

Supplementary information

**Targeted delivery of geranylgeranylacetone to mitochondria by triphenylphosphonium
modified nanoparticles: a promising strategy to prevent aminoglycosides induced hearing loss**

Zhenjie Wang, Xiao Kuang, Jia Shi, Weiling Guo, Hongzhuo Liu*

School of Pharmacy, Shenyang Pharmaceutical University, Shenyang 110016, China

* Corresponding author.

Hongzhuo Liu Mail address: School of Pharmacy, Shenyang Pharmaceutical University, No.
103 Wenhua Road, Shenyang 110016, P.R. China; Tel.: +8624 23986258; fax: +8624 23986293;
Email address: liuhongzhuo@syphu.edu.cn

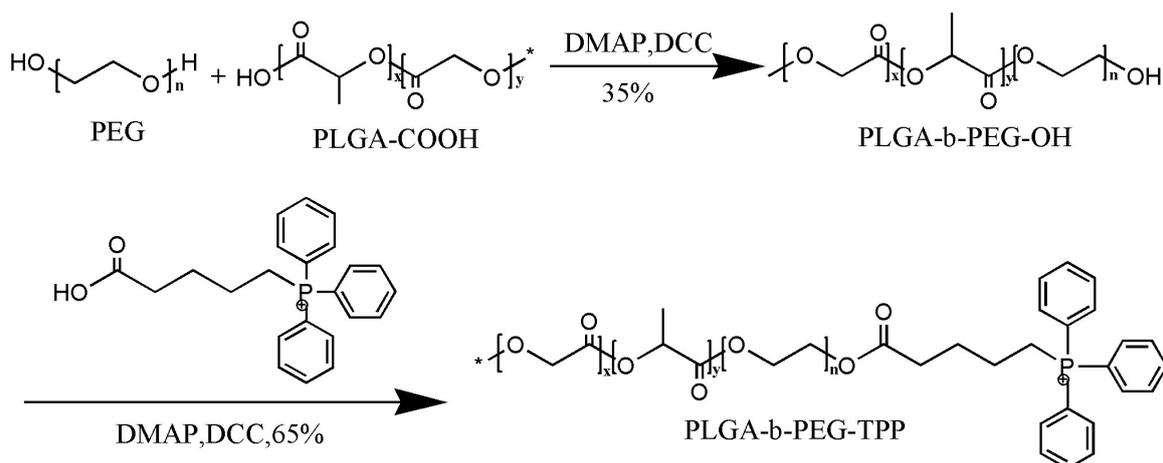


Fig S1. The roadmap for the synthesis of PLGA-b-PEG-OH and PLGA-b-PEG-TPP. The yield of PLGA-b-PEG-OH was about 35%, and PLGA-b-PEG-TPP was about 65%.

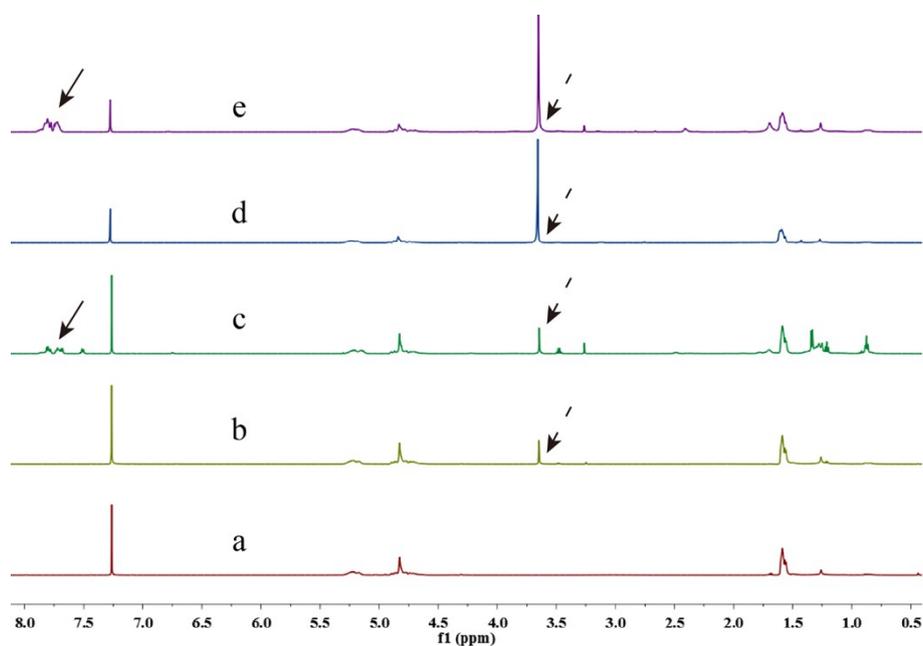


Fig S2. The $^1\text{H-NMR}$ (CDCl_3) spectra of PLGA(a), PLGA-b-PEG(b), PLGA-b-PEG-TPP(c), high PEG density of PLGA-b-PEG(d), high TPP density of PLGA-b-PEG-TPP(e). δ 7.8–7.5 [m, 15H(Ar)] , 7.3 [CDCl_3], 5.2 [m, (OCHCH₃C(O))], 4.8 [m, (OCH₂C(O))], 3.6 [s, (OCH₂)], 1.6 [m, (CH₃CH)]. The arrows of line point to the characteristic peaks of TPP and the arrows of dash line point to the characteristic peaks of PEG.

We did supplementary experiment to characterize polymer molecular weight via gel permeation chromatography (GPC, Waters, Milford, USA), GPC column (Waters Styragel HT 3 THF, Milford, USA). The mobile phase of GPC is tetrahydrofuran, the flow rate is 1 ml/min, the injection volume is 20 μ l, and the collection time is 15 min. The polymers were dissolved in tetrahydrofuran(THF) respectively(10 mg/ml) and we use polystyrene as the reference substance. The results of polymer molecular weight were shown in Tab.S1.

Tab.S1 The characterization of polymer molecular weight via GPC

Polymer	Mn(Da)	Mw(Da)	Mz(Da)	Mz+1(Da)
PLGA	4812	7869	10639	12596
PLGA-PEG	5598	8585	11190	13023
PLGA-PEG-TPP	6719	9037	11235	12931

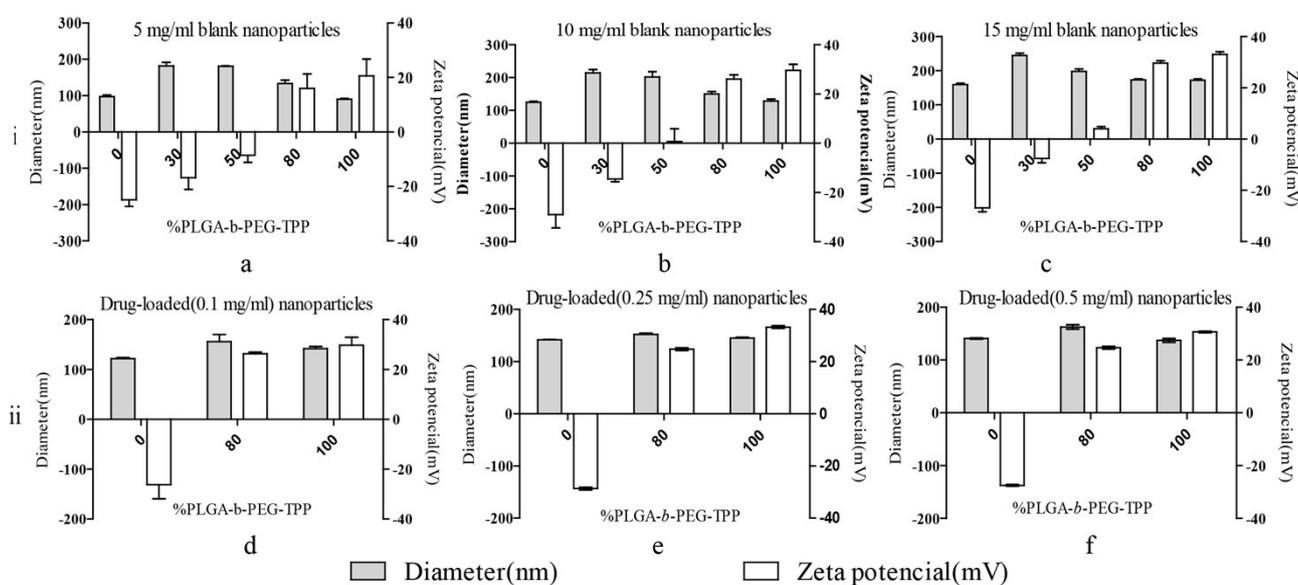


Fig S3. The screen of NPs on the mass ratio of polymer and drugs. The diameter and zeta potential of the blank NPs(i), which is consist of the different concentration of polymer: 5mg/ml(a), 10mg/ml(b), 15mg/ml(c). As can be seen from the figure, 5mg/ml NPs' zeta potential is too low and 15mg/ml NPs' diameter is too large. So we optimized 10mg/ml polymer to load different concentration of GGA drug(ii): 0.1mg/ml(d), 0.25mg/ml(e), 0.5mg/ml(f). Considering the particle size, zeta potential, encapsulation efficacy and drug loading, we finally chose 10mg/ml polymer to

load 0.25mg/ml GGA drug.

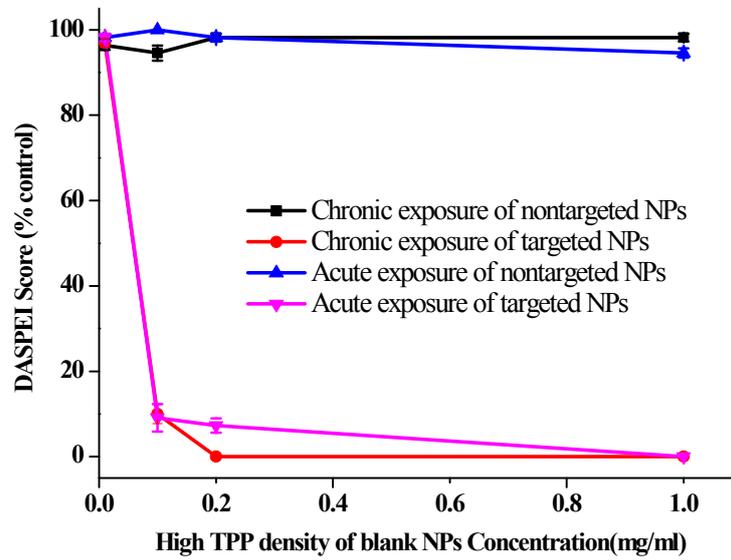


Fig S4. The toxicity of different concentrations(0.01,0.1,0.2,1mg/ml) of high PEG and TPP density of blank NPs to the 5 dpf zebrafish. For acute exposure, the blank NPs were incubated with 5 dpf zebrafish for 1 h. For chronic exposure, the blank NPs were incubated with 5 dpf zebrafish for 6 h.