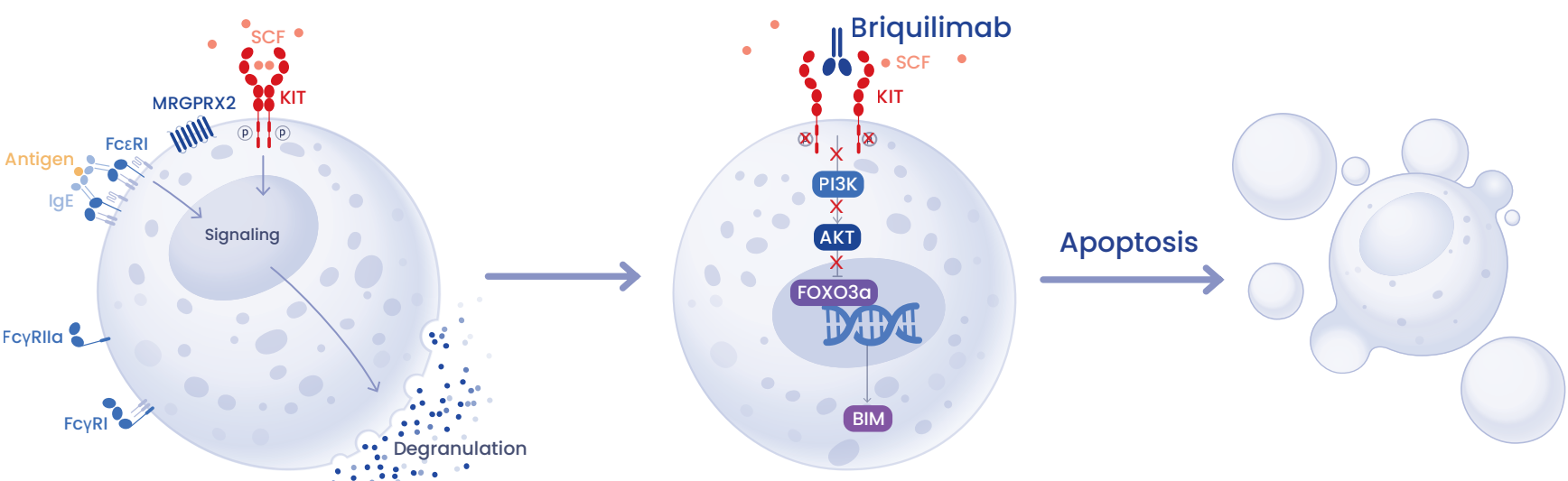


Targeting Mast Cells with Briquilimab, a Human KIT (CD117) Antibody, Mitigates COPD-Like Features in an Allergen and Cigarette Smoke-Exacerbated Asthma Model Using Humanized h/mCD117 Mice

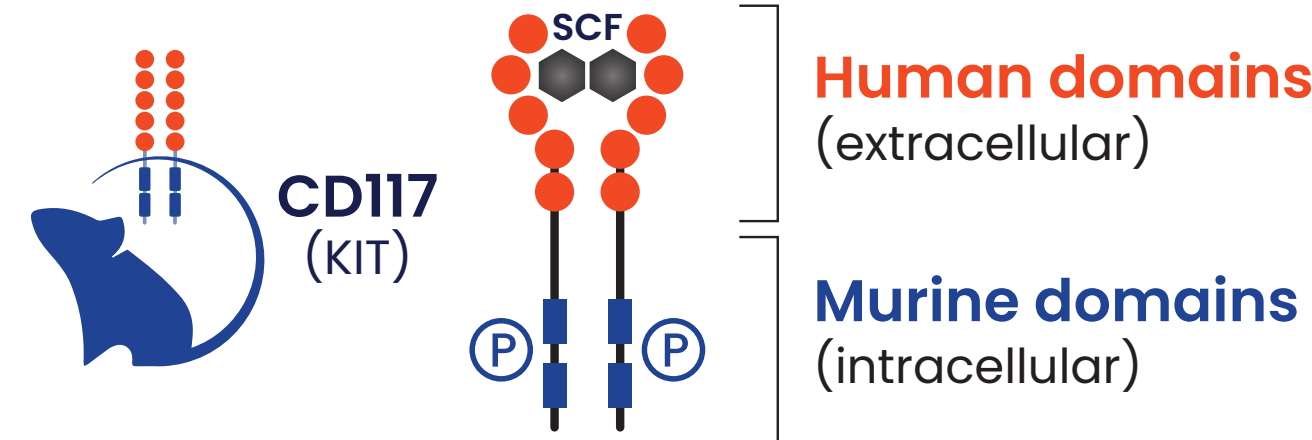
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Introduction

- Briquilimab is a humanized, aglycosylated anti-KIT monoclonal antibody that functionally blocks the interaction between KIT (CD117) and stem cell factor (SCF), thereby disrupting a key survival signal and inducing mast cell (MC) apoptosis



- Transgenic h/mCD117 mice, which express the functional human extracellular and murine intracellular domains of KIT, provide a clinically relevant platform for proof-of-concept efficacy testing

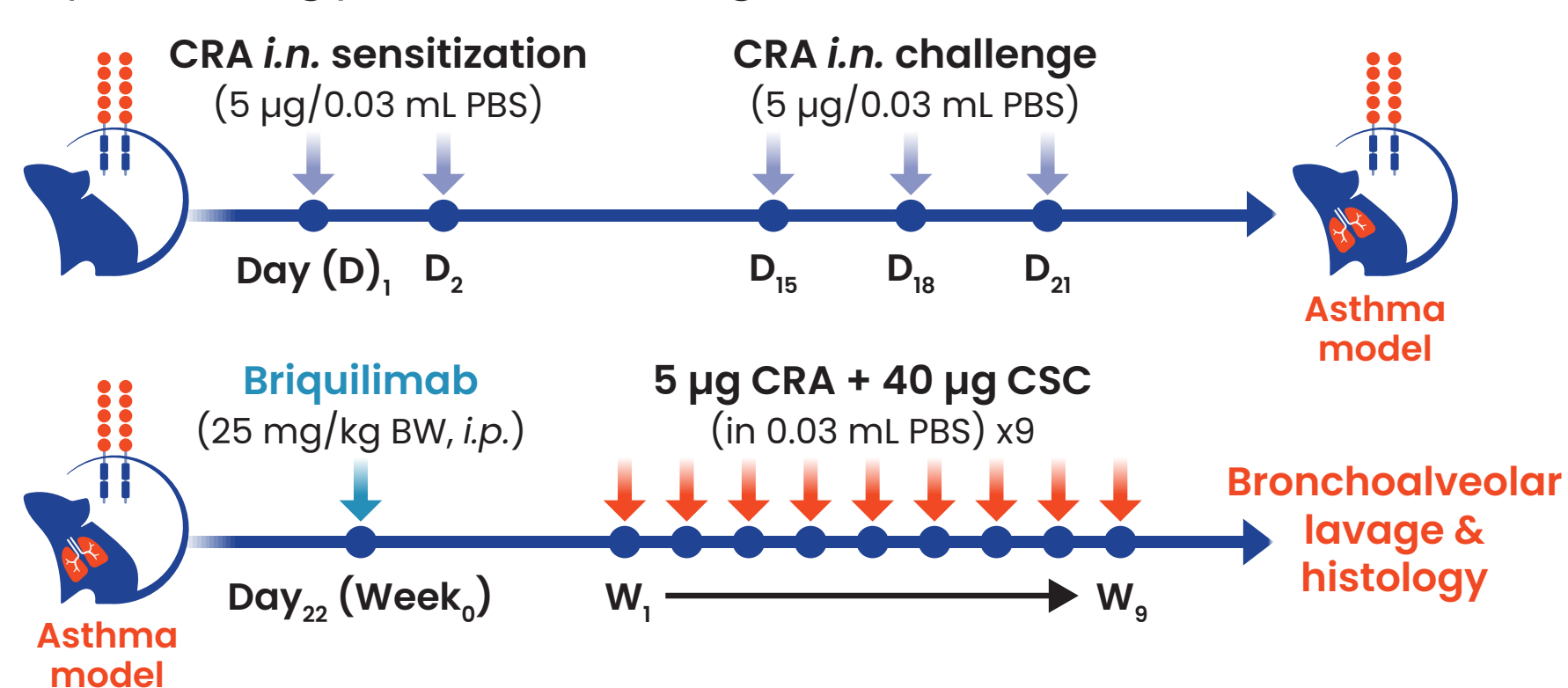


- A single dose of briquilimab previously demonstrated efficacy in an asthma model induced in h/mCD117 mice through intranasal (*i.n.*) exposure to cockroach allergen (CRA)

Methods

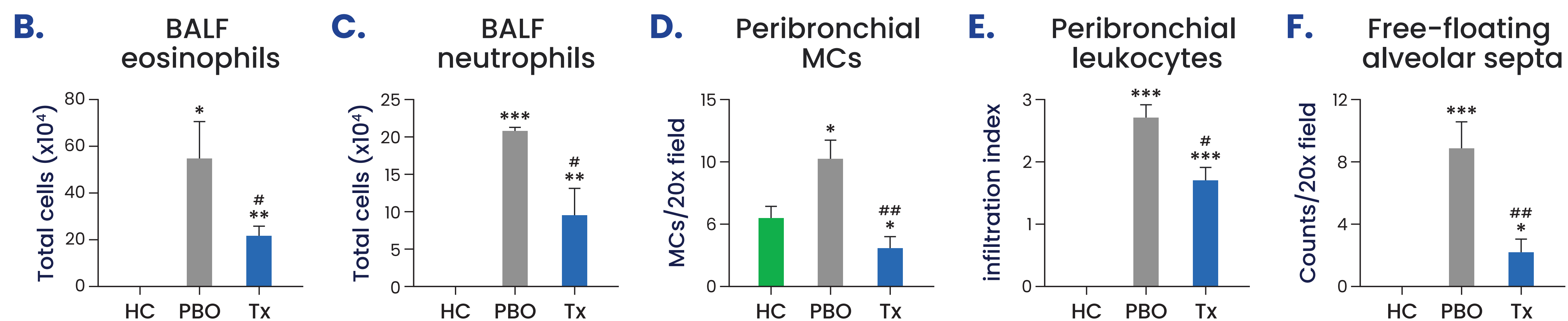
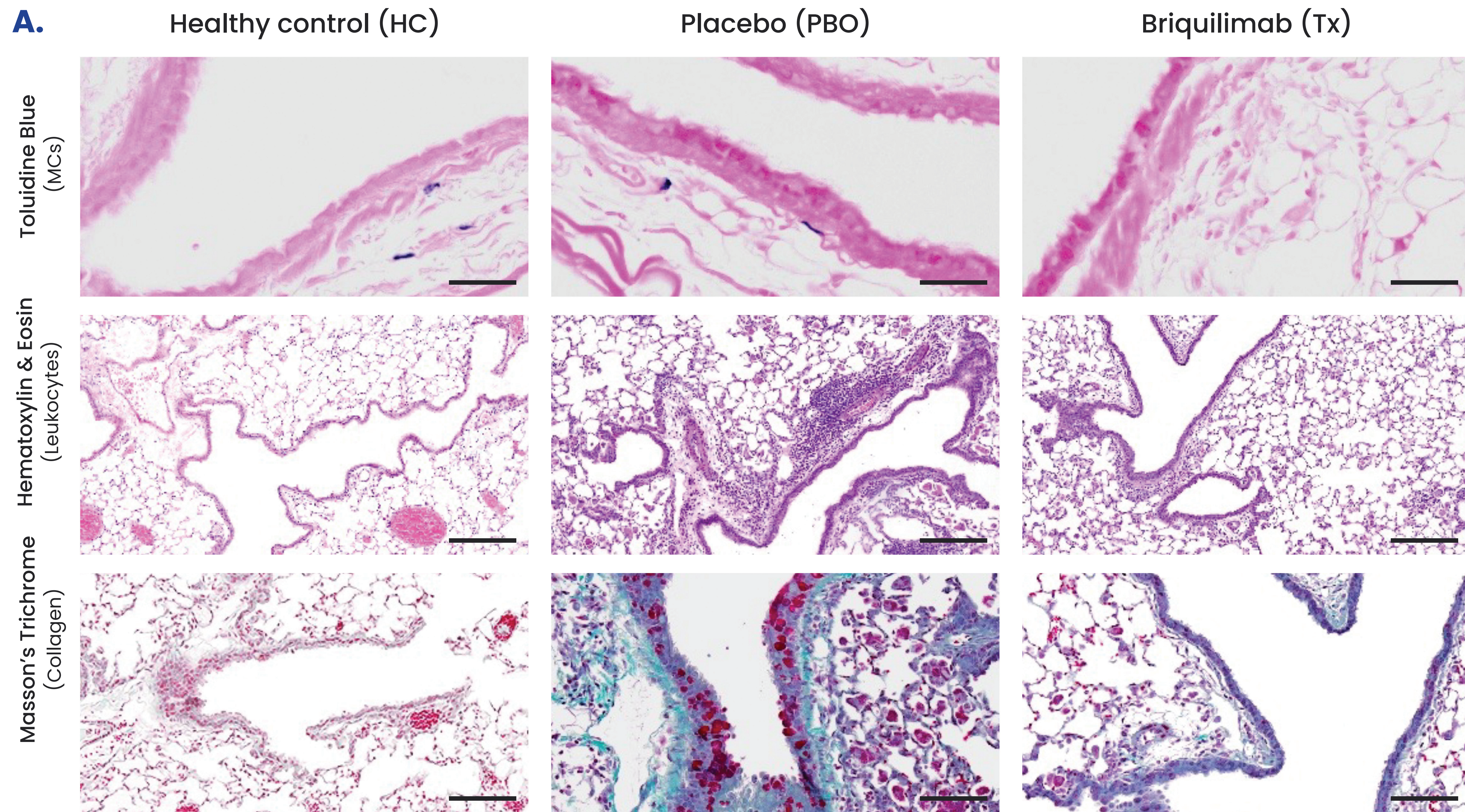
- In the present study, briquilimab- or placebo-treated asthmatic h/mCD117 mice were subjected to repeated *i.n.* challenge with a combination of CRA and cigarette smoke condensate (CSC) to induce asthma exacerbation with COPD-like features, including chronic airway inflammation and remodeling, and alveolar destruction

- The primary objective was to determine whether a single dose of briquilimab, effective in asthma, could also confer protection against asthma exacerbation and the development of COPD-like pathology in this setting



Results

Figure. Nine weeks after a single briquilimab treatment, the asthma exacerbation model exhibited a significant reduction in lung mast cell count, along with decreased airway inflammation, subepithelial collagen deposition, and alveolar destruction compared to placebo-treated model.



• Representative histological sections of peribronchiolar mast cells, leukocytes, and collagen depicted in A. Quantification of BALF eosinophils (B), BALF neutrophils (C), peribronchiolar mast cells (D), peribronchiolar leukocytes (E) and free-floating alveolar septa (F)

BALF – bronchoalveolar lavage fluid; *, **, or *** $P < 0.05$, 0.01, or 0.001 compared with the healthy control group; # or ## $P < 0.05$ or 0.01 compared with PBO group, $N = 3$ to 5 per group; Scale bar = 100 μm .

Conclusions

- A single dose of briquilimab conferred durable protection against airway inflammation, subepithelial fibrosis, and alveolar destruction in an asthma model caused by chronic exposure to allergen and cigarette smoke condensate, primarily through mast cell depletion
- These findings support the potential of briquilimab not only for asthma control but also for preventing COPD-like pathological features associated with chronic allergen and cigarette smoke exposure

Takeaways

- Mast cells play a key role in asthma exacerbation and COPD-like pathology
- A single-dose of briquilimab offered sustained mast cell-targeted protection, highlighting its potential in treating chronic inflammatory airway diseases

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Briquilimab is an investigational drug and is not approved for any indication.