Supplementary Information

ROS-scavenging Nanomedicine for "Multiple Crosstalk" Modulation in Non-alcoholic Fatty Liver Disease

Xiaofei Xin[a,b,#], Jingjing Li[a,#], Wantao Wu[a,#], Pengbo Zhao[a], Yang Yang[a], Ying Zhu[a], Lianjie Ren[a,d], Chao Qin[a,*], Lifang Yin[a,b,c,*]

[a] *Department of Pharmaceutics, China Pharmaceutical University, Nanjing, China*

[b] *NMPA Key Laboratory for Research and Evaluation of Pharmaceutical Preparations and Excipients, China Pharmaceutical University, Nanjing, China*

[c] *Key Laboratory of Drug Quality Control and Pharmacovigilance, China Pharmaceutical University, Nanjing, China; State Key Laboratory of Natural Medicine, China Pharmaceutical University, Nanjing, China*

[d] *Center for Drug Evaluation, National Medical Products Administration, Beijing, China*

Xiaofei Xin[a,#]

Jingjing Li[a,#]

Wantao Wu [a,#]

[#] These authors contributed equally to this work.

[*]Correspondence:

Lifang Yin, Department of Pharmaceutics, China Pharmaceutical University, Nanjing 210009, China; NMPA Key Laboratory for Research and Evaluation of Pharmaceutical Preparations and Excipients, China Pharmaceutical University, Nanjing 210009, China; Key Laboratory of Drug Quality Control and Pharmacovigilance, China

Pharmaceutical University, China; State Key Laboratory of Natural Medicine, China Pharmaceutical University, Nanjing, 210009, China.

Chao Qin, *Department of Pharmaceutics, China Pharmaceutical University, Nanjing 210009, China*.

Lifang Yin, Tel: +86 (025)83271018

E-mail addresses: lifangyin@cpu.edu.cn

Chao Qin, Tel: +86 (025)83271018

E-mail address: nada77@163.com

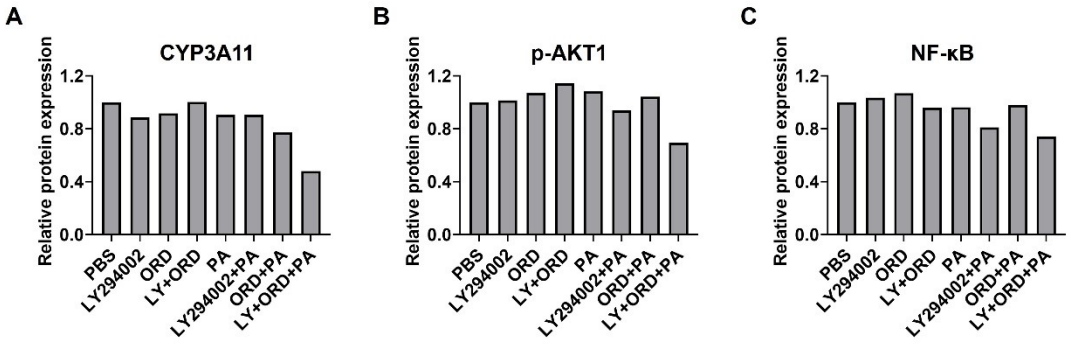

Fig. S1 Semi-quantitative Western blot analysis of AML-12 cells in Fig. 1C.

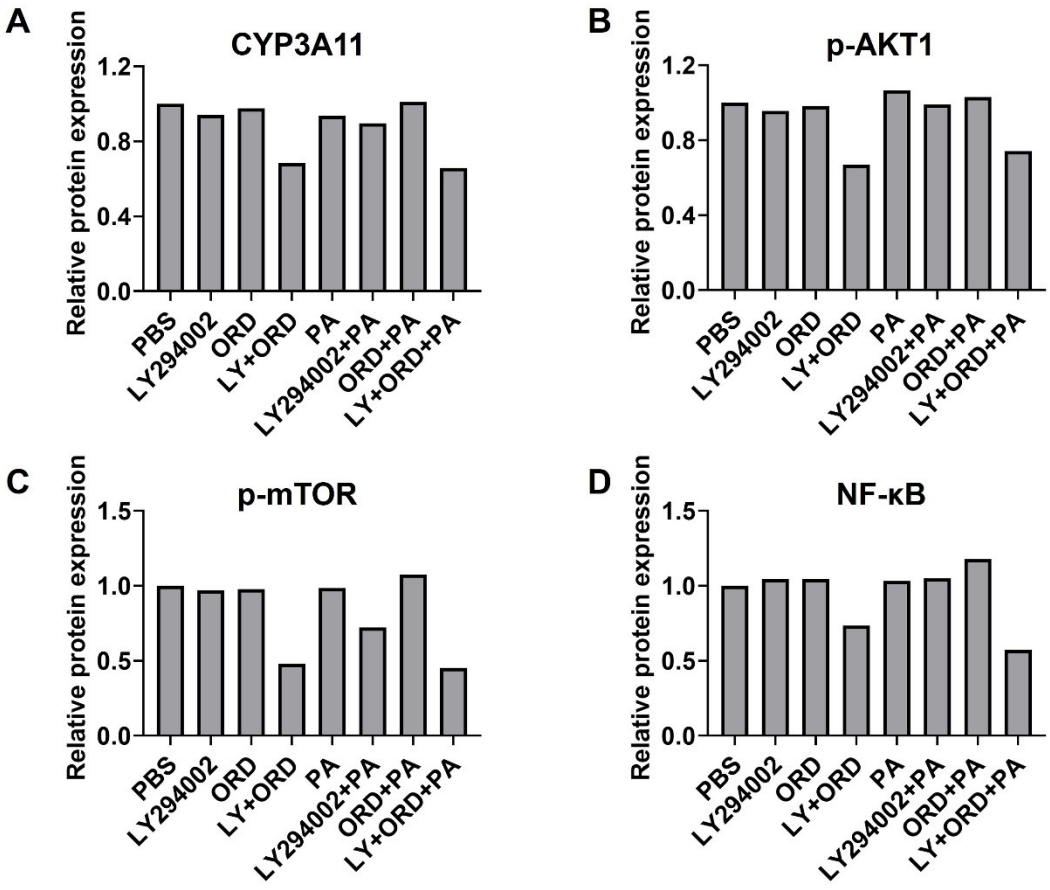

Fig. S2 Semi-quantitative Western blot analysis of LX-2 cells in Fig. 1C.

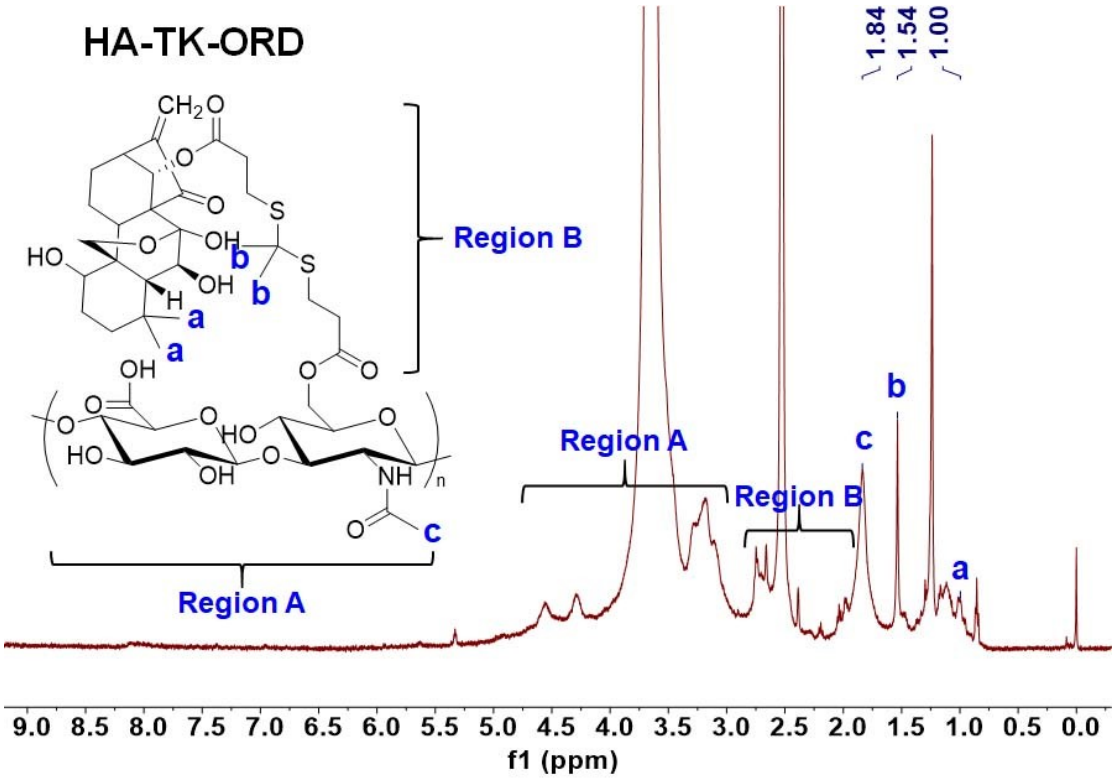

Fig. S3 ^{1}H NMR spectra of HA-TK-ORD in DMSO-*d6* : D_2O = 10 : 1.

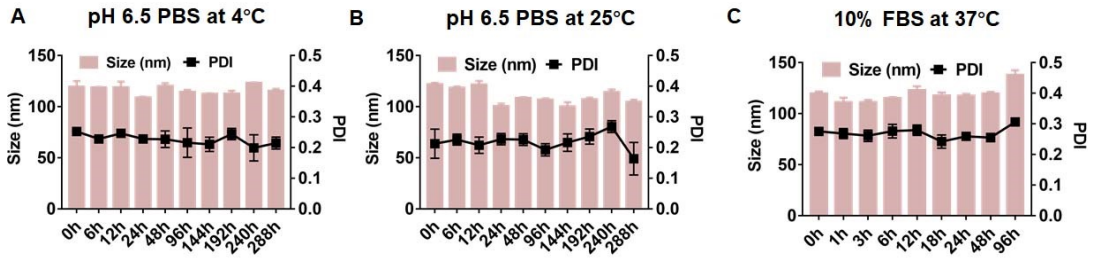

Fig. S4 Stability of RLLs in PBS with a pH level of 6.5 (**A**) at 4℃ and (**B**) at 25℃, and (**C**) in 10% FBS at 37℃, respectively.

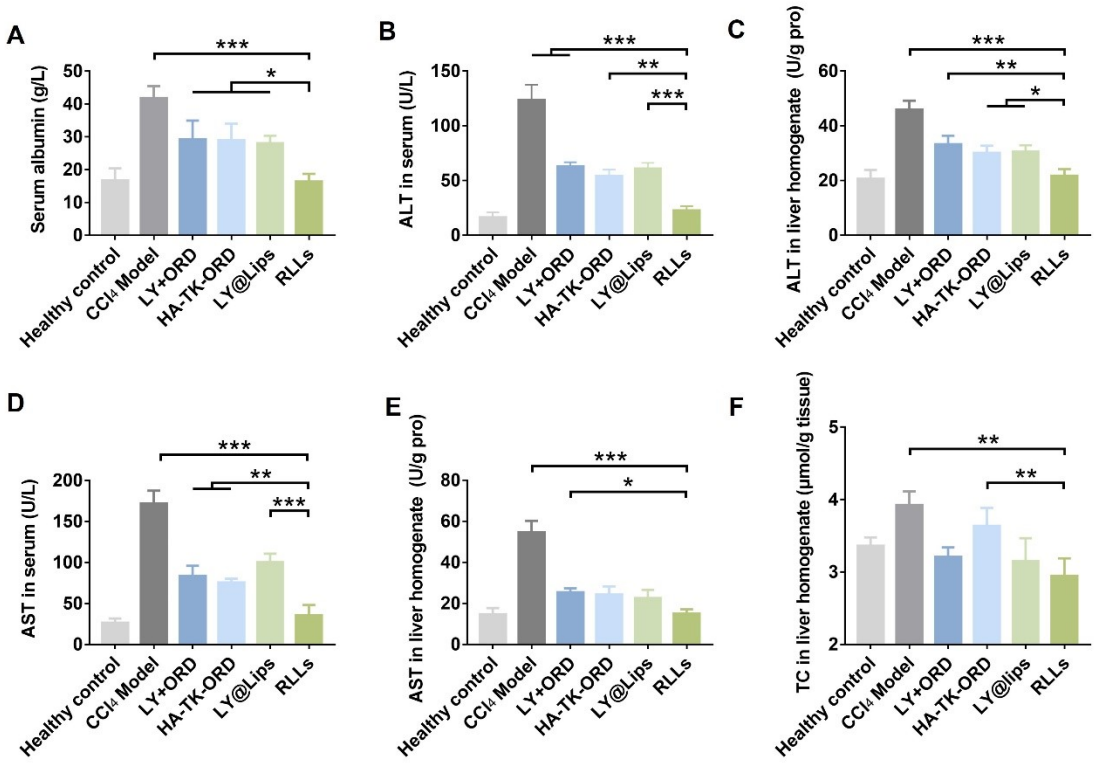

Fig. S5 (**A**) Serum albumin, ALT in (**B**) serum samples and (**C**) liver homogenates, AST (**D**) in serum samples and (**E**) liver homogenates, and (**F**) total cholesterol (TC) levels in liver homogenate, after LY+ORD, HA-TK-ORD, LY@Lips and RLLs treatment, using CCl_4-induced mice and healthy mice as positive and negative control, respectively. Results are presented as the mean ± SD (n=3). NS, not significant; $^{*}P<0.05$, $^{**}P<0.01$ and $^{***}P<0.001$, One-Way ANOVA test.

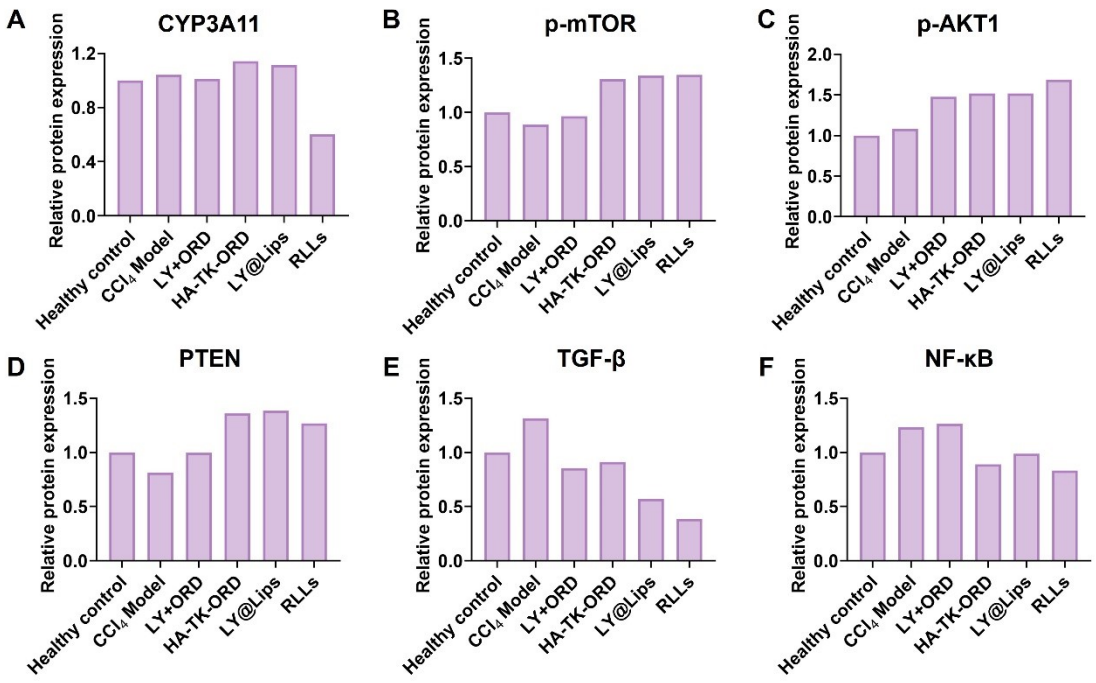

Fig. S6 Semi-quantitative Western blot analysis of Fig. 11B.

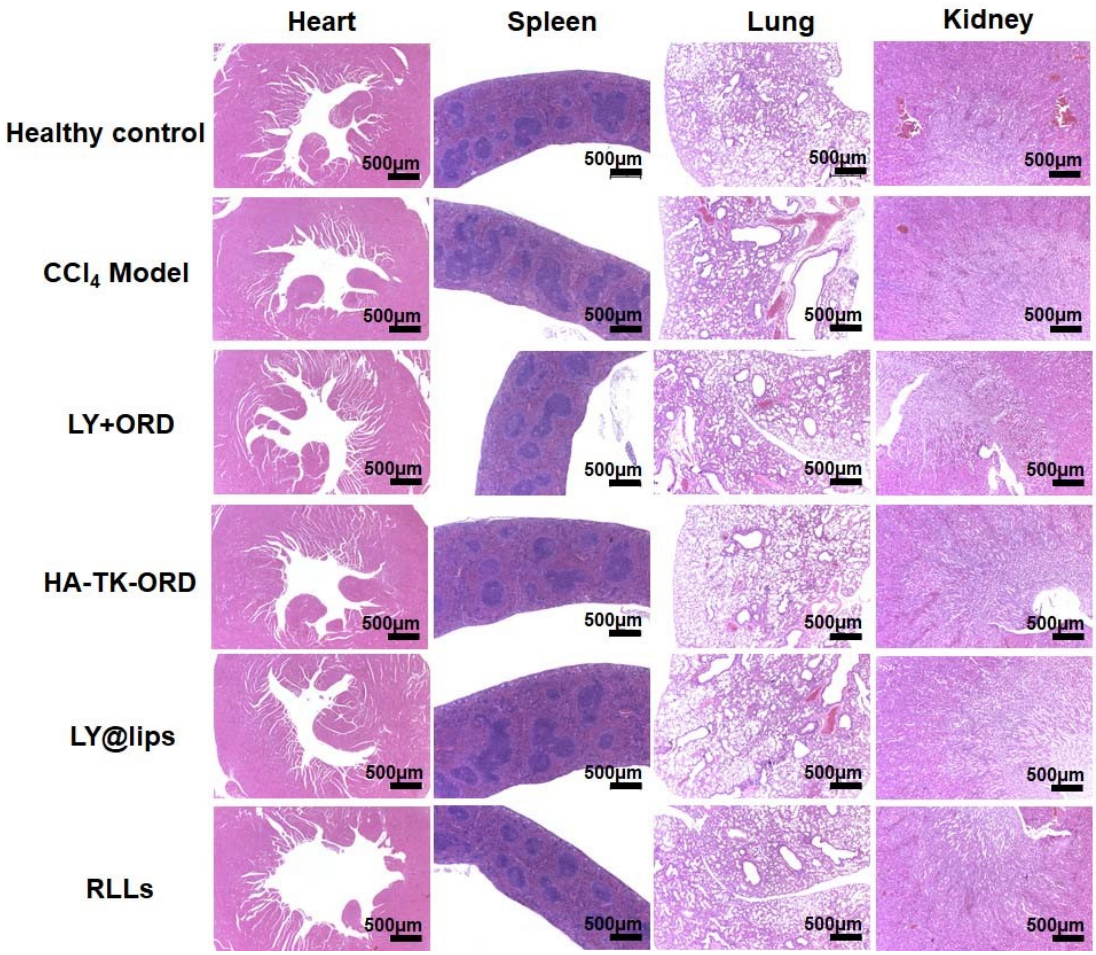

Fig. S7 H&E staining of heart, spleen, lung and kidney indicated the safety and biocompatibility of RLLs.

Table S1. PCR primer sequences

Genes	Forward primer (5'-3')	Reverse primer (5'-3')
Human β-actin	CATGTACGTTGCTATCCAGGC	CTCCTTAATGTCACGCACGAT
Human IRS1	CTGCACAACCGTGCTAAGG	CGTCACCGTAGCTCAAGTCC
Human INSR	CATCCGGGGATCACGACTG	ATCAGGTTGTAGAGGCCGAGT
Mouse β-actin	CGGTTCCGATGCCCTGAGGCTCTT	CGTCACACTTCATGATGGAATTGA
Mouse IRS1	CGATGGCTTCTCAGACGTG	CAGCCCGCTTGTTGATGTTG
Mouse INSR	ATGGGCTTCGGGAGAGGAT	GGATGTCCATACCAGGGCAC
Mouse SOCS3	ATGGTCACCCACAGCAAGTTT	TCCAGTAGAATCCGCTCTCCT