Introduction Rheumatoid arthritis (RA) and psoriatic arthritis (PsA) are both rheumatic autoimmune diseases, which share a number of similarities but also display differences. For example, the anti-IL17A biologic secukinumab turned out to be more effective in PsA than in RA. The anti-TNF biologic adalimumab on the other hand is equally indicated for both diseases. Synovial fibroblasts (SF) are one of the key effector cell types in the pathophysiology of RA and PsA.

Objectives We therefore investigated whether the effect of the two cytokines IL-17A and TNF- α as well as the effect of their corresponding biologics differs between RASF and PsASF, thus contributing to the difference seen in the therapeutic response. The effect of the IL-17A homolog IL-17F was also analyzed.

Methods SF were isolated from patients with PsA or RA, each undergoing surgery. SF from RA and PsA patients were stimulated with recombinant IL-17A, IL-17F and TNF- α alone or with respective combinations. Dose-response curve analysis was performed with IL-17A. The biologics secukinumab and adalimumab were used to block the effects on the SF. As a measure of the proinflammatory response, secretion of the cytokine IL-6 was quantified using an immunoassay.

Results RASF as well as PsASF responded to IL-17A (IL-17A: 13.7-fold vs 6.9-fold; $n=3$), while IL-17F alone caused no induction of IL-6 secretion in either SF type. However, when used in combination with TNF- α , both IL-17 isoforms, IL-17A and IL-17F, increased IL-6 secretion due to a strong synergistic effect with TNF- α . Surprisingly, these effects were notably stronger for RASF than for PsASF (IL-17A: 544-fold vs 127-fold, IL-17F: 54-fold vs 27-fold; $n=3$). However, adalimumab and secukinumab were similarly effective in abolishing the synergistic effect of IL-17A and TNF- α in RASF as well as PsASF.

Conclusions SF appear not to contribute to the differences in the therapeutic effectiveness of the anti-IL17A biologic secukinumab as the response to IL-17A alone and IL-17A together with TNF- α is not stronger for PsASF than for RASF. Furthermore, secukinumab was similarly effective for both SF types. The data also suggest that in a proinflammatory milieu with increased TNF levels IL-17A as well as IL-17F play a role in the SF-mediated pathophysiology of PsA and, therefore, approaches targeting TNF are effective in both diseases.

Acknowledgements Supported by an unrestricted educational grant from Celgene GmbH.

Disclosure of Interest K. Frommer Grant/research support from: unrestricted educational grant from Celgene GmbH, S. Rehart: None declared, U. Müller-Ladner: None declared, E. Neumann: None declared.

P092/O15 SYNOVIAL DERIVED TH17-LYMPHOCYTES FROM PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS INDUCE CARTILAGE DEGRADATION BY SYNOVIAL FIBROBLASTS MEDIATED BY MMP9 IN AN EXPERIMENTAL ANIMAL MODEL

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10.1136/annrheumdis-2018-EWRR2019.81

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Introduction The synovial fluid of Juvenile idiopathic Arthritis (JIA) is rich of Th17 and of Th-17-derived CD4+ CD161+

cells, also called non-classic-Th1. How such subpopulations drive the JIA joint damage is still a subject of great interest especially in light of the possible use of biological drugs able to selectively inhibit the activity of specific cytokines.

Objectives To clarify the role of Th17 and non-classical Th1 lymphocytes in the pathogenesis of joint cartilage destruction by synovial fibroblasts (SFbs).

Methods The role of different subsets of CD4+T cells was observed in the activation of SFbs in terms of cartilage degradation by normal and JIA SFbs and induction of proteases both *in vitro* and *in vivo*, using a SCID Mouse model through the 'inverse wrap' implantation technique.

Results JIA SFbs produce large amounts of MMP9 and efficiently degrade fragments of human cartilage wrapped in a collagen matrix containing the fibroblasts themselves and grafted under-skin on SCID mice (the 'inverse wrap model'). Similar effects were observed with SFbs of healthy subjects incubated with conditioned media of Th17 and of non-classic Th1. We shown that Th17 induce MMP9 in SFbs, while non-classic Th1 act mainly by inducing urokinase-plasminogen-activator over-activity.

Conclusions IL-17 triggers the pathogenic chain leading to joint damage in patients with JIA.

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Disclosure of Interest None declared.

P093/O16 IL-36 SIGNALING IN KERATINOCYTES IS MANDATORY IN IMIQUIMOD-INDUCED PSORIASIS IN MICE

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10.1136/annrheumdis-2018-EWRR2019.82

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Introduction A large body of evidence indicates that IL-36R signaling plays an important role in the pathogenesis of psoriasis. For instance, IL-36 receptor (IL-36R)-deficient mice showed impaired development of imiquimod (IMQ)-induced psoriasis, but the cells in which IL-36R signaling is involved have not been identified.

Objectives To assess the role of IL-36R signaling in keratinocytes in the development of IMQ-induced psoriasis.

Methods We constructed an IL-36R^{fl/fl} mouse line in which exons 1 and 2 from the *Il36r* gene are flanked by loxP sites. Crossing these mice with K5-Cre transgenic mice induced a progeny with a specific deletion of *Il36r* in keratinocytes (IL-36R^{ΔK}). The selectivity of *Il36r* gene targeting in keratinocytes was confirmed by RT-qPCR and *ex vivo* cell stimulation by

recombinant IL-36 using isolated keratinocytes and bone marrow differentiated dendritic cells. We then assessed the sensitivity of IL-36^{AK} mice to IMQ-induced psoriasis, and compared it to mice presenting a complete IL-36R deficiency (IL-36R^{-/-}) and to their respective littermate controls (IL-36^{+/+} and IL-36R^{fl/fl}). The severity of skin inflammation was assessed by ear thickness measured with a caliper. H and E staining was performed on treated and control ears. Total RNA was extracted from ears and mRNA levels of various cytokines were assessed by RT-qPCR.

Results IL-36R^{-/-} mice were strongly resistant to the induction of IMQ-induced psoriasis as assessed by ear thickness. IL-36^{AK} mice showed a similar macroscopic protection as IL-36R^{-/-} mice, demonstrating that IL-36 signaling in keratinocytes is critical in this model of psoriasis. Several pro-inflammatory genes upregulated by IMQ in IL-36R^{+/+} and IL-36R^{fl/fl} mice were not stimulated in neither IL-36R^{-/-} nor in IL-36^{AK} mice. These genes included notably IL-17A or IL-22, both known to be crucial in psoriasis. Histological findings in IMQ-induced psoriasis include keratinocyte altered differentiation and hyperproliferation as well as inflammatory cell infiltration. Surprisingly and in contrast to IL-36R^{-/-} mice, epidermis thickness was not reduced in IL-36^{AK} compared to IL-36R^{fl/fl} control mice. This finding suggests that IL-36 signaling in keratinocytes does not induce keratinocyte hyper-proliferation but rather controls the development of downstream inflammatory responses in IMQ-treated ears.

Conclusions IL-36R signaling in keratinocytes is mandatory for the development of IMQ-induced psoriasis in mice. FACS studies are ongoing to characterize the inflammatory cell infiltrates in the different mouse lines.

Disclosure of Interest None declared.

P094

EFFECTIVENESS AND SECURITY OF SECUKINUMAB IN PATIENTS WITH PSORIASIS ARTHRITIS IN REAL CLINICAL PRACTICE

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10.1136/annrheumdis-2018-EWRR2019.83

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Introduction Recently new therapeutic targets have been approved for the treatment of psoriatic arthritis (PSA). We have limited experience in real clinical practice.

Objectives To assess efficacy, safety and tolerability of secukinumab in patients with active PsA.

Methods Descriptive, retrospective observational study on the efficacy and safety of secukinumab in patients who met CASPAR classification criteria for PsA in follow-up in the Virgen de Valme hospital area. We evaluate, measures of disease activity by DAPSA in peripheral forms and ASDAS in axial forms. **Statistical analysis** The quantitative variables are expressed with means and standard deviations or medians and quartiles if the distributions are asymmetric, and the qualitative variables with percentages.

Results 12 patients were reviewed. 58.3% were male. The average age of these patients is 47.67 years. The mean time of evolution in years of the disease was 8.33. 75% of the sample was not a smoker, and 83.3% of patients didn't consume

alcohol excessively. 25% were hypertensive. 8.3% had an associated dyslipidemia, and 16.7% had a symptomatic hyperuricemia.

Oligoarthritis form was the most frequent patterns of presentation with 46%, followed by polyarthritis with 27%. All patients had previously failed at least one DMARD, the most frequent being Methotrexate (41.7%). Up to 75% of the patients were naïve to biological therapy. In patients refractory to biological therapy, the most commonly used drug in first choice was etanercept.

In peripheral presentation 80% of the patients had a moderate DAPSA at the beginning of the treatment and of these 62% passed to a low activity, while 38% they remained with moderate activity.

In patients with high activity, up to 70% went to a low activity DAPSA, and in 30% it decreased to moderate activity.

We have survival with the drug that has been 12.67 months with a DS of 7.07 months.

Treatment has been suspended in 3 patients, in one of them due to severe skin and joint breakout, in another due to nausea and headaches, and the last due to ineffectiveness.

Finally, regarding the safety data we have not had any severe adverse effects. 8.3% had mild adverse effects, the most frequent being infectious symptoms of the upper respiratory tract.

8.3% had a primary failure (no response at any time) compared to 25% that has presented a secondary failure after a good initial response to treatment.

Conclusions Secukinumab provided sustained improvements in signs and symptoms in patients of active and was well tolerated, with a safety profile consistent with that reported previously.

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Disclosure of Interest None declared.

P095

INFLAMMATORY BOWEL DISEASE, DURING ANTI IL 17 TREATMENT

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10.1136/annrheumdis-2018-EWRR2019.84

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Introduction IL 17-A blocking with Secukinumab (SEK) has proved efficacy in the treatment of psoriasis and psoriatic arthritis (PsoAr). Inflammatory bowel disease (IBD) is more common among patients with psoriasis and is considered as a part of the spectrum of spondyloarthritis. IL-17 is a cytokine required for the normal homeostasis of the bowel and its inhibition could initiate a subclinical disease.

Objectives We have observed 2 patients with IBD during therapy anti-IL17 for PsoAr.

Results Case 1 A 20-year-old woman with a diagnosis of plaque psoriasis since 12 years; she has been treated with topical treatment, phototherapy and Methotrexate. In November 2017 She presented skin worsening, (PASI 20, DLQI 20 and started treatment with SEK at a dose of 300 mg every 4