Expression of Th1/Th2 specific transcription factors T-bet and GATA-3 in pulmonary sarcoidosis

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PULMONARY SARCOIDOSIS

- a multisystem granulomatous disease accumulation of CD4+ Th1 T cells and macrophages
- sarcoidosis patients with extreme phenotypes differ in the disease course/ development
- limited information about the processes leading to various disease outcomes

an imbalance in the Th1/Th2 immune response may play a role in the disease outcome in sarcoidosis (hypothesis of Th1→Th2 switch)

Patient Characteristics

Patient group (S, n=61) (dg. - Statement on Sarcoidosis, 1999), clinical features + granuloma on biopsy + CD4+ lymphocytic alveolitis)
Control group (C, n=17) (patients without inflammation, normal BAL profile)

Subgroups based on disease phenotypes as assessed by chest X-ray (CXR) stage: CXR stage I (S-I, n=17), CXR stage II (S-II, n=34), CXR stage III (S-III, n=10) ; patients presenting with/without Löfgren´s syndrome (LS, n=11; nonLS, n=50)

ABBREVIATIONS

T-bet: T-box expressed in T-cells
GATA-3: GATA binding protein 3
BAL bronchoalveolar lavage

AIM

Based on the suppossed Th1→Th2 shift in more advanced stages of sarcoidosis, we aimed **to investigate mRNA expression of Th1 and Th2 specific transcription factors T-bet and GATA-3** (key players in the Th1/Th2 paradigm) in specific clinical phenotypes of sarcoidosis.

Fig.1 T–bet mRNA expression in S vs. C

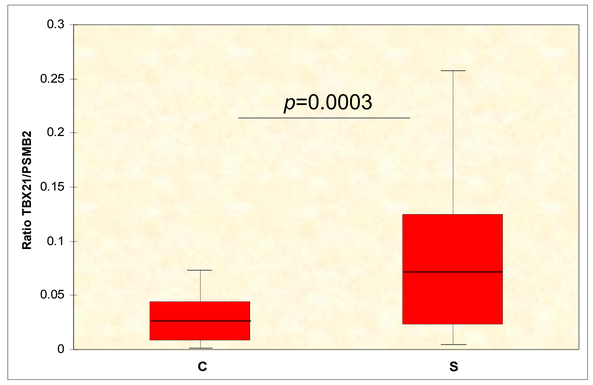
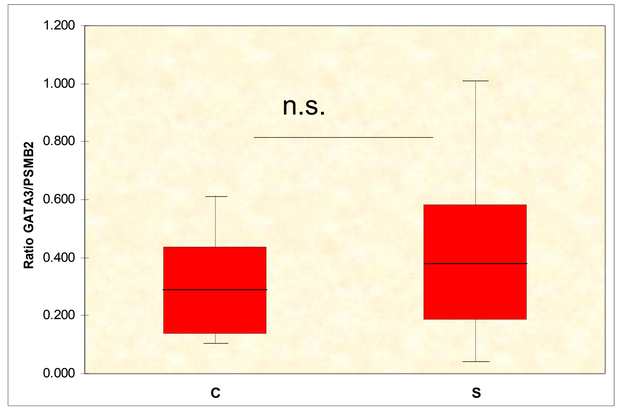


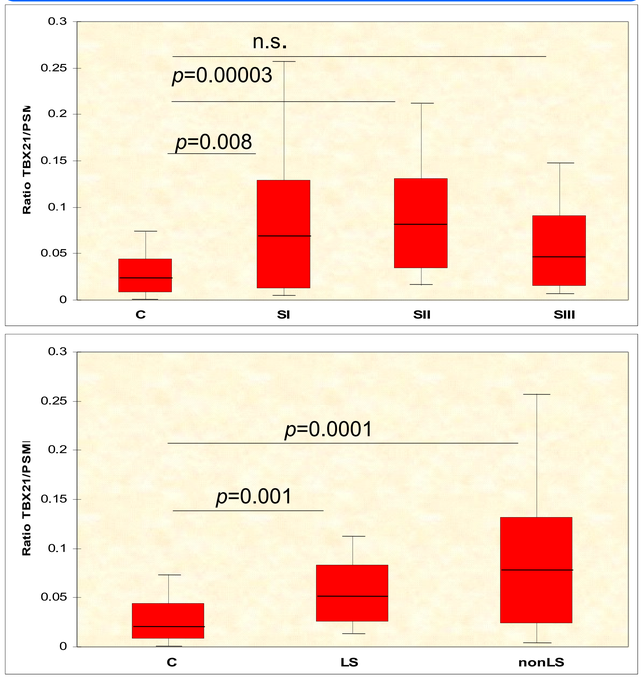
Fig.3 GATA-3 mRNA expression in S vs. C



RESULTS

- When comparing sarcoidosis patients and controls, patient BAL cells expressed higher T-bet mRNA levels (p=0.0003) **(Fig. 1)**.
- Subanalyses of T-bet mRNA expression in particular CXR-stages showed that T-bet was up-regulated in patients with CXR-stage I and II (p<0.008). Out of patient subgroups presenting with/without Löfgren´s syndrome (LS), lower T-bet mRNA expression was observed in patients with LS (p=0.001) than in patients without LS (p=0.0001) **(Fig. 2)**.
- mRNA expression levels of GATA-3 did not differ between sarcoidosis patients and controls (p=0.11) **(Fig. 3)** as well as among any patient subgroup (data not shown).

Fig.2 T–bet mRNA expression in clinical phenotypes



METHODS

Quantitative RT-PCR was used to investigate mRNA expression of T-bet and GATA-3 in unseparated BAL cells, PSMB2 was used as a reference gene.

- relative expression was calculated using second derivative method (RotorGene Software 6.1.71, Corbett Research)
- cDNA from human universal reference RNA (Stratagene) was used as a calibrator
- log-transformed relative expression values were used for statistical calculations by Student's t-test, one-way ANOVA.

Gene	Primers	LNA probe
T-bet	5´-GACTCCCCCAACACAGGAG-3´, 5´-GGGACTGGAGCACAATCATC-3´	#72
GATA-3	5´-CTCATTAAGCCCAAGCGAAG-3´, 5´-TCTGACAGTTCGCACAGGAC-3´	#71
PSMB2	5´-AGAGGGCAGTGGAACTCCTT-3´ 5´-AGGTTGGCAGATTCAGGTG-3´	#50

CONCLUSIONS

- mRNA expression of Th1 transcription factor T-bet was up-regulated in pulmonary sarcoidosis.
- No up-regulation of Th2 specific transcription factor GATA-3 was observed in sarcoidosis as a whole nor in any particular phenotype.
- Our data further support a role for the Th1 subset of T cells in the pathogenesis of pulmonary sarcoidosis.

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