Supporting Information for

Copper (II)/cis-platinum -loaded nanogels as an adjuvant potentiate

disulfiram antitumor efficacy

Yu Geng^{‡a,b}, Rui Sun ^{‡*a,b}, Yifan Zhang ^a, Zhuxian Zhou ^{a,b}, Youqing Shen ^{*a,b}

a Center for Bionanoengineering and Key Laboratory of Biomass Chemical Engineering of Ministry of Education, College of Chemical and Biological Engineering, Zhejiang University, Hangzhou, China ^b ZJU-Hangzhou Global Scientific and Technological Innovation Center, Hangzhou, Zhejiang 311215, China

*Corresponding author. E-mail: <u>sx19900108@126.com</u> (Rui Sun), <u>shenyq@zju.edu.cn</u> (Youqing Shen)

‡ Yu Geng and Rui Sun contributed equally to this work. The manuscript was written through contributions of all authors. All authors have given approval to the final version of the manuscript.

Fig. S1 SEC curve of PGMA.

Fig. S2 ¹H-NMR spectrums of PGMA (solvent: CDCl₃), PGMA-SAR, and PGMA-IDA (solvent: D₂O).

Fig. S3 Confocal microscopy imaging of the intracellular $^{RhB}PGMA$ and $^{RhB}NG_{Cu2^+}$ nanogels in 4T1 cells.

Fig. S4 Size distribution patterns of PGMA-SAR/CDDP at different molar ratios.

Fig. S5 The ITC titration and fitting curves of adding PGMA-SAR solution to CDDP.

Fig. S6 Size distribution patterns of NG_{CDDP} in water and cell culture medium containing 10% serum.

Fig. S7 The blood Pt concentration as a function of time in the ICR mice after *i.v.* injection of CDDP or NG_{CDDP} at a CDDP dose of 2 mg/kg.

Fig. S8 Histological analysis of major organs in 4T1 cancer model after *i.v.* injection of $CuCl_2$ or NG_{Cu2+} at a copper ions dose of 0.5 mg/kg.

Fig. S9 Histological analysis of kidney in 4T1 cancer model after *i.v.* injection of CDDP or NG_{CDDP} at a CDDP dose of 2 mg/kg.

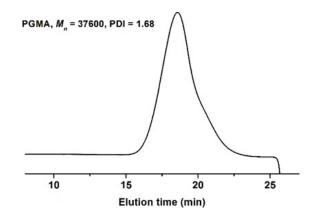


Fig. S1 SEC curve of PGMA.

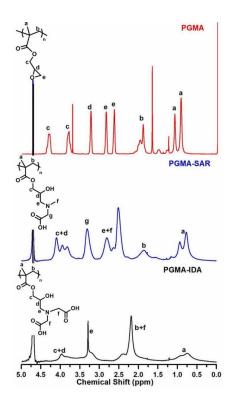


Fig. S2 ¹H-NMR spectrums of PGMA (solvent: CDCl₃), PGMA-SAR, and PGMA-IDA (solvent:

 D_2O).

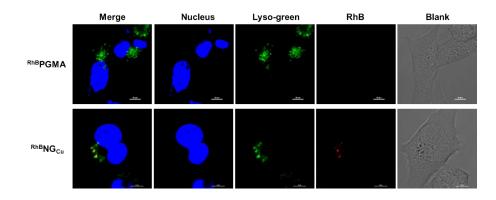


Fig. S3 Confocal microscopy imaging of the intracellular ^{RhB}PGMA and ^{RhB}NG_{Cu2+} nanogels in 4T1 cells. Confocal microscopy images taken from the RhB fluorescence channel (red) and merged with the images taken from the Hoechst fluorescence channel (blue) and Lyso-Tracker Green (green) of the cells after 2 h incubation with ^{RhB}PGMA and ^{RhB}NG_{Cu2+} nanogels (the RhB - eq. dose used for the experiments was 0.5 μ g/ mL). The cells were imaged using a 60× oil-immersion objective; scale bars: 20 μ m.

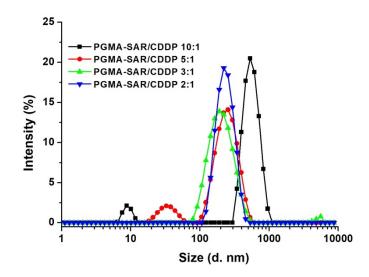


Fig. S4 Size distribution patterns of PGMA-SAR/CDDP at different molar ratios.

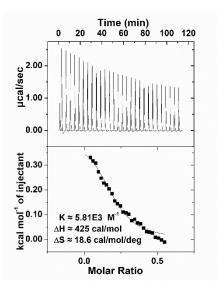


Fig. S5 The ITC titration and fitting curves of adding PGMA-SAR solution (50 mM) to CDDP (10 mM) at 25 °C

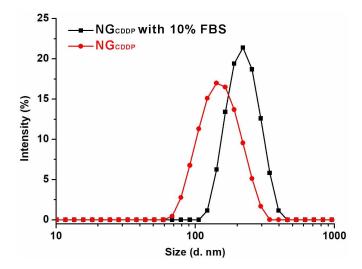


Fig. S6 Size distribution patterns of NG_{CDDP} in water and cell culture medium containing 10% serum.

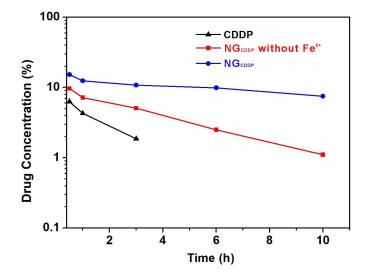


Fig. S7 The blood Pt concentration as a function of time in the ICR mice after *i.v.* injection of CDDP or NG_{CDDP} at a CDDP dose of 2 mg/kg.

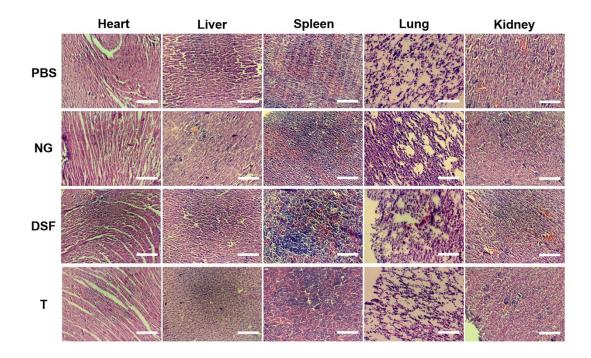


Fig. S8 Histological analysis of major organs in 4T1 cancer model after *i.v.* injection of CuCl₂ or NG_{Cu2+} at a copper ions dose of 0.5 mg/kg (scale bar: 1 mm).

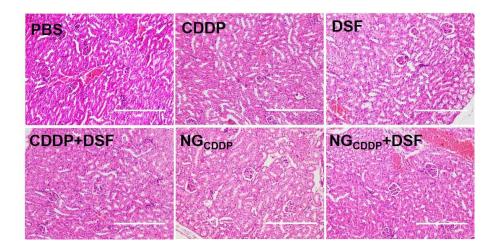


Fig. S9 Histological analysis of kidney in 4T1 cancer model after *i.v.* injection of CDDP or NG_{CDDP} at a CDDP dose of 2 mg/kg (scale bar: 1 mm).