systems, leading to changes in genes expression which are critical for T or B cell development and activation during the cellular immune response. In previous studies, it has been shown that *RasGRP1* and *RasGRP3* were dysregulated in peripheral blood mononuclear cells (PBMC) and synovium from rheumatoid arthritis (RA) patients leading to the question of *RasGRP1* and *RasGRP3* involvement in RA pathophysiology.

Objectives To measure *RasGRP1* and *RasGRP3* gene expression level in B and T cells from both RA and spondylarthropathy (SpA) patients compared to healthy controls (HC) in order to confirm their dysregulation in RA.

Methods PBMC were isolated from whole venous blood of 24 RA patients (53±15 years old (yo)) with active disease (DAS28=4.98±1.32), 18 patients with active SpA (45±12 yo; BASDAI=55.2±16.1/100) and 19 HC (32±9 yo). After negative cell selection, total RNA from B ant T cells were extracted. Immunofluorescence staining was performed to check the cell purity by flow cytometry. *RasGRP1* and *RasGRP3* expression levels were measured by qRT-PCR and their transcripts were compared by PCR.

Results *RasGRP1* was more expressed in T cells than in B cells (x 3.5; $p<0.0001$) while *RasGRP3* was more expressed in B cells than in T cells (x 8; $p<0.0001$). Moreover, *RasGRP1* was significantly overexpressed in T cells from RA ($p<0.05$) and SpA ($p<0.005$) patients in comparison with those from HC. Surprisingly, *RasGRP1* was also significantly overexpressed in B cells from RA patients ($p<0.05$) in comparison with those from HC. *RasGRP3* expression level was similar in RA or SpA patients and HC whatever the cellular lineage (B and T cells). Moreover, *RasGRP1* expression level in T cells was inversely correlated with the disease activity measured by DAS28 in RA patients ($p<0.05$). Otherwise, two *RasGRP1* variants are expressed in T cells from RA patients compared to HC. Moreover, a minority of RA patients have *RasGRP3* full length transcript in B cells.

Conclusions This study has shown for the first time the overexpression, in human, of *RasGRP1* in T cells and of *RasGRP3* in B cells. Moreover, *RasGRP1* is overexpressed in T and B cells from RA patients and only in T cells from SPA patients. Furthermore, the authors identified differents *RasGRP1* variants in B and T cells from RA patients compared to HC; these variants correspond to deletions of exons. Otherwise, the inverse correlation between *RasGRP1* expression in T cells from RA patients and disease activity score confirms the hypothesis of RasGRP1 anti-inflammatory role. In addition, expression of RasGRP1 in B cells induces apoptosis of these one. Therefore, specific overexpression of *RasGRP1* in B and T cells opens broad perspectives for research and therapy.

8 RASGRP1 AND RASGRP3 EXPRESSION IN LYMPHOCYTES OF RHEUMATOID ARTHRITIS PATIENTS

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Introduction RasGRP is a member of the CDC25 family of Ras guanyl nucleotide exchange factors. RasGRP1 is expressed in T and B cells whereas RasGRP3 is only expressed in B cells. These proteins are involved in T cell receptor and B cell receptor signalling. Indeed, Ras activation stimulates various effector