CerS6 gene methylation in peripheral blood is associated with asthma and the frequent exacerbator phenotype

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Abstract

Background Sphingolipids metabolism regulated by ceramide synthase (CerS) enzyme is closely related to asthma development, but the underlying biological mechanism remains unclear. Since epigenetics plays a critical role in the pathogenesis of asthma, we thus studied the DNA methylation of *CerS1-6*, genes coding CerS in asthma patients. **Methods** We enrolled 26 asthma patients and 6 healthy controls. After collecting demographic and clinical information, peripheral blood was collected to analyze the serum phospholipid profile and DNA methylation assay. Illumina Human Methylation EPIC BeadChip (Illumina, USA) was used to perform DNA methylation profiling. Linear mixed-effect models were applied to estimate the associations between asthma patients and healthy controls. Subgroup analyses by different asthma phenotypes, frequent acute exacerbation, levels of asthma control, overweight, allergic, early onset, and different genders were further conducted. **Results** Among 127 CpG sites mapped on *CerS1-6,* we found that four sites including cg18956199, cg21465008, cg03236449 and cg15455300 located on *Cers6* genes were significantly differentiated in asthma patients. Particularly, the locus cg15455300 had significantly lower methylation levels in asthma patients compared to controls. After controlling for potential covariates, compared to healthy control, the DNA methylation level of cg15455300 decreased 0.0202 (Standard error = 0.0055) robustly. This site further associated with patients with frequent acute exacerbation and poorly controlled asthma. A negative correlation between cg15455300 and ceramide metabolites was further observed. **Conclusion** Changes in CerS6 gene methylation in blood have the potential to serve as a surrogate biomarker for asthma and frequent acute exacerbation phenotypes.

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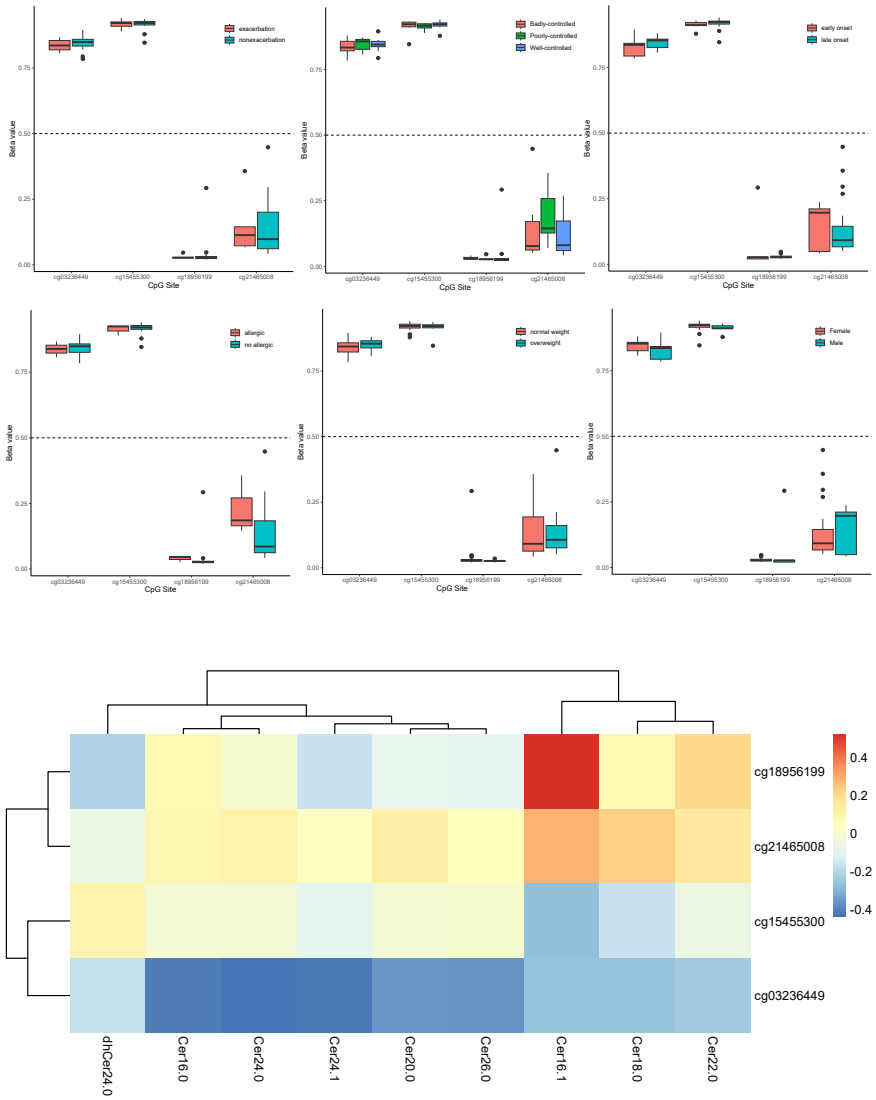

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