## **Supporting Information**

Colorimetric Aptasensor Based on Fluorescein as Temporal Controllable Light-Stimulated Oxidase Mimicking for Sensitive Detection of Exosomes in Mild Condition

Li-e Zheng<sup>1,2</sup>, Min Huang<sup>1,2</sup>, Yiyang Liu<sup>3</sup>, Qiufang Bao<sup>1,2</sup>, Yuxiu Huang<sup>1,2</sup>, Yuhong Ye<sup>4</sup>, Mengmeng Liu<sup>5\*</sup>, Pengming Sun<sup>6,7,8\*</sup>

<sup>1</sup> Department of Gynecology, The First Affiliated Hospital of Fujian Medical University, Fuzhou, Fujian 350005, China

<sup>2</sup> Department of Gynecology, National Regional Medical Center, Binhai Campus of the First Affiliated Hospital, Fujian Medical University, Fuzhou 350212, China

<sup>3</sup> Department of Epidemiology and Health Statistics, School of Public Health, Fujian Medical University, Fuzhou 350122, China

<sup>4</sup> Department of Pathology, The First Affiliated Hospital of Fujian Medical University, Fuzhou, Fujian 350005, China

<sup>5</sup> Department of Pharmacy, The First Affiliated Hospital of Fujian Medical University, Fuzhou, Fujian 350005, China

<sup>6</sup> Laboratory of Gynecologic Oncology, Fujian Maternity and Child Health Hospital, College of Clinical Medicine for Obstetrics & Gynecology and Pediatrics, Fujian Medical University, Fuzhou 350001, Fujian, China

<sup>7</sup> Fujian Key Laboratory of Women and Children' s Critical Diseases Research, Fujian Maternity and Child Health Hospital (Fujian Women and Children's Hospital), Fuzhou 350001, Fujian, China

<sup>8</sup> Fujian Clinical Research Center for Gynecological Oncology, Fujian Maternity and Child Health Hospital (Fujian Obstetrics and Gynecology Hospital), Fuzhou 350001, Fujian, China

Corresponding author

\*Mengmeng Liu, E-mail: <u>lmm0305@fjmu.edu.cn</u>

\*Pengming Sun, E-mail: <u>sunpengming854@163.com</u>, <u>fmsun1975@fjmu.edu.cn</u>

Name	Sequence (from 5' to 3')		
FITC labeled	Cholesterol-TTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTT		
DNA anchor			
EpCAM	Biotin-		
aptamer	GCACTACAGAGGTTGCGTCTGTCCCACGTTGTCATGGGGG		
	GTTGGCCTG		
Random	Biotin-		
sequence	TTCGTGCAGTCCATTGATGGGTGCAGTTAAATTCCTGCATG		
	AATTAATT		





**Figure. S1.** (A) The TMB oxidation by FITC under LED and xenon lights. (B) The TMB oxidation by FITC under LED lights with different wavelengths. (C) The photographs of TMB oxidation by FITC under LED lights with different wavelengths. (D) Effects of scavengers on the TMB-FITC chromogenic reaction under 365 LED

light irradiation.



**Figure S2.** The TMB oxidation by free FITC and DNA modified FITC under LED light.



Figure S3. Proposed mechanism for light-stimulated oxidase mimicking activity of FITC.



**Figure S4.** The optimization of experimental conditions. Influence of (A) aptamer concentration, (B) the capturing time for exosomes, (C) DNA anchor concentration, (D) incubation time between DNA anchor and exosomes, (E) the pH value for colorimetric reaction, (F) the light irradiation time.



**Figure S5.** (A) UV-vis absorbance toward different exosomes concentrations (from a to f represented 0, 20.0, 40.0, 60.0, 80.0,  $100.0 \times 10^5$  particles mL<sup>-1</sup>). (B) Linear calibration curve of detection exosomes.

LOD	Detection range	Ref.
(particles/mL)	(particles/mL)	
1.71×10 <sup>6</sup>	2.86×10 <sup>6</sup> -2.86×10 <sup>10</sup>	44
9.66×10 <sup>6</sup>	107-1010	45
4.8×10 <sup>5</sup>	1.66×10 <sup>6</sup> -1.66×10 <sup>9</sup>	46
9.38×10 <sup>4</sup>	4.66×10 <sup>6</sup> -9.32×10 <sup>9</sup>	47
8.7×10 <sup>4</sup>	2.5×10 <sup>5</sup> -2.5×10 <sup>10</sup>	48
1.161×10 <sup>4</sup>	5.00×10 <sup>4</sup> -5.00×10 <sup>8</sup>	49
5.0×10 <sup>4</sup>	0-106	50
4.5×10 <sup>4</sup>	1.0×10 <sup>5</sup> -1.0×10 <sup>6</sup>	51
1.027×10 <sup>6</sup>	2.0×10 <sup>6</sup> -4.0×10 <sup>7</sup>	52
2.170×10 <sup>6</sup>		
5.2×10 <sup>8</sup>	1.84×10 <sup>9</sup> -2.21×10 <sup>10</sup>	53
	(particles/mL) 1.71×10 <sup>6</sup> 9.66×10 <sup>6</sup> 4.8×10 <sup>5</sup> 9.38×10 <sup>4</sup> 8.7×10 <sup>4</sup> 1.161×10 <sup>4</sup> 5.0×10 <sup>4</sup> 4.5×10 <sup>4</sup> 1.027×10 <sup>6</sup> 2.170×10 <sup>6</sup>	(particles/mL)       (particles/mL)         1.71×106       2.86×106-2.86×1010         9.66×106       107-1010         4.8×105       1.66×106-1.66×109         9.38×104       4.66×106-9.32×109         8.7×104       2.5×105-2.5×1010         1.161×104       5.00×104-5.00×108         5.0×104       0-106         4.5×104       1.0×105-1.0×106         1.027×106       2.0×106-4.0×107         2.170×106       2.0×106-4.0×107

## Table S2. Comparison of the present aptasensor and other methods for exosomes

detection

DNA-capped single-walled carbon			
nanotubes			
Dual-modal aptasensor based on	1.3×10 <sup>5</sup>	5.0×10 <sup>6</sup> -1.0×10 <sup>9</sup>	54
acridone derivative			
A colorimetric aptasensor based on	1.77×10 <sup>5</sup>	0-100×10 <sup>5</sup>	This work
light-stimulated oxidase			
mimicking of FITC			



**Figure S6.** The WB images of EpCAM from different cell lines derived exosomes, including SKOV-3, HepG2, IOSE-8, GES-1, and MCF-10A.



**Figure S7.** PAGE results of the EpCAM aptamer. Lane M: marker, lane 1: EpCAM aptamer in PBS, lane 2: EpCAM aptamer in serum.

Table S3. Performance of exosomes and serum CA-125 in OC versus HD

Marker	Sensitivity (%)	Specificity (%)	Accuracy (%)	AUC
Exosomes	93.8	100	96.3	0.994
	(85.4 - 100)	(100)	(96.2 - 96.4)	(0.983 - 1.000)
Serum CA-	43.8	90.9	63.0	0.645
125	(26.6 - 60.9)	(78.9 - 100)	(62.1 - 63.8)	(0.496 - 0.793)

discrimination (Ninety-five percent CIs are indicated in parentheses)