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Th17/Treg ratio derived using DNA methylation analysis discriminates allergen-induced early from dual asthmatic responses

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Background

Atopic allergic asthmatic individuals experience acute bronchoconstriction (early response) upon allergen exposure. Several hours after the initial exposure, some individuals exhibit a chronic late phase (dual responders, DRs) whereas others do not (early responders, ERs). The purpose of this study is to determine changes in Th17 and regulatory T (Treg) cell numbers and their associated gene expression profiles in whole blood between allergen-induced ERs and DRs.

Methods

14 participants with mild, atopic asthma (8 ERs and 6 DRs) underwent a cat allergen inhalation challenge as part of the AllerGen Clinical Investigator Collaborative. Whole blood was collected immediately prior to challenge (pre) and 2 hours post-challenge. DNA methylation analysis was used to measure the frequency of Th17, Treg, B and T cells (Epiontis, Germany). Whole blood transcriptome profiling was performed using Affymetrix GeneChip® Human Gene 1.0 ST Arrays. Statistical analysis was performed using R.

Results

Sum of the T cell and B cell frequencies obtained using the methylation assays strongly correlated (r = 0.95) with the lymphocyte frequency obtained using a hematolyzer. Allergen inhalation did not significantly ($p>0.05$) change Th17, Treg, B and T cell counts between ERs and DRs. However, the Th17/Treg ratio was significantly ($p=0.03$) different between ERs and DRs post challenge. 199 genes positively correlated with Th17 cells at an FDR of 5%. 463 genes positively correlated with Treg cells at an FDR of 5%. Th17 genes were inversely correlated with Treg genes.

Conclusions

Th17/Treg ratio derived using DNA methylation analysis discriminates allergen-induced early from dual asthmatic responses. The inverse correlation between Th17 genes and Treg genes may be indicative of the inflammatory or suppressive phenotypes of these cells.

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