Introduction

Asthma endotypes may be associated with specific epigenetic signatures. The identification of differentially methylated loci associated with serum total IgE levels in adults with asthma may bring further insight into asthma heterogeneity.

Objective

To identify differentially methylated regions associated with serum total IgE levels in adults with asthma.

Methods

DNA methylation was measured in 599 blood samples from 357 adults with asthma participating to the EGEA cohort (241 individuals had 2 samples 10 years apart) using MethylC-Capture Sequencing. After quality control, 2.8 million CpG sites were analysed. A binomial mixed model was fitted for each CpG site, considering the proportion of methylated reads weighted for sequence read coverage as the dependent variable.
variable, IgE levels (log-transformed) as the predictor, and age, sex, active smoking, and proportion of leucocytes as confounders. At loci with CpG sites showing suggestive association with IgE levels at $p<10^{-4}$, we used the Comb-p method to identify differentially methylated regions (DMRs).

**Results**

Overall, 312 CpG sites were associated with IgE levels at $p<10^{-4}$, but none was significant at FDR≤5%. 11 DMRs were detected at Sidak $p<0.01$; one of them at 22q11 included the *IL17RA* gene involved in signalling in airway inflammation, while another one at 13q34 harboured the *TUBGCP3* gene, previously suggested as an epigenetic mark in respiratory allergy.

**Conclusions**

Using high-resolution methylome data, we identified DMRs associated with serum total IgE levels in adults with asthma, including biological relevant genes in the development of novel therapeutic targets or biomarkers for allergic asthma.