Acute wheeze-specific gene module shows correlation with vitamin D and asthma medication

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ABSTRACT

Background: Airway obstruction and wheezing in preschool children with recurrent viral infections are a major clinical problem, and are recognised as a risk factor for the development of chronic asthma. We aimed to analyse whether gene expression profiling provides evidence for pathways that delineate distinct groups of children with wheeze, and in combination with clinical information could contribute to diagnosis and prognosis of disease development.

Methods: We analysed leukocyte transcriptomes from preschool children (6 months–3 years) at acute wheeze (n=107), and at a revisit 2–3 months later, comparing them to age-matched healthy controls (n=66). RNA-sequencing applying GlobinLock was used. The cases were followed clinically until age 7 years. Differential expression tests, weighted correlation network analysis and logistic regression were applied and correlations to 76 clinical traits evaluated.

Findings: Significant enrichment of genes involved in the innate immune responses was observed in children with wheeze. We identified a unique acute wheeze-specific gene-module, which was associated with vitamin D levels ($p<0.005$) in infancy, and asthma medication and FEV_1%/FVC (forced expiratory volume in 1 s/forced vital capacity) ratio several years later, at age 7 years ($p<0.005$). A model that predicts leukotriene receptor antagonist medication at 7 years of age with high accuracy was developed (area under the curve 0.815, 95% CI 0.668–0.962).

Interpretation: Gene expression profiles in blood from preschool wheezers predict asthma symptoms at school age, and therefore serve as biomarkers. The acute wheeze-specific gene module suggests that molecular phenotyping in combination with clinical information already at an early episode of wheeze may help to distinguish children who will outgrow their wheeze from those who will develop chronic asthma.