Adaptive immunity (T cells and B cells) in rheumatic diseases

AB0010 LILRB3 EXPRESSION ON T CELLS CORRELATES WITH DISEASE ACTIVITY IN RA

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Background: Leukocyte immunoglobulin-like receptors (LILR) participate in the generation of immunological tolerance (1,2). LILRB3 can be expressed on T cells and is an inhibiting receptor (3).
Objectives: We wanted to study LILR expression on T cells in RA compared to SLE and controls.
Methods: Heparinised human blood from blood donors was obtained from the Institute of Transfusion Medicine, Medical School Hannover (Germany). Blood samples from RA (DAS28 <3.2 n=11; DAS28>3.2 n=8) and SLE patients (n=9) were obtained from Outpatients' Clinic of the Department of Rheumatology and Immunology after informed consent. PBMCs were stained with LILRA2 (Biolegend, APC), LILRB3 (Biolegend, PE), CD3 (Biolegend, APC-Cy 7), CD4 (BD, PerCP-Cy5.5), CD8 (Biolegend, V500), CD25 (Biolegend, PE/Cy5), CD28 (Biolegend, Pacific Blue). Results were compared to isotype controls.
Statistical analyses and figures were made with GraphPad Prism, ANOVA and the Mann-Whitney Test.
Results: The percentage of both CD4+ and CD8+ T cells expressing LILRB3 was significantly higher in both inactive as well as active RA compared to controls or SLE (See Fig. 1) (p=0.0397 ANOVA: RA all vs. SLE vs. controls). Within the group of RA patients, the percentage of LILRB3 expressing T cells was highest in active compared to inactive (DAS28<3.2) RA (p=0.0287). LILRA2 was not expressed on T cells.

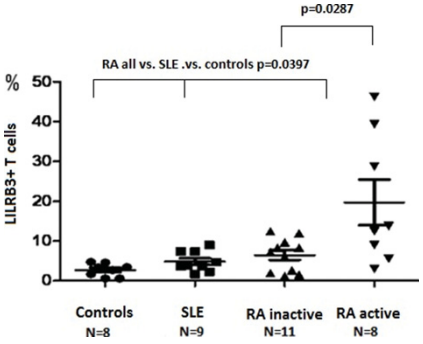

Figure 1

Conclusions: Expression of LILRB3 correlates with disease activity of RA and is decreased after successful treatment with DMARDS or biologicals. Since LILRB3 is an inhibiting receptor the increased expression in active RA may be a counterregulation to reduce disease activity.
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AB0011 KLRG1 AS A MARKER OF CD28 NEGATIVITY IN RHEUMATOID ARTHRITIS, COMPARISON WITH CD57 AND CD45RA

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Background: Our research has shown that patients with RA have higher proportions of peripheral blood CD3+CD8+CD28- Treg cells compared to healthy individuals. CD3+CD8+CD28- Treg cells in patients with RA have lost their ability to suppress lymphocyte proliferation[1]. Thus CD28 negativity may mark senescent T cells. CD57[2] CD45RA[3,4] and killer-cell lectin like receptor G1 (KLRG1)[5] cell surface molecules have been associated with CD8+ T cell activation and senescence. Defining the phenotypic signature of CD8+CD28- Treg cells will help establish their significance in the immunoregulation of RA.
Objectives: To use immunofluorescence and flow cytometry to define the phenotype of CD3+CD8+CD28+/- cells in relation to early RA progression.
Methods: The effector characteristics of peripheral blood CD8 T cells were evaluated by flow cytometry. RA patients with established (n=21) and early disease (n=20) were recruited, and compared to twenty four healthy controls. The mean age of the subjects was 59 (SD=12.5), 25/38 (66%) were female, 27/38 (71%) were anti-CCP positive and 25/38 (66%) rheumatoid factor positive. The mean age for the controls was 43 (SD=11.6), 14/20 (70%) were female.
Results: Confirming our previous work, a significantly higher proportion of CD3+CD8+CD28- cells was observed in RA patients compared to healthy individuals (P=0.03) (Figure 1).
Flow cytometric evaluation of peripheral blood demonstrated a significantly higher expression of CD57, CD45Ra and KLRG1 in CD28- compared to CD28+ T cells.

Table 1. CD57, CD45Ra, KLRG1 and CD28 on CD3+CD8+ T cells

	CD28–	CD28+	P value
CD57+	40	9	<0.0001
CD45Ra+	38	23	0.0026
KLRG1+	36	20	0.0012

A further evaluation of these markers revealed that 69% of the CD8+CD28- cell pool was KLRG1+, in comparison to 66% being CD57+ and 55% KLRG1+CD57+ double positive. This suggests that KLRG1 is a robust and clinically relevant marker of CD28- T cells in RA. Our current research is investigating the significance of KLRG1 and CD8+CD28- cells as prognostic markers in RA.

CD3+CD8+CD28- cells in Controls (n=24) v.s RA patients (n=41) with median.

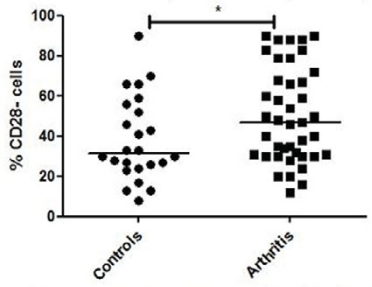

Figure 1: Graph showing the percentage of CD3+CD8+CD28- in RA patients and healthy controls.

Conclusions: CD3+CD8+CD28- cells are enriched in the peripheral blood of RA patients. KLRG1 expression is increased in line with CD57 and CD45Ra in CD8+CD28- cells, and will be used to evaluate the functional significance of these cells in relation to their activation status and potential senescence in the immunoregulation of RA pathogenesis.
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AB0012 IN THE ELDERLY ACPA-NEGATIVE RA IS MORE PREVALENT THAN ACPA-POSITIVE RA WHILE THE COMPOSITION OF THE ACPA-RESPONSE APPEARS IDENTICAL

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Background: Rheumatoid arthritis (RA) consists of two syndromes, one autoantibody-positive and one autoantibody-negative. This multi-cohort study