

PULMONARY DENDRITIC CELLS ARE HIGHLY ACTIVATED AND INDUCE CD4+ T-CELL PROLIFERATION AND DIFFERENTIATION IN SARCOIDOSIS

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Background

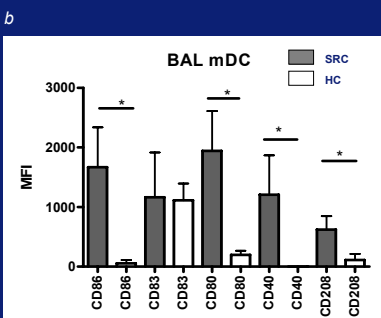
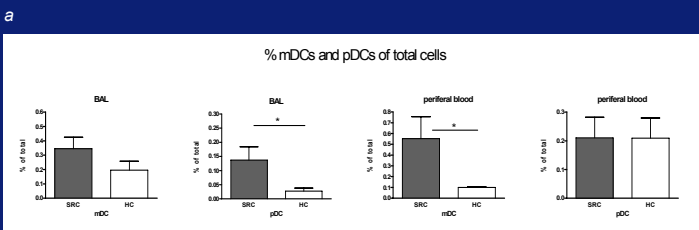
In sarcoidosis, dendritic cells (DCs) are thought to play a pivotal role by presenting an unknown antigen to naïve CD4+ T cells, initiating CD4+ T cell proliferation and Th1 polarization, in susceptible individuals. However, functional and detailed phenotypical information on DC's in the lungs and peripheral blood (PB) of sarcoidosis patients is lacking. In this study we investigate the subsets, phenotype and function of the dendritic cells in sarcoidosis

Method

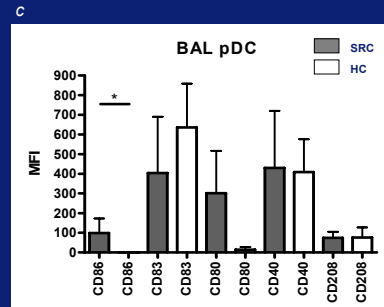
BAL samples were collected from in total 26 sarcoidosis patients and 11 healthy controls. The cells of 16 sarcoidosis and 6 healthy control patients were stained for Lin mix (CD3, CD14, CD16, CD19, CD56), CD11c, HLA-DR, CD123 and the costimulatory markers CD80, CD86, CD83, CD40 and CD208. The samples were measured on a FACS ARIA. From 10 patients and 5 healthy controls the myeloid dendritic cells were sorted using the FACS ARIA and evaluated in a mixed leukocyte reaction with allogenic naïve CD4+ T-cells.

Results

Compared with healthy controls (HC), sarcoidosis patients (SRC) have an increased number of plasmacytoid DCs (pDC) in the BAL and mDCs in the PB.



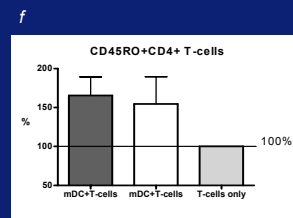
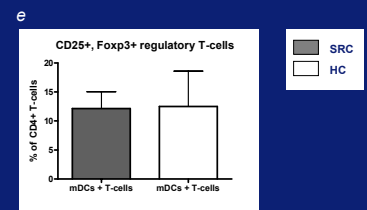
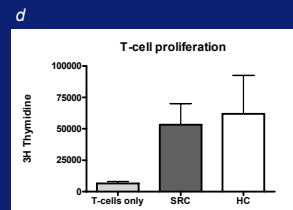
BAL mDCs of patients have a higher surface expression of costimulatory markers CD40, CD80, CD86 and CD208, involved in CD4+ proliferation and differentiation, compared to control mDCs.



pDC's from the BAL only demonstrate a higher expression of CD86.

There is no difference in marker expression between patients en healthy control mDCs and pDCs in the peripheral blood. (data not shown)

Despite the phenotypical differences between dendritic cells of sarcoidosis patients and healthy controls, our data show no significant functional differences between the two groups when naïve allogenic T-cells were stimulated with the sorted bronchoalveolar lavage mDCs



d) Proliferation of CD4+ T-cells after stimulation

e) CD25 and FoxP3 expression on CD4+ T-cells after stimulation

f) Expression of CD45RO (memory cell marker) on CD4+ T-cells after stimulation

Conclusion

In sarcoidosis a distinct, mature population of dendritic cells can be recognized in the pulmonary compartment. These cells are capable of inducing allogenic CD4+ T-cell proliferation and differentiation, however not different from mDC's from healthy controls.