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Briquilimab, an Anti-CD117 (c-Kit) Antibody, Prevents Cockroach Allergen-Induced Allergic Asthma in Mice Expressing Chimeric Human and Mouse CD117

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Jasper Therapeutics, Inc., Redwood City, CA

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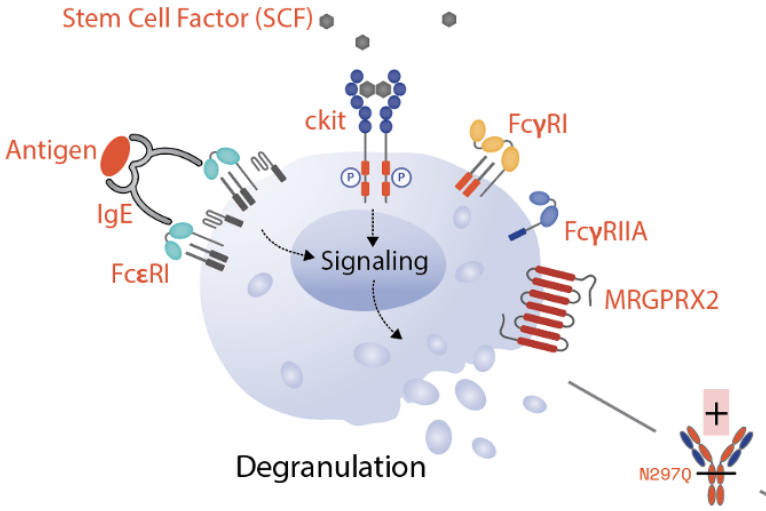
Briquilimab (humanized anti-human c-Kit mAb) inhibits c-Kit leading to mast cell (MC) apoptosis

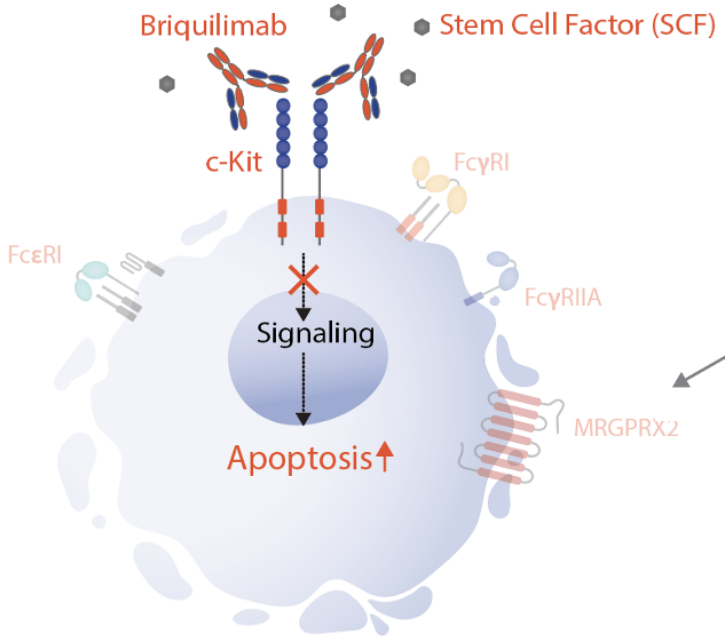
IgE/FcεRI-Mediated Mast Cell Activation



Prevents passive systemic anaphylaxis in mice (Poster# 024, yesterday)

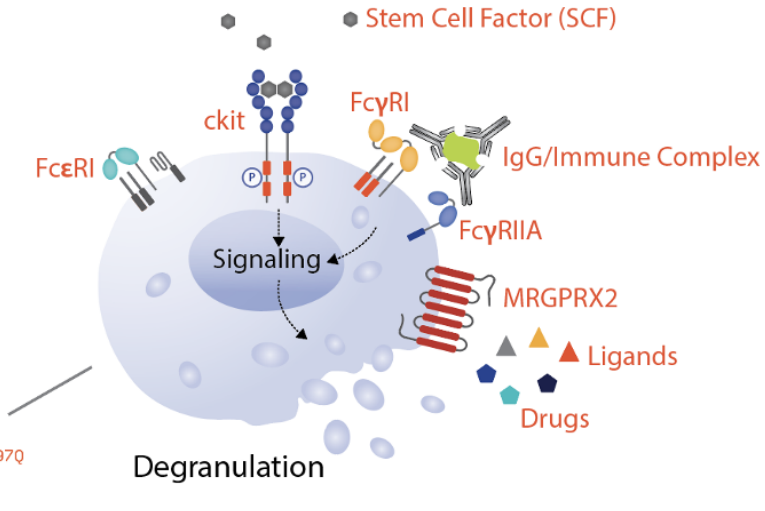
Briquilimab

- Aglycosylated and humanized antibody
- No intrinsic agonistic activity
- No ADCC and CDC activity
- No FcγR mediated-mast cell activation



Non IgE/FcεRI-Mediated Mast Cell Activation

- FcγR/IgG/immune complex-mediated
- MRGPRX2-mediated



Ameliorates Mrgprb2-mediated anaphylactoid drug reactions in mice (Poster# 747, tomorrow 4:15-6:15 PM)

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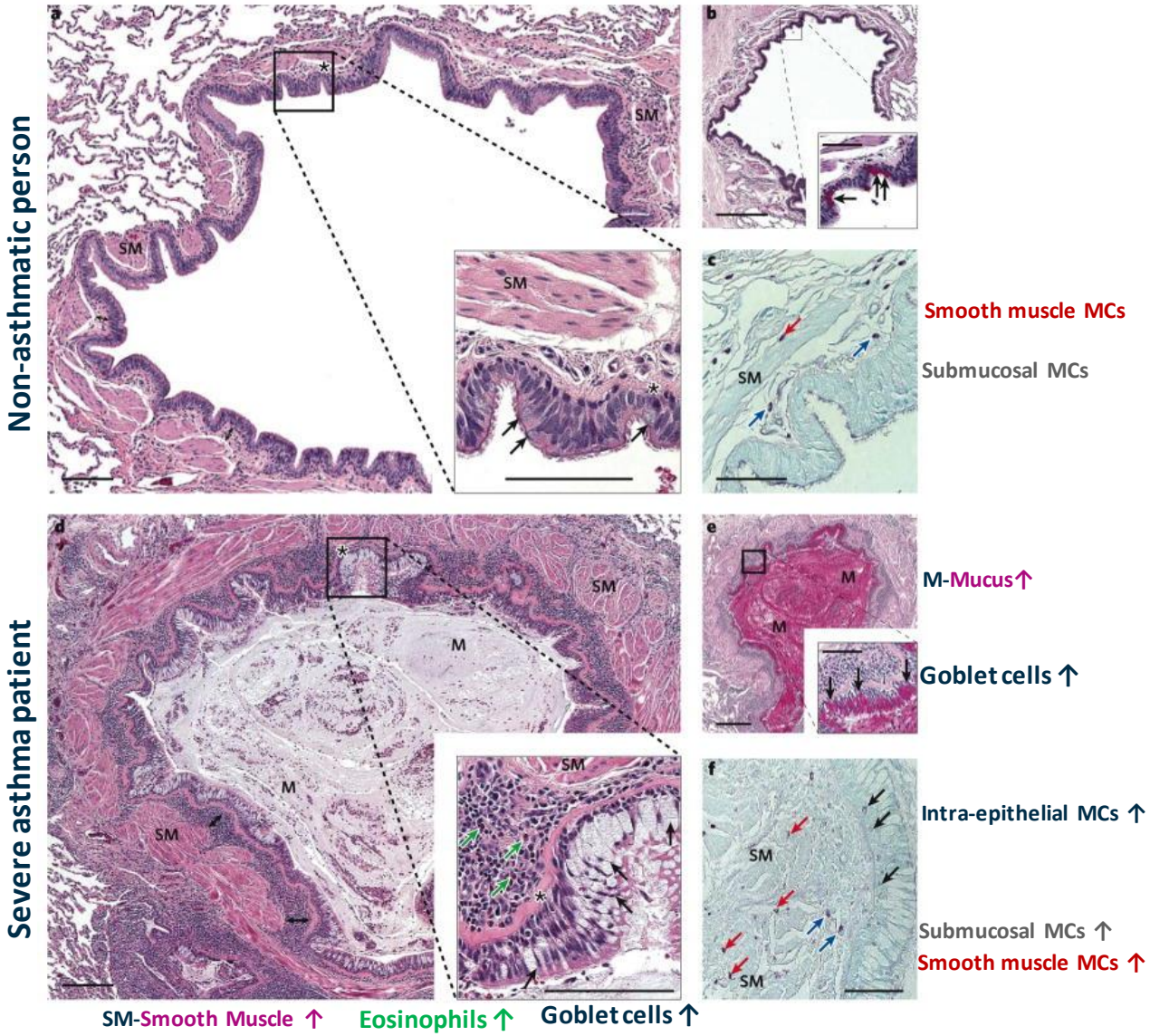
Mast Cells (MC) play a critical role in allergic inflammation and tissue remodeling in asthma



MC Lung Distribution

- Airway epithelium
- Submucosal glands
- Airway smooth muscle
- Alveolar epithelium

MC Pathological Mediators

- Proteases
- Proteoglycans
- Monoamines
- Neuropeptides
- Lipid mediators
- Cytokines/Chemokines/Growth factors

MC Pathophysiological Effects

- Airway hyperresponsiveness
- Inflammatory cell infiltration
- Airway barrier damage
- Smooth muscle hypertrophy
- Mucus over production
- Airway remodeling

Galli, *et al*. *Nature* (Insight). 2008; 454:445

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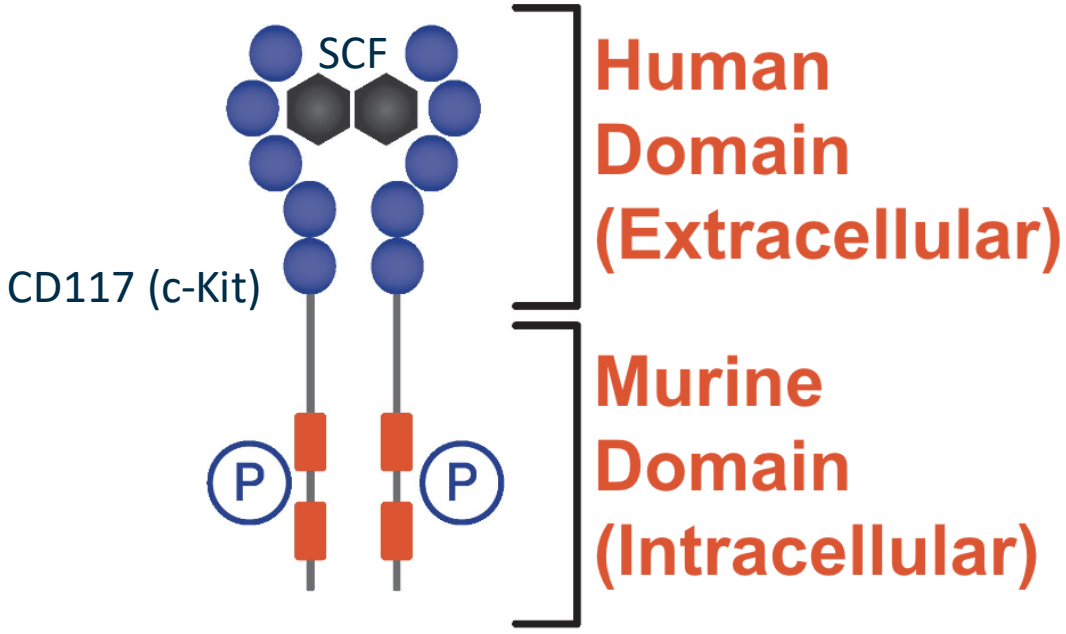
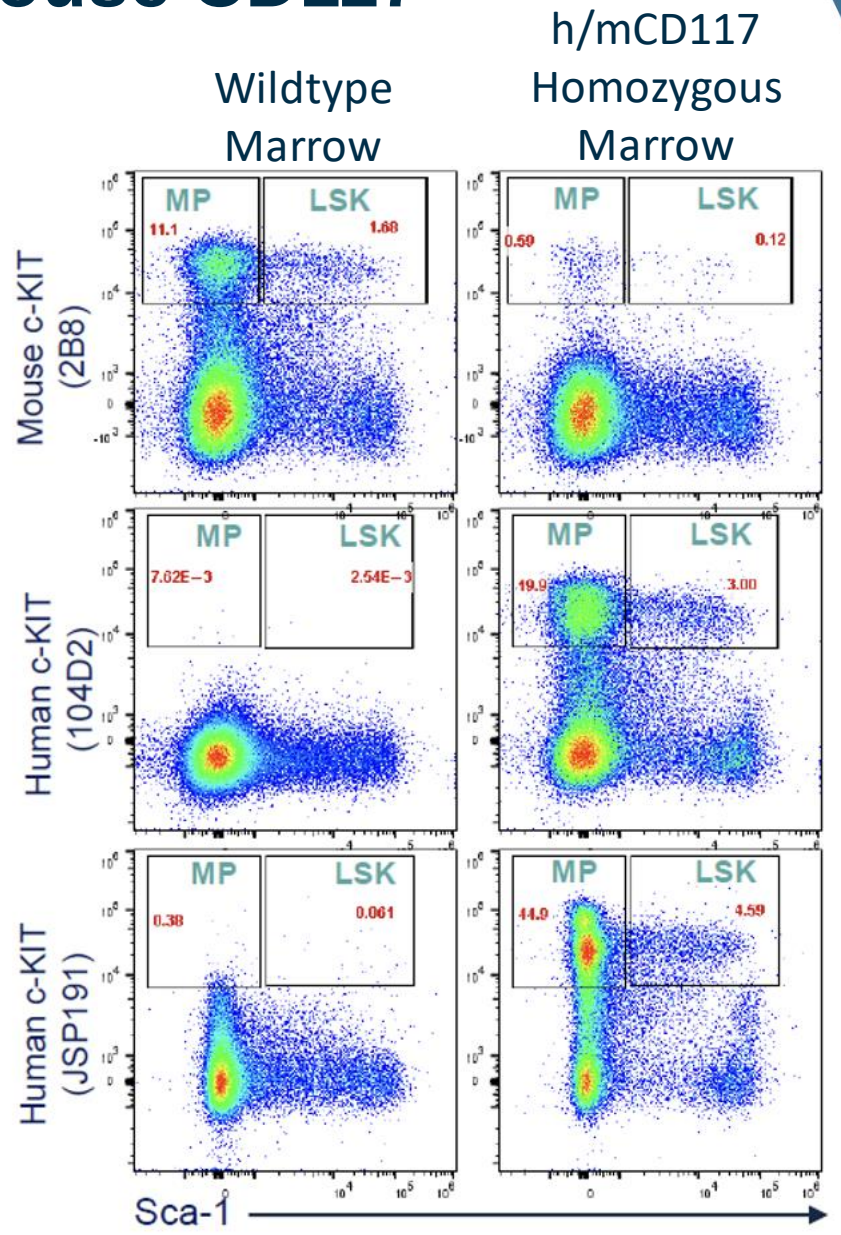
Chimeric human/mouse CD117 (h/mCD117) mice

B6 mice with h/mCD117 knock-in, replacing endogenous wildtype CD117





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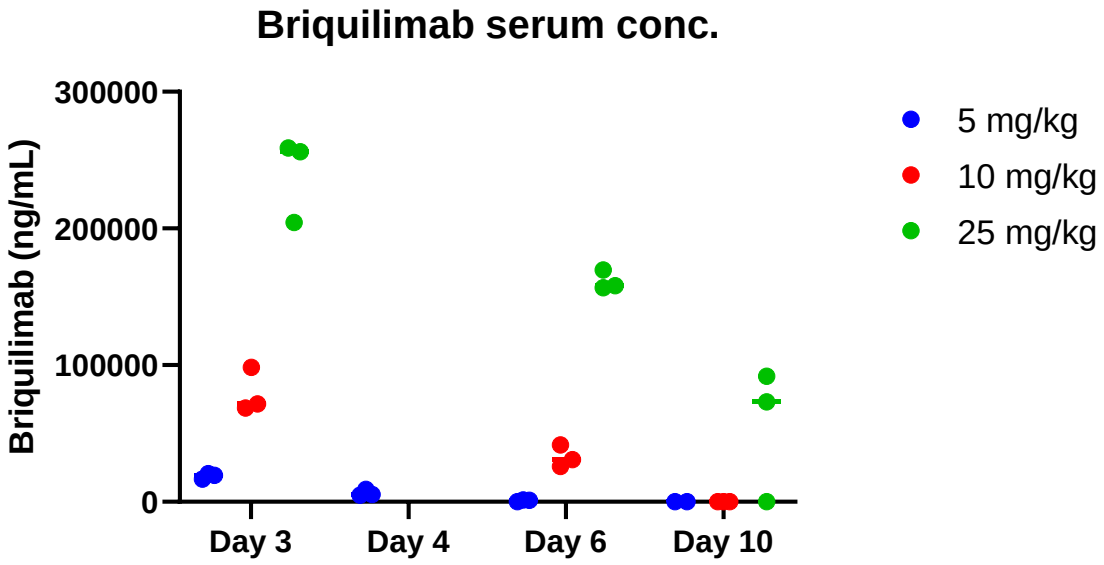
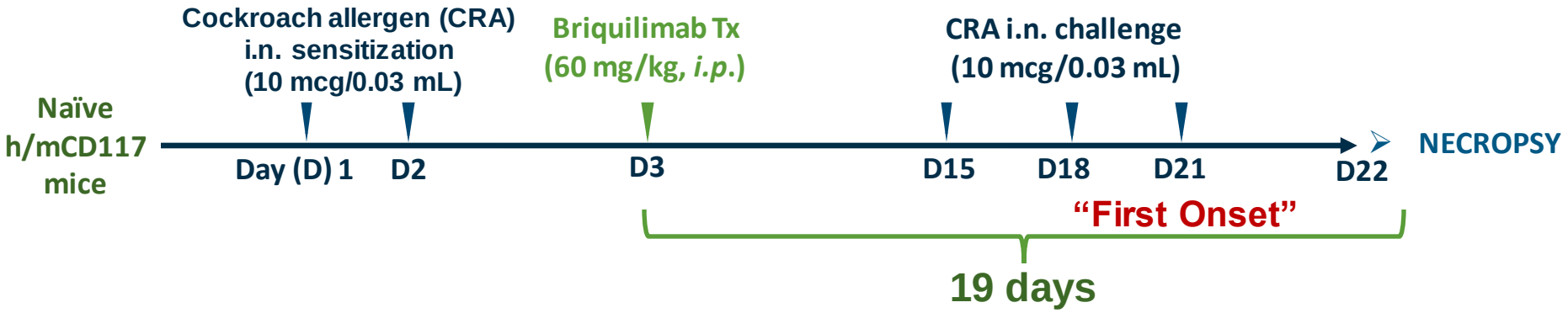
PK characterization of briquilimab in chimeric h/mCD117 mice



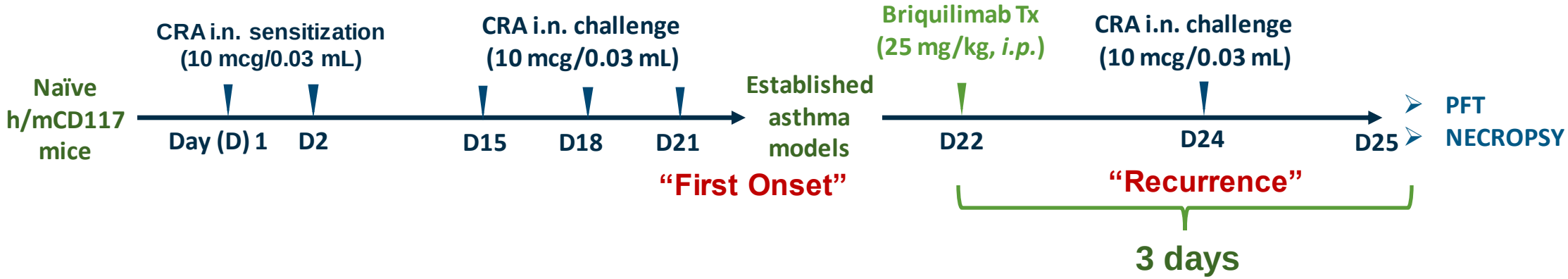
- Chimeric h/mCD117 mice received single dose of intravenous briquilimab
- Pharmacokinetic clearance of briquilimab is dose-dependent
- Pharmacokinetic clearance of briquilimab, at all evaluated dose levels, was faster in h/mCD117 mice compared to non-human primates (Kwon *et al*, *Blood*. 2019;133:2104), which is expected due to allometric scaling
- The 25mg/kg briquilimab dose in h/mCD117 mice corresponds to ~2 mg/kg in human, as determined through allometric scaling

Study design: preclinical prophylactic vs. therapeutic models of asthma in h/mCD117 mice

Prophylactic Model:



Therapeutic Model:



Yu, *et al*. *J Allergy Clin Immunol*. 2018;142:1618

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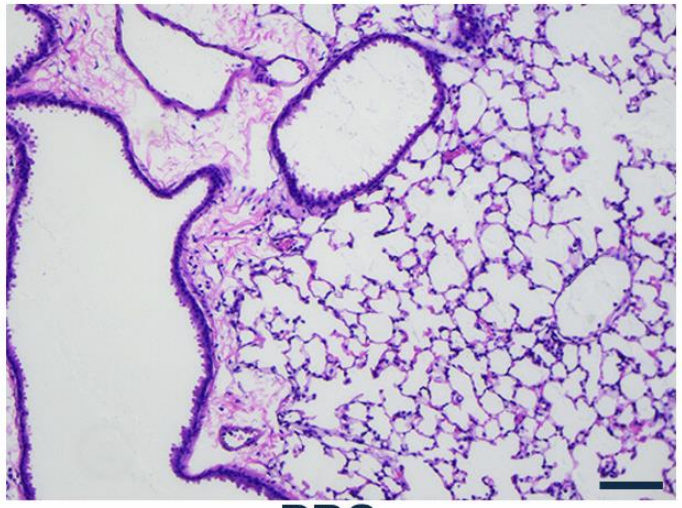
Prophylactic briquilimab (Briq) treatment inhibits the development of airway inflammation in h/mCD117 mice following cockroach allergen sensitization and challenge



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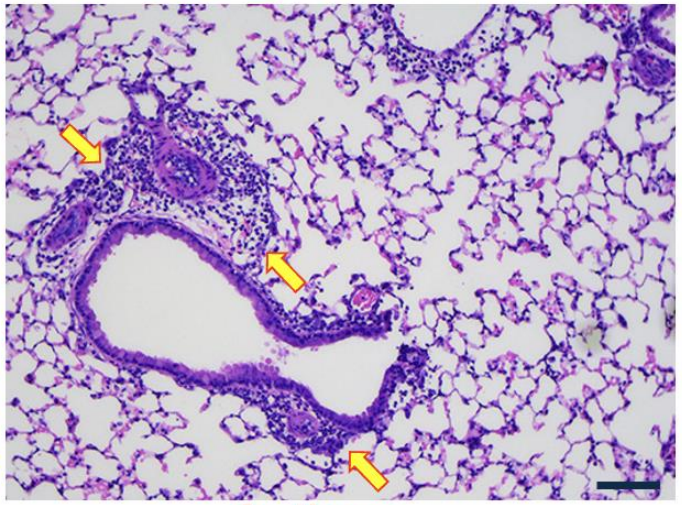
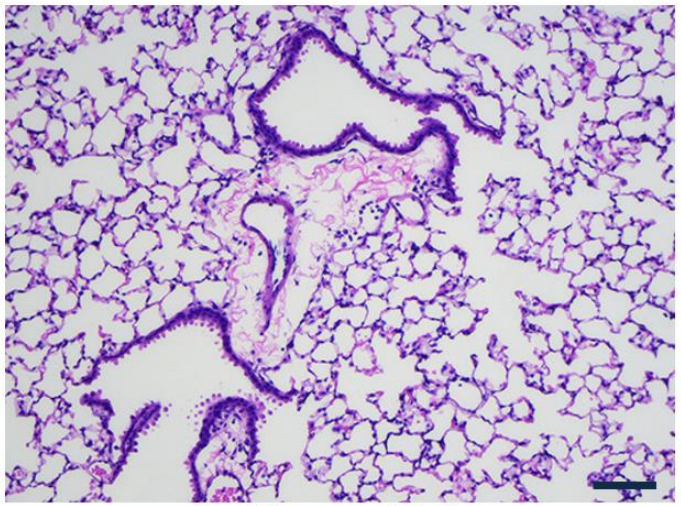
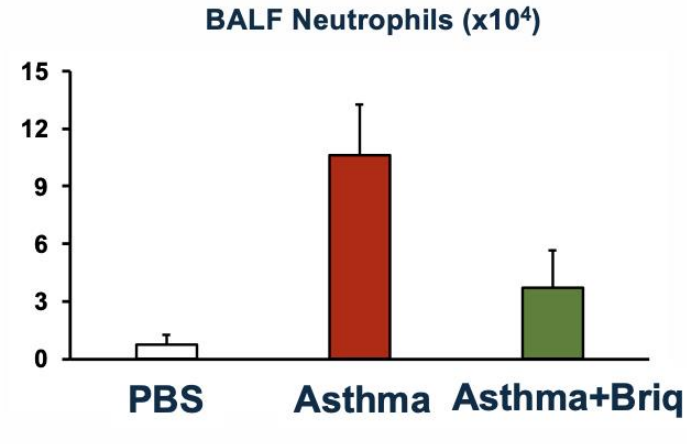
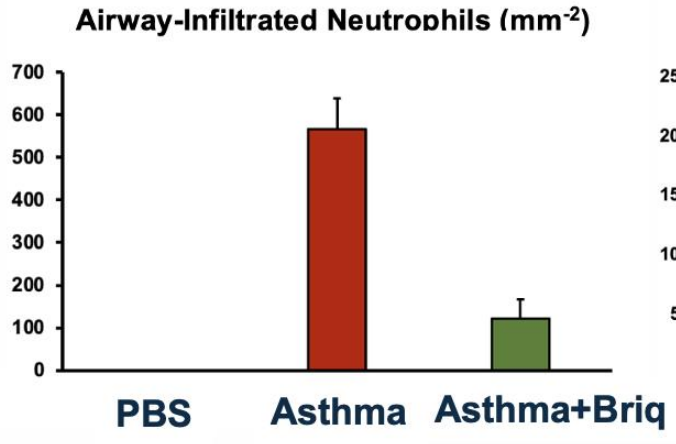


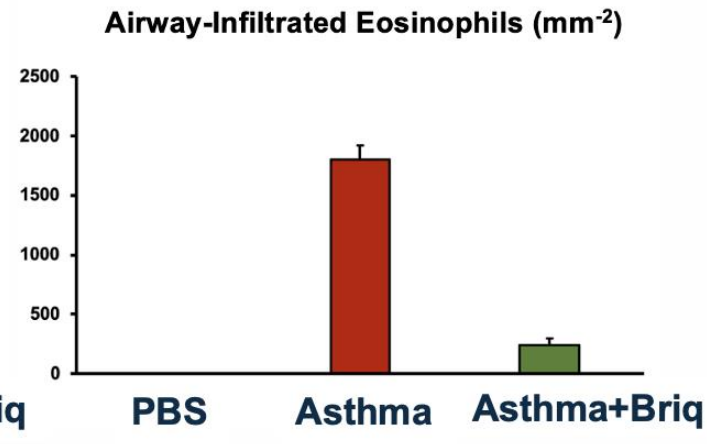
Asthma



Asthma+Briq







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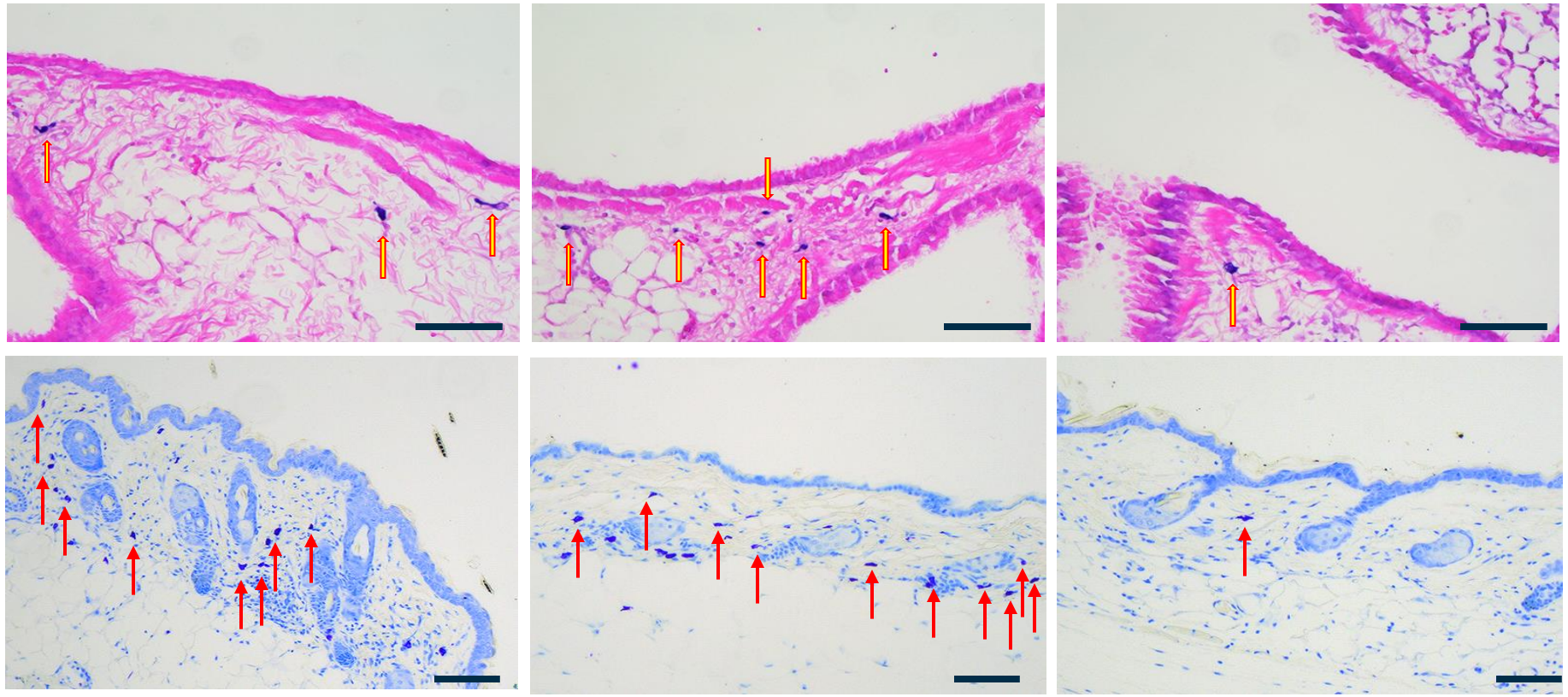
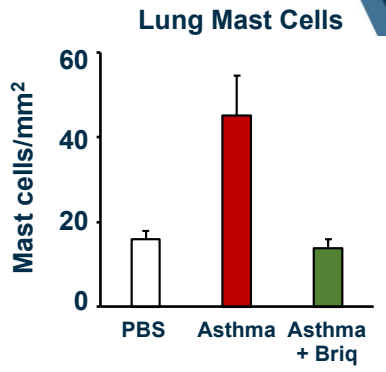
Nineteen days after one-time briquilimab (Briq) preventive treatment, cockroach allergen-sensitized and challenged h/mCD117 mice exhibited significantly decreased numbers of mast cells in the lung and back skin

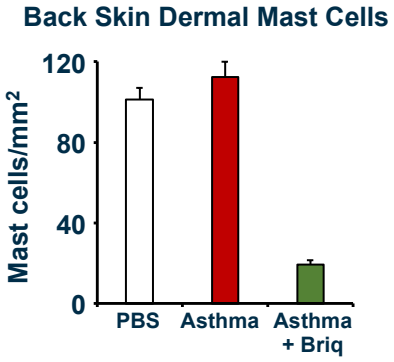
Lung MCs

Back Skin MCs



PBS | Asthma | Asthma+Briq





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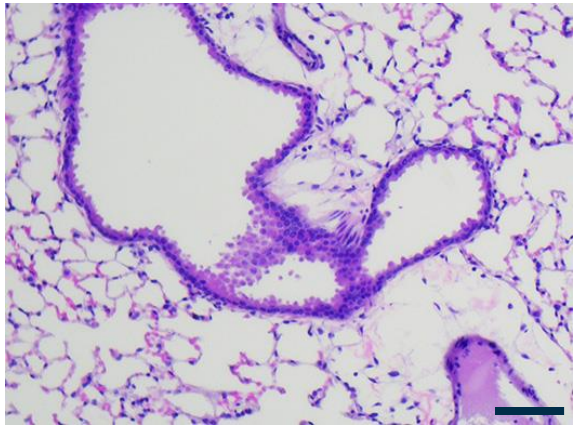
One-time therapeutic briquilimab (Briq) treatment prevented recurrence of asthma exacerbation following allergen exposure in established asthma models elicited in h/mCD117 mice



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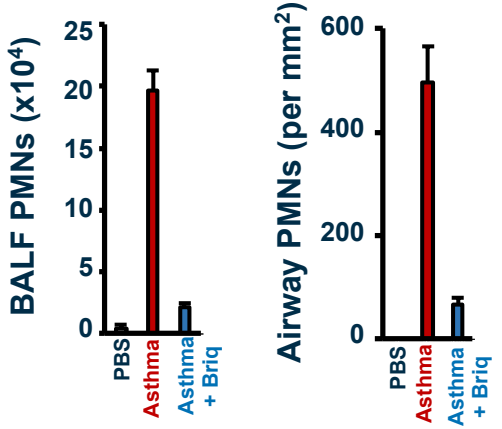
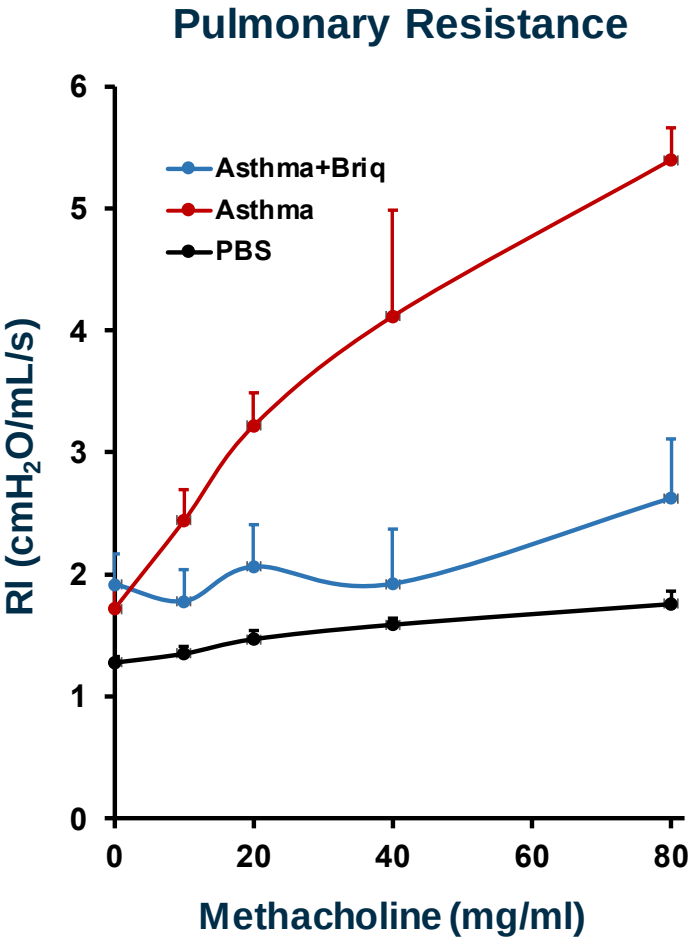
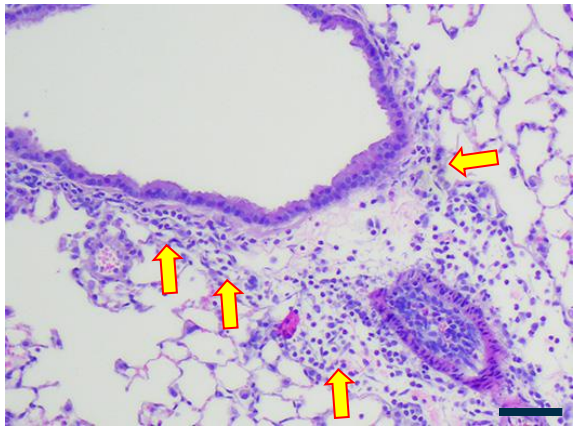
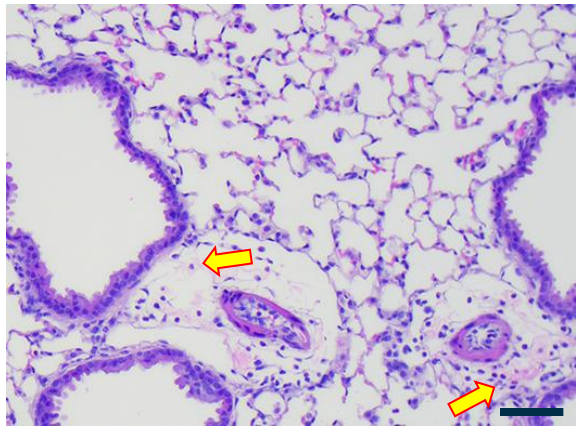






Asthma



Asthma+Briq

Three days post-briquilimab, mice exhibited significantly decreased airway inflammation (including neutrophilic infiltration) and pulmonary resistance following exposure to allergen.

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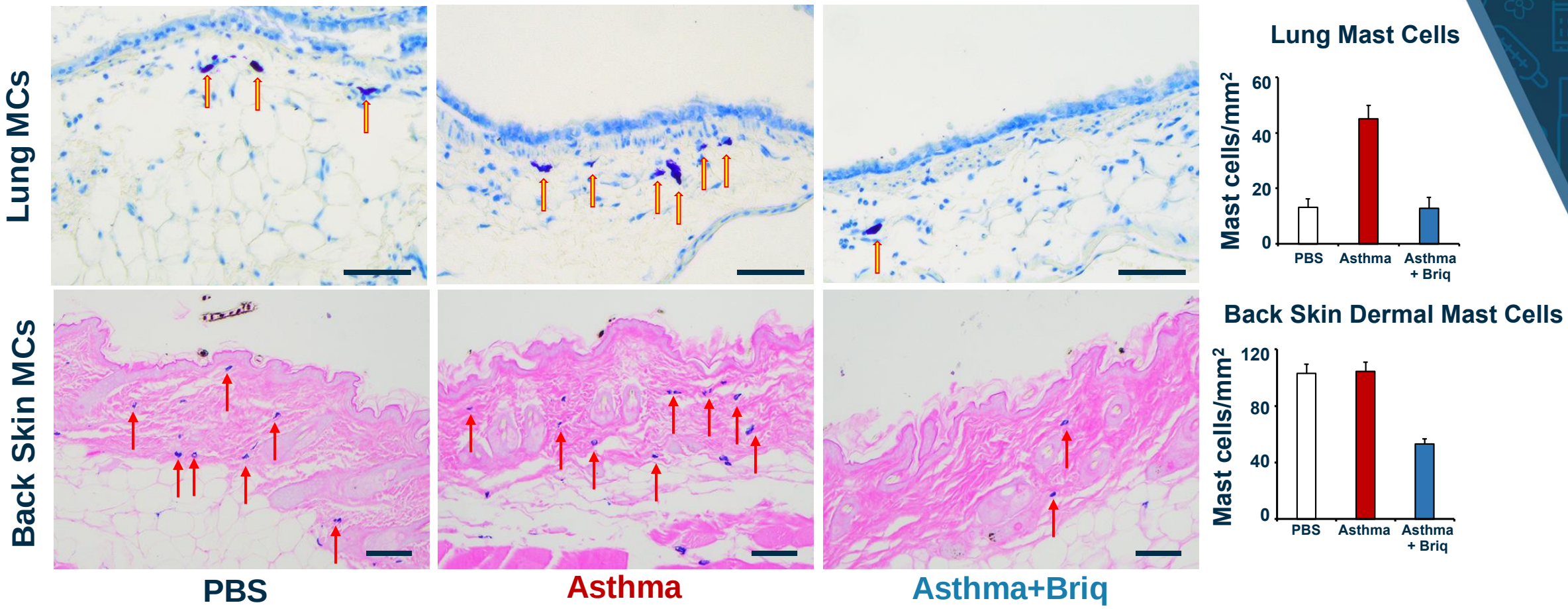
Three days after one-time therapeutic briquilimab (Briq) treatment, established asthma models in h/mCD117 mice exhibited significant decreases in the numbers of mast cells in the lung and back skin following allergen exposure



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Conclusions & Takeaways

- **Mast cells play a key role in asthma pathophysiology.**
- **Briquilimab can deplete mast cells in both inflamed (lung) and non-inflamed tissue (back skin) in an allergen-induced asthma model elicited in h/mCD117 mice.**
- **Briquilimab exhibits potential prophylactic and therapeutic benefits in an allergen-induced asthma model elicited in h/mCD117 mice.**
- **Jasper is actively enrolling participants in a phase 1a/2b trial evaluating briquilimab in patients with chronic spontaneous urticaria (NCT06162728).**

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Acknowledgements

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Judy Shizuru
Stephen Galli

JASPER THERAPEUTICS

Meet us at Jasper's booth #444.
Copies of the abstract are available on request