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Supplementory Information



Fig.S1 The relationship between added Zn^{2+} concentrations and free Zn^{2+} concentrations in the EGTA-buffered bath solution. The calculations were based on an online program WEBMAXC STANDARD by taking pH7.3, an ionic strength of 0.16, ATP (1.5 mM), Mg²⁺(3 mM), EGTA (1 mM) and 20 °C into account.²¹



Fig. S2 Effects of internal Zn²⁺ and GSH on inside-out macroscopic currents of Fe³⁺-insensitive C832A/H775A/D836A hCFTR across an excised *HEK*-293T patch. The control currents were evoked with 1.5 mM MgATP²⁻ and 12 units/ml PKA (low PKA) and then blocked by PKI before the addition of Zn²⁺. The final free [Zn²⁺]=2.5 nM until GSH was used to reverse the Zn²⁺ effect. The voltagedependent blocker glibenclamide (100 μ M) was applied to evaluate the total currents of hCFTR. The arrows indicate the final concentrations.



Fig. S3 Effects of internal Cd²⁺ on inside-out macroscopic currents of (A) Fe³⁺-sensitive WT or (B) Fe³⁺-insensitive H954A hCFTR across an excised *HEK*-293T patch. The control currents were activated with 1.5 mM MgATP²⁻ and 24 units/ml PKA and then blocked by PKI before the addition of 500 μ M Cd²⁺ to the EGTA-buffered bath solution. Because the stability constant *logK* of EGTA for Cd²⁺ is 16.5 at 25 °C,²⁰ the free [Cd²⁺]=2.3×10⁻¹³ M until EDTA reversed the Cd²⁺-induced potentiation.²¹ 5,5'-dithiobis-(2-nitrobenzoic acid) (DTNB) was used to modify thiol groups of endogenous cysteines and DTT was employed to reverse the DTNB effect. Inh₁₇₂ was applied to evaluate the total currents of CFTR. The arrows indicate the final concentrations. (C) Effects of 0.23 pM Cd²⁺ on the currents of WT and H954A hCFTR at the low level of PKA (n=3-4), *, p<0.05, versus WT hCFTR, from unpaired Student's *t* test).