Supplemental Data

Figure S1

A

		G5 -NH_2-PEG
Mn (g/mol)	67700	from GPC and NMR
Initial NO. of NH_2 Arms (via titration)		109
NO.of PEGS (via NMR)		8
NO. of Free NH_2 Arms		101
%PEGylation		7.9%

B

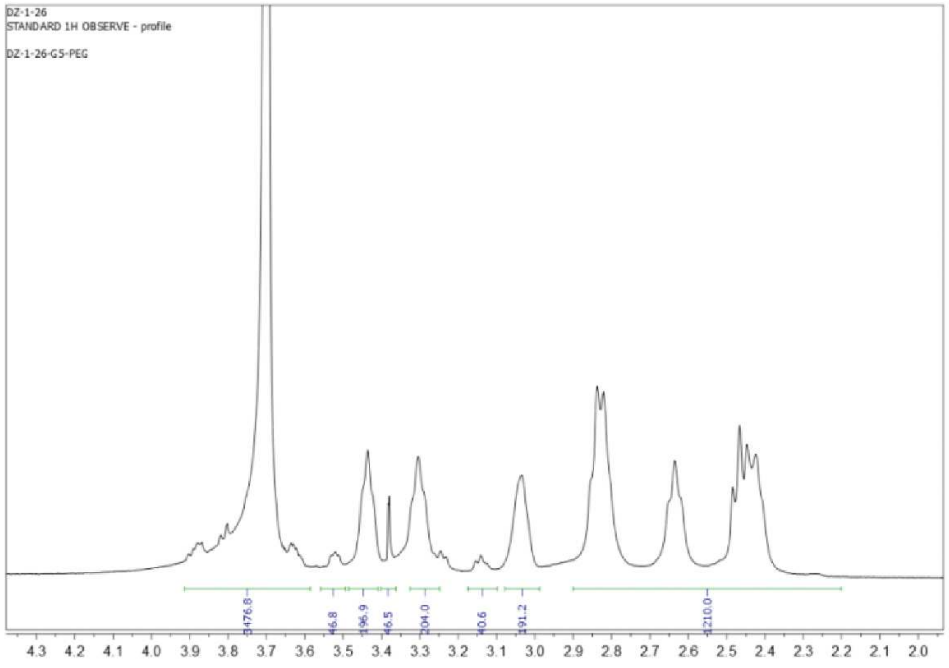

FIG. S1. Summary of characterization data (A) and ^{1}H NMR spectrum (B) data

for G5-PEG PAMAM dendrimer.

Figure S2

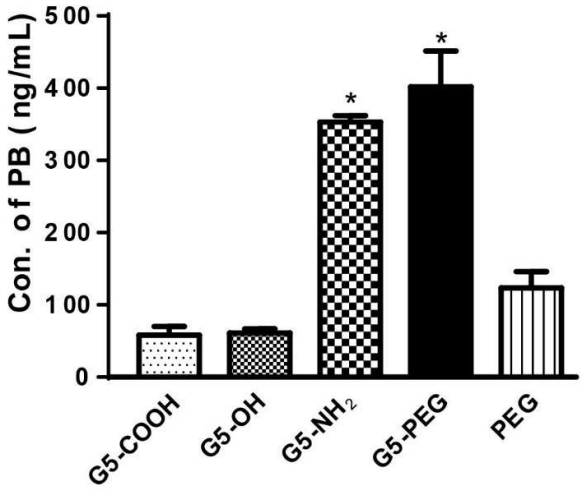

FIG.S2. Effects of different terminal groups and charges of G5 PAMAM dendrimers on water solubility of PB. * $p<0.05$ *vs* G5-COOH or G5-OH.

Figure S3

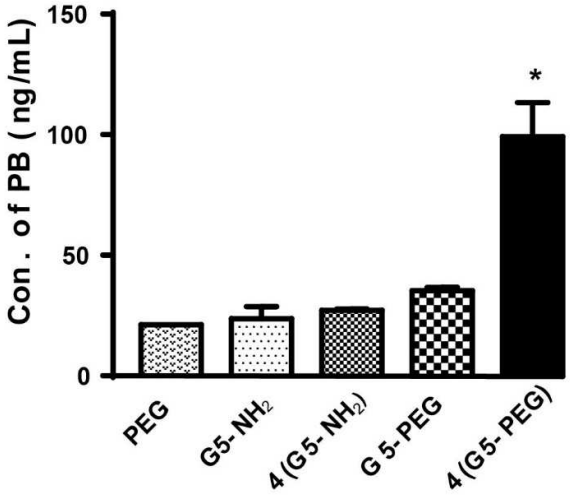

FIG. S3. Effects of terminal groups and charge concentration of G5

dendrimers on transport of PB across Caco-2 cell monolayers over 4 h. *P<0.05 *vs* 4(G5-NH_2).

Figure S4

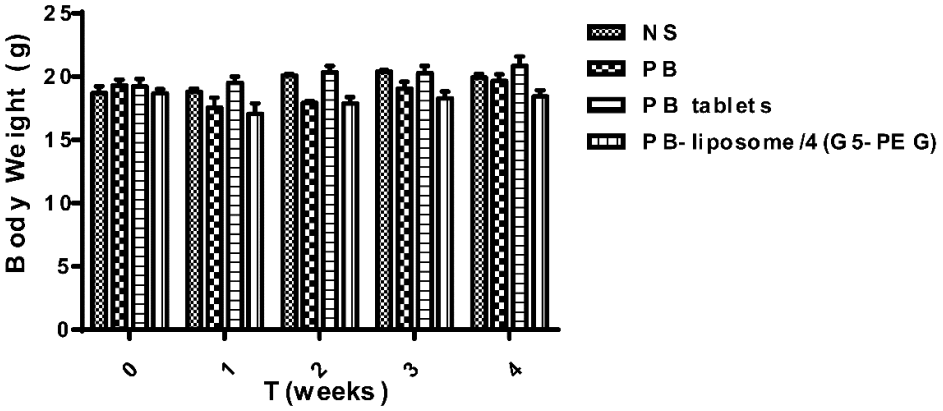

FIG. S4. Body weights of LDLR-/- mice in each group after being treated with different formulations for 4 weeks. Data were collected by week. NS means saline-treated group. n=4.

Supplemental Methods:

1. HPLC analysis

All PB samples were analyzed by HPLC (Shimadzu, Japan) on a C18 column (150 mm x 4.6 mm, 5 μm). The mobile phase was acetonitrile/water (95/5, v/v), and flow rate was 1.0 mL/min. The wavelength of the UV detector was 242 nm.

PB concentration (C) was calculated according to a formula: Peak area A = 50931C - 354.02, r = 0.9999. The linear relationship was good within 0.03~2.0 μg/mL PB.

2. Determination of the PB concentration encapsulated in the liposome

The PB concentration encapsulated in the liposome was calculated based on the total and free PB concentrations in the liposome system.

To determine the total PB concentration in the liposome system, 1 mL of the PB-liposome was diluted four-fold with HBSS to 5 mL and then 15 mL of methanol was added into the suspension to demulsify the liposomes. After ultrasonicated for 10 min, the suspension was centrifuged (Eppendorf 5810R, USA) at 1672 g for 20 min. PB concentration in the supernatant was determined by HPLC as the total PB concentration in the liposome system.

To determine the free PB concentration in the liposome system, the PB-liposome were centrifuged using an ultracentrifuge (Himac CP70-MX, Hitachi, Japan) at 100000 g and 4 °C for 2 h, and PB concentration in the supernatant was determined by HPLC as the free PB concentration in the liposome system.

The encapsulation efficiency of PB in the liposomes was calculated according to a formula as follows:

$$EE(\%) = \frac{M_{total}\text{-}M_{free\ drug}}{M_{total}} \times 100\%$$

M_{total} and $M_{free\ drug}$ are the concentrations of total and free PB in the liposome system, respectively.

3. Preparation of *in vivo* plasma samples

Mice plasma samples were processed before HPLC analysis. Briefly, 100 μL acetonitrile were added into 200 μL plasma sample in a screw-capped glass tube and vortexed for 60 s. Then 1.25 mL of n-hexane was added into the mixture and vortexed for 3 min followed by centrifugation (Eppendorf 5810R, USA) at 2612 g for 10 min. The upper organic layer in a volume of 1 mL was separated carefully into a clear centrifuge tube and evaporated under nitrogen. The dried residue was dissolved in 100 μL mobile phase, and 20 μL of the resultant solution was injected into HPLC for analysis of PB concentration.

4. Plasma TC and TG determination

The mice were fasted for 4 h, and the blood samples were collected by retro-orbital blood drawing. Plasma were then separated by centrifugation of the samples for 10 min at 4°C. Plasma TC and TG were determined by enzymatic methods (Sigma kits, MO, USA). Briefly, a standard was double diluted with ddH_2O, and 10 μL diluted standard or plasma sample were aliquoted into a cuvette. Then, 200 μL reaction reagent was added into each well followed by incubation for 10 min at 37°C. The OD value was acquired at a wavelength of 500 nm. Formula for determination of TC is $Y=323.17X-5.38$, $R^2=0.9996$, and TG is $Y=553.23X+1.93$, $R^2=0.9998$.