

# CD122 Antagonism Prevented Inflammation in a Murine Model of Celiac Disease and Inhibited the Activity of Cytotoxic CD8+ and Activated CD4+ T Cells from Celiac Patients In Vitro

Richard T. (Rik) Frank<sup>1</sup>, Valerie Abadie<sup>2</sup>, Tierney Kauffman<sup>3</sup>, John Sedy<sup>1</sup>, Matthew Hsu<sup>1</sup>, Cheryl Herrera<sup>1</sup>, Noah Siegel<sup>1</sup>, Yangsu Ren<sup>1</sup>, Stephen Parmley<sup>1</sup>, Martin Dahl<sup>1</sup>

<sup>1</sup>First Tracks Biotherapeutics, San Diego, CA, USA

<sup>2</sup>Department of Medicine, Section of Gastroenterology, Hepatology and Nutrition, Committee on Immunology, University of Chicago, Chicago, IL, USA

<sup>3</sup>University of Chicago, Chicago, IL, USA

19 October 2026 | Barcelona, Spain



# Disclosure of Conflicts of Interest

RTF, JS, MH, CH, NS, YR, SP, and MD are employees and shareholders of First Tracks Biotherapeutics, Inc.

VA's laboratory has, in addition to support from governmental bodies, received research funding from First Tracks Biotherapeutics, Inc. and from Tolerance Bio

TK has nothing to declare

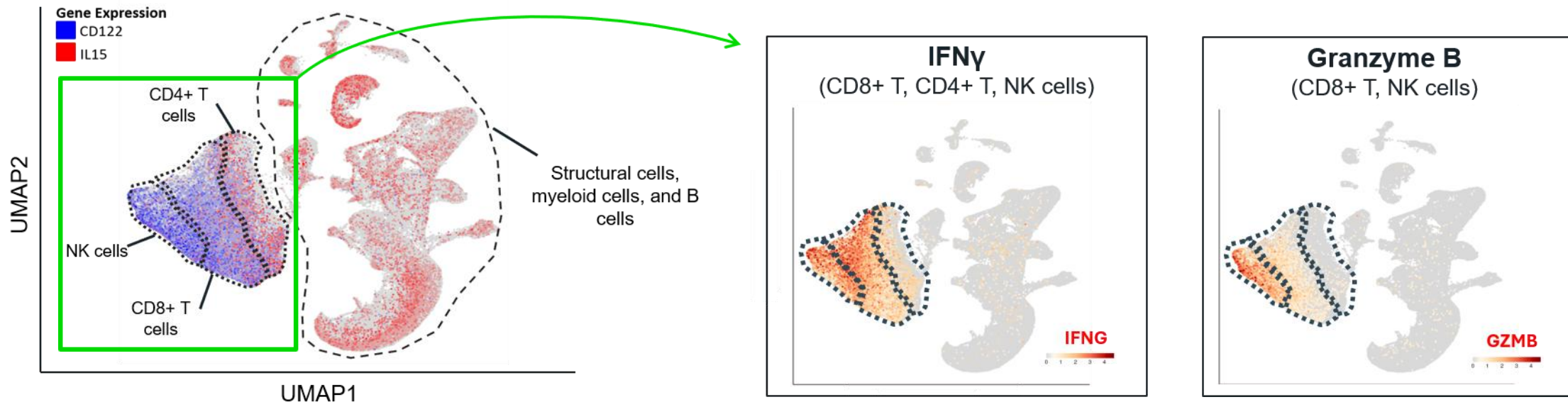
# scRNAseq of CeD Patient-Derived Biopsies Show Prominent Expression of IL-15 and the Presence of CD122+ Immune Cells

**CD122** (shared  $\beta$  subunit of the IL-15 and IL-2 receptors) is expressed on cytotoxic CD8+ T cell subsets, CD4+ T cell subsets, and NK cells<sup>1,2</sup>

## Celiac Disease Intestinal Tissue<sup>3</sup>

- Dense infiltration of inflammatory CD122+ immune cells (CD8+ T, NK, and CD4+ T cells)
- Broad IL-15 expression across structural cells
- About 3-fold increase in CD122+ cells expressing IFN $\gamma$  in CeD vs healthy

### Celiac Intestinal Biopsy



# ANB033 Mechanism of Action

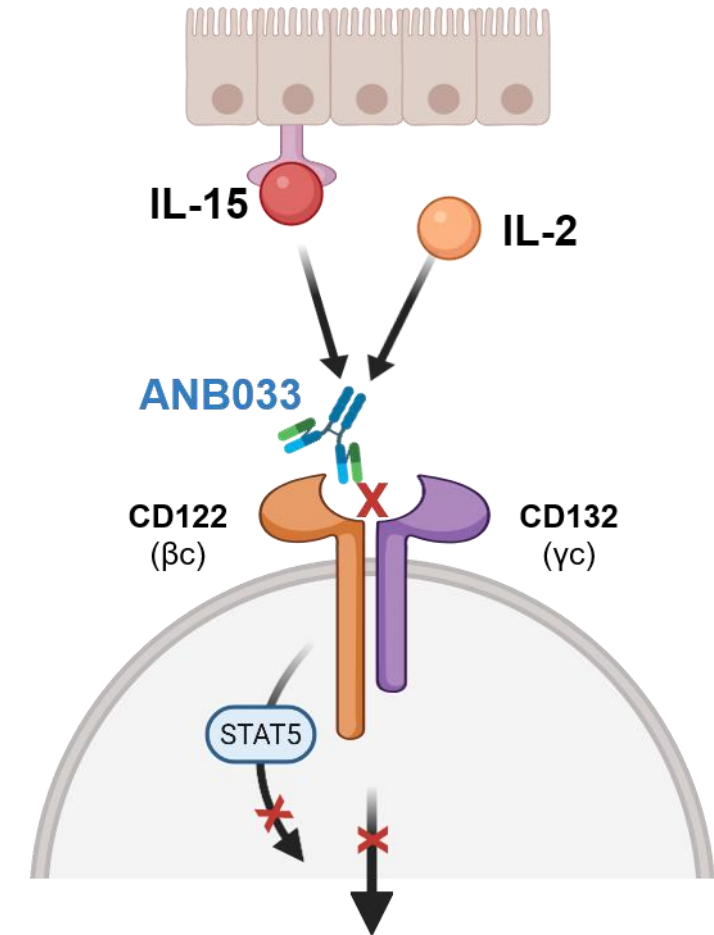
## ANB033

Investigational CD122 Antagonist Monoclonal Antibody

### Proposed Mechanism of Action

Inhibition of IL-15 and IL-2 signaling through CD122 antagonism results in<sup>1,2</sup>:

- Reduced activation, proliferation, and survival of CD122-expressing:
  - Intraepithelial lymphocytes (IELs) including CD8+ T and NK cells
  - Memory CD4+ T cells
- Reduced IL-15- and/or IL-2-dependent pro-inflammatory immune cell cytokine production



# ANB033 (CD122 Antagonist mAb) in Celiac Disease

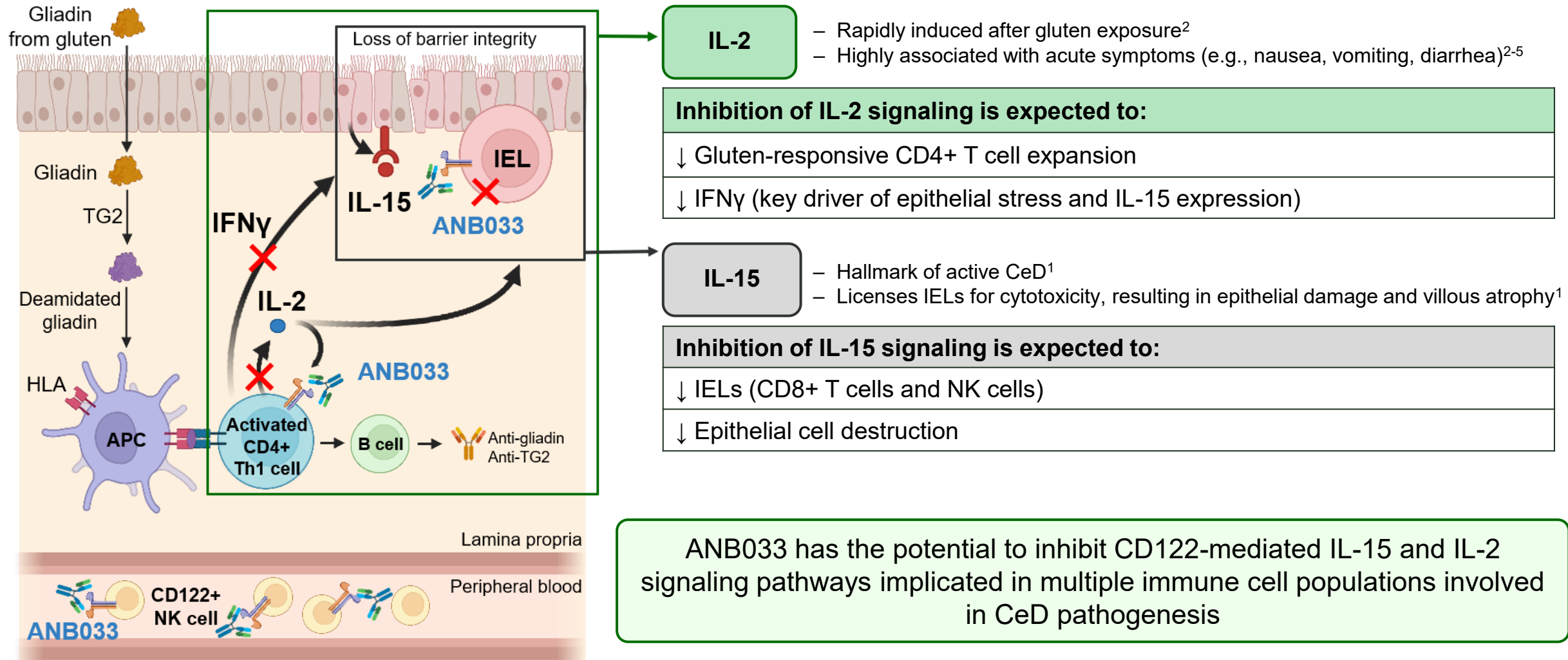
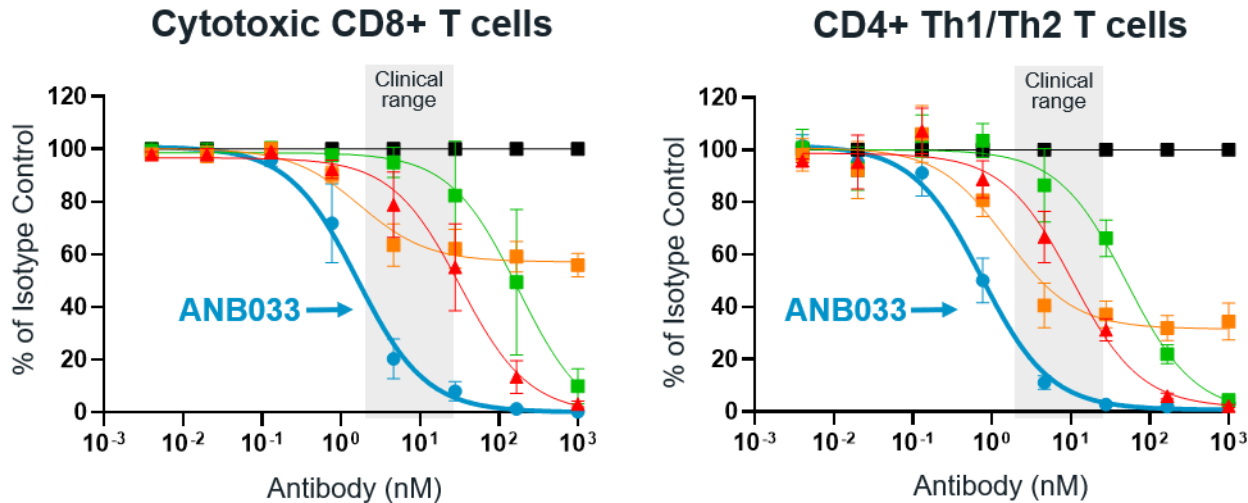


Figure adapted from Dieckman et al. *Curr Opin Pharmacol* 2022;66:102268.

# ANB033 Reduced Proliferation and Inflammatory Cytokines in CD8+ and CD4+ T cells in CeD Patient-Derived PBMCs In Vitro

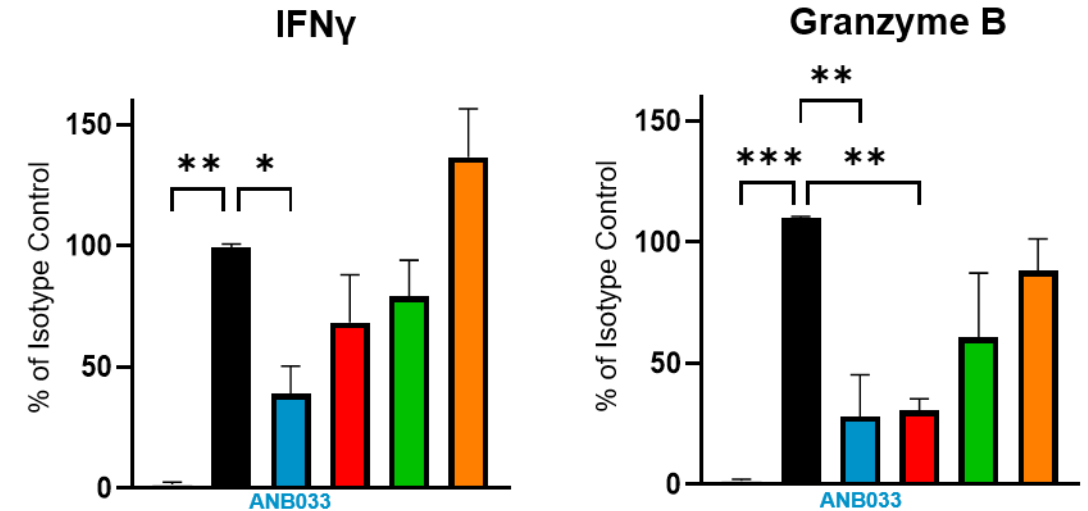
## Proliferation (Ki67)



ANB033 reduced IL-15- and IL-2-mediated proliferation of T cell subsets

CeD patient-derived PBMCs were stimulated for 6 days with IL-15 + IL-2 and assessed for proliferation (Ki67 staining) (N=4)

## Inflammatory Cytokines



ANB033 reduced IFN $\gamma$  and granzyme B production from T cells in response to TCR-stimulation

CeD patient-derived PBMCs were stimulated for 3 days with anti-CD3 and anti-CD28 (N=4); 100nM for all groups. Differences were assessed using one-way ANOVA with Dunnett's post-hoc test for 5 simultaneous comparisons (\*p<0.05, \*\*p<0.01).

Unstimulated Isotype Control ANB033 Anti-CD122 Reference 1 Anti-CD122 Reference 2 Anti-IL15 Reference

# Murine Model of Gluten Challenge in Celiac Disease

## Murine Model<sup>1,2</sup>

DQ8-D<sup>d</sup>-villin-IL-15tg mice

- Transgenic for HLA-DQ8
- D<sup>d</sup> promoter drives IL-15 expression in lamina propria (LP)
- Villin promoter drives epithelial IL-15 expression

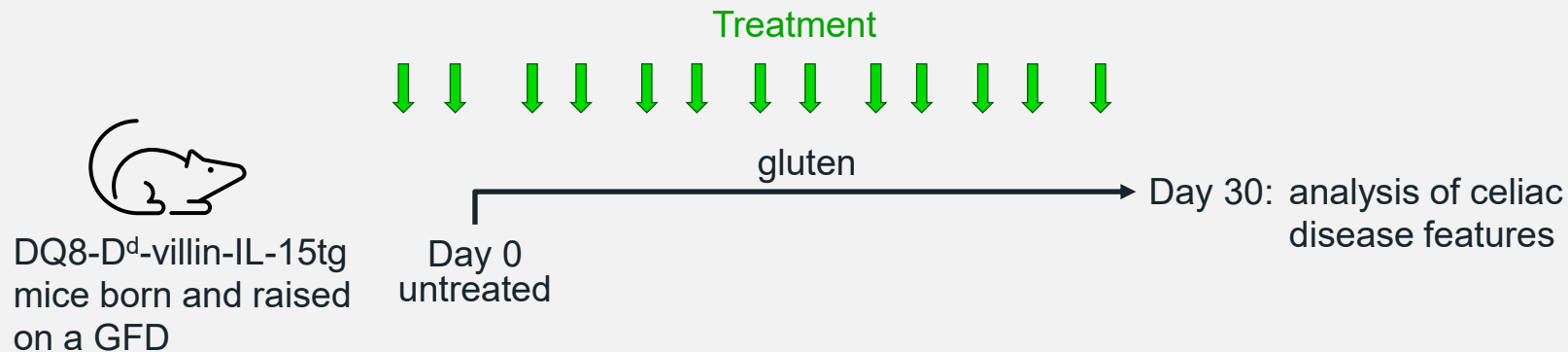
Model achieves main features of CeD<sup>1,2</sup>:

- Gluten-induced villous atrophy
- T<sub>H</sub>1 immune response (IFN $\gamma$  in LP)
- Increase in cytotoxic IEL
- Features recede on gluten free diet (GFD)

## ANB033 Surrogate Antibody

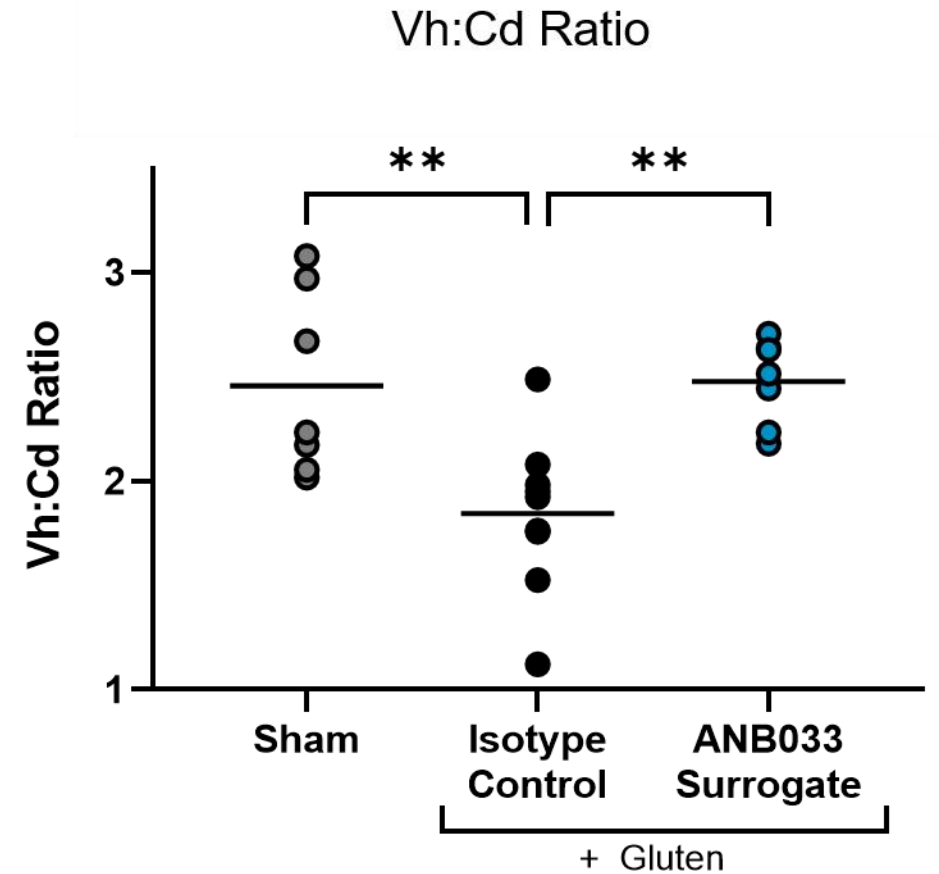
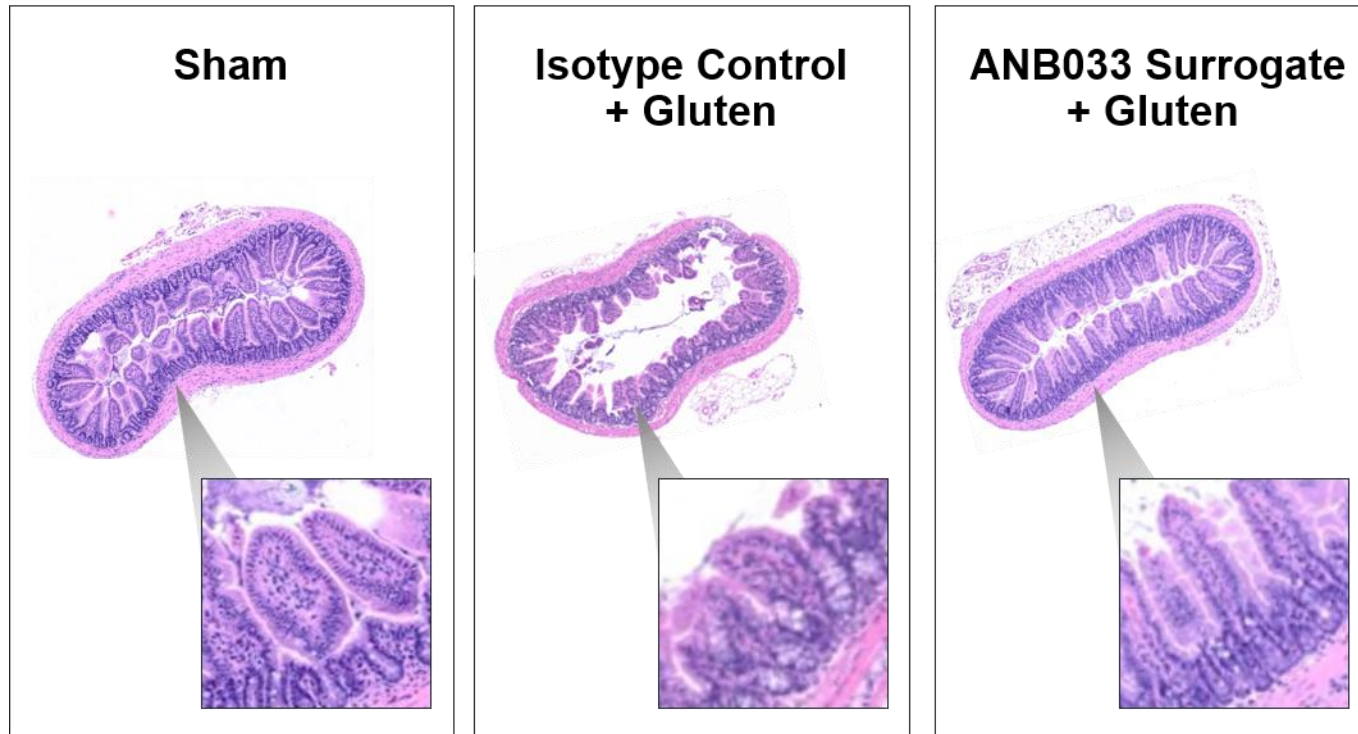
- Mouse-reactive anti-CD122 antibody engineered to have similar epitope, binding affinity, and isotype

## Study Schema

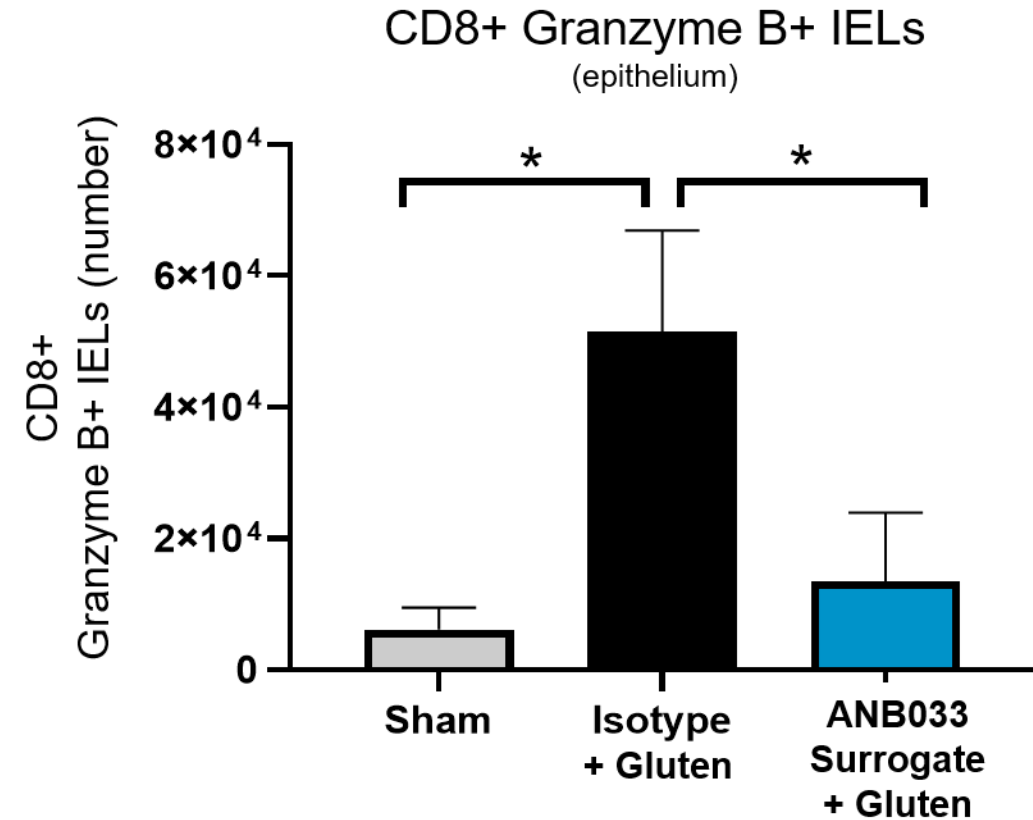
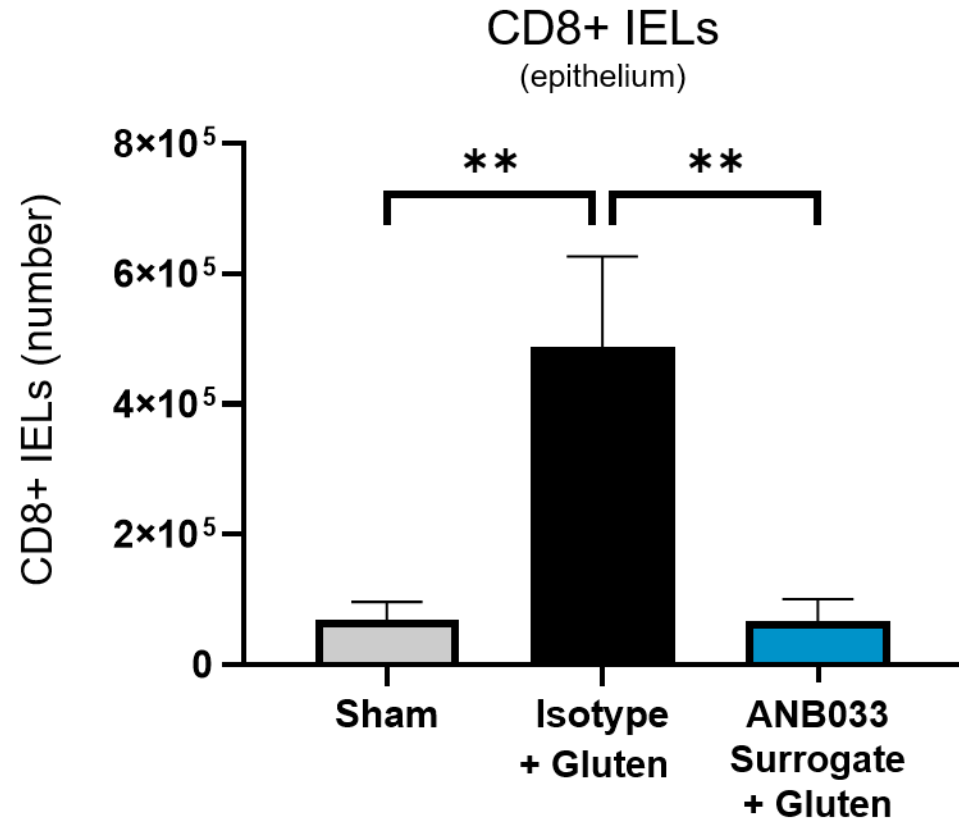


| Treatment Group               | Dosing Schedule |
|-------------------------------|-----------------|
| Sham (No Gluten)              | N/A             |
| Isotype Control               | BIW, 13 total   |
| Anti-CD122 (ANB033 surrogate) | BIW, 13 total   |

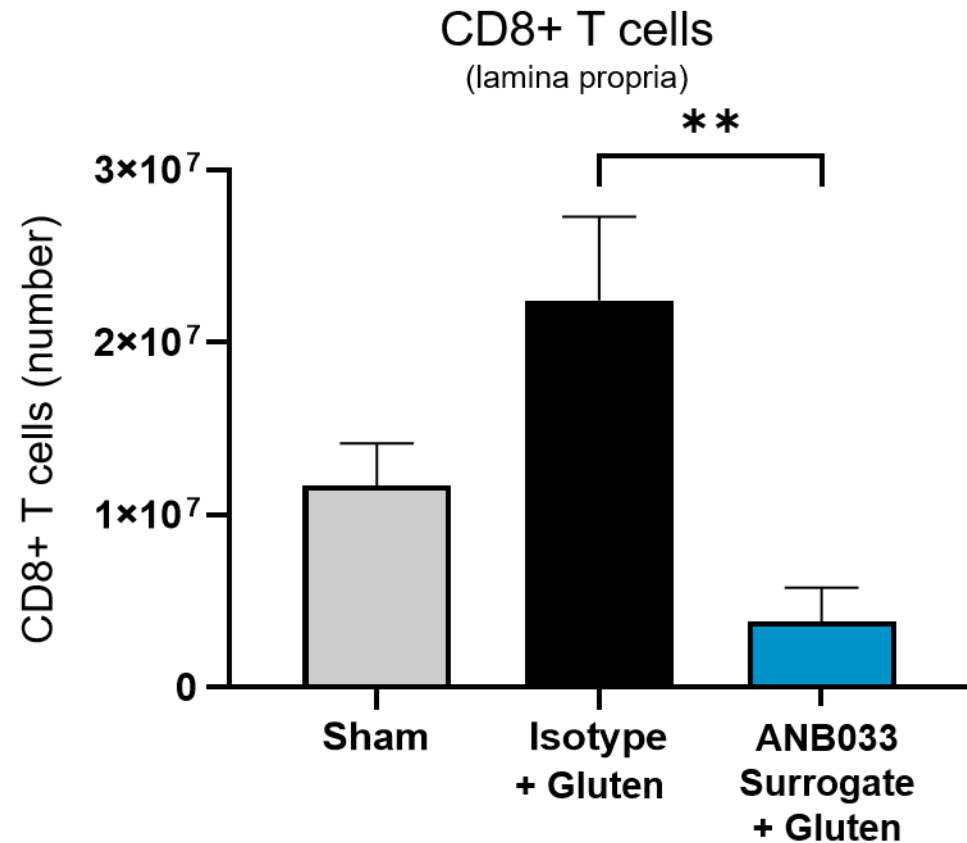
# ANB033 Surrogate Prevented Gluten-induced Villous Atrophy in Murine Model



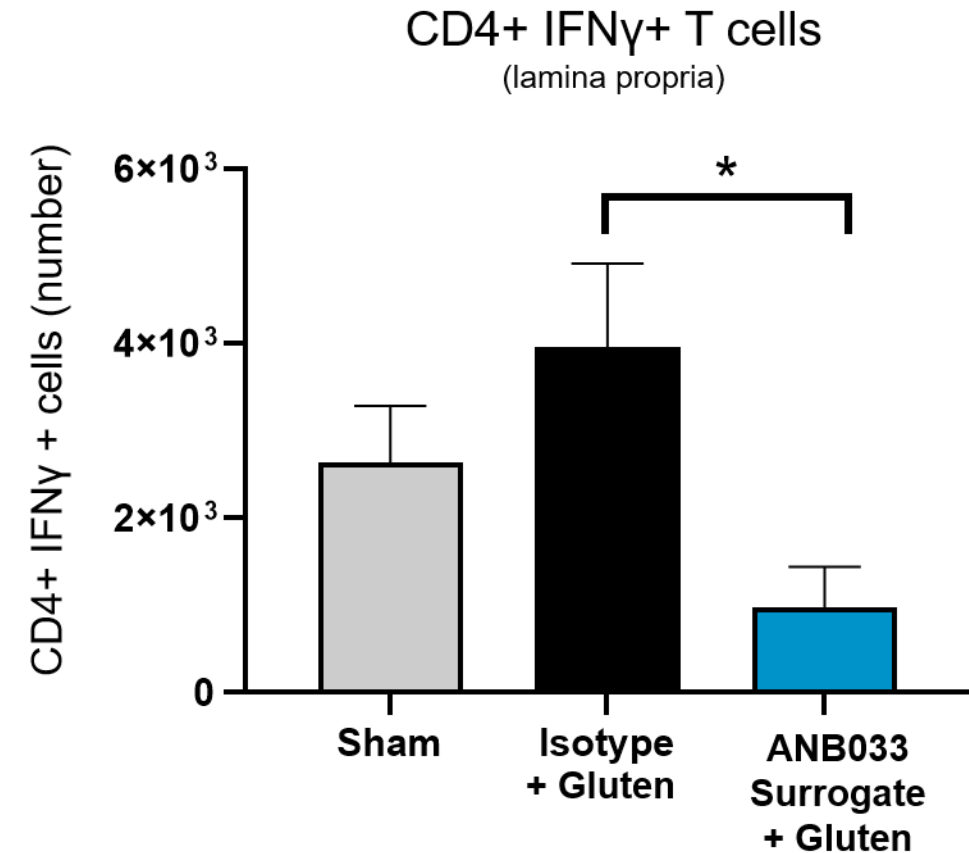
# ANB033 Surrogate Prevented Gluten-induced Inflammation in the Intestinal Epithelium In Vivo



# ANB033 Surrogate Prevented Gluten-induced Inflammation in the Lamina Propria In Vivo



Reduced gluten-induced expansion  
of total CD8+ T cells



Reduced number of CD4+ T cells  
expressing IFN $\gamma$

# Summary

- The prominence of IL-15, IL-2, and CD122-expressing immune cells in celiac disease supports CD122 targeting as a potential therapeutic strategy
- ANB033 inhibits CD122-mediated IL-15 and IL-2 signaling resulting in:
  - Reduced T cell proliferation and secretion of inflammatory cytokines and cytotoxic mediators in celiac disease patient-derived PBMCs in vitro
  - Prevention of villous atrophy and reduced gluten-induced inflammation in both the epithelium and lamina propria in mice treated with an ANB033 surrogate antibody in a preclinical model of celiac disease
- CD122 antagonism by ANB033 may provide a broader, upstream approach (vs IL-15 antagonism alone) for celiac disease by addressing two critical cytokine signaling pathways and key immune cells involved in inflammation and epithelial injury
- These data support the continued evaluation of ANB033 in a Ph1b study in celiac disease (ISRCTN16318446)

