## **Supporting Information**

Sensitive Detection of Intracellular Telomerase Activity via Double

Signal Amplification and Ratiometric Fluorescence Resonance Energy

## Transfer

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Figure S1. (A) Analysis of telomerase activity by TRAP assay, (B) Gel electrophoresis of SDR reaction.



Figure S2. (A) DLS results of  $MnO_2NS$  and  $MnO_2NS/DNAs$ . (B) Zeta potential of  $MnO_2NS$  and  $MnO_2NS/DNAs$ . (C) UV-vis absorption spectra of  $MnO_2NS$  and  $MnO_2NS/DNAs$ .



Figure S3. (A) Fluorescence quenching of FAM-H1 by  $MnO_2NS$ . The concentrations of  $MnO_2NS$  increased from 0 to 63  $\mu$ g·mL<sup>-1</sup>. The concentration of FAM-H1, TAMRA-H2, A-DNA/T-DNA and TS were 100 nM, 100 nM, 50 nM, 20 nM respectively. (B) Fluorescence recovery induced by 2 mM GSH.



Figure S4. Adsorption analysis of DNA loading efficiency on  $MnO_2NS$ . (a) the UVvis absorption spectrum of FAM-H1, TAMRA-H2, A-DNA/T-DNA and TS; (b) the UV-vis absorption spectrum of supernate after the centrifugation of the DNA/MnO<sub>2</sub>NS mixture.



Figure S5. Cytotoxicity assay of MnO<sub>2</sub>NS with different concentrations to HeLa cells.



Figure S6. (A) Effect of the concentration of FAM-H1 and TAMRA-H2 on the FRET ratio, (B) Effect of the concentration of A-DNA/T-DNA on the FRET ratio, (C) Effect of the different kinds of buffer on the FRET ratio, (D) Effect of the reaction time for SDR on the FRET ratio.



Figure S7. Counterstaining assay for locating the distribution of telomerase in HeLa cells. The nuclear dye is DAPI.

Name	Sequence
FAM-H1	FAM-5'-
	AAAATTAGGGTCTACCTTCAACACACAAGGTAGA
	CCCTAACCCTAACT-3'
TAMRA-H2	5'-
	ACCTTCAACACACAAGGAGTTAGGGTCTACCTTG
	TGTGTTGAAGGTAGACCCTAA-3'-TAMRA
	5'-
A-DNA	CCTAACCCTAACCCTAACCCTAACTCTGCTCCTAT
	-3'
T-DNA	5'-AGTTAGGGTTAGGGTCTACCTT-3'
TS	5'-AATCCGTCGAGCAGAGTT-3'
ACX	5'-GCGCGGCTTACCCTTACCCTTACCCTAACC-3'

Table S1. Sequences of the oligonucleotides used in the experiment.

Analytical Method	Linear range	Detection limit	Refs
Fluorometric assay	2000–40000 HeLa cells	220 HeLa cells	(Hong et al., 2016)
Fluorometric assay	200–100000 HeLa cells	200 HeLa cells	(Tian et al., 2013)
Fluorometric assay	500–10000 HeLa cells	185 HeLa cells	(Zhu et al., 2015)
Fluorometric assay	50–2000 HeLa cells	30 HeLa cells	(Zhu et al., 2018)
Fluorometric assay	50–1000 HeLa cells	33 HeLa cells	(Yang et al., 2017)
Chemiluminescence	100–1000 HeLa cells	100 HeLa cells	(Li et al., 2011)
Chemiluminescence	-	500 HeLa cells	(Xiao et al., 2004)
Colorimetry	$5 \times 10^3$ -10 <sup>6</sup> cells/mL	100 HeLa cells	(Feng et al., 2019)
Colorimetry	500–1000 HeLa cells	25 HeLa cells	(Yu et al., 2018)
Electrochemical assay	50–50×10 <sup>5</sup> cells/mL	20 HeLa cells	(Ling et al., 2020)
Electrochemical assay	300–1.04×10 <sup>7</sup> HeLa cells/mL	8.20 HeLa cells	(Wang et al., 2020)
Electrochemiluminesce nce	100–9×10 <sup>3</sup> HeLa cells	62 HeLa cells	(Zhang et al., 2014a)
Electrochemiluminesce nce	313–1×10 <sup>4</sup> HeLa cells	148 HeLa cells	(Zhang et al., 2014b)
Surface-Enhanced Raman Scattering	1-1000 HeLa cells	10 HeLa cells	(Li et al., 2019)
This work	20–1000 HeLa cells	20 HeLa cells	-

Table S2. Comparison of the analytical performance for telomerase activity detection.

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