CXCL8 and CCL20 Enhance Osteoblast-mediated Osteoclastogenesis

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INTRODUCTION

Osteoporosis is common in rheumatoid arthritis (RA). Osteoblasts express receptors for CXCL8 and CCL20, which are produced by inflammatory cells around the inflamed joints in RA and present in elevated levels in serum in RA.

We hypothesized that CXCL8 and CCL20 contribute to generalized osteoporosis in RA by affecting osteoblast proliferation, differentiation and osteoblast-osteoclast communication.

METHODS

- Primary human osteoblasts were cultured in the presence or absence of CXCL8 (2-200 pg/ml) or CCL20 (5-500 pg/ml) for 14 days.
- Osteoblast proliferation and differentiation were analyzed, as well as cytokine gene expression. IL-6 protein production was quantified by ELISA.
- Human peripheral blood mononuclear cells were cultured with CXCL8 and CCL20 or conditioned medium from CXCL8 and CCL20-treated osteoblasts in the presence or absence of IL-6 inhibitor for 21 days.
- The number of tartrate-resistant acid phosphatase-positive osteoclasts was counted, and osteoclast activity was determined by the resorption pit assay.

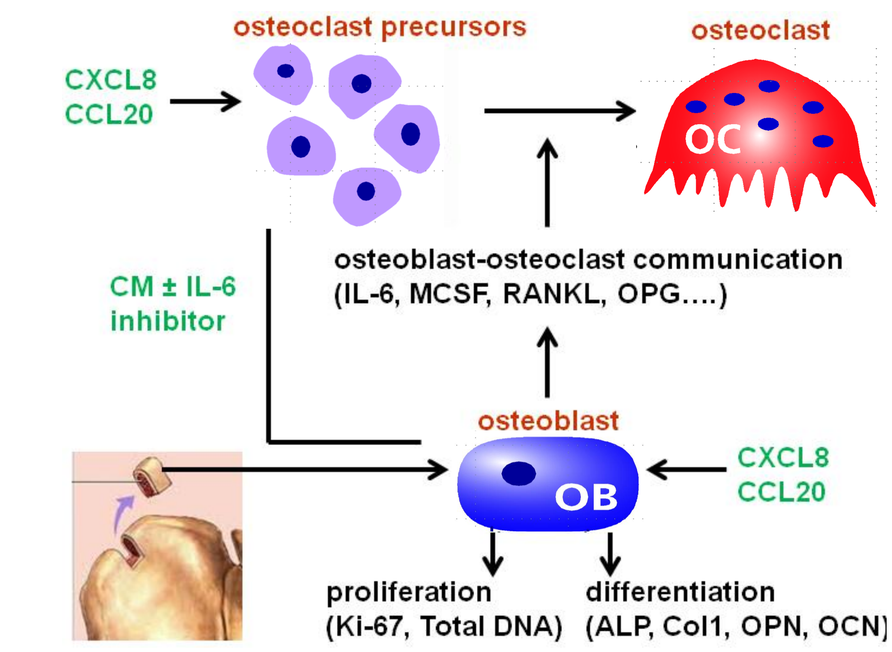

FIGURE 1. Experimetal set up

RESULTS

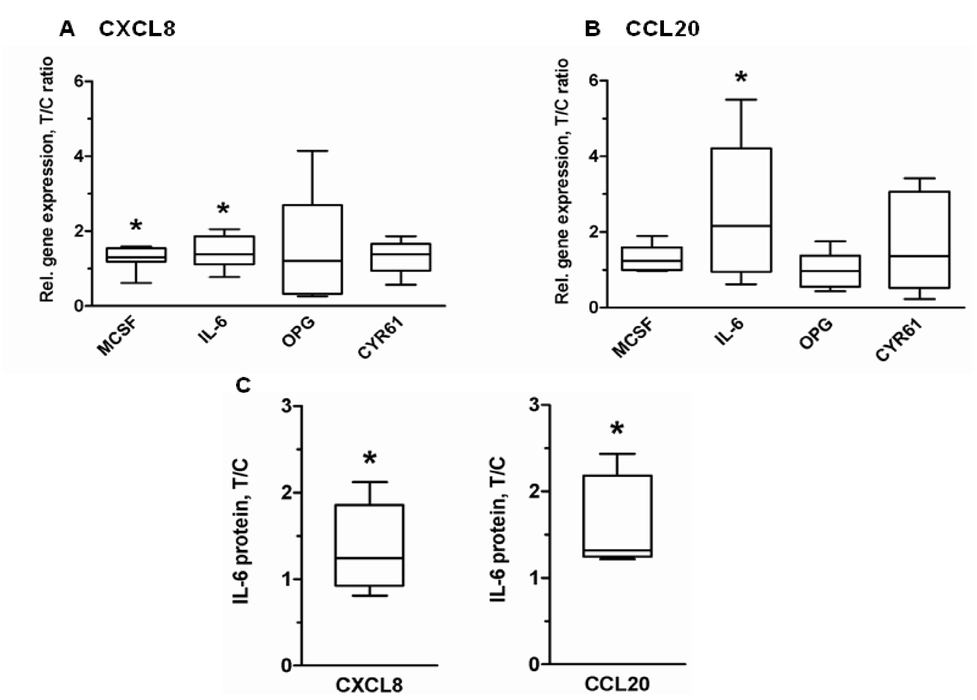

FIGURE 2. CXCL8 and CCL20 enhanced IL-6 gene expression and IL-6 protein production

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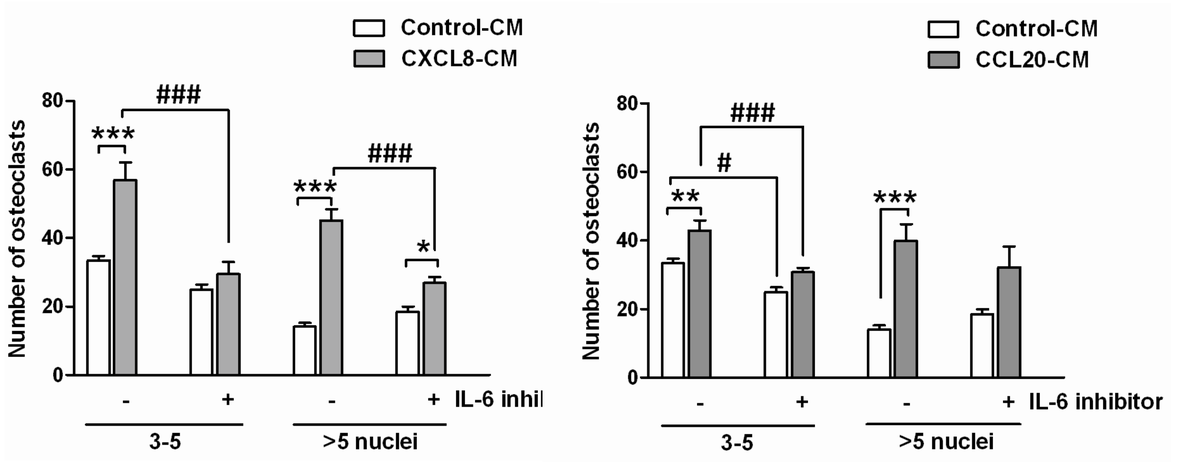

FIGURE 3. CXCL8-CM and CCL20-CM enhanced osteoclastogenesis which effect was reduced by inhibition of IL-6

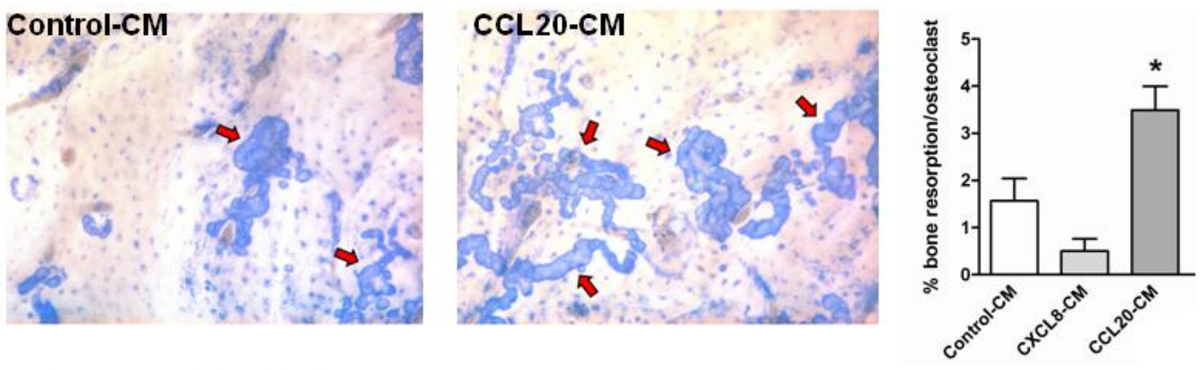

FIGURE 4. CCL20-CM enhanced osteoclastic bone resorption while CXCL8-CM had no effect

- **CXCR1 (receptor for CXCL8) and CCR6 (receptor for CCL20) were present on human osteoblasts (not shown).**
- **CXCL8 and CCL20 enhanced Ki-67 gene expression, but did not affect total DNA (not shown).**
- **CXCL8 and CCL20 enhanced ALP gene expression, but did not affect OPN and OCN gene expression, P1NP protein production, nor ALP activity (not shown).**
- **Gene expression of RANKL, IL-17, and TNF-α was below the detection level (not shown).**

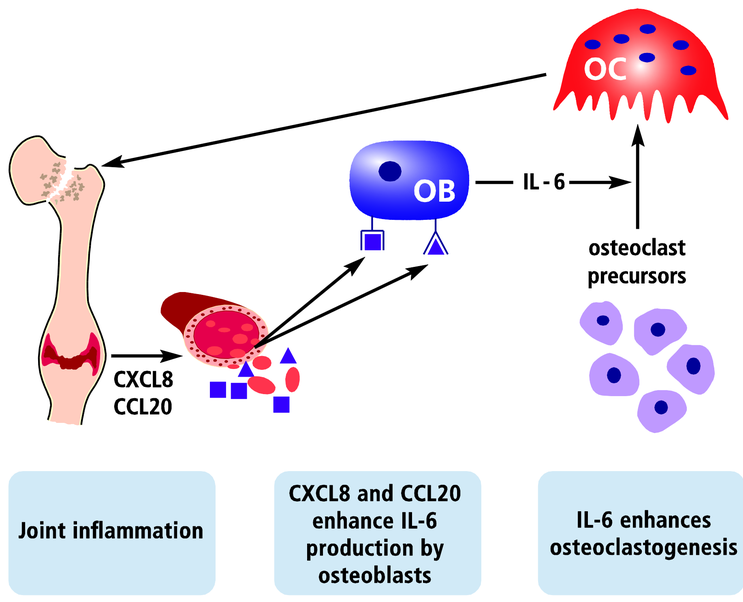

FIGURE 5. Pathophysiological model to illustrate how CXCL8 and CCL20 influence bone remodeling in RA

CONCLUSIONS

CXCL8 and CCL20 did not inhibit osteoblast proliferation or differentiation.

CXCL8 and CLC20 enhanced osteoblast-mediated osteoclastogenesis, partly via stimulation of IL-6 production, suggesting that CXCL8 and CCL20 contribute to localized and generalized osteoporosis in rheumatoid arthritis.

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