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Predicting asthma related phenotypes from genome-wide methylation profile

Xuefeng Wang

Harvard School of Public Health,USA

Abstract

DNA methylation at CpG sites is an important epigenetic modification that may regulate gene expression. There is a growing interest in understanding how the methylation inheritance contributes to the development of complex diseases. It has been shown that methylation modification may influence individual asthma risk and related phenotypes. The primary purpose of this study is to comprehensively assess—by using genome-wide DNA methylation data as markers—the contribution of epigenetic effects on asthma related quantitative traits. Results of variance component analyses on our data indicated that a considerable proportion of phenotypic variation in total serum IgE (an important biomarker for asthma) can be explained by the variation in epigenetic markers. To evaluate the clinical utility of epigenetic markers, we then constructed and compared various prediction models by including top ranked methylation loci from the genome-wide association scan, together with selected sets of known genetic markers from published genome-wide association studies (GWAS). A new prediction model based upon Best Linear Unbiased Prediction (BLUP) was further proposed where all CpG sites (on the Illumina Infinium 27K methylation array) were simultaneously modeled. The overall prediction accuracies of the proposed methods were extensively evaluated via the cross-validation analysis. We observed a significant increase of correlation coefficient between actual and predicted IgE level when methylation markers were included. Taken together, results from this study suggest that DNA methylation has important influence in asthma and it explains much larger variability in IgE level than known genetic variants. Our comprehensive assessment suggests that methylation has great potential in prediction of clinical phenotypes.

WANG@hsph.harvard.edu