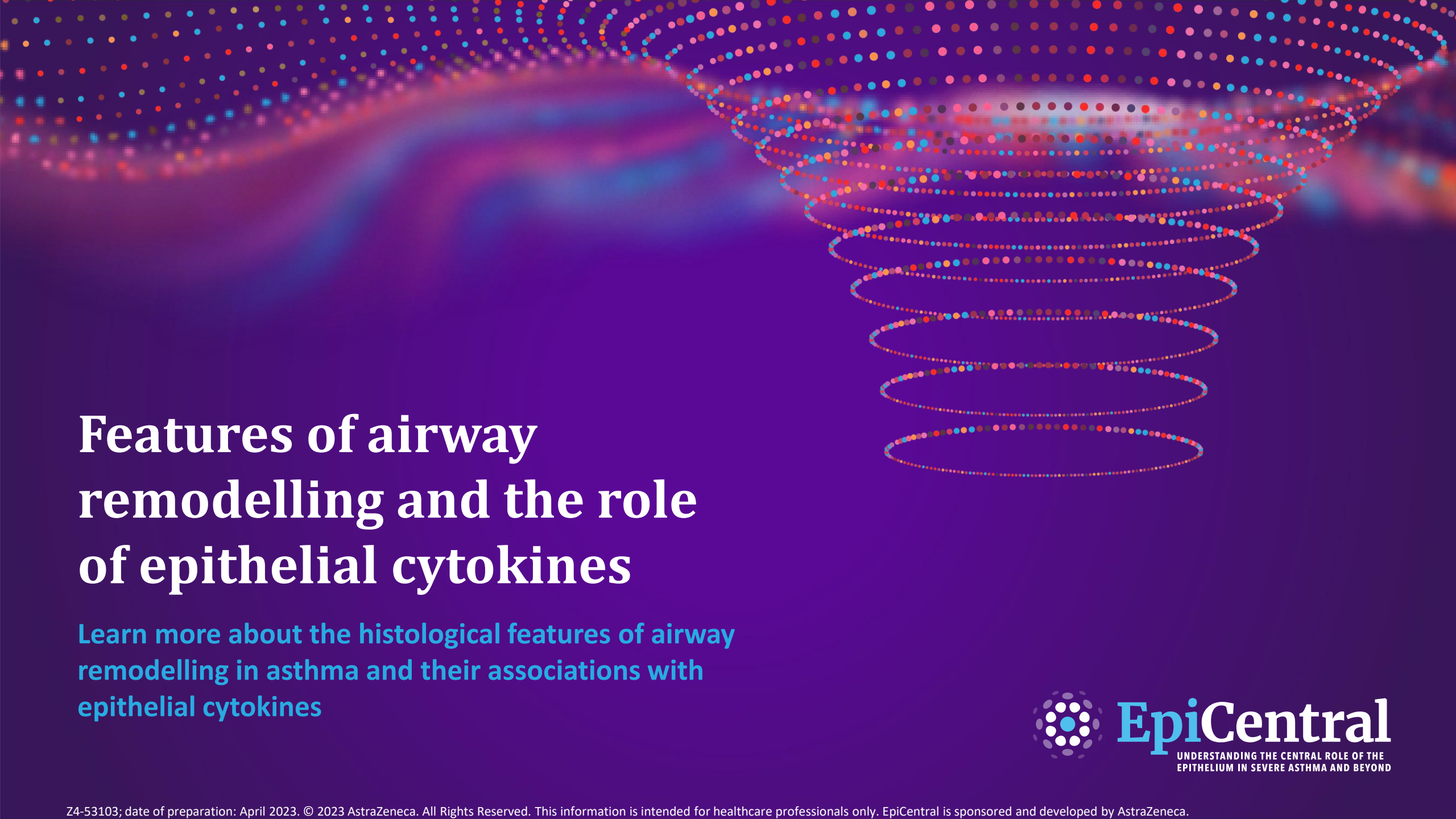
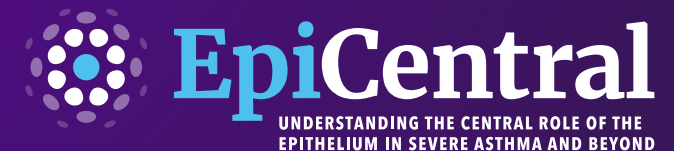




Features of airway remodelling and the role of epithelial cytokines

Learn more about the histological features of airway remodelling in asthma and their associations with epithelial cytokines



Features of airway remodelling in asthma

- Airway remodelling is **heterogeneous** and can be observed across the spectrum of asthma severity¹
- In asthma, airway remodelling refers to structural changes that can occur in both the **small and large airways**²
- These structural changes are orchestrated by crosstalk between a variety of **immune and non-immune cells** within the airway wall and submucosa^{2,3}

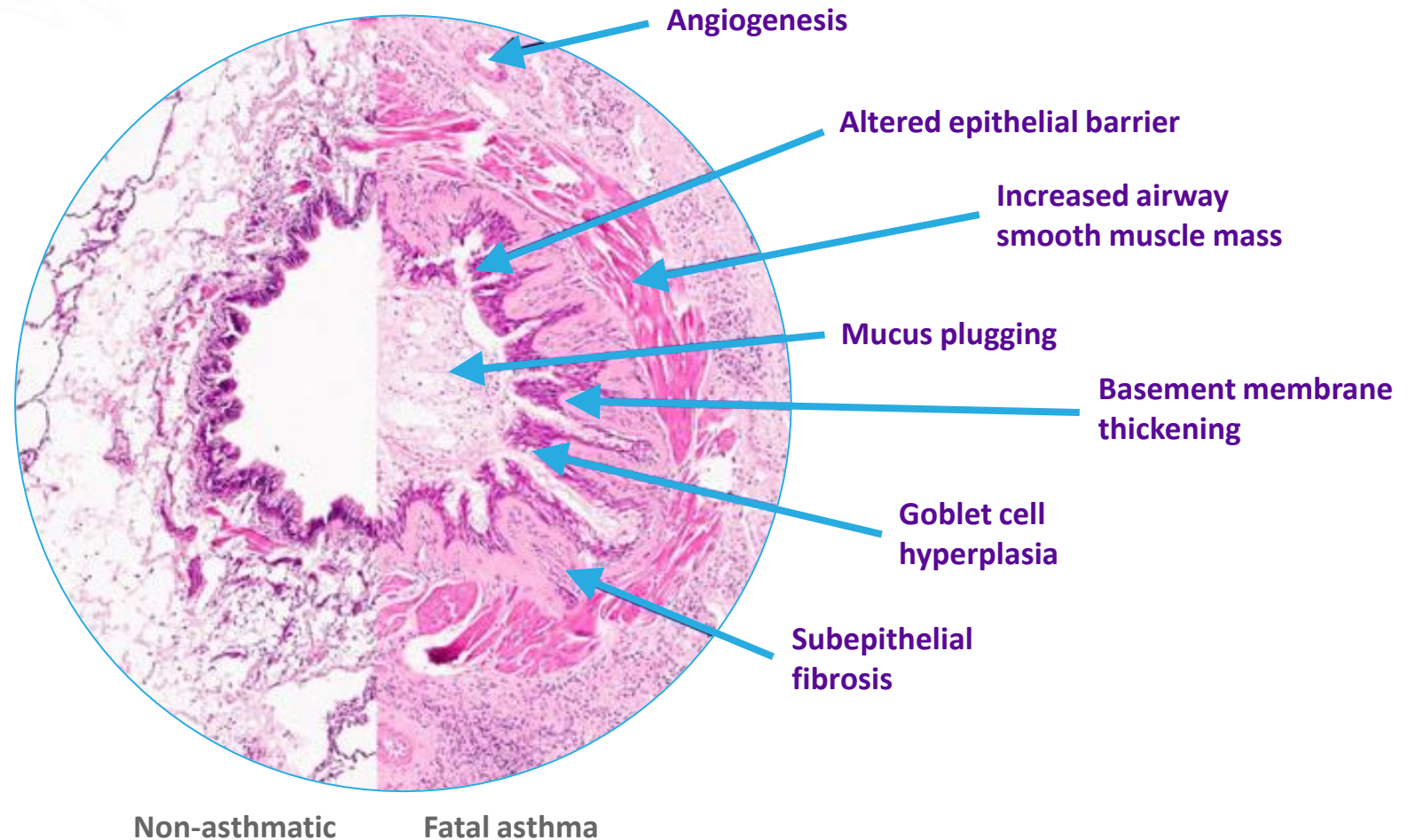


Figure adapted from Hsieh A, et al. Front Physiol 2023;14:1113100

1. Hsieh A, et al. Front Physiol 2023;14:1113100; 2. Varricchi G, et al. Allergy 2022;77:3538–3552; 3. Hough KP, et al. Front Med 2020;7:191

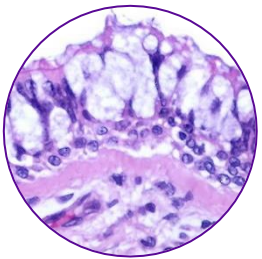
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Structural consequences of airway remodelling

**Goblet cell metaplasia
and increased mucus
production^{1,2}**



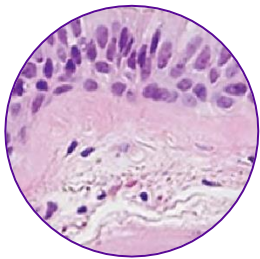
Airway blockage



**Increased basal
membrane thickness^{1,2}**



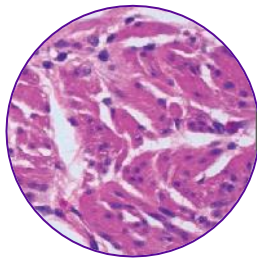
**Increased matrix
deposition leads to
airway narrowing**



**Airway smooth
muscle hyperplasia
and hypertrophy³**



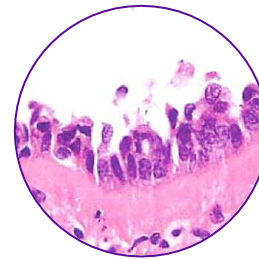
**Promotes airway
hyperresponsiveness**



Epithelial shedding^{2,4,5}



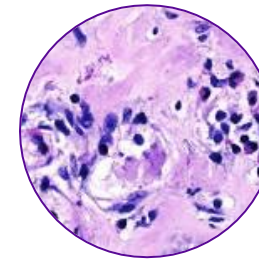
**May contribute to
damage as external
insults penetrate the
airway wall**



Subepithelial fibrosis^{2,6}



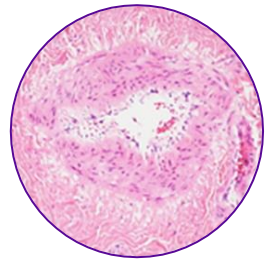
**Can lead to fixed
airway obstruction**



Angiogenesis⁷



**Promotes immune
cell infiltration**

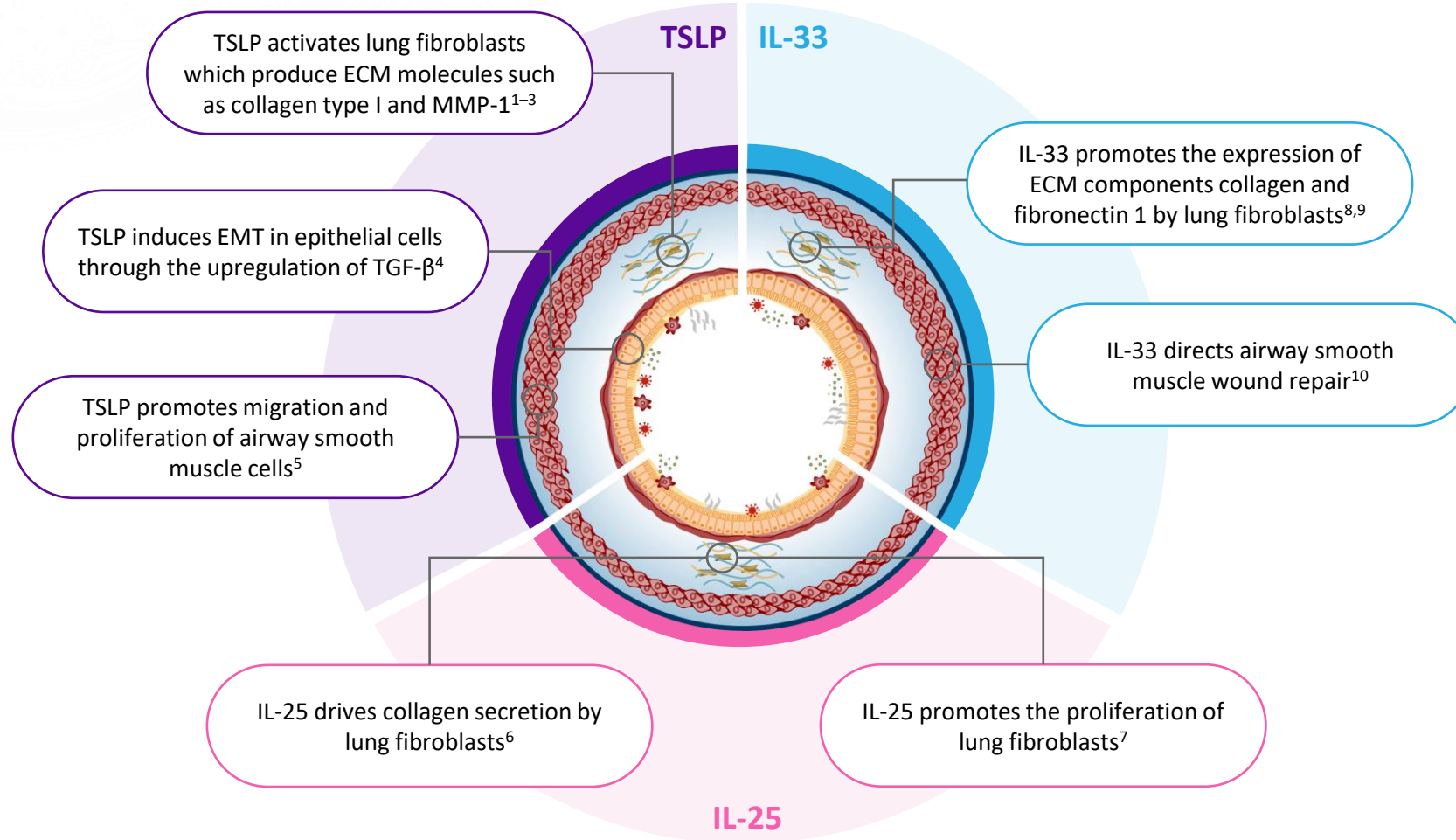


Images adapted from Rosen Y. Bronchial goblet cell hyperplasia. 2009. In: Atlas of pulmonary pathology. Available from: https://www.flickr.com/photos/pulmonary_pathology/3705951876 (Accessed 6 April 2023), Shifren A, et al. J Allergy (Cairo) 2012;2012:316049, Doeing DC, Solway J. J Appl Physiol (1985) 2013;114:834–843, Kubo T, et al. Lab Invest 2019;99:158–168, Gordon IO, et al. Arch Pathol Lab Med 2009;133:1096–1105 and Galambos C, et al. Ann Am Thorac Soc 2018;15:1359–1362

1. Bartemes KR, Kita H. Clin Immunol 2012;143:222–235; 2. Holgate ST. Immunol Rev 2011;242:205–219; 3. Doeing DC, Solway J. J Appl Physiol 2013;114:834–843; 4. Yang Y, et al. Clin Respir J 2021;15:1027–1045; 5. Calvén J, et al. Int J Mol Sci 2020;21:8907; 6. Cohen L, et al. Am J Respir Crit Care Med 2007;176:138–145; 7. Keglrich LF, Borger P. Open Respir Med J 2015;9:70–80

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Epithelial cytokines can play diverse, yet often overlapping, roles in airway remodelling in asthma



Evidence based on in-vitro experimental data

ECM, extracellular matrix; EMT, epithelial-mesenchymal transition; IL, interleukin; MMP-1, matrix metalloproteinase-1; TGF, transforming growth factor; TSLP, thymic stromal lymphopoietin

1. Cao L, et al. Exp Lung Res 2018;44:288–301; 2. Wu J, et al. Cell Biochem Funct 2013;31:496–503; 3. Jin A, et al. Biochim Biophys Acta Mol Cell Res 2021;1868:119083; 4. Cai L-M, et al. Exp Lung Res 2019;45:221–235;

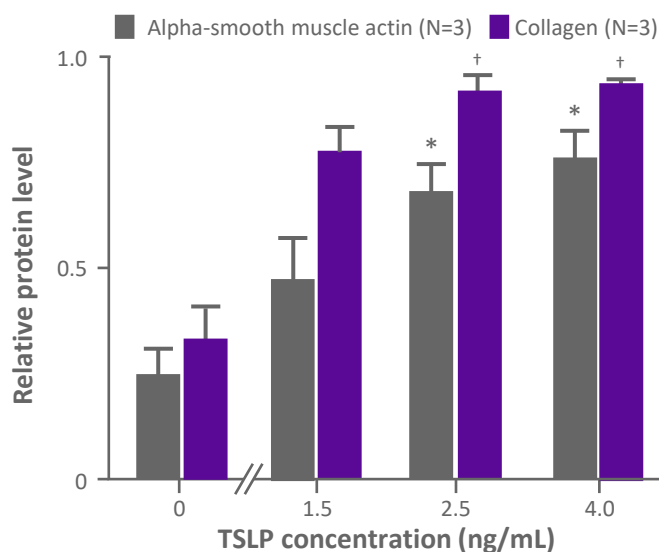
5. Redhu NS, et al. Sci Rep 2013;3:2301; 6. Gregory LG, et al. Thorax 2013;68:82–90; 7. Xu X, et al. Exp Biol Med (Maywood) 2019;244:770–780; 8. Saglani S, et al. J Allergy Clin Immunol 2013;132:676–685;

9. Guo Z, et al. J Asthma 2014;51:863–869; 10. Kaur D, et al. Allergy 2015;70:556–567

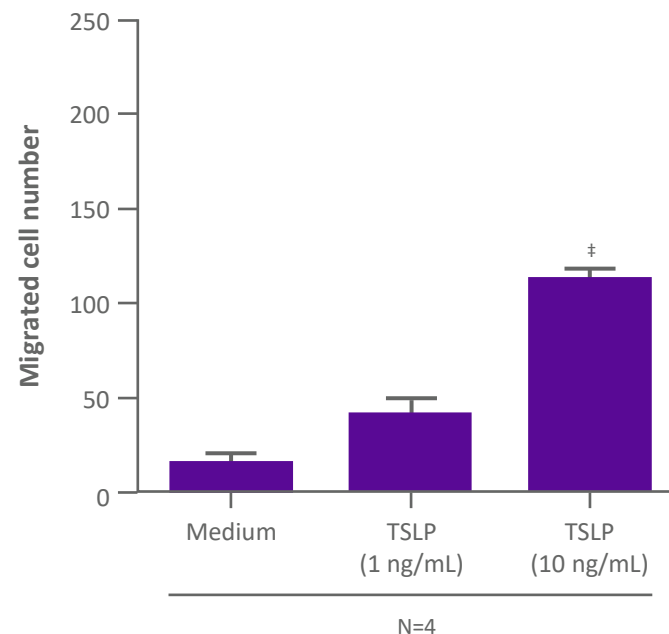
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Evidence for TSLP in airway remodelling in asthma

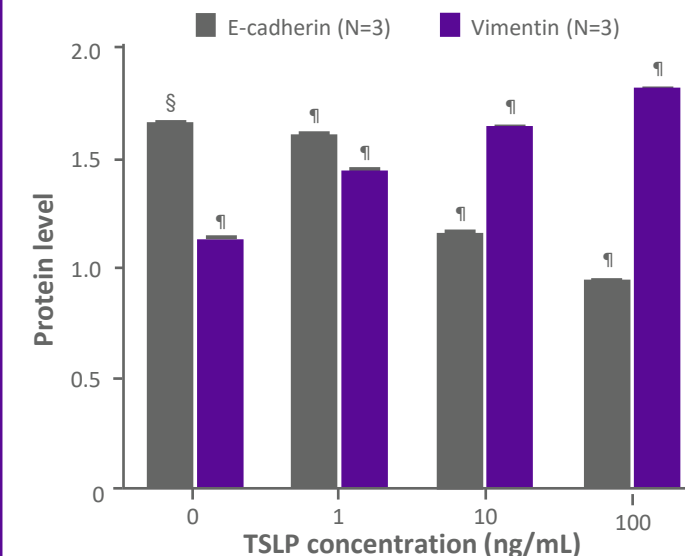
In human lung fibroblasts, TSLP increased expression of collagen and alpha-smooth muscle actin *in vitro*^{1,2}



In human airway smooth muscle cells, TSLP induced migration, which may contribute to increased smooth muscle mass *in vitro*³



In human airway epithelial cells, TSLP downregulated epithelial marker E-cadherin and upregulated mesenchymal marker vimentin *in vitro*⁴



Figures adapted from Cao L, et al. Exp Lung Res 2018;44:288–301, Redhu NS, et al. Sci Rep 2013;3:2301 and Cai L-M, et al. Exp Lung Res 2019;45:221–235

*P<0.05 vs GAPDH control (smooth muscle actin); [†]P<0.05 vs GAPDH control (collagen); [‡]P<0.001 vs medium control; [§]P<0.01; [¶]P<0.001

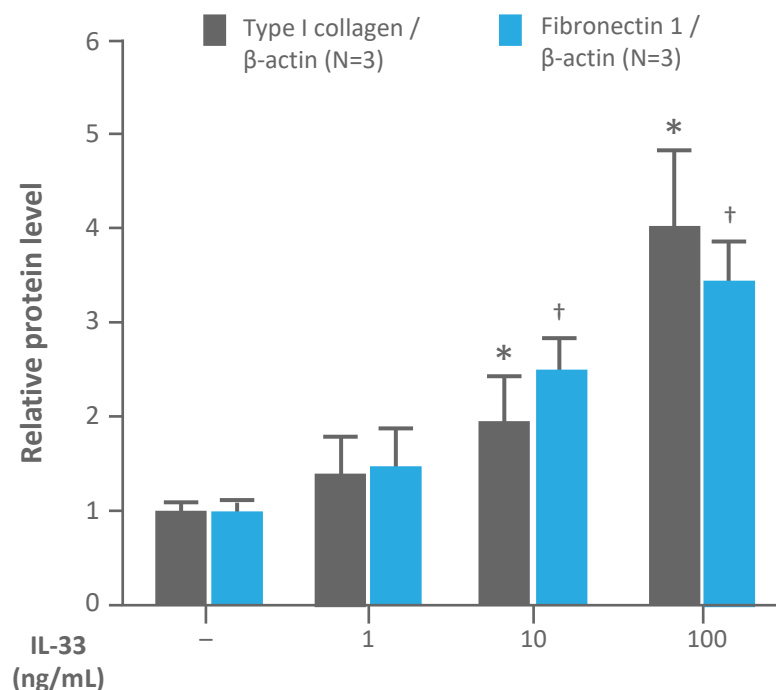
GAPDH, glyceraldehyde-3-phosphate dehydrogenase; TSLP, thymic stromal lymphopoietin

1. Cao L, et al. Exp Lung Res 2018;44:288–301; 2. Wu J, et al. Cell Biochem Funct 2013;31:496–503; 3. Redhu NS, et al. Sci Rep 2013;3:2301; 4. Cai L-M, et al. Exp Lung Res 2019;45:221–235

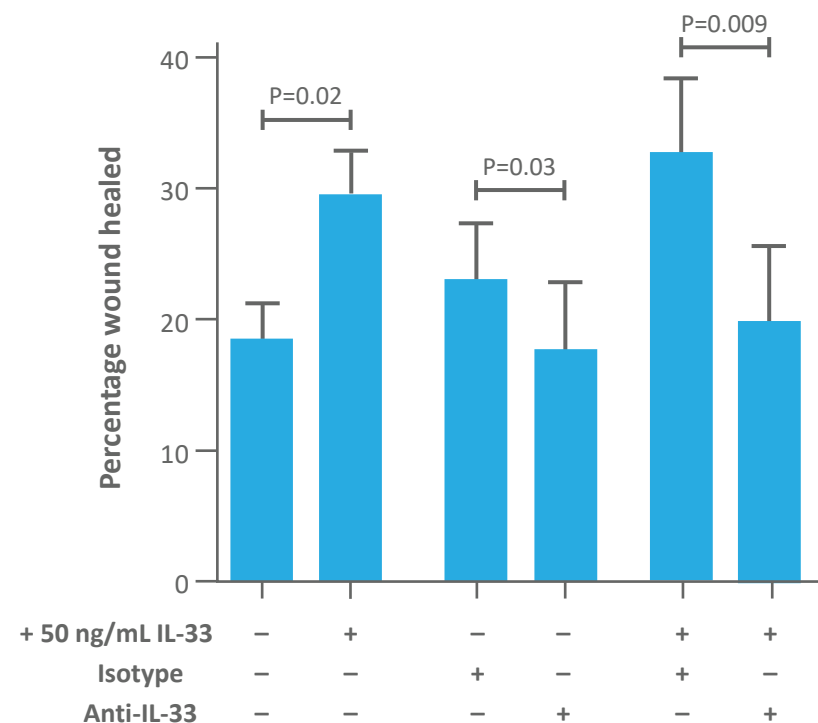
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Evidence for IL-33 in airway remodelling in asthma

In human lung fibroblasts, IL-33 increased expression of fibronectin 1 and type I collagen *in vitro*^{1,2}



In human airway smooth muscle cells, IL-33 directed wound closure *in vitro*, which may contribute to smooth muscle repair in response to physical or inflammatory damage³



Figures adapted from Guo Z, et al. J Asthma 2014;51:863–869 and Kaur D, et al. Allergy 2015;70:556–567

*P<0.05 vs controls; †P<0.01 vs controls

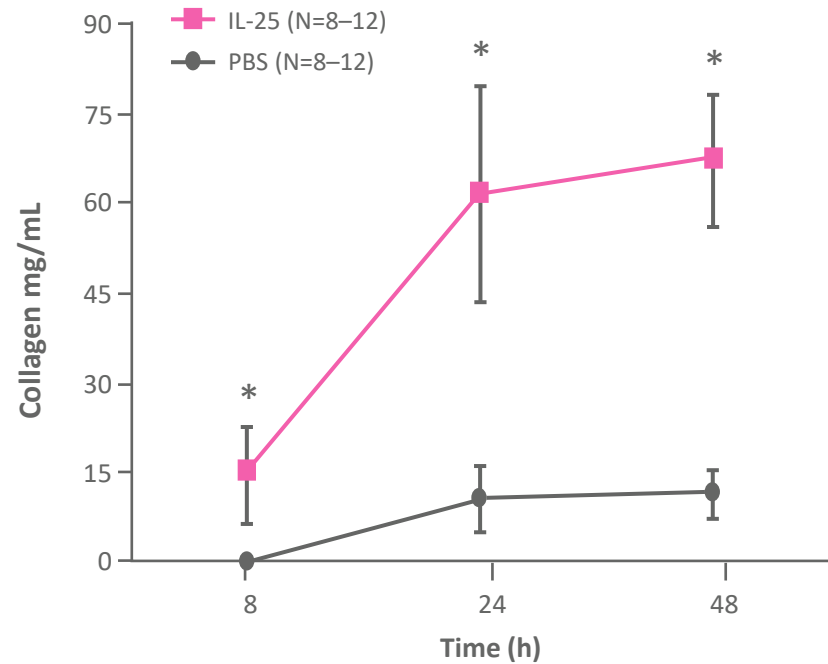
IL, interleukin

1. Guo Z, et al. J Asthma 2014;51:863–869; 2. Saglani S, et al. J Allergy Clin Immunol 2013;132:676–685; 3. Kaur D, et al. Allergy 2015;70:556–567

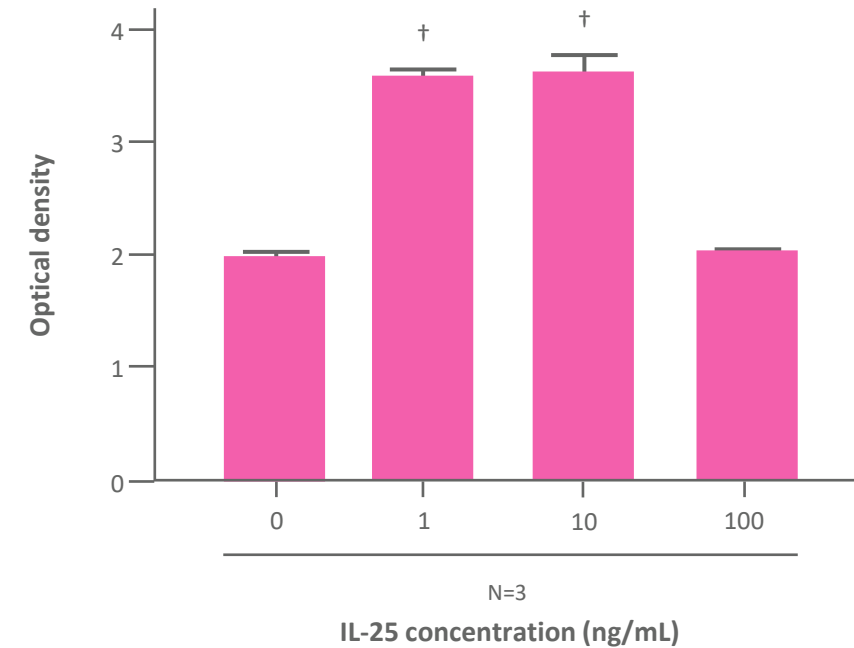
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Evidence for IL-25 in airway remodelling

In human airway lung fibroblasts, IL-25 induced extracellular collagen secretion *in vitro*¹



In human lung fibroblasts, IL-25 promoted cell proliferation *in vitro*²



Figures adapted from Gregory LG, et al. Thorax 2013;68:82–90 and Xu X, et al. Exp Biol Med (Maywood) 2019;244:770–780

*P<0.05 vs PBS control group; †P<0.01 compared with vehicle-treated fibroblasts after 72 hours

IL, interleukin; PBS, phosphate-buffered saline

1. Gregory LG, et al. Thorax 2013;68:82–90; 2. Xu X, et al. Exp Biol Med (Maywood) 2019;244:770–780

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