Electronic Supplementary Information (ESI)

Tailored polyethylene glycol grafting on porous nanoparticles for enhanced targeting and intracellular siRNA delivery

Jounghyun Yoo,‡[a] Kyunghwan Kim,‡[b] Suhyun Kim,[a] Hee Ho Park,*[c] Heungsoo Shin,*[c] and Jinmyoung Joo*[a]

[a] Department of Biomedical Engineering, Ulsan National Institute of Science and Technology, Ulsan 44919, Republic of Korea. E-mail: jjoo@unist.ac.kr

[b] Department of Chemistry, Ulsan National Institute of Science and Technology, Ulsan 44919, Republic of Korea

[c] Department of Bioengineering, Hanyang University, Seoul 04763, Republic of Korea. E-mail: hshin@hanyang.ac.kr, parkhh@hanyang.ac.kr

‡ These authors contributed equally to this work.

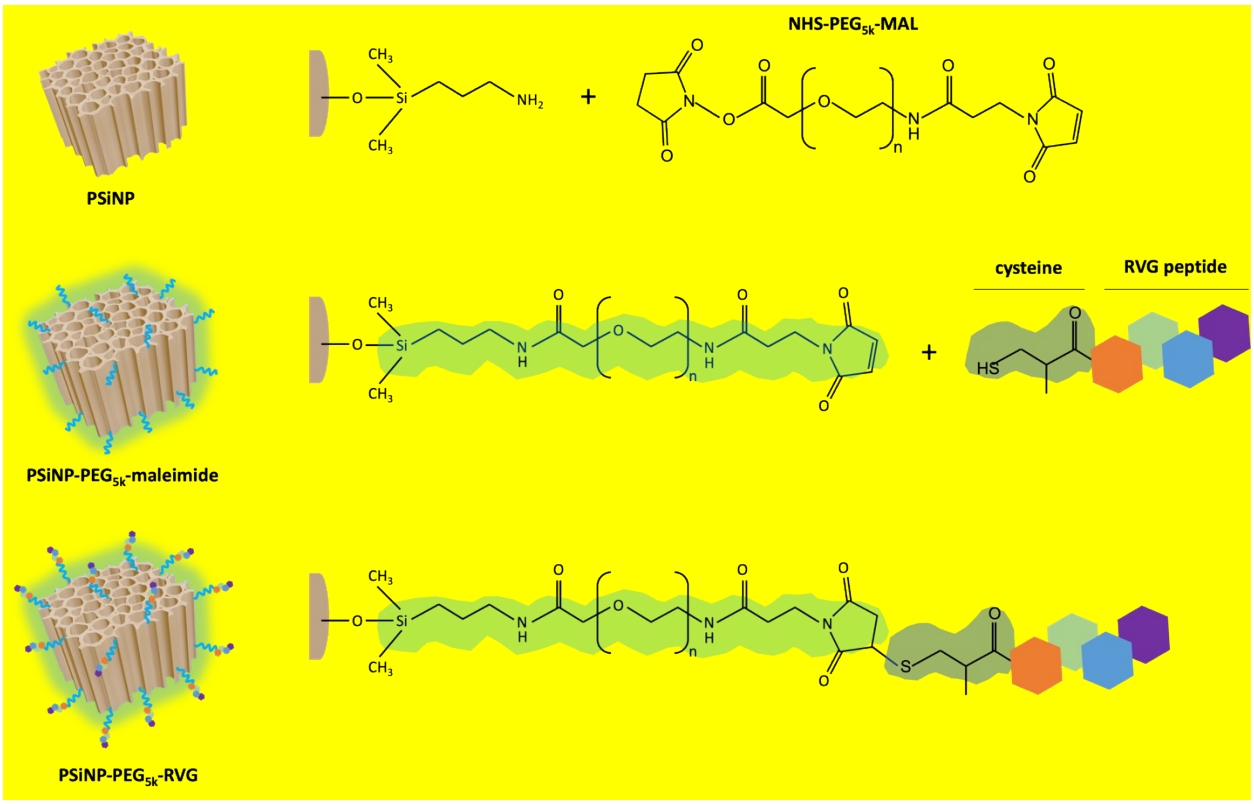

Figure S1. Schematic illustrations of RVG peptide conjugation on the PSiNPs.

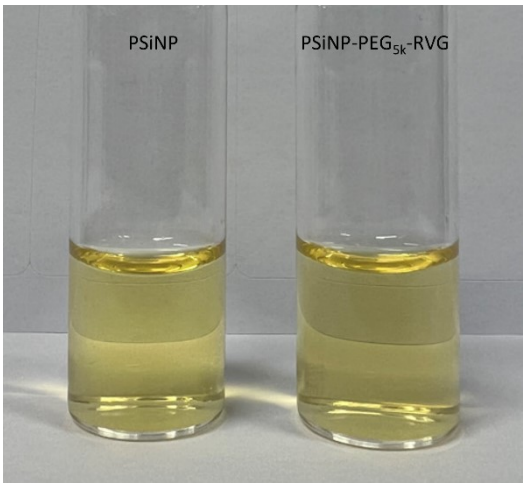

Figure S2. Photographs of aqueous PSiNPs before and after RVG peptide conjugation.

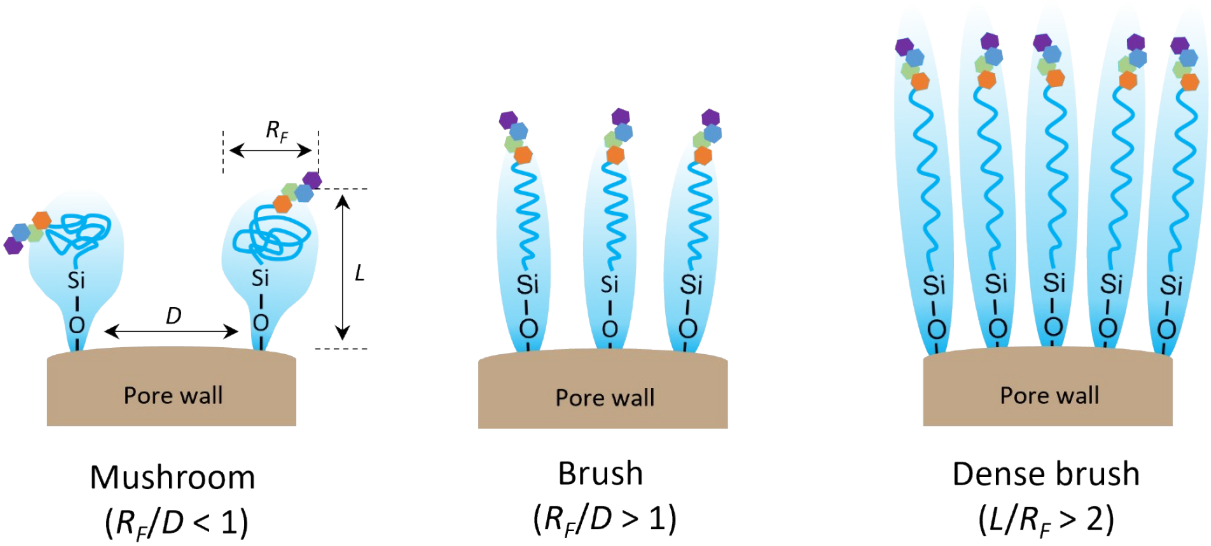

Figure S3. Schematic illustrations of PEG conformation depending on the grafting density.

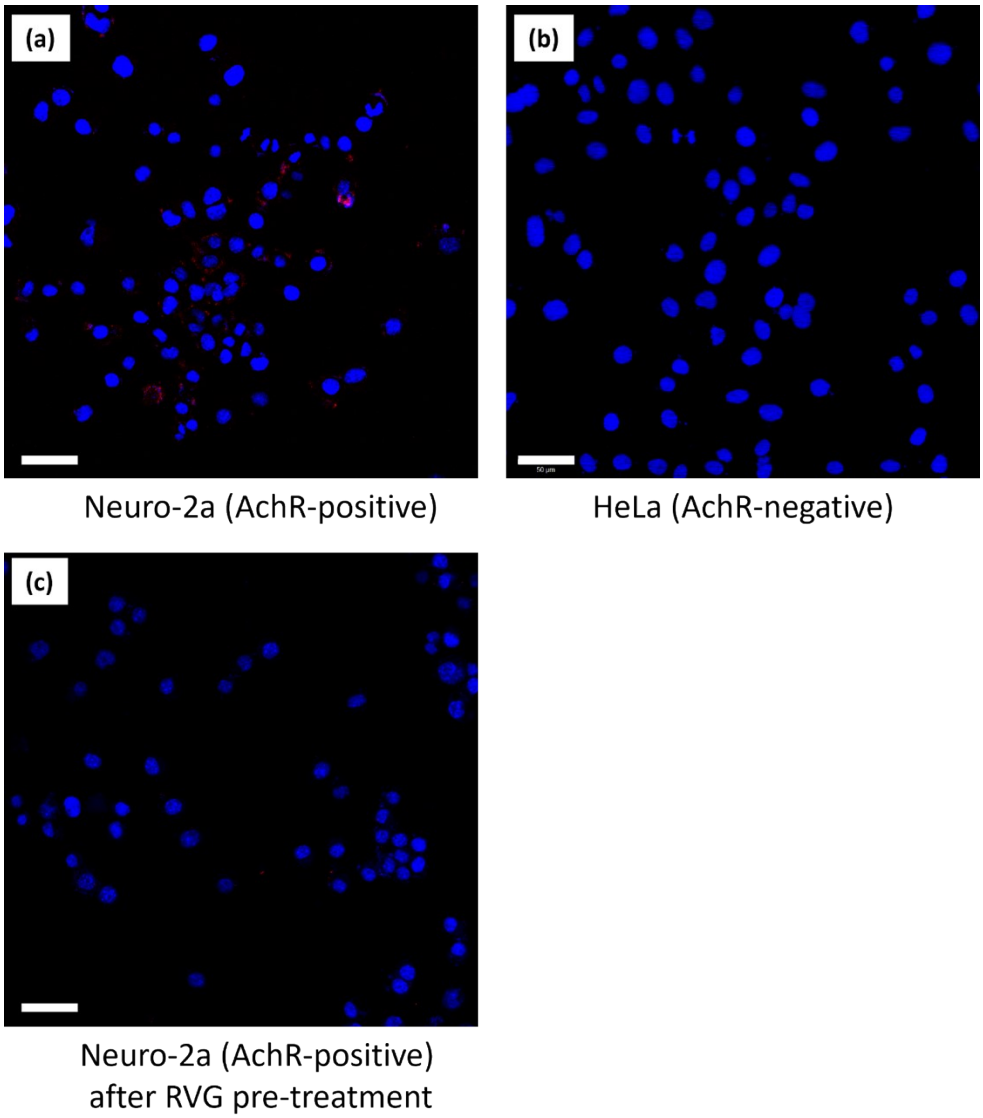

Figure S4. Confocal laser scanning microscopy images. (a) Neuro-2a and (b) HeLa cells treated with PSiNP-PEG_{5k}-RVG for 2 h. (c) Neuro-2a cells treated with free RVG peptide prior to incubation with PSiNPs-PEG_{5k}-RVG. Scale bar: 50 μm.

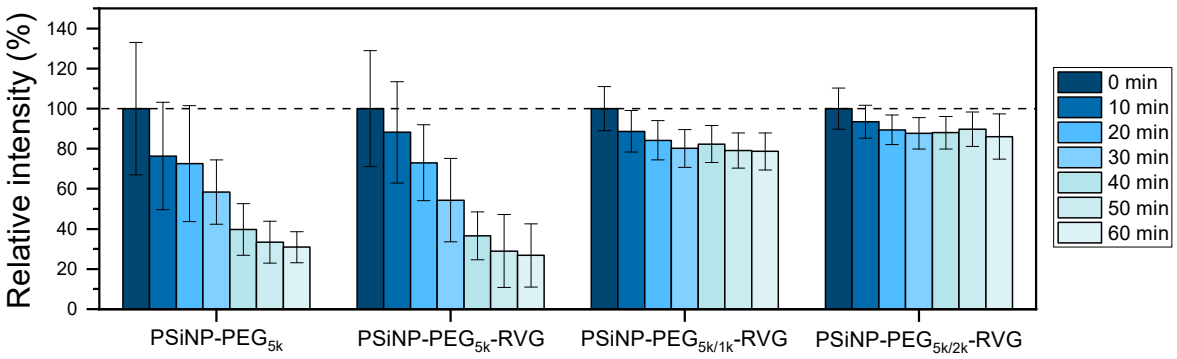

Figure S5. Reduced cellular uptake of PSiNPs upon pre-incubation in serum-containing culture media prior to cellular exposure. Relative photoluminescence intensity (± standard deviation) of PSiNPs found in a cell (n = 50) after pre-incubation in serum-rich cell culture media for designated time as indicated.

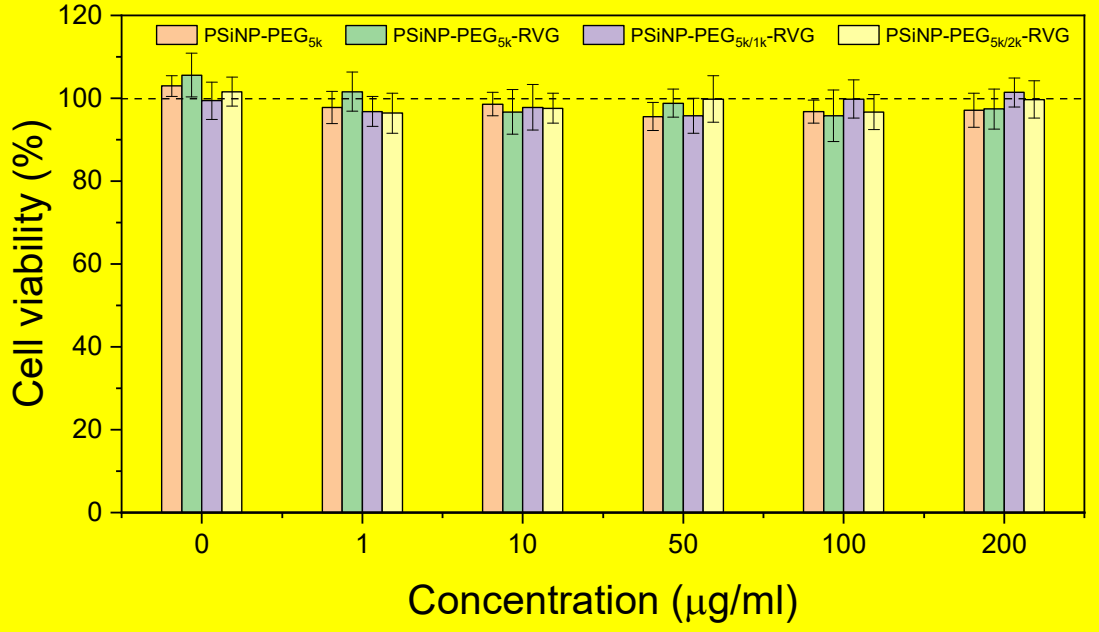

Figure S6. *In vitro* concentration-dependent cell viability towards Neuro-2a cells upon treatment for 24 h with PSiNPs containing PEG chains as indicated.

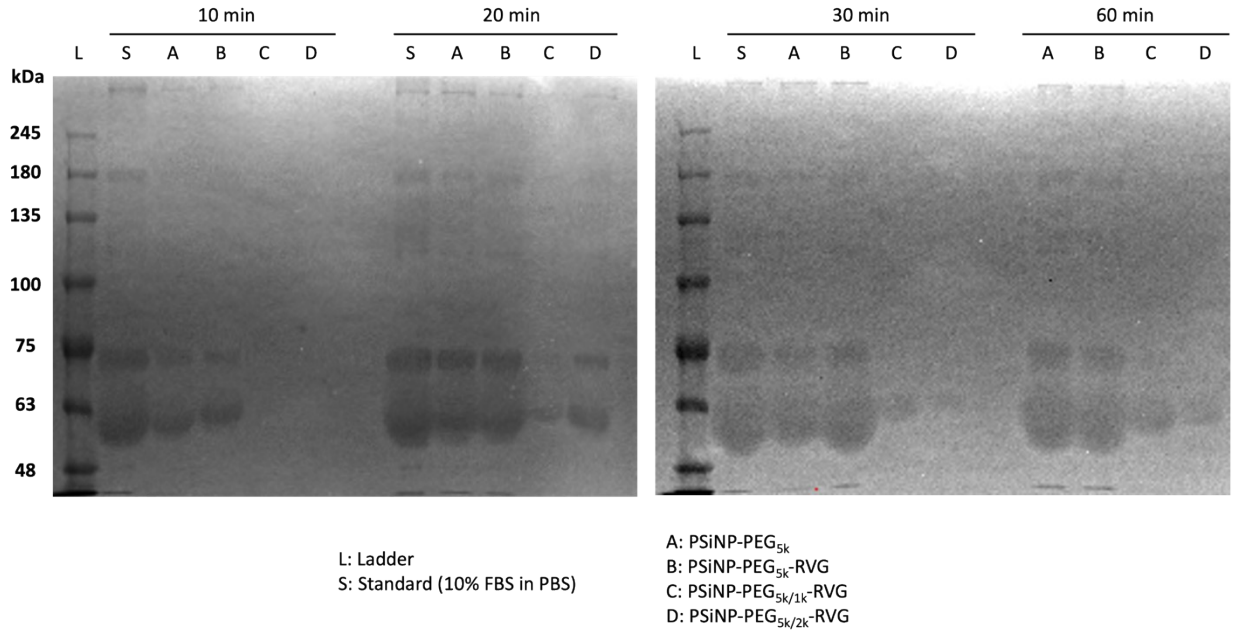

Figure S7. SDS-PAGE analysis of proteins adsorbed to the PSiNPs depending on surface PEG grafting types and pre-exposure time as indicated. Although the serum proteins were non-specifically adsorbed to all types of PSiNPs, the secondary packaging leads less protein binding. Note that PSiNP-PEG_{5k} and PSiNP-PEG_{5k}-RVG also slightly reduce the protein binding, indicating that the secondary packaging is essential for efficient prevention of non-specific protein adsorption on mesoporous nanoparticles such as PSiNPs.

Table S1. Conformational factors that determine the PEG types on PSiNPs.

PSiNP formulations	Primary grafting PEG	Secondary packaging PEG		L (nm)[b]	D (nm)[c]	R_F/D[d]	L/R_F[d]	PEG conformation
	Molecular weight (kDa)	Molecular weight (kDa)	R_F (nm)[a]					
PSiNPs-$PEG_{5k/1k}$-RVG	5	1	1.78	9.5	2.70	2.13	1.66	Brush
PSiNPs-$PEG_{5k/2k}$-RVG		2	3.10	17.0	1.13	5.09	2.96	Dense brush
PSiNPs-$PEG_{5k/3.4k}$-RVG		3.4	4.48	10.5	2.33	2.47	1.83	Brush
PSiNPs-PEG_{5k}-RVG		-	5.74	4.5	8.29	0.69	0.78	Mushroom

[a] Flory radius (R_F) is determined by the equation: $R_F = \alpha N^{3/5}$, where α is the monomer length (0.35 nm for PEG) and N is the number of PEG repeating unit.

[b] PEG layer thickness (L) is estimated from hydrodynamic radius and size of RVG peptide.

[c] Grafting distance (D) is obtained by the equation: $D = \left(\frac{N}{L}(\alpha^{5/3})\right)^{3/2}$, where α is the monomer length (0.35 nm for PEG), N is the number of PEG repeating unit, and L is the PEG layer thickness.

[d] R_F value of PEG 5 kDa is used since the major PEG chains for conformational transition induced by secondary packaging is PEG 5 kDa.