

How TSLP correlates with the clinical features of asthma



Multiple clinical features of asthma are associated with TSLP¹⁻⁹

TSLP



**Asthma
severity¹⁻²**



**Exacerbation
risk³**



**Reduced lung
function¹**



**Reduced
steroid
response⁴**



**Exaggerated T2
response to
viral
infections⁵⁻⁷**



**Potential
airway
remodeling^{8,9}**

T2, type 2; TSLP, thymic stromal lymphopoietin

1. Li Y, et al. *J Immunol*. 2018;200:2253–2262. 2. Shikotra A, et al. *J Allergy Clin Immunol*. 2012;129:104–111. 3. Ko H-K, et al. *Sci Rep*. 2021;11:8425. 4. Liu S, et al. *J Allergy Clin Immunol*. 2018;141:257–268. 5. Lee H-C, et al. *J Allergy Clin Immunol*. 2012;130:1187–1196. 6. Uller L, et al. *Thorax*. 2010;65:626–632. 7. Kato A, et al. *J Immunol*. 2007;179:1080–1087. 8. Cao L, et al. *Exp Lung Res*. 2018;44:288–301. 9. Wu J, et al. *Cell Biochem Funct*. 2013;31:496–503.

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Airway TSLP expression increases with asthma severity^{1,2}

- Two studies found that TSLP expression was higher in the airways of patients with asthma vs healthy controls ($p < 0.05$)^{1,2}
- TSLP concentration correlated with disease severity ($p < 0.05$)²

Airway TSLP concentration increased with asthma severity^{1,a}

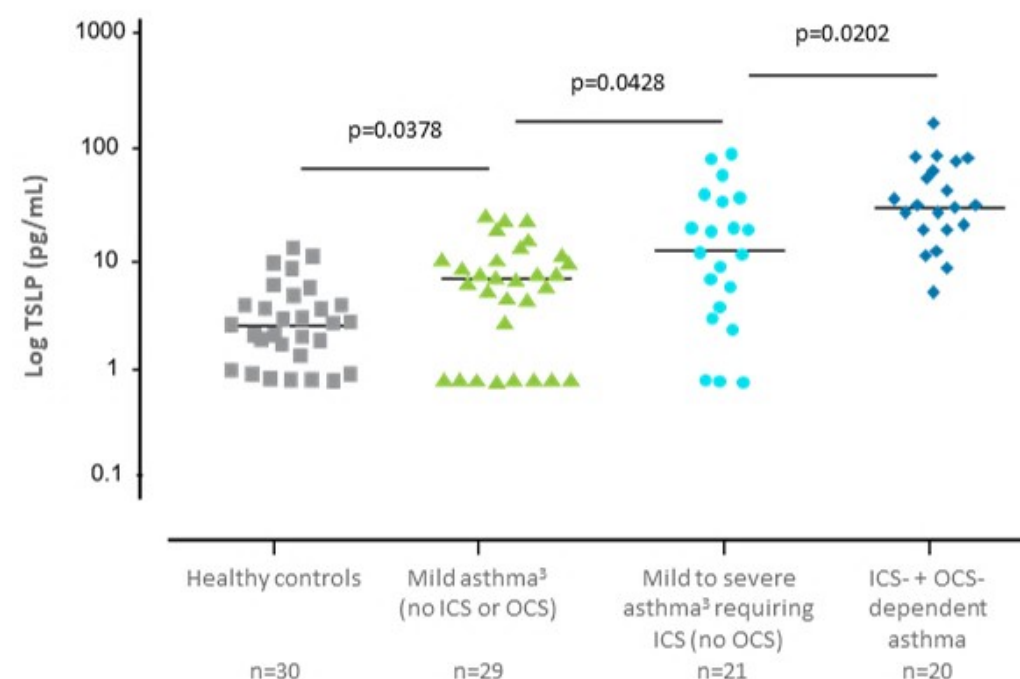


Figure adapted from Li Y, et al. *J Immunol.* 2018;200:2253–2262

In-house ELISA platforms developed by Novartis, with lower limits of detection of 1 and 2 pg/mL, were used to analyze TSLP in BALF

Normal control patients were healthy lifelong non-smoking volunteers who had no history of lung disease¹

^aBALF was used to measure the concentrations of TSLP (patients with asthma, n=70; controls, n=30)¹

BALF, bronchoalveolar lavage fluid; ELISA, enzyme-linked immunosorbent assay; ICS, inhaled corticosteroid(s); OCS, oral corticosteroid(s); TSLP, thymic stromal lymphopoietin

1. Li Y, et al. *J Immunol.* 2018;200:2253–2262. 2. Shikotra A, et al. *J Allergy Clin Immunol.* 2012;129:104–111. 3. Global Initiative for Asthma.

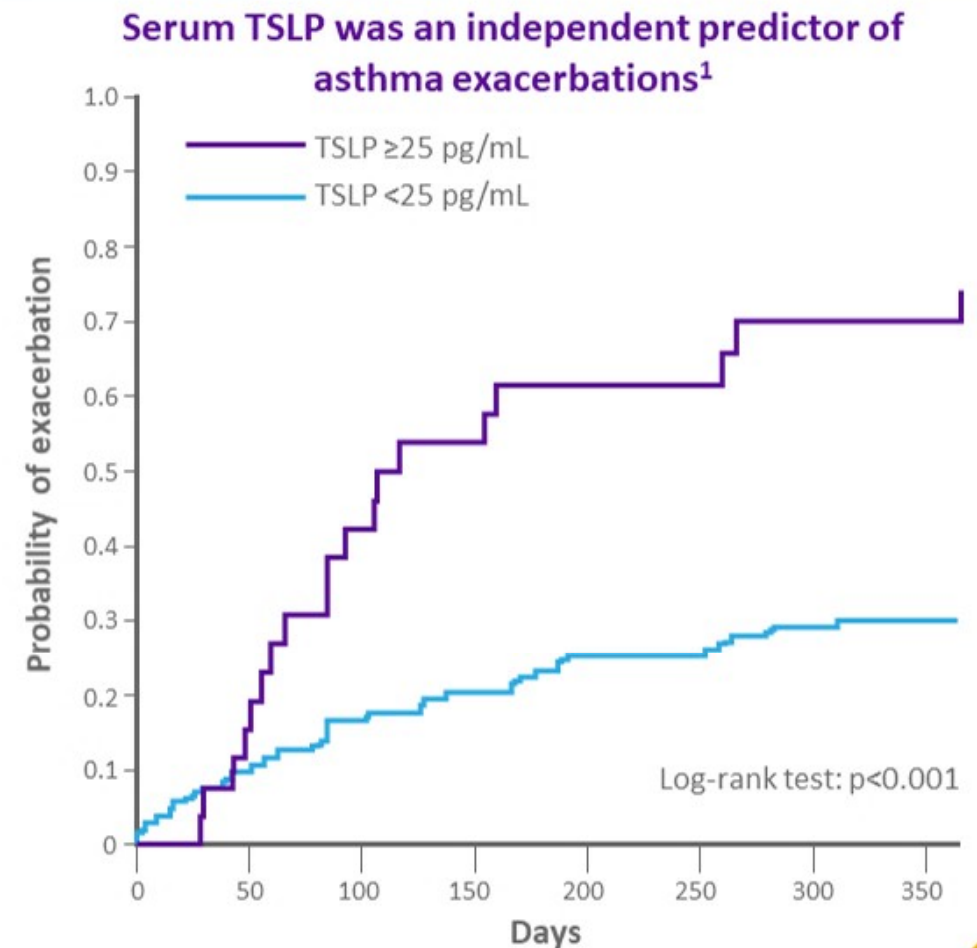
https://ginasthma.org/wp-content/uploads/2020/04/GINA-2020-full-report_-final_-wms.pdf. Accessed November 15, 2021.

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TSLP has been associated with exacerbation risk in severe asthma



- In a prospective, observational study of 132 patients with severe asthma:
 - **Serum TSLP** level was an **independent factor for predicting future risk of exacerbations**¹
 - **Higher serum TSLP** was associated with **8.7-fold higher odds of exacerbation** ($p < 0.001$)¹
- Previous exacerbations, blood eosinophil count, serum tryptase, and serum TSLP were **independent predictors** of asthma exacerbation risk¹
 - The authors concluded that TSLP may be playing a **pathogenic role across different asthma phenotypes**^{1,2}



TSLP, thymic stromal lymphopoietin

1. Ko H-K, et al. *Sci Rep*. 2021;11:8425. 2. Corren J, et al. *N Engl J Med*. 2017;377:936–946.

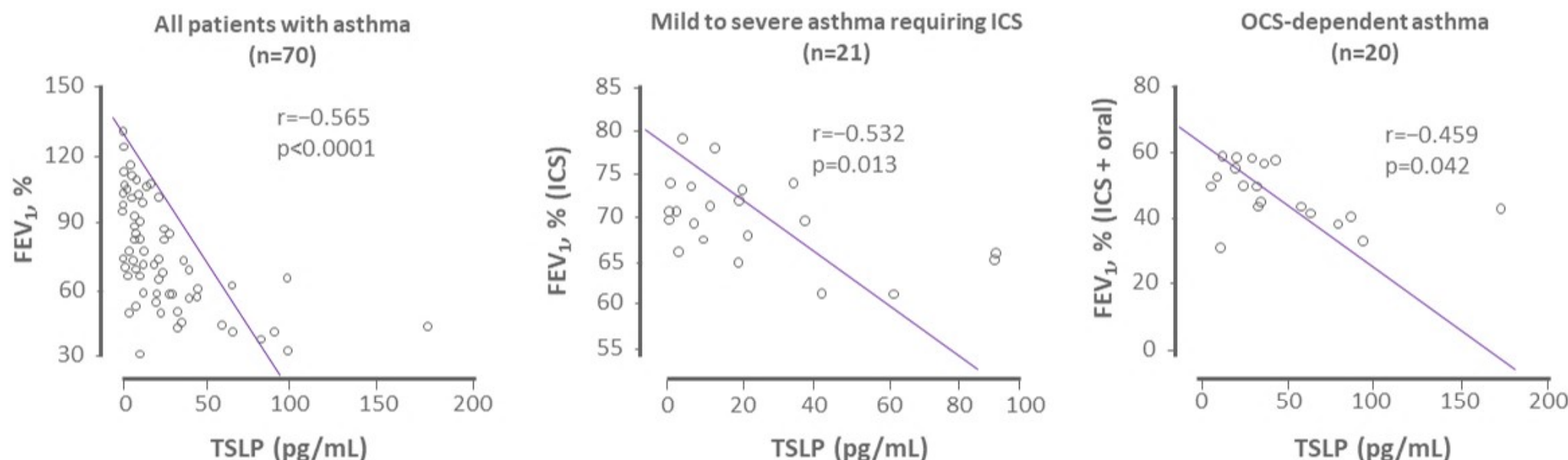
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Airway TSLP expression correlates with reduced lung function in patients with asthma¹



Concentration of TSLP is inversely correlated with FEV₁¹



Figures adapted from Li Y, et al. *J Immunol.* 2018;200:2253–2262

BALF was used to measure the concentrations of TSLP. Spearman rank-order method with correction for tied values was used to obtain correlation coefficients

BALF, bronchoalveolar lavage fluid; FEV₁, forced expiratory volume in 1 second; ICS, inhaled corticosteroid(s); OCS, oral corticosteroid(s); r, Spearman rank-order correlation coefficient;

TSLP, thymic stromal lymphopoietin

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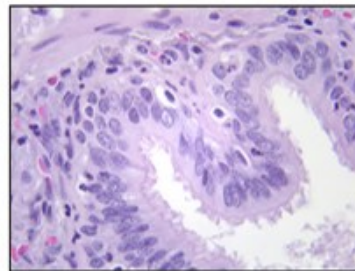
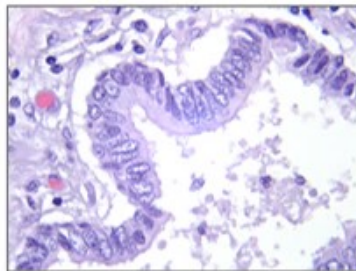
TSLP may drive airway remodeling in patients with asthma^{1,2}

Bronchial airway epithelial cells in asthma versus non-asthma lung³

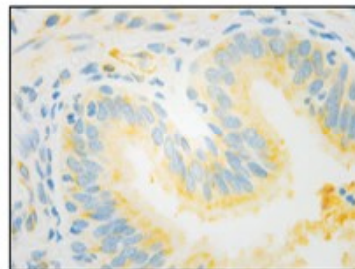
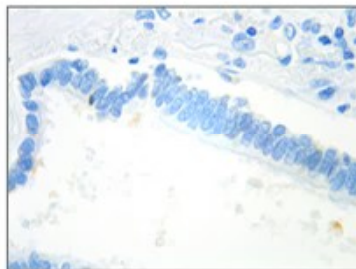
Non-asthma

Asthma

Standard
H&E
staining



TSLP
staining
(in yellow)



Images from Data on File, REF-108602, AZPLP

In human lung fibroblasts, TSLP increased expression of collagen and smooth muscle actin in a concentration-dependent manner ($p < 0.05^a$)^{1,2}

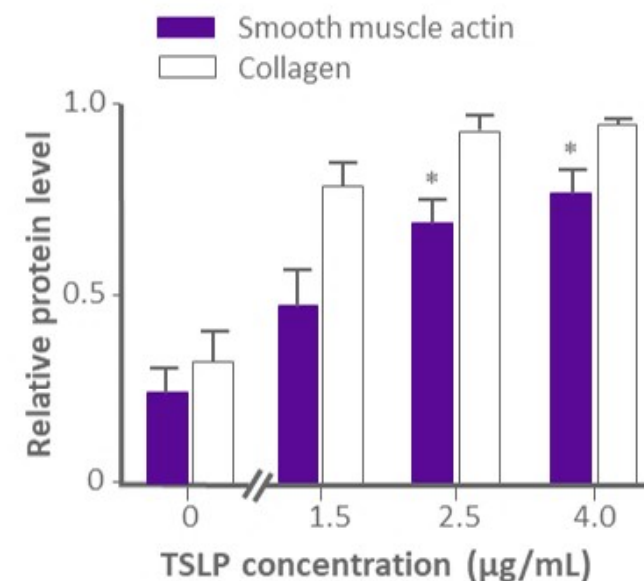


Figure adapted from Cao L, et al. *Exp Lung Res.* 2018;44:288–301

Human BECs were stained with H&E or Masson Trichrome

^aVs GAPDH control; * $p < 0.05$

BEC, bronchial epithelial cell; GAPDH, glyceraldehyde-3-phosphate dehydrogenase; H&E, hematoxylin and eosin; 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. Data on File, REF-108602, AZPLP.

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TSLP may drive reduced corticosteroid responses in patients with asthma¹



- ILC2s from BAL fluid of patients with asthma exposed to TSLP were resistant to steroids^{1,a}
- Reduced effect of dexamethasone was linked to higher airway TSLP expression¹
- Steroid resistance also correlated with higher BALF and blood eosinophils, and lower FEV₁ ($p \leq 0.003$)¹

In patients with asthma, TSLP levels correlated with reduced steroid response¹

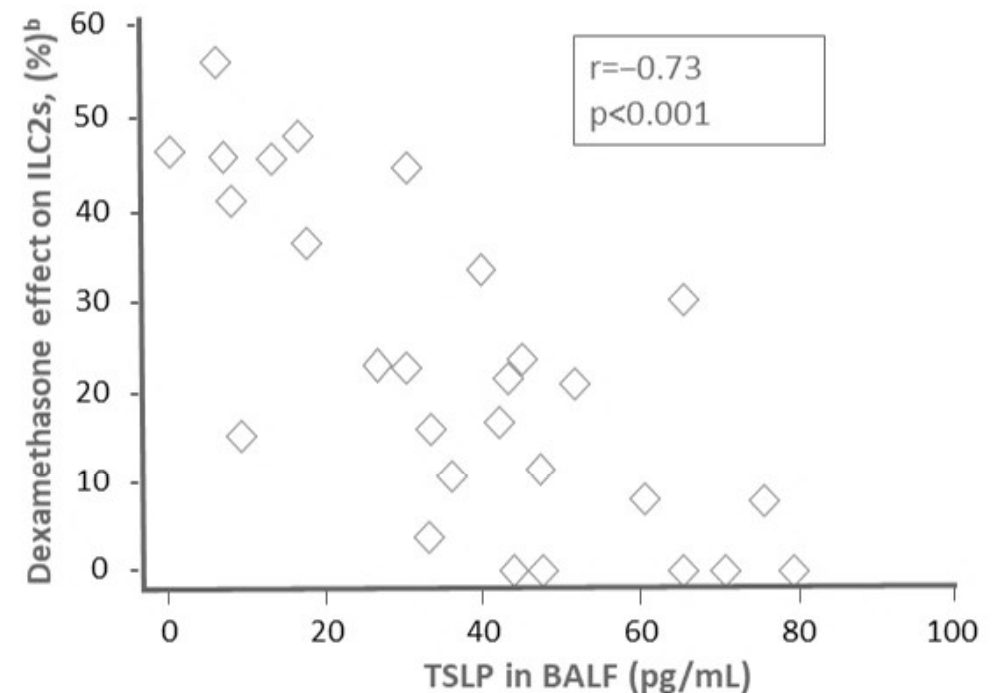


Figure adapted from Liu S, et al. *J Allergy Clin Immunol*. 2018;141:257–268

^aResistance to steroids meant a lack of inhibition of T2 cytokine expression by ILC2s

^bBALF ILC2s in patients with asthma were examined (n=50). Controller medications were maintained (SCS and ICS medications)

BALF, bronchoalveolar lavage fluid; FEV₁, forced expiratory volume in 1 second; ICS, inhaled corticosteroid(s); ILC2, type 2 innate lymphoid cell; r, Pearson correlation coefficient; SCS, systemic corticosteroid(s); T2, type 2; TSLP, thymic stromal lymphopoietin

1. Liu S, et al. *J Allergy Clin Immunol*. 2018;141:257–268.

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Exaggerated TSLP release following viral infection drives T2 response in patients with asthma¹⁻³



- After RSV infection, BECs of children with asthma produced higher levels of TSLP than BECs of healthy children¹
 - In adults, BECs produced increased TSLP when exposed to rhinovirus or dsRNA (viral RNA analog) ($p < 0.05$)^{2,3}
- This increased TSLP drives an exaggerated T2 response to viral infections^{2,3}
- These results may explain how viruses have the ability to drive exacerbations in patients with asthma¹⁻³

Following viral infection, TSLP release is increased from bronchial epithelial cells of patients with asthma¹

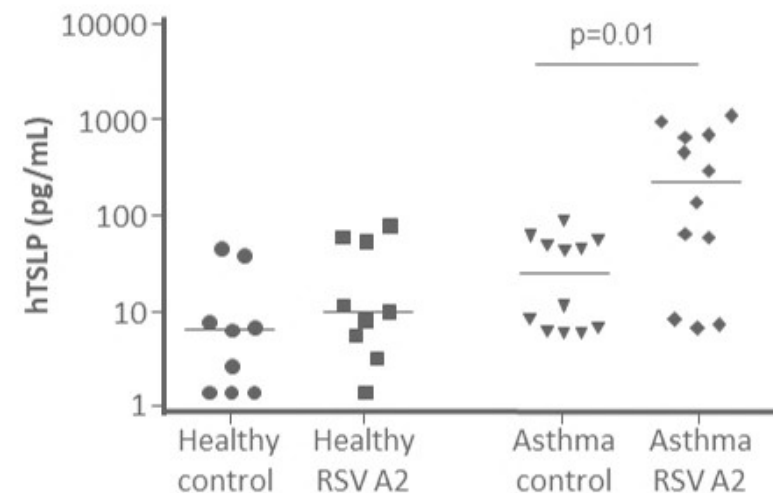


Figure adapted from Lee HC, et al. *J Allergy Clin Immunol.* 2012;130:1187–1196

BEC, bronchial epithelial cell; dsRNA, double-stranded RNA; hTSLP, human thymic stromal lymphopoietin; RSV, respiratory syncytial virus; T2, type 2; TSLP, thymic stromal lymphopoietin

1. Lee HC, et al. *J Allergy Clin Immunol.* 2012;130:1187–1196. 2. Uller L, et al. *Thorax.* 2010;65:626–632. 3. Kato A, et al. *J Immunol.* 2007;179:1080–1087.

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