Supporting Information

Quercetin covalently-linked lipid nanoparticles: Multi-faceted killing effect on tumor cells

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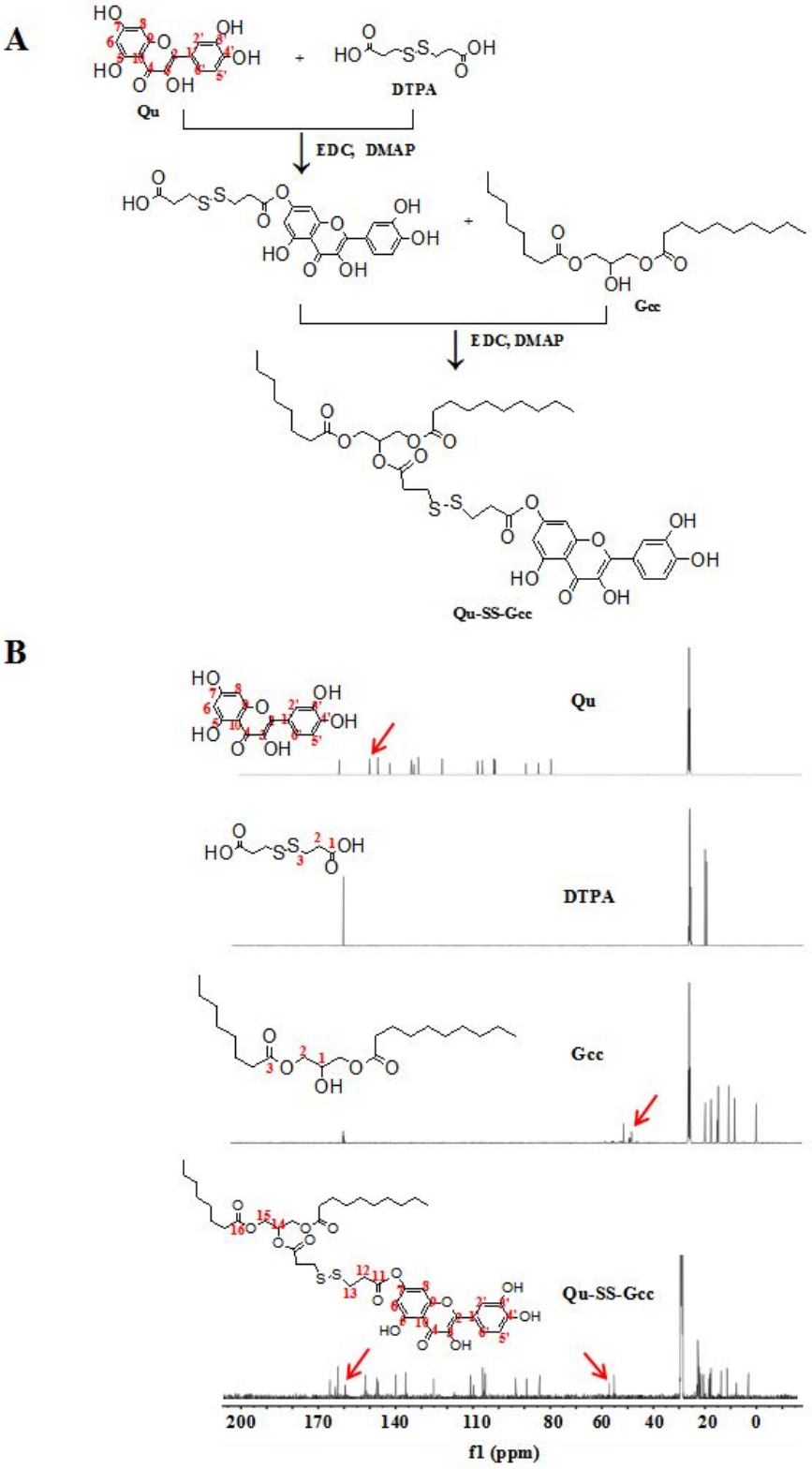
A
Qu
DTPA
EDC, DMAP
Gcc
EDC, DMAP
Qu-SS-Gcc
B
Qu
DTPA
Gcc
Qu-SS-Gcc
200
170
140
110
80
60
40
20
0
f1 (ppm)

Figure S1. Synthetic route to Qu-SS-Gcc and structural characterization. (A) Synthetic route to Qu-SS-Gcc. (B) ^{13}C NMR spectra of Qu, DTPA, Gcc and Qu-SS-Gcc. All the chemicals were dissolved in methanol.

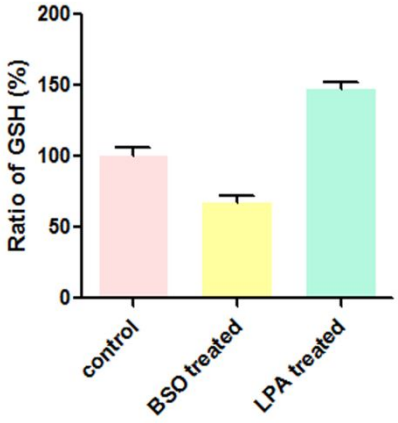

Figure S2. Change of glutathione content in MCF-7/ADR cells after treated with BSO or LPA.

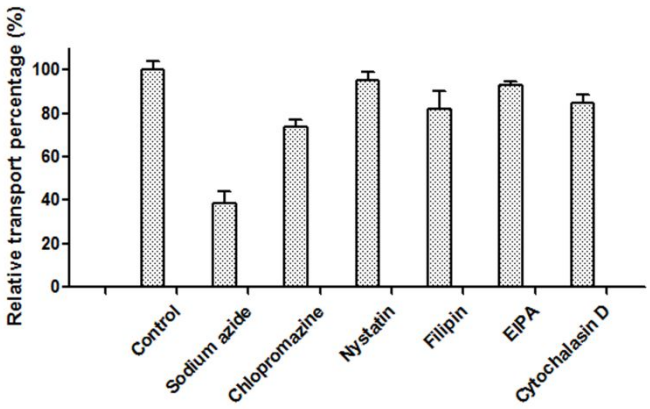

Figure S3. Effects of different inhibitors on the transport of Qu-SS-Gcc LNPs across MDCK cell monolayer.

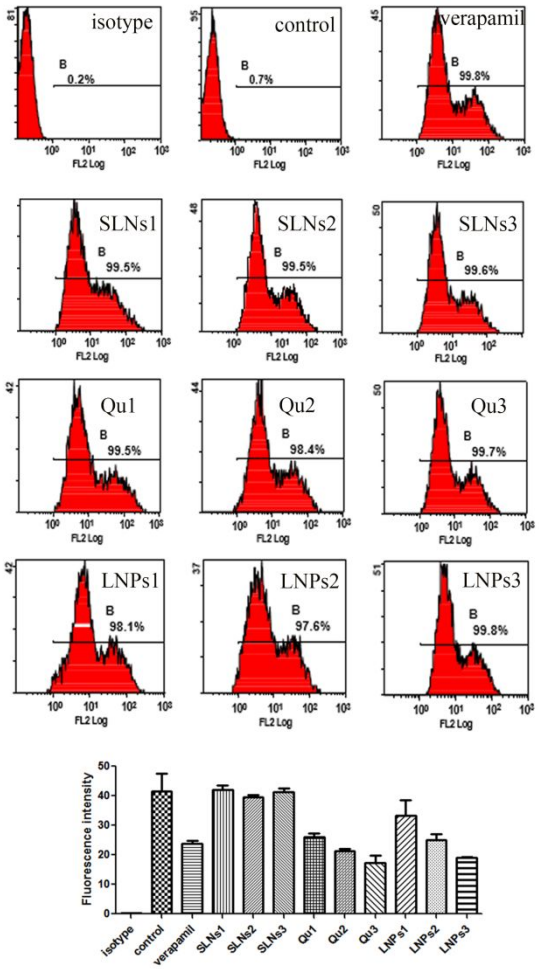

Figure S4. Flow cytometry of P-gp in MCF-7/ADR cells treated with indicated concentrations of Qu or Qu-SS-Gcc LNPs for 24 h. SLNs1, 2, 3 represent 20, 50, and 100 μM MS SLNs respectively; Qu1, 2, 3 represent 20, 50, and 100 μM Qu respectively; LNPs1, 2, 3 represent 20, 50, and 100 μM Qu-SS-Gcc LNPs respectively.

Table S1 Inhibitors used in this study and their functions as well as concentrations

Inhibitors	Function	Final concentration
sodium azide	Energy-Dependent Inhibitor active transport inhibitor	1 mg/mL
	Endocytosis Inhibitors	
nystatin	lipid raft/caveolae-mediated route	30 μM
filipin	lipid raft/caveolae-mediated pathway	5 μg/mL
chlorpromazine	inhibitor of clathrin-mediated pathway	30 μM
EIPA	inhibitor of macropinocytosis pathway	100 μM
cytochalasin D	disrupt actin filaments	5 μM