was added to assess IgA binding to FcRL4+ B cells. Single B cells were sorted from SF of RA patients and their constant region genes probed for identification of their Ig subclass by PCR.

Results: *Ex vivo*, FcRL4$^+$ B cells in SF of RA patients have a higher load of IgA bound to their surface compared to their FcRL4- counterparts. After in vitro removal of surface bound IgA, they can bind heat-aggregated IgA (p=0.0313). We also demonstrate that a significantly higher proportion of FcRL4+ B cells use IgA BCRs (p=0.0061) by flow cytometry and further more by probing constant region genes by PCR an enrichment for Ig genes for coding the IgA1 isotype (p=0.009) was found.

Conclusions: Both their ability to capture IgA immune complexes through binding to FcRL4 and their enrichment in IgA Ig gene expression suggest a potential role for synovial fluid FcRL4$^+$ B cells in the mucosal origin of joint inflammation.

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AB0016 B-CELL SUBSETS DIFFERENCES IN INFLAMMATORY RHEUMATIC DISEASES

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Background: Targeting humoral immunity has been proved effective in several inflammatory rheumatic diseases (IRD). Though clinical trials have shown some efficacy of B-cell depletion in ankylosing spondylitis (AS), results are less convincing. Other studies have revealed an association between mutations and expression of immune regulatory genes suggesting B-cell dysfunction in the development and progression of AS. Yet, there is still lack of data describing B-cell subsets in AS, how these compare to other IRD and an evaluation of B cell compartment homeostasis in the pathophysiology of this disease.

Table 1. Patient and healthy controls demographics, clinical variables and absolute cell counts.

	AS (n=22)	RA (n=20)	SLE (n=18)	HC (n=12)
Patients				
Male, Female; n (%)	11 (50); 11 (50)	9 (45); 11 (55)	5 (27.8); 13 (72.2)	3 (30); 7 (70)
Age; median (IQR)	56 (45.8-65.5)	55 (51-65.5)	44 (37.5-52.5)*	60.5 (32-64.5)
ESR mm/hour	14 (10-29.3)	21 (10.3-37.8)	23 (6-34.5)	11 (8-22.5)
CRP mg/dL	1.1 (0.9-1.7)	0.98 (0.7-3.2)	0.6 (0.5-1.6)	-
HLA B27+: n (%)	11 (68.8)	-	-	-
With csDMARS, n (%)	6 (30)	18 (90)	15 (83.3)	0
Ig seric levels, mg/dl; median (IQR)				
IgG	1165 (881.3-1247.5)	1021 (830.3-1265)	1140 (1003-1325	1033.5 (823.3-123
IgA	230 (158.8-340)	250.5 (164.3-315.3)	261 (205-323)	236.5 (150.3-339.8
IgM	95.3 (65.6-119.5)	112 (67.7-164.8)	103 (60.6-131.5	122 (71.5-158.3)
Absolute cell counts/µl blood; median (IQR)				
Lymphocytes	1685 (1217-2007.5)	1555 (1097.5-2085)	1250 (625-1892.5)	2170 (1830-2377)*
Total B-cells (CD20$^+$)	186.3 (110.9-238.6)	96.2 (50.3-180.6)***	65.8 (20.9-116.1)***	182.1 (100.9-269.3
Immature Transitional B-cells (CD5$^+$CD27$^-$IgD$^+$), median (IQR)				
CD24^{++}CD38^{++}(T1)	2.8 (1.8-3.9)	0.6 (0.1-2.7)**	1.5 (0.2-2.8)**	4.3 (2.3-6.5)
CD24^{++}CD38^{++}(T2)	8.3 (5.1-14.9)	2.6 (0.2-8.0)**	3.0 (1.0-8.0)**	13.7 (5.7-18.8)
CD24$^+$CD38$^+$(T3)	9.0 (5.5-17.7)	2.2 (0.3-4.6)**	1.9 (0.2-3.7)**	7.7 (4.1-12.3)
Mature B-Cells, median (IQR)				
CD27$^-$IgD$^+$ (*naïve*)	73.2 (49.7-121.7)	40.1(19.2-76.9)**	27.2(11.9-57.1) †	78.6 (48.4-163.4)
CD27$^+$IgD$^+$(mem. *MZ-like*)	25.9 (13.6-39.9)	13.0 (3.5-27.2)**	2.6 (1.8-9.6) †	18.9 (11.2-27.1)
CD27$^+$IgD$^-$(*switch mem.*)	18.8 (12.2-37.9)	13.5 (3.9-37.6)	4.9 (2.2-17.2)***	29.3 (14.51-37.9)
CD27$^-$IgD$^-$(*double neg.*)	2.4 (1.8-5.2)	3.1 (2.0-6.4)	2.9 (1.0-5.0)	5.2 (2.6-8.1)

Mann-Whitney and the Fisher´s exact test were used for comparison between AS and other groups
* p<0.05; **p<0.02; ***p<0.01; †p<0.0001

Objectives: To assess and compare the immature, naive and antigen differentiated subsets of peripheral B-cell compartment in AS with those in healthy controls (HC) and other IRD

Methods: Patients (pts) with AS, RA and SLE according to respective classification criteria were included in this study. Pts under biologic DMARDS were not included. Sociodemographic and clinical variables were recorded. Blood samples were collected for quantification of inflammatory markers (ESR and CRP), immunoglobulin serum levels and assessment of B-cell immature transitional stages and mature subsets by flow cytometry (figure). Mann-Whitney and Fisher's exact test were used for comparison of AS with other groups

Results: Overall, 60 pts and 12 HC were included (Table). All patient groups presented similar and rather low levels of inflammation, as measured by CRP, ESR and immunoglobulins, in addition to a decreased lymphocyte count by comparison with HC. There were no differences in the B-cell counts between AS pts and HC, with both groups having higher B-cell counts than RA and SLE pts. Regarding B-cell subsets, the immature transitional compartment of AS pts was found in normal range, but not in the RA and SLE groups. In fact, the latter presented a significant decrease in all transitional cell maturity stages (T1-T3). The next step in B-cell differentiation is mature naïve cells, also found in normal levels in AS and decreased in RA and in particular in SLE. AS pts presented slightly higher counts of CD27+IgD+ MZ-like and class able to switch memory cells with reference to HC and these cell numbers were found to be low in RA and even lower in SLE pts. Switched memory CD27+IgD- B-cells were reduced in all patient groups, however, only SLE pts presented highly decreased cell levels.

Conclusions: We found that while a severe dysfunction is present in the homeostasis of the B-cell compartment in RA and in particular SLE pts, which are lymphopenic in both immature and mature B-cell compartments, it appears that AS pts are not affected in the same way. At this stage, functional studies appear to be necessary in order to identify differences in key mechanisms of B cell development and differentiation that may play a role in the aetiology and progression of these inflammatory rheumatic diseases. Our first results, however, establish that pathophysiological mechanisms involving B-cells clearly differentiate AS from RA and SLE

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AB0017 THERAPEUTIC EFFECT OF UMBILICAL CORD-DERIVED MESENCHYMAL STEM CELLS TRANSPLANTATION IN A MOUSE MODEL OF PRIMARY BILIARY CIRRHOSIS

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Background: Primary biliary cirrhosis (PBC) is a cholestatic liver disease characterized by slowly progressive non-suppurative cholangitis with immune mediated destruction of intrahepatic bile ducts. Previous studies have shown beneficial effects of mesenchymal stem cells (MSCs) transplantation in many autoimmune diseases. However, few studies have focused on the effects of MSCs on PBC.

Objectives: In our study, we investigated the therapeutic effect of umbilical cord-derived mesenchymal stem cells (UC-MSCs) transplantation in a well-defined mouse model of PBC and explored the potential mechanism.

Methods: After 2OA-BSA-induced autoimmune cholangitis was created in C57BL/6 mice, cultured human UC-MSCs or a vehicle control was administered. Liver injury severity was assessed by clinical and histologic analysis. The immunity suppression effects and mechanism of UC-MSCs were tested.

Results: UC-MSCs administration alleviated bile duct damage and intrahepatic inflammatory cell infiltration in C57BL/6 mice that had undergone 2OA-BSA immunization. Serum levels of ALT and ALP were significantly decreased. Also, UC-MSCs reduced the production of anti-mitochondrial autoantibodies (AMA) in PBC mice. UC-MSCs downregulated inflammatory cytokine, such as IFN-γ, TNF-α, IL-12 and IL-17A production both in peripheral blood and local liver. Notably, Infusion of UC-MSCs resulted in an increase in regulatory T cells (Tregs) in peripheral blood but a decrease of this kind of cells in liver tissues. Furthermore, UC-MSCs significantly suppressed Th1- and Th17-cell responses and these alternations could be detected in spleen, peripheral blood and liver in PBC mice.

Conclusions: In summary, the current study shows that UC-MSCs based therapy has profound inhibitory effects on inflammatory responses and immunoregulatory effects both in local and systemic abnormalities in PBC. These findings also provide further evidence regarding the role of MSCs in the clinical trials of PBC.

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