## **Supplementary Information**

## Emerging integrated nanoclay-facilitated drug delivery system for papillary thyroid cancer therapy

Yi Zhang<sup>1,†</sup>, Mei Long<sup>1,†</sup>, Peng Huang<sup>2,†</sup>, Huaming Yang<sup>1,3,4,\*</sup>, Shi Chang<sup>2,\*</sup>, Yuehua Hu<sup>1,3</sup>, Aidong Tang<sup>5</sup>, Linfeng Mao<sup>2</sup>

- <sup>1</sup> Centre for Mineral Materials, School of Minerals Processing and Bioengineering, Central South University, Changsha 410083, China
- <sup>2</sup> Xiangya Hospital, Central South University, Changsha 410078, China
- <sup>3</sup> Hunan Key Lab of Mineral Materials and Application, Central South University, Changsha 410083, China
- <sup>4</sup> State Key Lab of Powder Metallurgy, Central South University, Changsha 410083, China
- <sup>5</sup> School of Chemistry and Chemical Engineering, Central South University, Changsha 410083, China
- \* Corresponding author, Email: H.Y.(email: <u>hmyang@csu.edu.cn</u>) or S.C.(email: <u>changshi@csu.edu.cn</u>), Fax: +86-731-88830549, Tel.: +86-731-88710804

<sup>†</sup> These authors contributed equally to this work.

## Supplementary movie, tables and figures

Movie 1 The supplementary movie 1 clearly shows the passive targeting research *in vivo* (Pig)

**Table S1** The loading amount, loading efficiency and cumulative release of DOX inDOX-Kaolin and DOX-modified-Kaolin

**Table S2** Parameters of Korsmeyer–Peppas Model of cumulative release of DOX inDOX-Kaolin and DOX-modified-Kaolin

**Figure S1** (a) XRD patterns, FTIR spectra, (c) zeta curves and (d) static water contact angle of the kaolin samples.

**Figure S2** DAPI images of DOX, DOX-Kaolin<sub>MeOH</sub> and KI@DOX-Kaolin<sub>MeOH</sub> at different concentrations

**Figure S3** CLSM images of thyroid cancer cells after the uptake of free DOX, Kaolin<sub>MeOH</sub>, DOX-Kaolin<sub>MeOH</sub>, KI@DOX-Kaolin<sub>MeOH</sub>

**Figure S4** (a) Inhibition of migratory potential of papillary thyroid cancer cells by wound healing assay before and after treatment with free DOX. (b) The percentages of migrated (\*P < 0.05) and (c) invasive (\*P < 0.05) cells determined by the migration and invasion assays

Figure S5 MTS assay and high-content screening of DOX-Kaolin<sub>MeOH</sub> with representative cancer cells

**Table S1** The loading amount, loading efficiency and cumulative release of DOX inDOX-Kaolin and DOX-modified-Kaolin

Sample	Loading amount of DOX (%)	Loading efficiency (%)	Cumulative release(pH=4.5, 31 h)			
Kaolin	54.41	90.69	43.84			
Kaolin <sub>MeOH</sub>	54.52	90.86	35.87			

**Table S2** Parameters of Korsmeyer–Peppas Model of cumulative release of DOX inDOX-Kaolin and DOX-modified-Kaolin

Sample	pH=4.5			pH=5.5			pH=7.4					
	n	k	b	$\mathbf{R}^2$	n	k	b	$\mathbf{R}^2$	n	k	b	$\mathbf{R}^2$
Kaolin	0.46	9.67	-1.58	0.99	0.54	3.74	-1.19	0.96	0.39	1.15	-0.23	0.93
Kaolin <sub>MeOH</sub>	0.42	9.05	-1.3	0.98	0.55	3.03	-0.86	0.91	0.58	0.59	0.262	0.87

 $M_t\!/M_\infty = kt^n + b$ 

k is a constant that incorporates the structure and geometric characteristics of the drug dosage form, n is the release exponent characteristic of the release mechanism, and b represents the burst effect in the release.



**Figure S1** (a) XRD patterns, (b) FTIR spectra, (c) zeta curves and (d) static water contact angle of the kaolin samples.

## DOX



Figure S2 DAPI images of DOX, DOX-Kaolin<sub>MeOH</sub> and KI@DOX-Kaolin<sub>MeOH</sub> at different concentrations



Figure S3 CLSM images of thyroid cancer cells after the uptake of free DOX, Kaolin<sub>MeOH</sub>,

 $DOX\text{-}Kaolin_{MeOH},\,KI@DOX\text{-}Kaolin_{MeOH}$ 



**Figure S4** (a) Inhibition of migratory potential of papillary thyroid cancer cells by wound healing assay before and after treatment with free DOX. (b) The percentages of migrated (\*P < 0.05) and (c) invasive (\*P < 0.05) cells determined by the migration and invasion assays



**Figure S5** MTS Assay and High-Content Screening of DOX-Kaolin<sub>MeOH</sub> with representative cancer cells