

Supplementary Material

Programmable Site-Specific Delivery of Alkaline Phosphatase-Activatable Prodrug and Mitochondria-Targeted Cyclopeptide for Combination Therapy in Colon Cancer

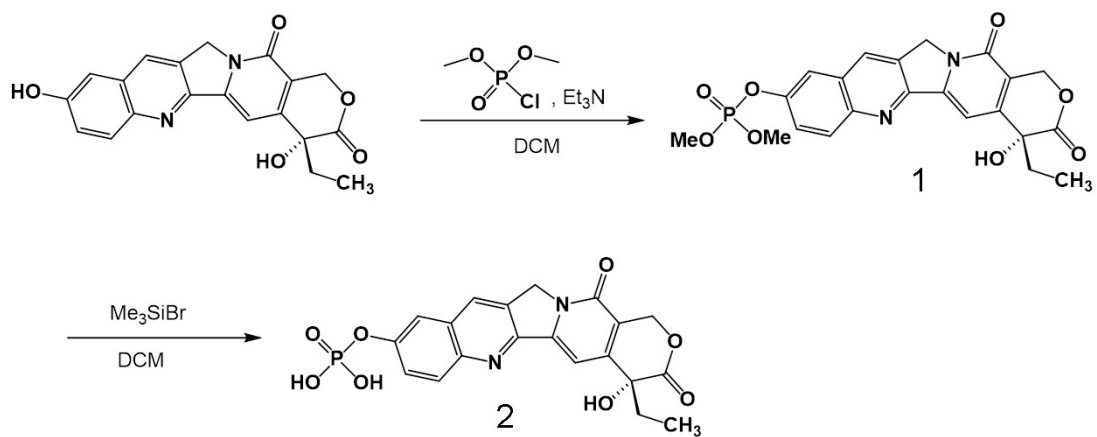
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Supplementary figures

1. **Scheme S1.** Synthesis of CPTP.
2. **Fig. S1** ¹H NMR spectrum of CPTP in DMSO.
3. **Fig. S2** ¹³C NMR spectrum of CPTP in DMSO.
4. **Fig. S3** ³¹P NMR spectrum of CPTP in DMSO.
5. **Fig. S4** MS spectrum of CPTP.
6. **Fig. S5** Long-term-stability study of the size of CPTP/RA-HALipo in PBS or DMEM with 10% FBS.
7. **Fig. S6** GSH depletion rate of CPTP/RA-HALipo, RA-S-S-Cy, and empty HALipo, calculated from the GSH/GSSG assay kit (n = 3).
8. **Fig. S7** Co-localization images of CPTP/RA-HALipo in cells.
9. **Fig. S8** Quantitative analysis of fluorescence intensity of tumor regions in Fig. 8.
10. **Fig. S9** Body weight variation of tumour-bearing mice during treatment.
11. **Fig. S10** H&E stained images of tissue sections from different organs of mice after CPTP/RA-HALipo treatment and the age-matched healthy mice without treatment (control).
12. **Fig. S11** Biochemical indexes analysis of aspartate aminotransferase (AST), alanine aminotransferase (ALT), creatinine (CREA) and blood urea nitrogen (BUN) of the mice after various treatments. All error bars present as mean±SD (n=6).
13. **Table. S1** The routine blood tests with mice after CPTP/RA-HALipo treatment and the age-matched mice without treatment (control).



Scheme S1 Synthesis of CPTP.

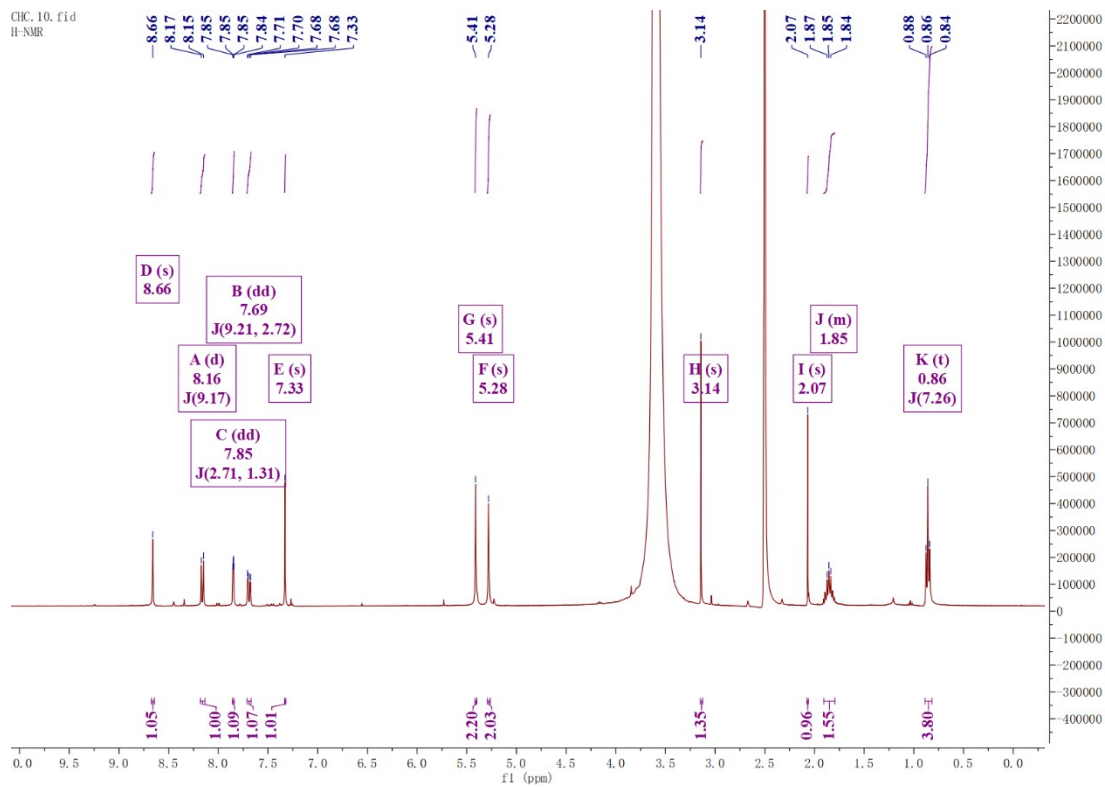


Fig. S1 ^1H NMR spectrum of CPTP in DMSO.

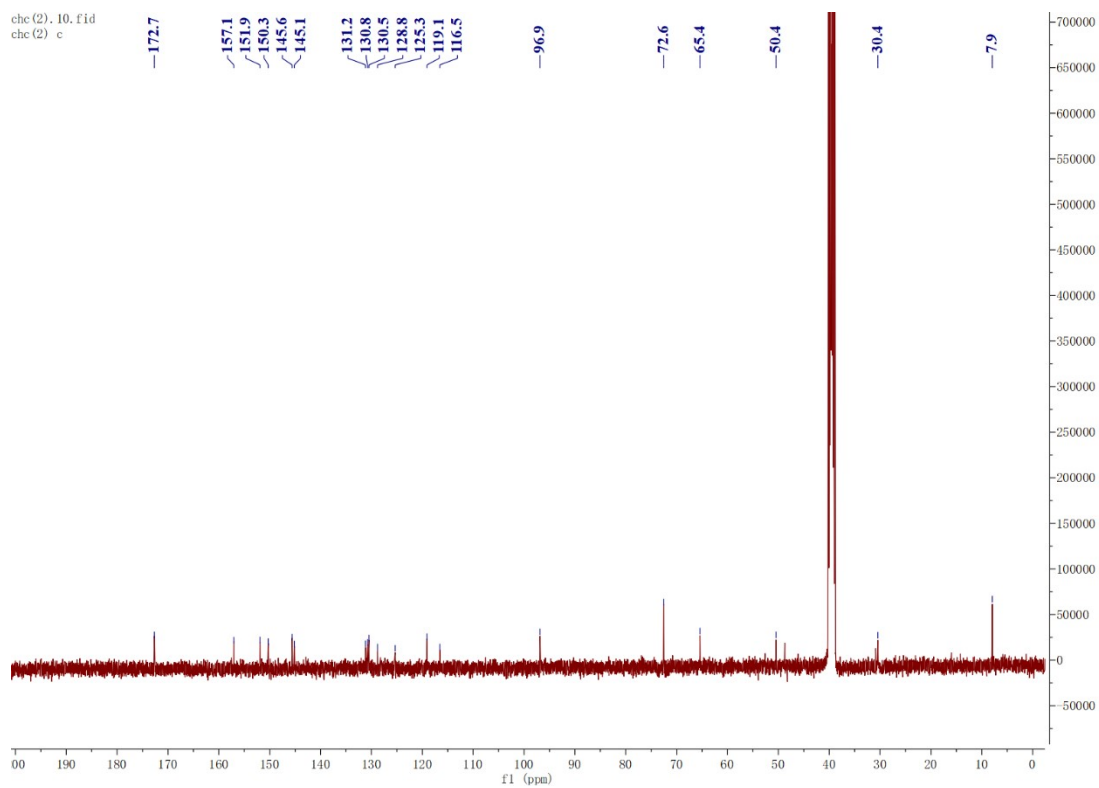


Fig. S2 ^{13}C NMR spectrum of CPTP in DMSO.

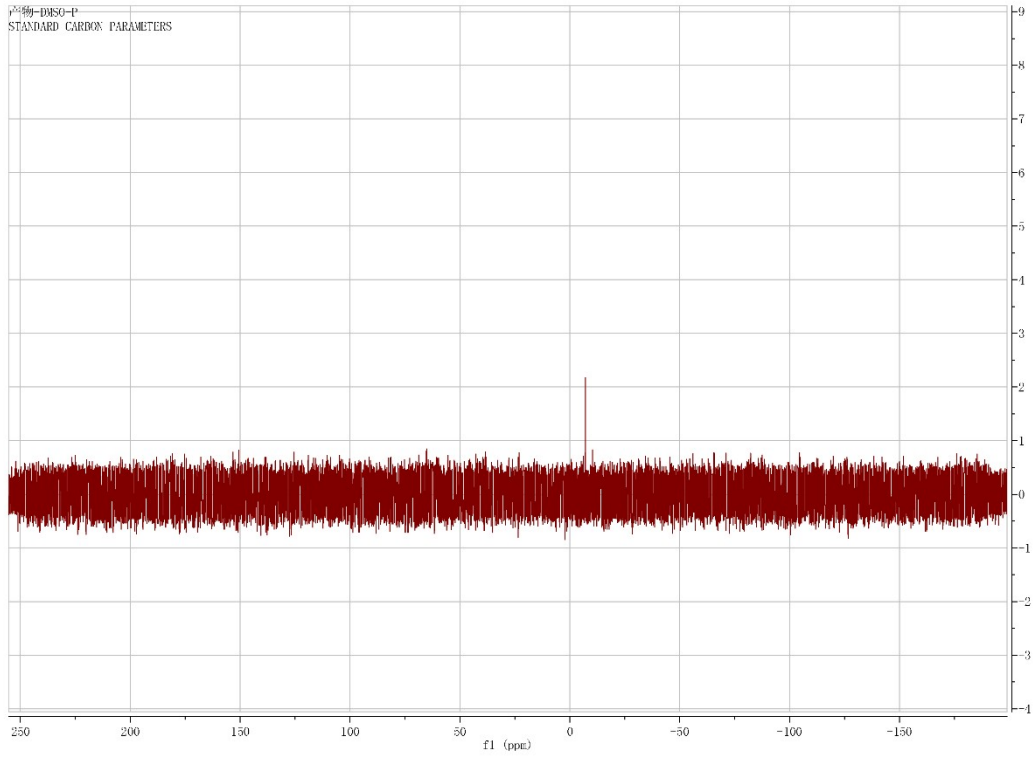


Fig. S3 ^{31}P NMR spectrum of CPTP in DMSO.

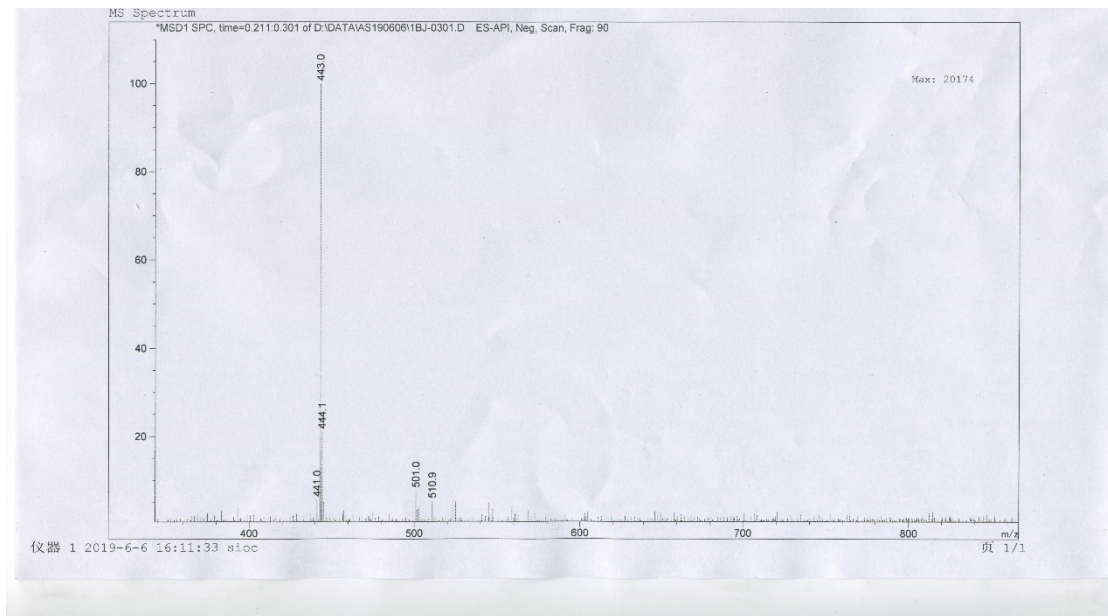


Fig. S4 MS spectrum of CPTP.

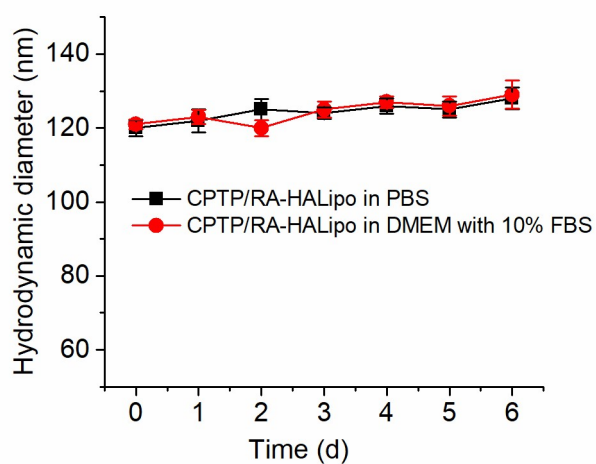


Fig. S5 Long-term-stability study of the size of CPTP/RA-HALipo in PBS or DMEM with 10% FBS.

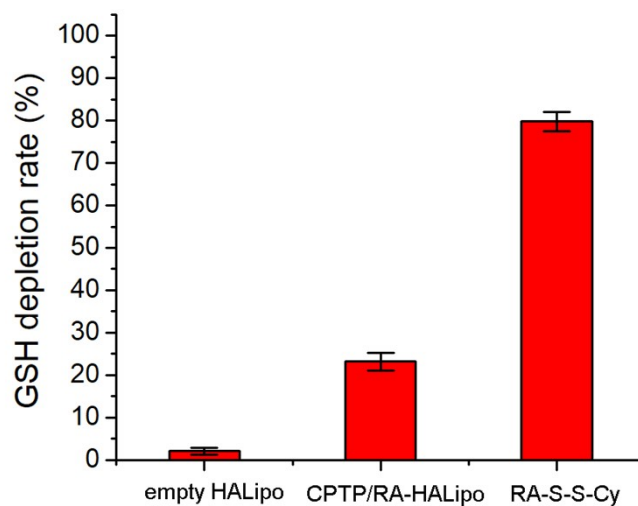


Fig. S6 GSH depletion rate of CPTP/RA-HALipo, RA-S-S-Cy, and empty HALipo, calculated from the GSH/GSSG assay kit (n = 3).

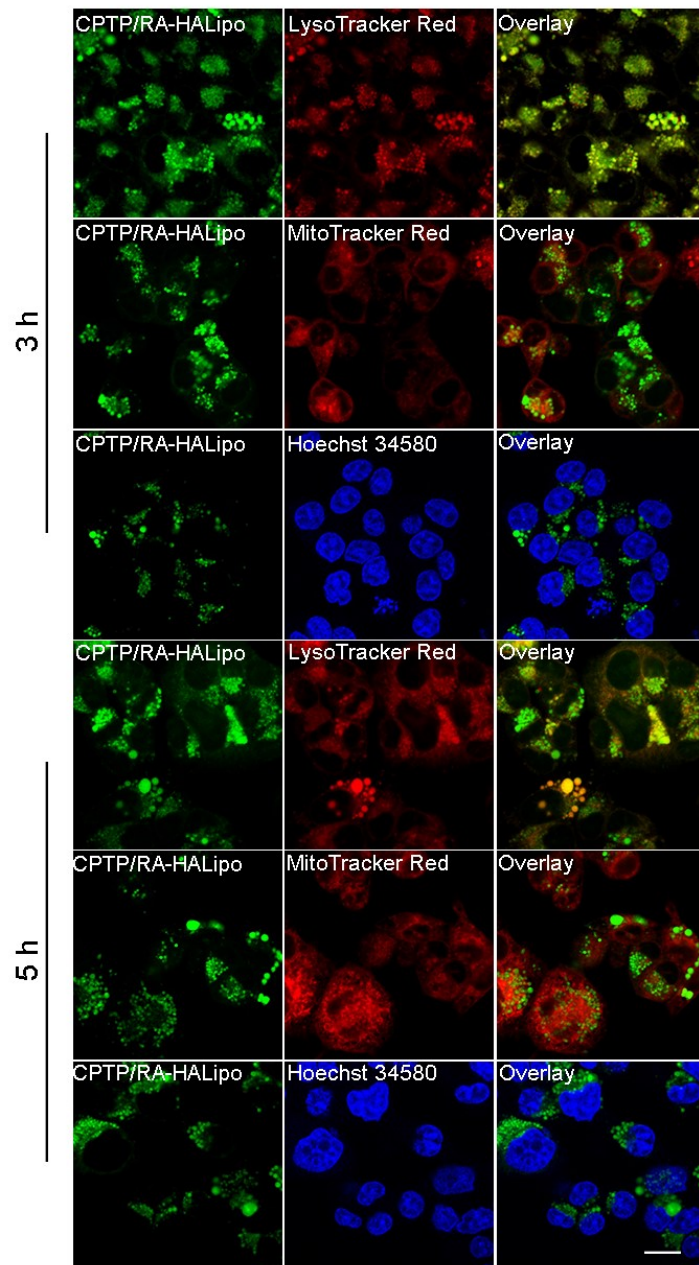


Fig. S7 Co-localization images of CPTP/RA-HALipo in cells. Caco-2 cells were incubated with CPTP/RA-HALipo at 37 °C for 3 h or 5 h, and then incubated with 100 nM LysoTracker Red, Hoechst 34580 and MitoTracker Red 10 min. Scale bar: 20 μ m.

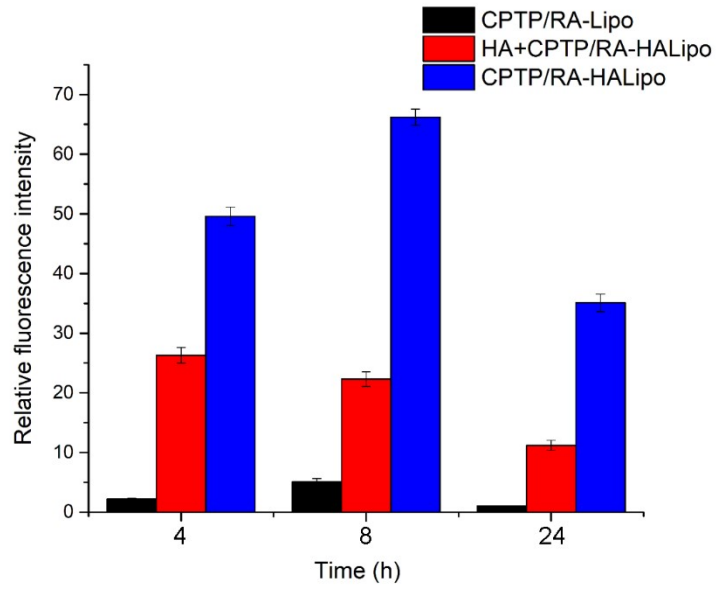


Fig. S8 Quantitative analysis of fluorescence intensity of tumor regions in Fig. 8.

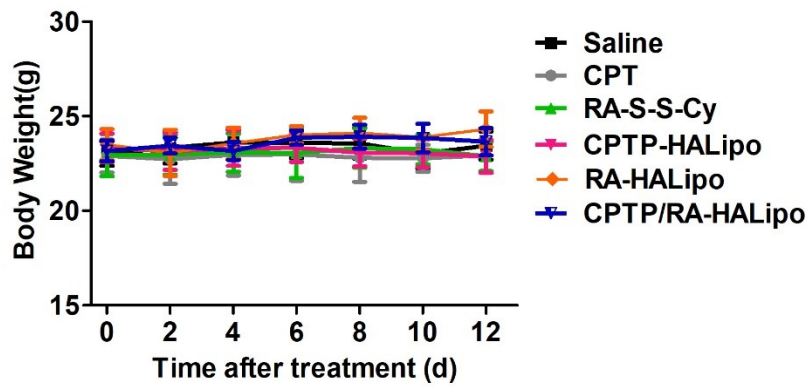


Fig. S9 Body weight variation of tumour-bearing mice during treatment.

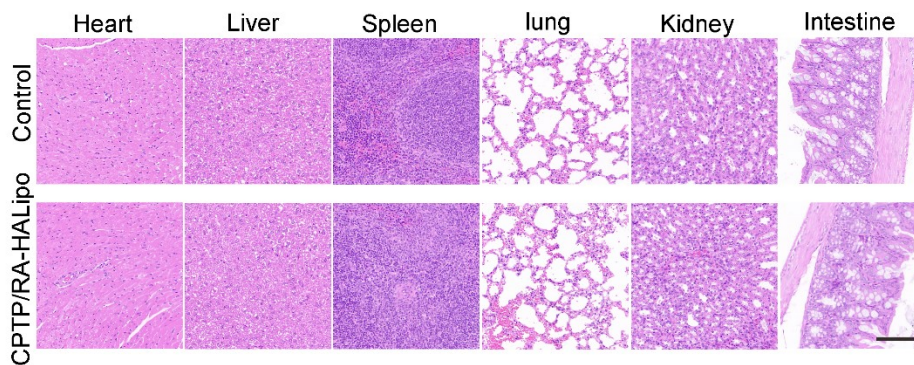


Fig. S10 H&E stained images of tissue sections from different organs of mice after CPTP/RA-HALipo treatment and the age-matched healthy mice without treatment (control).

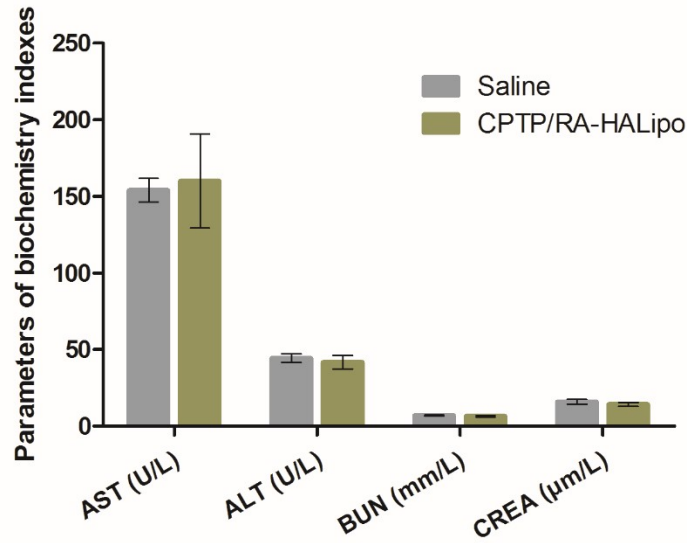


Fig. S11 Biochemical indexes analysis of aspartate aminotransferase (AST), alanine aminotransferase (ALT), creatinine (CREA) and blood urea nitrogen (BUN) of the mice after various treatments. All error bars present as mean±SD (n=6).

Parameters	Control	CPTP/RA-HALipo
WBC ($10^9/L$)	9.36 ± 1.92	7.51 ± 2.29
RBC ($10^{12}/L$)	10.6 ± 0.48	10.48 ± 0.2
HGB (g/dL)	14.89 ± 0.56	14.97 ± 0.57
HCT (%)	48.3 ± 2.13	48.03 ± 1.65
MCV (fL)	45.57 ± 0.58	45.83 ± 1.48
MCH (pg)	14.04 ± 0.28	14.27 ± 0.53
MCHC (g/dL)	30.81 ± 0.58	31.11 ± 0.27
PLT ($10^9/L$)	663.29 ± 61.47	620.86 ± 27.97
NEU (%)	14.37 ± 2.52	11.03 ± 4.73
LYM (%)	73.13 ± 7.17	71.74 ± 4.42
MONO (%)	1.34 ± 0.45	1.43 ± 0.42
EOS (%)	4.21 ± 0.93	6.9 ± 3.82
BASO (%)	0.33 ± 0.08	0.37 ± 0.11
NEUT ($10^9/L$)	1.37 ± 0.48	0.91 ± 0.5
LYMP ($10^9/L$)	6.35 ± 1.29	4.75 ± 1.79
MONO ($10^9/L$)	0.12 ± 0.07	0.07 ± 0.04
EOS ($10^9/L$)	0.39 ± 0.13	0.61 ± 0.25
BASO ($10^9/L$)	0.03 ± 0.01	0.03 ± 0.01

CHCM (g/dL)	31.21 ± 0.72	31.26 ± 0.21
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Table. S1 The routine blood tests with mice after CPTP/RA-HALipo treatment and the age-matched mice without treatment (control).