# Supporting Information

# Label-Free and Ultrasensitive APE1 Detection Based on Hybridization Chain Reaction Combined with G-Quadruplex

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## 1. Optimization of the experimental conditions of the system

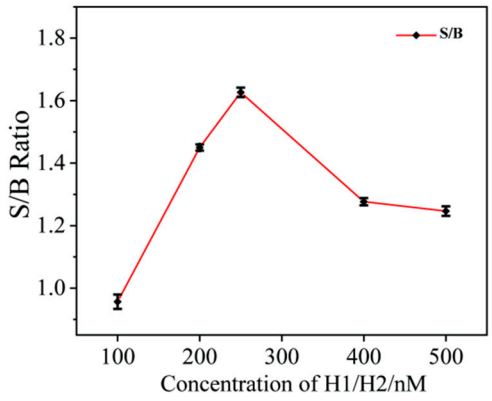



**Figure S1.** Optimization the concentration of H1 and H2 (Error bars: n=3).

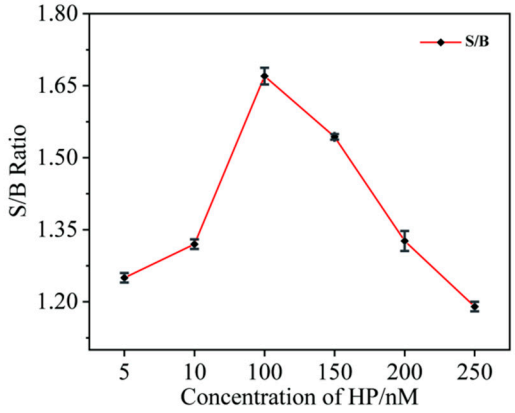



**Figure S2.** Optimization the concentration of HP (Error bars: n=3).

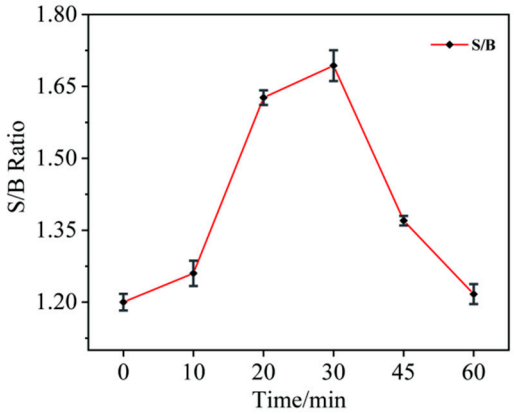



**Figure S3.** Optimization of the reaction time (Error bars: n=3).

## 2. Effects of HCR

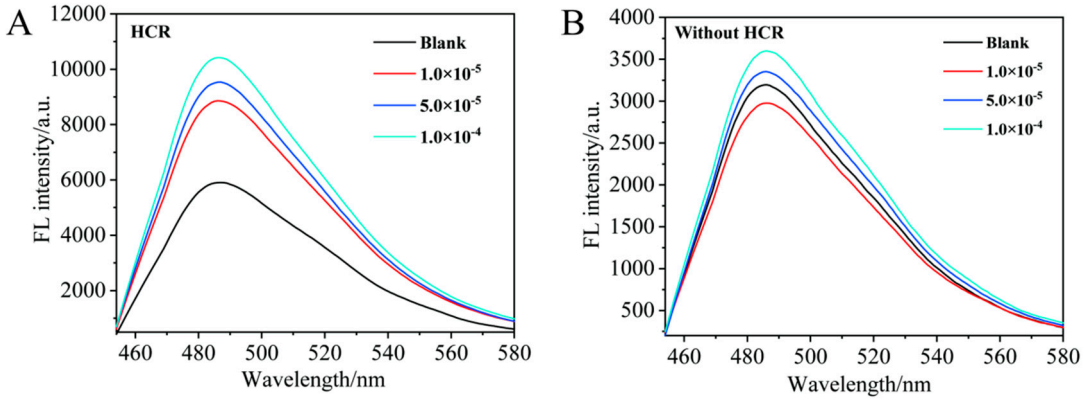



**Figure S4.** Effects of HCR. (A)Fluorescence spectra of the system with HCR amplification; (B) Fluorescence spectra of the system by only use H1 as the fuel. Concentration of APE1($1\times10^{-5}$、$5\times10^{-5}$、$1\times10^{-4}$ U/mL）

## 3. Repeatability and stability analysis of the biosensor

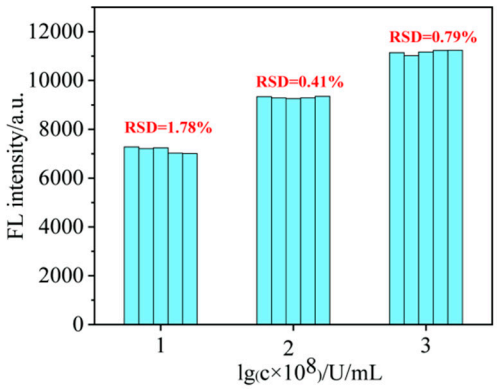



**Figure S5.** Repeatability of the proposed APE1 assay (APE1 concentration: $1\times10^{-7}$、$1\times10^{-6}$、$1\times10^{-5}$ U/mL, Error bars: n=3).

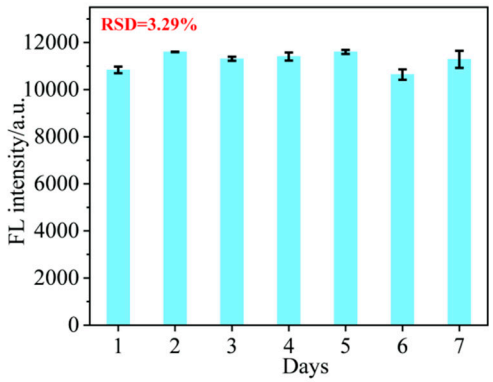



**Figure S6.** Stability of proposed APE1 assay (APE1 concentration: $1\times10^{-5}$ U/mL, Error bars: n=3)

## 4. Application of the proposed assay in actual samples

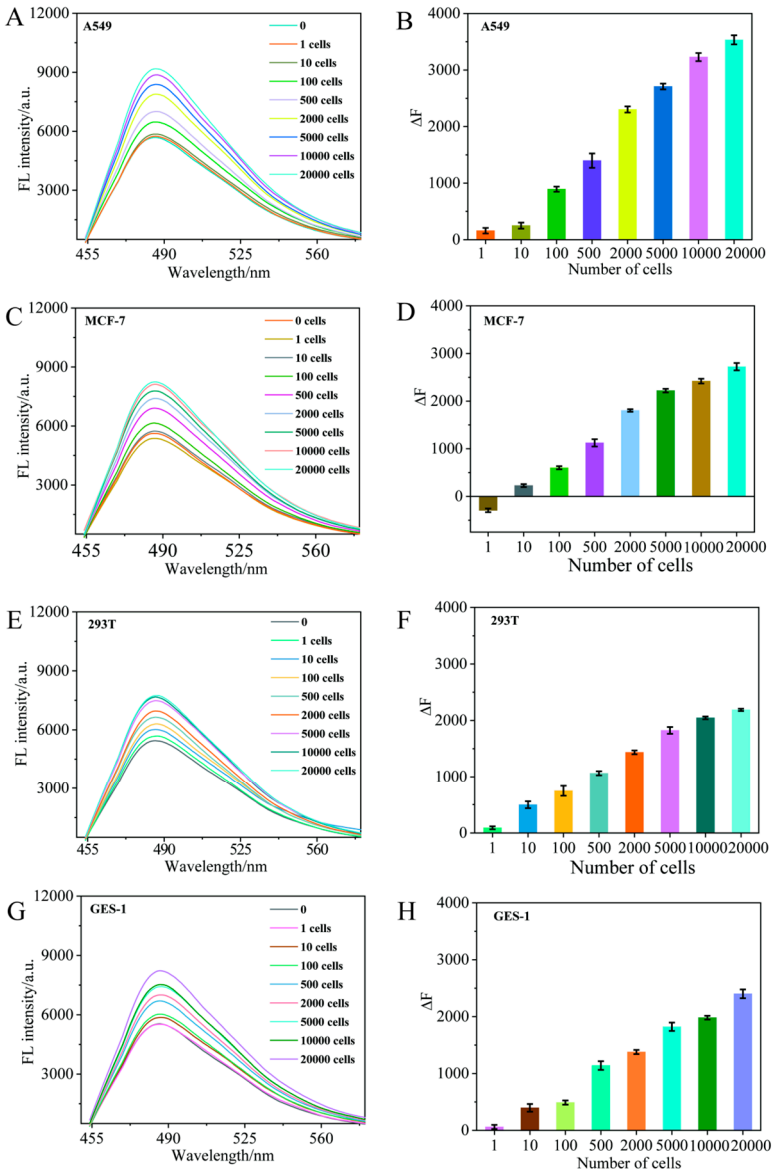



**Figure S7.** (A) Fluorescence spectra of A549 cell lysates (0–20,000 cells). (B) Corresponding

fluorescence intensity quantification for A549 cells. (C) Fluorescence spectra of MCF-7 cell lysates (0–20,000 cells). (D) Corresponding fluorescence intensity quantification for MCF-7 cells. (E) Fluorescence spectra of 293T cell lysates (0–20,000 cells). (F) Corresponding fluorescence intensity quantification for 293T cells. (G) Fluorescence spectra of GES-1 cell lysates (0–20,000 cells). (H) Corresponding fluorescence intensity quantification for GES-1 cells (Error bars: n=3).

## 5. APE1 mRNA expression level

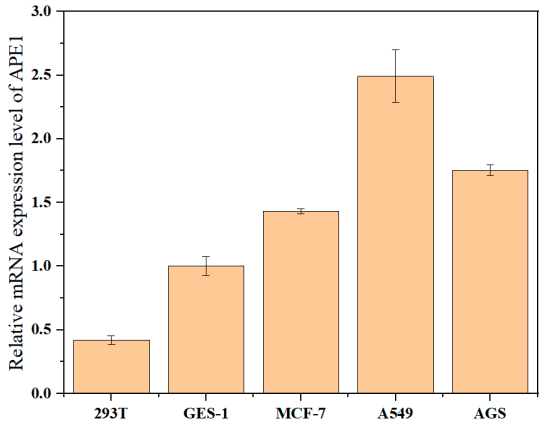



**Figure S8.** Relative mRNA expression level of APE1 (Error bars: n=3).

## 6. APE1 inhibition assay

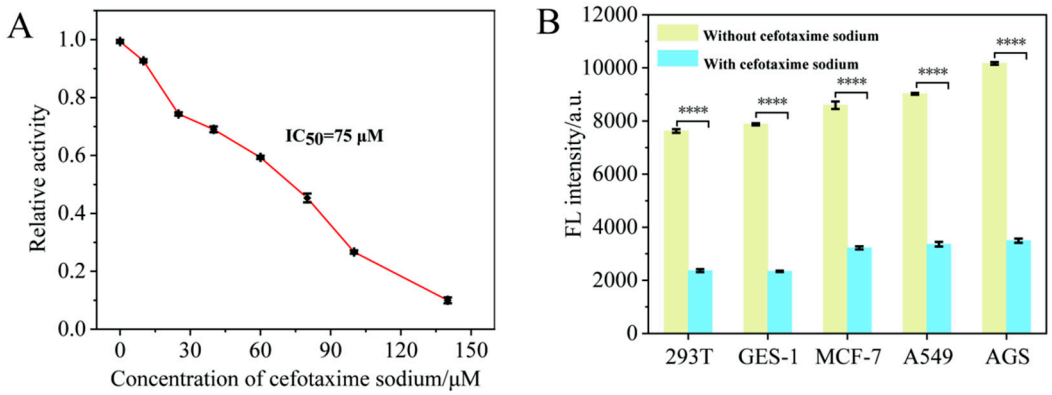



**Figure S9.** (A) Relative APE1 activity changes under varying concentrations of cefotaxime sodium (APE1 concentration: $1\times10^{-5}$ U/mL). (B) Fluorescence intensity comparison of five cell lysates with/without cefotaxime sodium treatment (Error bars: n=3).