## **Supporting Information**

## Crosslinked Histone as a Nanocarrier for Gut Delivery of Hydrophobic Cargos

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**Figure S1**: A) UV-VIS spectrum of ONc,BPc and ZnBNc in DCM (left) and after protein loading (right) **B**) Agarose gel electrophoresis of dye-loaded proteins, the gel was prepared using 7% agarose, run time 30 minutes at 70V, negative electrode to the left. Agarose gel was dissolved at concentration of 0.7% in TAE buffer and after loading the proteins, the gel was run at 70 V for 50 minutes and the gel was imaged using Bio-Rad ChemiDoc imager.



Figure S2: Size (left) and zeta potential (right) as measured with DLS for genipin-crosslinked Histone/ONc.



**Figure S3**: Flow cytometry showing uptake of histone nanoparticles crosslinked with genipin following 4 hr incubation with murine RAW 264.7. RAW264.7 murine macrophage cells were obtained from the American Type Culture Collection and cultured in Dulbecco's modified Eagle's medium with 10% fetal bovine serum (FBS) and 1% penicillin/streptomycin. For the in vitro uptake studies, RAW264.7 cells  $(5 \times 10^5 / \text{ well})$  were cultured in a 24-well plate overnight to reach 70–80% confluence. Cells were then treated with 1 µg/mL genipin crosslinked histone nanoparticles.



**Figure S4: Murine RAW 264.7 activation with histone nanoparticles.** RAW264.7 murine macrophage cells were obtained from the American Type Culture Collection and cultured in Dulbecco's modified Eagle's medium with 10% heat inactivated fetal bovine serum (FBS) and 1% penicillin/streptomycin. LPS was used at 10 ng/mL while histone nanoparticles were used at total protein concentration of 50  $\mu$ g/mL. Non-crosslinked histone was degraded or separated from genipin crosslinked histone nanoparticles either by addition of 1 mg/mL pepsin for 2 hr at pH =1.5 then adjusting the pH to 7.4 to inactivate the pepsin or by centrifugal filtration through a 100 KDa filter. TNF- $\alpha$  was measured by ELISA. Analysis was done with one way ANOVA with posthoc Dunnett test compared to control (\*\*\*\*P<0.0001)