

# IL-25, IL-33, TSLP AND THE MULTIPLE ROLES OF MAST CELLS IN ASTHMA

Together, IL-25, IL-33, TSLP and mast cells play important roles in allergic T2 and beyond T2 pathways

## ALLERGIC T2 PATHWAYS

## BEYOND T2 PATHWAYS

IL-25, IL-33, TSLP and mast cells can promote airway inflammation via allergic pathways and contribute to airway hyperresponsiveness<sup>1-7</sup>

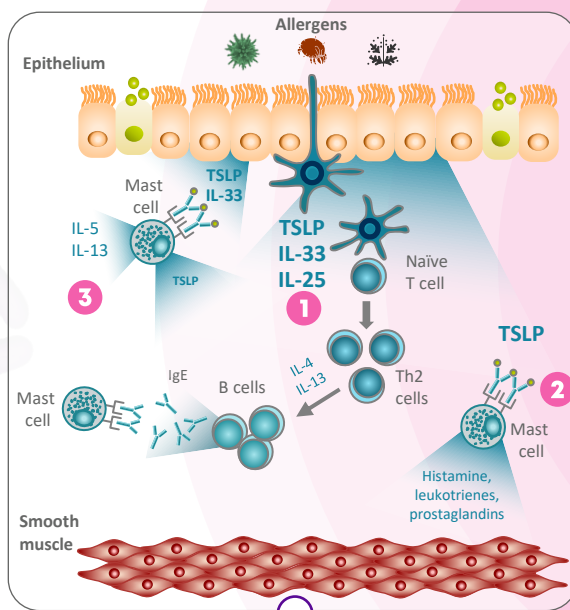
Infiltration of airway smooth muscle by mast cells that secrete mediators, including IL-33 and TSLP, is associated with airway hyperresponsiveness and structural changes;<sup>3,7,16-21</sup> any interaction between IL-25 and mast cells in these pathways has not yet been elucidated

**1** IL-25, IL-33 and TSLP are released from the epithelium after exposure to allergens, driving Th2 cell differentiation and allergic inflammation<sup>1,3,6-9</sup>

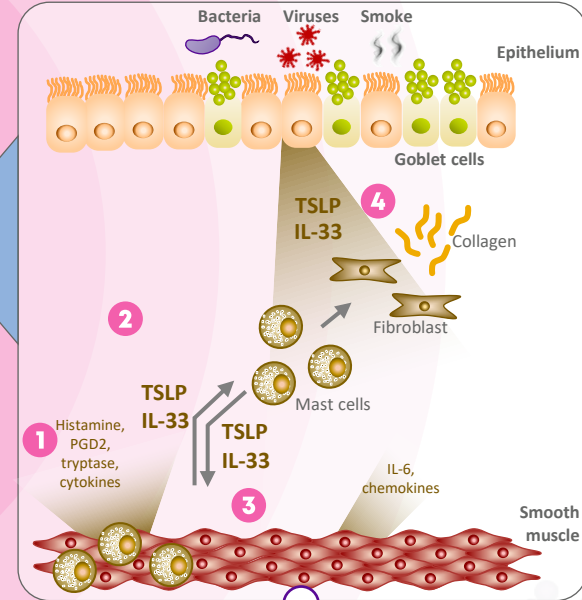
**2** Mast cells initiate allergic inflammation following allergen binding of IgE, triggering mast cell degranulation and bronchospasm (the early allergic response)<sup>3,10,11</sup>

**3** The late allergic response occurs 2-9 hours after the early allergic response and is associated with increased airway hyperresponsiveness<sup>11,12</sup>

Allergen challenge is associated with increased airway IL-25+, IL-33+ and TSLP+ cells; IL-33+ and TSLP+ cells also correlate with baseline FEV<sub>1</sub> and FEV<sub>1</sub> decline during the late allergic response<sup>13</sup>



Airway inflammation and hyperresponsiveness<sup>3-5,7,9</sup>



Airway hyperresponsiveness and structural changes<sup>3-5,8,21</sup>

Initiation and persistence of asthma pathophysiology<sup>3-5,7,9,14,15</sup>

**1** Mast cells are recruited to the airway smooth muscle bundle and are activated, releasing mediators such as histamine, PGD2, tryptase, TSLP, IL-33 and IL-13<sup>3,14,17,19-24</sup>

**2** IL-33 and TSLP are produced by both mast cells and smooth muscle cells; TSLP has been implicated in an autocrine feedback loop<sup>3,6,8,19,21,25</sup>

**3** Mediator release, including IL-33 and TSLP, can result in bronchoconstriction and increased smooth muscle mass; IL-33 release can also result in airway smooth muscle wound repair<sup>10,20-30</sup>

**4** IL-33 and TSLP stimulate fibroblasts to produce collagen, potentially promoting airway remodelling<sup>3,8,15\*</sup>