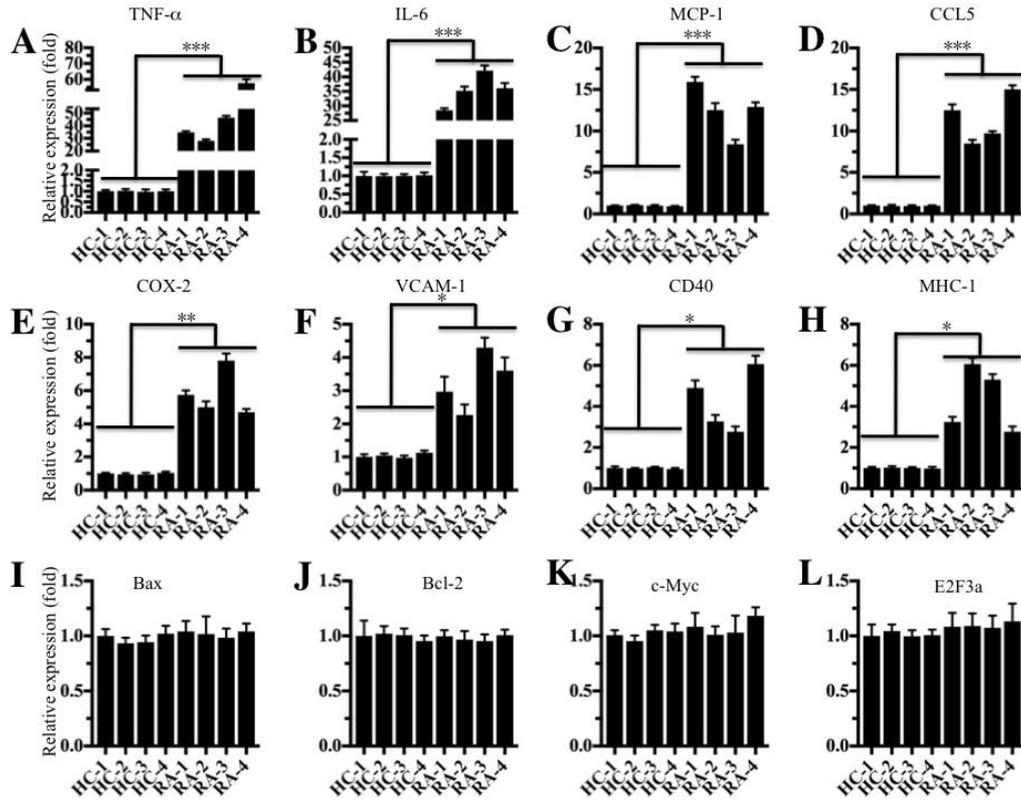


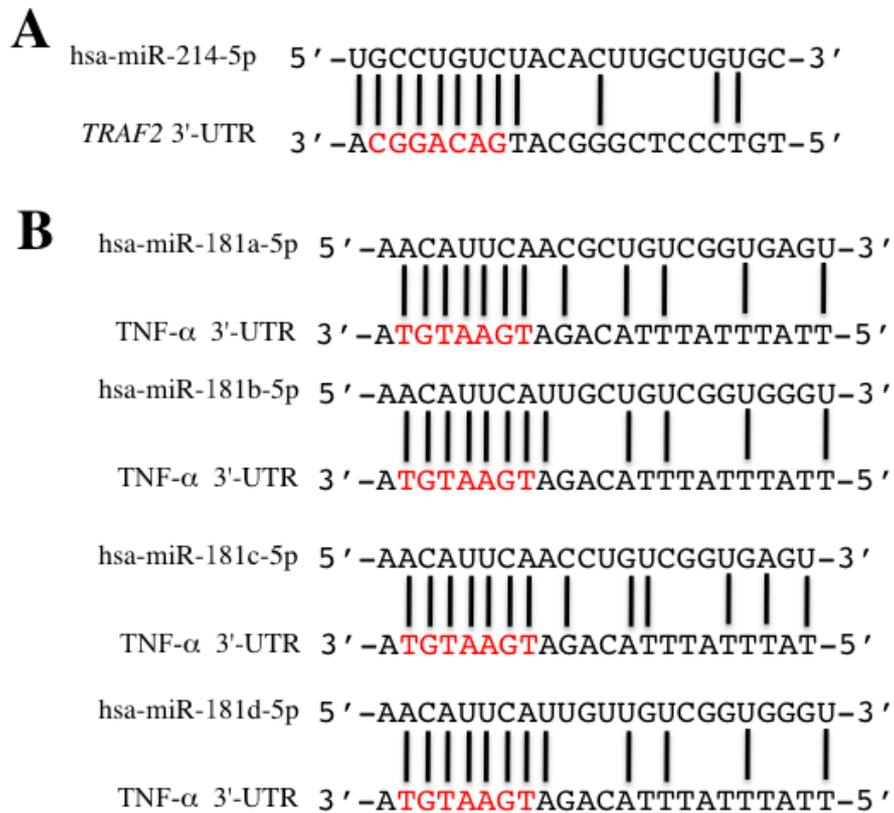
Supplementary Figure 1. The mRNA and protein levels of p65 in overexpressing and knockdown cells.

(A) The RNA from SW982 cells, SW982 cells overexpressing p65 (S-OE), SW982 cells with the knockdown p65 (S-KD), HFLS-RA (HFLS) cells, HFLS-RA cells overexpressing p65 (H-OE), and HFLS-RA cells with the knockdown p65 (H-KD) were subjected to qRT-PCR analysis. ** $P < 0.001$; *** $P < 0.0001$. (B) The total proteins from SW982, S-OE, S-KD, HFLS, H-OE and H-KD cells were subjected to Western blot analysis to examine their p65 level. GAPDH was used as a loading control.



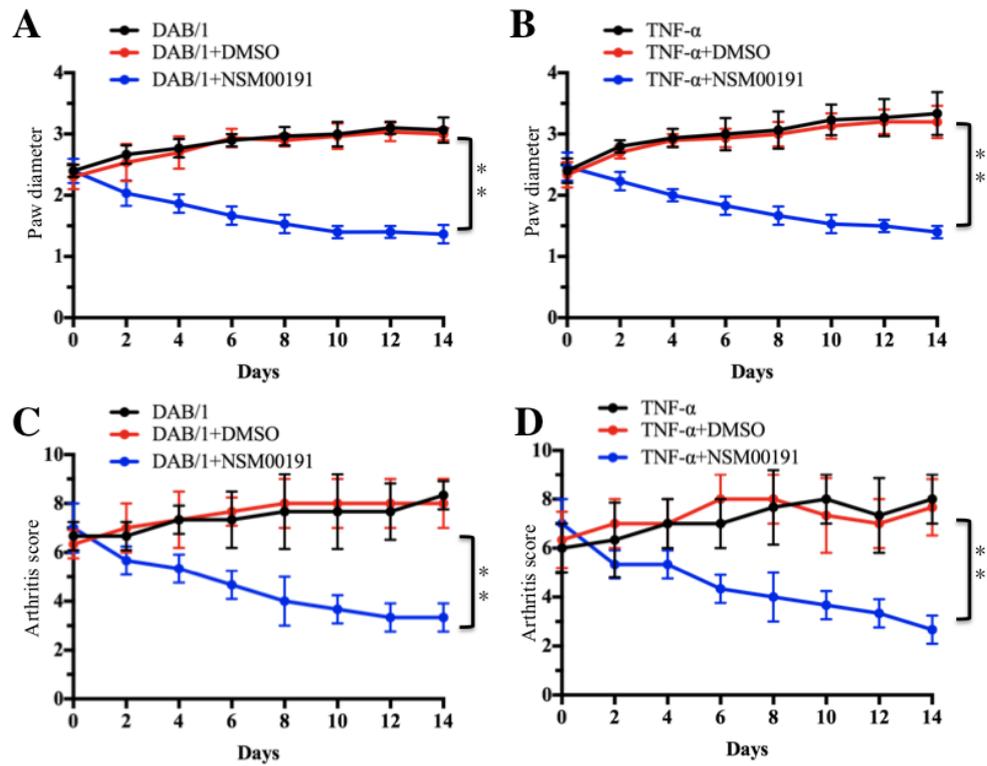
Supplementary Figure 2. The inflammatory targets of NF- κ B were activated in RA patients.

RNA samples from four paired joint tissue specimens that were used in Figure 2A were subjected to qRT-PCR analysis to examine the expression of a number of genes, including TNF- α (A), IL-6 (B), MCP-1 (C), CCL5 (D), COX-2 (E), VCAM-1 (F), CD40 (G), MHC-1 (H), Bax (I), Bcl-2 (J), c-Myc (K), and E2F3a (L). * $P < 0.05$; ** $P < 0.001$; *** $P < 0.0001$.



Supplementary Figure 3. Schematic diagrams of several miRNAs that might target the members of the TNF- α /NF- κ B pathway.

(A) The 3'-UTR of *TRAF2* contains a putative miR-214-5p binding site. (B) The 3'-UTR of *TNF- α* contains a putative binding site for miR-181a-5p, miR-181b-5p, miR-181c-5p and miR-181d-5p.



Supplementary Figure 4. NSM00191 treatment decreased the severity of arthritis.

The six-week old DBA/1 and TNF- α mice were injected with or without NSM00191, or DMSO, and then the paw diameter and clinical arthritis scores were measured for 14 days (n=15 mice in each group). **(A)** The paw diameter in DBA/1 mice. **(B)** The paw diameter in TNF- α mice. **(C)** The arthritis scores in DBA/1 mice. **(D)** The arthritis scores in TNF- α mice. $**P < 0.001$.

Supplementary Table-1. Clinical features of the RA patients

Patient	Age	Sex	Disease duration	Source of synovium
1	48	Female	2	Foot
2	55	Female	5	Ankle
3	56	Female	6	Ankle
4	58	Female	8	Ankle
5	59	Female	12	Ankle
6	61	Female	10	Foot
7	63	Female	7	Foot
8	65	Female	15	Ankle
9	65	Female	6	Foot
10	66	Female	8	Ankle
11	66	Female	10	Ankle
12	67	Female	8	Foot
13	68	Female	7	Foot
14	69	Female	11	Ankle
15	69	Female	6	Foot
16	70	Female	12	Foot
17	70	Female	5	Ankle
18	72	Female	17	Ankle
19	72	Female	11	Ankle
20	72	Female	10	Foot
21	73	Female	6	Foot
22	74	Female	8	Foot
23	74	Female	13	Foot
24	75	Female	15	Ankle
25	44	Male	4	Ankle
26	46	Male	5	Ankle
27	49	Male	8	Foot
28	55	Male	10	Ankle
29	57	Male	4	Foot
30	57	Male	6	Ankle
31	60	Male	8	Foot
32	61	Male	12	Foot
33	62	Male	3	Ankle
34	62	Male	15	Ankle
35	65	Male	3	Foot
36	65	Male	7	Foot
37	68	Male	6	Ankle
38	69	Male	5	Ankle
39	70	Male	8	Foot
40	70	Male	9	Ankle
41	72	Male	10	Foot
42	72	Male	6	Foot
43	72	Male	5	Ankle
44	74	Male	15	Foot
45	74	Male	20	Ankle
46	75	Male	13	Ankle

47	75	Male	11	Foot
48	76	Male	8	Foot

Supplementary Table-2 Primers used for qRT-PCR analyzes

Gene	Forward Primers	Reverse primers
TNF- α	5'-AGACTTCCTTGAGACACGGAG-3'	5'- CCTATTGTTTCAGCTCCGTTTTTCAC- 3'
IL-6	5'-AGTATGAGCGTTAGGACACTA-3'	5'- CTGCATAGCCACTTTCATTATT- 3'
MCP-1	5'-GATACAGAGACTTGGGGAAAT-3'	5'- TAGTTACAAAATATTCATTTCC-3'
CCL5	5'-GCCTAGAAGAGCTTCTGAGGC-3'	5'- TAAGCTCCTGTGAGGGGTTGAG- 3'
COX-2	5'-GATAGGCCTATGTGCTAGCCC-3'	5'-AATACTATTATCTGTAATCAG- 3'
VACM-1	5'-TGCCCATCTATGTCCCTGCTG-3'	5'- TTAAGCAATCTTGCTATGGCA-3'
CD40	5'-CATCAGCAGGAGACTGGCTAA-3'	5'- ATCCATAGGCAATATACATACA- 3'
MHC-1	5'-CCCACGCTGACCTGTGCTCCCT-3'	5'-ATGGCAAGAATTTGAGAAAGT- 3'
Bax	5'-TCATCAGATGTGGTCTATAATG-3'	5'-TCAGAGGGTCATCAATGAAC-3'
Bcl-2	5'-TACCAAGCTGAGCACAGAAGA-3'	5'-CTCTTGCAAATTCTACCTTG-3'
c-Myc	5'-AGACAGATCAGCAACAACCGA-3'	5'-CTCCTCTGCTTGGACGGACAG- 3'
E2F3a	5'-AGTGTGTTTATATGTACAGAGT-3'	5'- AACAAGAGCCACAACAAAGAA-3'