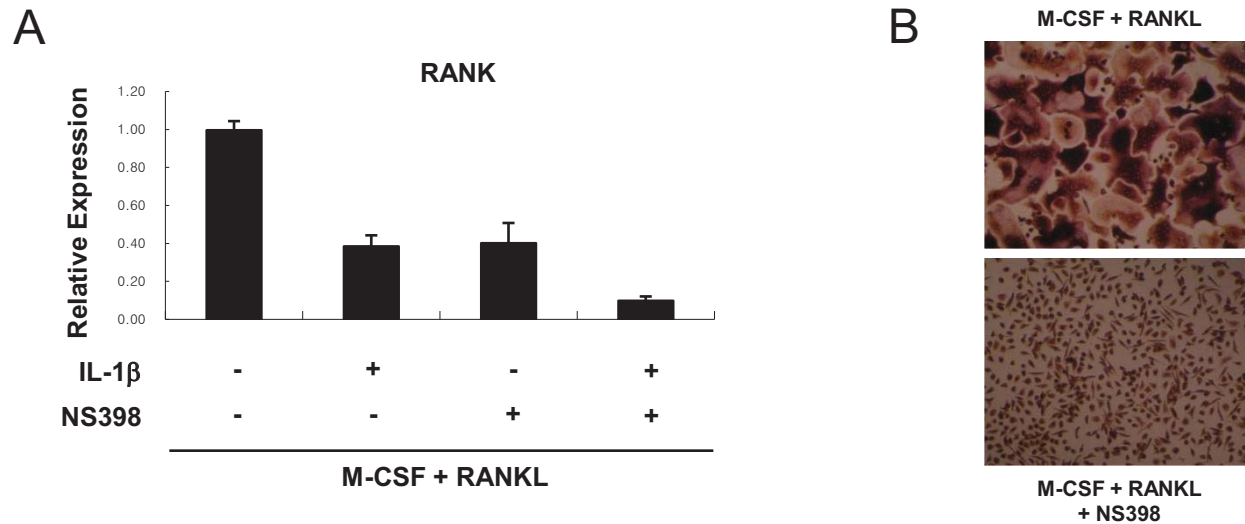


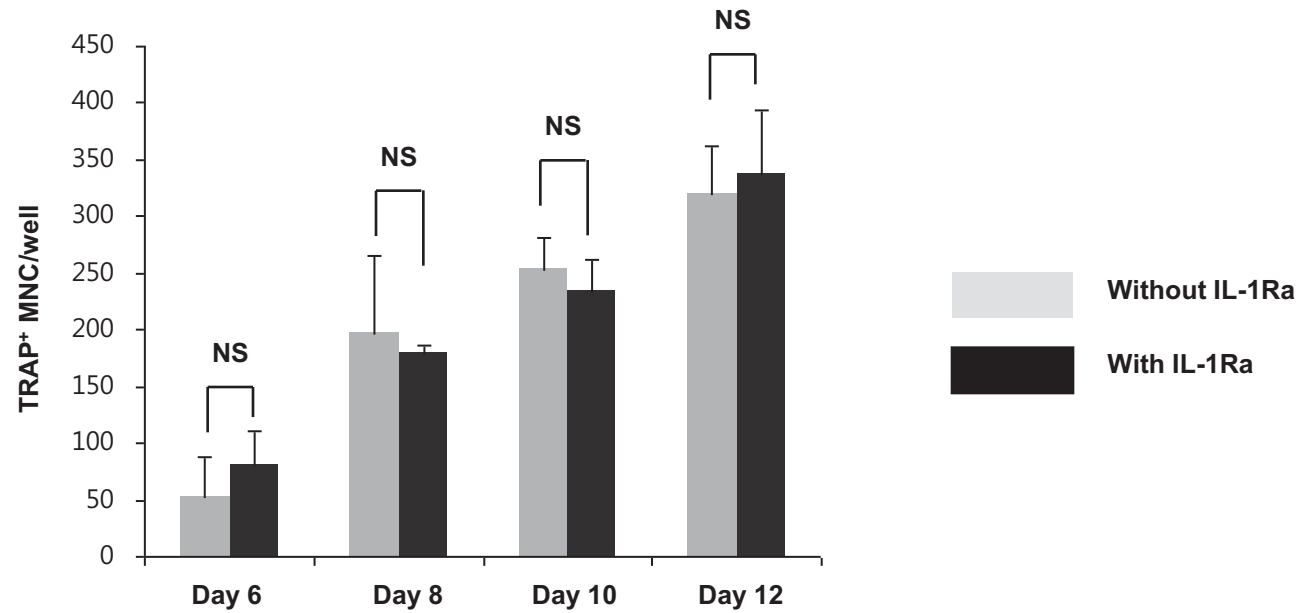
**Fig. S1. IL-1 $\beta$  significantly inhibited osteoclastogenesis when added prior to addition of RANKL.**

Human monocytes were cultured with M-CSF (20 ng/mL) in the presence or absence of IL-1 $\beta$  (10 ng/mL) for 2 days, and then M-CSF and RANKL (40 ng/mL) was added in the presence or absence of IL-1 $\beta$  (10 ng/mL) for an additional 6 days. Cells were stained for TRAP expression. TRAP-positive multinucleated (> 3 nuclei/cell) cells were counted as osteoclasts. Data are shown as means  $\pm$  SD of triplicate determinants and are representative of more than three experiments. \* =  $P < 0.05$  versus control..



**Fig. S2. NS398 itself inhibits RANK expression and osteoclast differentiation in human osteoclast precursors.**

(A) Human monocytes were cultured with M-CSF (20 ng/mL) for 2 days, and then M-CSF and RANKL (40 ng/mL) was added in the presence or absence of IL-1 $\beta$  (10 ng/mL) and/or NS398 (a COX-2 inhibitor;  $10^{-7}$  M) overnight, and mRNA was isolated and analyzed using real time PCR and were normalized relative to the expression of GAPDH. Data are shown as means  $\pm$  SD of triplicate determinants and are representative of more than three experiments. (B) Human monocytes were cultured with M-CSF (20 ng/mL) for 2 days, and then RANKL (40 ng/mL) was added for an additional 6 days. NS398 ( $10^{-7}$  M) was added with RANKL. Cells were stained for TRAP expression. TRAP-positive multinucleated (> 3 nuclei/cell) cells were counted as osteoclasts. Data are shown as means  $\pm$  SD of triplicate determinants and are representative of more than three experiments.



**Fig. S3. IL-1Ra do not reverse inhibited osteoclastogenesis in RA synovial fluid macrophages.**

RA synovial macrophages were cultured with M-CSF (20 ng/mL) and RANKL (40 ng/mL) in the presence or absence of IL-1Ra (200ng/ml) for indicated times. Cells were stained for TRAP expression. TRAP-positive multinucleated (> 3 nuclei/cell) cells were counted as osteoclasts. \*NS, not significant.