Electronic Supplementary Information

Combo-targeted Nanoassemblies as a Chemotherapy Delivery System against Peritoneal Carcinomatosis Colorectal Cancer

Ming-Yin Shen^{a,b,§}, Siou-Han Chang^{a,§}, Te-I Liu^a, Ting-Yu Lu^a, Arjun Sabu^a, Hsin-Hung Chen^a, Hsin-Cheng Chiu^{a,*}

^aDepartment of Biomedical Engineering and Environmental Sciences, National Tsing Hua University, Hsinchu 300, Taiwan

^bDepartment of Surgery, China Medical University Hsinchu Hospital, Hsinchu County 30272, Taiwan

*Corresponding Author: Email: hscchiu@mx.nthu.edu.tw

[§]These authors contributed equally to this work



Figure S1. Synthetic routes, chemical structures and ¹H-NMR spectra of (a) NAcHis-TPGS in DMSO-d₆ and (b) FA-TPGS in CDCl₃ at 25 °C.



Figure S2. DLS size distribution profiles of various drug-free NPs in phosphate buffer (pH 7.4, I 0.1 M) at 25 °C.



Figure S3. Cumulative SN38 release of various drug-loaded nanoformulations in phosphate buffers of pH 6.6 and 6.0.



Figure S4. Cell viability of CT26 cells treated with drug-free NPs at varying concentrations for 6 h. Error bars represent mean \pm s.d (n = 6).



Figure S5. (a) CLSM fluorescence images of three types of cancer cells incubated with SN-TNPs and SN-FNPs at pH 7.4. Nile red was shown in red and the nucleus was stained with Hoechst 33242 in blue. Scale bars are 10 μ m. IOD was obtained by analyzing 10 randomly selected fluorescence images. (b,c) Intracellular SN38 fluorescence intensity of the cancer cells incubated with various NP formulations at pH 7.4 (b) with and (c) without addition of free FA (2 mM). Error bars represent mean \pm s.d (n = 6).



Figure S6. *In vivo* fluorescence images of CT26.Luc tumor-bearing mice at (a) day 1 and (b) 3 after tumor inoculation.



Figure S7. (a) Fluorescence images and quantification analyses of tumor sections harvested from pcCRC tumor-bearing mice at day 7 after treatments (n = 10). Cell nuclei and apoptosis were stained with Hoechst 33342 (blue) and caspase-3 marker (green), respectively. Scale bars are 50 µm. (b) Histological examination of the sections of tumors harvested from pcCRC tumor-bearing mice treated with various NP formulations by H&E staining. Scale bars are 200 µm.



Figure S8. (a) Body weights (n = 8) and (b) liver function index of pcCRC-bearing mice receiving various treatments (n = 8). Liver index was obtained on day 14.



Figure S9. Histological examination of the sections of major organs and colon harvested from pcCRC tumor-bearing mice treated with various NP formulations by H&E staining. Scale bars are 200 μm.