Electronic Supplementary Information

On-Demand Responsive Nanoplatform Mediated Targeting CAFs

and Down-Regulating mtROS-PYK2 Signaling

for Antitumor Metastasis

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Figure S1 The equation of TPP-RSV synthesis



Figure S2 The equation of PLGA-BM synthesis



Figure S3 The equation of PLGA-β-CD synthesis



Figure S4 ESI-MS spectrum of TPP-RSV prodrug



Figure S5 FTIR spectrum of $PLGA_{2k}$ -CD polymer.



Figure S6 Cytotoxicity of blank P/NPs, blank PBC/NPs and blank HPBC/NPs were

estimated by MTT method at various concentrations.



Figure S7 H&E staining images of heart, liver and kidneys of 4T1/NIH3T3 tumor bearing mice. Scale bar: 200 μm.



Figure S8 The vascular normalization in tumors. (A) CLSM images of immunofluorescence staining of tumor vessels (anti-CD31 staining) at the end point of treatments. (B) Quantitative analysis of tumor vessels (CD31⁺) in tumor tissue by Image J software. *P < 0.05, ** P < 0.01.

Table S1 The characterization of P@TR/NPs, PBC@TR/NPs and HPBC@TRP/NPs formulations, including particle size and Zeta potential.

| | P@TR/NPs | PBC@TR/NPs | HPBC@TRP/NPs |
|-----------|-------------------|-------------------|-------------------|
| Size (nm) | 146.2 ± 8.4 | 150.7 ± 2.3 | 162.4 ± 3.9 |
| PDI | 0.111 ± 0.037 | 0.109 ± 0.018 | 0.124 ± 0.001 |
| Zeta (mV) | 52.8 ± 5.2 | 49.2 ± 2.1 | -35.7 ± 0.4 |

Data are given as mean \pm SD (n = 3).

Table S2 The EE% and DL% analysis of prodrug TPP-RSV and PFD in various

| | | P@TR/NPs | PBC@TR/NPs | HPBC@TRP/NPs |
|---------|-----|------------------|------------------|------------------|
| TPP-RSV | EE% | 75.92 ± 1.32 | 73.92 ± 3.96 | 86.42 ± 2.53 |
| | DL% | 5.32 ± 0.09 | 5.18 ± 0.28 | 4.16 ± 0.12 |
| PFD | EE% | | | 63.72 ± 1.03 |
| | DL% | | | 6.14 ± 0.10 |

formulations. Data are given as mean \pm SD (n = 3).

Table S3 The evaluation of IC_{50} for 4T1 cells after RSV, TPP-RSV, P@TR/NPs,

PBC@TR/NPs and HPBC@TRP/NPs treatments.

| Mean±SD | RSV | TPP-RSV | P@TR/NPs | PBC@TR/NPs | HPBC@TR/NPs |
|----------------------------|-------------|------------|------------|------------|-------------|
| IC ₅₀ (nmoL/mL) | 108.40±6.65 | 31.73±1.23 | 60.62±1.73 | 45.83±1.3 | 38.49±1.10 |

Data are given as mean \pm SD (n = 3).