Supporting Information

A Flexible Smart Membrane Consisting of GO Composite Fibres and Upconversion MSNs for microRNA Detection

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Materials

Tetraethoxysilane (TEOS), cetyltrimethylammonium bromide (CTAB), ethanol, calcium acetate monohydrate (99%), anhydrous N,N-dimethyl-formamide (DMF), tetrahydrofuran(99%) were acquired from Sinopharm Chemical Reagent Co., Ltd. Lysine, n-octane (99%), 2, 2'-azobis(2-amidinopropane) dihydrochloride (AIBA), styrene (99%, contains 4-tert-butylcatechol as stabilizer), trifluoroacetic acid (TFA, 99.5%), 1-ethyl-3-(3-(dimethylamino)propyl) carbodiimide hydrochloride (EDC), N-hydroxysulfosuccinimide (sulfo-NHS), 3-aminopropyltriethoxysilane (APTES) were purchased from Sigma-Aladdin Industrial Co., Ltd. Ytterbium(III) acetate hydrate (99.9%), holmium(III) acetate hydrate (99.9%) were purchased from Thermo Fisher Scientific. All chemicals were used as received without further purification. TPU was purchased by Bayer A.G. (Germany).
DNA oligonucleotides with a concentration of 100 nM were ordered from Sangon Biotech (Shanghai) Co., Ltd., and the sequence are listed in Table 1.

Characterization

The morphology of materials was investigated via a Hitachi SU-70 field-emission scanning electron microscopy (FESEM) and a FEI Tecnai F20 high-resolution transmission electron microscope (HRTEM). The X-ray diffraction (XRD) pattern was recorded by using a Thermo ARL X'TRA powder diffractometer. Surface textural characterization was implemented according to the Brunauer–Emmett–Teller (BET) method by using a Coulter OMNISORP-100 apparatus. FTIR spectra were evaluated using a Perkin-Elmer 580B infrared spectrophotometer. UV/Vis absorption values were measured with a TU-1810 spectrophotometer. The upconversion photoluminescence spectra were recorded using a fluorescence spectrophotometer (PL, FLSP920, Edinburgh) under the excitation of a 980 nm laser.

Synthesis of CaF_2: Yb/Ho @MSN

100 mg CTAB were dissolved in 30 ml deionized water, and stirred at 60℃. After stirred magnetically for 30 min, 25.2 ml octane, 1000 mg TEOS, 22 mg lysine, styrene (30 mg/ml) and AIBA (0.84 mg/ml) were subsequently added to the system and stirred for 3 h. After 4 h, the solution was cooled down to the ambient temperature. The products were collected by centrifugation at 10000 rpm for 10 min and then washed 3 times. The template was completely removed by heat treatment at 550℃ under atmospheric conditions. To incorporate CaF_2:RE^{3+} nanocrystals within mesoporous silica nanoparticles, a precursor solution should be prepared beforehand. $Ca(OAc)_2$, $Yb(OAc)_3$, and $Ho(OAc)_3$ were dissolved in deionized water to make a 0.5 M solution, and added with 12 ml TFA under stirring for 24 h. Subsequently, 300 mg MSN was added into 20 ml precursor solution and immersed for 24 h under stirring at 35℃. The particles were then centrifugated at 8000 rpm for 5 min, and stood for 4 h at room temperature. After being air-dried at 80℃ overnights, the particles were further calcined at 600℃ for 3 h.

Conjugation of CaF_2: Yb/Ho @MSN with probe oligonucleotides

100 mg CaF_2: Yb/Ho @MSN was dispersed in 100 ml ethanol under sonication for 10 min, and then 3 ml APTES was added under stirring at 50℃ for 24 h. The samples were collected by centrifugation and dried at 80℃. 100 μl ssDNA probe was dissolved in 5 ml PBS solution. 0.8 ml EDC (2 mg/ml) and 0.4 ml NHS (2 mg/ml) were added and the reaction was allowed to react for 30 min at 37℃ under shaking. 10 mg CaF_2: Yb/Ho @MSN which modified with amino group was then added, and the reaction was incubated for 12 h. After reaction, the products were centrifuged, washed with PBS and then resuspended in 5 ml PBS solution.

Preparation of smart substrate

The precursor solution for electrospinning was prepared by a sol−gel method. In a typical process, 15 wt% TPU dissolved in 10 ml DMF and 10 ml THF, all the stuff had been stirring for 3 h at room temperature until got homogeneous spinnable precursor sols. For the electrospinning procedure, the electrospinning sol was fed into the conducting nozzle (2.5 mm ID) using an infusion pump (KDS-100, KD Scientific, USA) at a constant flow rate of 1 mL/h. The distance between the needle tip and the grounded aluminum foil was 12.5 cm. And the voltage was set to be 6 kV (PS/FC30P04.0-22, Glassman High voltage Inc., USA). The as-spun fibers were dried at 37 °C for 12 h.

The TPU fiber substrate was cut into the area of 0.8 cm x 0.5 cm small pieces, and added in 2 mg/ml GO solution under magnetic stirring for 24h at room temperature. The samples were dried at 37 °C. These small pieces were added in the solution which contained CaF_2: Yb/Ho @MSN-ssDNA probe as-prepared under gentle shaking for 12h at 37 °C. Finally, the substrate was washed with PBS solution for 3 times.

Hybridization assay and PL measurements

The smart substrates were incubated with different concentration of target analog miRNA at 37℃ under shaking for 1 h in PBS and 10 vol% fetal bovine serum, and then washed with PBS solution gently. Photoluminescence spectrum measurements were done all these smart substrates at 980 nm excitation.

Table S1. Structural parameters of nanoparticles before and after CaF_2: Yb/Ho crystals combination

	Surface area [$m^2 g^{-1}$]	Pore volume [$cm^3 g^{-1}$]	Pore size [nm]
MSN	747	1.54	8.27
CaF_2:Yb/Ho @MSN	454	0.98	8.63

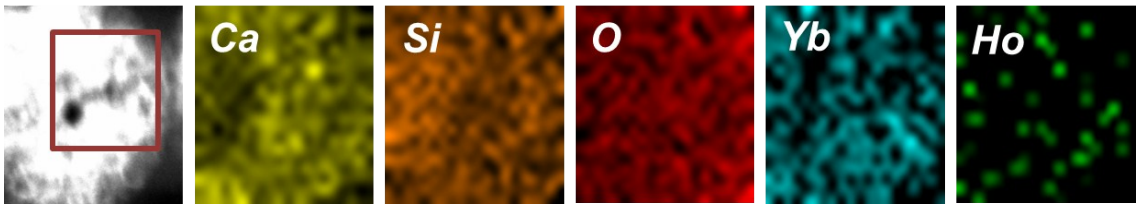

Fig. S1 Elemental mapping images of an ultrathin section through part of CaF_2: Yb/Ho@MSN.

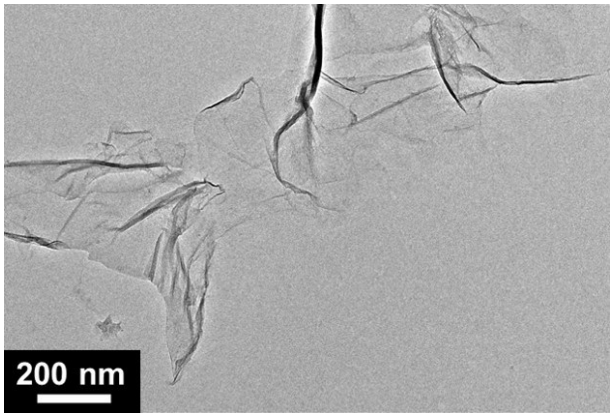

Fig. S2 TEM image of GO film.

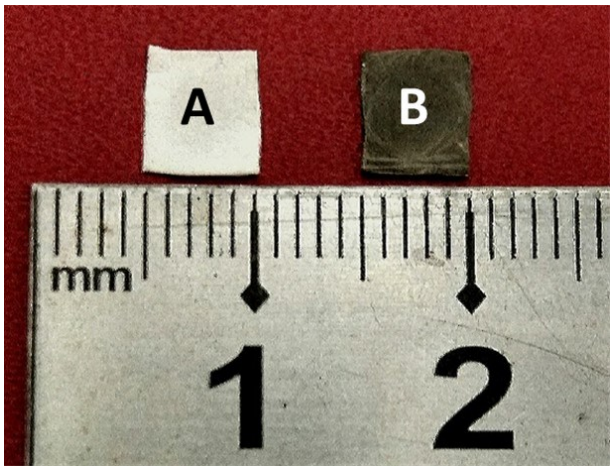

Fig. S3 Optical photograph of TPU fiber membrane [A] and TPU@GO membrane [B]

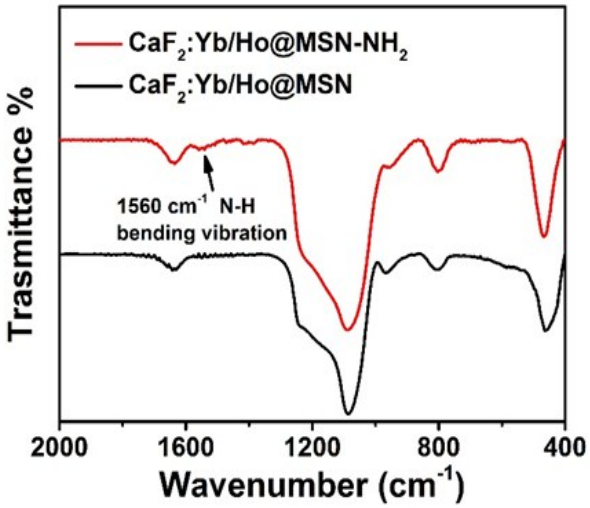

Fig. S4 FTIR spectra of CaF_2: Yb/Ho@MSN and CaF_2: Yb/Ho@MSN modified with APTES.

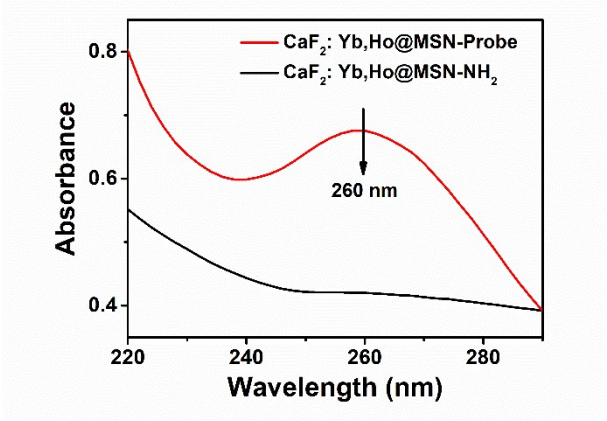

Fig. S5 UV-vis absorption of CaF_2: Yb/Ho@MSN modified with NH_2 and DNA probe.

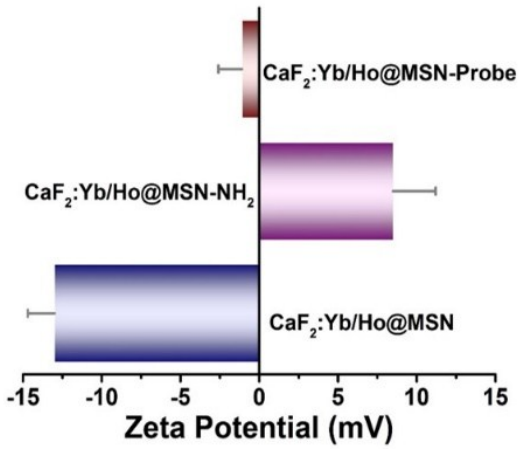

Fig. S6 ζ-potential of CaF_2: Yb/Ho@MSN, CaF_2: Yb/Ho@MSN modified with-NH_2 and DNA probe.

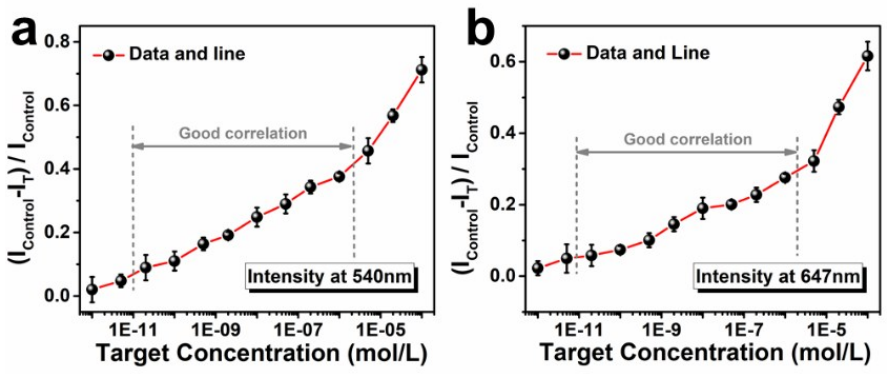

Fig. S7 Representation of the maximum fluorescence relative intensity of the smart membrane measured at (a) 540nm and (b) 647nm as a function of the target miR-21 concentration.

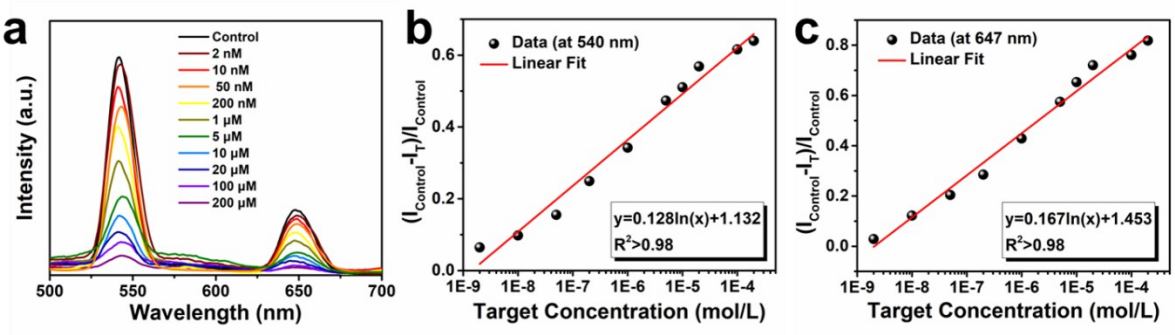

Fig. S8 (a) UCL spectra of the smart membrane after treating with solutions with different miR-21 concentration in 10 vol% fetal bovine serum, and the relationship between the relative intensity of UCL, at (b) 540 nm and (c) 647 nm, and miR-21 concentration at a certain range.

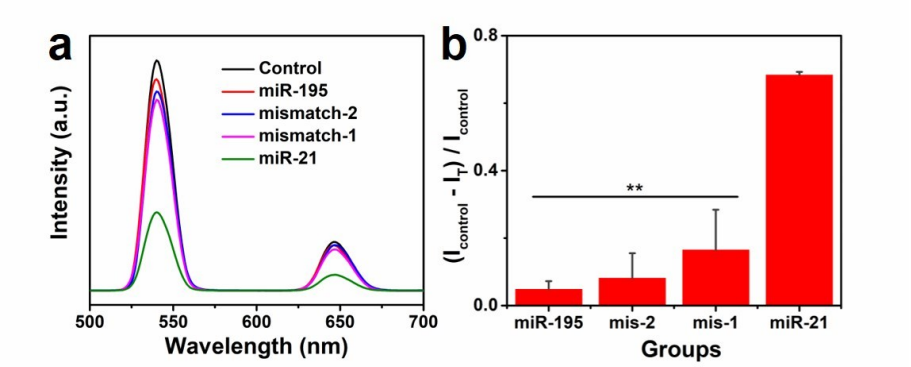

Fig. S9 Specific detection of miR-21, miR-21 with single base mismatch, miR-21 with three base mismatch and miR-195. (a) UCL spectra of the smart membrane after treating with different samples at 1 μM. (b) The relationship between the relative intensity of UCL and samples at 647 nm.