Reduced T-bet in addition to enhanced STAT6 and GATA3 expressing T cells contribute to human allergen-induced late responses.

Abstract:
T-bet and GATA-3 are transcriptional factors involved in Th1 and Th2 cell differentiation, although their concomitant roles at protein levels in target organs during human allergic disease have not been assessed. We investigated the expression of T-bet and GATA-3 in nasal and cutaneous models of Th2 (grass-pollen allergen) and a cutaneous model of Th1 (PPD) responses in man. Nasal biopsies were obtained at 8 h and skin biopsies at 8 and 48 h after allergen and PPD challenges, respectively, from 10 allergic rhinitics and 6 non-atopic controls. T cells were assessed using immunofluorescence microscopy. There were increases in CD3(+)STAT6(+) cells (P = 0.01 for nose and skin) and CD3(+)GATA3(+) cells (P = 0.03 for skin) in response to allergen compared with diluent in allergics. When compared with non-atopics after allergen challenge the difference between the two groups was also significant for CD3(+)STAT6(+) (P = 0.001 and 0.03) and for CD3(+)GATA3(+) cells (P = 0.04 and 0.001) for nose and skin respectively. Following PPD challenge CD3(+)STAT4(+) cells and CD3(+)T-bet(+) cells increased in both groups compared with diluent (P = 0.02 and 0.03 for both TFs), whereas only CD3(+)T-bet(+) cells were significantly greater in non-atopics compared with allergics.
The ratio of GATA3(+) : T-bet(+) T cells in allergen-induced responses was significantly greater in the allergics (P = 0.008 and 0.01 nose and skin respectively), whereas the ratio of T-bet : GATA3(+) T cells was significantly higher in the non-atopics during PPD-induced responses (P = 0.003). Dysregulation of Th1 transcription may contribute to heightened expression of STAT6 and GATA3 leading to exaggerated Th2-driven manifestations of allergic disease.