Lymphotoxin-beta receptor signaling complex: role of tumor necrosis factor receptor-associated factor 3 recruitment in cell death and activation of nuclear factor kappaB.Proc Natl Acad Sci U S A 1997;94:2460-5.

45. Chang YH, Hsieh SL, Chen MC, Lin WW. Lymphotoxin beta receptor induces interleukin 8 gene expression via NF-kappaB and AP-1 activation. Exp Cell Res 2002;278:166-74.

Figure 1. Levels of LIGHT in synovial fluid from RA patients compared with those from OA patients, as determined by enzyme-linked immunosorbent assay. Data are shown as box plots. Each box represents the 25th to 75th percentiles. Error bars represent the 10th to 90th percentiles. Lines inside the boxes represent the median. * = $P < 0.05$.

Figure 2. Expression of LIGHT, HVEM, and LTβR mRNAs in synovial tissues and fibroblast-like synoviocytes. A, Expression of LIGHT, HVEM and LTβR mRNAs in synovial tissues from RA patients OA patients. The expression level of LIGHT mRNA was evaluated by real-time PCR; results are represented as relative ratios to GAPDH levels, and are shown as box plots. B, Expression of LIGHT, HVEM, LTβR, and

GAPDH in RA FLS. RT-PCR was performed using total RNA extracted from FLS from 7 different RA patients. * = $P < 0.05$.

Figure 3. LIGHT induces the proliferation of RA FLS via LTβR. A, LIGHT induces RA FLS proliferation. RA FLS were stimulated with the indicated concentrations of LIGHT or EGF for 48 hours, and proliferation was determined by a BrdU assay. B, RA FLS were transfected with control, HVEM or LTβR siRNAs using Lipofectamine 2000, and cultured for 96 hours prior to the extraction of total RNA from the cells. Expression of HVEM and LTβR mRNA was analyzed by real-time quantitative PCR. C, After the transfection of cells with siRNAs, the cells were stimulated for 48 hours with 10 ng/ml LIGHT. Cell proliferation was determined by a BrdU assay. Values are shown as means ± SD fold change compared with controls. All analyses were carried out on 5 RA FLS lines. * = $P < 0.05$.

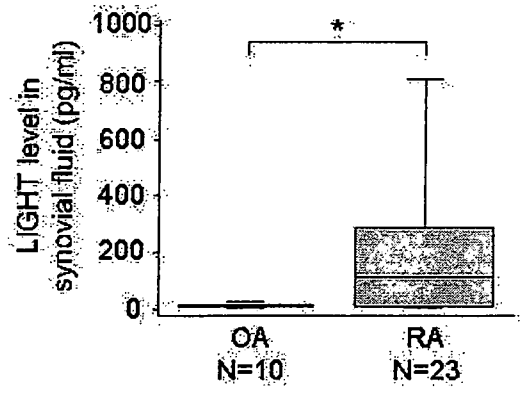
Figure 4. Up-regulation of IL-8, MCP-1 and ICAM-1 expression in RA FLS by LIGHT. A, RA FLS were stimulated with the indicated concentrations of LIGHT for 3 hours, and real-time quantitative PCR was performed to determine the levels of IL-8, MCP-1, and ICAM-1 mRNA expression. Values are shown as means ± SD fold change compared with controls. B, RA FLS were stimulated with the indicated concentrations

of LIGHT for 72 hours. The concentrations of IL-8 and MCP-1 in the cell culture supernatants were determined by multiplex bead array assays. Values are shown as means ± SD pg/ml. ICAM-1 surface expression on RA FLS was detected by FACS after stimulation with 10 ng/ml LIGHT for 24 hours. All analyses were carried out on 4 RA FLS lines; the FACS profiles of one representative result are shown. * = $P < 0.05$.

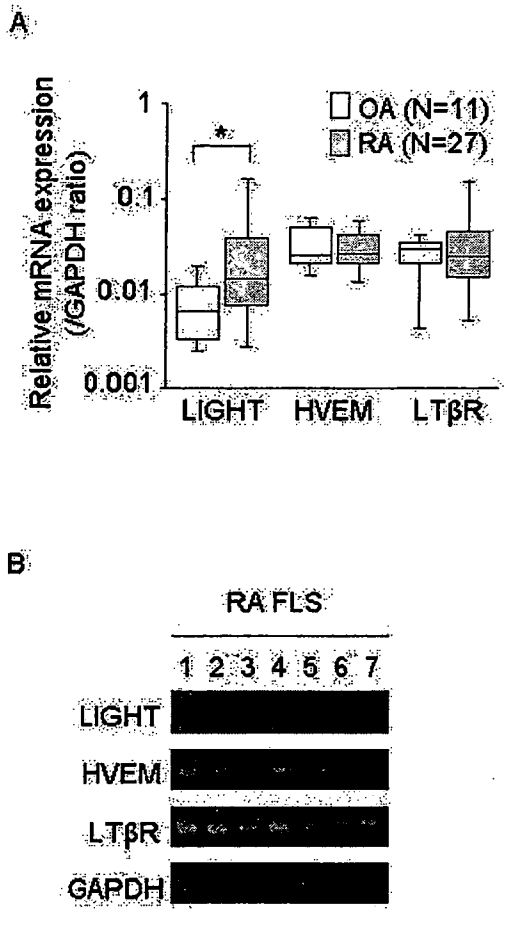
Figure 5. LIGHT-induced expression of IL-8, MCP-1, and ICAM-1 in RA FLS via LTβR. RA FLS were transfected with control, HVEM or LTβR siRNAs using Lipofectamine 2000. Following 96 hours of incubation, the cells were stimulated with 10 ng/ml LIGHT for an additional 3 hours. The expression levels of IL-8, MCP-1 and ICAM-1 mRNAs were analyzed by real-time quantitative PCR. Values are shown as means ± SD fold change compared with controls. All analyses were carried out on 4 RA FLS lines. * = $P < 0.05$.

Figure 6. LIGHT-induced expression of IL-8, MCP-1 and ICAM-1 through NF-κB-mediated pathways. A, FLS were stimulated with 10 ng/ml LIGHT for 3 hours with or without preincubation for 30 minutes with 30 μM PDTC. The expression levels of IL-8, MCP-1 and ICAM-1 mRNAs were analyzed by real-time quantitative PCR. Values

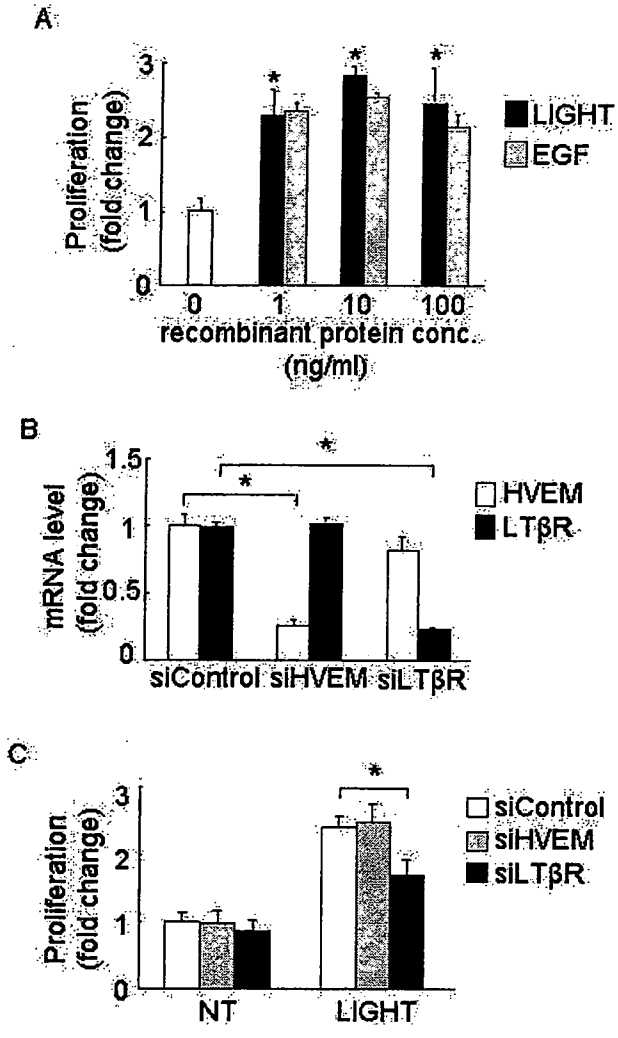
are shown as means ± SD fold change compared with control. All analyses were carried out on 4 RA FLS lines. * = $P < 0.05$. B, Immunofluorescence staining for NF-κB p65 in RA FLS; control in which primary antibodies were replaced with control IgG (left); unstimulated RA FLS (middle) and RA FLS stimulated with 10 ng/ml LIGHT for 30 minutes (right). Results are representative of 2 experiments using 2 FLS lines. C, Ninety-six hours after siRNA transfection, the cells were stimulated with 10 ng/ml LIGHT for 40 mins. IκBα degradation was analyzed by immunoblotting. Results are representative of 2 experiments using 2 RA FLS lines.



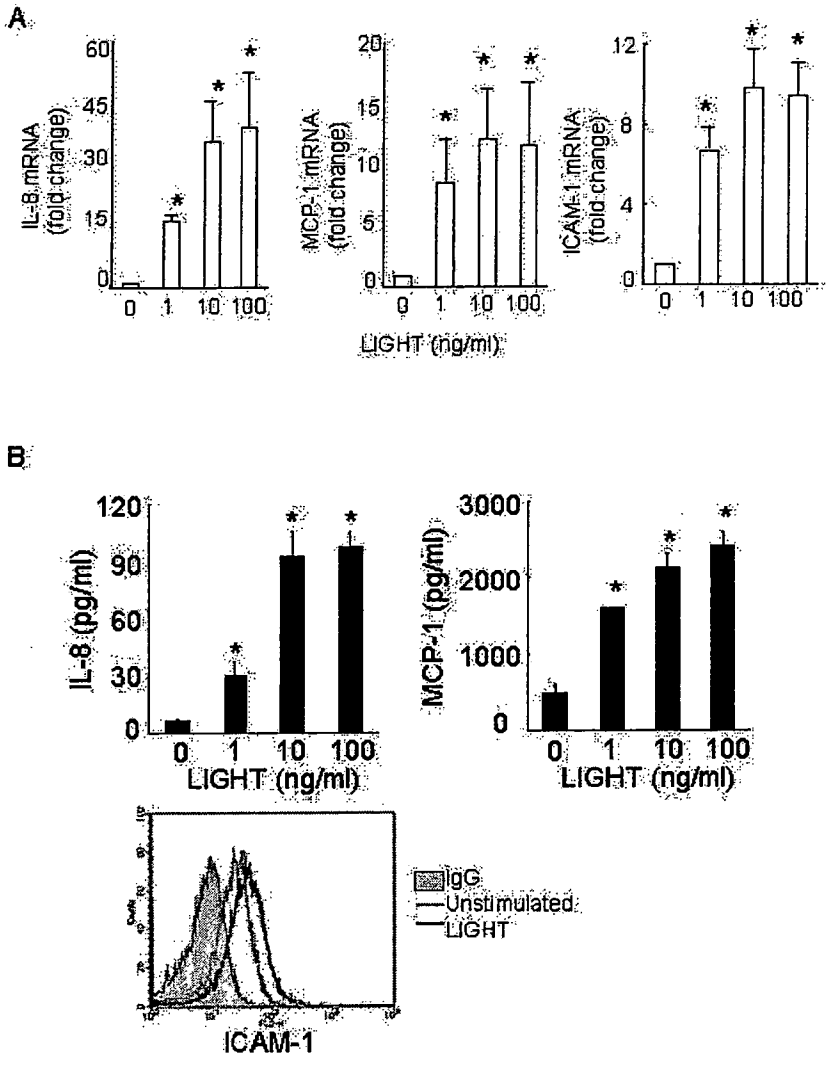
190x254mm (72 x 72 DPI)



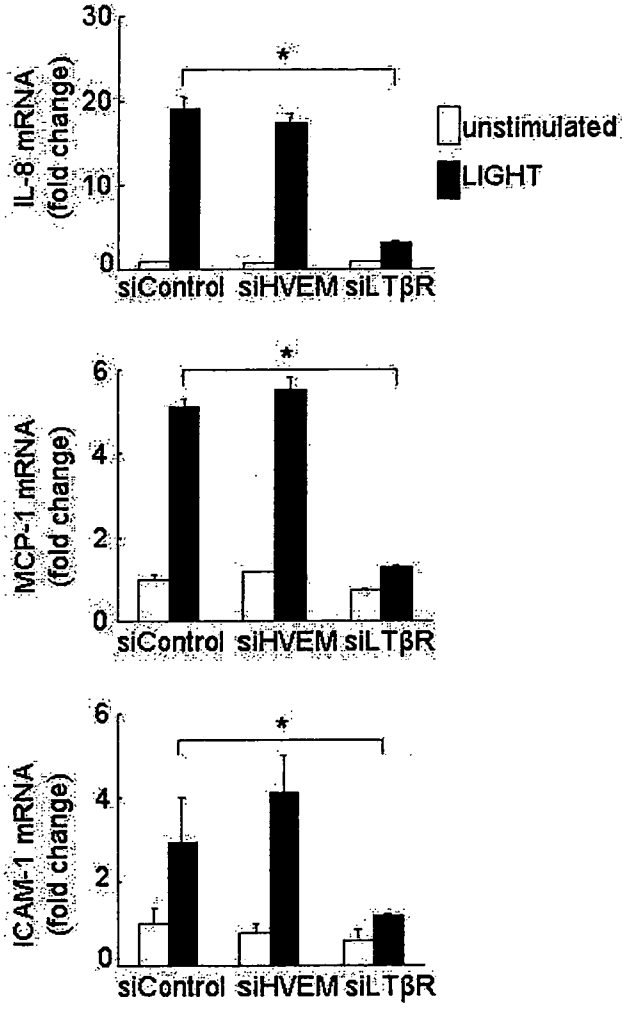
190x254mm (72 x 72 DPI)



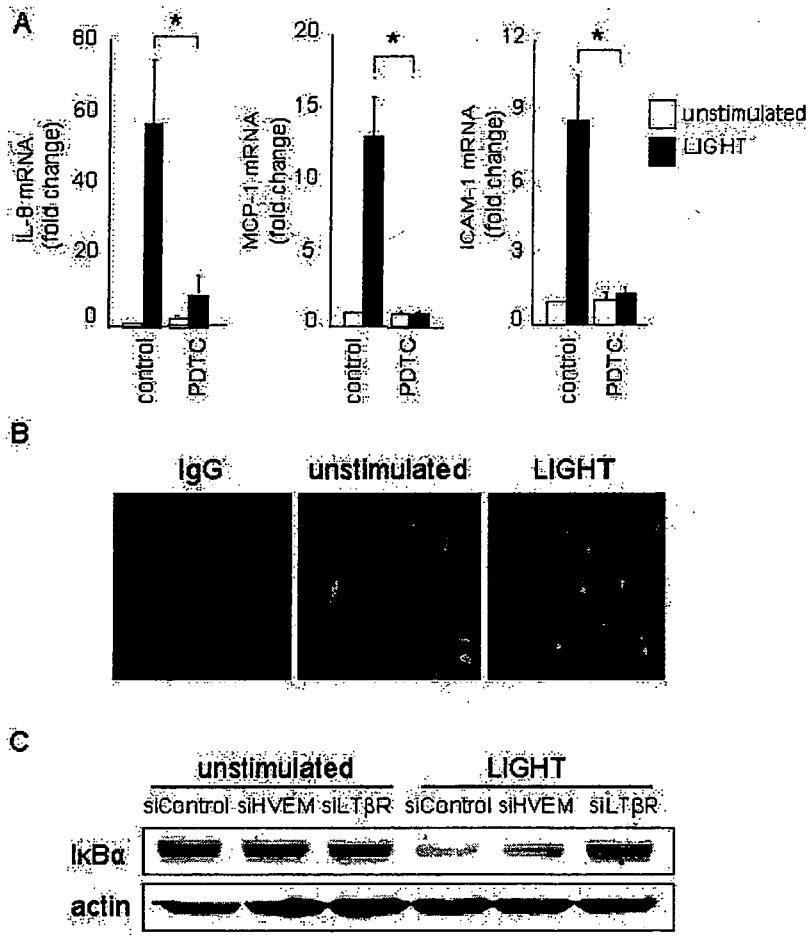
190x254mm (72 x 72 DPI)



190x254mm (72 x 72 DPI)



190x254mm (72 x 72 DPI)



190x254mm (72 x 72 DPI)