



## Polymer Chemistry

### ARTICLE

### Supporting Information

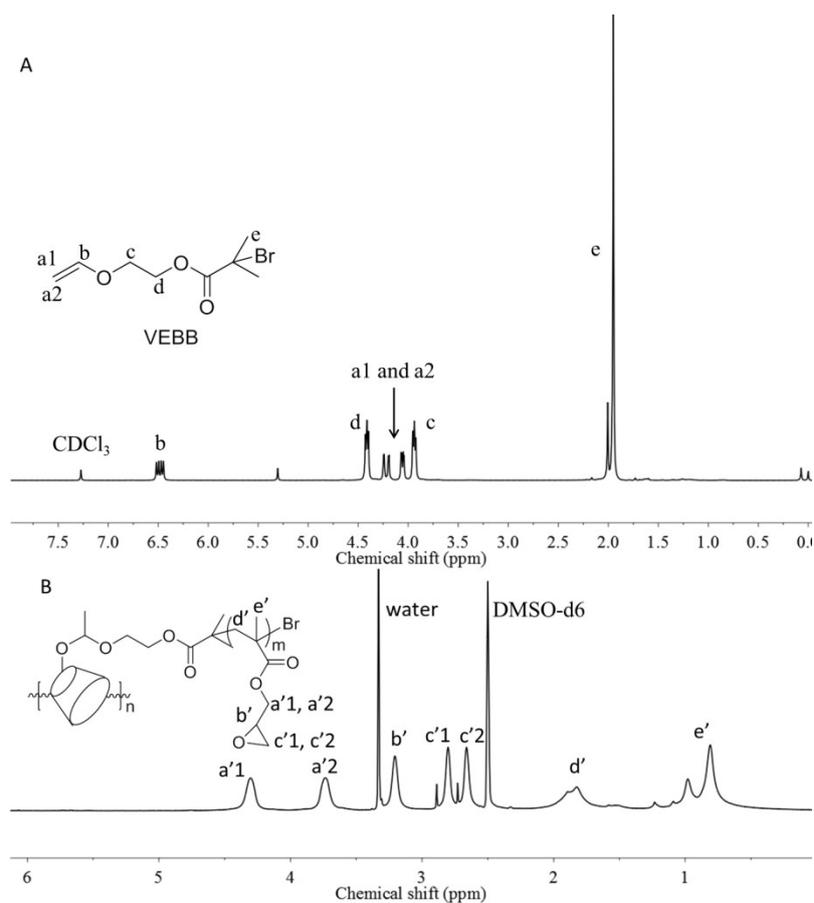
#### Acid-sensitive poly( $\beta$ -cyclodextrin)-based multifunctional supramolecular gene vector

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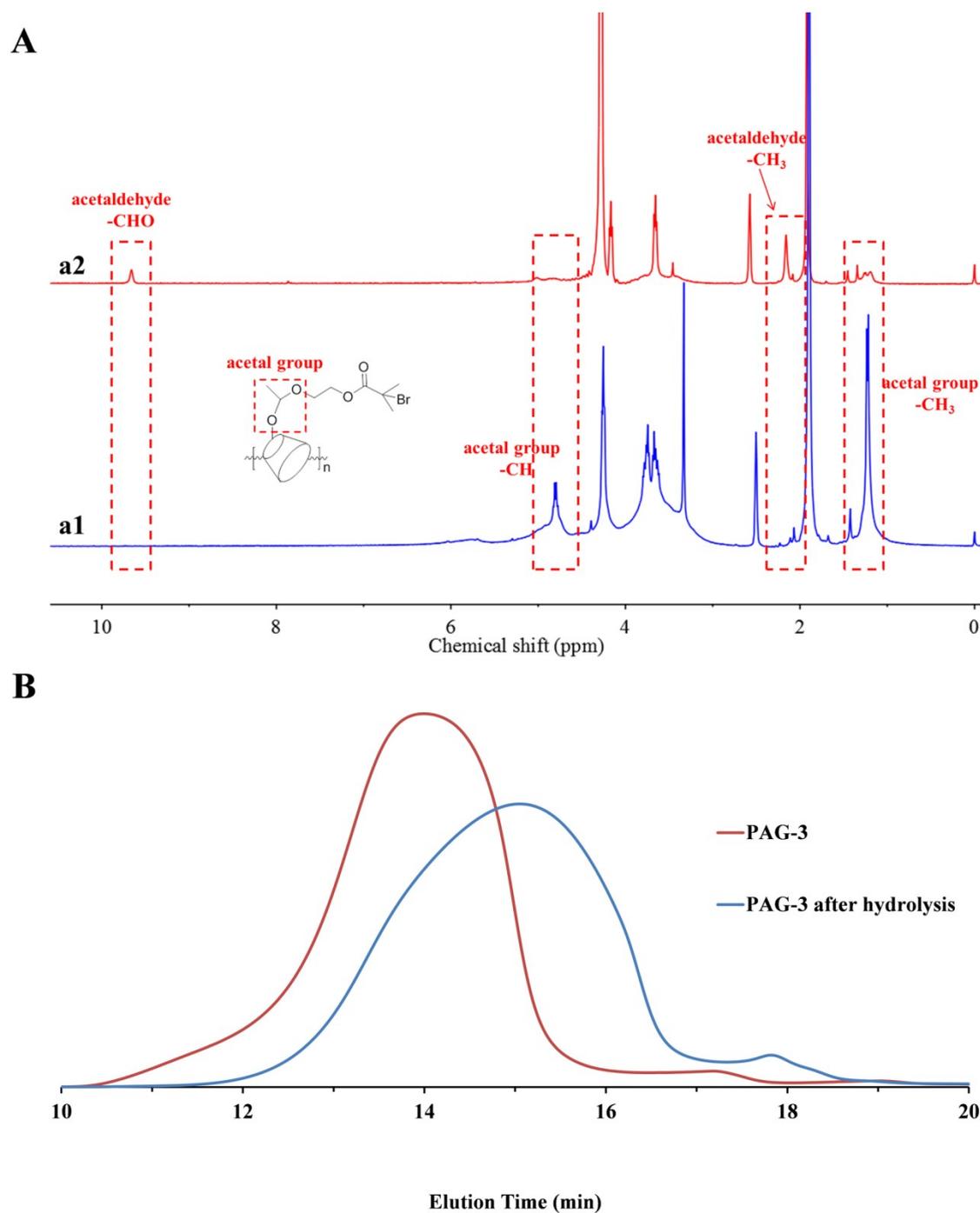


**Fig. S1** <sup>1</sup>H NMR spectra of VEBB (A) in CDCl<sub>3</sub> and PCD-acetal-PGMA (B) in DMSO-d<sub>6</sub>.

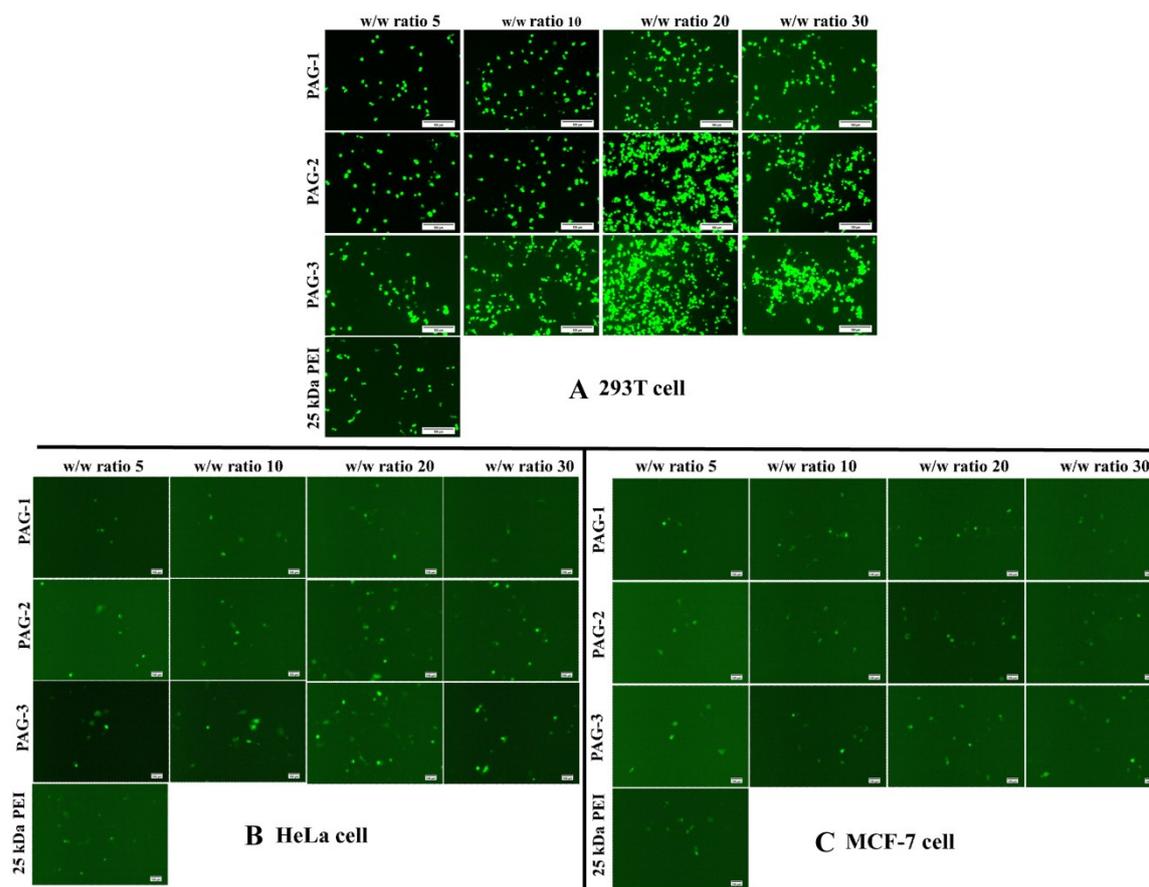
### Calculation of the Modification Degree of VEBB to PCD.

Assuming  $x$  mol VEBB successfully grafted for every mole cyclodextrin unit, 70 mol H from the protons of cyclodextrin, based on the <sup>1</sup>H NMR spectrum of PCD-acetal-BIB in Fig. 1, there are  $(70+5x)$  mol H at  $(a+c+d+e)$  and  $6x$  mol H at  $f$ . Therefore,  $x$  can be calculated by following equation:

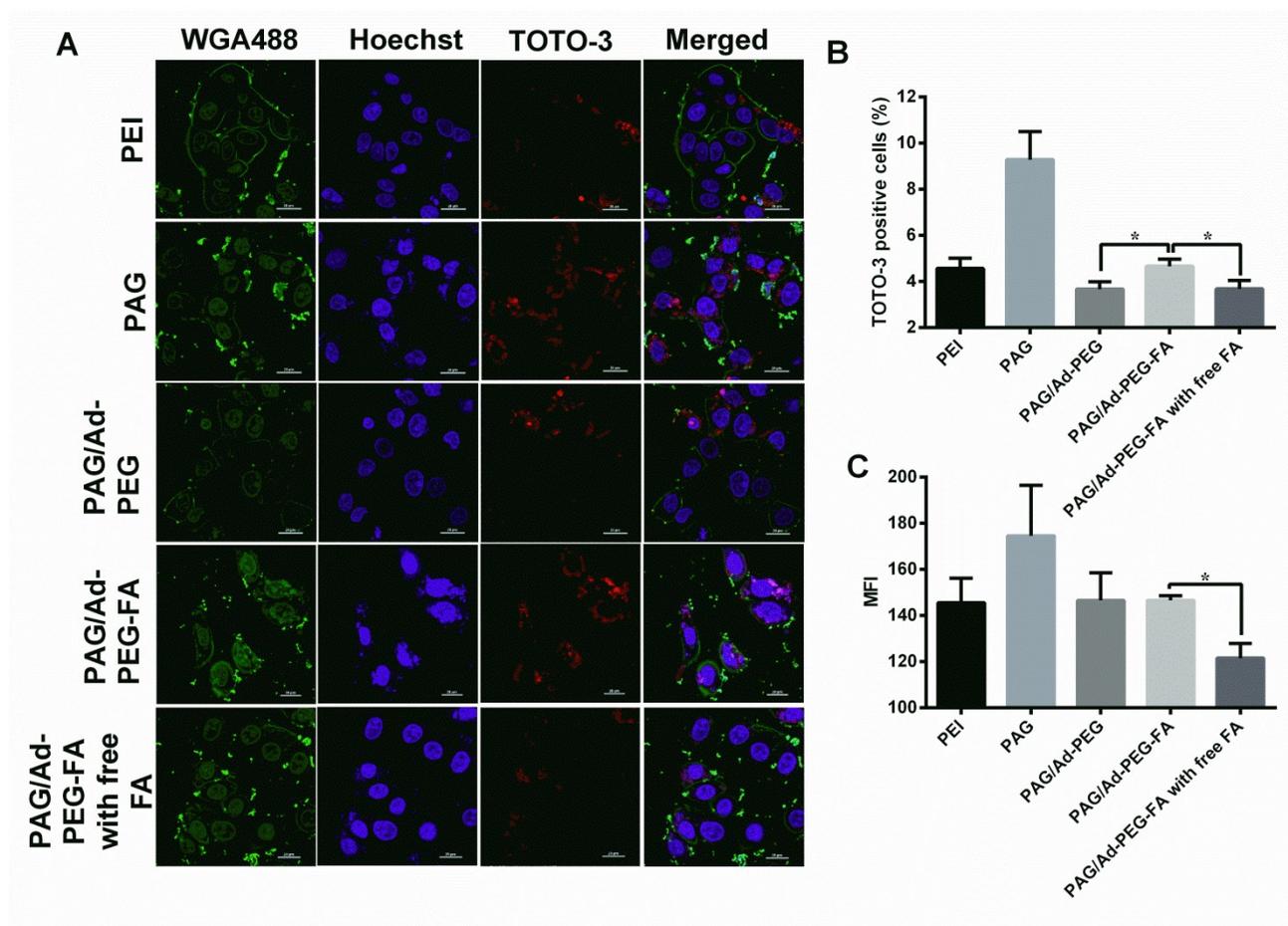
$$\frac{6x}{70 + 5x} = \frac{f}{a + c + d + e}$$



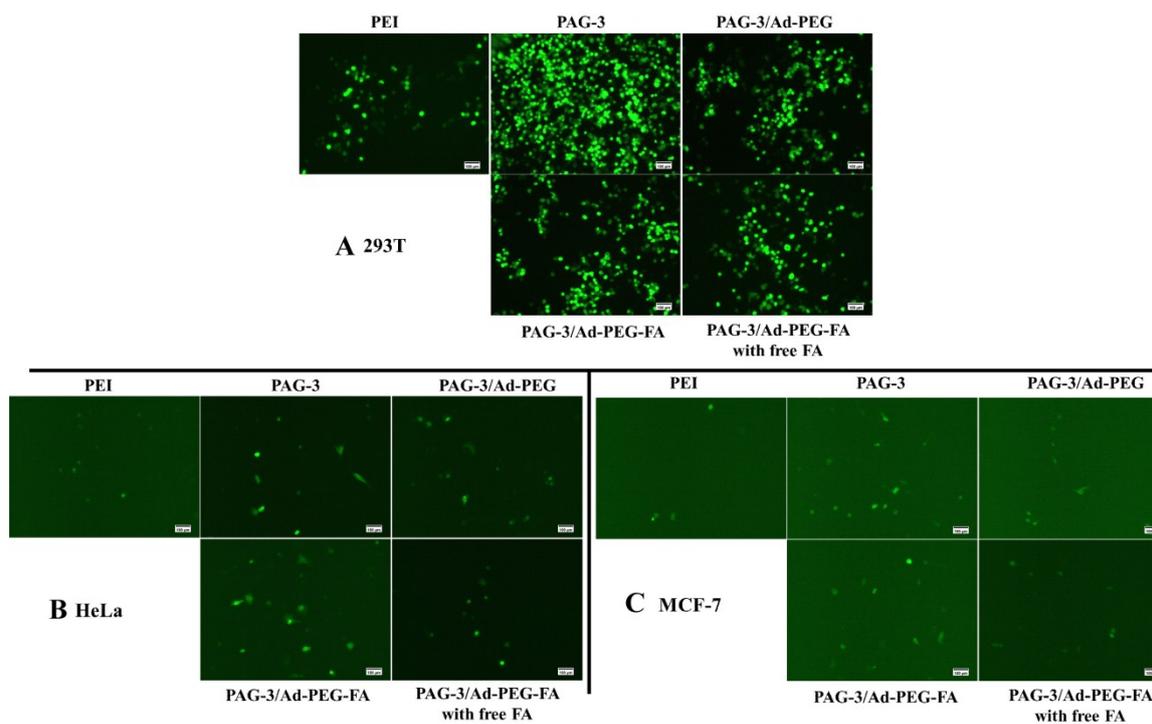
**Fig. S2** (A) Typical  $^1\text{H}$  NMR spectra of PCD-acetal-BIB (a1) before and (a2) after incubated in pH 5 cosolvent mixture of  $\text{DMSO-d}_6$  and  $\text{D}_2\text{O}$  containing trace amounts of  $\text{DCI}$  and (B) SEC-RI traces of PAG-3 before (red line) and after (blue line) incubated in pH 5.0 acetate buffer solution.



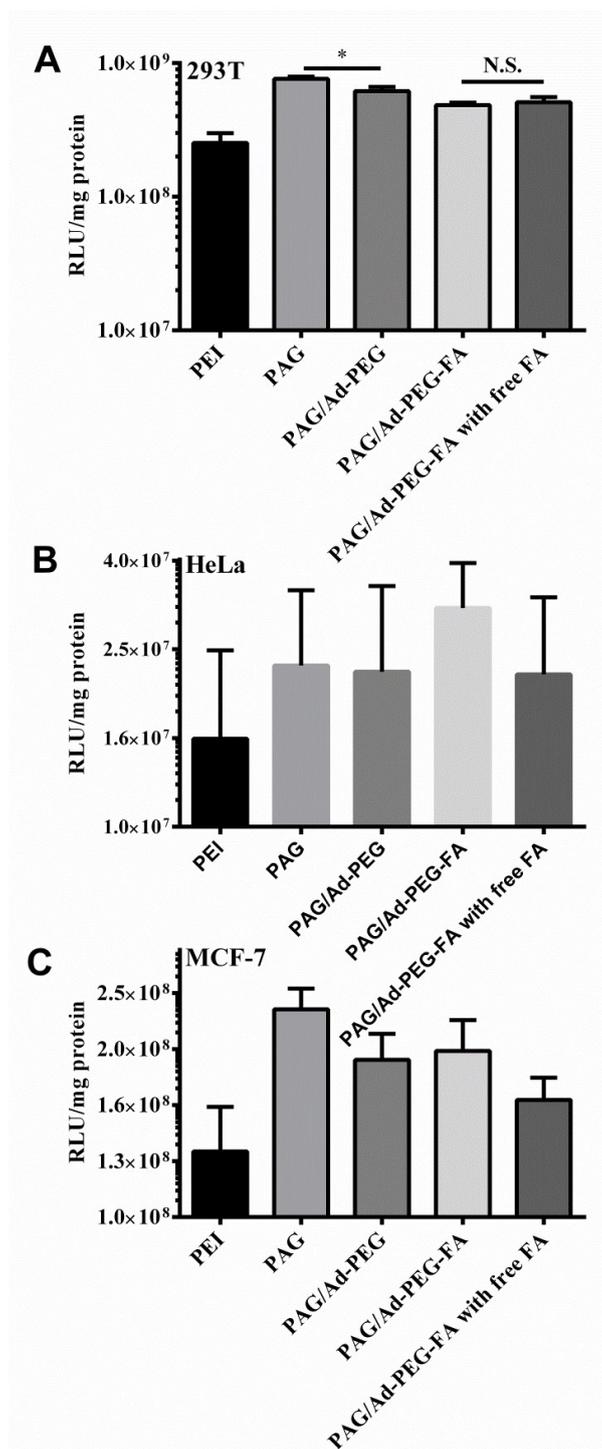
**Fig. S3** The photos of EGFP expression mediated by PAG/pDNA polyplexes prepared using different weight ratios ranging from 5 to 30 in 293T (A), HeLa (B) and MCF-7 (C) cell lines. 25 kDa PEI at N/P ratio of 10 was used as control. The scale bar is 100  $\mu\text{m}$ .



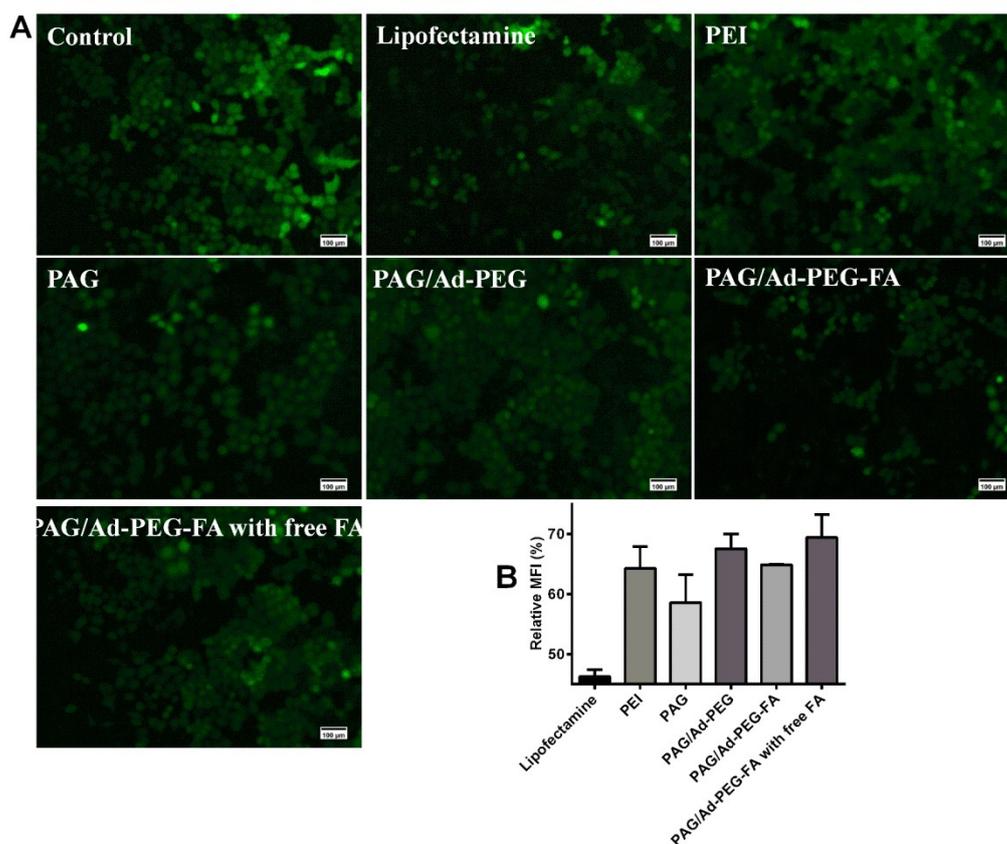
**Fig. S4** Confocal laser scanning images (A) and the quantification of flow cytometry (B: percentage and C: mean fluorescent intensity (MFI) of TOTO-3 positive cells) of FR positive MCF-7 cells after being incubated with polyplexes prepared with the TOTO-3-stained plasmid DNA (red) for 4 h in the medium without or with free folate (1 mM). The nuclei was stained by Hoechst 33342 (blue) and the cell membrane was stained by wheat germ agglutinin 488 (WGA-488, green) (\* $p < 0.05$ , student's t-tests). The scale bar is 20  $\mu\text{m}$ .



**Fig. S5** Image of EGFP expression of PAG-3, PAG-3/Ad-PEG-OH, and PAG-3/Ad-PEG-FA based polyplexes at the w/w ratio of 20 in 293T (A, low expression of folate receptors), HeLa (B, high expression of folate receptors) and MCF-7 (C, high expression of folate receptors) cells. The scale bar is 100  $\mu\text{m}$ .



**Fig. S6** Quantification of luciferase transfection activity of PAG-3, PAG-3/Ad-PEG-OH, and PAG-3/Ad-PEG-FA based polyplexes at the w/w ratio of 20 in 293T (low expression of folate receptors), HeLa (high expression of folate receptors) and MCF-7 (high expression of folate receptors) cell lines (\* $p < 0.05$ , N.S., not significant, student's t-tests). Data are shown as mean  $\pm$  SD ( $n = 3$ ).



**Fig. S7** siRNA transfection efficiency of supramolecular polyplexes. EGFP fluorescence images (A) of the HeLa\_EGFP cells treated with PAG-3/siRNA based polyplexes prepared at the w/w ratio of 20. The scale bar is 100 µm. Relative mean EGFP fluorescence intensity (B) of the HeLa cells treated with PAG-3/siRNA based polyplexes determined by flow cytometry.