

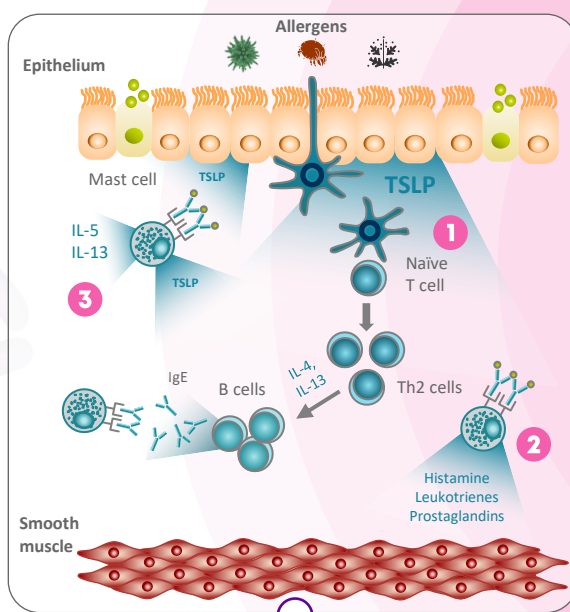
# TSLP AND THE MULTIPLE ROLES OF MAST CELLS IN ASTHMA

Together, TSLP and mast cells play important roles in allergic T2 and T2-independent pathways

## ALLERGIC T2 PATHWAYS

TSLP and mast cells can promote airway inflammation via allergic pathways and contribute to airway hyperresponsiveness<sup>1-5</sup>

- 1 TSLP is released from the epithelium after exposure to allergens, driving Th2 cell differentiation and allergic inflammation<sup>1,3,6,7</sup>
- 2 Mast cells initiate allergic inflammation following allergen binding of IgE, triggering mast cell degranulation and bronchospasm (the early allergic response)<sup>3,8,9</sup>
- 3 The late allergic response occurs 2-9 hours after the early allergic response and is associated with increased airway hyperresponsiveness<sup>9,10</sup>  
Airway TSLP+ cells correlate with baseline FEV<sub>1</sub> and FEV<sub>1</sub> decline during the late allergic response<sup>11</sup>

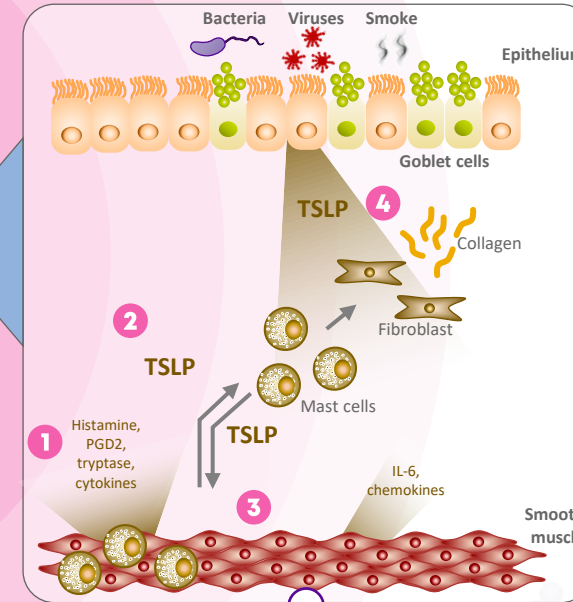


Airway inflammation and hyperresponsiveness<sup>3-5</sup>

## T2-INDEPENDENT PATHWAYS

Infiltration of airway smooth muscle by mast cells that secrete mediators, including TSLP, is associated with airway hyperresponsiveness and structural changes<sup>3,12-17</sup>

- 1 Mast cells are recruited to the airway smooth muscle bundle and are activated, releasing mediators such as histamine, PGD<sub>2</sub>, tryptase, TSLP, IL-33, and IL-13<sup>3,12,15,17-21</sup>
- 2 TSLP is produced by both mast cells and smooth muscle cells in an autocrine feedback loop<sup>3,6,7,12,22</sup>
- 3 Mediator release results in bronchoconstriction and increased smooth muscle mass<sup>15,18-20,22-27</sup>
- 4 TSLP stimulates fibroblasts to produce collagen, potentially promoting airway remodeling<sup>3\*</sup>



Airway hyperresponsiveness and structural changes<sup>3-5</sup>

Initiation and persistence of asthma pathophysiology<sup>3-5,13</sup>

\*This has been demonstrated *in vitro*; additional evidence is required *in vivo*  
 FEV<sub>1</sub>, forced expiratory volume in 1 second; Ig, immunoglobulin; PGD<sub>2</sub>, prostaglandin 2; T2, type 2; Th, T helper; TSLP, thymic stromal lymphopoietin; TSLP+, thymic stromal lymphopoietin positive.  
 Figures adapted from Gauvreau GM, et al. *Expert Opin Ther Targets* 2020;24:777-792, which was based on Brusselle G, Bracke K. *Ann Am Thorac Soc* 2014;11(Suppl. 5):S322-S328; Brusselle G, et al. *Nat Med* 2013;19:977-979 and Lambrecht BN, Hammad H. *Nat Immunol* 2015;16:45-56.  
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