# Supporting Information

## Experimental

***Materials*****:** Graphite and hydrogen peroxide solution (30 wt %) were purchased from Sinopharm Chemical Reagent Co. Ltd (Shanghai, China). Single-walled carbon nanotubes (SWNT) were purchased from Nanotech Port Co. Ltd. (Shenzhen, China). Tetramethylbenzidine (TMB) and N-Hydroxysulfosuccinimide sodium (sulfo-NHS) were purchased from BBI (Ontario, Canada). $H_2O_2$ was obtained from Beijing Chemicals Inc (Beijing, China). Poly (allyl amine hydrochloride) (PAH, $M_W = 60000$), 1-Ethyl-3(3-dimethylaminopropyl) carbodiimide hydrochloride (EDC) and hemin were purchased from Alfa Aesar (Ward Hill, MA). Tetraethylorthosilicate (TEOS, >98 %) and Folic acid (FA) was purchased from Sigma-Aldrich. All other regents were of analytical reagent grade. Aqueous solutions were prepared with double-distilled water ($ddH_2O$) from a Millipore system (>18 MΩ cm). SWNT-COOH and mesoporous silica were prepared according to the previous approaches. [1]

***Synthesis of PAH-Functionalized Graphene (GP):*** Graphite oxides (GO) were synthesized from graphite powder by a modified Hummers method.[2] The graphene-PAH (GP, as shown in Scheme 1A) was prepared by vigorously stirring a solution of 20 mg of the graphene oxides, 100 mg of PAH, and 100 mg of KOH in 50 mL of $H_2O$ at 70 $^0$C for 24 h. [3] Then 10 mL of 1M $NaBH_4$ solution was added, and the reaction was kept on at 70 $^0$C for 2 h. After that, the GP was collected and purified by

centrifugation and adequately washed with water several times to remove the impurities and the excess of PAH by physical absorption.

***Synthesis of Folic Acid-Functionalized Graphene (GF):*** To conjugate the graphene-PAH with folic acid (FA), free folic acid (10 mg, 0.0227 mmol) was firstly dissolved in 4 mL 50mM MES buffer (pH 6.0). The solution of FA was then mixed with a 2 mL aqueous solution of (EDC) (0.068 mmol) and sulfo-NHS (0.068 mmol).[4] After agitating overnight at temperature in the dark, the solution of GP (20 mg) was added to the mixture. The resulting solution was stirred at room temperature for 24 h and then centrifuged at 13000 rpm to separate the precipitate. The resulting black precipitate was sonicated and extensively washed eight times with dd$H_2O$ to remove the physisorbed folic acid.

***Synthesis of Folic Acid Conjugated Graphene-Hemin Composite (GFH):*** To prepare GFH, hemin (20 mg) was firstly dissolved in 5mL dd$H_2O$. Then, 20 mg GF was added to the solution. The resulting mixture was stirred at room temperature in the dark for 72 h and then centrifuged at 10000 rpm to separate the precipitate. The resulting brown precipitate was washed three times to give GFH.

***Characterization:*** Atomic-force microscopy (AFM) measurements were performed using Nanoscope V multimode atomic force microscope (Veeco Instruments, USA). Samples for AFM images were prepared by depositing a dispersed GFH/$H_2O$ solution (20 μg $mL^{-1}$) onto a freshly cleaved mica surface and washed with dd$H_2O$. Tapping mode was used to acquire the images under ambient conditions.[5] FTIR characterization was carried out on a BRUKE Vertex 70 FTIR spectrometer. UV-vis

absorbance measurements experiments were carried out on a Jasco－V550 UV/Vis spectrophotometer. Thermogravimetric analysis (TGA) was recorded on a PE TGA-7 thermal analyzer at 10 $^{o}C \cdot min^{-1}$ in an $N_2$ atmosphere. EDX was carried out using a HITACHI S-4500 instrument. The zeta potential of GFH in solution (~0.05 mg/mL in millipore water) was determined using a Zeta PALS, zeta potential analyzer (Brookhaven Instruments Corp. Holtsville, NY).

***Bioassay:*** Kinetic measurements of GFH peroxidase reactions were performed using a Jasco-V550 UV-Vis spectrophotometer in time course mode at 652 nm.[5] Experiments were carried in a reaction volume of 500 μL buffer solution (25 mM $Na_2HPO_4$, pH 7.0), with 800 μM TMB and 5 mM $H_2O_2$ as substrate.

***Cell Culture and Treatment:*** The human cervical cancer cells (HeLa), human breast cancer cells (MCF-7) and the mouse fibroblasts cells (NIH-3T3, used as negative control) were grown in Iscove's modified Dulbecco's medium (Gibco BRL) supplemented with 10% fetal calf serum in a humidified 37 °C incubator with 5% $CO_2$. For the bright field microscope images, cells were plated in 24 well plate at density of 6000 cells per well and allowed to incubate with 20 $\mu gmL^{-1}$ GFH for 1.5 h. For control experiment, cells in 24 well plate were firstly treated with 200 $\mu g\ mL^{-1}$ FA in IMDM medium for 30 min and then incubate with 20 $\mu g\ mL^{-1}$ GFH for 1.5 h. Afterwards cells were washed with PBS buffer three times and then visualized using an Olympus BX-51 optical system microscope (Tokyo, Japan) equipped with 40×objective lenses and Olympus digital camera.[6] For the colorimetric method, 20 $\mu gmL^{-1}$ of GFH were incubated with different cells lines in IMDM medium at 37 °C

for 1.5 h, then harvested by centrifugation at 2000 rpm, and washed three times with phosphate buffered saline (PBS). Finally, cells were dispersed in detection buffer (25 mM $Na_2HPO_4$, pH 7.0) for color reaction. Cell numbers were determined by Trypan blue exclusion in a hemocytometer chamber.[6]

**References**

1 (a) X. Li, Y. H. Peng, X. G. Qu, *Nucleic Acids Res.***2006**, *34*, 3670; (b)X. Li, Y. H. Peng, J. S. Ren, X. G. Qu, *Proc. Natl. Acad. Sci. U.S.A.* **2006**, *103*, 19658; (C) C. Y. Lai, B. G. Trewyn, D. M. Jeftinija, K. Jeftinija, S.Xu, S. Jeftinija, V. S. Y. Lin, *J. Am. Chem. Soc.* **2003**, *125*, 4451.

2 (a) Hummers, W. S.; Offeman, R. E. *J. Am. Chem. Soc.* **1958,** *80*, 1339; (b) Kovtyukhova, N. I.; Ollivier, P. J.; Martin, B. R.; Mallouk, T. E.; Chizhik, S. A.; Buzaneva, E. V.; Gorchinskiy, A. D. *Chem. Mater.* **1999,** *11*, 771.

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6 Wang, X. H.; Song, Y. J.; Ren, J. S.; Qu, X. G.. *PLoS ONE* **2009,** *4*, e6665.

# Supporting Figures

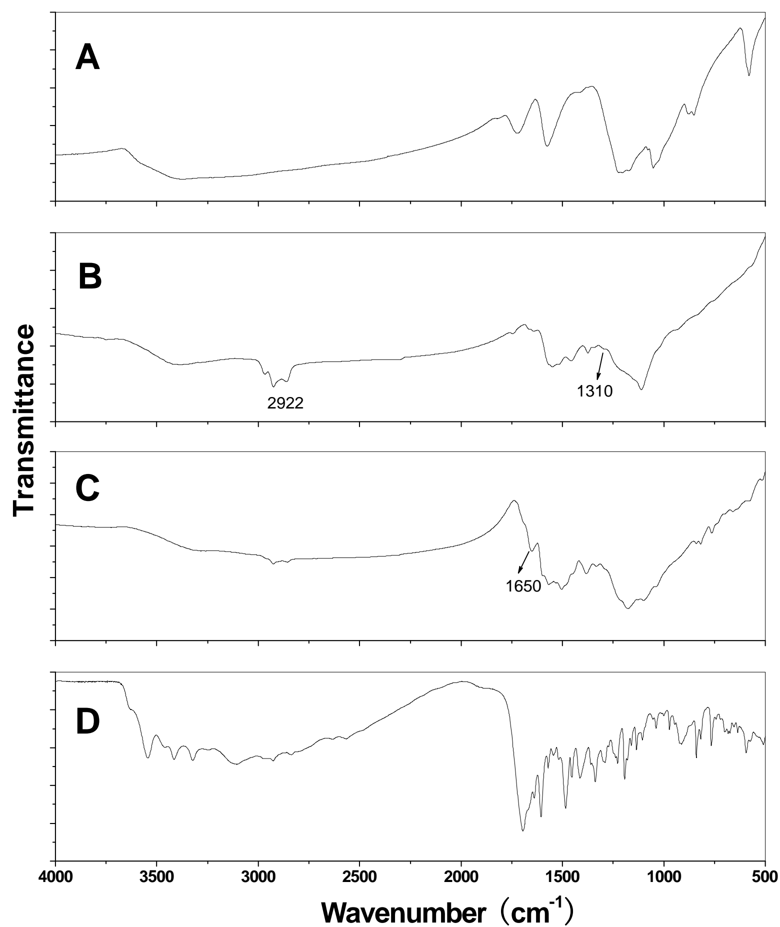


**Figure S1.** FTIR spectra of (A) GO, (B) GP, (C) GF and (D) FA.

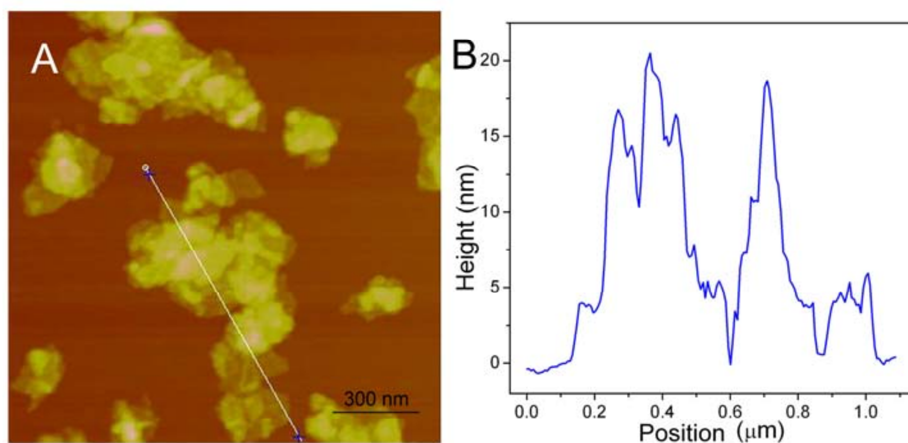


**Figure S2.** A) AFM image of GFH; B) Height profile taken across the white line in (A).

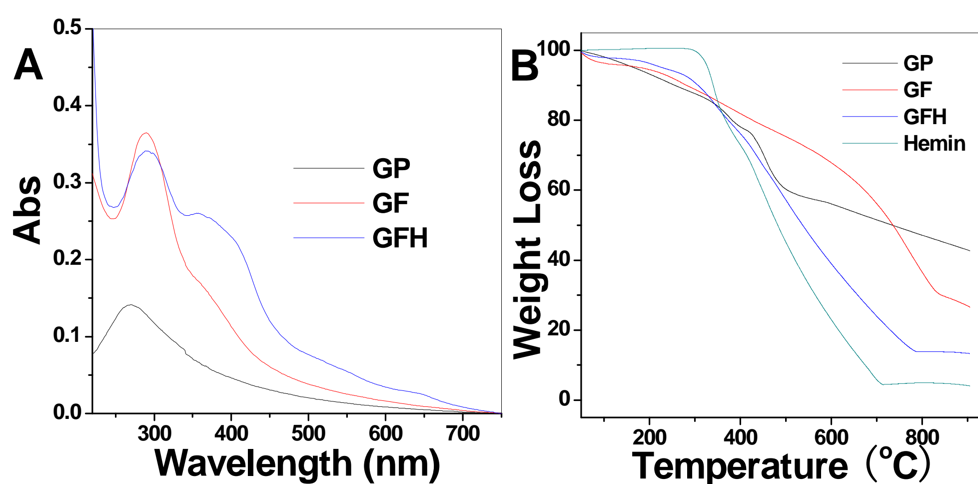


**Figure S3.** (A)UV/Vis spectra for GP, GF and GFH in dd$H_2O$. (B)Thermogravimetric analysis for GP (black), GF (red), GFH (blue) and hemin (cyan) in $N_2$ atmosphere with a ramp of 10 °C/min.

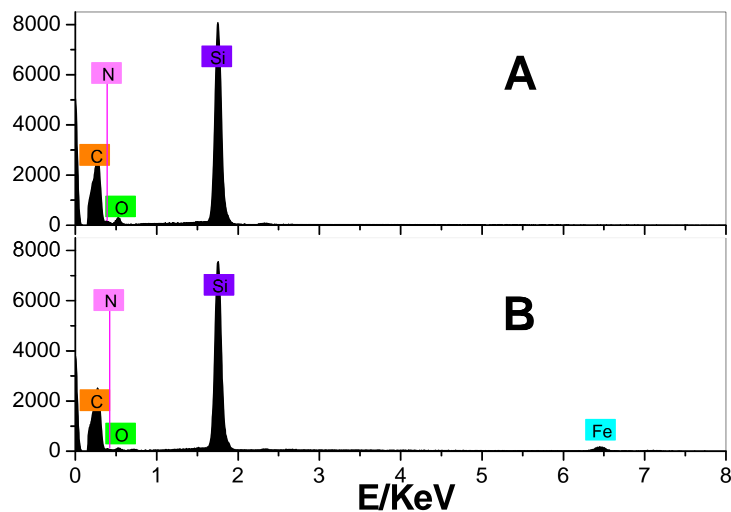


**Figure S4.** EDX spectra of (A) GF and (B) GFH.

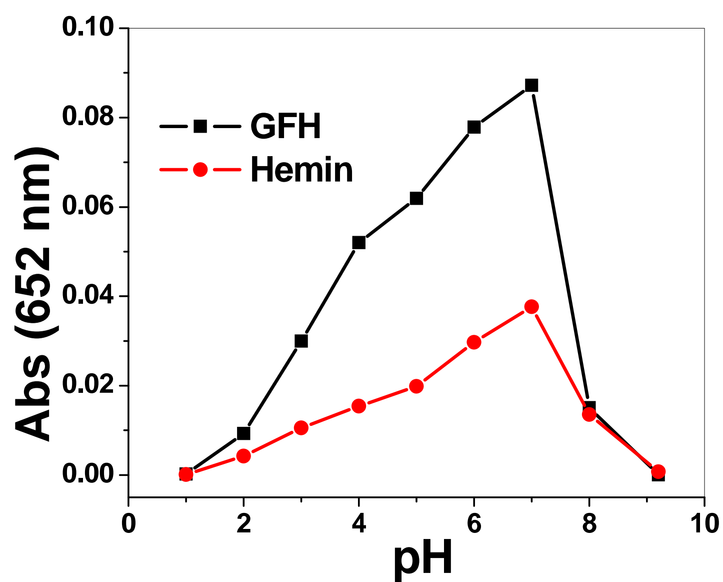


**Figure S5.** The peroxidase-like activity of GFH (black) and hemin (red) is pH dependence. GFH and hemin show the optimal pH of 7.0.

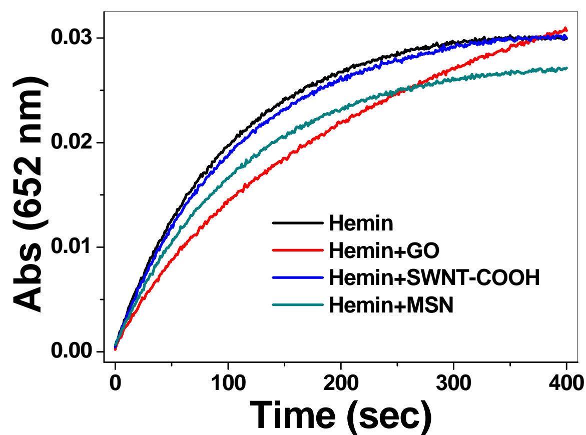


**Figure S6.** The time-dependent absorbance changes at 652 nm of 20 ng·ml$^{-1}$ Hemin in the absence (black) or presence of 80 ng·ml$^{-1}$ GO (red), 80 ng·ml$^{-1}$ SWNT-COOH (blue), or 80 ng·ml$^{-1}$ mesoporous silica (MSN, cyan) in phosphate buffer (25 mM $Na_2HPO_4$, pH 7.0) at room temperature.

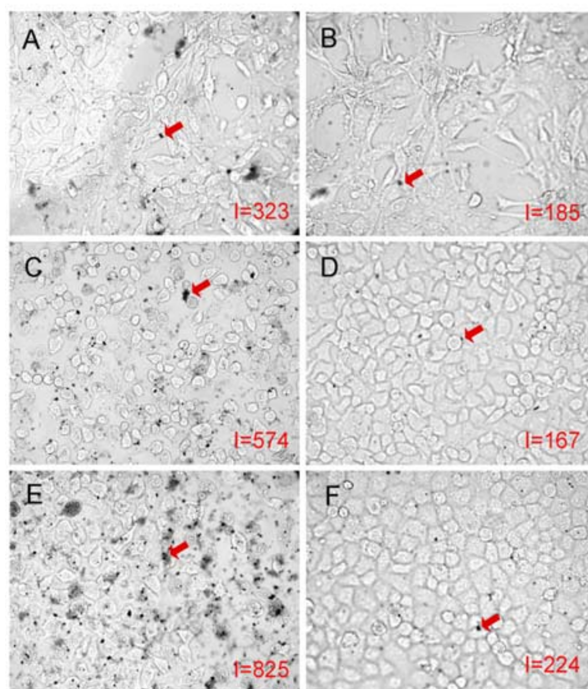


**Figure S7** Bright field images of three cell lines that were incubated with GFH in vitro. (A), (C), (E)GFH bind to NIH-3T3 cells, HeLa cells or MCF-7 cells; (B), (D), (F)The binding of GFH to NIH-3T3 cells, HeLa cells or MCF-7 cells can be blocked by folic acid; GFH was visualized as dark spots under conventional bright field microscopy (arrow points to GFH). Dark counts (I) were determined manually using cell count plugins and Image J software.