Objectives To explore the importance of IL-23 signalling in MAIT-cell-derived IL-17A and IL-17F production, examine the presence of MAIT cells in psoriatic lesional skin and assess the contribution of MAIT-cell-derived IL-17A and IL-17F using *in vitro* models of skin inflammation.

Methods IL-17A and IL-17F production by MAIT cells was assessed by flow cytometry, ELISA, qPCR and CyTOF upon activation by anti-CD3/CD28 or fixed *E. coli* via MR1-presented riboflavin metabolites, $\pm$ recombinant cytokines or an IL-23-neutralising antibody. RNAscope was utilised to observe MAIT cells in psoriatic lesional skin. MAIT cell supernatant, generated by FACS sorting, was cultured with normal human dermal fibroblasts (NHDFs) in the presence of IL-17-isoform-specific antibodies, including bimekizumab, a monoclonal antibody that potently and selectively neutralises both IL-17A and IL-17F.

Results Optimal MAIT cell IL-17A and IL-17F production occurred upon T-cell receptor triggering with IL-12 and IL-18, independently of IL-23. IL-17F expression was greater at both gene and protein levels than IL-17A. The kinetics and threshold of activation for IL-17A and IL-17F suggest tighter regulation compared with other inflammatory cytokines, including IFN γ and TNF. Optimal MAIT cell IL-17A and IL-17F production requires monocytes, which contribute to IL-12 production upon IL-18 stimulation. MAIT cells were abundant in psoriatic lesional skin. NHDFs cultured with supernatant generated from activated MAIT cells produced inflammatory mediators IL-6, IL-8 and CCL2, which were reduced upon inhibition of either IL-17A or IL-17F, with optimal suppression achieved following dual neutralisation with bimekizumab.

Conclusions IL-17A and IL-17F can be produced from MAIT cells independently of IL-23, and contribute to inflammatory responses in NHDFs. These results support dual neutralisation of IL-17A and IL-17F as a complete and targeted approach to suppress IL-17-driven inflammatory responses.

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Disclosure of Interest S. Cole Employee of: UCB Pharma, A. Maroof Employee of: UCB Pharma (also has a patent pending).

P090 PRO-INFLAMMATORY CYTOKINES AND CELL INTERACTIONS BETWEEN PBMC AND SYNOVIOCYTES INDUCE RETRACTION AND FORMATION OF PSEUDOPODIA

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Introduction Rheumatoid synovitis is infiltrated by immune cells, which interact with synovioocytes inducing abnormal proliferation and massive production of pro-inflammatory cytokines.

Objectives The aim was to evaluate the effect of inflammatory environment and cell interactions on morphological parameters of synovioocytes alone or in co-culture with peripheral blood mononuclear cells (PBMC).

Methods Synovioocytes from different donors: healthy (HE) or rheumatoid arthritis (RA) were exposed or not to inflammatory conditions (IL-17 alone, TNF alone and their combination) during 48 hours and observed with different microscopes (optical, digital holographic and holographic-tomographic). Quantification of morphological parameters included cell confluence, area, motility speed and number of pseudopodia/cell. Co-cultures between normal PBMC and synovioocytes with or without phytohemagglutinin (PHA) or cytokines (IL-17/TNF) were used to mimic the *in vivo* situation.

Results Inflammatory cytokines induced a change in synovioocyte morphology, inducing a retracted cell with a higher number of pseudopodia. Several parameters decreased in inflammatory conditions: cell confluence (Ctrl:31.7% $\pm$ 2.5%, IL-17:21.8% $\pm$ 2.0%, TNF:19.2% $\pm$ 1.5%, IL-17/TNF:19.8% $\pm$ 1.6%, $p<0.01$), area (Ctrl:4491 $\pm$ 254 μ m², IL-17:3537 $\pm$ 265 μ m², TNF:2862 $\pm$ 217 μ m², IL-17/TNF:2583 $\pm$ 211 μ m², $p<0.01$) and motility speed (Ctrl:446 $\pm$ 7 μ m/h, IL-17:177 $\pm$ 2 μ m/h, TNF:161 $\pm$ 2 μ m/h, IL-17/TNF:159 $\pm$ 1 μ m/h, $p<0.01$). The cell membrane exhibited a much larger number of pseudopodia in inflammatory conditions (ctrl: only 18% of cells had more than 4 pseudopodia vs. IL-17/TNF: 82%, $p<0.01$). The same impact on cell morphology was observed in co-culture of synovioocytes and PBMC, affecting both cell types: synovioocytes were retracted (HE: Ctrl:5092 $\pm$ 274 μ m², cocult:3037 $\pm$ 168 μ m², cocult +PHA:3644 $\pm$ 184 μ m², cocult +IL-17/TNF: 2949 $\pm$ 154 μ m², $p<0.01$) and inversely PBMC proliferated in inflammatory and PHA conditions (HE: Ctrl:47.9 $\pm$ 1.4 μ m², cocult:80.6 $\pm$ 3.2 μ m², cocult +PHA:94.2 $\pm$ 2.9 μ m², cocult +IL-17/TNF:114.6 $\pm$ 3.4 μ m², $p<0.01$), indicating that cell activation induced a morphological change of cells. With RA but not normal synovioocytes, co-culture was not sufficient to activate both PBMC and synovioocytes. The morphological effect came only from the inflammatory environment and not from cell interactions as if it did not exist and did not occur (RA: Ctrl:4491 $\pm$ 254 μ m², cocult:4573 $\pm$ 275 μ m² (ns), cocult +PHA:3220 $\pm$ 184 μ m², cocult +IL-17/TNF:2313 $\pm$ 122 μ m², $p<0.01$).

Conclusions The inflammatory environment or cell interactions induced massive changes in synovioocytes, with cell retraction and increase of pseudopodia number, leading to better interactions with other cells. Except in the case of RA, the inflammatory environment was absolutely required for such changes.

Disclosure of Interest None declared.

P091 EFFECTS OF BIOLOGICS ON IL-17A AND TNF INDUCED CYTOKINE SECRETION ON SYNOVIAL FIBROBLASTS FROM RHEUMATOID AND PSORIATIC ARTHRITIS PATIENTS

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