Electronic Supplementary Material (ESI) for Journal of Materials Chemistry B.

Supporting information

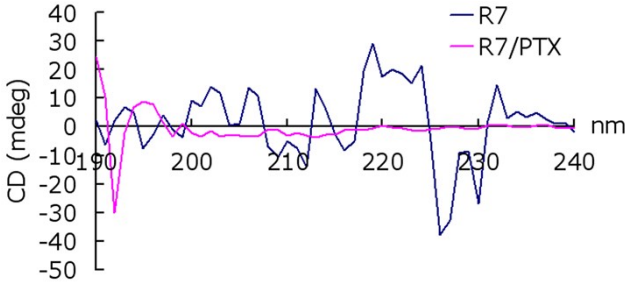

Fig. S1 The CD analysis for the secondary structure of R7 and R7/PTX.

The secondary structure of Hb was determined using a CD spectrometer (Jasco-J810, Japan). The spectra were scanned at 200 nm/min with a response time of 1 s and recorded in the range of 190-240 nm and in the Soret region. The results were expressed as ellipticity in mdeg.

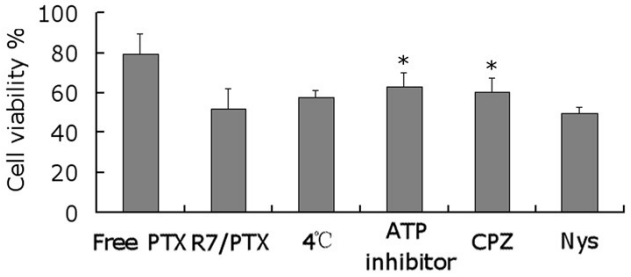

Fig. S2 Cytotoxicity analysis of effects of low temperature, ATP depletion and endocytosis inhibitors on PA9/PTX uptake. The HeLa cells were treated with 4°C, NaN_3/2-D-G, CPZ and Nys in the presence of R7/PTX for 30min.

As shown in Fig. S2, the internalization routes were evaluated based on the results from the ATP depletion and endocytosis inhibition test. The HeLa cell was treated with low temperature (4°C), ATP depletion (NaN_3/2-D-G) and endocytosis inhibition (CPZ and Nys) in the presence of R7/PTX for 30min following the pretreatment of low temperature, ATP

depletion and endocytosis inhibition for 30 min. The untreated cells were used as negative control (Blank) and the results are presented as percentage of the negative control value (100 %). The cells treated with R7/PTX were used as positive control. The cell viability increased in the presence of NaN_3/2-D-G and CPZ group whereas was still lower than free PTX, indicating both the direct translocation and endocytosis participated in the R7/PTX complex uptake.

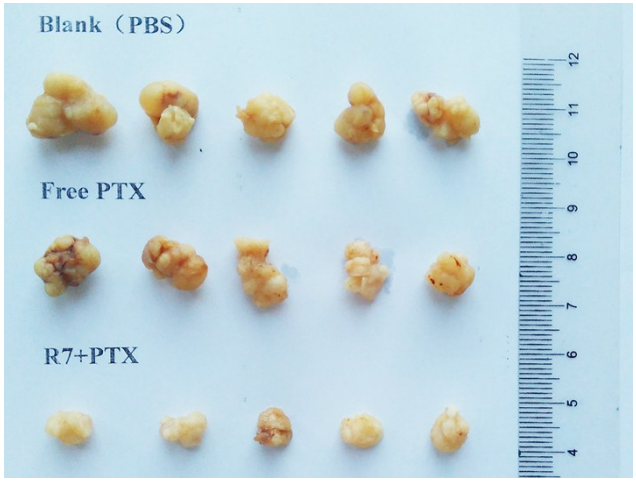

Fig. S3 The photo images of the tumor separated from mice after treatments for 14 day.

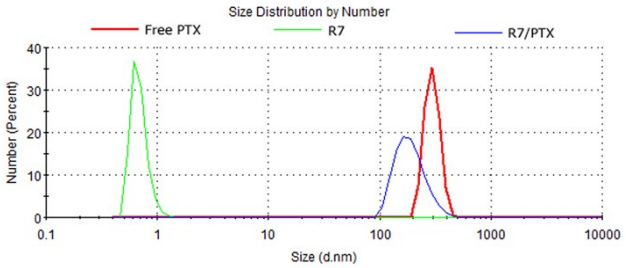

Fig. S4 The size distribution by number of free PTX, R7 and R7/PTX complex. The concentrations of free PTX and R7 were 1.7μM. R7/PTX (1.7μM) was obtained by adding R7 to free PTX. All the solutes were dissolved in PBS.

Due to the low water solubility of PTX, it is not able to characterize the interaction between R7 and PTX in aqueous phase using classic methods such as Nuclear Magnetic Resonance Spectroscopy (NMR) and Surface Plasmon Resonance (SPR). In our study, the size distribution of free PTX, R7 and R7/PTX were measured using a Zetasizer instrument and analyzed using DTS software (Malvern, UK). As shown in Fig. S2, the size of free PTX was about 310 nm, suggesting that PTX undergoes aggregation, which was consistent with previous studies [1]. In contrast, the size of R7 was about 0.8 nm, indicating that R7 was present as a monomer in solution instead of aggregate. Interestingly, the size of R7/PTX changed to about 170 nm when R7 and PTX were mixed. *Suh et al* [2]. showed that the size of LMWP/miR-29b complexes was significantly reduce from 500 nm to 50 nm by the addition of excess amount of LMWP (arginine-rich CPPs), suggesting LMWP have interactions with miR-29b or LMWP/miR-29b. Thus, the significantly change of free PTX, R7 and R7/PTX in size distribution suggested that there are interactions between R7 and PTX.

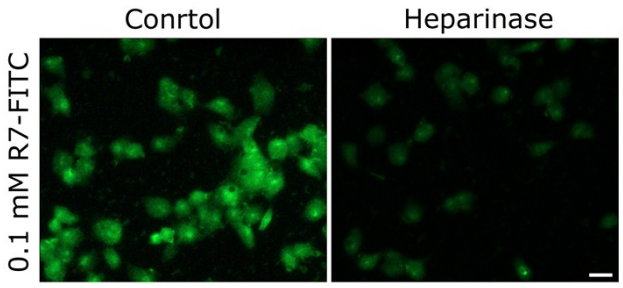

Fig. S5 The effect of heparinase on R7 uptake. The HeLa cells were treated with heparinase I/II/III in the presence of 0.1 mM R7-FITC. Bar = 50 μm.

The cells were incubated in the complete culture medium overnight and then treated with the culture medium (1% FBS) containing 15 mIU/mL of heparinase I, 8 mIU/mL of

heparinase II, 10 mIU/mL of heparinase III, at 37 ^{o}C for 1 h. After two PBS washes, the cells were incubated for 60 min incubation with 0.1 mM R7-FITC. The untreated cells were used as negative control.

References

[1] S.A. Lorenz, B.P. Jr, S.V. Balasubramanian, G.J. Fetterly, R.M. Straubinger, T.D. Wood, Noncovalent dimerization of paclitaxel in solution: evidence from electrospray ionization mass spectrometry, Journal of pharmaceutical sciences, 91 (2002) 2057-2066.

[2] S.S. Jin, J.Y. Lee, Y.S. Choi, P.C. Chong, Y.J. Park, Peptide-mediated intracellular delivery of miRNA-29b for osteogenic stem cell differentiation, Biomaterials, 34 (2013) 4347-4359.