Electronic Supplementary Information

Electrochemical current rectifier as high sensitive and selective cytosensor for cancer cell detection

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Experimental section

Materials. 16-mercaptohexadecanoic acid (MHDA), FA, potassium hexachloroiridate(IV), N-(3-Dimethylaminopropy)-N'-ethylcarbodiimide hydrochloride (EDC) and N-hydroxysuccinimide (NHS) were purchased from Aldrich and used as received. 11-undecanethiol-1-ferrocene (UDT-Fc) was from Dojindong Co**.** Dulbecco's modified Eagle's medium (DMEM) was obtained from HyClone Corp. (USA). Trypsin was obtained from Amresco (USA). Fetal bovine serum (FBS) was obtained from Gibco (USA). All other chemicals used were of analytical grade and were used without further purification. The phosphate buffered saline (PBS) contains 8.0 g L^{-1} NaCl, 0.2 g L^{-1} KCl, 1.44 g L^{-1} Na_2HPO_4, and 0.24 g L^{-1} KH_2PO_4 (pH: 7.4). MHDA was dissolved in ethanol at the concentration of 1 mM, so was UDT-Fc. The water used throughout all experiments was purified through a Millipore system.

Preparation of FA-modified Gold Bead Electrode. A gold bead electrode with 0.11 cm^2 was firstly annealed with a hydrogen flame and then cooled to room

temperature gradually. Afterwards, the electrode was rinsed with Milli-Q water. Subsequently, the electrode was immersed into the mixture of UDT-Fc and MHDA (1:15, V/V). A compact mixed monolayer is necessary to achieve electrochemical current rectification and guarantee the stability of the system. Toward this goal, various factors were taken into account, including kinetic and thermodynamic factors, monomer ratio, and so on.[1] In our investigations, it was found that compact mixed monolayer can be formed by immersing an electrode into a mixture of UDT-Fc and MHDA (1:15, v/v) at 60 1C for 4 h, resulting in a modified electrode Au/(UDT-Fc)-MHDA. MHDA-modified electrode was similarly prepared using only MHDA solution. Before measurement, the prepared electrode was carefully rinsed with large amount of ethanol and Milli-Q water. To further conjugate FA, the electrode was firstly immersed in the mixture of 15 mM NHS/75 mM EDC in water for 40 min at ambient temperature to activate the terminal carboxylate group of MHDA and then rinsed with water. Finally, the activated gold bead electrode was immersed in 25 mM FA aqueous solution for 15 min and then rinsed with Milli-Q water.

Cell Culture and Preparation of Cell Suspensions. The folate receptor-rich HeLa cell and folate receptor-lack normal cells (human embryonic kidney cell: HEK 293) were cultivated for in vitro experiments. Both of HeLa and HEK 293 were obtained from Kunming Institute of Zoology, Chinese Academy of Sciences. All the cells were cultured in DMEM, supplemented with 10% fetal bovine serum (FBS) at 37 ºC in a humidified 5% CO_2 incubator. After the concentration of cells reached

about 1×10^6 cells mL^{-1}, HeLa and HEK 293 cells were trysinized in the presence of 0.25% trypsin solution and collected from the medium by centrifugation at 3000 rpm for 5 min. The collected cells were washed with saline twice and resuspended in saline to achieve the desired concentration for experimental measurement.

Electrochemical Experiments. Cyclic voltammetry (CV) and differential pulse voltammetry (DPV) were performed in a classical three-electrode cell. Platinum foil and a saturated calomel electrode (SCE) worked as counter and reference electrodes, respectively. PBS (pH: 7.4) was used as supporting electrolyte. The cyclic voltammograms and differential pulse voltammograms were recorded with CHI 900 (Co. Chenhua, China). The parameters of DPVs: amplitude, 50 mV; pulse width, 0.05 s; pulse period, 0.2 s.

Results:

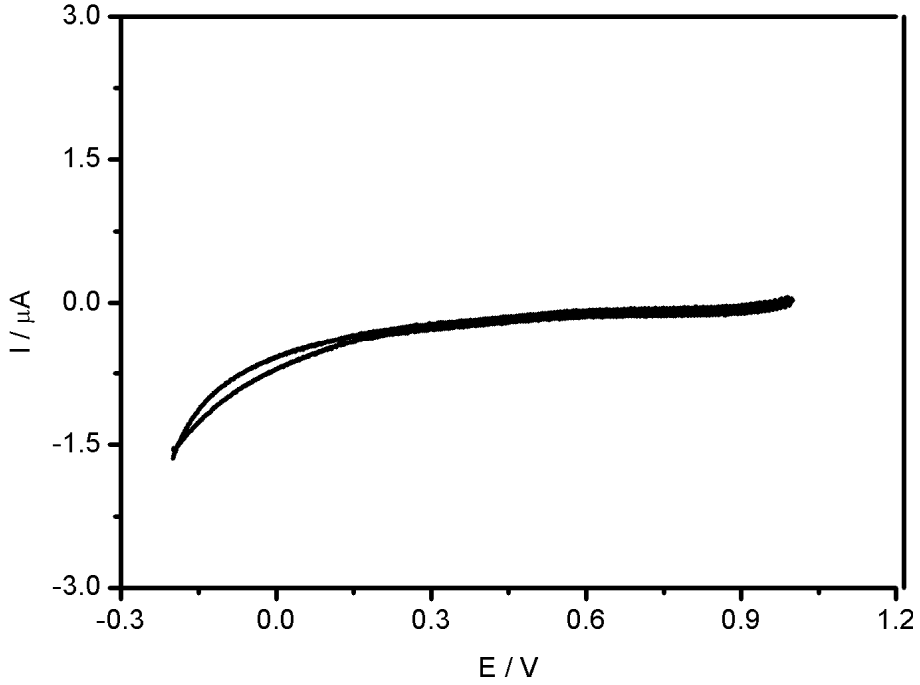

Fig. S1 Cyclic voltammogram of MHDA modified electrode in 5 mM K_2IrCl_6 solution. Scan rate: 50 mV s^{-1}.

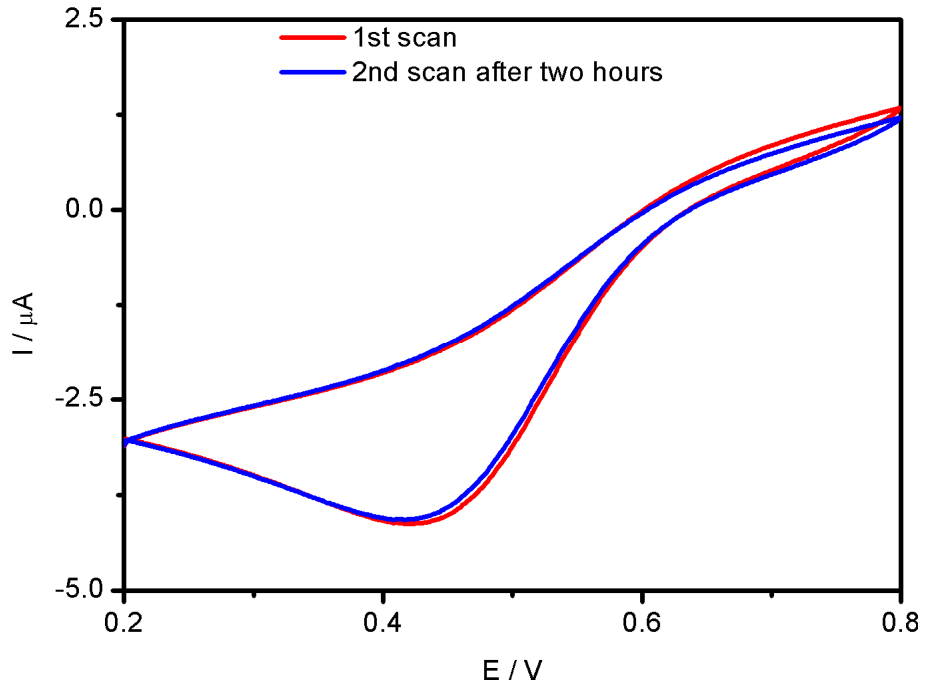

Fig. S2 Cyclic voltammograms of UDT-Fc/MHDA modified gold bead electrode electrode in 1 mM K_2IrCl_6 solution recorded at different time. Scan rate: 50 mV s^{-1}.

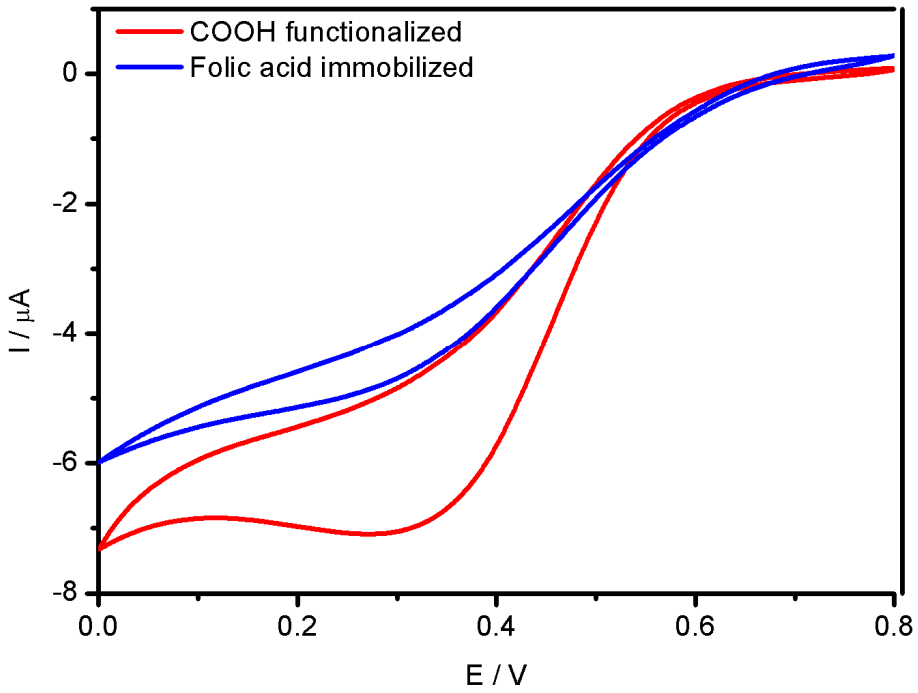

Fig. S3 Cyclic voltammograms of Au/(UDT-Fc)-MHDA in 1 mM K_2IrCl_6 solution before and after FA conjugation through amide bond. Scan rate: 50 mV s^{-1}.

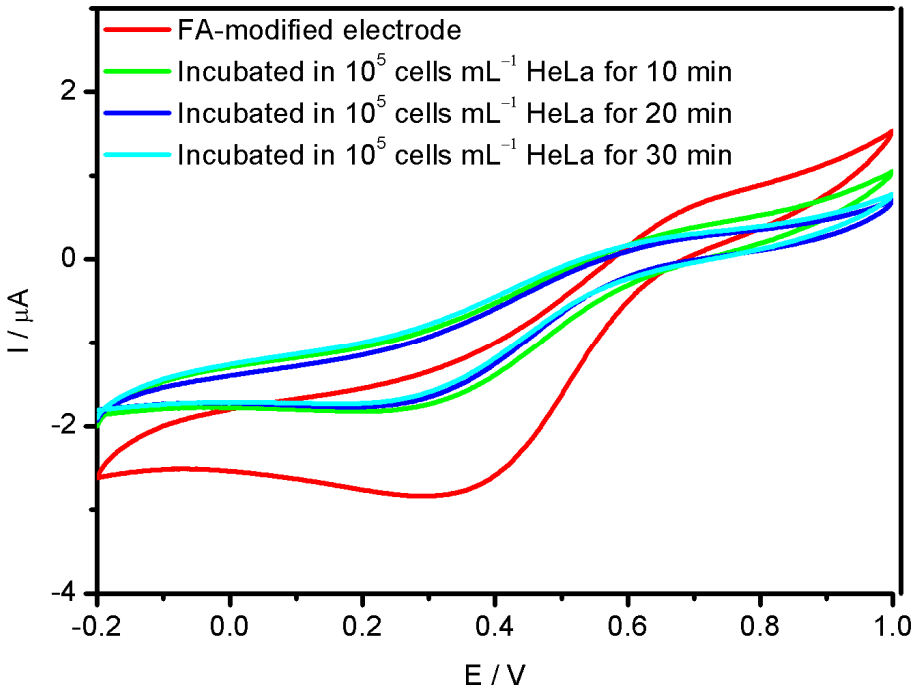

Fig. S4 Cyclic voltammograms of FA-modified gold bead electrode in 1 mM K_2IrCl_6 solution after being incubated in 10^5 cells mL^{-1} suspension in saline for different time. Scan rate: 50 mV s^{-1}.

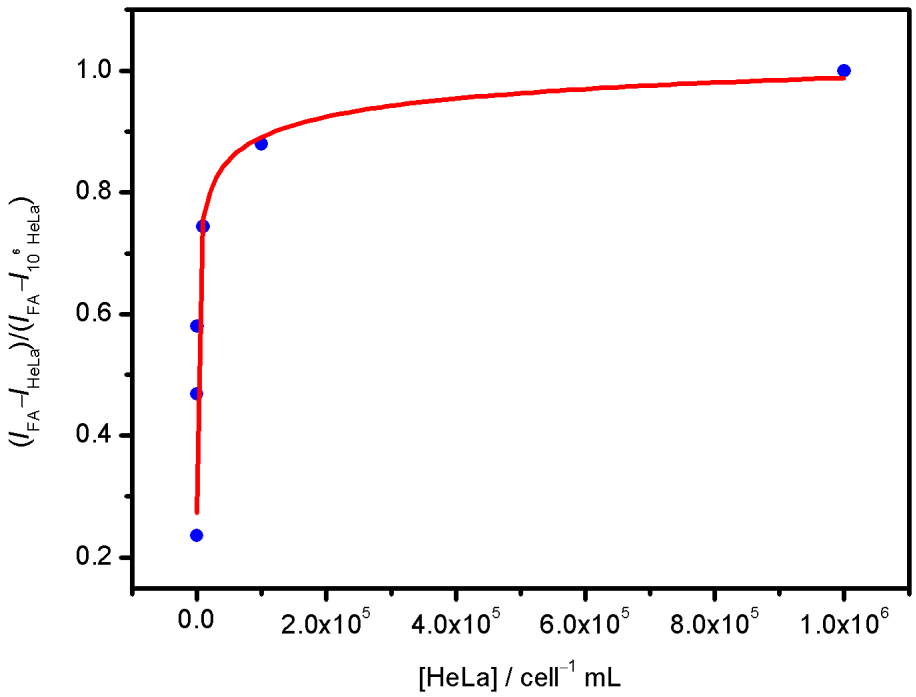

Fig. S5 The non-linear Langmuir fitting of the current change $(I_{Blank}-I_{HeLa})/(I_{Blank}-I_{10^6\ HeLa})$ against cell concentrations, where I_{Blank}, I_{HeLa} and $I_{10^6\ HeLa}$ are the peak current intensities in the absence of cells, different concentrations of HeLa cells and 10^6 cells mL^{-1} (HeLa), respectively.

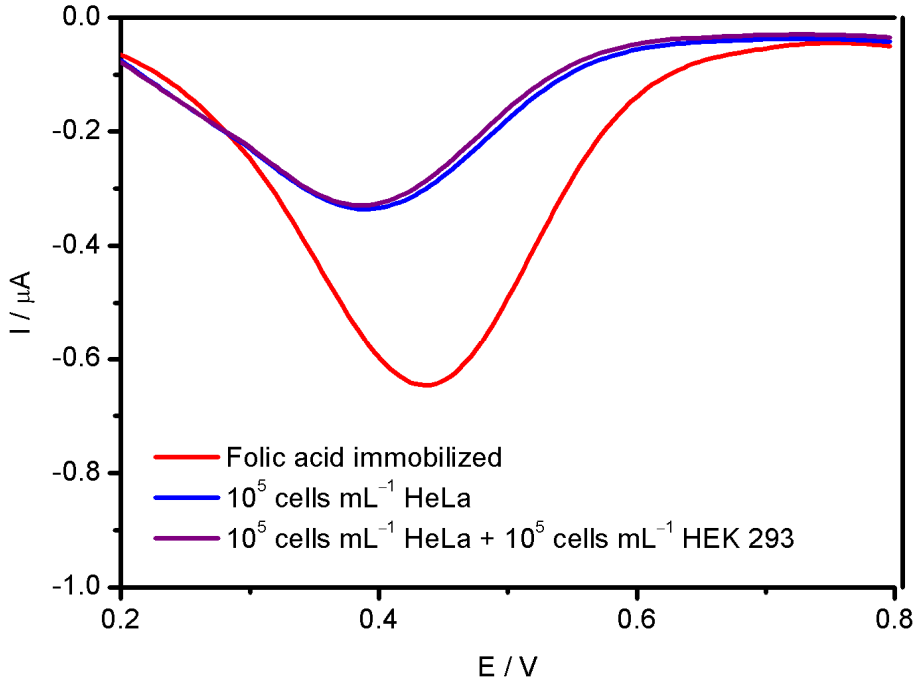

Fig. S6 DPV responses of the FA-modified electrode in 5 mM K_2IrCl_6 solution after being incubated with suspensions of 0 cells mL^{-1}, 10^5 cells mL^{-1} HeLa, 10^5 cells mL^{-1} HeLa + 10^5 cells mL^{-1} HEK 293, respectively.

Reference:

1. (a) L. T. Zhang, T. B. Lu, G. W. Gokel and A. E. Kaifer, Langmuir, 1993, 9, 786; (b) C. D. Bain, J. Evall and G. M. Whitesides, J. Am. Chem. Soc., 1989, 111, 7155; (c) J. P. Folkers, P. E. Laibinis and G. M. Whitesides, Langmuir, 1992, 8, 1330.