

# 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

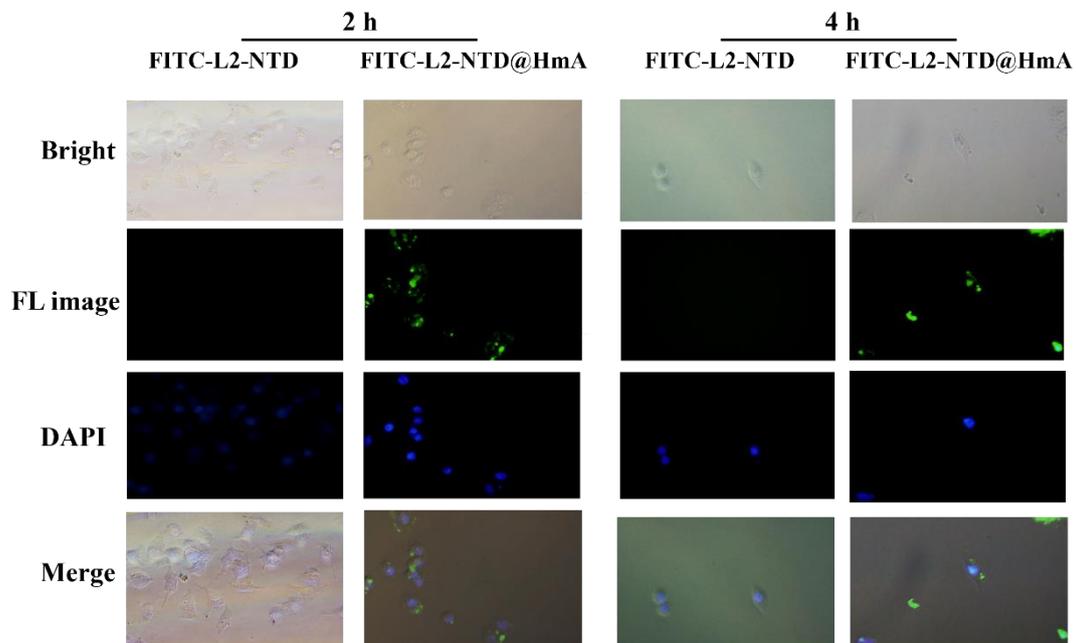
The UV-vis data can be found in the "Supporting Information" folder, specifically within the Excel tables named "UV-vis raw data".

### 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

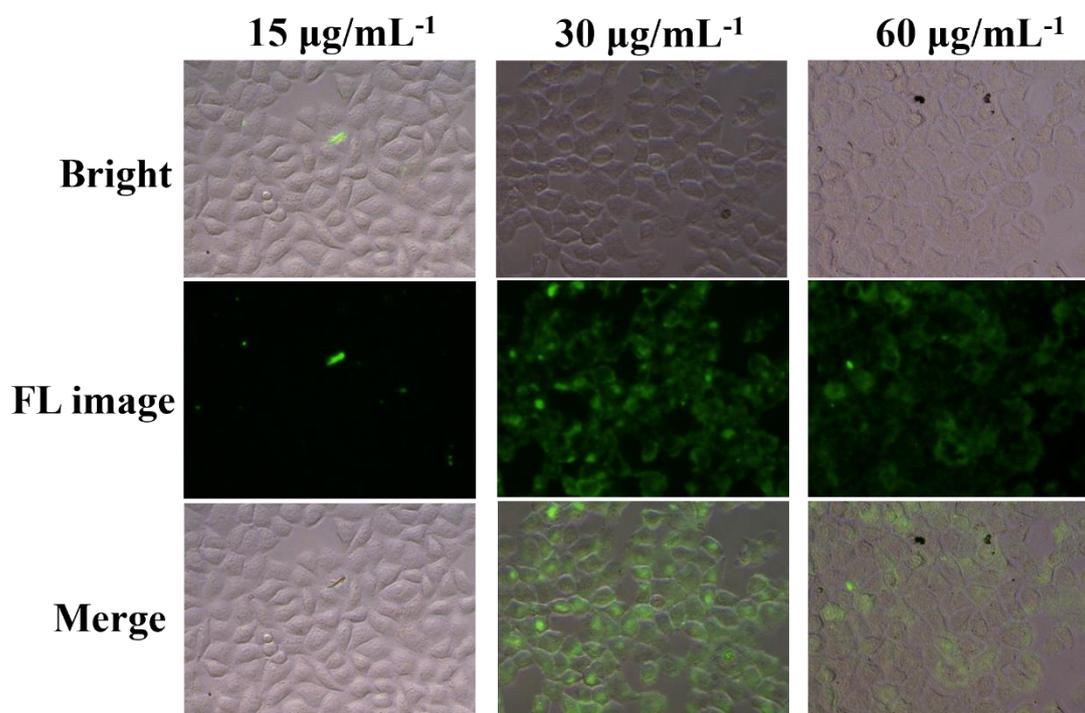
To determine whether HmA could efficiently carry the small peptide into cells, HeLa cells were transfected with L2-NTD and FITC-L2-NTD@HmA, respectively. Figure S1 shows unprocessed plots of the corresponding fluorescence microscopy results after 2 and 4 h of incubation.



**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  $\mu\text{g}/\text{mL}$ .

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  $\mu\text{g}/\text{mL}$ , 30  $\mu\text{g}/\text{mL}$ , and 60  $\mu\text{g}/\text{mL}$  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  $\mu\text{g}/\text{mL}$  (Fig. S2).



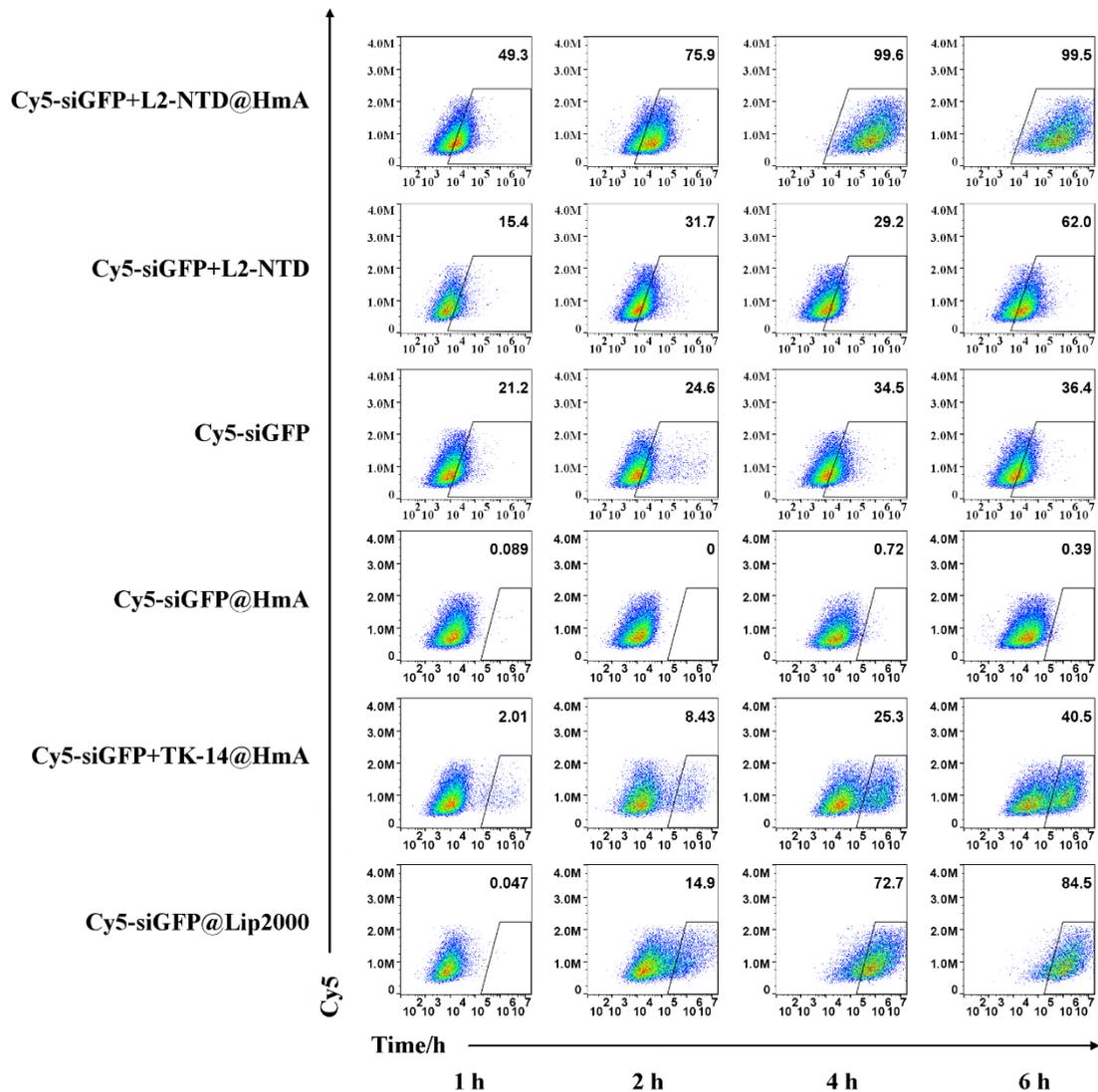
**Fig. S2** Fluorescence imaging of HeLa cells after transfected with FITC-L2-NTD@HmA constructed from different concentrations of FITC-L2-NTD@HmA for 4 h, the green is shown for FITC.

#### 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  $3 \times 10^5$  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  $\beta$ -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".