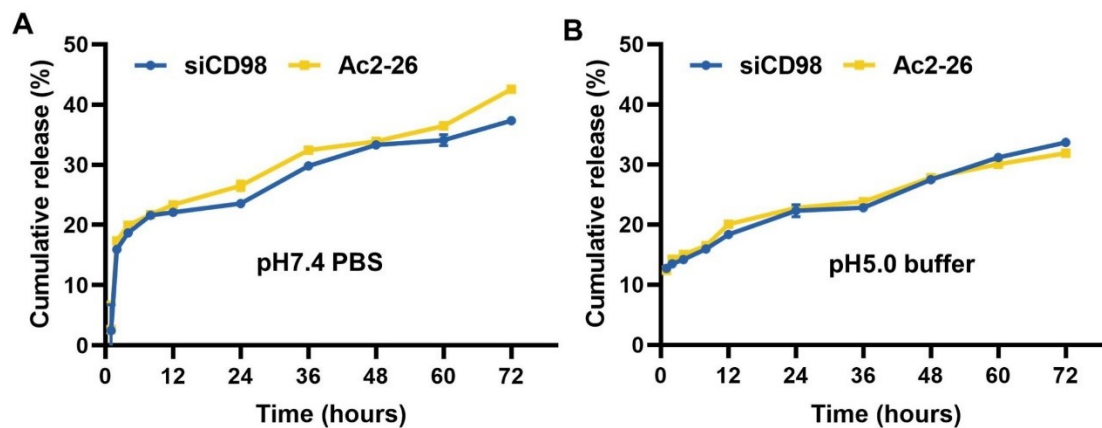
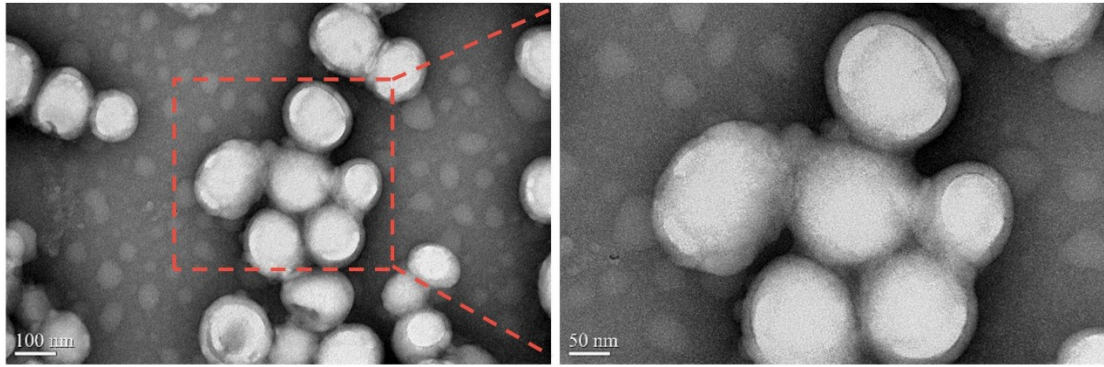


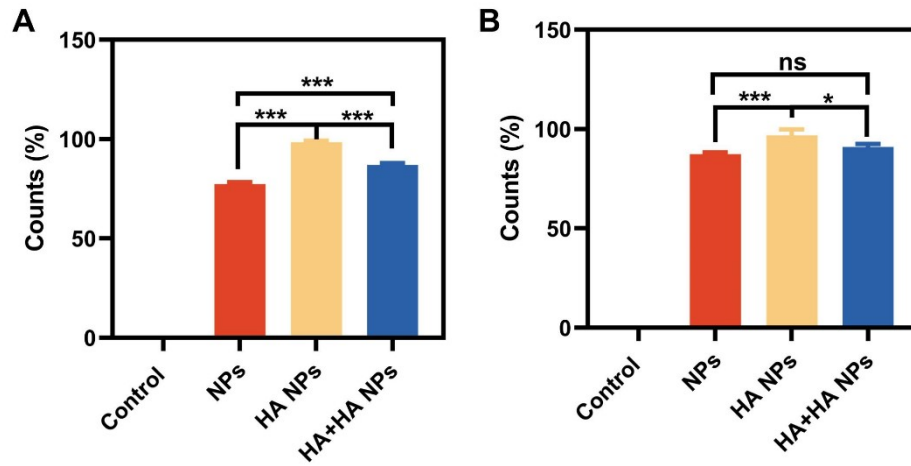
## Supporting information



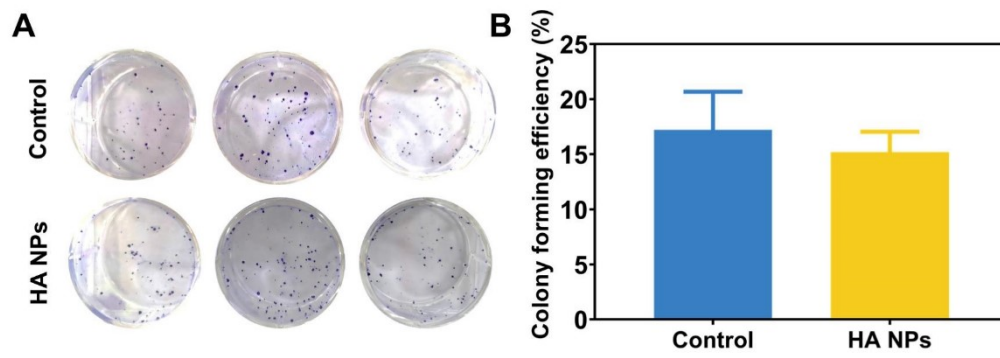
**Supplementary Figure 1.** The cumulative release profile of siCD98 and Ac2-26 from nano-bomb nanoparticles in different pH PBS. (A). The cumulative release profile of siCD98 and Ac2-26 in pH 7.4 PBS. (B). The cumulative release profile of siCD98 and Ac2-26 in pH 5.0 buffer.



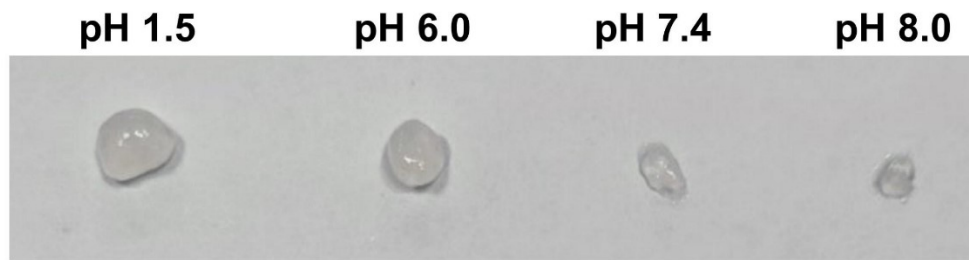
**Supplementary Figure 2. TEM images of HA NPs in PBS.**



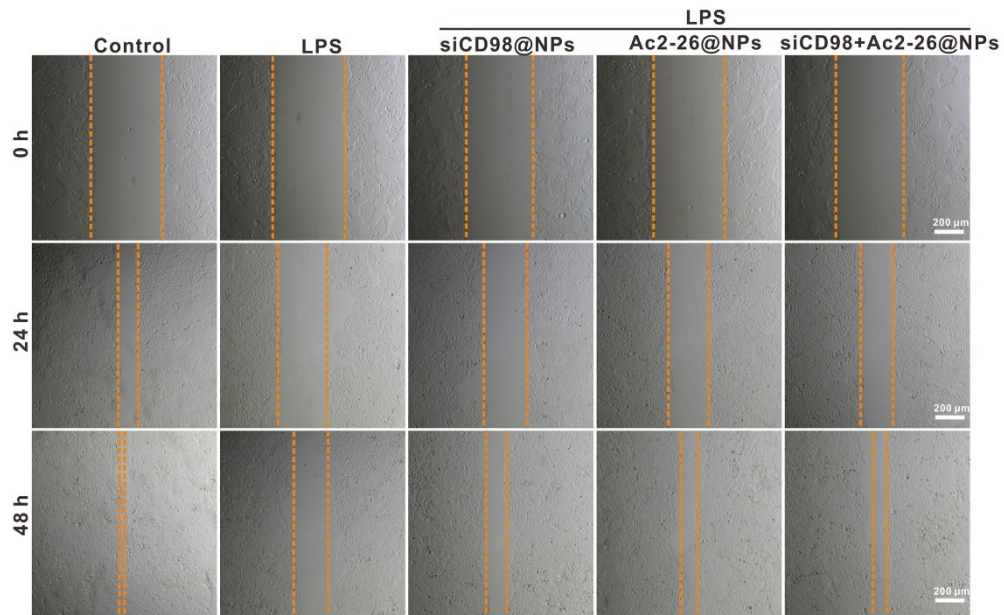
**Supplementary Figure 3. Statistical analysis of the detection of cellular uptake of different nanoparticles by flow cytometry.** (A). Statistical analysis of Colon-26 cells uptake efficiency of NPs, HA NPs and free HA+HA NPs by flow cytometry. (B). Statistical analysis of RAW 264.7 cells uptake efficiency of NPs, HA NPs and free HA+HA NPs by flow cytometry.  $n = 3$ ,  $*P < 0.05$ , and  $***P < 0.001$ , ns” represents no significant difference.



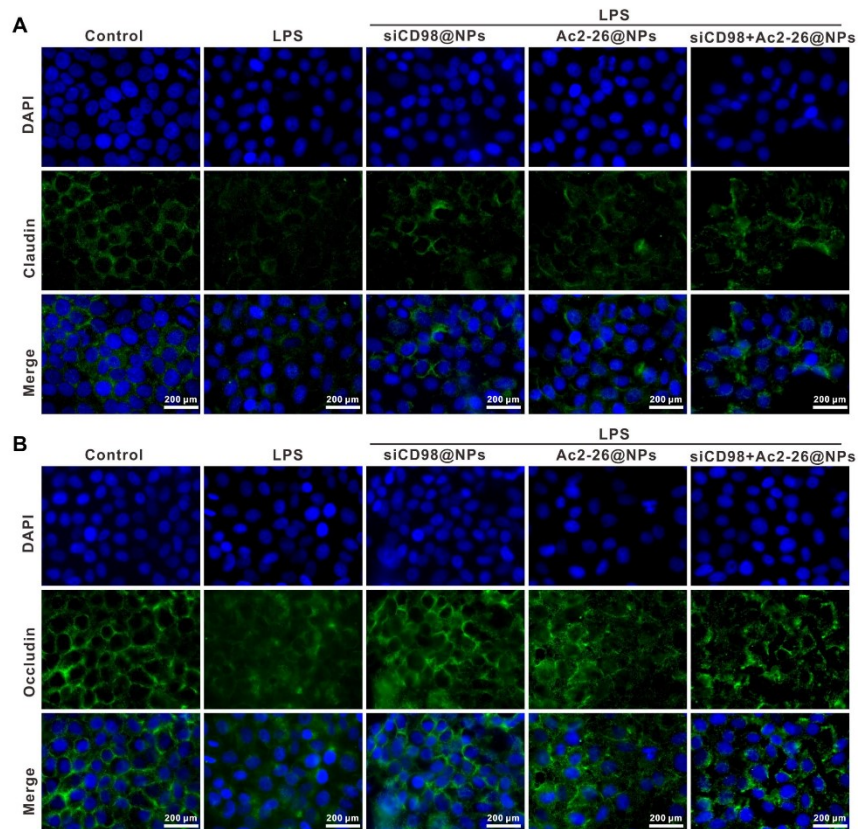
**Supplementary Figure 4. Colony formation assay was used to evaluate the biocompatibility of HA NPs. (A).** Crystal violet stain of HT-29 cells with treated with HA NPs (n = 3). **(B).** Statistical analysis of the clone formation rate of HT-29 cells using ImageJ software.



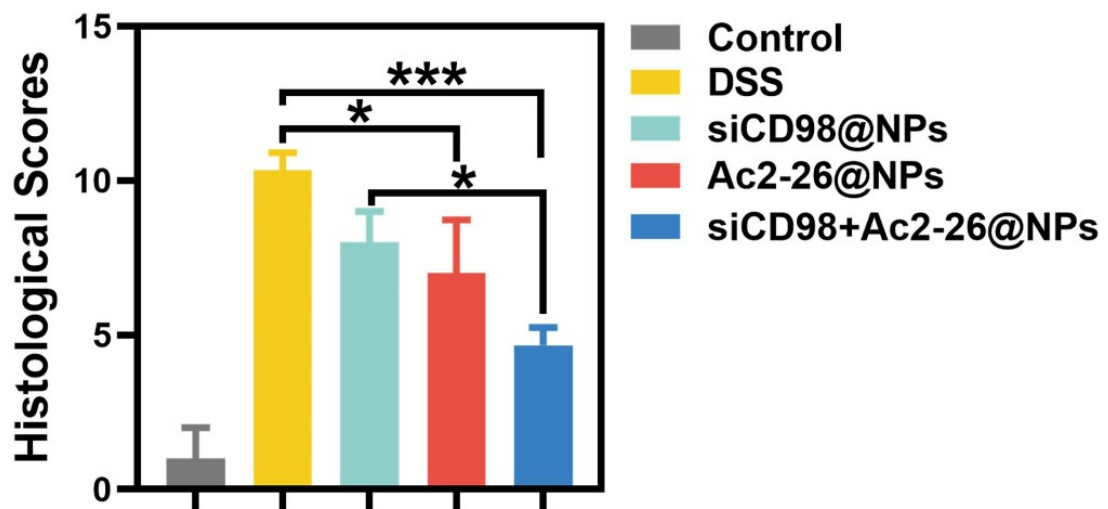
**Supplementary Figure 5. The gelling ability of chitosan/alginate hydrogel in different pH buffer solutions.** 100  $\mu\text{L}$  chitosan solution and sodium alginate were mixed with chelating solution (30 mM  $\text{Na}_2\text{SO}_4$  and 70 mM  $\text{CaCl}_2$ ) in different pH buffer (pH 1.5, 6.0, 7.4, 8.0), then collected respectively.



**Supplementary Figure 6. Wound healing assay analysis of Caco2 cells after different treatments in different times.** Caco-2 cells were incubated with siCD98@NPs and/or Ac2-26@NPs for 0 h, 24 h, 48 h. And LPS (500 ng/mL) was incubated with cells at the same time (n = 3).



**Supplementary Figure 7. Immunofluorescence image of tight junction protein in Caco-2 cells.** Caco-2 cells were incubated with siCD98@NPs and/or Ac2-26@NPs for 12 h. Then LPS (500 ng/mL) was added to the cells and incubated for a further 4 h (n = 3). Photographs were taken using an inverted fluorescence microscope. (A). The fluorescence images of Claudin in Caco-2 cells with different treatments (n = 3). (B). The fluorescence images of Occludin in Caco-2 cells with different treatments (n = 3).



Supplementary Figure 8. Histopathological scoring of colonic tissue in different treatment groups of mice.  $n = 3$ ,  $*P < 0.05$ , and  $***P < 0.001$ .



**Table S1. Primers used for Real-time PCR.**

| <b>Gene name</b> | <b>Forward primer (5'-3')</b> | <b>Reverse primer (5'-3')</b>   |
|------------------|-------------------------------|---------------------------------|
| <b>CD98</b>      | GAGGACAGGCTTTTGATTGC          | TCCAGGCTTTGGGCATCA              |
| <b>TNF-alpha</b> | AGGCTGCCCCGACTACGT            | GACTTTCTCCTGGTATGAGATAGCAA<br>A |
| <b>IL-6</b>      | AGGCTGCCCCGACTACGT            | TTGCCATTGCACAACCTCTTTTC         |
| <b>IL-1beta</b>  | TCGCTCAGGGTCACAAGAAA          | CATCAGAGGCAAGGAGGA AAAC         |
| <b>iNOS</b>      | CCCTTCCGAAGTTTCTGGCAGC        | CCAAAGCCACGAGGCTCTGACAGCC       |
| <b>CD86</b>      | TCAGTCAGGATGGGAGTGGTA         | ATCCAAGAGCCATTCCTACCT           |
| <b>MR</b>        | CATGAGGCTTCTCTTGCTTCTG        | TTGCCGTCTGAACTGAGATGG           |
| <b>GAPDH</b>     | TGTGTCCGTCGTGGATCTGA          | TTGCTGTTGAAGTCGCAGGAG           |