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SOLUBLE FACTORS DERIVED FROM INFRAPATELLAR FAT PAD ADIPOCYTES OF OA PATIENTS MODULATE CD4+T CELL CYTOKINE PRODUCTION

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Background and objectives As shown in previous studies, the infrapatellar fat pad (IFP) of OA patients has an inflammatory phenotype and could contribute to the biological processes in the OA knee joint. The authors have previously characterised the immune cell infiltrate in the IFP and have shown the presence of CD4+T cells. Because several studies have shown that the phenotype of CD4+T cells in adipose tissue is changing with the adiposity of the individual, the authors hypothesised that this effect could be due to the modulation of infiltrating T cells by the tissue-resident adipocytes. Therefore, the authors investigated whether adipocytes from IFP can modulate CD4+T cell cytokine production.

Materials and methods CD4+T cells were purified from peripheral blood mononuclear cells isolated from buffycoats obtained from healthy volunteers. The purity of the CD4+T cells isolated using magnetic beads coated with antihuman CD4 was above 95%. Plate-bound anti-CD3 and soluble anti-CD28 antibodies were used to activate T cells. Adipocytes were isolated from IFP of OA patients by collagenase digestion and were either cultured with purified CD4+T cells or were cultured in vitro for 24 h in DMEM/F12 medium supplemented with 0.5% bovine serum albumin to generate adipocyte-conditioned medium (ACM). Cytokine/adipokine production was measured by intracellular cytokine staining (ICS), ELISA or cytokine multiplex. Lipids were isolated using hapten and lipid profiling was performed by liquid chromatography combined with mass spectrometry.

Results CD4+T cells produced increased levels of interferon γ (IFN γ) when activated in the presence of adipocytes. This effect is mediated by soluble mediators, as shown in transwell and ACM transfer experiments. Other T cell cytokines, such as tumour necrosis factor α , IL-17 and IL-5 were also modulated by IFP-derived ACM, indicating a general effect on memory T cells. Several cytokines, adipokines and lipid species were detected in ACM and current research aims at identifying the main soluble mediator responsible for T cell modulation. Finally, IFP of OA patients contained more IFN γ -competent CD4+T cells than peripheral blood in three out of three patients tested, suggesting a possible in vivo consequence of our results.

Conclusions Soluble mediators secreted by IFP of OA patients can modulate cytokine production of CD4+T cells. Although the precise mechanism involved in this modulation is still unknown, in vivo comparison of IFN γ -producing cells in IFP and peripheral blood indicates a possible in vivo relevance of this finding.