Methylation risk scores for childhood aeroallergen sensitization: Results from the LISA birth cohort

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Abstract

Background It has been hypothesized that epigenomic modifications such as genomic methylation changes are an intermediate step linking environmental exposures with allergic disease development. Associations between individual DNA methylation CpG sites and allergic diseases have been reported, but they have not been assessed regarding their joint predictive capability. Methods Data were obtained from 240 children of the German LISA cohort. Blood-based DNA methylation was measured at six and ten years. Aeroallergen sensitization, at least RAST class 1, was measured in blood at six, ten and 15 years. We calculated six methylation risk scores (MRS) for allergy-related phenotypes based on available publications and assessed their performance both cross-sectionally and prospectively. Dose-response associations between aeroallergen sensitization and MRS, their correlation and mapping of common hits were evaluated. Results All six atopy-related MRS were highly correlated ($r>0.86$) and seven CpGs were included in more than one MRS. Cross-sectionally, we observed an 80% increased risk for aeroallergen sensitization at six years with an increased risk score by one standard deviation (best MRS: relative risk = 1.81, 95% confidence interval = [1.43; 2.27]). Significant associations were also seen at ten years and in prospective models, though the effect of the latter was attenuated when only including participants not sensitized at baseline. A clear dose-response relationship with RAST classes of aeroallergen sensitization could be established cross-sectionally, but not prospectively. Conclusion We found good classification and prediction capabilities of calculated allergy-related MRS, particularly cross-sectionally for the allergy prevalence, underlining the relevance of altered gene-regulation in allergic diseases.

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