRY LIAISON
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TECHNOLOGY ABSTRACT

Secretin Receptor Agonists for Targeted Immune Modulation and Anti-Inflammatory Therapy

Reference No.: INV-2025018

BACKGROUND

G-protein coupled receptors (GPCRs) are critical regulators of cellular signaling and are widely targeted in drug development. Existing GPCR-based therapies, such as GLP-1 receptor agonists, have shown success in treating metabolic diseases like diabetes and obesity. However, these therapies may produce undesirable side effects and lack specificity in modulating immune responses. There is a growing need for therapies that can precisely regulate inflammation without broad immunosuppression. In particular, diseases driven by innate immune activation, such as inflammatory bowel disease, sepsis, and metabolic disorders, require targeted approaches that can modulate immune signaling pathways more effectively and safely.

TECHNOLOGY OVERVIEW

This technology introduces a novel class of synthetic secretin receptor (SR) agonists designed to selectively modulate neuroimmune pathways along the gut-brain-immune axis. The agonists are based on engineered peptide sequences with high homology to native secretin, combined with non-peptidic moieties such as lipid chains or polymers to enhance pharmacokinetic performance. The peptide component maintains strong binding affinity to the secretin receptor, while substitutions and addition of specific amino acid improve stability without compromising activity, extends systemic half-life, enhances tissue residency, and enables sustained receptor engagement. These agonists act on secretin receptors expressed in key regions of the gut-brain-immune axis, including enteric and vagal neurons, allowing pharmacological activation of neuroimmune circuits that regulate inflammation. Unlike conventional anti-inflammatory drugs that broadly suppress immune responses, this approach provides targeted modulation of innate immunity, particularly by attenuating toll-like receptor (TLR)-mediated signaling pathways. Preclinical data shows that the lead compound (BI-3434) effectively suppresses pro-inflammatory cytokines such as TNF-α, IL-6, and IL-1β, and reduces inflammation in models of endotoxemia and colitis. Importantly, the efficacy is comparable to GLP-1 receptor agonists but achieved through a more selective and potentially better-tolerated mechanism.

APPLICATION(S)

- Inflammatory bowel diseases (Crohn's disease, ulecratives colitis)
- Sepsis and endotoxemia
- Metabolic disorders -related inflammation (Type 2 diabates, obesity)
- Autoimmune and inflammatory conditions (e.g. arthritis)
- Neuroimmune and inflammatory disorders

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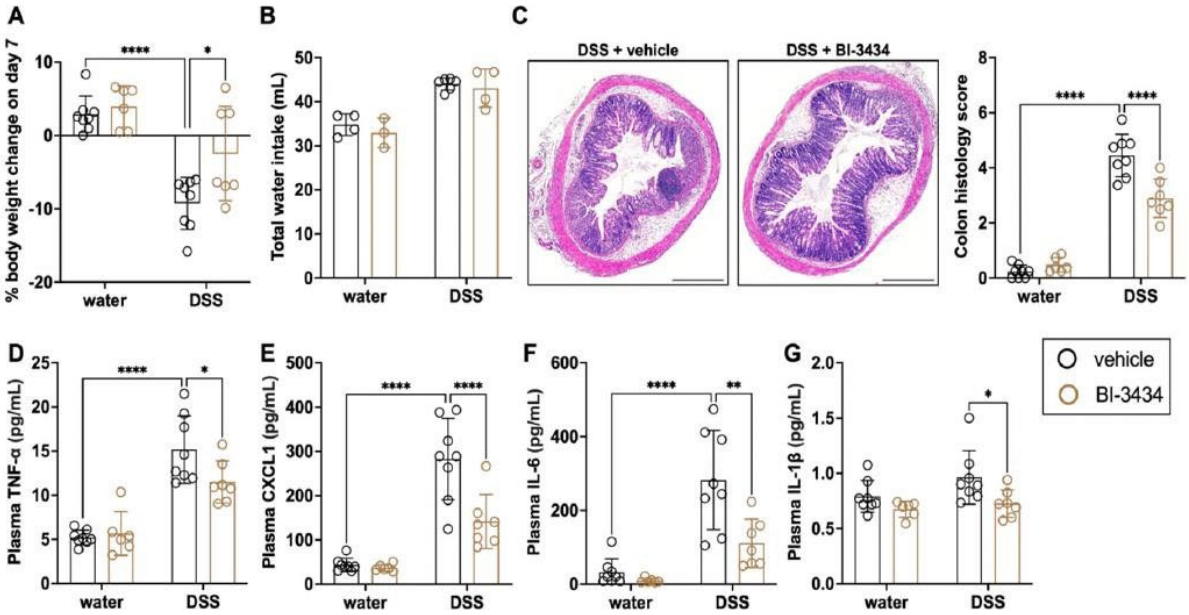

Figure 1. Secretin receptor agonist BI-3434 attenuates disease severity, tissue damage, and systemic inflammation in a DSS-induced colitis model. (A) Percentage body weight change over the study period demonstrates that BI-3434 treatment reduces disease-associated weight loss compared to DSS + vehicle controls. (B) Total water intake remains comparable across groups, indicating that observed differences in disease severity are not due to altered fluid consumption. (C) Representative H&E-stained colon sections (left) and corresponding histological scores (right) show that BI-3434 treatment reduces key markers of colonic damage, including crypt distortion, inflammatory cell infiltration, muscle thickening, goblet cell depletion, and crypt abscess formation. (D–G) Plasma concentrations of pro-inflammatory cytokines and chemokines are significantly reduced following BI-3434 treatment, including (D) TNF-α, (E) CXCL1, (F) IL-6, and (G) IL-1β, demonstrating suppression of systemic inflammatory responses.

COMPETITIVE ADVANTAGE(s):

- Targeted immune modulation: selectively regulates innate immune responses via the secretin receptor along the gut-brain-immune axis, avoiding broad immunosuppression.
- TLR pathway suppression: Inhibits key Toll-like receptor–driven inflammation, including TLR-4 (LPS) and TLR-1/2 (Pam3CSK) signaling.
- Cytokine reduction: Reduces major pro-inflammatory mediators such as TNF-α, IL-6, IL-1β, and CXCL1.

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- Enhanced stability C-terminal lipidation improves systemic stability, prolongs half-life, and supports sustained receptor engagement.
- Broad therapeutic scope: Applicable to acute and chronic diseases driven by innate immune activation, including metabolic, infectious, and autoimmune conditions.
- Improved tissue outcomes: Reduces histological markers of inflammation and tissue damage, including those seen in colitis models.
- Flexible delivery: Compatible with multiple routes of administration, including systemic and non-invasive options.

RESEARCH TEAM:

- Daniel Drucker,
- Profiles of Daniel Drucker,
- Lab Website Drucker Lab

PATENT STATUS: US Provisional Patent Application filed

PUBLICATION: N/A

COMMERCIAL OPPORTUNITIES:

Collaborations and partnerships in:

- Development of next-generation metabolic peptides
- Novel immune-modulating pathways
- Metabolic disease and anti-inflammatory drug development

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