Supporting Information

Experimental Section

Chemicals. Peptides (SH-PEG-CALNNGPLGVRGRAK-N_2H) were synthesized by GL Biochem (Shanghai). MMP-2 was purchased from Sino Biological Inc. Co., Ltd.. 4-aminophenylmercuric acetate (APMA) was purchased from Shanghai Genmed Gene Pharmaceutical Technology. Co., Ltd.. 6-mercaptohexano (MCH), N-(3-dimethylaminopropyl)-N'-ethylcarbodiimide (EDC) and N-Hydroxysuccinimide (NHS) were received from Shanghai Medpep Co., Ltd. All other chemicals were of analytical grade.

All solutions were prepared with using Milli-Q reagent water (Milli-Q, Millipore, 18.2-MΩ resistivity). Peptide buffer solution was prepared by dissolving 4.5 mg peptide into TCNB buffer (50 mM Tris-HCl with 10 mM $CaCl_2$, 150 mM NaCl, and 0.05% Brij 35; pH 7.5). Electrochemical buffer solution: (10 mM Tris-HCl with 10 mM $MgCl_2$, and 500 mM KCl, pH 7.4).

The preparation of Fc-labeled peptide. Fc-labeled peptide was prepared according to the previous reports. Firstly, 10 mg/mL of ferrocene acetic acid was added to the solution containing EDC/NHS (0.1 mol/L for each) for 3 h to activate the COOH group of ferrocene acetic acid. Next, 150 μL of activated ferrocene acetic acid mixture solution was incubated with 50 μL peptide solution at room temperature overnight. Then, the resulted solution was stored in refrigerator at 4 ^{o}C for the following experiments.

The fabrication of peptide-modified electrode. A gold electrode (2 mm in diameter,

CH Instruments, Shanghai, China) was immersed into freshly prepared piranaha acid (V_{H2SO4}:V_{H2O2}=1:1) for 1 h, and then polished with aqueous slurries of 1.0 μm, 0.3μm and 0.05μm α-Al_2O_3 powders on a polishing microcloth and sonicated with deioned water, ethanol for 3 min, respectively. After rinsing with deioned water, the above electrode was electrochemically activated by consecutively cycling in the potential range of 0 ~ +1.6 V in 0.5 mol/L sulfuric acid until a cyclic voltammogram was achieved, which means that a clean gold electrode was obtained. This treated electrode was then interacted with 10 μL as-prepared Fc-labeled peptide solution for 90 min to achieve a peptide-modified electrode.

MMP-2 detection. Firstly, MMP-2 solutions were prepared by dissolving MMP-2 into TCNB buffer. Before the analysis, MMP-2 was activated with APMA according to the provided protocols by the manufacturer. Briefly, 20 μL of MMP-2 at different concentrations were mixed with 2 mM APMA (final concentration) in 37 ^{o}C water bath for 1 h. And then the proposed peptide-modified electrode was immersed into the actived MMP-2 solution for 60 min at room temperature followed by the electrochemical measurement.

Electrochemical measurement. All electrochemical measurements were carried out using CHI 660D electrochemical system (CH Instruments, Shanghai, China) at room temperature. A three-electrode electrochemical cell was used. Above peptide-modified gold electrode was used as the working electrode. Platinum wire and Ag/AgCl (saturated with KCl) were used as counter and reference electrodes, respectively. Differential pulse voltammetry (DPV) was used as scan mode. The

parameter was set as follow: the potential interval from 0 to +0.4 V vs. Ag/AgCl, modulation amplitude 0.05V, pulse width 0.06 s, and sample width 0.02 s.

Treatment of blood serum. Blood sample was kept in EP tube for overnight at 4 ^{o}C. After centrifugation for 20 min at 4 ^{o}C, the clear supernatant layer was collected via 0.45 μm milli-pore filter to obtain blood serum sample. The collected serum was diluted to certain volume using double distilled de-ionized water for the following experiment.

Results and Discussion

Optimized condition.

In order to achieve better assay results, some conditions are optimized. Immobilization time of peptides is an important factor for the performance of the sensor. As shown in Fig. S1A, upon increasing assembly time, more Fc-peptide is immobilized on the gole electrode, resultin in the DPV signal enhances. While the assembly time exceeds 60 min, DPV signal reaches a plateau due to the steric hindrance. Thus, 60 min is used as the assembly time of peptide for the following experiment. Additionally, the hydrolytic time of peptides is also investigated. The results are shown in Fig. S2B. It is found that DPV signal decreases sharply until the hydrolytic time opproaches 90 min. Hence, 90 min is set as the optimal hydrolytic time.

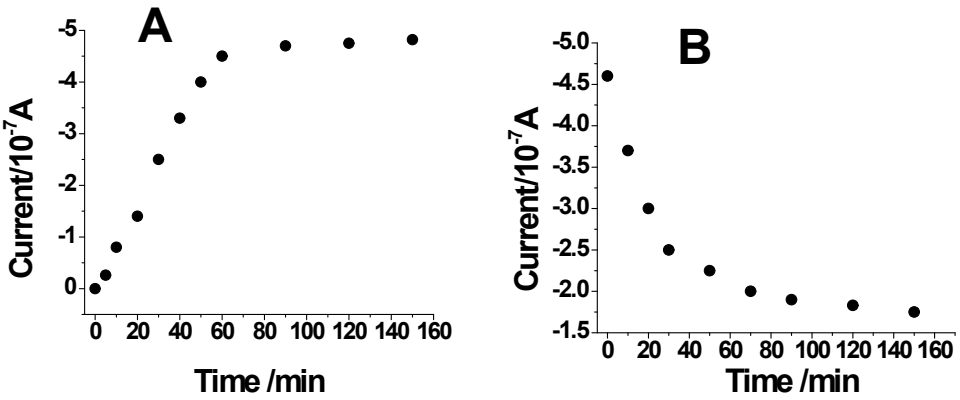

Figure S1 A) Optimization of the measuring system. Influence of: (A) immobiled time (B) incubation time.

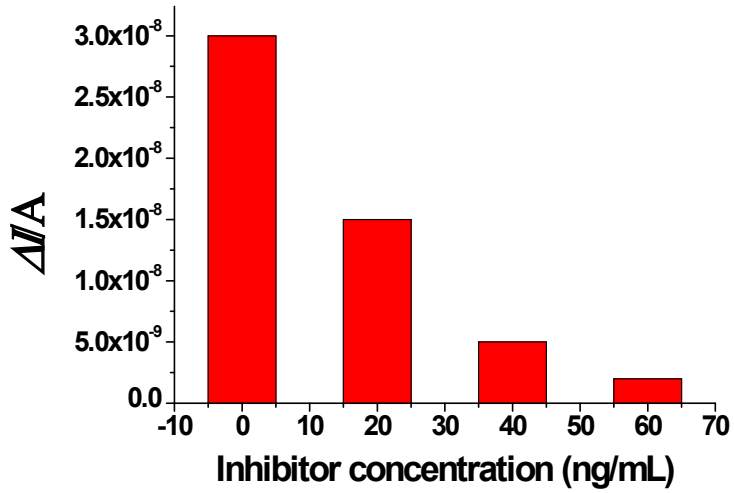

Figure S2 Current response of the sensor upon the introduction of different concentration of the inhibitor.