is limited understanding on the mode of action of glycans in RA. We hypothesise that the glycans on ACPA interact with glycan binding receptors and thus modulate immune responses in RA. Therefore, our aim is to elucidate the glycan effect of ACPA and other glycans on immune cells of RA patients to increase our understanding of RA pathogenesis.

Methods A whole blood flow assay was used to study glycan interactions with leukocytes. Leukocytes were isolated from blood and cells were incubated for 2 hours at 4°C with 15 µg/ml highly glycosylated ACPA and immunomodulatory glycoconjugates, such as sialic acid, Lewis-x, Lewis-y, mannose and as a negative control GlcNAc. Glycan binding and identification of immune cell subsets was assessed with flow cytometry using a whole blood flow antibody panel.

Results This study examined the glycan-binding capacity of leukocytes in healthy donors via the whole blood flow assay. B cells appear to be superior in their interaction capacity with a variety of glycans, including the Fab glycan on APCA. This is an important finding because B cells play a key role in the pathogenesis of RA, through their antigen presenting capacity as well as their production of ACPA. In future studies RA patients material will be used to assess the glycan binding capacity to immune cell and to elucidate their role in the pathogenesis of RA.

Conclusions This study examined the glycan-binding capacity of leukocytes in healthy donors via the whole blood flow assay. B cells appear to be superior in their interaction capacity with a variety of glycans, including the Fab glycan on APCA. This is an important finding because B cells play a key role in the pathogenesis of RA, through their antigen presenting capacity as well as their production of ACPA. In future studies RA patients material will be used to assess the glycan binding capacity to immune cell and to elucidate their role in the pathogenesis of RA.

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Disclosure of interest None declared

P003 IGF1R SIGNALLING IS ESSENTIAL FOR NEUROLOGICAL SYMPTOMS IN RA

^{1,2}KM Andersson, ¹L Juzokaite, ¹C Wasen*, ²A Stokowska, ¹L Leifsdottir, ¹MC Erlandsson, ²M Pekna, ¹M Pekny, ³K Olmarker, ⁴M Kalm, ¹MI Bokarewa. ¹Dept Rheumatology and Inflammation Research, Inst Medicine; ²Department of Clinical Neuroscience and Rehabilitation, Institute of Neuroscience and Physiology; ³Department of Medical Chemistry and Cell Biology, Institute of Biomedicine; ⁴Department of Pharmacology, Institute of Neuroscience and Physiology, Göteborg, Sweden

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Introduction In addition to inflammation of the joints, rheumatoid arthritis (RA) has a neurological part consisting of pain, fatigue, depression and cognitive deterioration. These symptoms are critical for the patients' ability to cope with daily life, but are not alleviated completely with modern anti-rheumatic drugs. Sufficient IGF1R signalling is important for neurogenesis in the hippocampus. Its misbalance correlates with depression and anxiety.

Objectives The aim of this study was to evaluate the pathological changes in the brain during experimental RA and investigate their connexion to IGF1R.

Methods Characteristics of pain, depression and anxiety were collected among 214 RA patients and analysed in relation to IGF1R expression in WBC. Experimental RA was induced by immunisation with collagen II. Inhibition of IGF1R was achieved by injection of shRNA-producing lentiviral construct. The behavioural pattern of each mouse was recorded by filming. The hippocampus was analysed morphometrically, and gene and protein expression were analysed by qPCR and immunohistochemistry, respectively.

Results The RA patients' perception of depression and anxiety was associated with high IGF1R expression in WBC. This group of patients was also less physically active. In experimental RA, an enrichment of IBA1 +microglia and high expression of CD68 and IL-1b was found in the hippocampus. This was followed by an increased density of IGF1R+cells in cornu ammoni, and a decreased neurogenesis by limited expression DCX in the subgranular layer of the dentate gyrus. This results in a significant reduction of the hippocampus area. These changes in the brain were associated with immobility in RA mice. Treatment with shRNA targeting IGF1R improved arthritis, but led to increased immobility.

Conclusions RA induces remote inflammation in the hippocampus reducing neurogenesis and physical activity. The neurological symptoms in patients and in experimental RA are connected to IGF1R expression and signalling, and further expands our knowledge of neurological processes in RA.

Disclosure of interest None declared

P004 ABSTRACT WITHDRAWN

P005 INFLUENCE OF MACROPHAGE POLARISATION ON EXPRESSION OF PEPTIDYLARGININE DEIMINASES 2 AND 4 THAT CATALYSE CITRULLINATION OF THE PROTEINS TARGETED BY ANTI-CITRULLINATED PROTEIN/PEPTIDE AUTOANTIBODIES (ACPA)

M-C Méchin, G Serre, C Clavel*. UDEAR UMR 1056 INSERM – UNIVERSITÉ DE TOULOUSE, TOULOUSE Cedex 9, France

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Introduction Autoantibodies to citrullinated proteins (ACPA) are specifically associated to rheumatoid arthritis (RA) and probably involved in its pathophysiology. ACPA are produced in the inflamed synovial tissue (ST). We demonstrated that peptidylarginine deiminases (PAD) 2 and 4 are present in the tissue and probably responsible for fibrin citrullination, and consequently for genesis of the epitopes targeted by ACPA. PAD2 and 4 are expressed in the intima and the subintimal inflammatory infiltrates, essentially by CD68 +mononuclear cells.¹ We suspected macrophages (MΦ) of the ST to be responsible for synthesis and release of PADs in the interstitium, inducing citrullination of the local fibrin deposits. We generated *in vitro* various subsets of MΦ in the presence of IFN-γ, IL-4, IL-10 or M-CSF, and observed a major influence of the phenotype of polarised MΦ on cytokine response to ACPA-containing immune complexes.²

Objectives The aim of the current study was to evaluate expression of PAD2 and 4 by various subsets of polarised MΦ.