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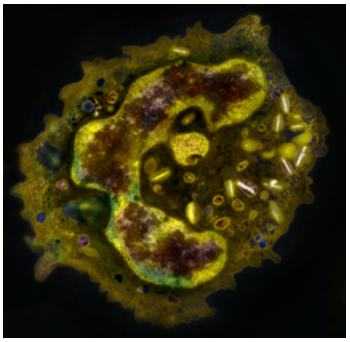
OESOPHAGUS

TSLP–basophil axis important in eosinophilic oesophagitis

A new study shows that thymic stromal lymphopoietin (TSLP, a cytokine that promotes allergic inflammation) and basophils contribute to the pathogenesis of eosinophilic oesophagitis (EoE). These results suggest that the TSLP–basophil pathway could be a potential target for new therapeutic approaches to treat EoE," note authors David Artis, Mario Noti and Elia Tait Wojno.

EoE is an inflammatory disorder characterized by oesophageal dysfunction and eosinophil infiltration. Previous studies have shown that a range of immune cells are probably involved in the pathogenesis of EoE and that there is a genetic component. One gene under scrutiny is *TSLP* after it was shown to be strongly associated with EoE in children. Now, the role of TSLP in EoE has been investigated.

First, the researchers developed a new mouse model of EoE-like disease that was associated with increased Tslp production and mimicked some of the clinical features of human disease (oesophageal eosinophilia and food impaction). Using this model, they observed that the development of this EoE-like disease was dependent on Tslp,



A computer-enhanced electron microscopic image of a mouse basophil. Image courtesy of M. Noti, E. Tait Wojno, D. Artis and the UPenn Electron Microscopy Resource Laboratory.

but independent of IgE, a key mediator of allergic inflammation.

Given that TSLP expression is associated with selective expansion of certain basophil populations, the study authors considered that basophils might also have a role in EoE. By depleting basophils through various means, the investigators noted reduced accumulation of eosinophils in those mice upon sensitization and challenge.

Importantly, Tslp and basophils proved to be a useful target to treat EoE-like disease. In mice with established EoE-like disease, treatment with a Tslp-specific monoclonal antibody resulted in decreased oesophageal eosinophilia and no food impaction; similar results were observed following treatment with a basophil-depleting monoclonal antibody.

Translating findings from studies in mice to humans can be an issue, but the researchers took steps to confirm the importance of the TSLP–basophil axis in human EoE. Oesophageal biopsy samples from children with inactive or active EoE, and control samples from children without EoE, were examined. *TSLP* expression was highest in individuals with active EoE, and these samples also stained positive for TSLP. Basophil counts were also highest in active EoE samples. Similar findings were observed in biopsy samples from adults. Finally, the gain-of-function $TSLP^{risk}$ polymorphism was found to be associated with increased basophil responses in patients with EoE.

The authors now plan to use their new mouse model to "further interrogate the function and regulation of the TSLP–basophil pathway in the context of oesophageal inflammation".

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Original article Noti, M. *et al.* Thymic stromal lymphopoietin-elicted basophil responses promote eosinophilic esophagitis. *Nat. Med.* doi:10.1038/nm.3281