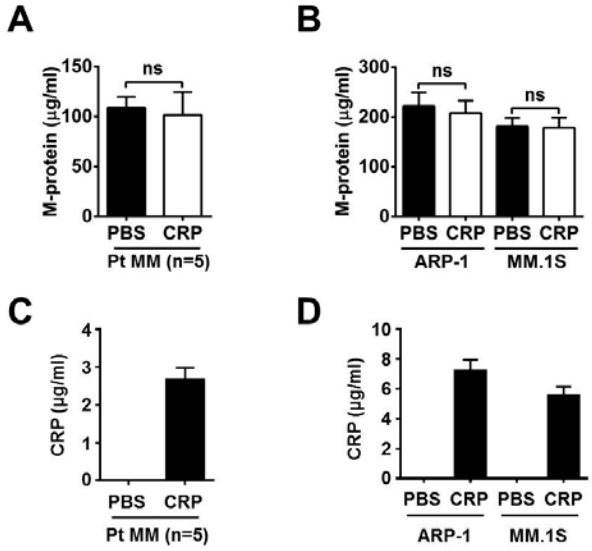

Figure S1. Injection of CRP does not affect tumor growth in vivo. (A to D) Serum levels of M-protein in (A, C) SCID-hu mice bearing primary myeloma cells isolated from myeloma patients (n = 5) and (B, D) SCID mice (n = 10 per group) bearing myeloma after injection with ARP-1 or MM.1S and treated with CRP (20 μg/mouse; twice a week for 8 weeks) or PBS at 8 weeks after tumor injection. M-protein or CRP levels were measured by ELISA. Data from three independent experiments are shown. ns: not significant, by student's t test.

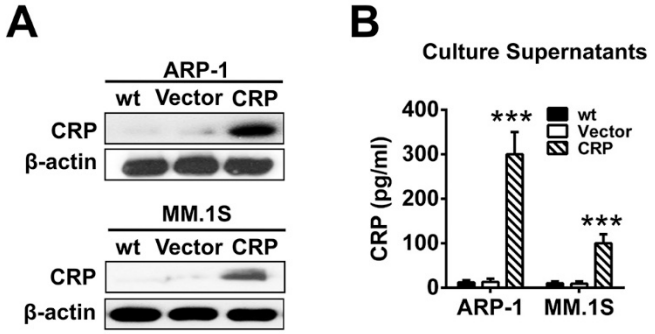

Figure S2. Generation of CRP-expressing myeloma cells. (**A**) Western blot analysis shows expression of CRP proteins in ARP-1 (upper panels) and MM.1S (lower panel) cells transfected with lentivirus carrying human *CRP* cDNA (CRP). Wild type (wt) cells and cells transfected with lentivirus vector control (Vector) served as controls. β-actin served as a protein loading control. (**B**) ELISA shows the levels of secreted CRP in the culture supernatants of CRP-expressing ARP-1 and MM.1S cells, compared with controls. Representative results or data from three independent experiments are shown. $^{***}P < 0.001$ by student's t test.

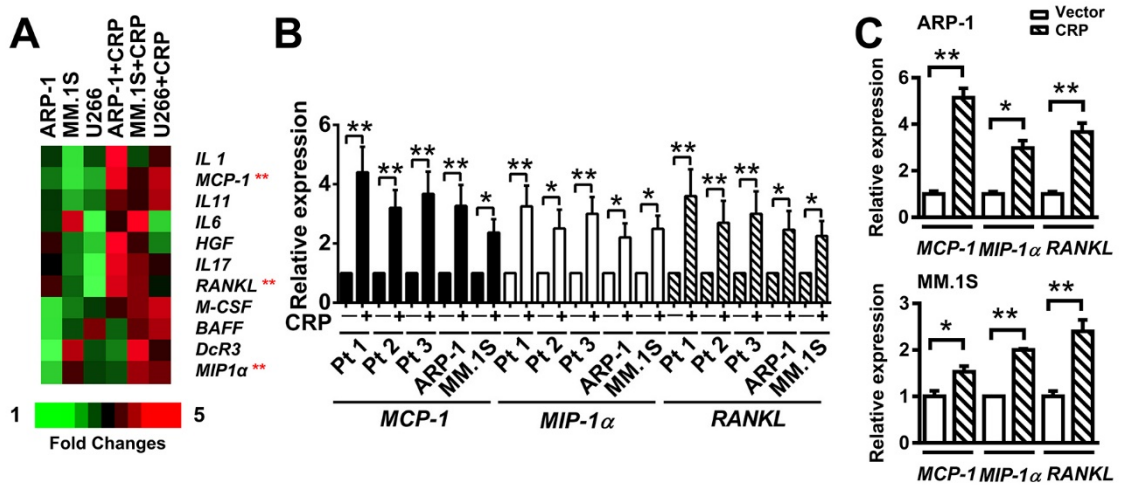

Figure S3. CRP upregulates myeloma cell production of cytokines important for OC activation. (**A**) Expression pattern of OC differentiation-associated cytokines in the medium of ARP-1, MM.1S or U266 cells cultured in the presence or absence of CRP (5 μg/mL). **(B)** Real-time PCR shows the mRNA level of three cytokines (*MCP-1*, *MIP-1α*, and *RANKL*) in cultured primary myeloma cells from 3 of 5 patients (Pt1-Pt3) and myeloma cell lines (ARP-1, MM.1S, CAG, U266) in the presence or absence of CRP (5 μg/mL). (**C**) Real-time PCR shows the mRNA level of three cytokines (*MCP-1*, *MIP-1α,* and *RANKL*) in CRP-expressing ARP-1 and MM.1S cells in comparison with control myeloma cells. $^{*}P < 0.05$, $^{**}P < 0.01$ by student's t test. Data from five independent experiments are shown.

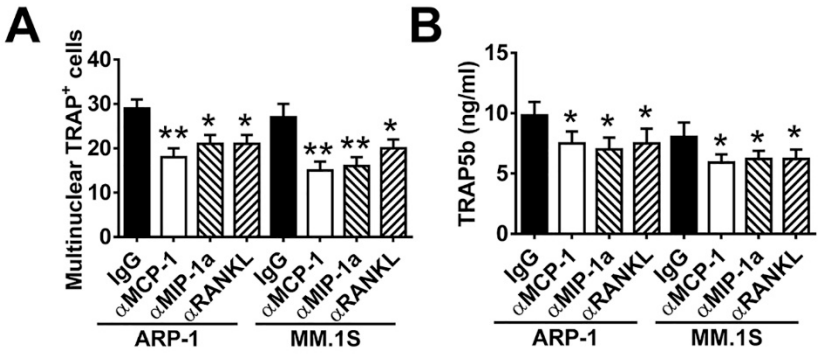

Figure S4. Antibodies specific for OC-activating cytokines inhibit CRP-induced OC activation. (**A**) Number of multinuclear TRAP^{+} cells and (**B**) amount of secreted TRAP5b in culture medium of OC precursors cocultured with ARP-1 or MM.1S cells without RANKL but with CRP (5 μg/mL) and blocking antibodies (1 μg/mL) against MCP-1, MIP-1α, or RANKL, as compared with those in coculture with addition of control (IgG). $^{*}P < 0.05$, $^{**}P < 0.01$ by student's t test. Data from five independent experiments are shown.

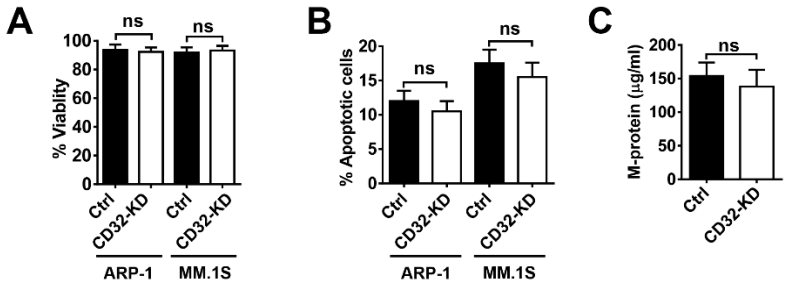

Figure S5. Knockdown or overexpression of CD32 does not affect myeloma cell proliferation or survival. (**A**) Viability of cultured non-targeted shRNA (Ctrl) or CD32-knockdown (CD32-KD) ARP-1 or MM.1S cells. (**B**) Percentages of apoptotic control or CD32-KD ARP-1 or MM.1S cells in a 48-hour culture. Results represent average values from five independent experiments. (**C**) Serum M-protein (secreted by myeloma cells) of SCID mice (n = 10 per group) injected with control or CD32-KD ARP-1 cells. Results represent average values from three independent experiments. Results represent average values from three independent experiments.

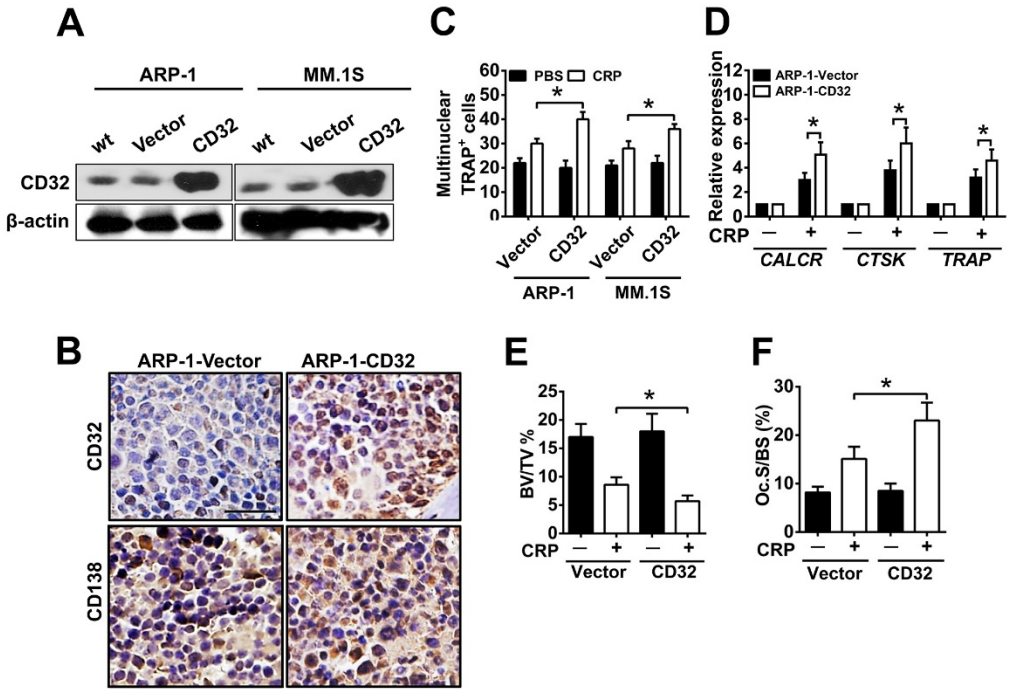

Figure S6. Overexpression of CD32 in myeloma cells enhances CRP-induced OC differentiation. (A) Expression of CD32 proteins in cultured wild-type (wt), vector control (vector), and CD32-overexpressing (CD32) ARP-1 or MM.1S cells. β-actin served as the protein loading control. (**B**) Expression of CD32 and CD138 in bone sections of SCID mouse femurs (n = 10 per group) injected with vector or CD32 ARP-1 cells. Scale bar, 50 μM. (**C**) Numbers of

multinuclear $TRAP^+$ OCs generated from OC precursors cocultured with CD32 ARP-1 or MM.1S cells in the presence of CRP (5 μg/mL), compared with those of cells generated from precursors cocultured with vector myeloma cells. (**D**) Real-time PCR analysis shows an enhanced OC gene expression in OCs cocultured with CD32 ARP-1 cells in the presence of CRP (5 μg/mL), compared with cells cocultured with vector-ARP-1 cells. (Co)cultures with addition of PBS served as controls. (**E-F**) Histomorphometric analysis shows (**E**) decreased bone volume (BV/TV) and (**F**) increased numbers of OCs on the bone surface (Oc. S/BS) in the bone sections of distal femurs of SCID mice (n = 10 per group) injected CD32 ARP-1 cells, compared with those of mice injected with control (vector) ARP-1 cells. Mice receiving no CRP injection served as control. $^*P < 0.05$ by student's t test. Representative results of three independent experiments are shown.

Table S1. Primers used for real-time PCR.

Gene	**Direction**	**Sequence**
GAPDH	Forward	CTGGGCTACACTGAGCACC
CTSK	Forward	CCATATGTGGGACAGGAAGA
	Reverse	CCTCTTCAGGGCTTTCTCAT
CALCR	Forward	GGGAATCCAGTTTGTCGTCT
	Reverse	ACAAAGAAGCCCTGGAAATG
TRAP	Forward	AGATCCTGGGTGCAGACTTC
	Reverse	AAGGGAGCGGTCAGAGAATA
MCP-1	Forward	CAGCCAGATGCAATCAATGCC
	Reverse	TGGAATCCTGAACCCACTTCT
MIP-1α	Forward	CTGCTCAGAATCATGCAGGT
	Reverse	ATGCAGAGAACTGGTTGCAG
RANKL	Forward	ATCGTTGGATCACAGCACAT
	Reverse	TTATGGGAACCAGATGGGAT