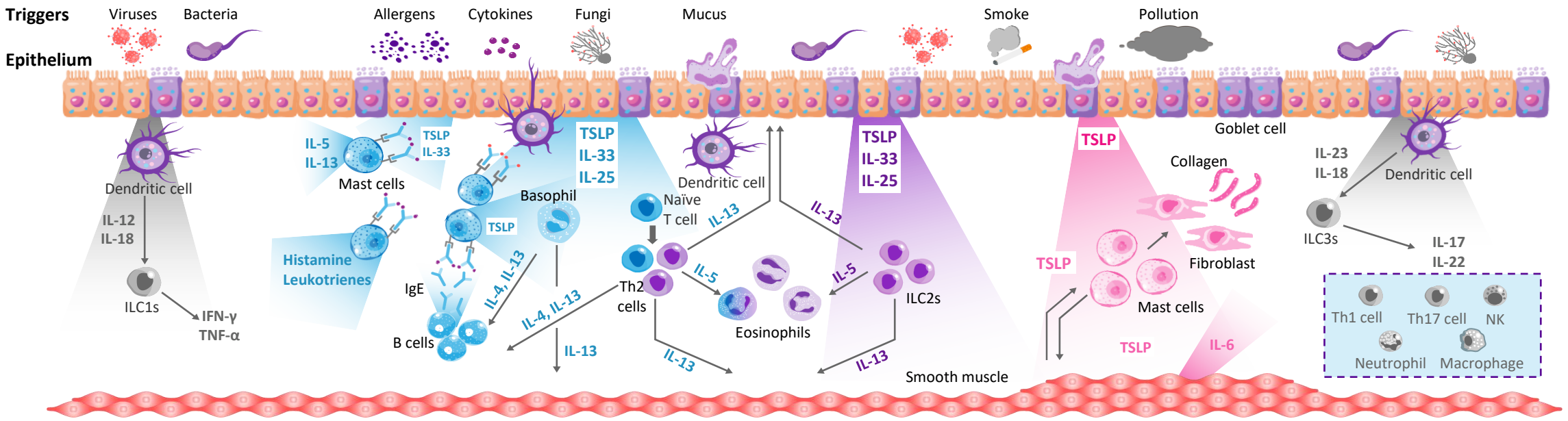
Similar inflammatory processes are associated with both upper and lower airway diseases[1–3]

Inflammation in upper airways disease

Inflammation in asthma



Type 2 inflammation has a role in both upper and lower airway diseases;[1–5] in response to various triggers, the epithelial cytokines initiate pathways involving Th2 cells, basophils, ILC2s and mast cells contributing to airway eosinophilia.[4] Upper airways disease can also be characterized by T1 and T3 inflammation, the proposed pathways for which are illustrated here.[5–7] Finally, TSLP also has a role in mediating structural mechanisms that contribute to airway remodelling in lower airways disease,[4] shown here as the beyond T2 pathway. Note, that the information presented in this image has been simplified for illustration purposes only and does not imply clinical benefit or relevance

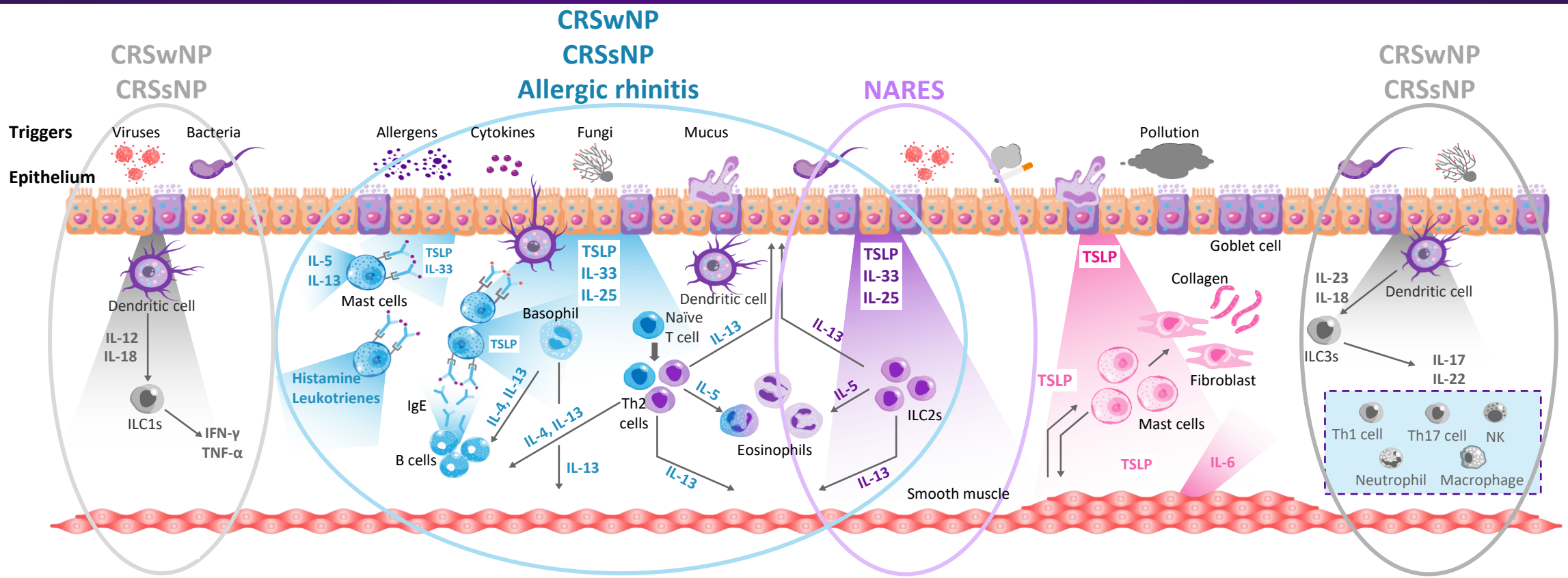
Figure adapted from Caminati M, et al. Allergy 2024;79:1134–1145, which was based on Gauvreau GM et al. Expert Opin Ther Targets. 2020;24:777–792

Cells thought to be involved in T1 and T3 inflammation; exact roles and pathways are hypothesized and further elucidation is required[7]

IFN, interferon; IgE, immunoglobulin E; IL, interleukin; ILC1, Type 1 innate lymphoid cell; ILC2, Type 2 innate lymphoid cell; ILC3, Type 3 innate lymphoid cell; NK, natural killer; T1, Type 1; T2, Type 2; T3, Type 3; Th, T helper; TNF, tumor necrosis factor; TSLP, thymic stromal lymphopoietin

1. Yii ACA, et al. Allergy 2018;73:1964–1978; 2. Laulajainen-Hongisto A, et al. Front Cell Dev Biol 2020;8:204; 3. Fokkens W, Reitsma S. Otolaryngol Clin North Am 2023;56:1–10; 4. Caminati M, et al. Allergy 2024;79:1134–1145; 5. Fokkens WJ, et al. Rhinology 2020;58(Suppl S29):1–464; 6. Victor AR, et al. J Immunol 2017;199:2333–2342; 7. Staudacher AG, et al. Ann Allergy Asthma Immunol 2020;124:318–325

Similar inflammatory cascades are implicated in CRSwNP, CRSsNP, AR and NARES[1–11]

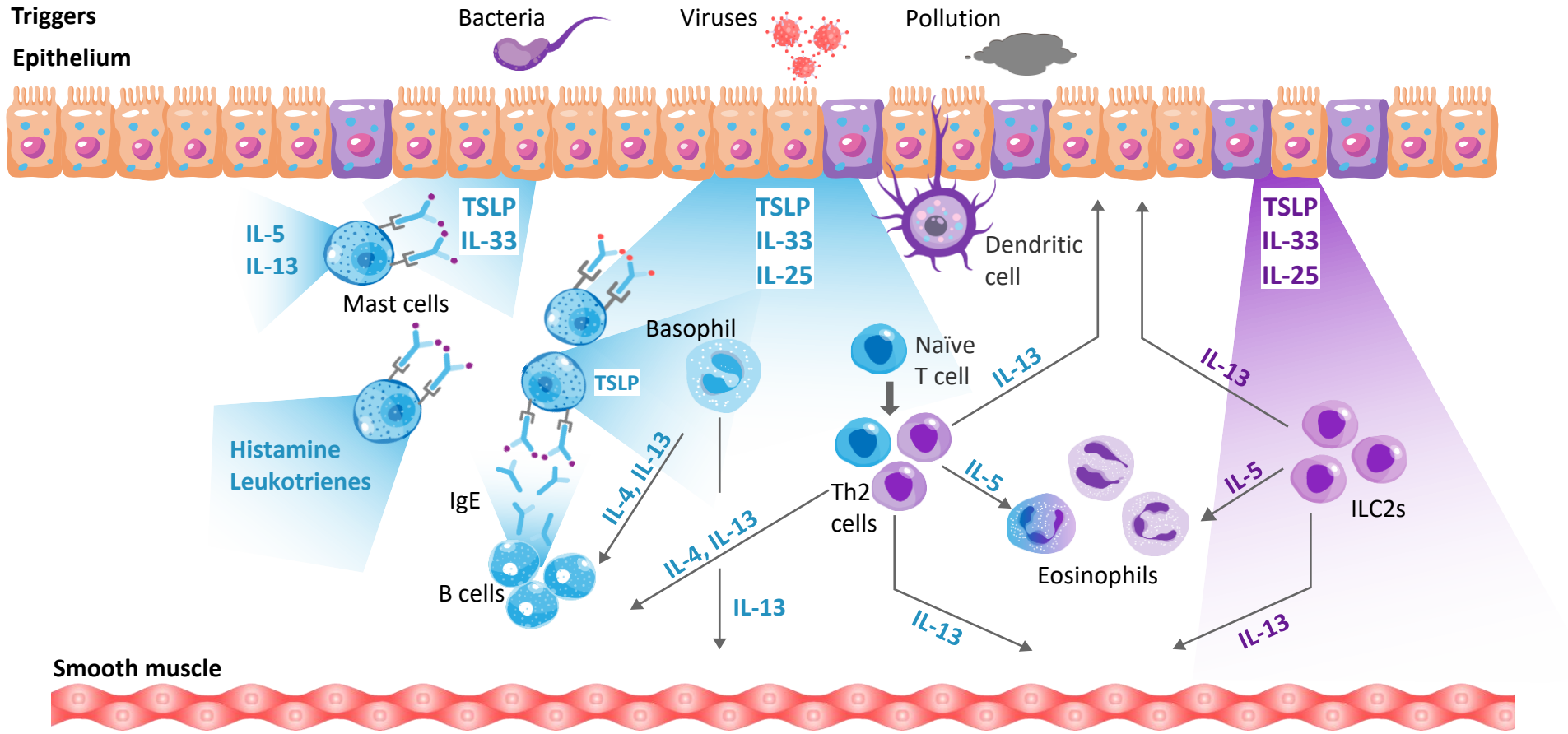


CRSwNP can present with a T1, T2, T3, mixed or unidentifiable endotype.[1] Prevalence of the different endotypes appears to vary geographically, and in 80% of Caucasian cases, CRSwNP is associated with a T2 signature.[2] CRSsNP was historically characterized by T1 inflammation, but there is now evidence that T2 inflammation may be the predominant endotype albeit with lower levels of T2 cytokines and eosinophils compared with CRSwNP.[1,3] Similarly, allergic rhinitis is characterized by T2 inflammation;[4,6,9] whereas, mechanisms underlying NARES require further elucidation, and the illustrated pathway is a hypothesis only[4]

Figure adapted from Caminati M, et al. Allergy 2024;79:1134–1145, which was based on Gauvreau GM et al. Expert Opin Ther Targets. 2020;24:777–792
Figure is for illustrative purposes only. Specific and definitive role of many cells and cytokines across the disease states shown require further elucidation
AR, allergic rhinitis; CRSsNP, chronic rhinosinusitis without nasal polyps; CRSwNP, chronic rhinosinusitis with nasal polyps; IFN, interferon; IgE, immunoglobulin E; IL, interleukin; ILC1, Type 1 innate lymphoid cell; ILC2, Type 2 innate lymphoid cell; ILC3, Type 3 innate lymphoid cell; NARES, non-allergic rhinitis with eosinophilia syndrome; NK, natural killer; T1, Type 1; T2, Type 2; T3, Type 3; Th, T helper; TNF, tumour necrosis factor; TSLP, thymic stromal lymphopoietin

1. Staudacher AG, et al. Ann Allergy Asthma Immunol 2020;124:318–325; 2. Laidlaw TM, et al. J Allergy Clin Immunol Pract 2021;9:1133–1141; 3. Cho SH, et al. J Allergy Clin Immunol Pract 2016;4:575–582; 4. Yii ACA, et al. Allergy 2018;73:1964–1978; 5. Stevens WW, et al. J Allergy Clin Immunol Pract 2016;4:565–572; 6. Kortekaas Krohn I, et al. Allergy 2018;73:837–850; 7. Fokkens WJ, et al. Rhinology 2020;58(Suppl S29):1–464; 8. Wang X, et al. J Allergy Clin Immunol 2016;138:1344–1353; 9. Bousquet J, et al. Nat Rev Dis Primers 2020;6:95; 10. Sin B, Togias A. Proc Am Thorac Soc 2011;8:106–114; 11. Victor AR, et al. J Immunol 2017;199:2333–2342

CRSwNP is most commonly associated with T2 inflammation[1–5]



CRSwNP can present with a T1, T2, T3, mixed or unidentifiable endotype.[1] Prevalence of the different endotypes appears to vary geographically, and in 80% of Caucasian cases, CRSwNP is associated with a T2 signature.[2] In patients with a T2 endotype, triggers such as bacteria, viruses and pollution interact with the epithelium causing the release of TSLP and IL-33 leading to the production of IL-4, IL-5 and IL-13 through the activation of ILC2s and mast cells[1,2,5]

Figure adapted from Caminati M, et al. Allergy 2024;79:1134–1145, which was based on Gauvreau GM et al. Expert Opin Ther Targets. 2020;24:777–792
Figure is for illustrative purposes only. Specific and definitive role of some cells and cytokines shown require further elucidation
CRSwNP, chronic rhinosinusitis with nasal polyps; IgE, immunoglobulin E; IL, interleukin; ILC2, Type 2 innate lymphoid cell; T1, Type 1; T2, Type 2; T3, Type 3; Th, T helper; TSLP, thymic stromal lymphopoietin

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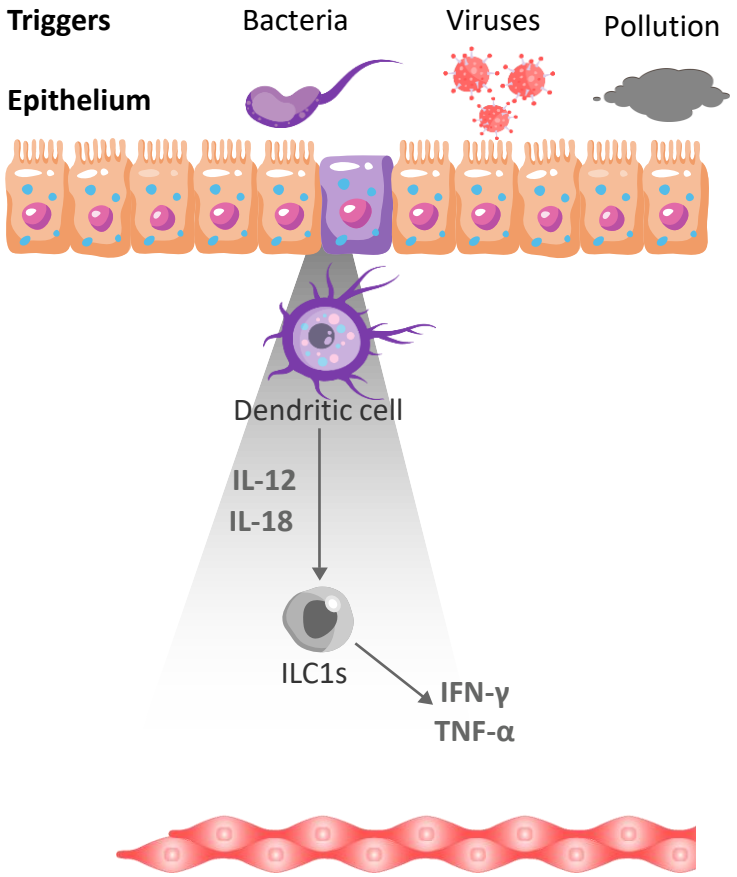
CRSsNP has historically been characterized by T1 inflammation but is now considered to include a range of endotypes[1–4]



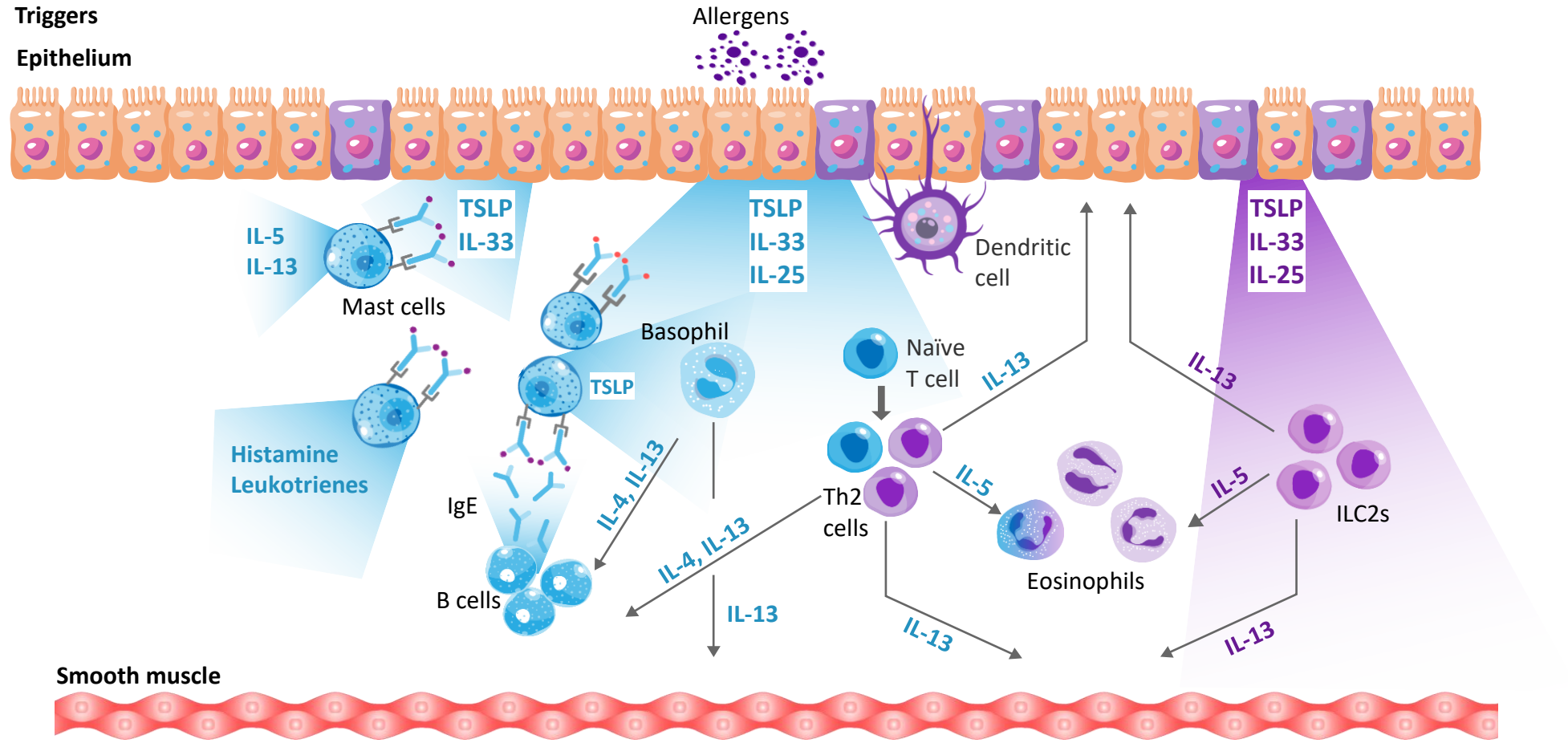
CRSsNP was historically characterized by T1 inflammation, but there is now evidence that T2 inflammation may be the predominant endotype albeit with lower levels of T2 cytokines and eosinophils compared with CRSwNP.[1,3] Common triggers of CRSsNP include bacteria, viruses and pollution,[4] and in those patients with a T1 endotype, dendritic cells produce IL-12 and IL-18 which act on ILC1s to release IFN-γ and TNF-α most often in response to pathogens[4]

Figure is for illustrative purposes only. Specific and definitive role of some cells and cytokines shown require further elucidation

CRSsNP, chronic rhinosinusitis without nasal polyps; CRSwNP, chronic rhinosinusitis with nasal polyps; IFN, interferon; IL, interleukin; ILC1, Type 1 innate lymphoid cell; T1, Type 1; T2, Type 2; TNF, tumour necrosis factor

1. Staudacher AG, et al. Ann Allergy Asthma Immunol 2020;124:318–325; 2. Wang X, et al. J Allergy Clin Immunol 2016;138:1344–1353; 3. Cho SH, et al. J Allergy Clin Immunol Pract 2016;4:575–582; 4. Fokkens WJ, et al. Rhinology 2020;58(Suppl S29):1–464

Allergic rhinitis is an IgE-mediated response to inhaled allergens characterized by T2 inflammation[1–5]



In patients with allergic rhinitis TSLP, IL-33 and IL-25 are released following allergen exposure, leading to T2 inflammation through the cytokines IL-4, IL-5 and IL-13[2,3,5]

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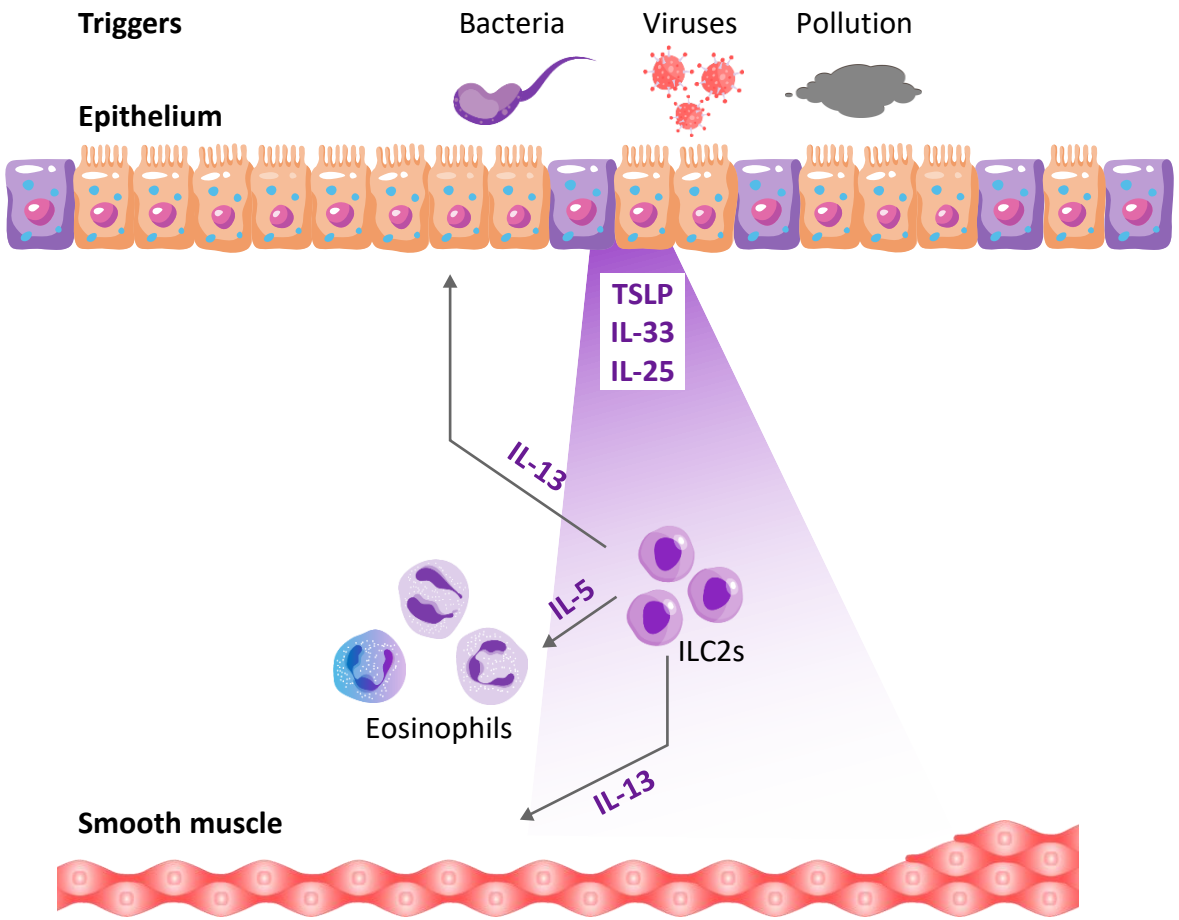
Figure is for illustrative purposes only. Specific and definitive role of some cells and cytokines shown require further elucidation
IgE, immunoglobulin E; IL, interleukin; ILC2, Type 2 innate lymphoid cell; T2, Type 2; Th, T helper; TSLP, thymic stromal lymphopoietin

1. Bousquet J, et al. Nat Rev Dis Primers 2020;6:95; 2. Yii ACA, et al. Allergy 2018;73:1964–1978; 3. Sin B, Togias A. Proc Am Thorac Soc 2011;8:106–114; 4. Kortekaas Krohn I, et al. Allergy 2018;73:837–850; 5. Wise SK, et al. Int Forum Allergy Rhinol. 2018;8:108–352

NARES may manifest as T2 inflammation without evidence of IgE-mediated hypersensitivity[1]



In patients with NARES, it is hypothesized that TSLP, IL-33 and IL-25 activate ILC2s, which leads to eosinophil activation via IL-5.[1] Common triggers may include bacteria, viruses and pollution.[1] However, mechanisms underlying NARES require further elucidation, and the illustrated pathway is a hypothesis only

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