Supporting Information

Poly(L-lactide)-Vitamin E TPGS Nanoparticles Enhanced the Cytotoxicity of Doxorubicin in Drug-Resistant MCF-7 Breast Cancer Cells

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1. Catalyst

The synthetic routes of new ligand **1** and their Zn complex **2** are outlined in Fig. 1. The ligand **1** was prepared in a moderate yield by the condensation reaction of 2-(tosylaminomethyl)aniline[1] with one molar equivalent of the o-anisaldehyde in ethanol. ^{1}H and ^{13}C NMR spectra, elemental analysis, and Mass spectroscopic data were consistent with the formation of the ligand, **1.** Further reaction of the **1,** with a stoichiometric amount of $ZnEt_2$ resulted in the compound **2.** Compound **2** has been characterized on the basis of ^{1}H and ^{13}C NMR spectroscopic studies, as well as by elemental analysis. All the spectroscopic data are given in the experimental section.

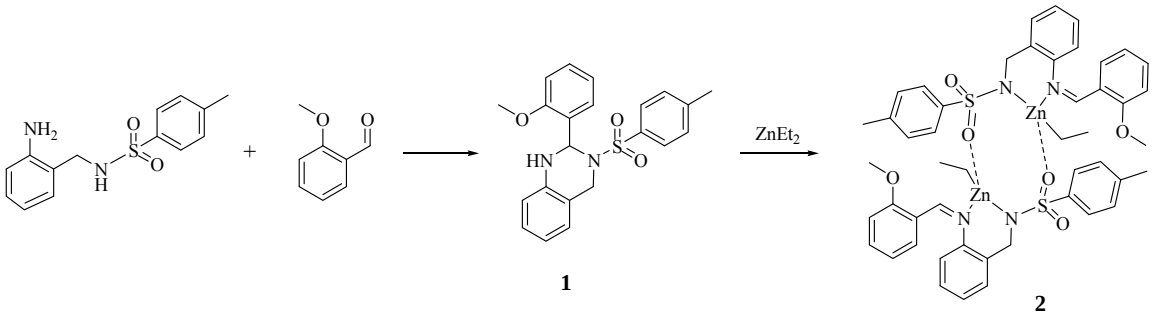

Fig S1. Synthesis of zinc compound

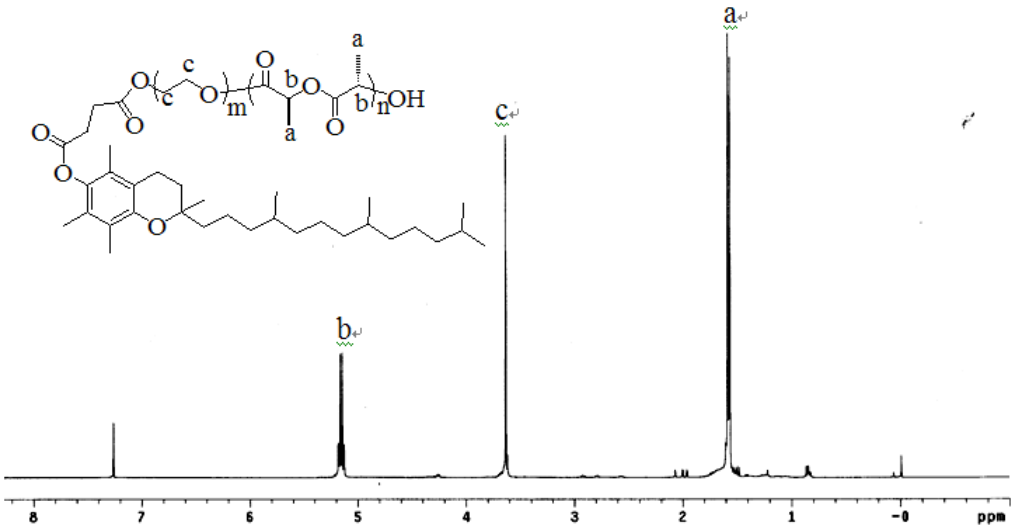

Fig. S2. ^{1}H NMR spectrum of PLA_{40}-TPGS (40 indicates $[LA]_0/[TPGS] = 40$).

2. Stability of Nanoparticles

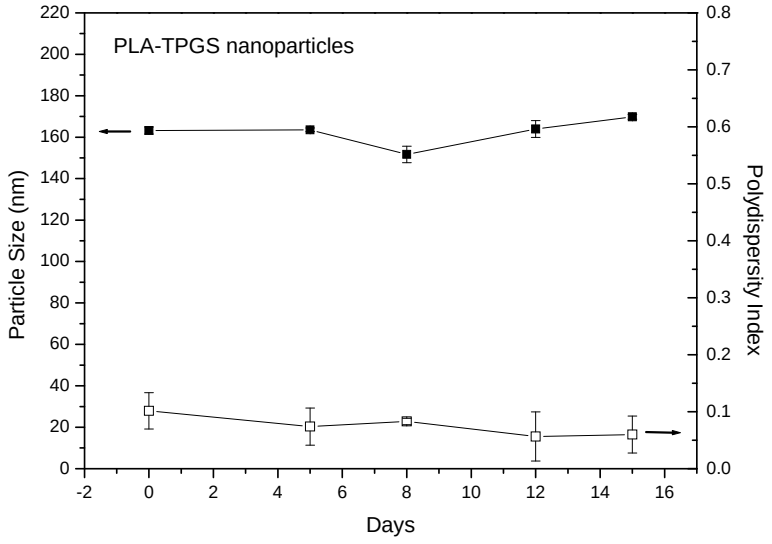

Fig. S3. Stability of doxorubicin-loaded PLA_{40}-TPGS nanoparticlels (polymer/drug ratio : 10/1).

3. P-glycoprotein Expression: Western Blot Analysis

MCF-7/ADR cells were treated with PLA-TPGS or TPGS for 24h, respectively. For Western Blot analysis, cell extracts were first prepared in lysis buffer,[2] and the extracts containing equal amounts of proteins were separated on SDS-PAGE and transferred onto nitrocellulose membranes. The membranes were blocked, washed, and then probed with primary anti-P-gp C19 antibody (sc1517; Santa Cruz Biotechnology, Santa Cruz, CA). After washing, membranes were incubated with horseradish peroxidase-conjugated secondary antibody for 2 h. The labeling was then detected by an enhanced chemiluminescence according to the manufacturer's protocol (Amersham Biosciences, Piscataway, NJ, USA).

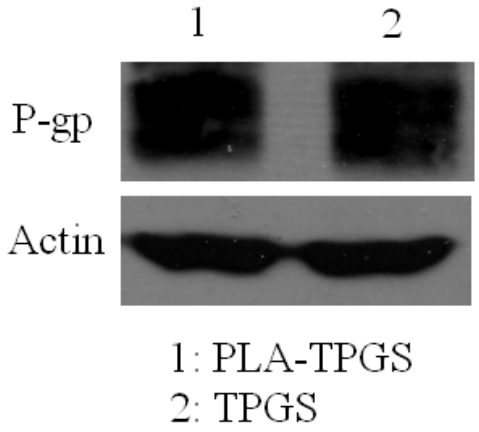

Fig. S4. P-gp expression after PLA-TPGS or TPGS treatment in MCF-7/ADR cells.

4. Intracellular Distribution of Doxorubicin

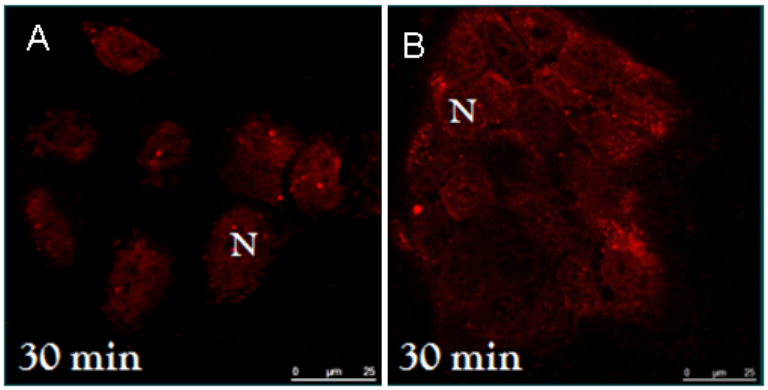

Fig. S5. Intracellular distribution of (A) free doxorubicin in solution and (B) doxorubicin-loaded PLA-TPGS nanoparticles in MCF-7 cells. The concentration of doxorubicin was 20 μM.

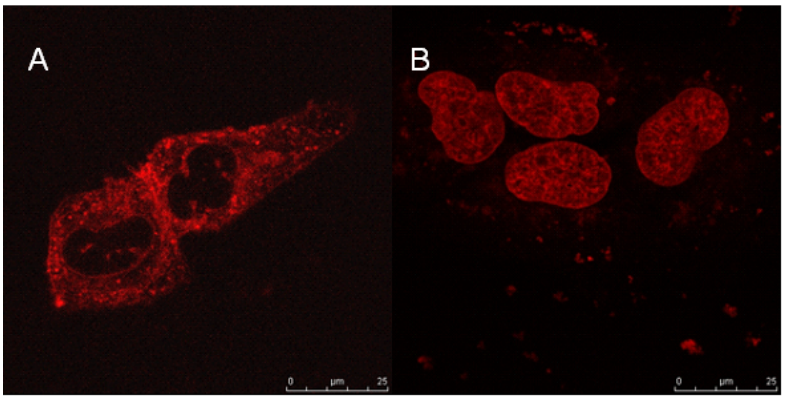

Fig. S6. Intracellular distribution of free doxorubicin in MCF-7/ADR cells detected by confocal microscopy. MCF-7/ADR cells were treated with either free doxorubicin (10 μM) (A) or free doxorubicin (10 μM) plus TPGS (0.03%) for 1 h.

Reference:

(1) Sanmartín, J.; Novio, F.; García-Deibe, A. M.; Fondo, M.; Bermejo, M. R. *New J. Chem.* **2007**, *31*, 1605-1612.

(2) Hsin, Y. H.; Chen, C. F.; Huang, S.; Chih, T. S.; Lai, P. S.; Chueh, P. J. *Toxicology Letters* **2008**, *179*, 130-139.