**Supporting Information**

# Nano Metal-Organic Framework (NMOF)-Based Strategies for Multiplexed MicroRNA Detection in Solution and Living Cancer Cells

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Y. F. Wu and J. Y. Han contributed equally to this work.

**Figure S1** Nitrogen adsorption-desorption isotherm obtained at 77 K and corresponding pore size distribution of the NMOF (UiO-66).

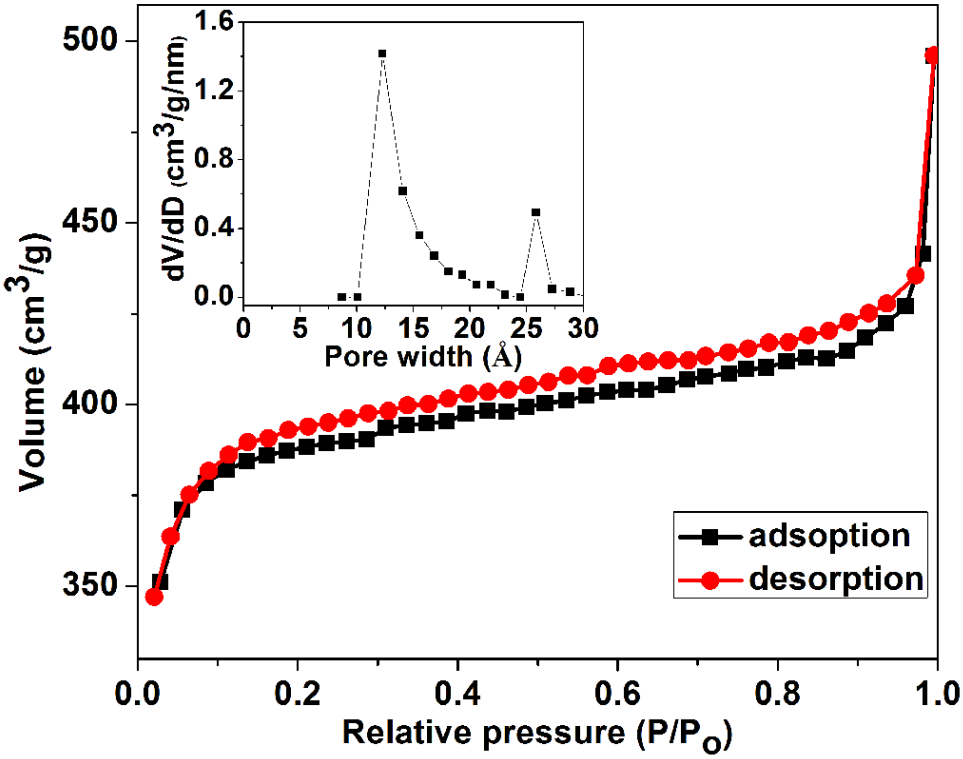

**Figure S2** Fluorescence emission spectra (excitation at 480 nm) of dye-labeled probe FAM-PNA21 (5 μM) under different conditions: (a) probe FAM-PNA21 in Tris-HCl buffer; (b) probe FAM-PNA21 + NMOF; (c) probe FAM-PNA21 + NMOF + 1 nM miR-21.

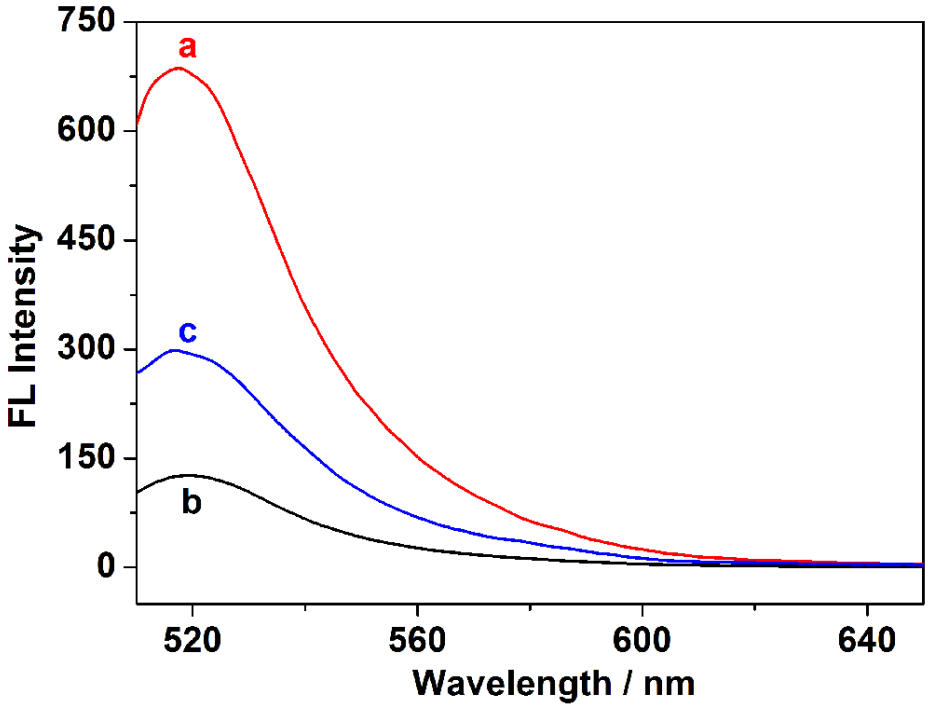

**Figure S3** Fluorescence intensity of three different PNA probes upon the introduction of NMOF of different concentrations. The fluorescence intensity is measured at 518 nm. The analysis revealed that the addition of 10 μL, 16 μL and 8 μL of 20 μg/mL NMOF resulted in complete fluorescence quenching of 5 μM of FAM-PNA21, ROX-PNA125b and Cy5-PNA96 within 10 min, respectively. These optimized ratios were used for detection of miRNAs unless otherwise indicated.

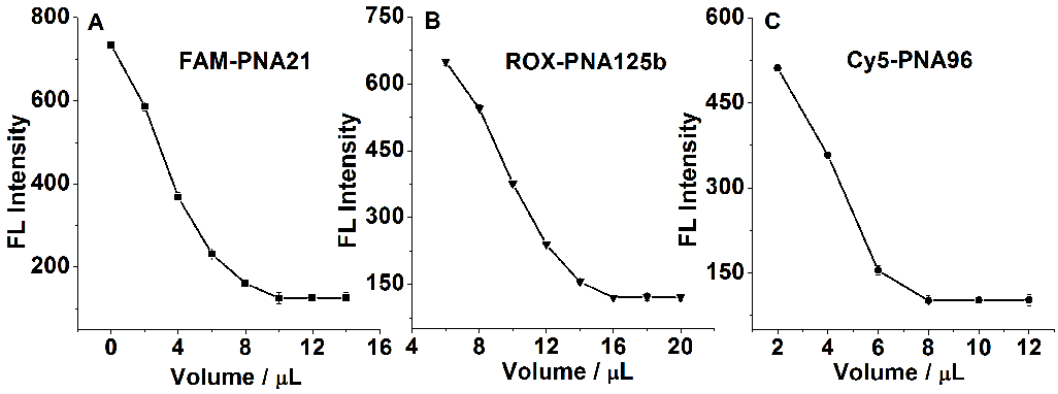

**Figure S4** The influence of the incubation time between the probe complex PNA-NMOF and target on the fluorescence intensity. The fluorescence emission was at 518 nm. The fluorescence recovery was done with vibration in 37 ºC water bath. Upon increasing incubation time, more adsorbed probe PNA was released from NMOF, resulting in the recovery of fluorescence gradually. When the incubation time exceeded 2 h, 3 h and 1.5 h, respectively, the intensity no longer increase, showing a balance between probe PNA/NMOF and probe PNA/target. Thus, 2 h, 3 h and 1.5 h were chosen as the incubation time for these three probes complexes, respectively.

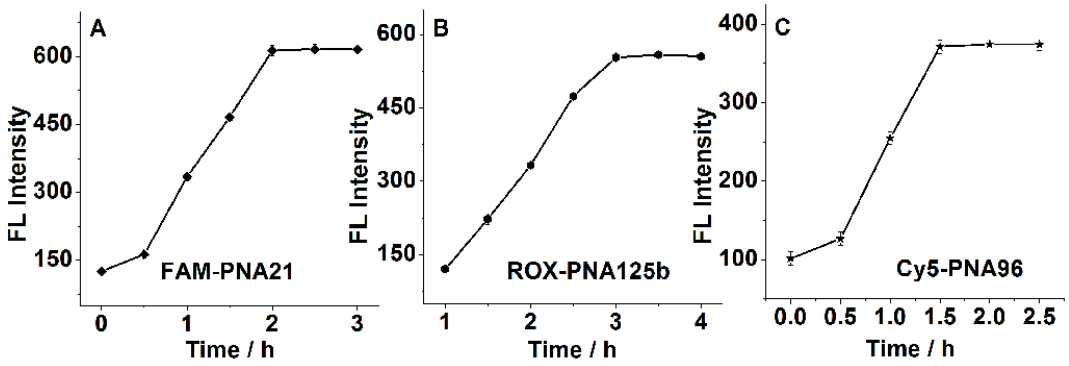

**Figure S5** Fluorescence emission spectra of dye-labeled probe FAM-PNA21 of different concentrations (0.0025, 0.025, 0.25, 2.5, 5 μM) in Tris-HCl buffer with 1 mM miR-21.

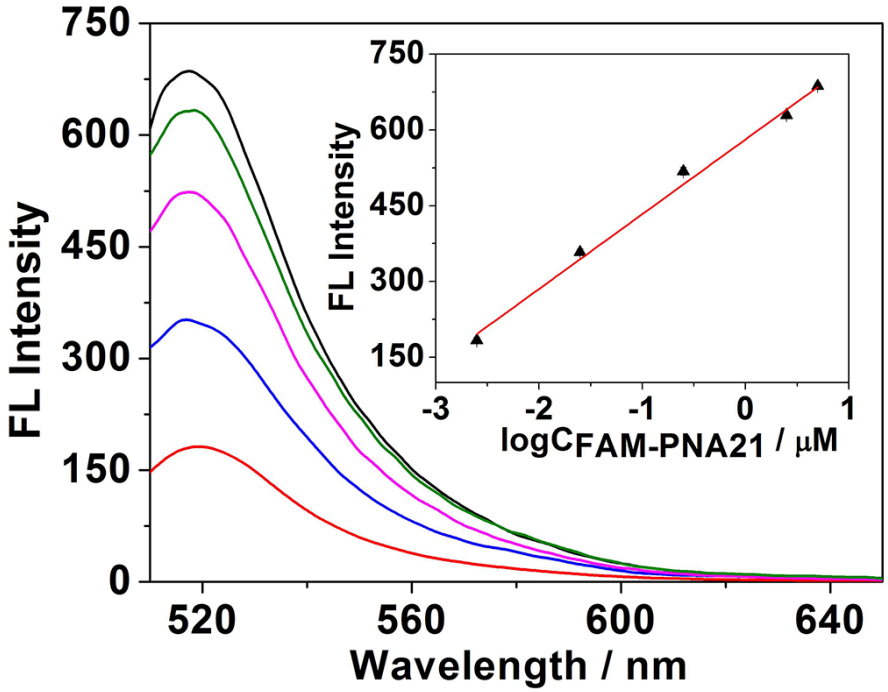

**Figure S6** The fluorescence images of the MDA-MB-231 cells that were treated with NMOF alone or each PNA probe alone (left side: phase contrast images, right side: overlay of fluorescence images of FAM, ROX, Cy5 channels for each PNA probe and blue for nuclei stained with DAPI).

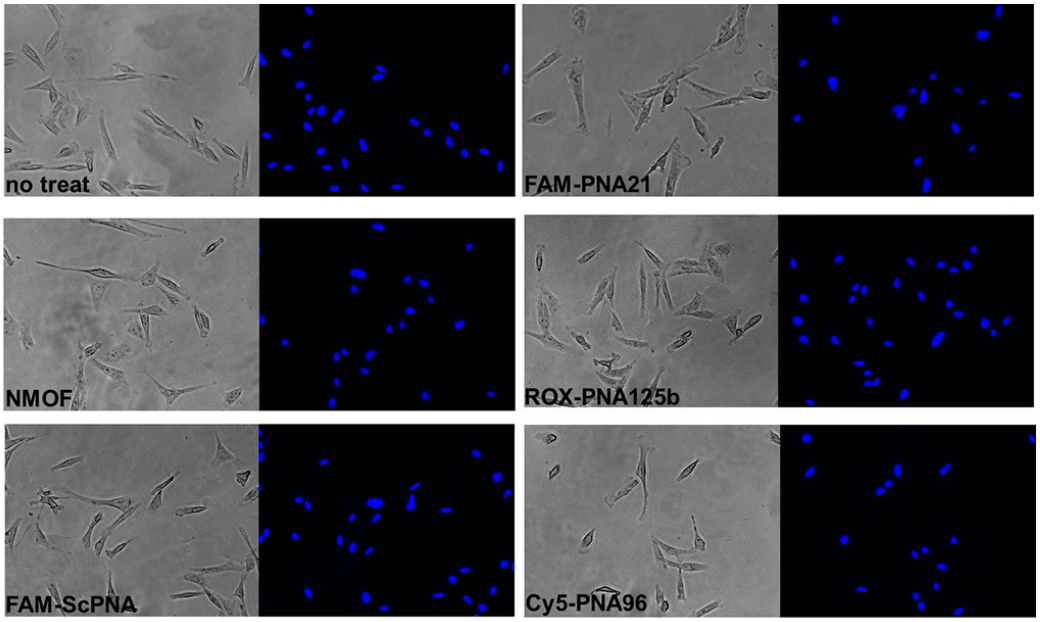

**Figure S7** The fluorescence images of MCF-10A cells that were treated with FAM-PNA21-NMOF.

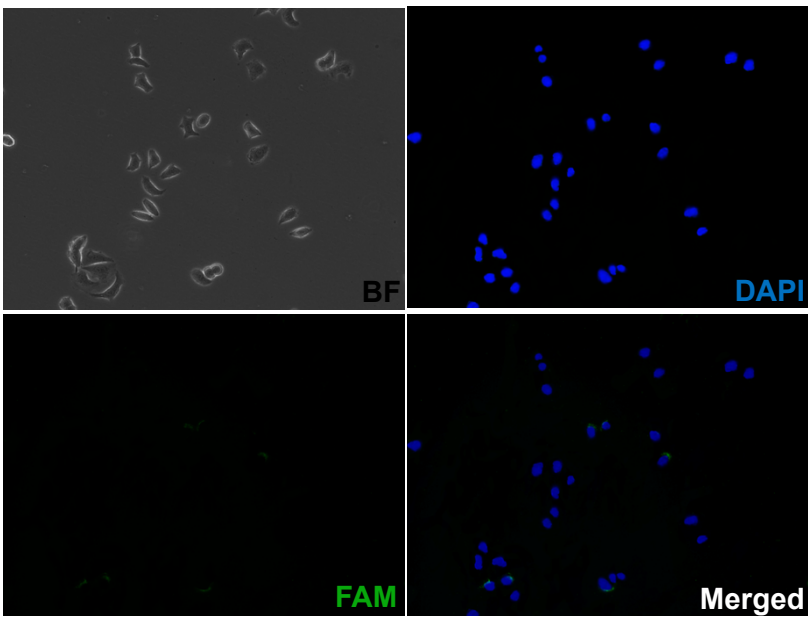

**Figure S8** Cytotoxicity test of the NMOFs in two cell lines (MCF-7 and MDA-MB-231). The viabilities of cells incubated with different concentrations of NMOF for 14 h were measured by MTT assay. Throughout the present study for miRNA sensing, the concentration of NMOF was maintained at 20 μg/mL, which ensured ~100% cell viability.

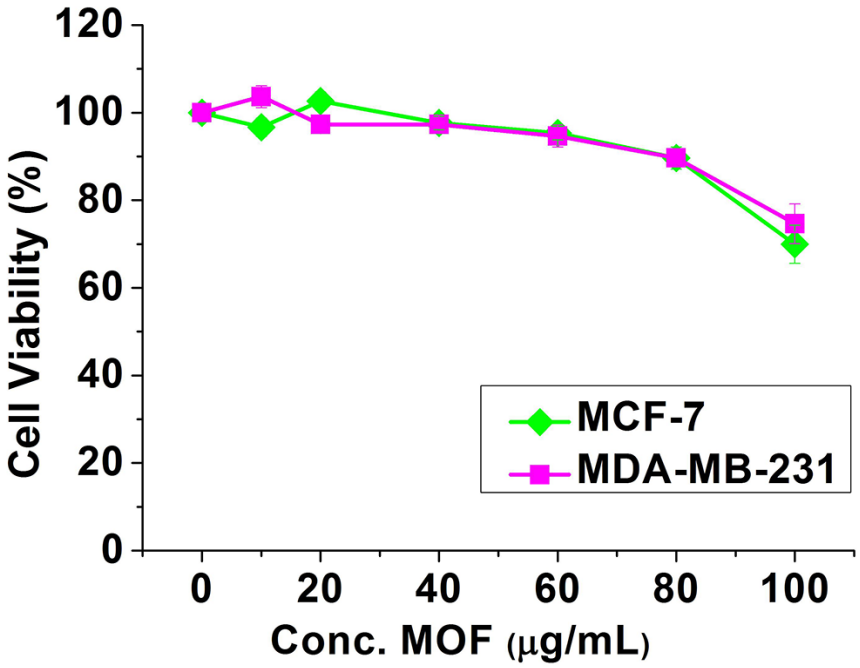

**Figure S9** (a) The fluorescence images of MCF-7 cells after the treatment of FAM - scPNA-NMOF complex. Before the addition of scPNA-NMOF, curcumin (5 μM) was treated to the cells for miR-21 induction for different time period (0, 8, 16, 24 and 32 hours). (b) In the control experiments in which the MCF-7 cells were treated with NMOF only, FAM-scPNA alone or FAM-PNA21 alone, no fluorescence of FAM was observed inside cells.

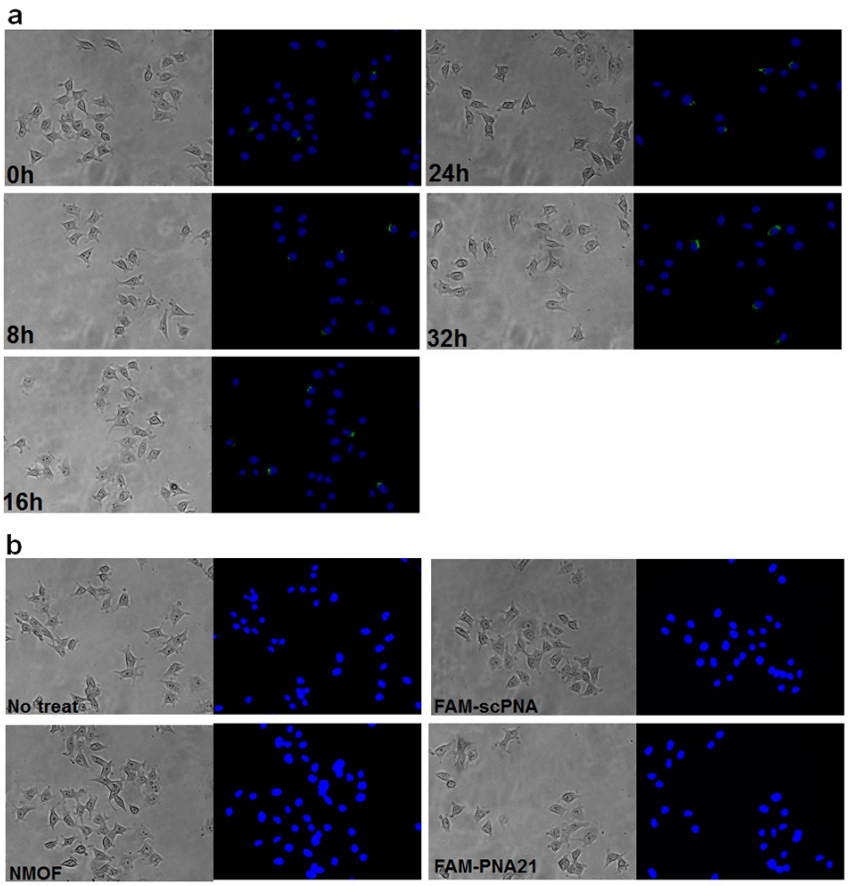

**Figure S10** The expression levels of the three miRNAs were investigated using RT-PCR. The data were shown as mean ± SD ($n$ = 4, *$p$ value <0.05 between two groups).

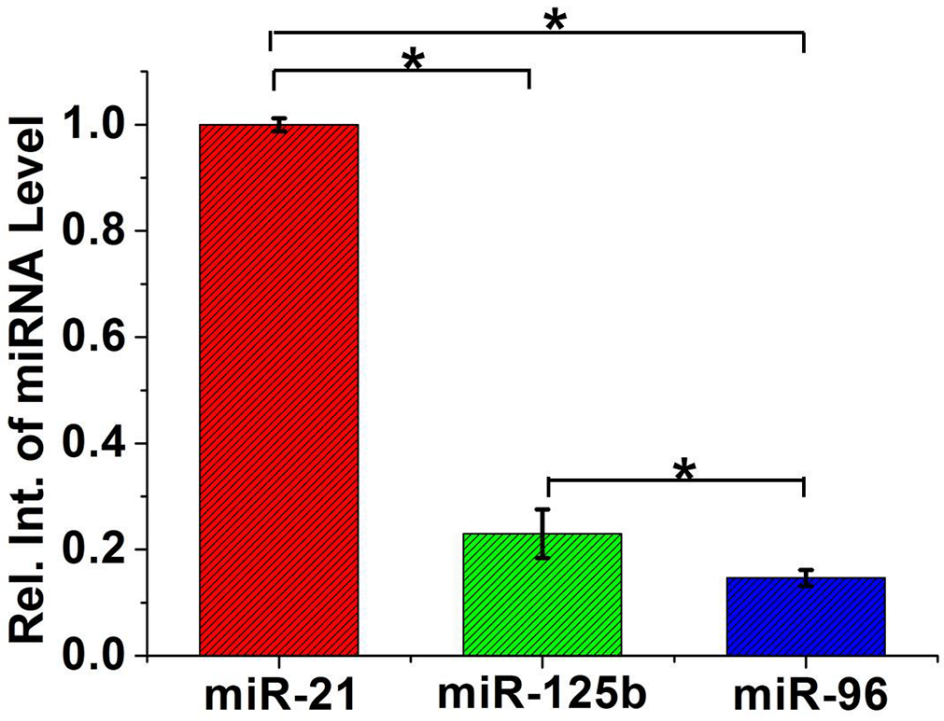

**Table S1** Fluorescence quench of the dye-labeled PNA probes in different solutions.

| Fluorescence of FAM-PNA21 | + $ZrCl_4$ | + Terephthalic acid | + NMOF(UiO-66) |
|---|---|---|---|
| $F_0$: (Intensity in the absence of fluorescence quencher) | 675 | 690 | 686 |
| $F_M$: (Intensity in the presence of fluorescence quencher) | 137 | 642 | 126 |
| Quenching efficiency $Q_E = (1 - F_M / F_0)$ | 79.7% | 6.96% | 81.6% |

**Table S2** Experimental data for the intra-assay and inter-assay of PANMOF-based miRNA sensor. Concentration of NMOF, FAM-PNA21 and miR-21 were 20 μg/mL, 5 μM and 1 nM, respectively.

| Intra-assay | | | | | | |
|---|---|---|---|---|---|---|
| Test # | 1 | 2 | 3 | 4 | 5 | RSD (%) |
| Fluorescence intensity | 309 | 310.1 | 310.6 | 309.2 | 308.6 | 8.2 |
| Inter-assay | | | | | | |
| Sensor # | 1 | 2 | 3 | 4 | 5 | RSD (%) |
| Fluorescence intensity | 309 | 308.7 | 308.9 | 310.3 | 310.7 | 9.1 |

**Table S3** Sequence information of miRNAs and complementary peptide nucleic acid probes.

| | |
|---|---|
| **miR-21** | **5’-UAGCUUAUCAGACUGAUGUUGA-3’** |
| **miR-125b** | **5’-UCCCUGAGACCCUAACUUGUGA-3’** |
| **miR-96** | **5’-UUUGGCACUAGCACAUUUUUGCU-3’** |
| **ScRNA** | **5'-UGCGCUCCUGGACGUAGCCUU-3'** |

| | |
|---|---|
| **FAM-PNA21** | **5’-/56-FAM/TCAACATCAGTCTGATAAGCTA-3’** |
| **ROX-PNA125b** | **5’-/56-ROXN/TCACAAGTTAGGGTCTCAGGGA-3’** |
| **Cy5-PNA96** | **5’-/5Cy5/AAAATGTGCTAGTGCCAA-3’** |
| **FAM-ScPNA** | **5’-/56-FAM/ATCGAATAGTCTGACTACAACT-3’** |

**Table S4** Fluorescence intensity of three types of PANMOF complexes in response to seven different combinations of miRNAs.

| | FAM-PNA21-NMOF | ROX-PNA125b-NMOF | Cy5-PNA96-NMOF |
|---|---|---|---|
| miRNA | Fluorescence intensity | Fluorescence intensity | Fluorescence intensity |
| miR-21 | 603.7 | 63.3 | 64 |
| miR-125b | 90.3 | 542.5 | 92.4 |
| miR-96 | 85 | 87.3 | 374.7 |
| miR-21+ miR-125b | 606.5 | 545.1 | 69 |
| miR-21+miR-96 | 599.1 | 77 | 376.4 |
| miR-125b+miR-96 | 90 | 540 | 380 |
| miR-21+ miR-125b+miR-96 | 600 | 543.1 | 381.3 |