# Porous PLGA Microspheres with Recruited Ions and Doxorubicin for Triple-Combination Therapy of Larger Hepatocellular Carcinoma $\dagger$ 

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Scheme S1. Schematic illustration of the preparation of porous PLGA microspheres as MW-chemoembolization agent via several procedures.

## 1. Experimental Sections

### 1.1. In Vitro Release of $\mathrm{DOX} \cdot \mathrm{HCl}$

The absorbance of phosphate-buffered saline (PBS, pH 7.2, containing $0.1 \%(\mathrm{w} / \mathrm{v})$ Tween 80) with different concentration of $\mathrm{DOX} \cdot \mathrm{HCl}$ at 485 nm was obtained using UV absorption of a Spectrophotometer (U-3010, Hitachi, Japan), and their results were changed into a standard curve with the goodness of fit about 0.99 , to evaluate the release rate at different conditions. Briefly, P-PLGA@DN microparticles ( $5 \mathrm{mg} / \mathrm{mL}, 1 \mathrm{~mL}$ ) in EP tube were gently shaken at $37{ }^{\circ} \mathrm{C}$ under the microwave irradiation of 0 W and 2 W , and another isometric PBS is added. When the supernatant is completely collected at $0.5,1,2,4,8,12$ and 24 min , respectively. Every test was performed three times.


Fig. S1. SEM images of P-PLGA microspheres with low porosity via using $10 \mathrm{mg} / \mathrm{mL} \mathrm{NH}_{4} \mathrm{HCO}_{3}(0.5 \mathrm{~mL})$ as pore-forming agent.


Fig. S2. IR imaging of P-PLGA microspheres dispersed into saline with concentration of $35 \mathrm{mg} / \mathrm{mL}$ and irradiated by MW ( $0.6 \mathrm{~W}, 1.2 \mathrm{~W}$ and 1.8 W ) for 5 min , saline as control was performed simultaneously with 1.8 W power.



Fig. S3. Cell viability of VX2 cells and H22 cells indicating the effect of treatment time when cells were incubated with P-PLGA-DN microparticles for $1,2,4$ and 8 days at $37^{\circ} \mathrm{C}$. P-PLGA-DN has significant cell inhibition abilities in comparison with the control ( $p<0.01$ ) after 1 days. Error bars indicate the standard deviation.


Fig. S4. Curves of relative body weight in Control, P-PLGA@DN, MW, DOX, P-PLGA@N+MW and PPLGA@DN+MW after 16 days treatment.


Fig. S5. Representative images of organs (heart, liver, spleen, lung and kidney) in different groups after 16 days treatment, and scale bar is $100 \mu \mathrm{~m}$.


Fig. S6. Representative photographs of the tumours in control, DOX, MW, P-PLGA@DN, P-PLGA@N+MW and P-PLGA@DN+MW after 16 days treatment.

