A178 MESENCHYMAL STEM CELLS PARTICIPATE IN THE LOOP LEADING TO AMPLIFICATION OF INFLAMMATION THROUGH SECRETION OF INTERLEUKIN (IL)6, IL1B AND IL8

A Eljaafari, M-L Tartelin, P Miossec *Immunogenomics Unit, EA 4130, Hospices Civils de Lyon, France*

10.1136/ard.2010.129668o

Background Mesenchymal cells and subsets of T cells interact in the rheumatoid arthritis (RA) synovium leading to the local production of inflammatory cytokines. These high levels suggest a defect in the regulation of cytokine secretion, but the respective contribution of Th1 and Th17 cells remains to be clarified.

Objectives Mesenchymal stem cells (MSC) are known to play a role in the regulation of the immune response and are present in the synovium. The authors investigated the effects of exogenous Th1 and Th17 cytokines on their functions. The impact on RA synoviocytes (fibroblast-like synoviocytes (FLS)) was investigated in parallel because FLS derive from MSC and are the most abundant cells in synovium.

Methods MSC were isolated from the bone marrow of healthy controls and were developed by culture of adherent cells in α-MEM+10%FCS. RA FLS were obtained from hip surgery and were cultured in DMEM+10%FCS. Cells were treated for 24 h with interleukin (IL)7A (50 ng/ml), tumour necrosis factor (TNF)α (1 or 10 ng/ml) or interferon (IFN)γ (50 ng/ml), alone or in combination. mRNA levels of inflammatory cytokines (IL6, IL1β, IL8) were measured by Q-RT-PCR.

Results Culture of MSC with IL17A or TNFα for 24 h resulted in increased expression of IL6, IL1β and IL8 mRNA, with a synergistic effect when IL17α and TNFα were combined. In contrast, IFNγ induced a weak increase in IL6 mRNA expression, with

almost no effect on IL1β or IL8 mRNA expression. However, when used in combination with IL17 plus TNFα, a massive effect was observed on IL6, IL1β and TNFα mRNA expression (amplification of 34, 53 and 4386-fold, respectively). Similar enhancing effects of IL17A, TNFα and IFNγ were seen when RA FLS were used instead of MSC.

Conclusion These results suggest that, in an inflammatory environment, MSC as well as FLS participate in the amplification of inflammation through secretion of high levels of inflammatory cytokines. Moreover, while IFNγ and IL 17 often have opposite effects, here the authors show that these two cytokines, plus or minus TNFα, can also combine their effects, especially to amplify inflammation.