A129 ANTI-TYPE II COLLAGEN-IMMUNE COMPLEX-INDUCED PRODUCTION OF INTERLEUKIN 1β AND TUMOUR NECROSIS FACTOR α STIMULATE PRODUCTION OF MATRIX METALLOPROTEINASES FROM MONOCYTE/ RHEUMATOID ARTHRITIS SYNOVIAL FIBROBLAST CO-CULTURES

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Objective We have previously reported that anti-CII-containing immune complexes (anti-CII IC) induced production of tumour necrosis factor (TNF) β, interleukin (IL)1α and IL8 from monocytes via FcγRIIa.1 We have also shown that high levels of anti-CII were associated with IC-induced production of pro-inflammatory cytokines in vitro and increased laboratory signs of inflammation 2 and increased radiological erosions at the time of diagnosis. 3 The objective of this study was to establish an in vitro model that might explain the association between early joint destruction and the appearance of anti-CII in patients with early rheumatoid arthritis (RA). This RA pannus tissue model utilises IC-containing anti-CII antibodies as a stimulus and monocytes and synovial fibroblasts as responder cells.

Methods Peripheral blood mononuclear cells (PBMC) and RA synovial fibroblasts (RASF) were stimulated with IC individually as well as in co-cultures. Monocytes were depleted to define the responder cells and TNFα and IL1β were neutralised to study the effect of the individual cytokines on MMP production. TNFα, IL1β, matrix metalloproteinase (MMP)-1, MMP-8 and MMP-13 were measured in cell culture supernatants using ELISA.

Results Anti-CII-containing IC induced production of TNFα, IL1β and MMP-1 in PBMC cultures and TNFα, IL1β, MMP-1 and MMP-8 in PBMC/fibroblast co-cultures in a dose-dependent manner. IC-induced MMP-1 responses were stronger and more associated with induced production of IL1β compared with MMP-8 responses. Baseline production of IL1β and MMP-1 increased significantly in co-cultures compared with individual cultures, whereas these effects were not observed for TNFα and MMP-8. Monocyte depletion decreased TNFα, IL1β and MMP-1 production, while the effect on MMP-8 production was variable. Cytokine neutralisation revealed that IL1β was a stronger inducer of MMP-1 than was TNFα. No production of MMP-13 was found in any cell cultures.

Conclusion Synergistic actions between RASF and PBMC resulted in enhanced anti-CII IC-induced production of IL1β and MMP-1. IL1β and MMP-1 are regulated in parallel as anti-CII IC-induced IL1β supports the production of MMP-1. MMP-8 seems to be regulated by other means. Anti-CII IC-induced TNFα seems to be inferior to IL1β concerning MMP-1 induction. The fact that anti-CII IC stimulated synovial macrophages and fibroblasts to produce MMP, which are the first enzymes to cleave the interstitial collagens, may explain the anti-CII-associated joint destruction apparent in early RA.

REFERENCES

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