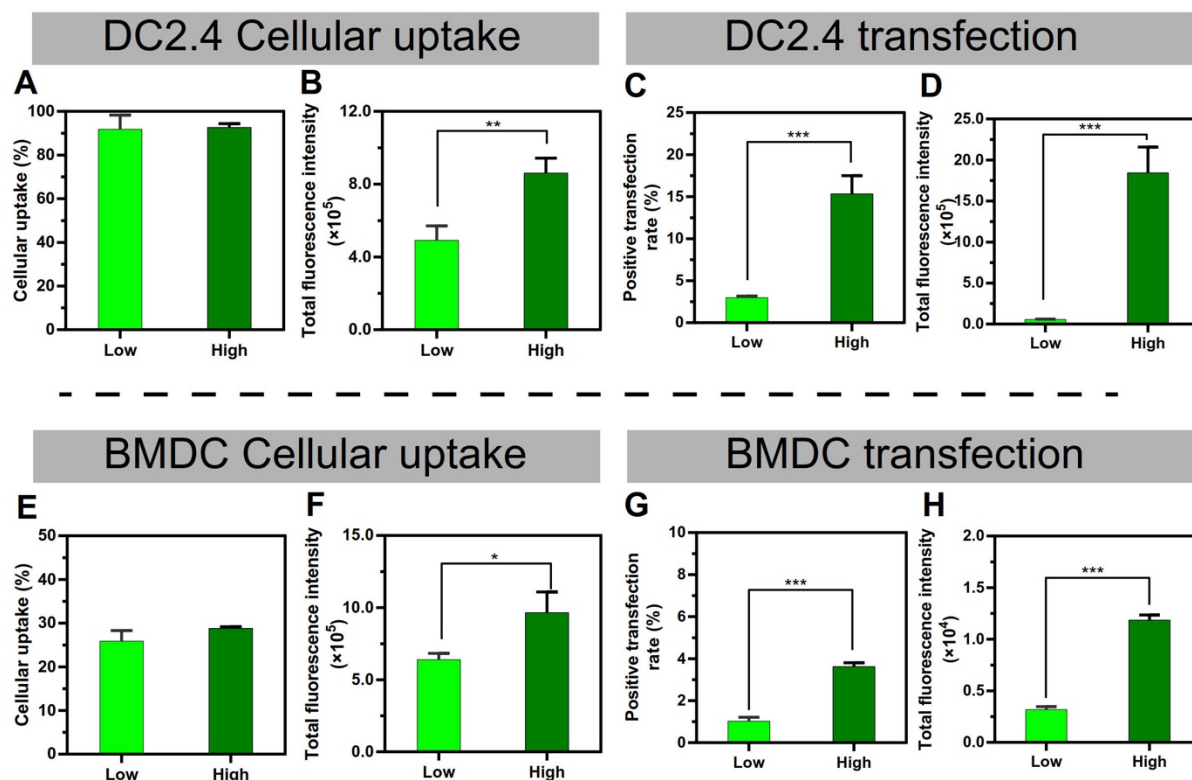


## Supporting Information

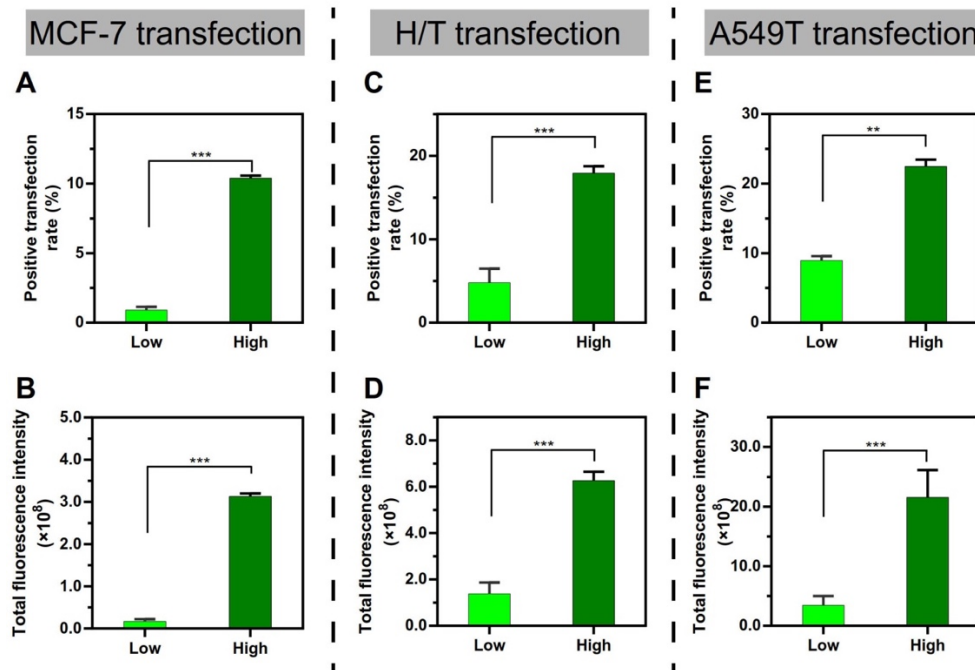
### Nano-structural effects on gene transfection: large, botryoid-shaped nanoparticles enhance DNA delivery via macropinocytosis and effective dissociation

Wenyuan Zhang<sup>1,2</sup>, Xuejia Kang<sup>1,3</sup>, Bo Yuan<sup>4</sup>, Huiyuan Wang<sup>1</sup>, Tao Zhang<sup>1</sup>, Mingjie Shi<sup>1</sup>, Zening Zheng<sup>1,3</sup>, Yuanheng Zhang<sup>1</sup>, Chengyuan Peng<sup>1</sup>, Xiaoming Fan<sup>1</sup>, Huaiyu Yang<sup>1,5</sup>, Youqing Shen<sup>6</sup>, Yongzhuo Huang<sup>1,2</sup>\*

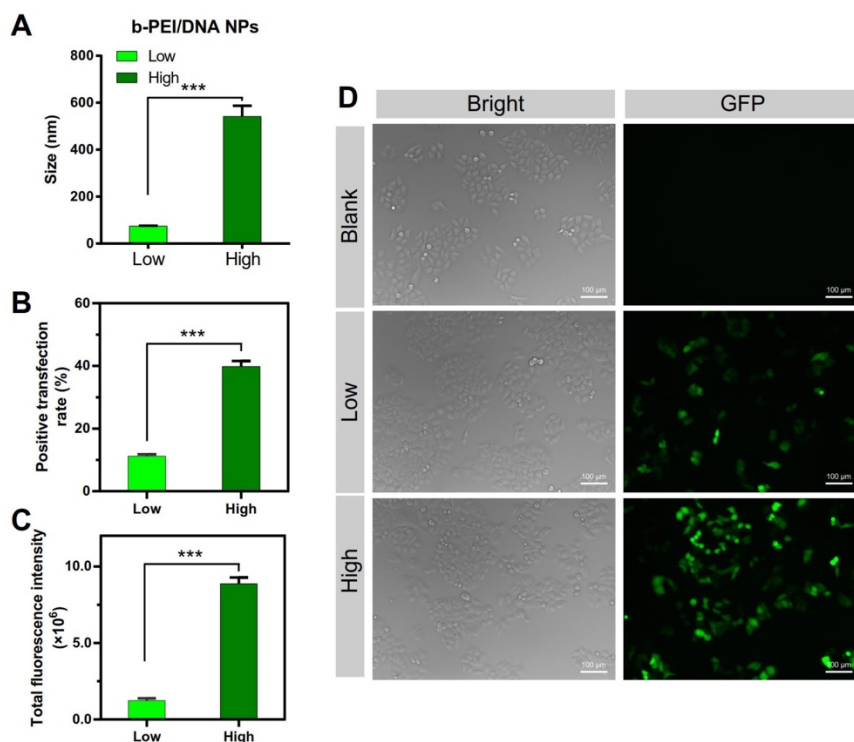
**Figure S1. Cellular uptake and transfection results of DC2.4 cells and BMDCs. (A-B, E-F)** The quantitative analysis of the cellular uptake rate and total fluorescence intensity. **(C-D, G-H)** The quantitative analysis of positive transfection rate and total fluorescence intensity.



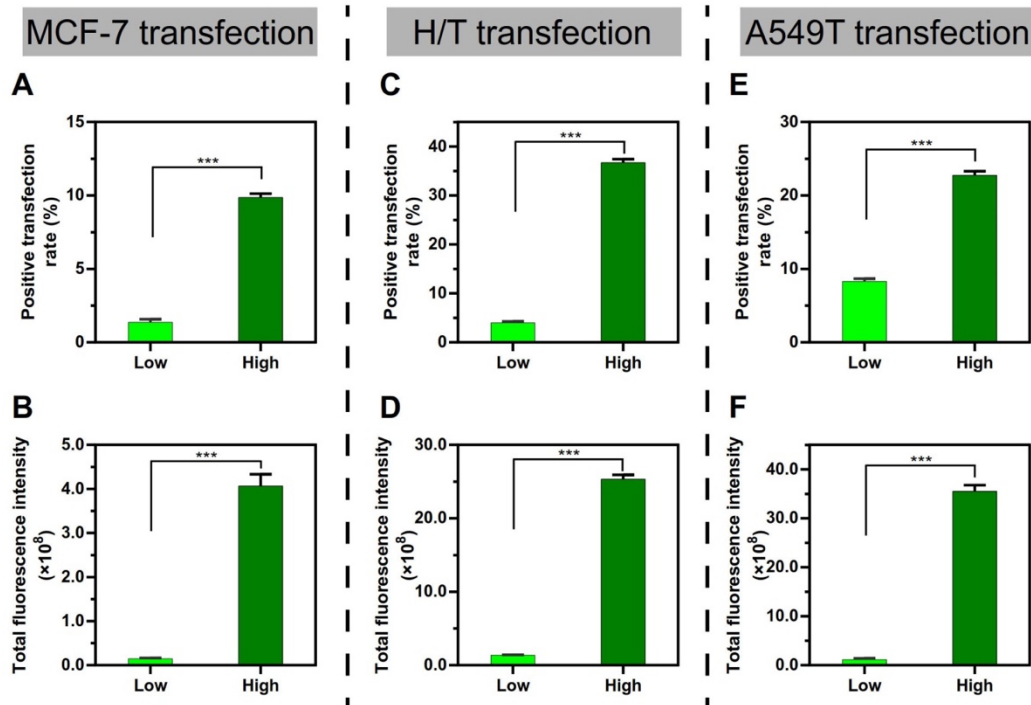
**Figure S2. Transfection of the two groups of PEI/DNA NPs in MCF-7, H/T, and A549T cells. (A, C, E) The quantitative analysis of positive transfection rate. (B, D, F) The quantitative analysis of total fluorescence intensity.**



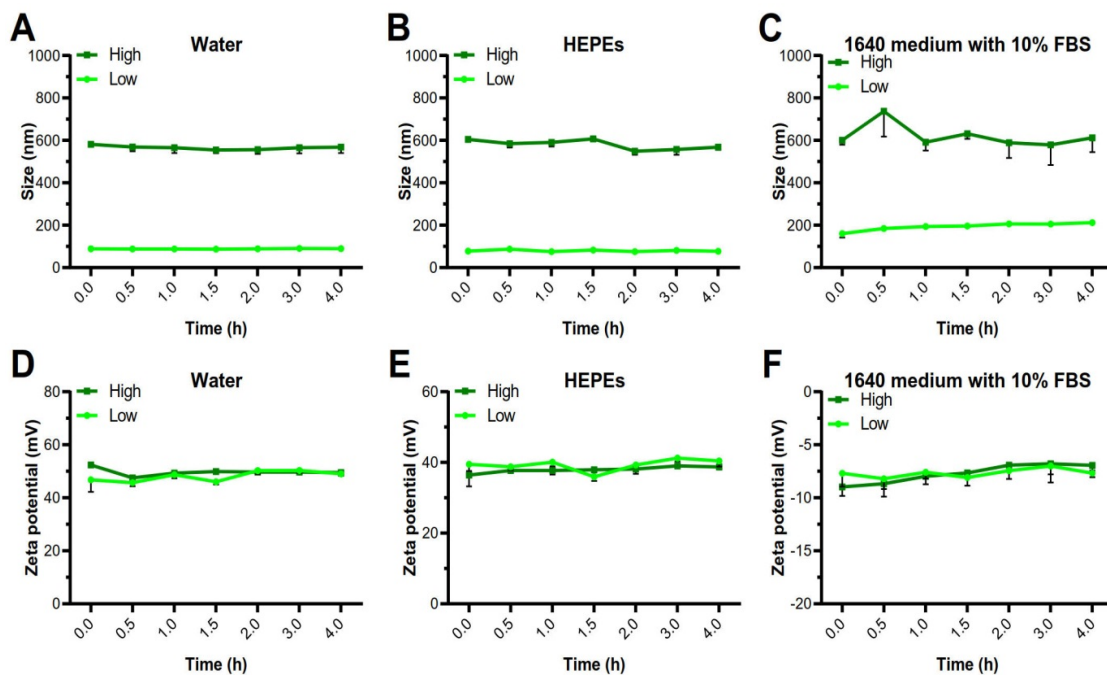
**Figure S3. The results of transfection experiments of the b-PEI/DNA NPs in HeLa cells. (A) Particle size of the b-PEI/DNA<sub>low</sub> and b-PEI/DNA<sub>high</sub> NPs. FACS analysis of positive transfection rate (B) and total fluorescence intensity (C). (D) Fluorescence images of GFP expression. Scale bar, 100  $\mu$ m.**



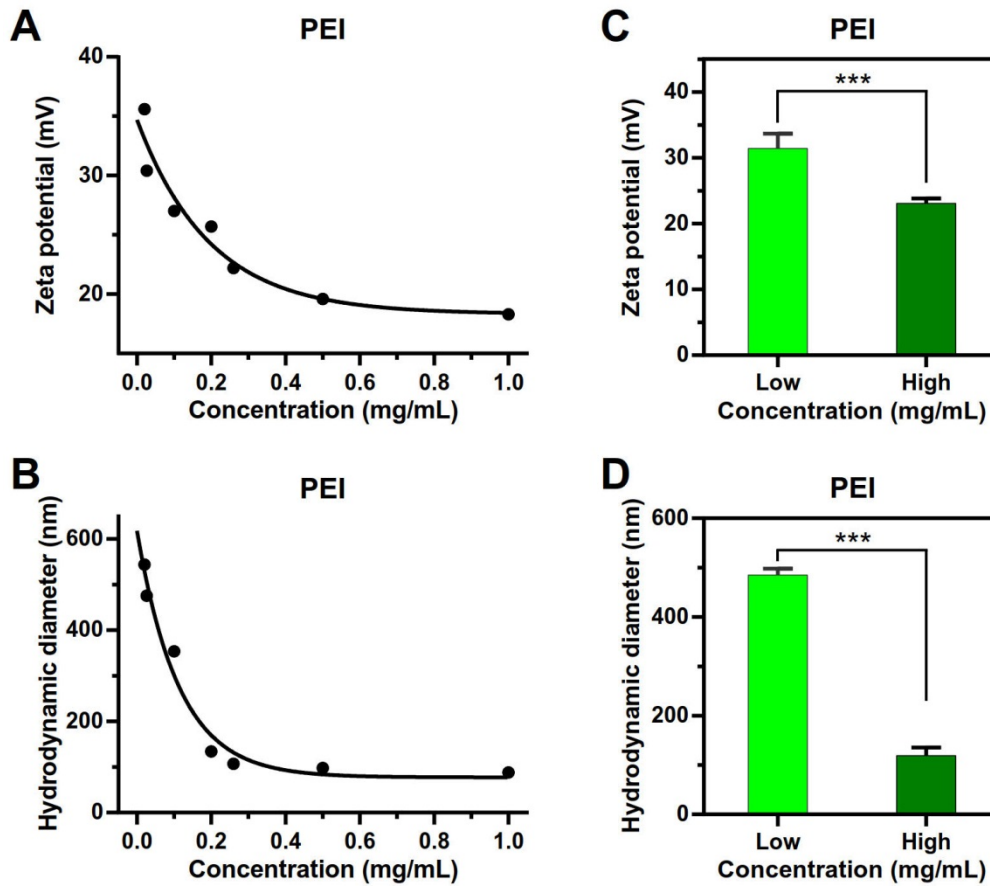
**Figure S4. Transfection results of the b-PEI/DNA NPs in MCF-7 cells, H/T cells, and A549T cells. (A, C, E) The quantitative analysis of positive transfection rate. (B, D, F) The quantitative analysis of total fluorescence intensity.**



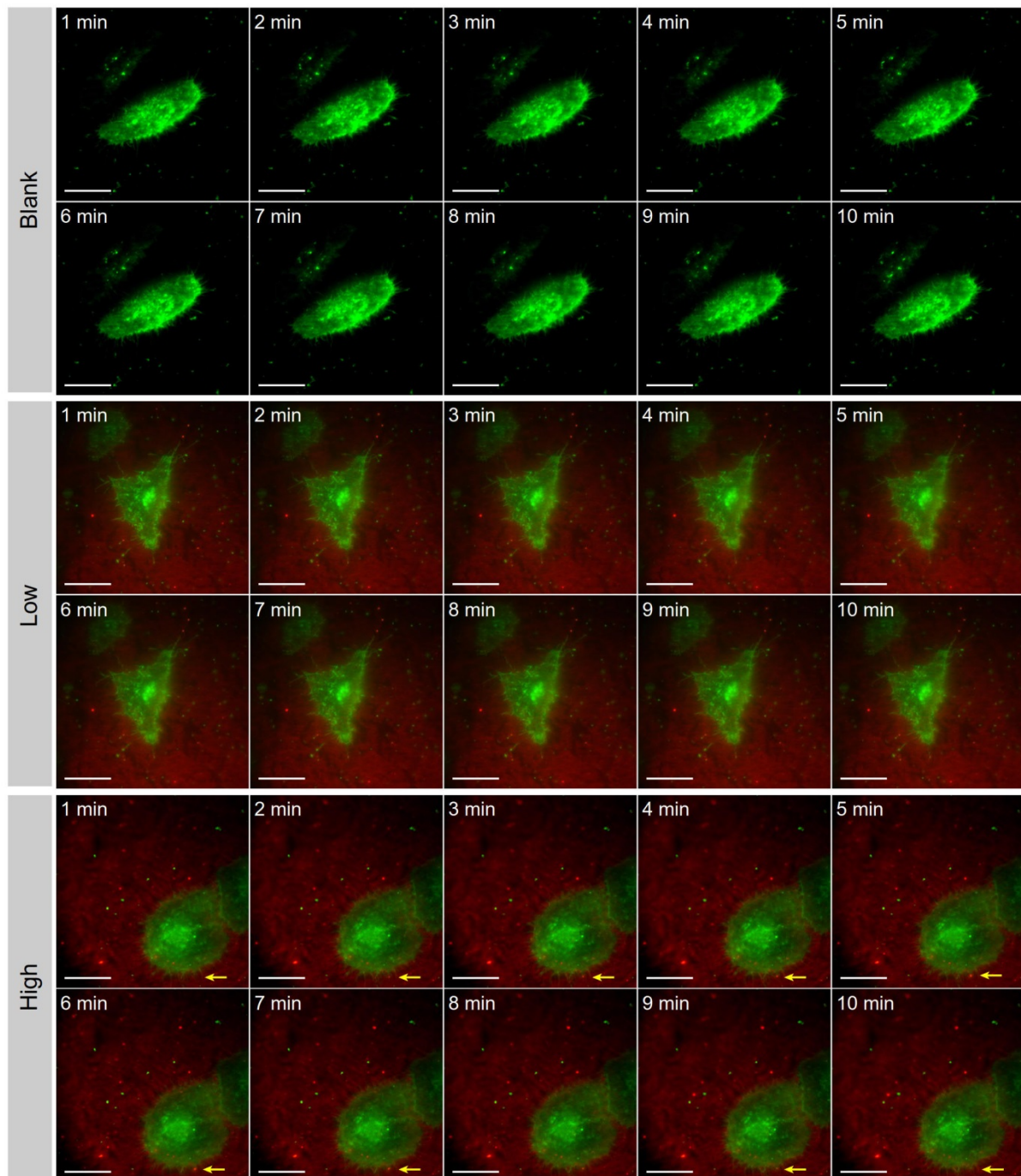
**Figure S5. The particle size and zeta potential results of the two groups of NPs in different solvents. (A-C) Particle size results. (D-F) Zeta potential results.**



**Figure S6.** (A) The zeta potential of PEI varies with the concentration. (B) The hydrodynamic diameter of PEI varies with the concentration. (C) The zeta potential of PEI in the low concentration group and the high concentration group were compared. (D) The hydrodynamic diameter of PEI in the low concentration group and the high concentration group were compared.

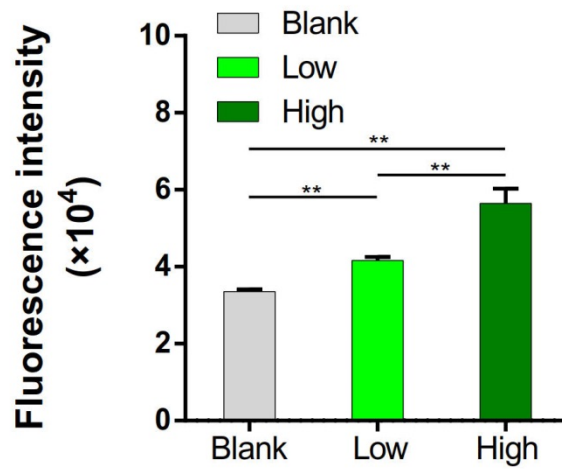


**Figure S7. TIRFM images of the cellular uptake.** The cell membrane is shown in green, and the NPs are shown in red.





**Figure S8.** The ROS levels in the HeLa cells after 24-h transfection of the PEI/pTRAIL NPs determined by a ROS detection kit.



**Figure S9.** The preliminary valuation of side toxicity. **(A)** The body weight changes over the regimen. **(B)** The organ coefficients. **(C)** Histological examination of the major organs after treatment. Scale bar, 50  $\mu$ m.

