Supporting Information for

Regulation of Drug Release by Tuning Surface Textures of Biodegradable Polymer Microparticles

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Supporting figures:

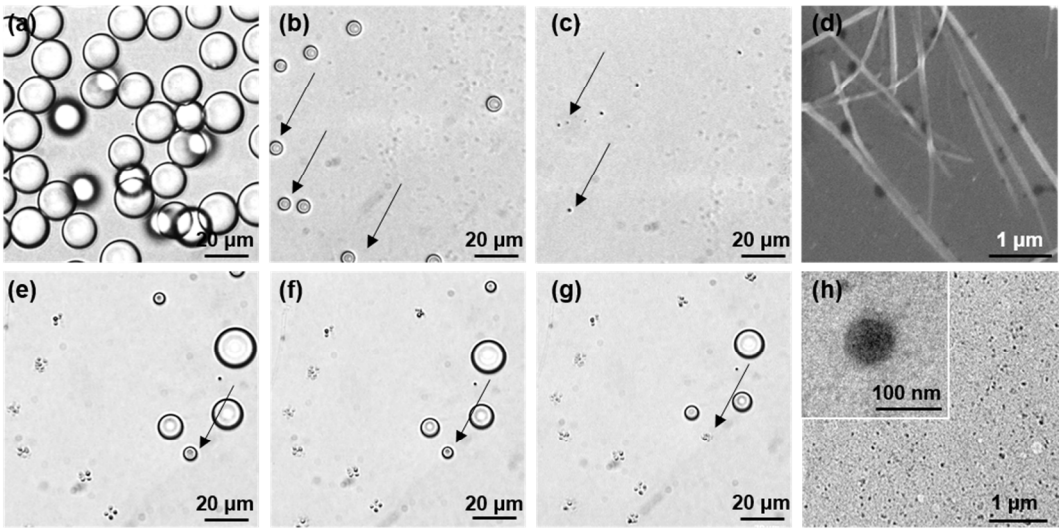

Figure S1. Optical microscopy images for the evolution of emulsion droplets containing: (a-c) $PLGA_{5k}$-*b*-PEG_{5k} and (e-g) $PLGA_{10k}$-*b*-PEG_{20k}. 10 mg/mL polymers were dissolved in DCM. The droplets shrank first, and then break into tiny droplets. Arrows show the shrinkage and breakage of the emulsion droplets. (d) is the representative SEM image showing the wormlike micelles obtained from $PLGA_{5k}$-*b*-PEG_{5k} while (h) is the bright field TEM image showing the spherical micelles obtained from $PLGA_{10k}$-*b*-PEG_{20k}. Inset in image (d) is the magnified TEM image for a spherical micelle.

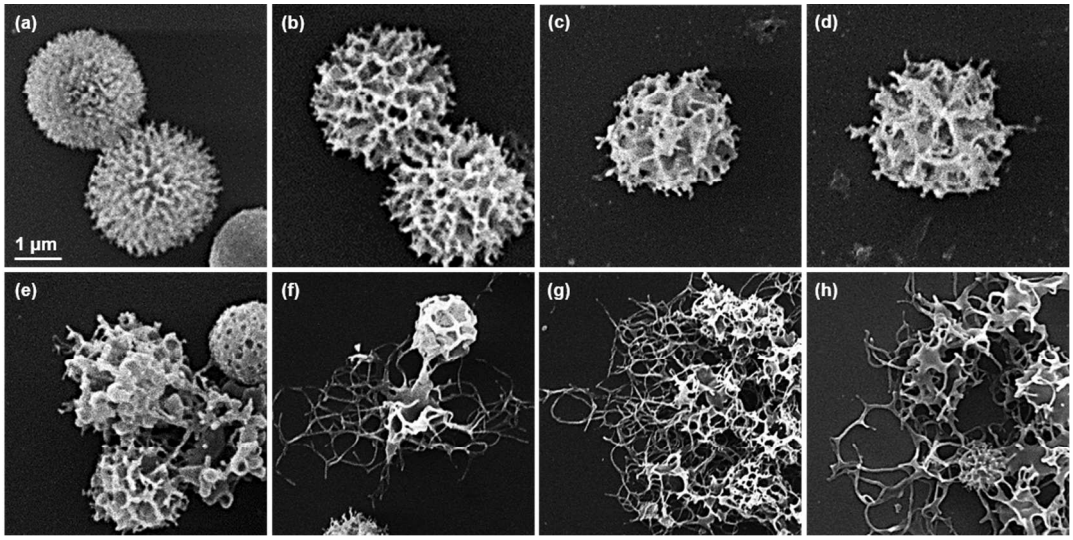

Figure S2. SEM images of the assemblies obtained from the binary blends of $PLGA_{50k}$-*b*-PEG_{5k} with $PLGA_{10k}$-*b*-PEG_{20k}. The total polymer concentration of the blends was same (10 mg/mL) in all cases while the ratio of $PLGA_{10k}$-*b*-PEG_{20k} in the blends was: (a) 10%, (b) 20%, (c) 30%, (d) 40%, (e) 50%, (f) 60%, (g) 70% and (h) 80%. (a-e) Roughness of the microparticles increased when increasing the ratio of $PLGA_{10k}$-*b*-PEG_{20k} in the blends up to 50%. Further increase of $PLGA_{10k}$-PEG_{20k} causes qualitively different interfacial instability in the system and leads to the formation of polymer micelles (f-h). Scale bar shown in (a) applies to all other images.

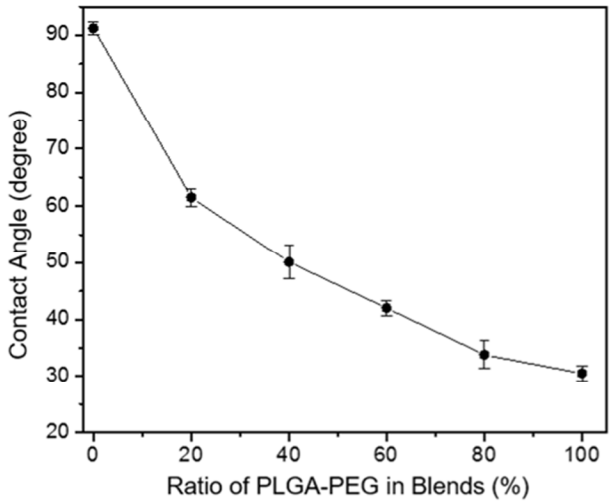

Figure S3. Plot shows the water contact angle on films of $PLGA_{50k}$-*b*-PEG_{5k}/$PLGA_{100k}$ blended microparticles. Clearly, contact angle decreases with the increase of $PLGA_{50k}$-*b*-PEG_{5k} in the polymer blends, indicating that the hydrophilicity of the polymer particles increase with the increase of surface area. Error bar represents the standard deviation.

We note that water contact angle usually increases with the increase of surface area.[1-2] However, in this case, with the increase of the surface area, component of the polymers will change since we used polymer blends. In general, as the PLGA-*b*-PEG content increase in the blends of PLGA-*b*-PEG/PLGA, the hydrophilic content will increase and the surface rough will enlarge (Figure 3). With the increase of surface area (roughness), more hydrophilic component (*e.g.*, PEG) will expose on the surface of the particles, resulting in the increase of the hydrophilicity.

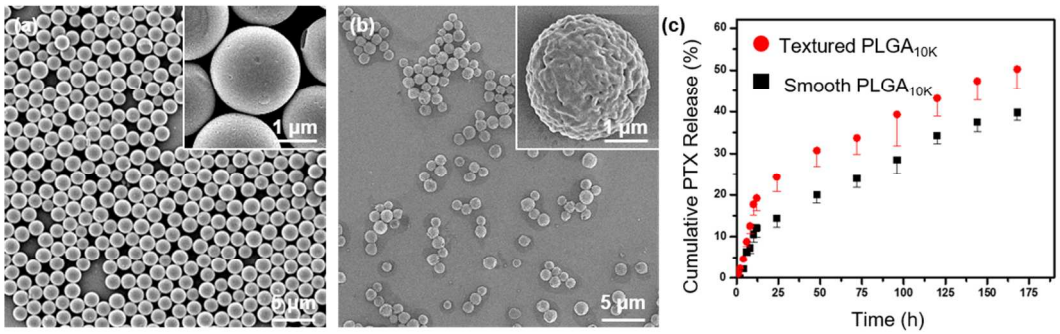

Figure S4. SEM images of PTX loaded (a) smooth and (b) textured $PLGA_{10k}$ microparticles. (c) Plot shows the PTX release profile for the PTX-poaded smooth and textured PLGA particles. Clearly, textured particles demonstrate enhanced drug release compared to the smooth ones.

Smooth PTX-loaded $PLGA_{10k}$ microparticles were produced in the same procedure, as deacribed in the text. To produce the rough $PLGA_{10k}$ microparticles, $PLGA_{10K}$ and PTX (weight ratio of $PLGA_{10k}$/PTX 10:1) were dissolved in DCM. 3 mg n-hexadecanol (HD, acting as a co-surfactant) was added to the above $PLGA_{10k}$/PTX solution. The resulting solution was then emulsified with SDS (5 mg/mL) aqueous solution through microfluidic technique, as described in the text. The formed emulsion droplets were allowed in the evaporation device. Upon solvent extraction, the emulsion droplets changed their morphologies as a result of vanished interfacial tension with the assistance of added HD.[1] After complete removal of organic solvent, polymer microparticles with textured surfaces were obtained.

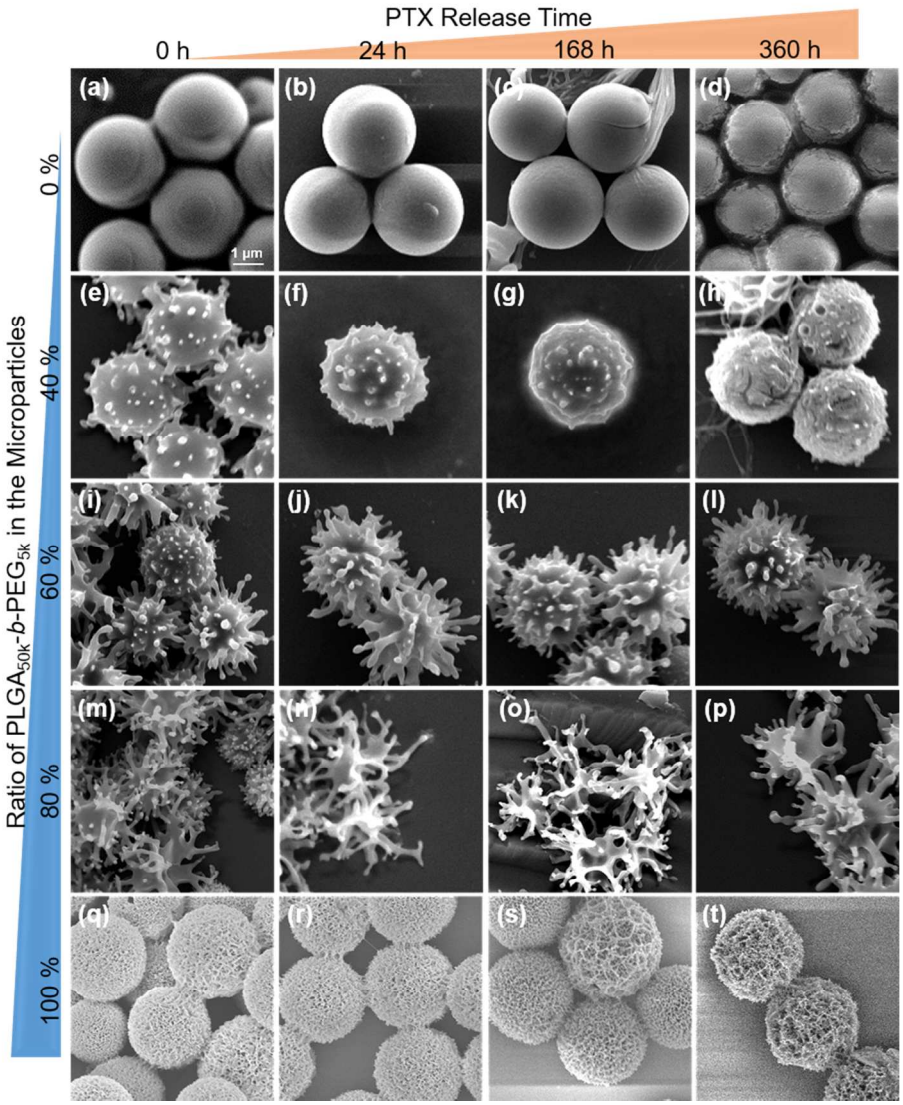

Figure S5. SEM images of the $PLGA_{50k}$-*b*-PEG_{5k}/$PLGA_{100k}$ polymer microparticles with diffrerent $PLGA_{50k}$-*b*-PEG_{5k} ratios at various period of drug release. Clearly, surface morphology of the polymer particles did not significantly change during the period of drug release investigation, indicating that the drug release pattern is a diffusion controlled mode. The scale bar in (a) applies to all other images.

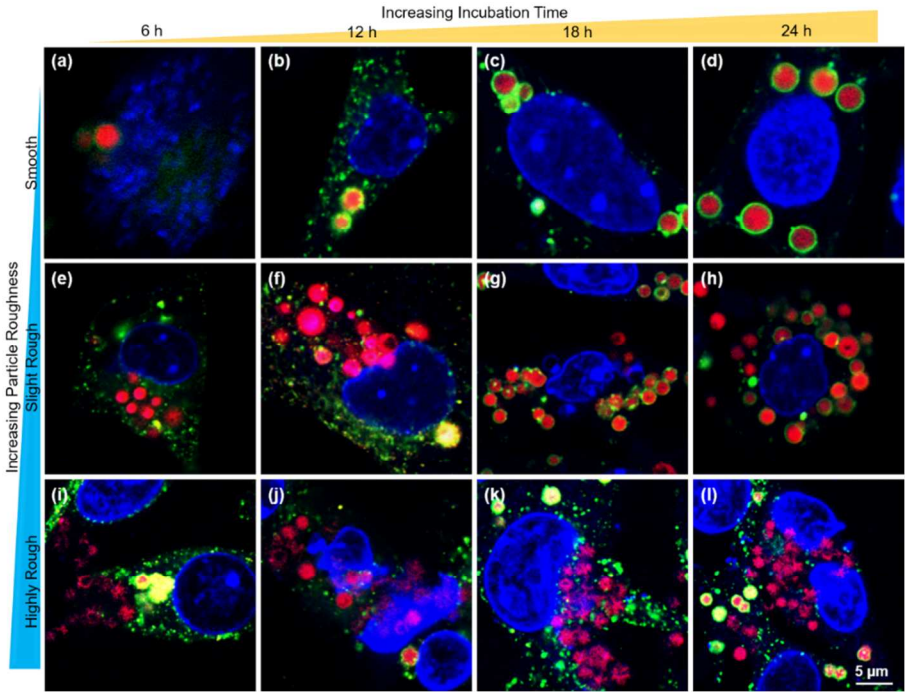

Figure S6. CLSM images showing the cellular uptake of Nile Red labelled smooth (a-d), slight rough (e-h) and highly rough (i-l) polymer microparticles by B16-F10 melanoma cell for (a, e, i) 6h, (b, f, j) 12h, (c, g, k) 18h and (d, h, l) 24 h, respectively. Cell lysosomes were stained with Lyso Tracker Green DND-26 (green) while blue Hoechst was used to lable the nuclei. The microparticles in images (a-d) are the smooth (Neat $PLGA_{100k}$), (e-h) slightly rough ($PLGA_{100k}$/$PLGA_{50k}$-b-$PLGA_{5k}$=60:40) and (i-l) are highly rough ($PLGA_{100k}$/$PLGA_{50k}$-b-$PLGA_{5k}$=20:80). The microparticles were co-cultured with cells in well plates and imaged after a given time period. The scale bar in image (l) can be applied to all other images.

Clearly, the polymer microparticles can be observed inside the B16-F10 cells, indicating that the microparticles are uptaken by the cancer cells, and the microparticles can act as drug carriers to successfully transport hydrophobic drugs to the cancer cells.

Supporting movies:

Movie 1. Real-time evolution of the emulsion droplets containing neat $PLGA_{50k}$-*b*-PEG_{5k} as DCM evaporates. During the extraction of solvent, the droplets shrink and then expand. Tiny protrusions start to appear due to the interfacial instability, and finally yielding particles with rough surface.

Movie 2. Real-time evolution of the emulsion droplets containing neat $PLGA_{5k}$-*b*-PEG_{5k} as DCM evaporates. During the extraction of solvent, the droplets shrink and then break into tiny droplets, finally disappearing in the aqueous phase.

Movie 3. Real-time evolution of the emulsion droplets containing binary blends of $PLGA_{50k}$-*b*-PEG_{5k}/$PLGA_{100k}$ with $PLGA_{50k}$-*b*-PEG_{5k} content of 70% as DCM evaporates. The emulsion droplets shrink first and then expand. Spiky and rough surfaces start to appear. Morphology of the droplets is finally frozen, and microparticles with highly rough surfaces are observed.

Movie 4. Real-time evolution of emulsion droplets containing $PLGA_{10k}$ in DCM. 3 mg HD was added to the oil phase to lower the oil/water interfacial tension. During the process of solvent evaporation, the emulsion droplets change their morphologies a little under optical microscopy investigation and give rise to the formation of textured microparticles.

References:

(1) Liu, S.; Deng, R.; Li, W.; Zhu, J. Polymer Micoparticles with Controllable Surface Textures Generated through Interfacial Instabilities of Emulsion Droplets. *Adv. Funct. Mater.* **2012**, *22*, 1692-1697.

(2) Wenzel, R. N. Resistance of Solid Surfaces to Wetting by Water. *Ind. Eng. Chem.* **1936**, *28*, 988-994.