Supporting Information

Experimental Section

Materials and reagents

DNA sequences, shown as following, were synthesized by Sangon Biotech (Shanghai) Co., Ltd with purification using PAGE method:

DNA primer: 5'-HS $(CH_2)_6$-TTTTTTAATCCGTCGAGCAGAGTT-3',

Complementary DNA (cDNA): 5'-NH_2-TTTTTTCCCAAT CCCAAT-3'.

The dNTP mix is purchased from Bioer Technology CO., Ltd. Glycol-bis-(2-aminoethylether)-N,N,N',N'-tetraacetic acid (EGTA), Phenylmethylsulfonyl fluoride (PMSF), 3-[(3-cholamidopropyl) dimethylammonio]- 1-propanesulfonate (CHAPS) are obtained from Bio Basic Inc. (Canada) and use as supplied. Invertase from baker's yeast (S. cerevisiae), 1, 4-phenylene diisothiocyanate (PDITC), and Tris(2-carboxyethyl) phosphine hydrochloride (TCEP) are bought from Sigma. Other chemicals employed are all of analytical grade. All the solutions are prepared with double-distilled water, which has been purified with a Milli-Q purification system.

Buffer solutions involved in this work were as follows: immobilization buffer solution (10 mM Tris–HCl containing 1 mM EDTA, 100 mM NaCl and 10 mM TCEP, pH 7.4), hybridization buffer solution (10 mM Tris–HCl containing 1 mM EDTA, 300 mM NaCl and 1 mM $MgCl_2$, pH 7.4), extension solution (20 mM Tris-HCl (pH 8.3), containing 4 mM $MgCl_2$, 1 mM EGTA, 63 mM KCl, 0.05% Tween 20, and 2 mM dNTP), and electrochemical impedance spectroscopy (EIS) test solution ($K_4[Fe(CN)_6]/K_3[Fe(CN)_6]$ and 0.1 M KCl, pH 7.4).

Preparation of telomerase extractions

Telomerase extractions are prepared according to the previous method. HeLa cells are removed from the substrate by trypsinization, washed with phosphate buffer solution (pH 7.4) twice and pelletted at 2000 rpm for 10min at 4°C. Next, about 1×10^5 cells/mL cells are resuspended in a cold CHAPS lysis buffer (10 mM Tris-HCl, pH 7.4, 1 mM $MgCl_2$, 1 mM EGTA, 0.1 mM PMSF, 0.5% CHAPS, and 10% glycerol), incubated for 30 min in ice, and then centrifuged for 20 min(12 000 rpm, 4 °C). The

supernatant was flash frozen and stored at -20 °C.

Preparation of inverse-modified cDNA

Inverse-functional cDNA (Invertase-cDNA) was prepared firstly. Briefly, 100 μL of 1 μM cDNA was mixed with 20 mg of PDTIC dissolved in 1 mL DMF with shaking at room temperature in the dark for 2 h. Next, 3 mL Millipore water and 3 mL 1-butanol were added into above solution with shaking slightly. After 10 min, the upper organic phase was discarded. And then the aqueous phase was extracted with 2 mL 1-butanol 3 times, and purified by Amicon-10K using hybridization buffer solution for 3 times to achieved PDITC-activated cDNA. 1 mg of invertase was introduced above activated DNA in the buffer solution with shaking overnight, and then the above solution was purified by Amicon-100K 3 time to achieved invertase-labeled cDNA.

Immobilization of primer on SPGE

SPEG (L3.3×W1.0×H0.05, cm) was bought from DropSens (Spain), containing a 4 mm diameter disk gold working electrode, Pt counter electrode and a silver pseudo-reference electrode. Before the experiment, the electrode was rinsed with ultrapure water, and dried with nitrogen. For the immobilization, 20 μL of primer buffer solution contain 0.1 μM primer was dropped on gold working electrode for 120 min in dark, and the electrode was rinsed to decrease physical adsorption. Then, primer-modified SPGE surface was passivated using 1 mM MCH solution for 60 min.

Elongation of primer

Known amounts of telomerase extracts were mixed into 100 μL 20 mM Tris-HCl (pH 8.3), containing 4 mM $MgCl_2$, 1 mM EGTA, 63 mM KCl, 0.05% Tween 20, and 2 mM dNTP, as the final reaction solution. Next, the reaction solution was introduced on the primer-immobilized electrode surface to extend the primer at 37 ^{o}C for a certain time. For control experiment, telomerase extracts were heated at 85 ^{o}C for 5 min.

Assay of telomerase activity using the PGM

The solution containing invertase-cDNA was doped on the above treated electrode surface for 1 h. For blank experiment, invertase- cDNA was doped on the

only primer-immobilized electrode surface with extension reaction. The electrode was rinsed with ultrapure water to remove away unreacted cDNA. Subsequently, 20 μL of 1 M sucrose was dripped on the electrode surface for 15 min at room temperature. The resulted solution was detected using the PGM to generate readout signal.

Results and Discussions

Feasibility of this proposed method for telomerase. In addition, above changes in the interface of the electrode surface can be also verified by the EIS. The impedance spectra include the semicircle portion at higher frequencies related to the electron transfer-limited process, and the linear part at lower frequencies corresponding to diffusion. The semicircle diameter change reflects the change in the interfacial charge-transfer resistance (R_{ct}), which is associated to the situation on the electrode. Figure 1S showed the impendance spectra at different modified electrode in 5 mmol/L $[Fe(CN)_6]^{3-/4-}$ solution. It is obvious that compared to bare electrode (curve a), R_{ct} enhances from 121.5 Ω to 327.6 Ω following the immobilization of primer on the electrode (curve b) due to the repulsion between the negative change phosphate backbone of the oligonucleotides and $[Fe(CN)_6]^{3-/4-}$. A similar semicircle is observed when the modified electrode is incubated with extension solution without the telomerase (curve c, 412 Ω). Further, with the extension reaction (curve d), R_{ct} is up to is 1431 Ω. It is ascribed to the generation of amounts of negative charge DNA. However, after preheating the telomerase, the R_{ct} is similar with that of primer-modified electrode (curve e), showing that no extension reaction occurs. The results of EIS are corresponding to those of the PGM and the color changes of control window.

Figure S1

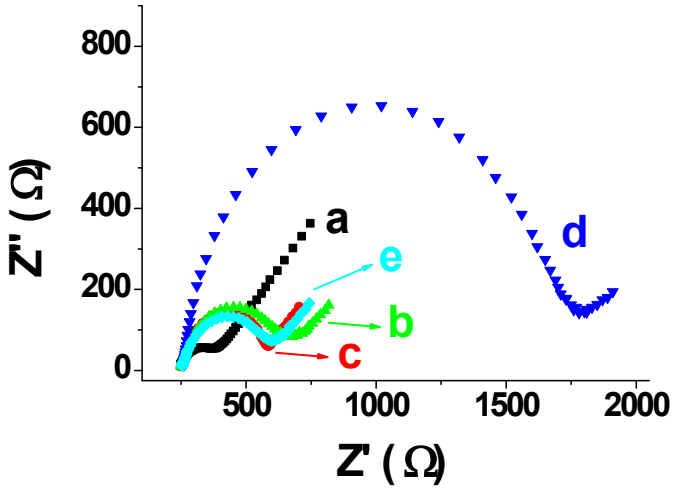

Figure S1 Impedance spectra of different modified SPGEs. a) bare electrode; b) primer-modified electrode; c) primer-modified electrode without the telomerase; d) primer-modified electrode with the telomerase; e) primer-modified electrode with the preheated telomerase.

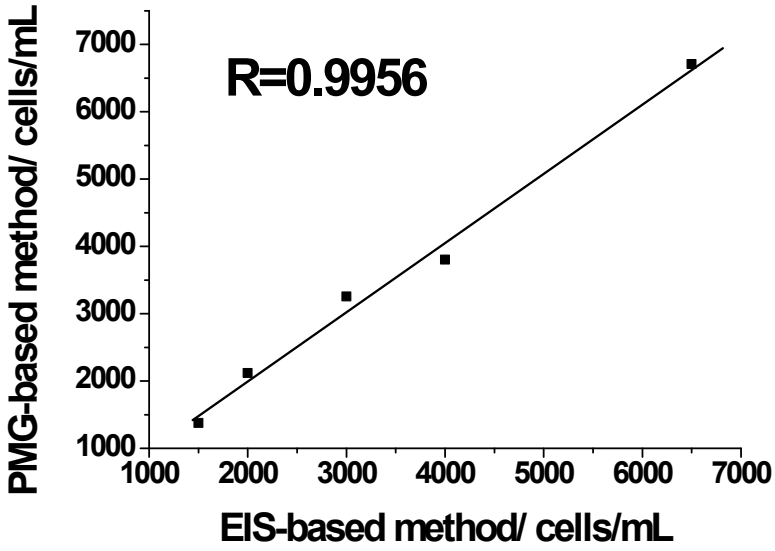

Figure S2 Comparison between the proposed PGM-based method and the previous EIS-based method. Correlation coefficient of this regression equation is 0.9956.