Supporting Information

Combination Therapy for Ulcerative Colitis: Orally Targeted Nanoparticles Prevent Mucosal Damage and Relieve Inflammation

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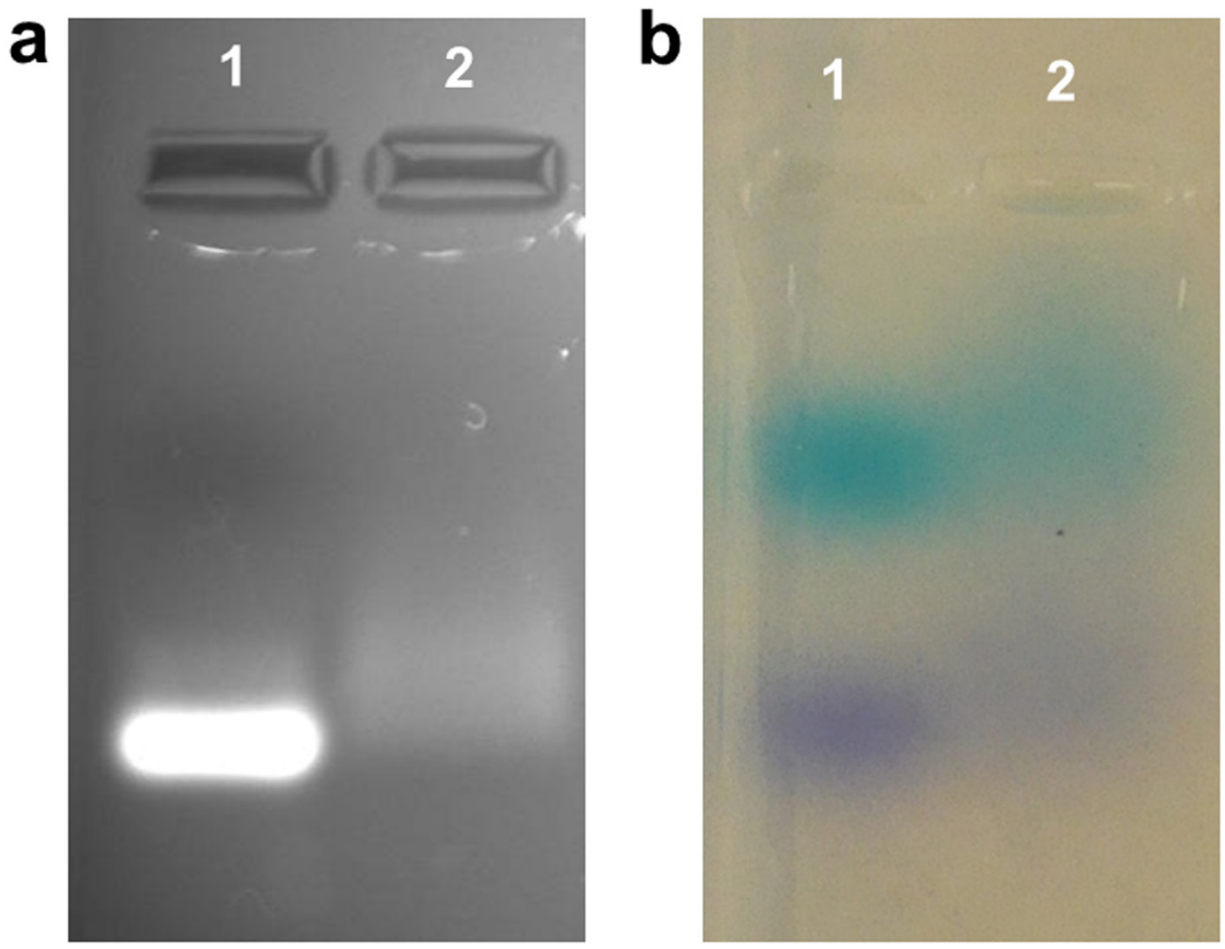

Figure S1. (a) Agarose gel electrophoresis of siRNA and (b) corresponding photo of agarose gel. Lane 1, control siRNA; Lane 2, siRNA extracted from HA-siCD98-NPs.

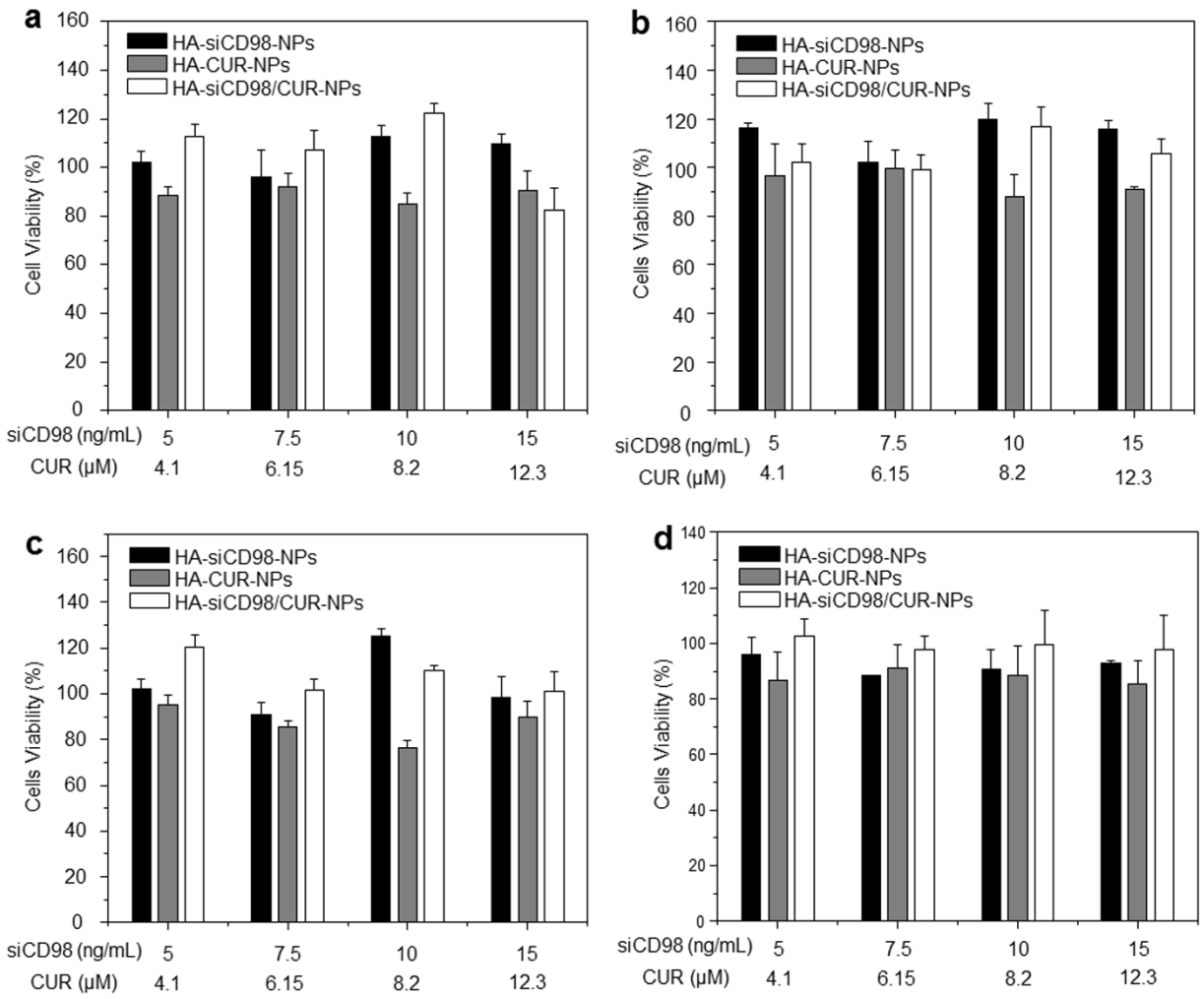

Figure S2. *In vitro* cytotoxicity assays of HA-siCD98-NPs, HA-CUR-NPs and HA-siCD98/CUR-NPs against (a) Colon-26 cells for 24 h, (b) Raw 264.7 macrophages for 24 h, (c) Colon-26 cells for 48 h and (d) Raw 264.7 macrophages for 48 h. Triton X-100 was used as the positive control to produce a maximum cell death rate (100%). Cell culture medium was used as a negative control (death rate defined as 0%). Toxicity is given as the percentage of viable cells remaining after treatment for 24 h. Each point represents the mean ± S.E.M. (n=5). Statistical significance was assessed using Student′s *t*-test (**P*<0.05 and ***P*<0.01).

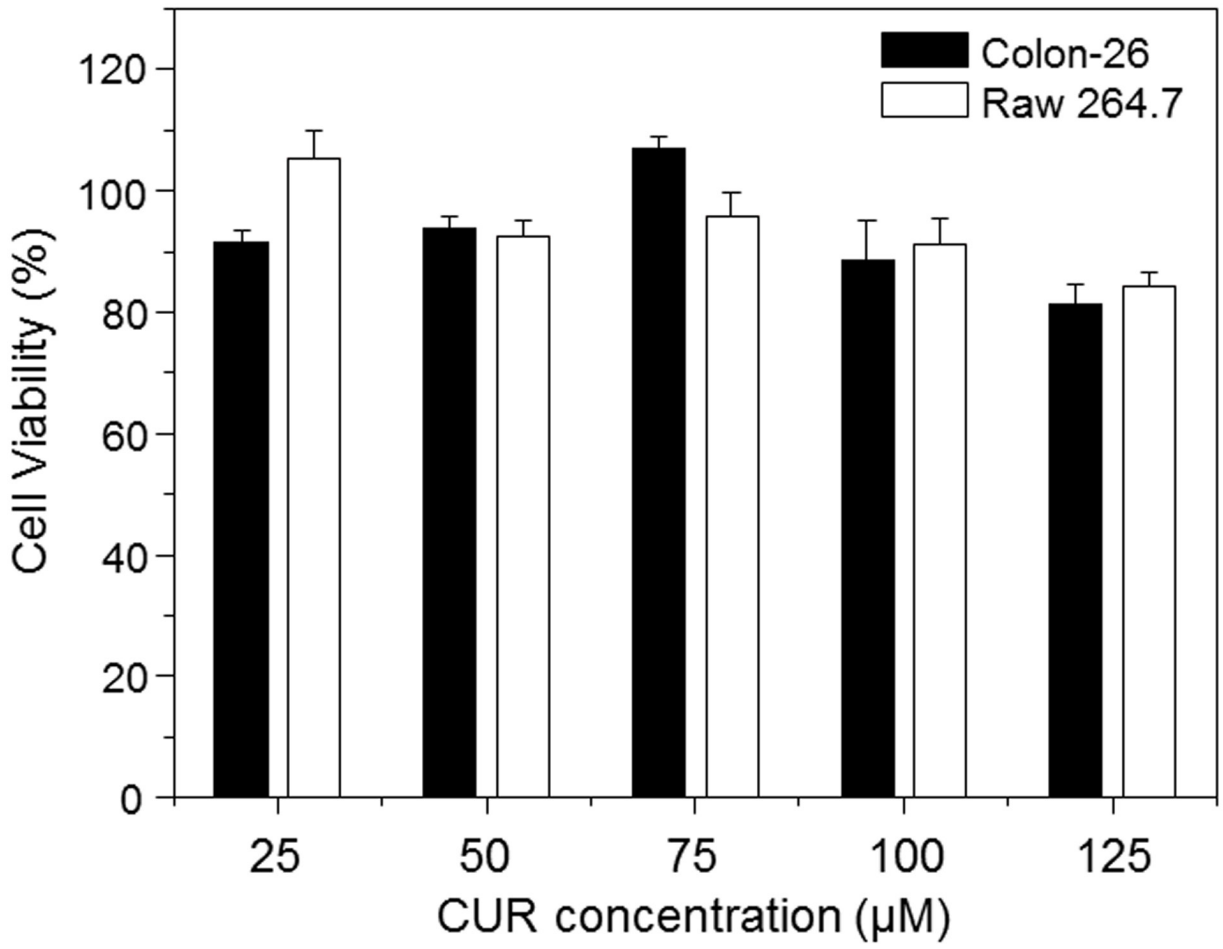

Figure S3. *In vitro* cytotoxicity assays of HA-CUR-NPs against (a) Colon-26 cells and (b) Raw 264.7 macrophages for 5 h. Triton X-100 was used as the positive control to produce a maximum cell death rate (100%). Cell culture medium was used as a negative control (death rate defined as 0%). Toxicity is given as the percentage of viable cells remaining after treatment for 24 h. Each point represents the mean ± S.E.M. (n=5). Statistical significance was assessed using Student′s *t*-test (*P<0.05 and **P<0.01).

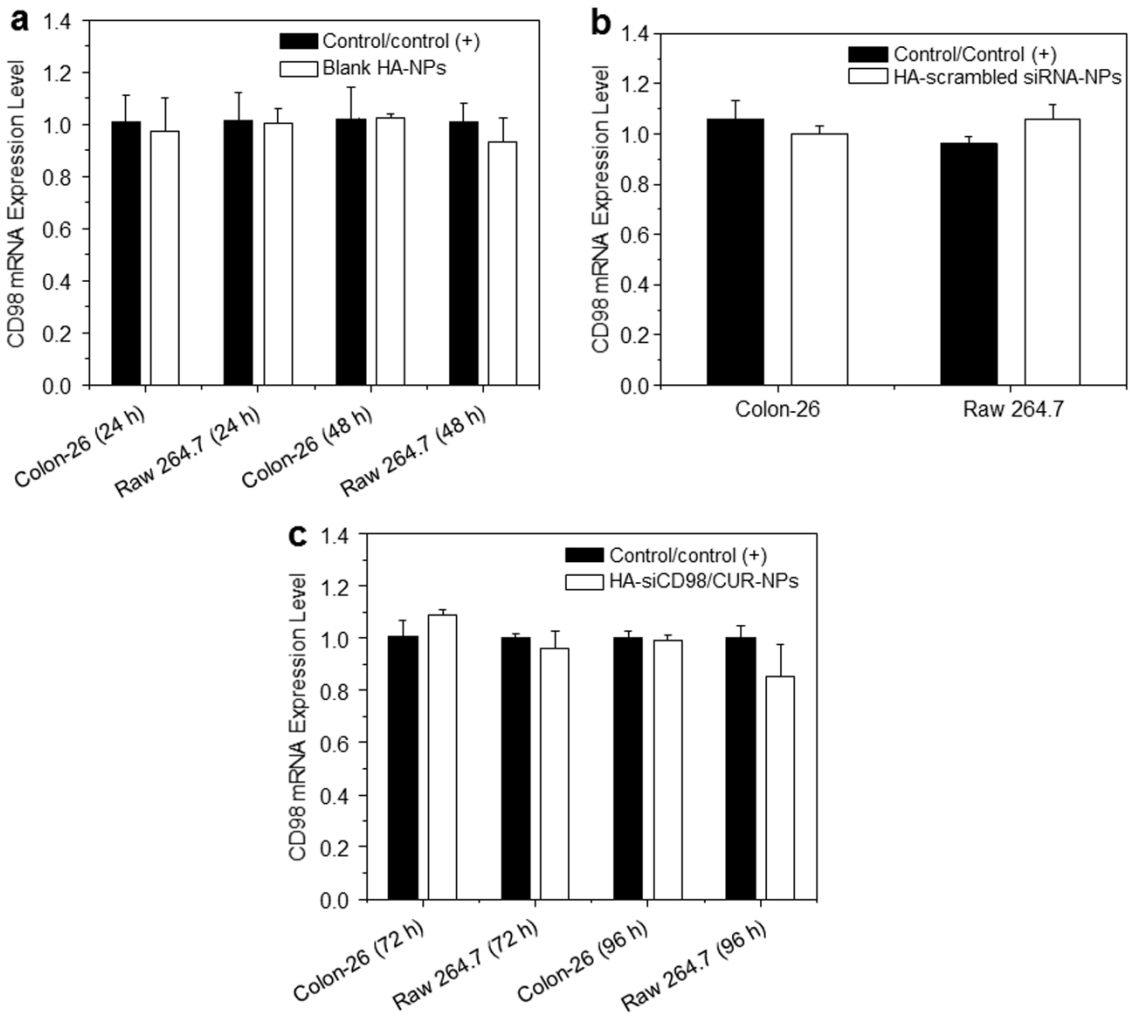

Figure S4. *In vitro* down-regulation capability of CD98 mRNA expression by various NPs. (a) CD98 mRNA expression levels in Colon-26 cells and Raw 264.7 macrophages treated by blank HA-NPs for 24 h or 48 h. (b) CD98 mRNA expression levels in Colon-26 cells and Raw 264.7 macrophages treated by HA-scrambled siRNA-NPs for 24 h. (c) CD98 mRNA expression levels in Colon-26 cells and Raw 264.7 macrophages treated by HA-siCD98/CUR-NPs for 72 h or 96 h. Each point represents the mean ± S.E.M. (n=3).

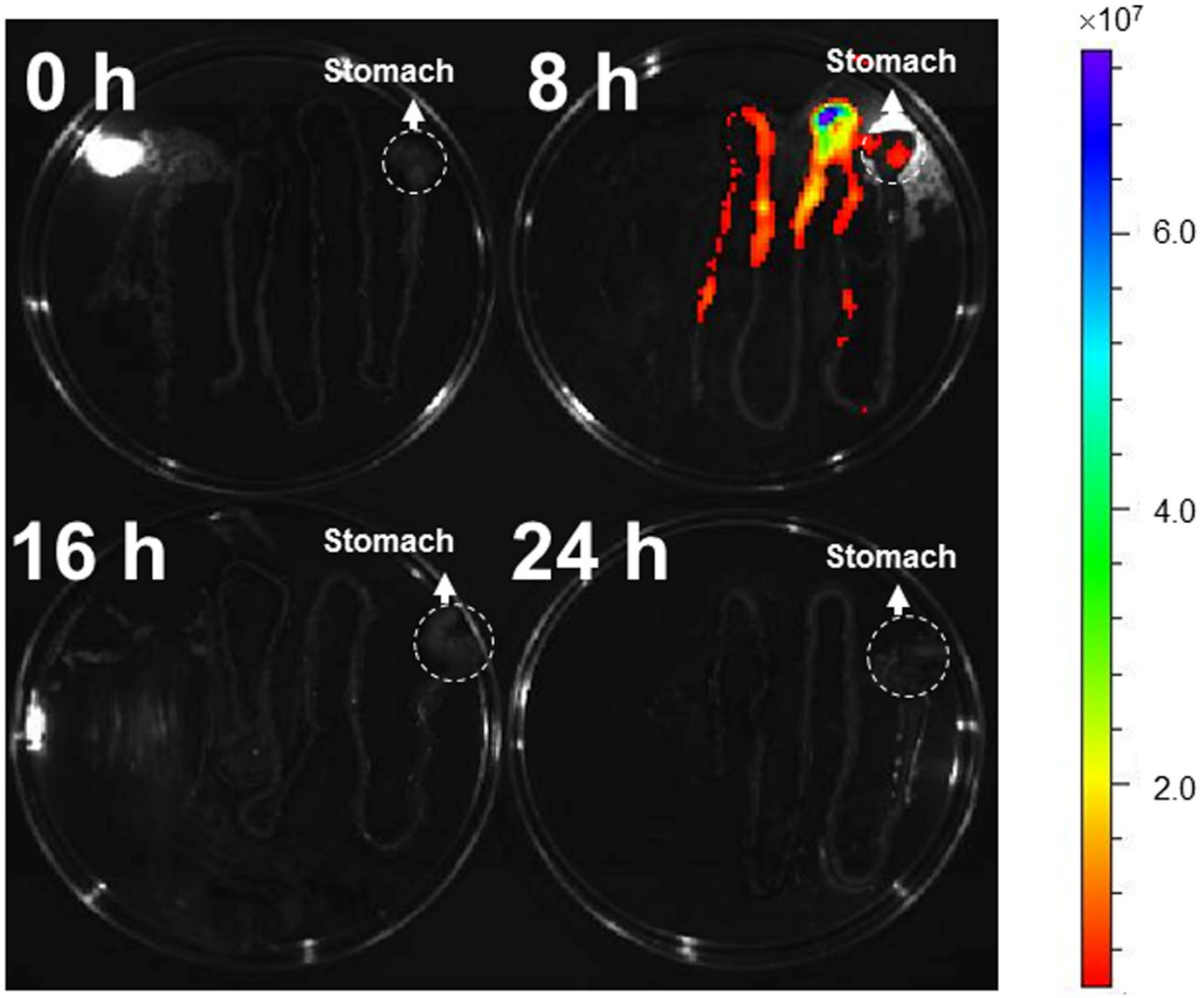

Figure S5. Typical images of stomach, small intestine and caecum imaging showing the distribution of orally HA-functionalized NPs embedded in hydrogel at four different time points (0, 8, 16 and 24 h).

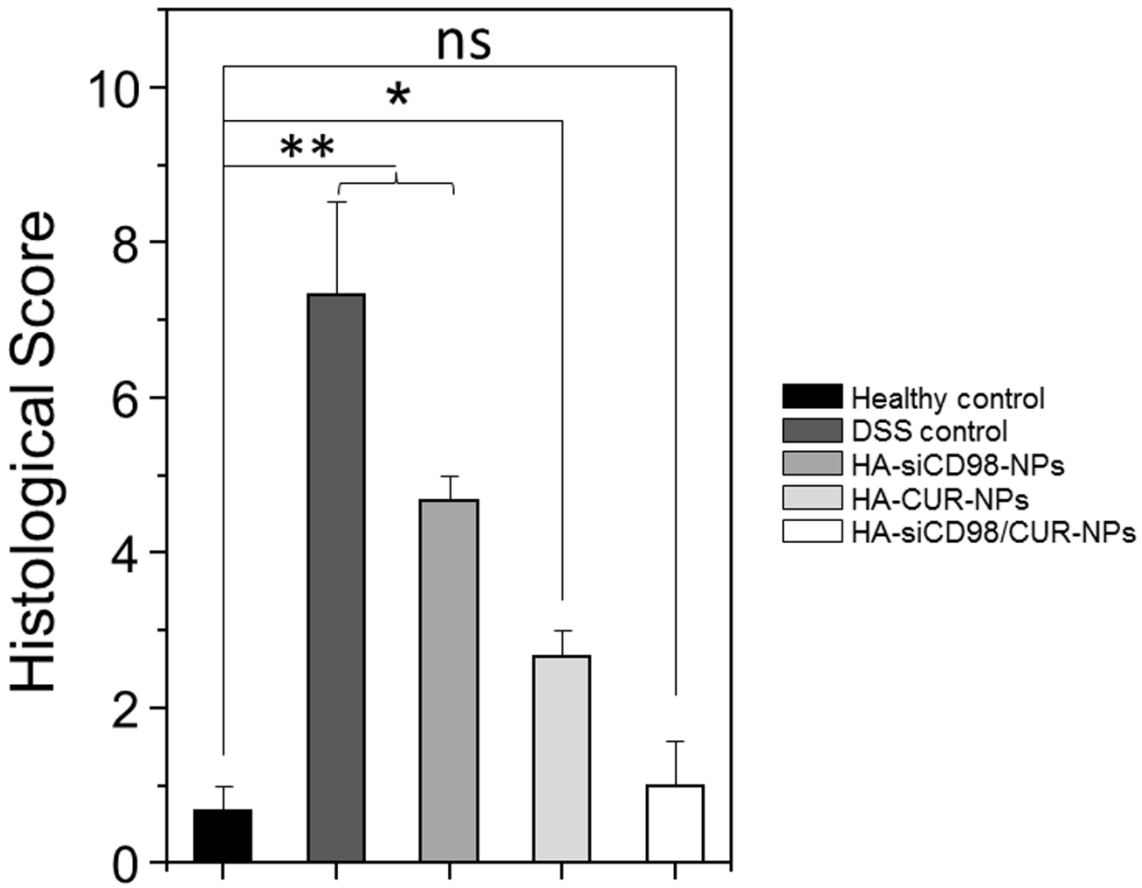

Figure S6. Histological scores determined from H&E-stained colons. Each point represents the mean ± S.E.M. (n = 3).

Table S1

Primers used in this study.

Primer name	Sequence	Description
CD98-F	5’-GAGGACAGGCTTTTGATTGC-3’	CD98 gene RT-PCR forward primer
CD98-R	5’-ATTCAGTACGCTCCCCAGTG-3’	CD98 gene RT-PCR reverse primer
TNF-α-F	5’-AGGCTGCCCCGACTACGT-3’	Tumor necrosis factor gene RT-PCR forward primer
TNF-α-R	5’-GACTTTCTCCTGGTATGAGATAGCAAA-3’	Tumor necrosis factor gene RT-PCR reverse primer
36B4-F	5’-TCCAGGCTTTGGGCATCA-3’	36B4 gene RT-PCR forward primer
36B4-R	5’-CTTTATCAGCTGCACATCACTCAGA-3’	36B4 gene RT-PCR reverse primer