

Supporting Information

1. Plasmid design

The L2-NTD plasmid was designed by integrating the N-terminal sequence of the L2 peptide from HPV 16, (aa: 396-439, GenBank: AAD33258.1), with the NTD of SARS-COV-2 N protein (GenBank: QHD43423.2). The plasmid of L2-NTD was synthesized by Genscript Biotechnology Co. and a comprehensive map, named PET-28A L2-NTD, is provided within the "Supporting Information" folder.

2. Construction of FITC-L2-NTD@HmA and its cell entry assay

2.1. UV-vis absorption spectra of FITC-L2-NTD@HmA

The UV-vis data can be found in the "Supporting Information" folder, specifically within the Excel tables named "UV-vis raw data".

2.2. DLS raw data

We characterized the particle sizes of HmA, L2-NTD@HmA, TK-14@HmA, siGFP+L2-NTD@HmA, siGFP+TK-14@HmA, siBCL-2+L2-NTD@HmA, The raw data of DLS mapping is shown in "Supporting Information" folder, named as "DLS raw data".

2.3. Fluorescence imaging of HeLa cells

To determine whether HmA could efficiently carry the small peptide into cells, HeLa cells were transfected with L2-NTD and FITC-L2-NTD@HmA, respectively. Figure S1 shows unprocessed plots of the corresponding fluorescence microscopy results after 2 and 4 h of incubation.

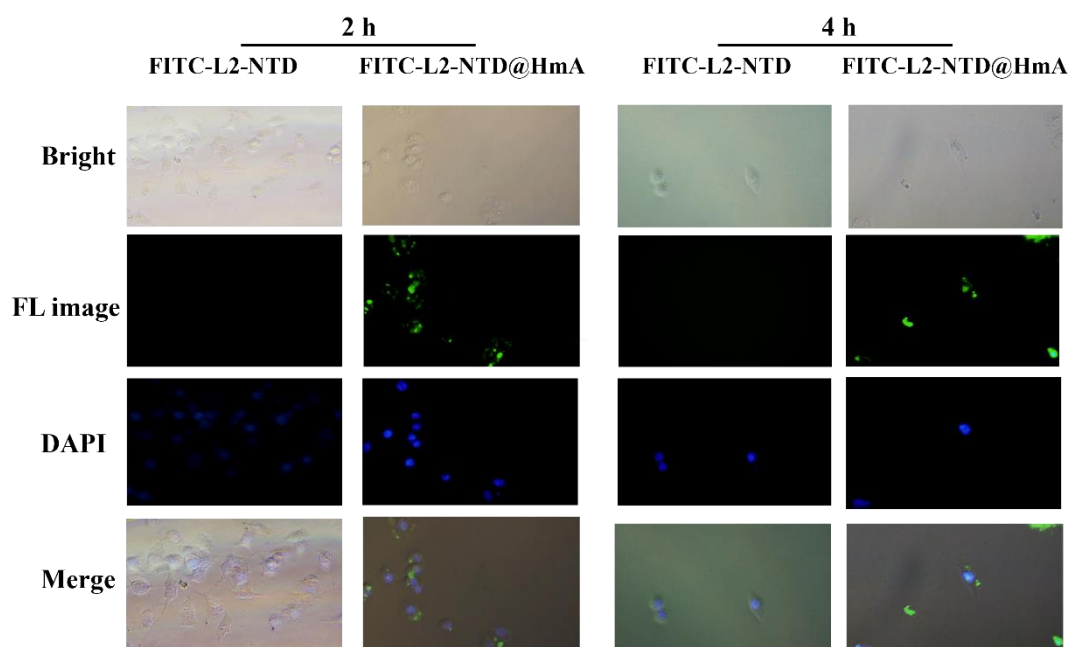


Fig. S1 Fluorescence imaging of FITC-L2-NTD and FITC-L2-NTD@HmA (blue: nucleus; green: FITC) after transfection of HeLa cells for 2 h and 4 h. The concentration of the transfected particles was 30 µg/mL.

Different amounts of the constructed FITC-L2-NTD@HmA were then added to the culture medium for a cell transmembrane assay. After 4 h of incubation, fluorescence images were observed for the test HeLa

cells using a fluorescence microscope, proving that FITC-L2-NTD@HmA successfully entered the cells. Among the three concentrations of 15 $\mu\text{g/mL}$, 30 $\mu\text{g/mL}$, and 60 $\mu\text{g/mL}$ of FITC-L2-NTD@HmA used for the assay, the fluorescence images in HeLa cells were the brightest and the cell morphology was mostly intact at a concentration of 30 $\mu\text{g/mL}$ (Fig. S2).

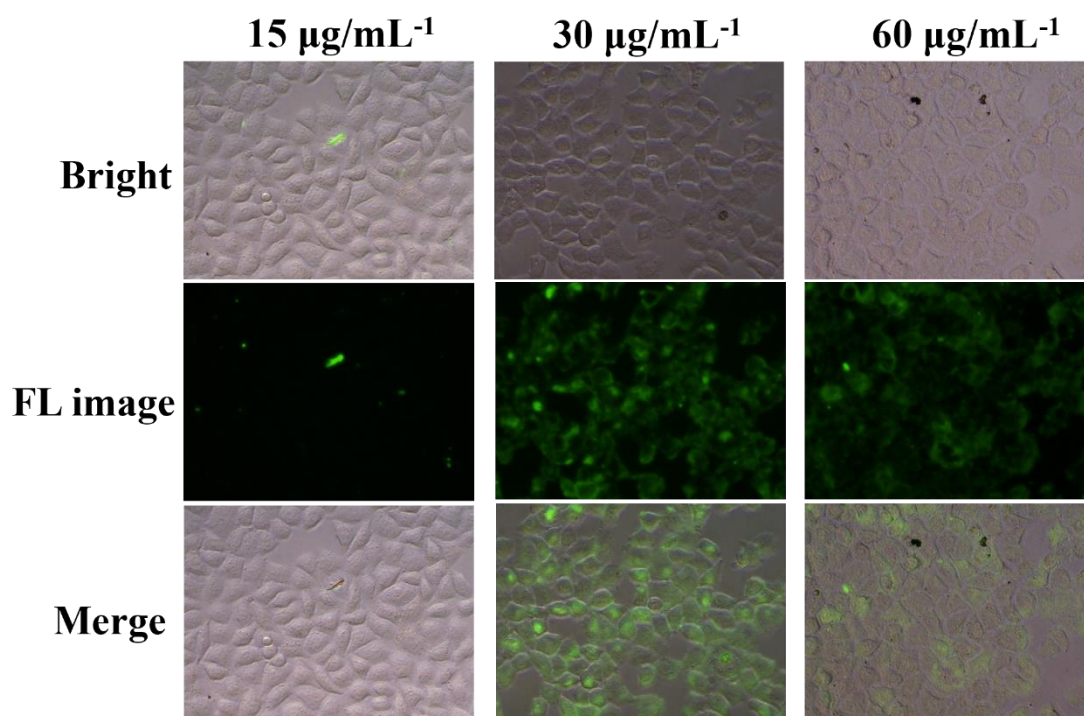


Fig. S2 Fluorescence imaging of HeLa cells after transfected with FITC-L2-NTD@HmA constructed from different concentrations of FITC-L2-NTD@HmA for 4 h, the green is shown for FITC.

2.4. CCK-8 毒性测试

The cell viability was assessed using the CCK-8 assay, After transfecting the cells with L2-NTD@HmA at different concentration gradients, the cells were incubated overnight and the cytotoxicity of the transfected cells was detected by CCK-8 kit. the plates were read at 450 nm using a microplate reader (Varioskan LUX Multimode Thermo, USA). Three replicates were performed for each concentration. Raw data measured at 450 nm are in the "Supporting Information" folder, named as "CCK-8 raw data"

3. Transmembrane assays of siRNA+L2-NTD@HmA co-assembly

To investigate if the encapsulation of siRNA+L2-NTD in HmA assembly can promote the transmembrane delivery of nanoparticles to cells, we analyzed the intracellular distribution of Cy5-labeled siGFP (Cy5-siGFP) after co-assembly with L2-NTD and HmA in living cells using both confocal fluorescence imaging and flow cytometry. Figure 8 is the Outline of flow-cytometry results for HeLa cells after being treated with the constructed materials at different time gradients. The flow-cytometry results is shown in Fig. S3.

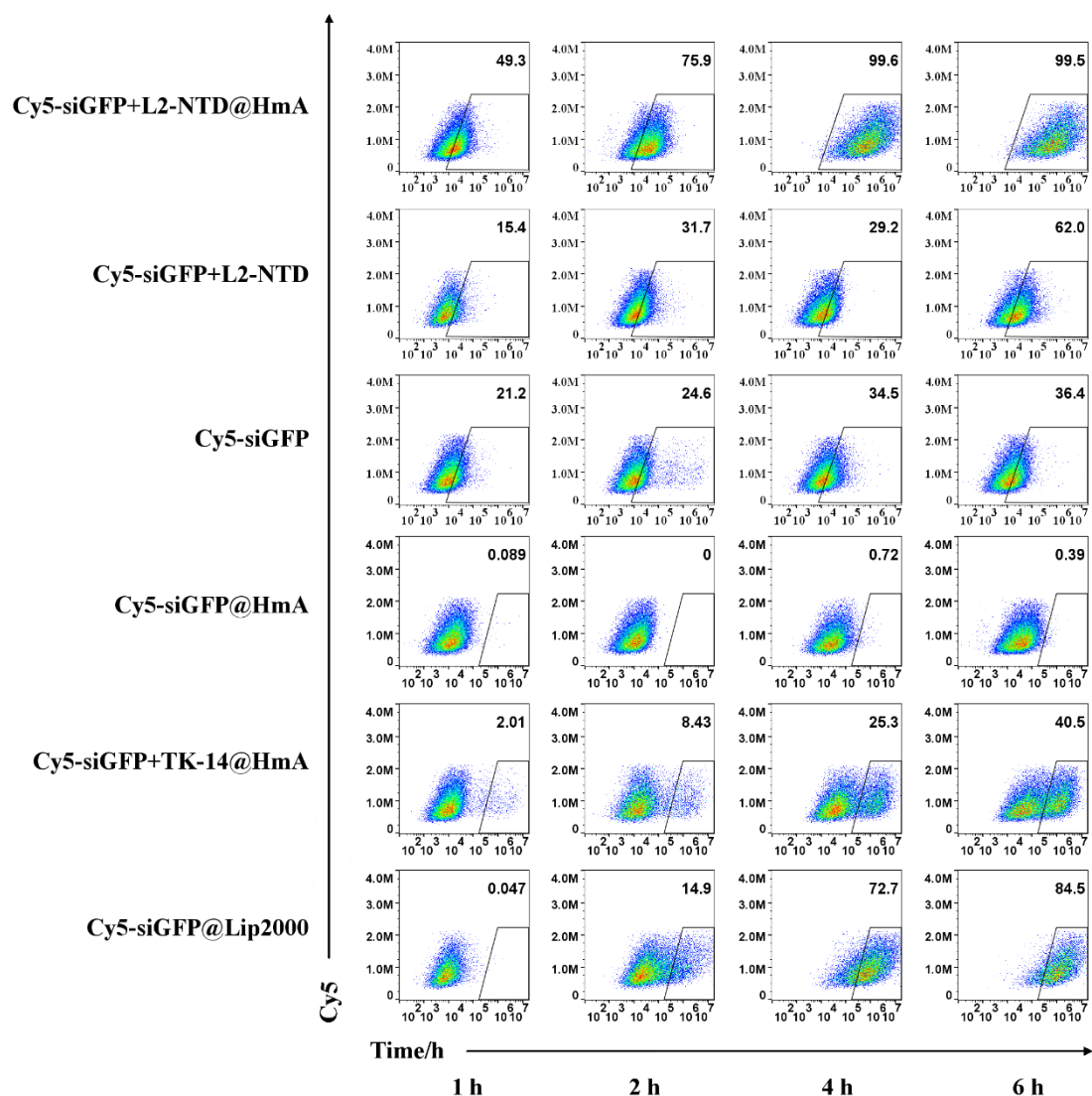


Fig. S3 flow-cytometry results for HeLa cells after being treated with the constructed materials at different time gradients.

4. Western-blot assay for BCL-2 expression in cells

HeLa cells were inoculated respectively in a 6-well plate at a density of 3×10^5 cells/well, following being cultured for 24 h to grow well. After the addition of each sample, the cells were continued to be cultured for another 48 h. Standard Western-blot experiments were then performed for each repeated wells after cell lysate. Standard Western-blot experiments were then performed for each repeated wells after cell lysate. The chromogenic bands obtained were analyzed semi-quantitatively by Image J for the gray value ratio of BCL-2 to β -tubulin, and GraphPad was used to graphically compare the BCL-2 protein expression levels of the test and control groups. The gray value raw data is shown in "Supporting Information" folder, named as "WB gray value".