

## Fabrication of Redox- Responsive Doxorubicin and Paclitaxel Prodrug Nanoparticles with Microfluidics for Selective Cancer Therapy

Xiaodong Ma,<sup>a,b</sup> Ezgi Özliseli,<sup>b</sup> Yuezhou Zhang,<sup>\*b</sup> Guoqing Pan,<sup>c</sup> Dongqing Wang,<sup>\*a</sup> and Hongbo Zhang,<sup>\*a,b,d</sup>

<sup>a</sup> Department of Radiology affiliated Hospital of Jiangsu University Jiangsu university 212001 Zhenjiang, P.R.China

<sup>b</sup> Pharmaceutical Sciences Laboratory, Faculty of Science and Engineering, Åbo Akademi University FI-00520, FI.

<sup>c</sup> Jiangsu University, Institute for Advanced Materials, School of Material Science and Engineering 301Xuefu Rd Zhenjiang, Jiangsu, CN212013

<sup>d</sup> Turku Centre for Biotechnology, University of Turku and Åbo Akademi University Turku, FI

### High performance liquid chromatography (HPLC) to identify the prodrug

Quantification of PTX and DOX was performed by following the method. Gradient analytical HPLC assay was performed on an Agilent 1100 instrument and 20  $\mu$ L of solution was loaded onto Waters reverse phase column (250  $\times$  4.6 mm). Acetonitrile (TFA 0.1%): water (TFA 0.1%) (Acetonitrile increase from 5 to 95% with 20 minutes) was eluted at a flow rate of 1 mL/min and all the compounds were detected at 254 nm by UV detector (UV-975, Jasco). A gradient of 5-95% solvent B over 20 min for a 25 min run time was used to determine the retention time of starting material DOX·HCl, PTX and DOX-S-S-PTX was 4.889 min, 17.950 min and 19.826 min individually.

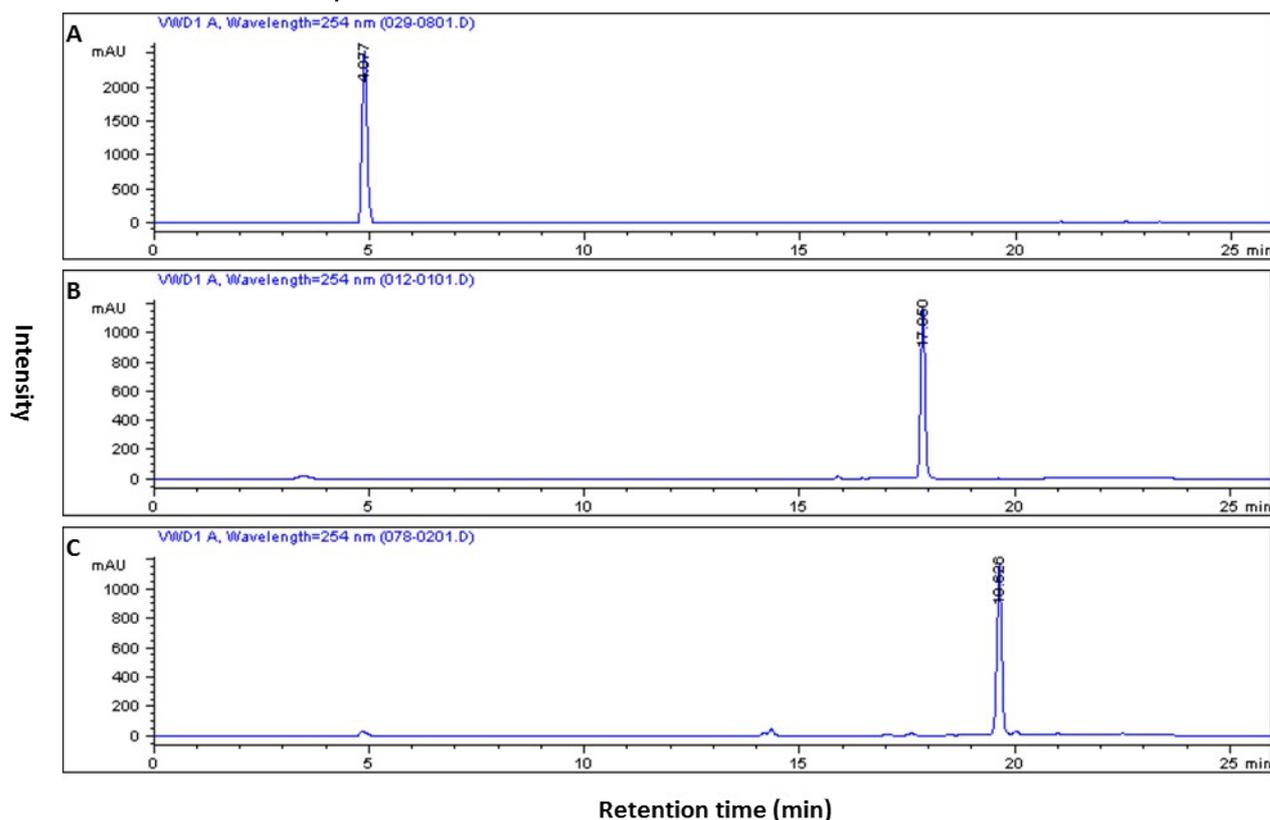


Fig. S1 Chromatography spectra of (A) DOX·HCl; (B) PTX and (C) DOX-S-S-PTX

### Standard curves of parent drug

The standard curves were established from known concentrations of DOX·HCl in aqueous and PTX in ethanol.

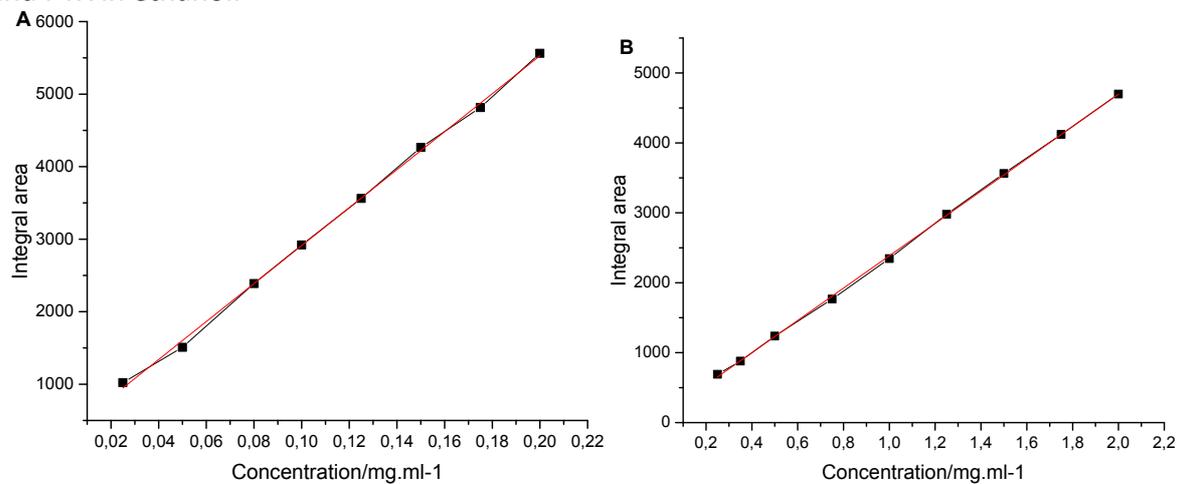


Fig. S2 Standard curves of (A) DOX.HCl; (B) PTX

The equation of standard curves for Doxorubicin

$$y = 293.3076 + 26181.03777x \quad R^2 = 0.99941$$

Here y is UV absorption integral of DOX at 254 wavelengths; x is the concentration of DOX.

The equation of standard curves for Paclitaxel

$$y = 75.24836 + 2310.54168x \quad R^2 = 0.99983$$

Here y is UV absorption integral of PTX at 254 wavelengths; x is the concentration of PTX.

The peak areas corresponding to individual compounds were integrated by comparison with external standard calibration curves. Validation of quantitative method was performed with samples for three times. The results of the three injections from the same samples showed similar retention time.

### Q-TOF(HRMS)

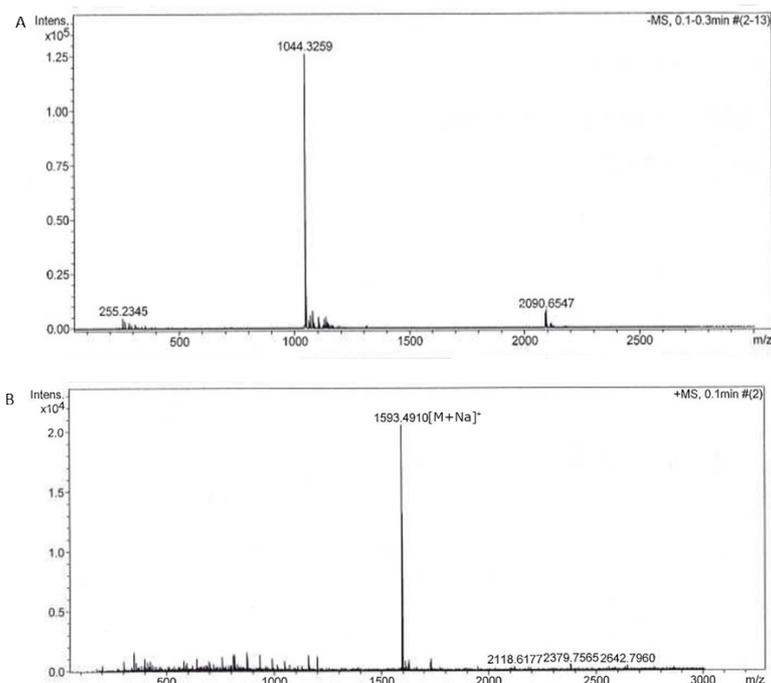


Fig. S3 High resolution mass spectra of (A) DOX-S-S-COOH; (B) PTX-S-S-DOX

Table S1 The size comparison of particles fabricated with different methods<sup>a</sup>

Prodrug concentration/mg.ml <sup>-1</sup>	Approach	Microfluidics	Bulk
1		99.04(0.106)	350.1(0.212)
2		106.8(0.161)	454.5(0.287)
3		181.9(0.084)	602.0(0.334)
4		223.4(0.221)	792.6(0.796)

<sup>a</sup> the numeric results in the table are showed as such that the average size of triple readouts are followed by corresponding PDI average values in brackets at fixed inner: outer (I: O) fluid flow of 2:40.

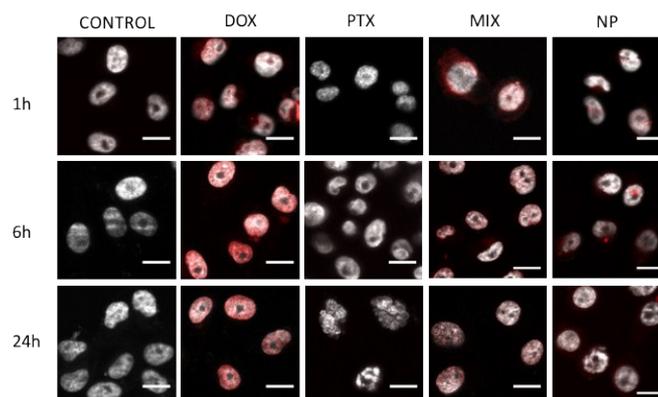


Fig. S4 The fluorescence microscopy images of MDA-MB-231 cells with Scale bar 10  $\mu$ m