

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 hyperresponsiveness¹⁻⁷

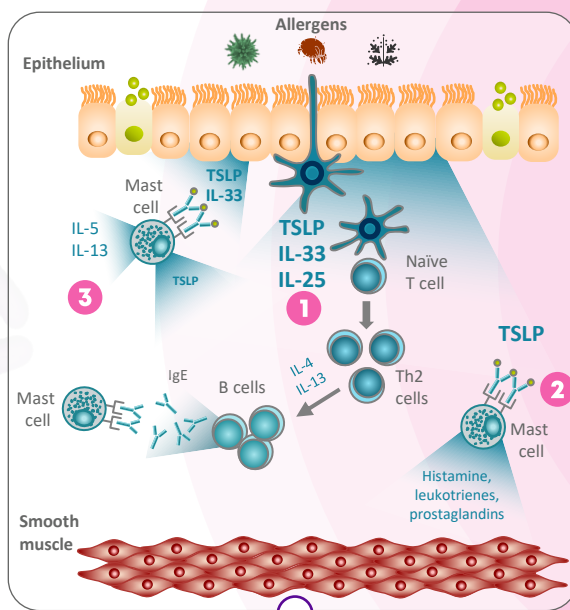
Infiltration of airway smooth muscle by mast cells that secrete mediators, including IL-33 and TSLP, is associated with airway hyperresponsiveness and structural changes;^{3,7,16-21} any interaction between IL-25 and mast cells in these pathways has not yet been elucidated

1 IL-25, IL-33 and TSLP are released from the epithelium after exposure to allergens, driving Th2 cell differentiation and allergic inflammation^{1,3,6-9}

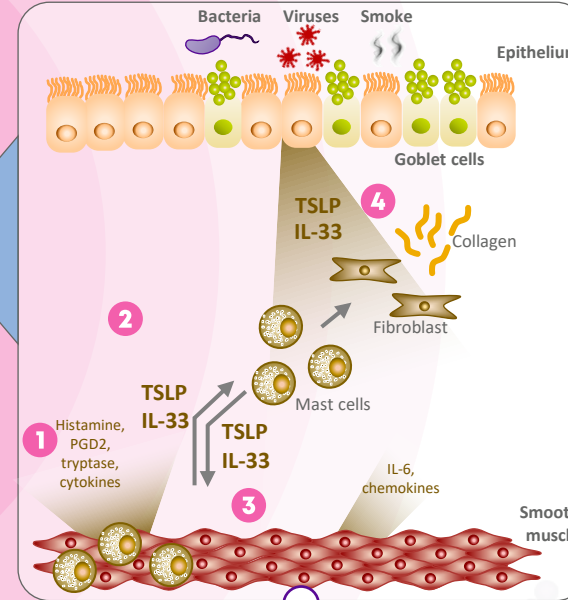
2 Mast cells initiate allergic inflammation following allergen binding of IgE, triggering mast cell degranulation and bronchospasm (the early allergic response)^{3,10,11}

3 The late allergic response occurs 2–9 hours after the early allergic response and is associated with increased airway hyperresponsiveness^{11,12}

Allergen challenge is associated with increased airway IL-25+, IL-33+ and TSLP+ cells; IL-33+ and TSLP+ cells also correlate with baseline FEV₁ and FEV₁ decline during the late allergic response¹³



Airway inflammation and hyperresponsiveness^{3-5,7,9}



Airway hyperresponsiveness and structural changes^{3-5,8,21}

Initiation and persistence of asthma pathophysiology^{3-5,7,9,14,15}

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^{3,14,17,19-24}

2 IL-33 and TSLP are produced by both mast cells and smooth muscle cells; TSLP has been implicated in an autocrine feedback loop^{3,6,8,19,21,25}

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^{10,20-30}

4 IL-33 and TSLP stimulate fibroblasts to produce collagen, potentially promoting airway remodelling^{3,8,15*}