different anti-inflammatory treatment, stronger in RA than OA patients, with resulting poor control of inflammation in OA.

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P065

INSULIN-LIKE GROWTH FACTOR 1 RECEPTOR REGULATES THE PHENOTYPE AND FUNCTION OF CD21+ B CELLS

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Introduction Ligand to the inducible T cell costimulator (ICOSL) on B cells is essential for the ICOS-dependent follicular recruitment of activated T cells. In patients with Rheumatoid arthritis (RA) the IGF1-IGF1R axis is altered. Inhibition of IGF1R alleviated arthritis by reducing IL-6-dependent formation of Th17 cells. Here we study the role of IGF1R on CD21 +cells in experimental arthritis.

Methods Female Balb/c mice were immunised with methylated BSA or with CII. Consequences of the IGF-1R inhibition for arthritis were studied in mBSA and CII-immunised mice treated with NT157 compound promoting degradation of insulin receptor substrates (mBSA) or using shRNA producing construct (mBSA +CII). At termination three sub-populations of CD21 +cells were analysed: follicular dendritic cells (FDc, CD21 +CD19-CXCR5-); marginal zone B cells (MZBc, CD21 +CD19+CXCR5-); follicular B cells (FBc, CD21 +CD19+CXCR5+). Supernatants of LPS-stimulated splenocytes and serum were analysed for production of antigen specific and autoantibodies.

Results In spleen of mBSA-immunised mice, ICOSL expression on CD21 +cells correlated to IGF1R ($r=0.70$). Inhibition of IGF1R induced a 20% reduction in ICOSL expression in all CD21 +subsets followed by an increase in MZBc ($p=0.003$), while FDc and FBc were unchanged. ICOSL +MZBc were mostly IgMhi, while ICOSL +FBc were mostly IgDhi. Inhibition of IGF1R had no effect on the expression of ICOS +on CD4 T cells and the subset of CXCR5 +follicular T cells. Reduction of the ICOSL +CD21 +B cells, reduced production of mBSA-specific IgM and increased production of autoreactive RF-IgM levels.

Conclusions The study shows that IGF1R controls expression of ICOSL on CD21 +cells. ICOSL on MZBc is required to balance between antigen-specific response and autoantibody production.

Disclosure of interest None declared

P066

ABSTRACT WITHDRAWN

P067

IL-17 RESULTING FROM CELL INTERACTIONS DURING CHRONIC INFLAMMATION: COMPARISON BETWEEN JOINT-DERIVED- AND SKIN-DERIVED-MESENCHYMAL CELLS

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Introduction IL-17, mainly produced by Th17 cells, is a major pro-inflammatory cytokine involved in several chronic inflammatory diseases. Furthermore, during chronic inflammation, immune cells, notably Th17 cells, migrate to the inflammatory site, synovium or skin for example, and interact with the local mesenchymal cells (synoviocytes or skin fibroblasts).

Objectives The aim is to study and compare the effect of cellular interactions between immune cells and mesenchymal cells (MC) from different origins on pro-inflammatory cytokine production, with a focus on IL-17, and to identify the involved mechanisms.

Methods A co-culture system with MC (synoviocytes or skin fibroblasts) and PBMC was developed. MC were cultured overnight and PBMC were seeded at a 5:1 ratio for 48 hour, in the presence or not of TCR activation with PHA. Transwell system was used to study cell-cell contact. Monocytes were removed to study their involvement. An antibody against podoplanin was pre-incubated with PBMC before co-culture. Supernatants were collected at 48 hour and IL-6, IL-1 β and IL-17 production measured by ELISA. Extracellular (CD3, CD4) and intracellular (IL-17) staining of PBMC was analysed by flow cytometry.

Results In control conditions, IL-6 and IL-1 β production was increased more than 20 fold and 10 fold respectively, in PBMC-MC co-culture compared to PBMC alone ($p\leq 0.05$). No additional effect was observed with PBMC activation. Flow cytometry showed no significant difference in the percentage of Th17 cells in activated-PBMC alone or co-cultured with MC ($p=0.4$). Conversely, IL-17 production was highly increased at least 10 fold only in co-cultures with activated-PBMC ($p\leq 0.02$). Transwell experiments confirm that cell-cell contact was critical for IL-17 secretion. The removal of monocytes highly decreased the IL-1 β production by 80%–90% ($p\leq 0.05$) with both MC, while the IL-17 secretion was decreased with skin fibroblasts by 60% but not with synoviocytes. The inhibition of podoplanin, interaction molecule involved in the modulation of IL-8 secretion during synoviocyte-platelet interactions, was tested. The addition of an anti-podoplanin antibody decreased significantly IL-17 secretion by 60%, similarly with skin fibroblasts and synoviocytes.

Conclusions Cellular interactions between mesenchymal cells and immune cells play a major role in the pro-inflammatory cytokine production, leading to a heightened IL-17 secretion. The podoplanin molecule seems play a crucial role in this mechanism. Nevertheless, the inhibition of IL-17 remains only