



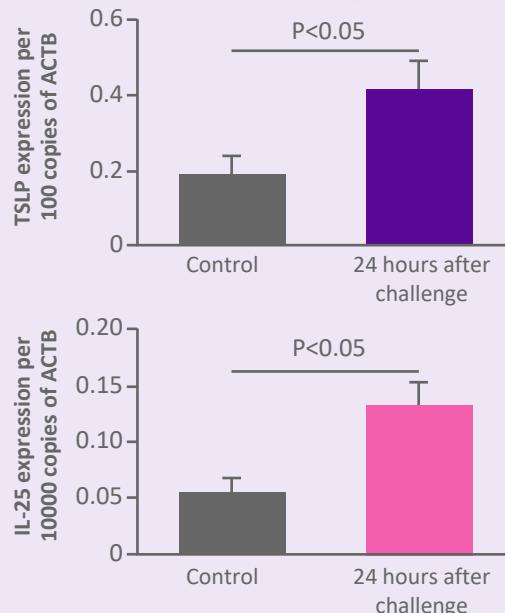
# Eosinophilic esophagitis (EoE) mouse model data

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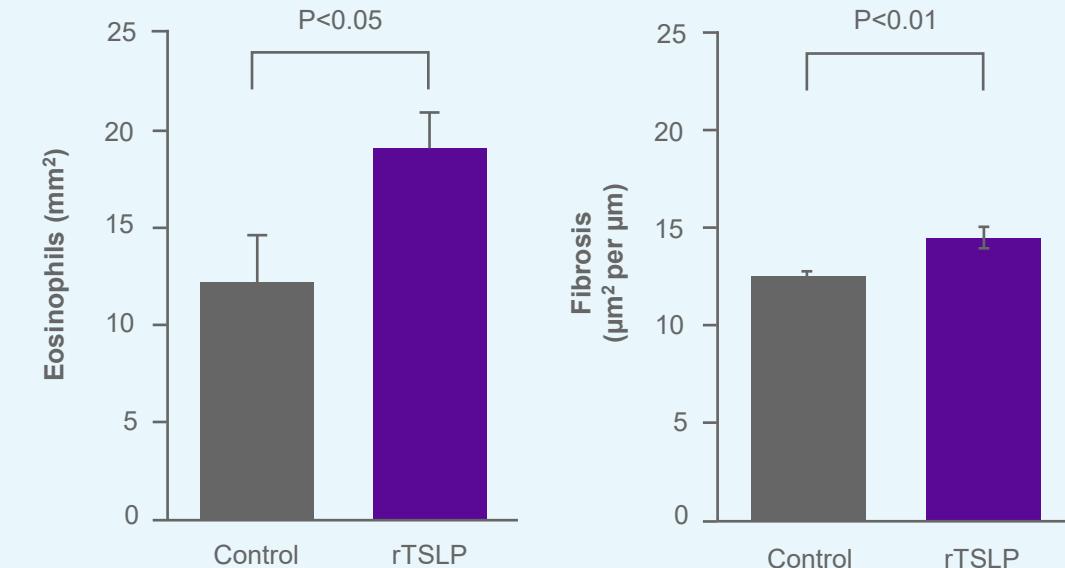
# TSLP and IL-25 are elevated following allergen challenge and TSLP is implicated in the pathogenesis of EoE

## Expression of TSLP and IL-25 following allergen challenge



- Aspergillus fumigatus induced EoE in mice, with TSLP and IL-25 expression observed during the challenge period in epithelial and smooth muscle cells\*
  - After 3 weeks of allergen challenge, TSLP expression remained elevated versus control; IL-25 expression was not elevated<sup>†</sup>

## Induction of oesophageal eosinophilia and fibrosis by rTSLP in a TRAIL-deficient mouse model of EoE



- In a murine model of EoE, TRAIL deficiency is associated with reduced TSLP expression and reduced EoE-type pathology
- Treatment with rTSLP is sufficient to induce oesophageal eosinophilia and fibrosis in TRAIL-deficient mice

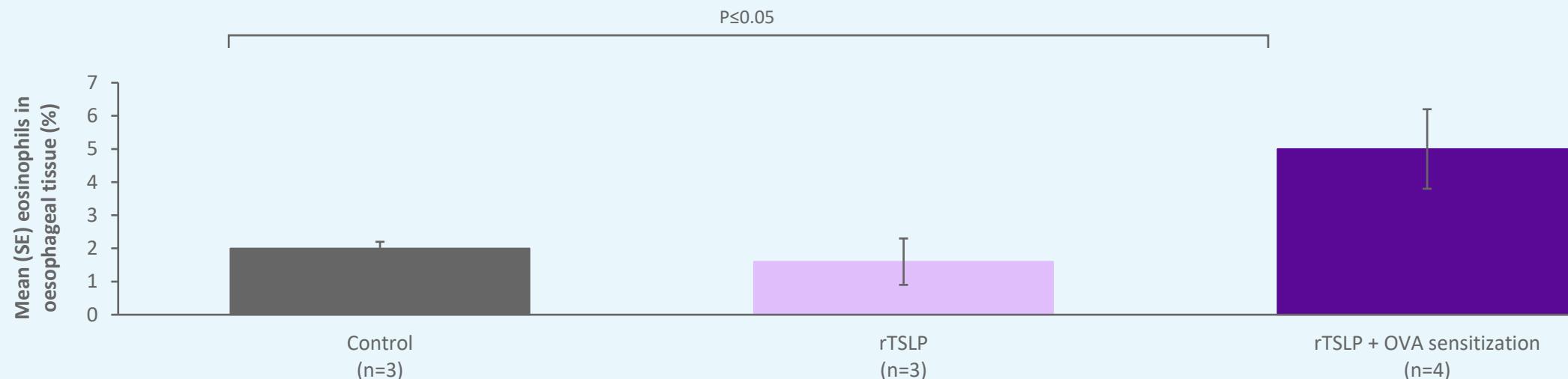
\*MID1 and CCL20 expression was also observed; <sup>†</sup>TRAIL and CCL20 expression was also not elevated, whereas MID1, CCL11, and CCL24 expression persisted versus control

ACTB,  $\beta$ -actin; EoE, eosinophilic esophagitis; IL, interleukin; rTSLP, recombinant thymic stromal lymphopoietin; TRAIL, tumour necrosis factor-related apoptosis-inducing ligand; TSLP, thymic stromal lymphopoietin  
Collison AM, et al. J Allergy Clin Immunol 2015;136:971–982

## In another murine model, the disruption of TSLP signalling prevents EoE development

- TSLPR-deficient mice did not develop experimental EoE
- Sensitisation of wild-type mice with rTSLP leads to an EoE-like phenotype following oral challenge

### Oesophageal eosinophilia in mice following intradermal injection of rTSLP and oral challenge\*



\*Data depicted are from one experiment, and are representative of three independent experiments

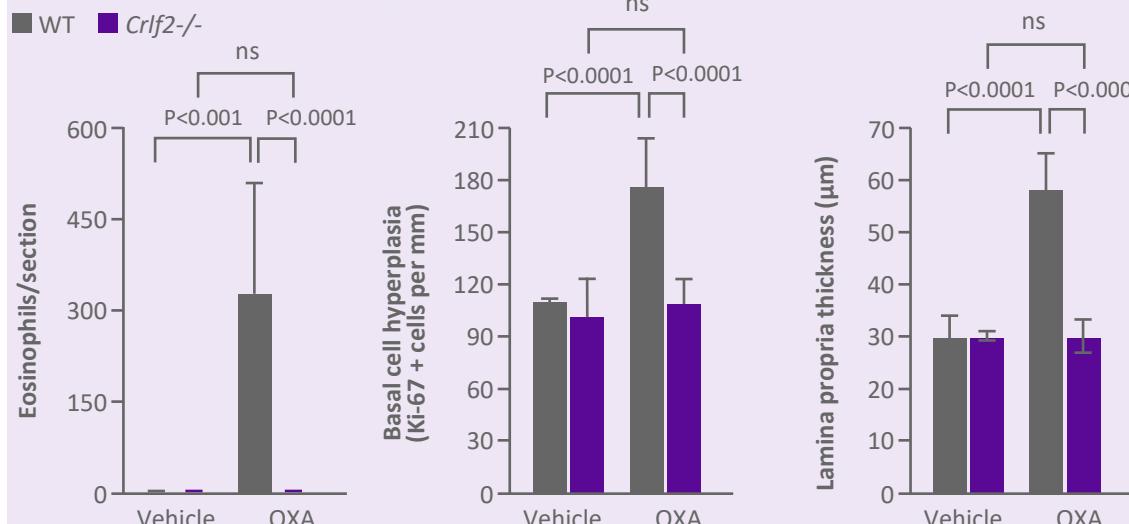
EoE, eosinophilic esophagitis; IL, interleukin; OVA, ovalbumin; rTSLP, recombinant thymic stromal lymphopoitin; SE, standard error; TSLP, thymic stromal lymphopoitin; TSLPR, recombinant thymic stromal lymphopoitin receptor

1. Noti M, et al. Nat Med 2013;19:1005–1013; 2. Noti M, et al. Nat Med (suppl) 2013;19:1005–1013

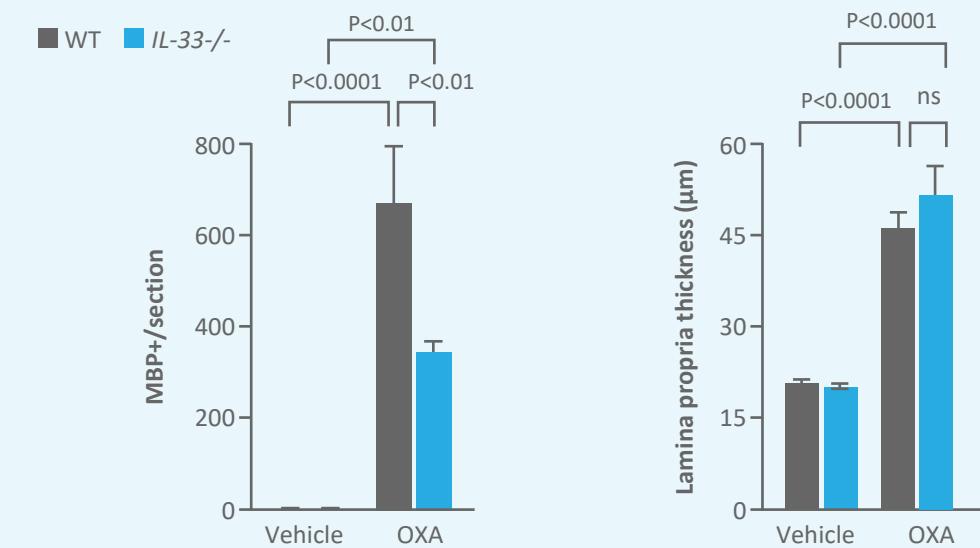
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# Distinct roles for TSLP and IL-33 in EoE

## Markers of experimental EoE in *TSLPR*-deficient mice\*



## Markers of experimental EoE in *IL33*-deficient mice



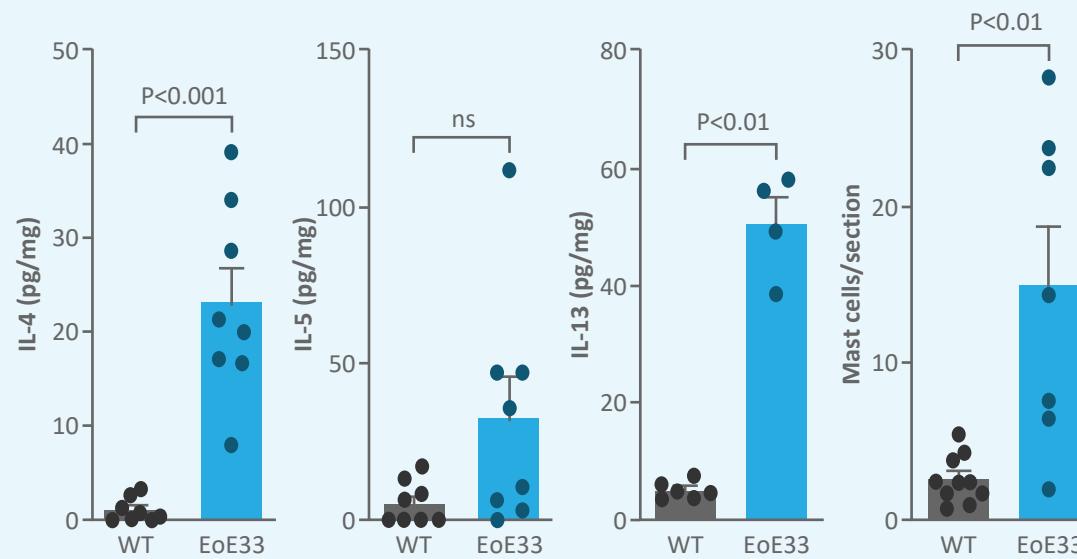
- TSLP was associated with eosinophil infiltration, basal cell proliferation and thickening of the lamina propria
  - Pharmacological blockade of TSLP resulted in a decrease in eosinophilia, basal cell proliferation and lamina propria thickening and vascularisation
- IL-33 was associated with eosinophil infiltration, but other structural changes were independent of IL-33

\**CRLF2* encodes TSLP

EoE, eosinophilic esophagitis; IL, interleukin; ns, not significant; OXA, oxazolone; TSLP, thymic stromal lymphopoitin; TSLPR, thymic stromal lymphopoitin receptor; WT, wild-type  
Dsilva A, et al. Allergy 2025;80:3095–3107

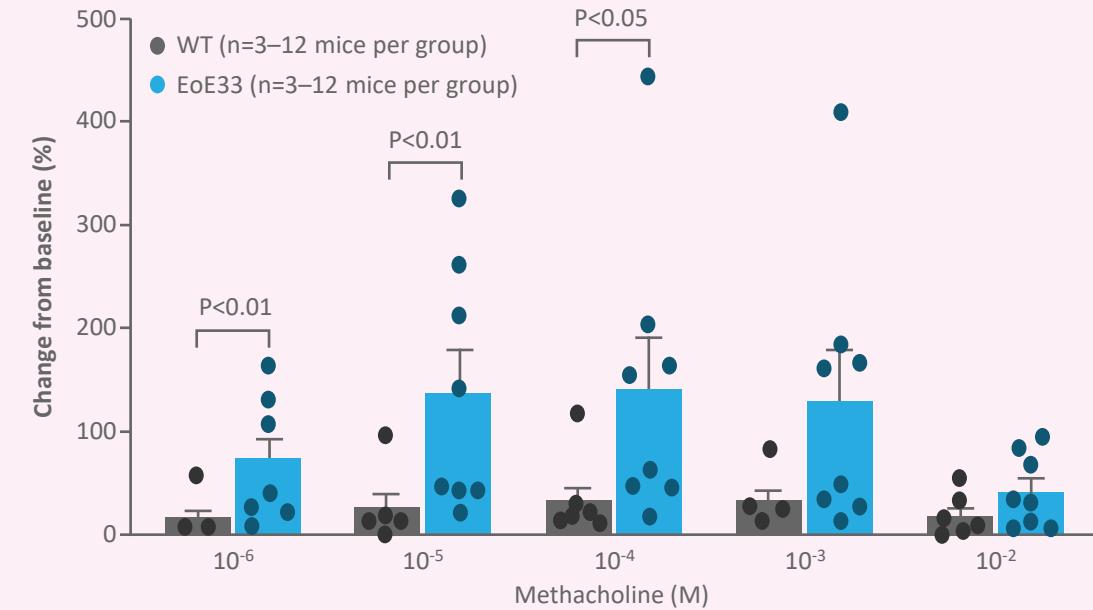
# IL-33 is implicated in symptomology and pathophysiology of EoE

## Oesophageal levels of T2 cytokines and mast cells<sup>1</sup>



- Mice with increased expression of IL-33 (EoE33 mice) in the oesophageal epithelium demonstrated **EoE-like pathology**, as well as a **failure to thrive**<sup>1</sup>
  - Increased T2 cytokines, including IL-13 and IL-4, eosinophil and mast cell infiltration, and tissue remodelling were observed<sup>1</sup>

## Muscle tension in response to methacholine challenge<sup>1</sup>



- Oesophageal muscle tension in response to methacholine was increased in mice with **IL-33-induced EoE**, compared with WT<sup>1</sup>
- The **IL-33-ST2 axis** has also been implicated in the **development of EoE** in a murine model<sup>2</sup>