Supplementary Materials:

Polymer Characterization

Glass transitional temperature (*Tg*) was measured by differential scanning calorimetry (DSC) using a DSC 2910 (TA instrument, New Castle, DE). Fourier transformed infra-red (FTIR) spectra were obtained using a Perkin Elmer Spectrum 1000 spectrometer (Perkin Elmer, Waltham, MA). The molecular weight (MW) of the polymer was determined by a calibration curve of standard polystyrene (TOSOH, Japan) measured with a gel permeation chromatography (GPC) column (Jordi lab, Bellingham, MA) at 0.5 mL/min flow rate in THF.

The PGMD polymer has a *Tg* temperature of 42.2°C measured by DSC. The *Tg* (~42°C) of the PGMD polymer allowed increased drug release with exposure of the NPs to an external heat stimulus. The FTIR showed an intense C=O stretch at 1735 cm^{-1}, indicating a typical esteric bond (Fig. S1). The MW measured by GPC column and Evaporative Light Scattering Detector (ELSD) is around 3000 Da.

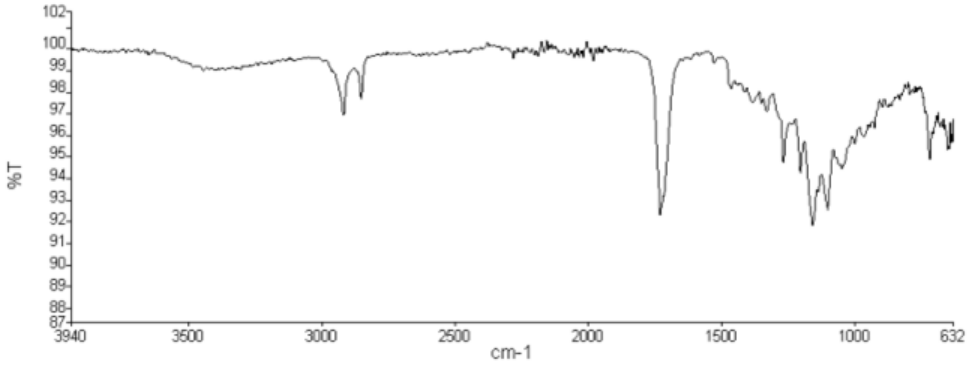

Fig. S1. FTIR spectrum shows the appearance of a C=O stretch at 1735 cm^{-1}, typical of ester bonds.

Synthesis of NPs

Briefly, approximately 2 mg DOX-HCl and 2 mg IR820 were measured and added to 0.4 mL methanol, then mixed with 0.8 ml acetonitrile containing approximately 12 mg PGMD polymer. The mixed solution was added to 12 ml 0.1% pluronic solution while stirring at 930 rpm. The organic phase was removed by evaporation for 24 hours at room temperature. The NPs were then collected and centrifuged at 5000 rpm for 5 minutes to remove large NPs. Next, the supernatant was collected and subjected to dialysis (membrane MWCO 1000 Da) for 24 hours. Finally, the particles were freeze-dried and lyophilized for 48 hours. Void PGMD NPs were prepared following a similar method except for the addition of DOX and IR820. IR820-PGMD NPs were also prepared following the same protocol, except that no DOX was added.

Drug loading measurements

Serial dilutions of the sample were done to reach the linear range. The maximum peak intensities were corrected with DMSO blank subtraction, plotted, and fitted to a linear model. The concentrations of DOX and IR820 in the NPs were determined using a standard calibration curve of DOX and IR820 in DMSO that was created using the same spectrophotometer.

Dynamic light measurement (DLS) and Scanning Electron Microscopy (SEM)

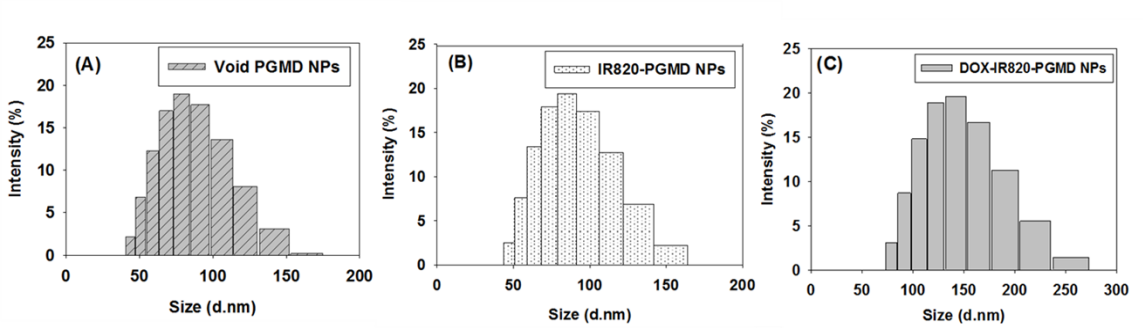

Fig. S2. (A) DLS measurement of void PGMD NPs; (B) DLS measurement of IR820-PGMD NPs; and (C) DLS measurement of DOX-IR820-PGMD NPs.

The shape and size of NPs were confirmed with scanning electron microscopy (SEM, JEOL-JEM). The SEM images showed that void PGMD NPs were nearly spherical and uniformly distributed (Fig. S3).

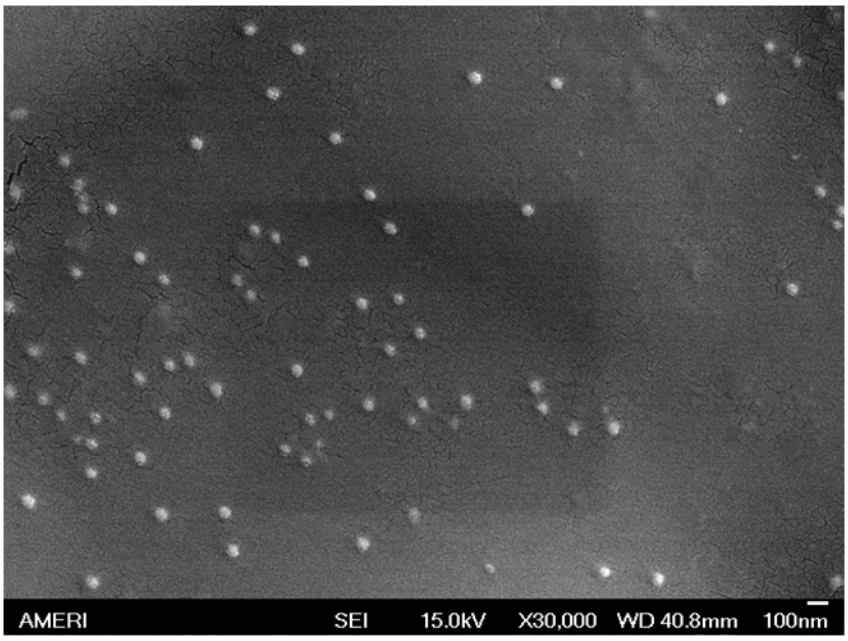

Fig. S3. SEM image of void PGMD NPs.

Cellular uptake experiments

Two cell lines (MES-SA and Dx5) were used to study the cellular uptake of unencapsulated DOX and IR820 (designated as free DOX + IR820) versus the uptake of the NP formulation (DOX-IR820-PGMD NPs). On the first day, the cells were seeded into 24-well plates at a cell density of around 200,000 cells per well. On the second day, the cell medium was removed, and free DOX + IR820 or DOX-IR820-PGMD NPs in growth medium was added to the plates at a normalized DOX concentration of 5 μM (2.9 μg/mL). The plates were then placed back in a cell incubator for 24 hours. The control group means no drug was added. After 24 hours, the cell medium was removed, and the cells were washed with ice cold DPBS four times and then lysed with 1 mL of DMSO. The supernatants were centrifuged at 14,000 rpm for 10 minutes and collected to obtain cell lysates. The DOX fluorescence intensity of cell lysates was measured by a spectrofluorometer (Jobin Yvon Horiba, NJ) at λex = 482 nm, λem = 590 nm to determine DOX concentration. To adjust the background fluorescence from cellular components, a DOX calibration curve was created by dissolving DOX and IR820 in DMSO and adding the solution to untreated cells. The protein content in the cell lysates was measured using a micro BCA protein assay kit, and the absorption data was acquired at 562 nm with the same spectrophotometer. Cellular uptake of DOX for different treatments was calculated by normalizing the DOX amount to the protein amount. An average value was obtained from three wells in each treatment for each experiment, and an average (± SD) intracellular uptake of DOX from three experiments was plotted.

Cumulative percent release of IR820 from DOX-IR820-PGMD NPs

The release of IR820 from DOX-IR820-PGMD NPs is shown in Fig. S4. IR820 release was enhanced when NPs were placed in an acidic environment. Approximately 48% IR820 was released in 5 hours in acidic PBS (pH=5.0), and up to 52% IR820 was released in 24 hours. Since the PGMD NPs are pH sensitive, it was expected that an acidic environment would induce higher amount of IR820 release from NPs as compared to a neutral environment (pH=7.4). IR820 measurements were performed only up to 24 hours because the fluorescence intensity of IR820 becomes unstable after 24 hours. Also, IR820 release was not measured after laser exposure to NPs since photobleaching would occur after laser excitation.

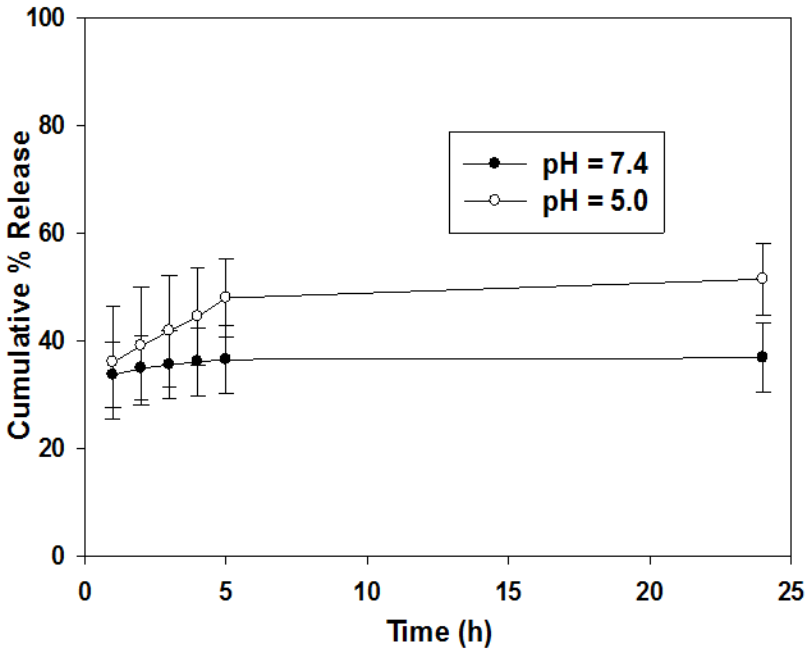

Fig. S4. Cumulative percent release of IR820 from DOX-IR820-PGMD NPs under different experimental conditions.

Void PGMD NPs cytotoxicity profile

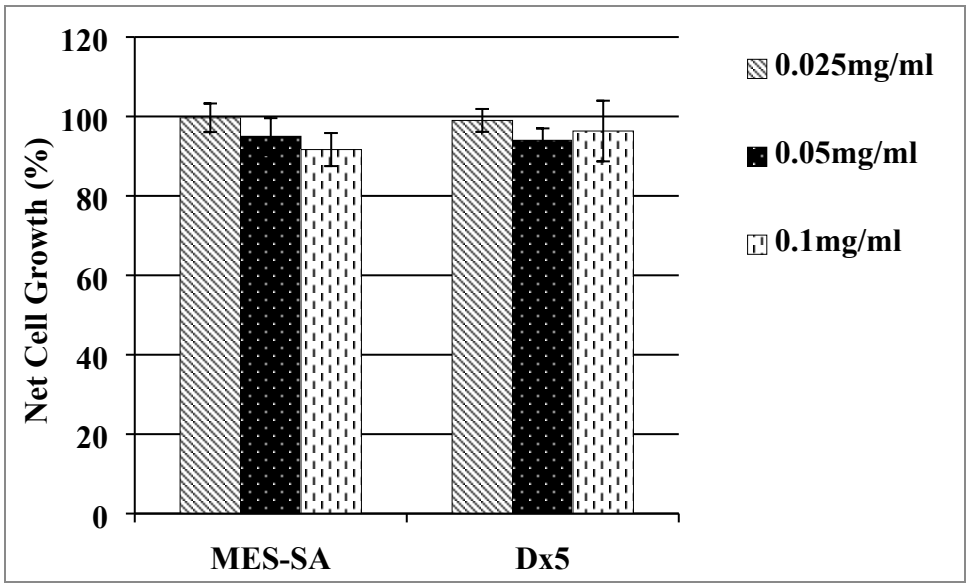

Fig. S5. 24-hour cytotoxicity profile of void PGMD NPs in MES-SA and Dx5.