Supplementary Material

A programmable hierarchical-responsive nanoCRISPR elicits robust activation of endogenous target to treat cancer

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# These authors contributed equally to this work.
| Name       | Sequence information                  |
|------------|---------------------------------------|
| TRAIL-F    | GAGCTGAAGCGAGATGCAGGAC                |
| TRAIL-R    | TGACGGAGTTGCCACTTGACT                 |
| HBG1-F     | AATGTGGAAGATGCTGGAGG                  |
| HBG1-R     | GCCAAAGCTGTCAAAGAACC                  |
| SIM1-F     | CGCGGACTAGGAGGGAGAA                   |
| SIM1-R     | GTCGTGAGTCTGATTATGGATGC               |
| DMD-F      | CAACTTTTGCGCATGAGGAGGTTC              |
| DMD-R      | GTAGGTCACTGAAGAGGTTCTC                |
| MIAT-F     | TGGCTGGGGGTCTTGAACCTTT                |
| MIAT-R     | AGGAAGCTGTTCCAGACTGC                  |
| FASLG-F    | AAAGGAGCTGAGGAAAGTGGG                 |
| FASLG-R    | CATAGGTGTCTTCCCATTCCAG                |
| LATS2-F    | AACTCACAGATTTGCAGCCTC                 |
| LATS2-R    | ACACCGACAGTTAGACACATC                 |
| ACTB-F     | CGGGAAATCGGCTGACATTAAG                |
| ACTB-R     | TGACTCTTCTTCTGCATCTCTGG               |
| TRAIL loci | AGAAGAGAGAAATGGGCTTG                  |
| HBG1 loci  | TCCCTGAACCTTTTACAAAAAT                |
| SIM1 loci  | AGACTGAAGAGCAACATGTC                  |
| DMD loci   | ACTCTACTATTGTACAGT                   |
| MIAT loci  | GCGCCCAGAAATTTTAATG                  |
| FASLG loci | CATAGCCTACTAACCTGTTC                 |
| LATS2 loci | CAAATAGGTCCAGAGGCCC                  |
Figure S1. The synthetic route (A), $^1$H NMR (B) and FTIR spectra (C) of the shell.
Figure S2. $^1H$ NMR spectra of the core.

Figure S3. Investigation of the expression of CD44 receptor on surface of HeLa cells by flow cytometry.
Figure S4. Evaluation of the transfection efficiency of different compounds.

(A) Fluorescent photographs of HeLa cells after transfected for 24 h. (B-D) Quantitative analysis by flow cytometry analysis.
Figure S5. Quantitative analysis of transfection efficiency under 0~20% FBS medium.

Figure S6. The repeated experiment of western blot.
Figure S7. (A) Tumor weight and (B) body weight of mice after different treatments.

Figure S8. H&E staining of main organs for toxicity analysis.