

## OESOPHAGUS

# Genome-wide association study reveals the tissue-specific nature of eosinophilic oesophagitis

An oesophageal-specific epithelial pathway that interfaces with the adaptive immune system in patients with eosinophilic oesophagitis (EoE) has been reported in a paper published in *Nature Genetics*. “Our findings explain the tissue-specific nature of this allergic disease and provide a paradigm for understanding why people develop different manifestations of allergic diseases,” says author Marc Rothenberg (Cincinnati Children’s Hospital Medical Center, USA).

The research team hypothesized that determining the genetic aetiology of EoE would provide insight into the basic disease aetiology, and could have therapeutic relevance. To test this theory, the team conducted a genome-wide association study that involved screening ~2.5 million genetic variants in thousands of people with and without EoE (736 cases and 9,246 control individuals). This approach enabled them to identify regions of the genome associated

with EoE. With further analysis, the team identified plausible genetic variants and a novel pathway involved in eliciting the tissue-specific allergic response.

One of the identified genetic variants was *CAPN14*, which encodes calpain 14 (a calcium-dependent protease) and is located in an epigenetic hotspot modified by IL-13. The gene was specifically expressed in the oesophagus and was upregulated as a function of disease activity and genetic haplotype and when epithelial cells were exposed to IL-13.

On the basis of these findings, Rothenberg and colleagues propose a model to explain the tissue-specific nature of EoE. This model involves interaction between allergic sensitization and an oesophageal response that is induced by IL-13 and involves *CAPN14*.

Although the molecular mechanisms underlying this model are unknown, they could involve the inflammatory substrates of calpain 14. “We are working full speed

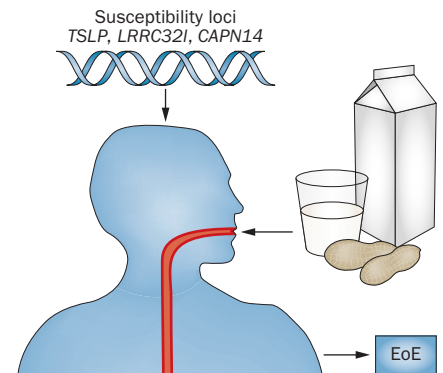


Image produced in consultation with L. C. Kottyan and M. E. Rothenberg.

to understand exactly how calpain 14 contributes to allergic responses, particularly EoE, and how we can modify the identified response for therapeutic intervention,” explains Rothenberg.

*Claire Greenhill*

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