Supporting Information

Electrical and Label-Free Quantification of Exosomes with Reduced Graphene Oxide Field Effect Transistor Biosensor

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Figure S1. The schematic diagram of exosomes detection by CD63-modified FET biosensor.

Figure S2. (a) The concentration range and particle size distribution of exosomes were assayed with nanoparticle tracking analysis system. The total concentration was calculated to be 3.3×10^{10} particles/mL. (b) Zeta potential distribution of exosome.

Figure S3. AFM imaging before and after anti-CD63 modification. (a) RGO modification. (b) Anti-CD63 functionalization on RGO surface.

Figure S4. TEM image of exosome purified from serum with a size of approximately 100 nm in diameter.

 Table 1. Comparison of different exosome detection techniques

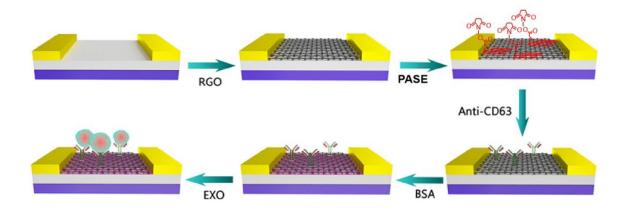


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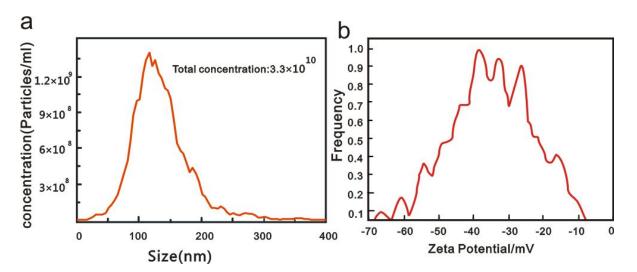


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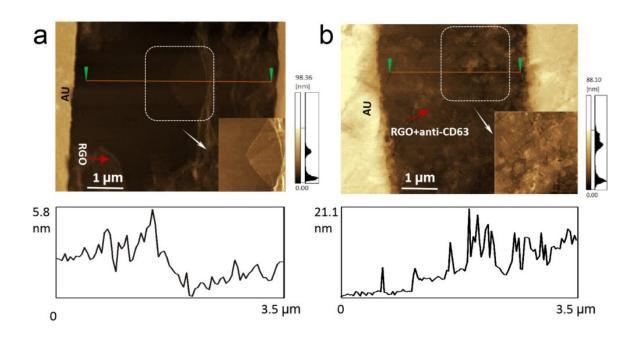


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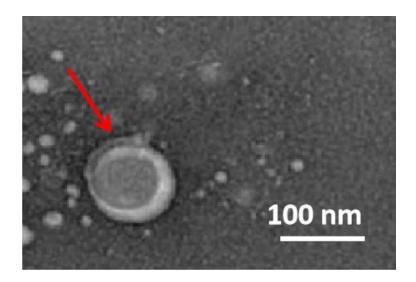


Figure S4. TEM image of exosome purified from serum with a size of approximately

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No	Detection	Method	LOD(part	Time	Ref
	platform		icles/µL)		
1	Electrochemistry	nanotetrahedron(NTH)-assisted aptasensor	20	30min	1
2		Electrochemical sandwich immunosensor	2×10 ²	60min	2
3		Aptamerrecognitioninduced multi-DNA release and cyclic enzymatic amplification	70	~5 h	3
4		Aptamer-based electrochemical biosensor	10×10 ³	~60 min	4
5	Fluorescence	Immuno-capture on GO/PDA nano interface and Fluorogenic ELISA	50	~60 min	5
6		Aptamer/Go captures exosomes and enzymatic amplification	1.6×10 ²	~30 min	6
7	Optical	Single particle Interferometric Reflectance Imaging Sensor	3.94×10 ⁶	>12 h	7
8		Colorimetric aptasensor	5.2×10 ⁵	~40 min	8
9	SPR	Antibody modified nano-plamsonic array	3×10 ³	~60 min	9
10	FET	Anti-CD63functionalized field effect transistor	33	~30 min	This work

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REFERENCE

- Wang, S.; Zhang, L.; Wan, S.; Cansiz, S.; Cui, C.; Liu, Y.; Wu, Y. Aptasensor with expanded nucleotide using DNA nanotetrahedra for electrochemical detection of cancerous exosomes. *ACS Nano*. 2017, *11*, 3943-3949.
- (2) Doldán, X.; Fagúndez, P.; Cayota, A.; Laíz, J.; Tosar, J. P. Electrochemical sandwich immunosensor for determination of exosomes based on surface marker-mediated signal amplification. *Anal. Chem.* 2016, 88, 10466-10473.
- (3) Dong, H.; Chen, H.; Jiang, J.; Zhang, H.; Cai, C.; Shen, Q. Highly sensitive electrochemical detection of tumor exosomes based on aptamer recognition-induced multi-DNA release and cyclic enzymatic amplification. *Anal. Chem. Anal. Chem.* 2018, *90*, 4507-4513.
- (4) Zhou, Q.; Rahimian, A.; Son, K.; Shin, D. S.; Patel, T.; Revzin, A. Development of an aptasensor for electrochemical detection of exosomes. *Methods* 2016, 97, 88-93.
- (5) Zhang, P.; He, M.; Zeng, Y. Ultrasensitive microfluidic analysis of circulating exosomes using a nanostructured graphene oxide/polydopamine coating. *Lab Chip* 2016, *16*, 3033-3042.
- (6) Jin, D.; Yang, F.; Zhang, Y.; Liu, L.; Zhou, Y.; Wang, F.; Zhang, G. J. ExoAPP: Exosome-Oriented, Aptamer Nanoprobe-Enabled Surface Proteins Profiling and Detection. *Anal. Chem.* 2018, 90, 14402-14411.

- (7) Daaboul, G. G.; Gagni, P.; Benussi, L.; Bettotti, P.; Ciani, M.; Cretich, M.;Prosperi, D. Digital detection of exosomes by interferometric imaging. *Sci. Rep.* 2016, 6, 37246.
- (8) Xia, Y.; Liu, M.; Wang, L.; Yan, A.; He, W.; Chen, M.; Chen, J. A visible and colorimetric aptasensor based on DNA-capped single-walled carbon nanotubes for detection of exosomes. *Biosens.Bioelectron.* 2017, *92*, 8-15.
- (9) Im, H.; Shao, H.; Park, Y. I.; Peterson, V. M.; Castro, C. M.; Weissleder, R.; Lee, H. Label-free detection and molecular profiling of exosomes with a nano-plasmonic sensor. *Nat. Biotechnol.* 2014, *32*, 490.