healthy control subjects and DNA microarrays were performed. Flow cytometry and real time PCR were used to verify the expression of de-regulated genes in RA pDCs. Finally, *in vitro* cultures of pDCs activated with CpG A in the presence or absence of recombinant IL-6 (rIL-6) were performed to assess the functional importance of these gene signatures.

Results pDCs from RA patients (n=5) exhibited a differential gene signature (6741 deregulated genes) compared to pDCs from healthy controls (n=5). Notably, IL-6 receptor (IL-6R) gene, exhibited increased expression levels in pDCs isolated from RA patients compared to healthy pDCs and the surface expression levels of IL-6 receptor were verified in a subsequent cohort of patients responding to therapy (n=9) versus active patients or healthy donors. Moreover, assessment of IL-6 signalling pathway in RA patients versus healthy donors revealed a significant increase of pSTAT1 expression levels in RA patients (n=9) compared with healthy donors (n=6) (MFI±SEM, 7.98 ±0.8 versus 12.65±1.18, p=0.0076). Importantly, IL-6-treated pDCs exhibited a vast decrease in TNF-α production (p=0.0002) whereas no differences were found in the production of IFN-α and in their antigen presenting capacity between CpG-treated pDCs in the presence or absence of rIL-6. Moreover, confocal experiments in progress will assess the expression levels of TNF-α in pDCs isolated from RA patients in remission versus active or healthy donors. The functional importance of the previous findings will be addressed in coculture experiments of IL-6 stimulated pDCs with neutrophils isolated from healthy donors and monitor the neutrophil extracellular trap formation.

Conclusions We found that pDCs from RA patients in remission display increased IL-6R expression levels and an activated IL-6 signalling pathway. Activation of IL-6 signalling on pDCs *in vitro* significantly decreases the production of TNF-α whereas it does not alter IFN-α production and their antigen presenting capacity. This novel finding that may drive pDCs towards a previously described tolerogenic phenotype, need to be further addressed.

Disclosure of interest None declared

P010 ABSTRACT WITHDRAWN

P011 EXPANDED T-CELL CLONES ARE PRESENT IN THE SYNOVIUM BEFORE THE ONSET OF CLINICAL RHEUMATOID ARTHRITIS

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10.1136/annrheumdis-2018-EWRR2018.36

Introduction T-cells are thought to be key players in the initiation and progression of rheumatoid arthritis (RA). Earlier we showed that already at the seropositive *at-risk* stage uninflamed synovial tissue contains T-cell infiltrates.[1] In another study we showed that inflamed synovium harbours expanded T-cell clones.[2]

Objectives Following up on these observations, we longitudinally investigated whether the expanded T-cell clones found in the inflamed synovial tissue at onset of RA are already present in the *at-risk* stage.

Methods Next-Generation Sequencing of the TCRβ repertoire was performed on 20 randomly selected individuals with elevated IgM-RF and/or ACPA levels. Ten individuals did not develop RA during at least 3 years of follow-up, and 10 individuals did. Peripheral blood and synovial tissue samples were analysed during the *at-risk* phase and, for individuals that developed RA, again after RA onset. T-cell clones were identified by their unique TCRβ sequence.[3] For each sample 3,570 TCRβ sequences were analysed.

Results During the *at-risk* phase the TCRβ repertoire in the synovium is characterised by expanded clones. This is observed both in *at-risk* individuals that did and did not develop RA. Interestingly, a higher impact of expanded clones inversely correlated with a longer disease-free follow-up time (p=0.02). During progression to RA, the *at-risk* TCRβ repertoire is largely maintained in the tissue. Further characterisation of the synovial CDR3 sequences showed no significant differences between clones that were maintained in the tissue during progression to clinical disease and clones that were uniquely present in the *at-risk* phase or at RA onset.

Conclusions Expanded T-cell clones are present in the synovial tissue in the *at-risk* phase regardless of future development of RA, and are maintained after onset of clinical disease. The resemblance in TCRβ repertoires indicates that the process leading to disease – at least at the T-cell level – constitutes a smooth development. Elucidating the role of these synovial T cells (resident memory, regulatory or autoreactive) might help understanding the earliest pathogenic events in RA.

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Acknowledgements MED, NdV, DMG and PPT received support from BTCURE, a research project from the Innovative Medicines Initiative Joint Undertaking (grant no 115142–2), NdV from the Dutch Arthritis Foundation, and from ZonMw, the Netherlands Organisation for Health Research and Development, in the program 2Treat (Grant 436001001).

Disclosure of interest None declared

P012 PEPTIDYL ARGININE DEIMINASE IMMUNISATIONINDUCES ANTI-CITRULLINATED PROTEIN ANTIBODIES IN HLA-DRB1*04:01 TRANSGENIC MICE

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10.1136/annrheumdis-2018-EWRR2018.37

Introduction Autoantibodies to citrullinated proteins (ACPAs) are highly associated with rheumatoid arthritis (RA). ACPAs are produced in the absence of T cell responses to citrullinated proteins.

Objectives Peptidyl arginine deiminase 4 (PAD4), which binds numerous different proteins and citrullinates them, is the target of autoantibodies in early RA. This suggests a model to explain the production of ACPAs in the absence of T cells to citrullinated proteins. ACPAs could arise because, at first, PADs are recognised by T cells, which, in turn help the production of autoantibodies to proteins being citrullinated by