Electronic Supplementary Material (ESI) for Journal of Materials Chemistry B.

Supplementary Information for

Ratiometric and amplified fluorescent nanosensor based on DNA tetrahedron for miRNA imaging in living cells

Liuting Mo, Danlian Liang, Wanqi He, Chan Yang, and Weiying Lin*

Guangxi Key Laboratory of Electrochemical Energy Materials, Institute of Optical Materials and Chemical Biology, College of Chemistry and Chemical Engineering, Guangxi University, Nanning, Guangxi 530004, P. R. China

*Email: weiyinglin2013@163.com

Table of contents

1. Supplementary Table……1

1.1 Table S1……..……1

1.2 Table S2……..……2

2. Supplementary Figures……..…….3

2.1 Figure S1……...…….…….3

2.2 Figure S2……...…….…….4

2.3 Figure S3……...…….…….5

2.4 Figure S4……...…….…….6

2.5 Figure S5……...…….…….7

2.6 Figure S6……...…….…….8

2.7 Figure S7……...…….…….9

2.8 Figure S8……...…….……...10

2.9 Figure S9……...……...……..…11

2.10 Figure S10..……...…….…….12

2.11 Figure S11……...……...…….13

2.12 Figure S12……...…….....….14

2.13 Figure S13……...…….....…....15

3. Reference……...……...…..…16

Supplementary Table

Table S1. Sequence of oligonucleotides used in this work.

Oligonucleotides	Sequence (5'-3')
S1	AACTATACAACCTACTACCTCAGAGTCAGTTTTTACATTCCTAAGT CTGAAACATTACAGCTTGCTACACGAGAAGAGCCGCCATAGTA
S2	AACTATACAACCTACTACCTCAGAGTCAGTTTTTTATCACCAGGCA GTTGACAGTGTAGCAAGCTGTAATAGATGCGAGGGTCCAATAC
S3	AACTATACAACCTACTACCTCAGAGTCAGTTTTTTCAACTGCCTGG TGATAAAACGACACTACGTGGGAATCTACTATGGCGGCTCTTCC
S4	AACTATACAACCTACTACCTCAGAGTCAGTTTTTTTCAGACTTAGG AATGTGCTTCCCACGTAGTGTCGTTTGTATTGGACCCTCGCATC
F	FAM-ATGACTCTGAGGTAGTAGGTTGACAGAGTCAT-TAMRA
S5	ACATTCCTAAGTCTGAAACATTACAGCTTGCTACACGAGAAGAGC CGCCATAGTAAGTAACGTCTAGTAT
S6	TATCACCAGGCAGTTGACAGTGTAGCAAGCTGTAATAGATGCGAG GGTCCAATACAGTAACGTCTAGTAT
S7	TCAACTGCCTGGTGATAAAACGACACTACGTGGGAATCTACTATG GCGGCTCTTCCAGTAACGTCTAGTAT
S8	TTCAGACTTAGGAATGTGCTTCCCACGTAGTGTCGTTTGTATTGGA CCCTCGCATCAGTAACGTCTAGTAT
H	TGACTCTGAGGTAGTAGGTTGTTTATATTTATTTATAATACTAGAC GTTACT
let-7a	UGAGGUAGUAGGUUGUAUAGUU
let-7i	UGAGGUAGUAGUUUGUGCUGUU
let-7d	AGAGGUAGUAGGUUGCAUAGUU
miR-429	UAAUACUGUCUGGUAAAACCGU
miR-200b	UAAUACUGCCUGGUAAUGAUGAC
let-7a mimics	TGAGGTAGTAGGTTGTATAGTT
anti-let-7a	AACTATACAACCTACTACCTCA

Table S2. Comparison of different sensors for intracellular miRNA analysis.

Method	Linear Range	Sensitivity	Ref. No.
DNA Triangle-Protected Molecular Beacon	0.3-50 nM	100 pM	1
DNAzyme-based amplification strategy	0.1-10 nM	44 pM	2
Protein scaffolded DNA tetrads	0.05-100 nM	6 pM	3
ATP-fueled DNA nanomachine	0.1-2 nM	100 pM	4
qTDN-mediated hyperbranched HCR	0.2-1.2 nM	2.14 pM	5
CHA-assisted DNA tetrahedron nanoprobe	0.1-10 nM	120 pM	6
DTN-based naosensor	0.5-25 nM	22 pM	This work

Supplementary Figures

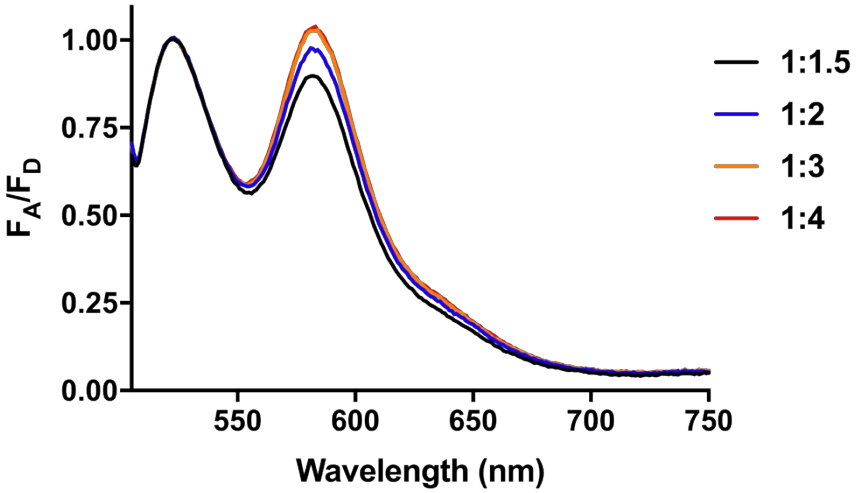

Fig. S1 Fluorescence spectra of the DTN nanosensor with different ratios between DTN-F and DTN-H.

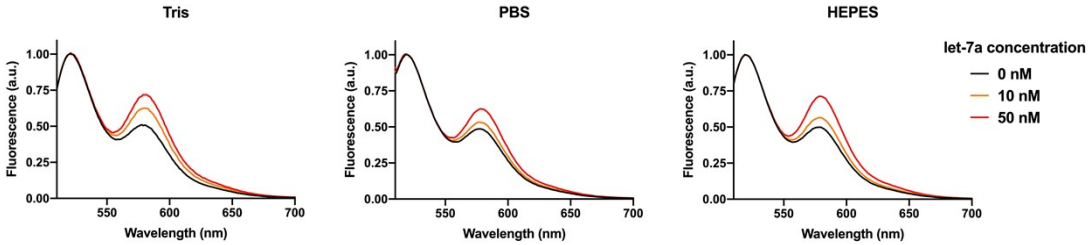

Fig. S2 Fluorescence spectra of the DTN nanosensor in response to let-7a in Tris, PBS and HEPES buffers.

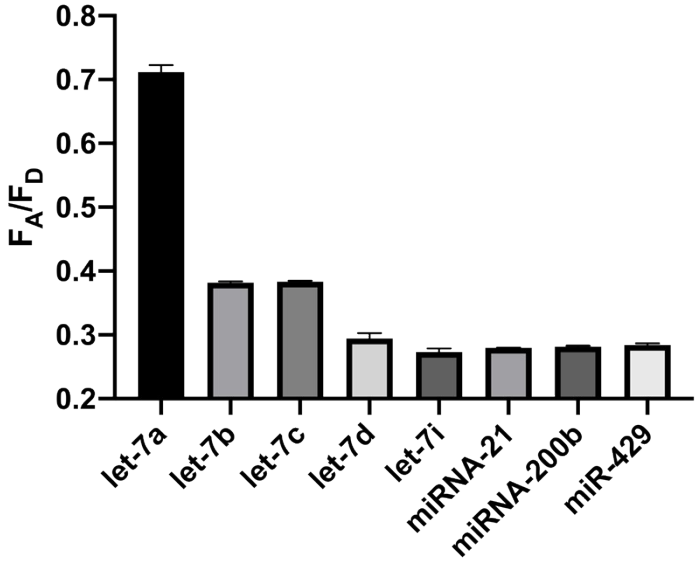

Fig. S3 Selectivity of the DTN nanosensor to different miRNAs.

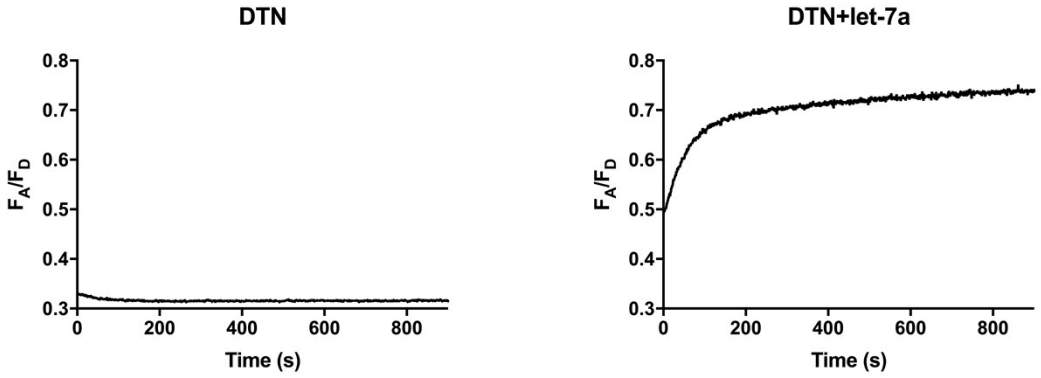

Fig. S4 Kinetic study of the DTN nanosensor in the absence and presence of let-7a.

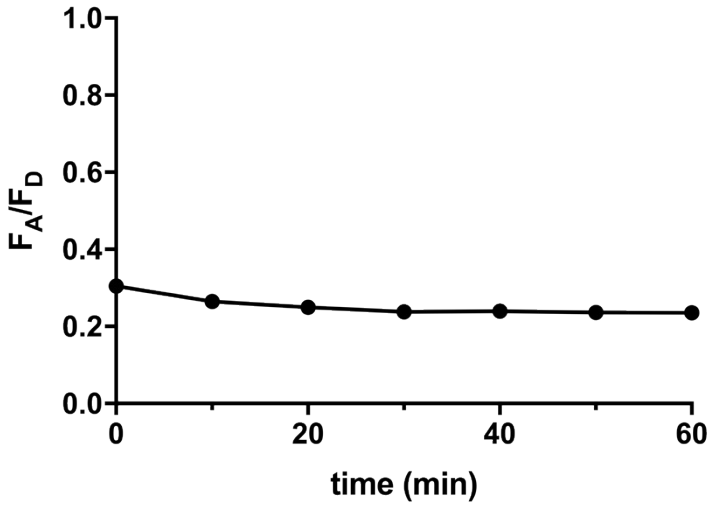

Fig. S5 Fluorescence spectra of the DTN nanosensor with the treatment of 0.5 U/mL DNase I for 0, 10, 20, 30, 40, 50 and 60 min.

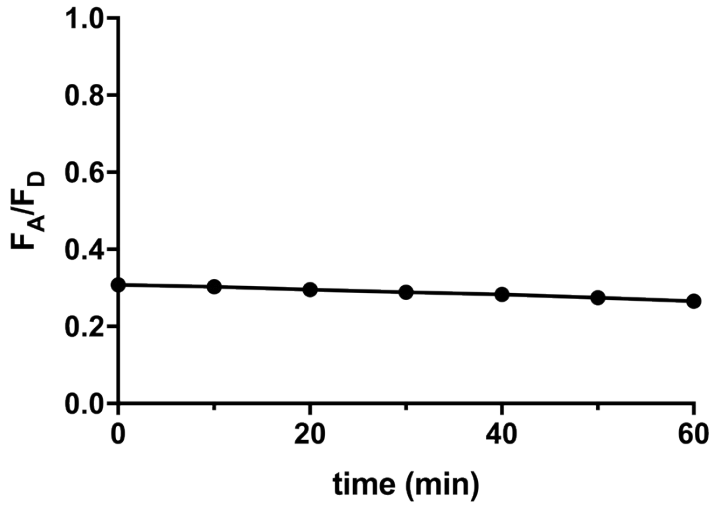

Fig. S6 Fluorescence spectra of the DTN nanosensor with the treatment of 10% FBS for 0, 10, 20, 30, 40, 50 and 60 min.

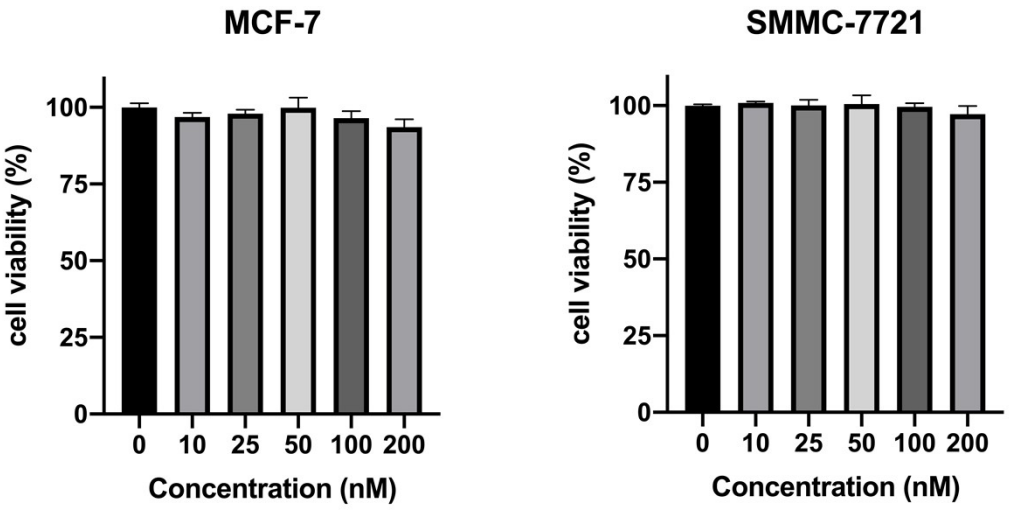

Fig. S7 Cell viability assay of the DTN nanosensor incubated with MCF-7 and SMMC-7721 cells at various concentrations for 24 h.

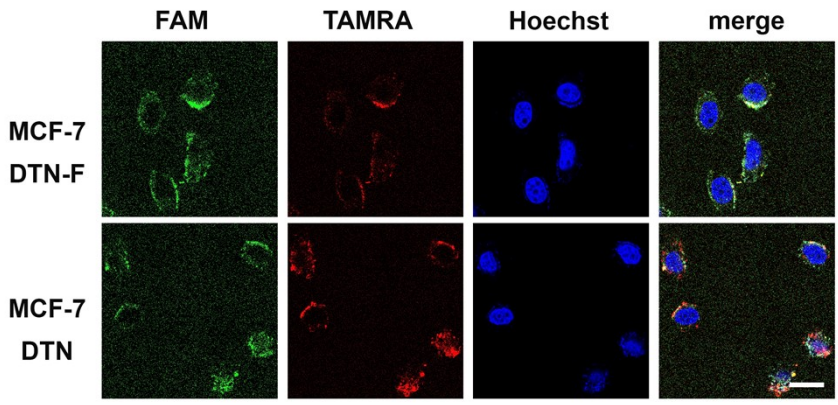

Fig. S8 Co-localization imaging of DTN-F and the DTN nanosensor in MCF-7 cells. The green and red fluorescence indicate the location of the nanosensor, and the blue fluorescence represents the nucleus. Scale bar: 25 μm.

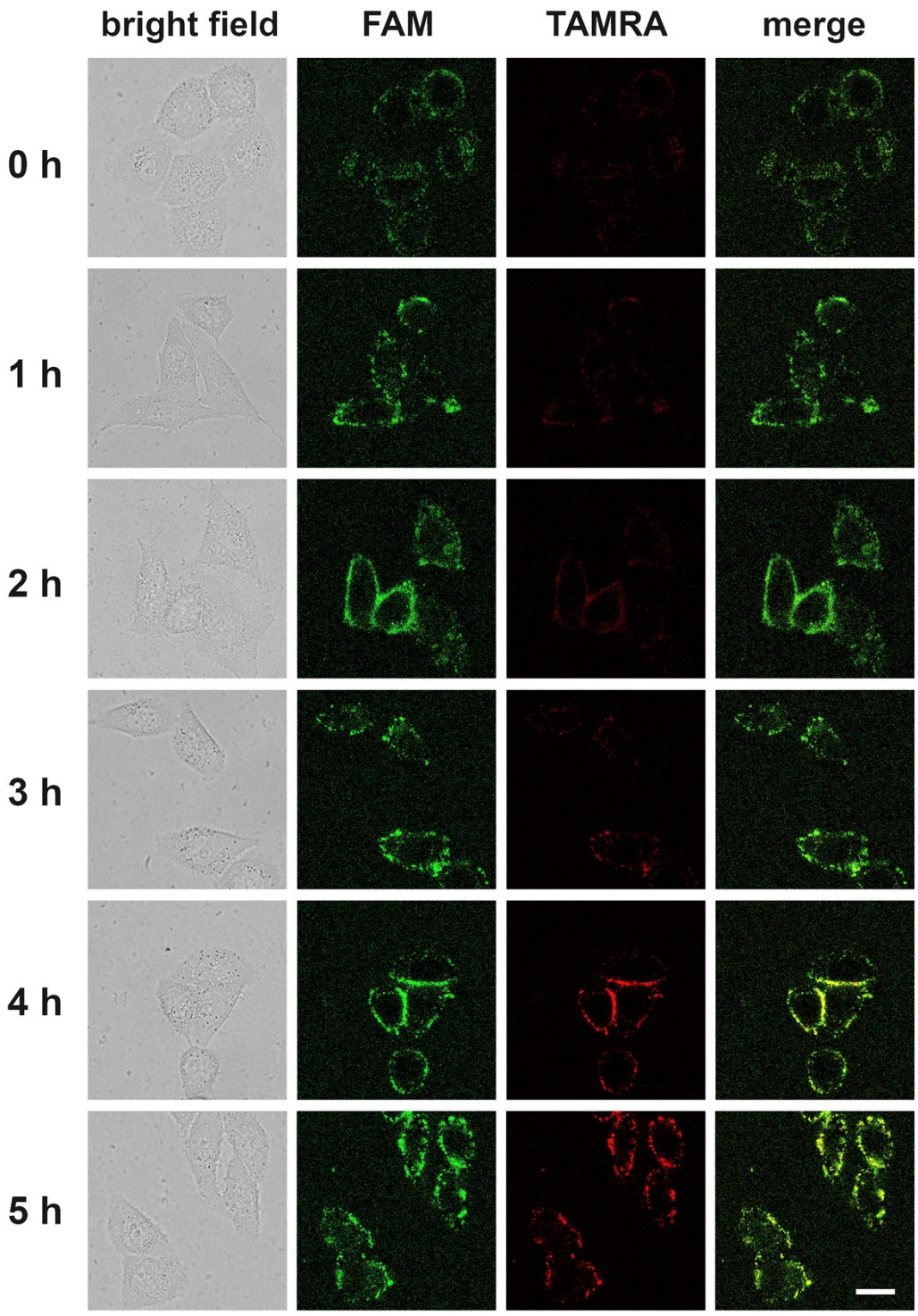

Fig. S9 Optimization of incubation time for the DTN nanosensor in living cells. MCF-7 cells were incubated with the DTN nanosensor for 0, 1, 2, 3, 4, 5 h. Scale bar: 25 μm.

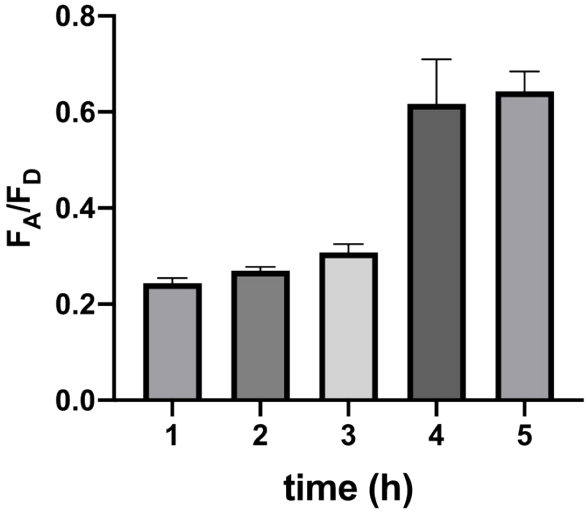

Fig. S10 Statistical analysis of FRET signal in MCF-7 after incubation with the DTN nanosensor for 0, 1, 2, 3, 4, 5 h.

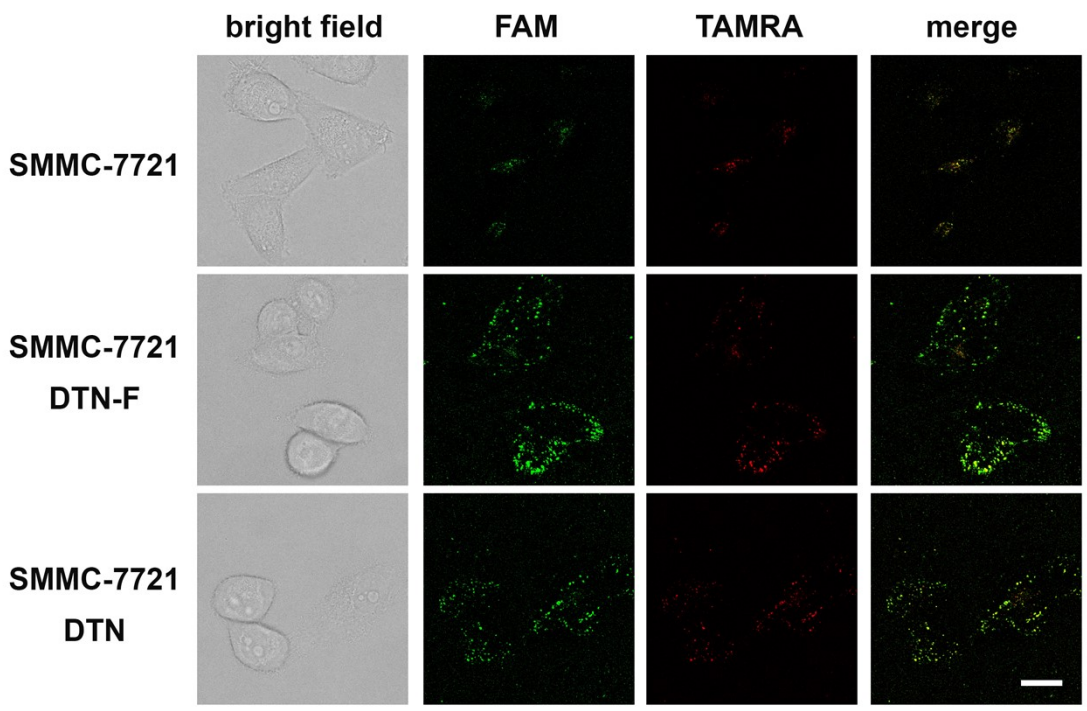

Fig. S11 Confocal fluorescence imaging of let-7a in SMMC-7721 cells after incubation with medium, DTN-F and the DTN nanosensor, respectively. Scale bar: 25 μm.

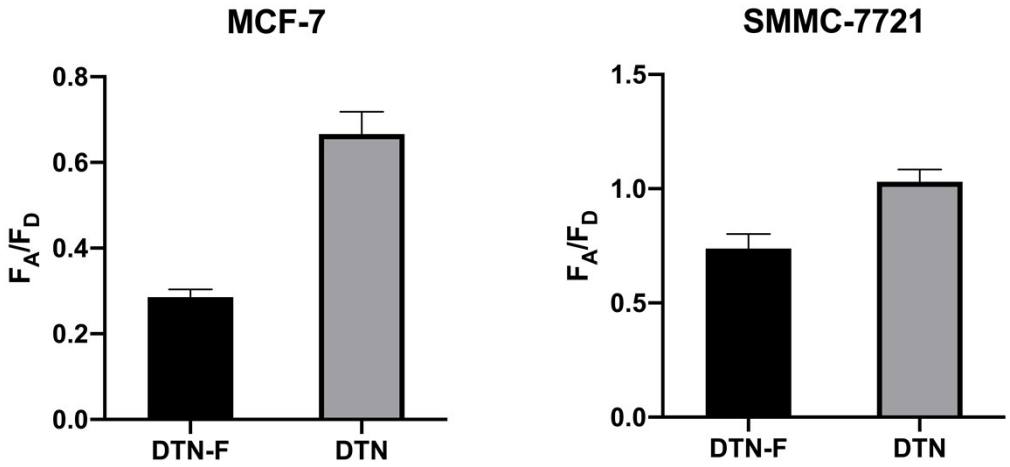

Fig. S12 Statistical analysis of FRET signal in MCF-7 and SMMC-7721 cells before and after incubation with DTN-F or the DTN nanosensor.

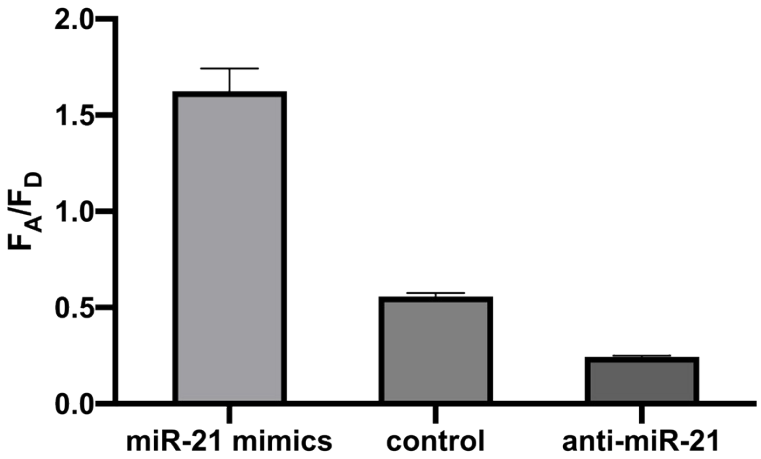

Fig. S13 Statistical analysis of FRET signal in MCF-7 cells before and after transfected with let-7a mimics and anti-let-7a.

Reference

1. C. Li, M. Luo, J. Wang, H. Niu, Z. Shen and Z. Wu, *ACS Sens.*, 2020, **5**, 2378-2387.
2. P. Li, M. Wei, F. Zhang, J. Su, W. Wei, Y. Zhang and S. Liu, *ACS Appl. Mater. Interfaces*, 2018, **10**, 43405-43410.
3. D. Huang, Z. Huang, H. Xiao, Z. Wu, L.Tang, J. Jiang, *Chem. Sci.*,2018, **9**, 4892-4897.
4. P. Ma, C. Liang, H. Zhang, B. Yin, B. Ye, *Chem. Sci.*, 2018, **9**, 3299-3304.
5. J. Wang, D. Wang, J. Ma, Y. Wang, D. Kong, *Chem. Sci.*, 2019, **10**, 9758-9767.
6. Q. Huang, P. Ma, H. Li, B. Yin, B. Ye, ACS Appl. Bio Mater., 2020, **3(5)**, 2861-2866.