Supporting Information

Analysis of carbohydrate-carbohydrate interactions using sugar-functionalized silicon nanoparticles for cell imaging

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Synthesis and characterization of COOH@SiNPs

Alkenyl-terminated silicon nanoparticles

Anhydrous octane (300 mL) was added into 500 mL flask with Mg_2Si (1.0 g, 7.8 mmol). Then, Br_2 (3.2 mL, 62 mmol) was added slowly, stirred at room temperature for 2 h and the reaction was refluxing for 72 h. After cooling down to room temperature, octane was removed by vacuum and new 100 mL dried THF was added. To the solution, 3-butenylmagnesium bromide (0.5 M, 100 mL, 50 mmol) was added slowly and stirred at room temperature overnight. It was quenched with $NH_4Cl_{(aq)}$, washed twice with 2M $HCl_{(aq)}$ and washed with DI water until neutral pH was reached. The organic layers were collected and dried with $MgSO_4$. Finally, the nanoparticles were purified by size exclusion chromatography (biobeads S-X1) to obtain a yellow wax.

Carboxylic acid terminated silicon nanoparticles (COOH@SiNPs)

$NaIO_4$ (877 mg, 4.1 mmol) was dissolved in a mixture of CH_3CN : ethyl acetate : H_2O = 6:6:9 mL. Alkenyl-terminated silicon nanoparticles and $RuCl_3$ (5 mg, 0.02 mmol) were subsequently added. The solution was stirred at room temperature for 4 h. Ethyl acetate was subsequently added and washed with deionized water twice. All organic layers were collected and dried with $MgSO_4$. The final product was purified by size exclusion chromatography (LH-20) to obtain a yellow wax.

XPS measurement

X-ray Photoelectron Spectroscopy (XPS) measurements were performed using a Thermo Scientific K-Alpha X-ray Photoelectron Spectrometer using a monochromatic AlKα radiation (hv= 1486.6 eV). 200 eV analyzer pass energy and a 1 eV energy step size were used in survey scan measurements. Element scans were performed with a 50 eV analyzer pass energy and a 0.1 eV energy step size. All the obtained binding energies were referenced to carbon 1s peak at 284.8 eV. The samples were prepared on the gold thin film substrates.

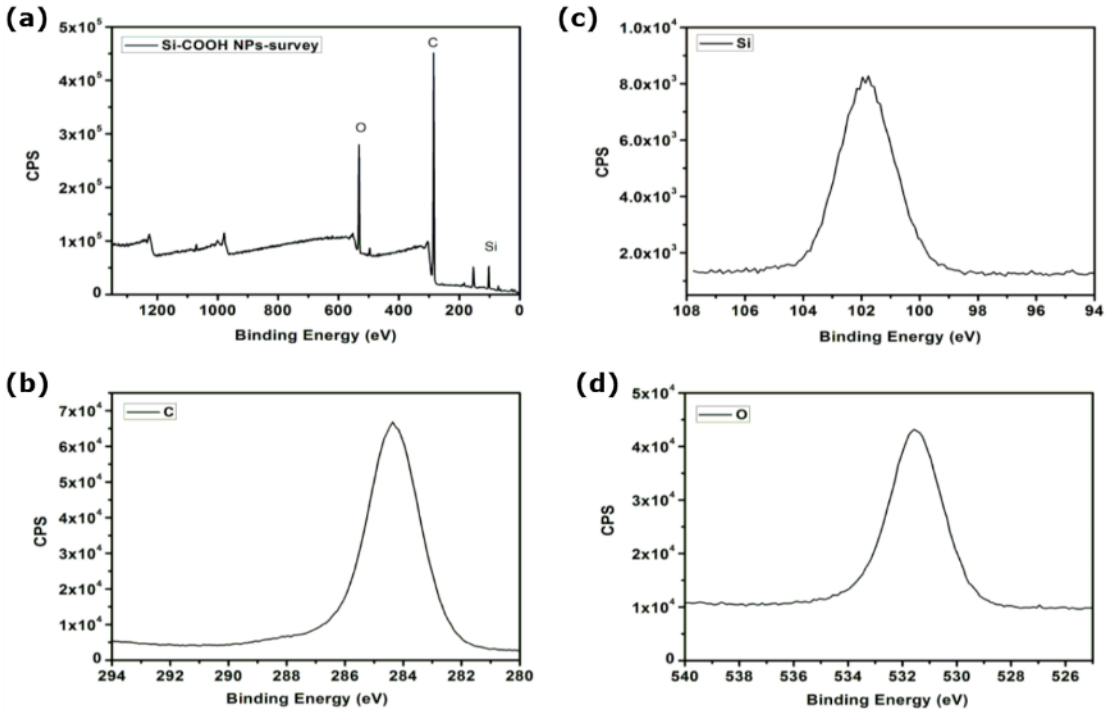


Figure S1. XPS data of **COOH@SiNP**s. (a) Survey scan of **COOH@SiNP**s. (b), (c), (d) Si, C, O elemental scan of **COOH@SiNP**s.

Table S1. XPS data of **COOH@SiNP**s

Element	Peak BE	FWHM eV	Area (P) CPS.eV	Atomic %
C1s	284.80	2.88	1220912	75.66
O1s	531.95	3.02	624249	16.01
Si2p	102.09	1.87	135063.3	8.33

Molecular weight determination of COOH@SiNPs by analytical ultracentrifugation (AUC)

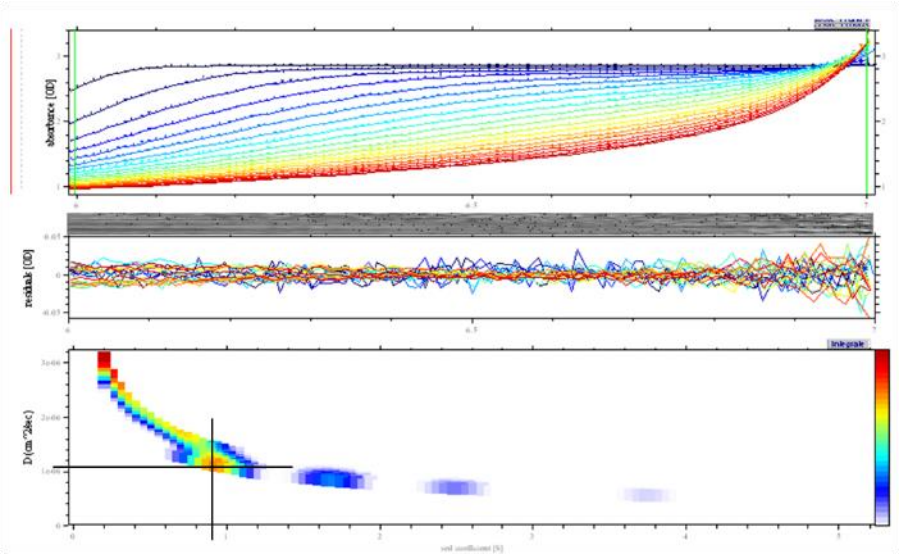


Figure S2. Analytical ultracentrifugation data.

$$\rho_p = \rho_s + 18\eta_s s\left(\frac{1}{D}\frac{k_b T}{3\pi\eta_s}\right)^{-2}$$

$$M = \frac{sRT}{D}\left(1-\frac{\rho_s}{\rho_p}\right)^{-1}$$

$$d_p = \sqrt{\frac{18\eta_s s}{(\rho_p - \rho_s)}}$$

AUC measurements were performed in an Optima Max-E centrifuge (Beckman-Coulter) equipped with a ML-80 fixed angle rotor. The sample was dispersed into EtOH and spun (45000 rmp) at 20 °C for 18–20 h. The hydrodynamic Stokes' diameter was obtained from the Svedberg equation and the Stoke-Einstein relation, giving the well-known expression for Stoke-equivalent spherical diameters in AUC[1] which is shown above. ρ_P: particle density, ρ_s: solvent density, η_S: the viscosity of the liquid, M: molecular weight, d_P: diameter of NPs, k_b: Boltzmann's constant, T: temperature, D: diffusion coefficient, S: sedimentation coefficient.

In the most intense point (cross line), the diffusion coefficient and sedimentation coefficient were $1.1\text{x}10^{-10}$ m^2 sec^{-1} and S = 0.9, respectively. The size of the **COOH@SiNPs** was calculated using the above equation resulting in a diameter of 3.25 nm, a molecular weight of 10546 Dalton, and a density of 973 kg m^{-3}.

Determination of carboxylic acid content on COOH@SiNPs

The amount of carboxylic acid group can be quantified by acid-base titration. The NaOH aqueous solution (5 x 10^{-3} M) was added dropwise to the **COOH@SiNP**s (20.0 mg) solution and then the pH change was monitored till the end point of titration. The equivalent point was calculated from the second derivative of the titration curve corresponding to 5.0 mL (Figure S3). Thus, the amount of carboxylic acid groups was 1.17 µmol per 1 mg SiNPs. Based on the particle size and molecular weight determined by AUC measurement, 15 carboxylic acid groups were present on one single **COOH@SiNP**.

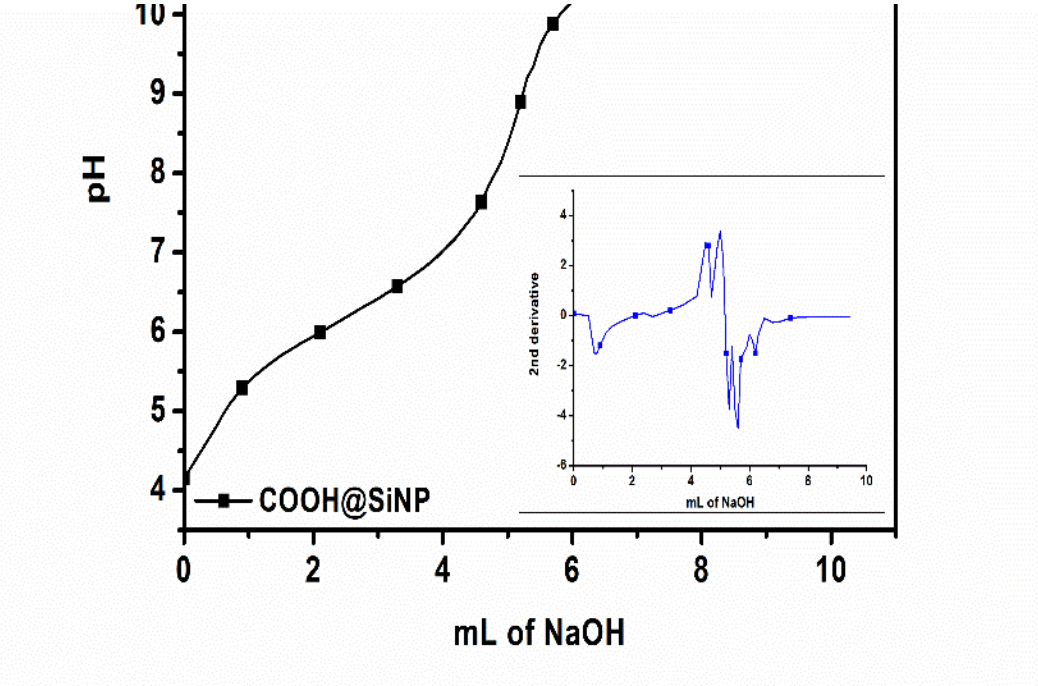


Figure S3. The acid-base titration curve of **COOH@SiNP**s.

Synthesis and characterization of sugar-dye@SiNPs

Synthesis of COOH-dye@SiNPs

To a solution of **COOH@SiNP**s (30.0 mg, corresponding to 35.1 µmol carboxylic acid groups) in DMF (1.0 mL), dye-ATTO647-NH_2 stock solution (586 µL of 1.25 mM, 0.73 µmol, ATTO-TEC) was added under Ar. EDC (13.5 mg, 70.2 µmol), HOBT (10.8 mg, 70.2 µmol) and NEt_3 (10 µL, 71.7 µmol) were then added to the reaction mixture in the dark under Ar and at room temperature for 24 h. When the reaction was completed, the DMF was evaporated. The residues of nanoparticles were dissolved in ethyl acetate (EtOAc) and were extracted with 1N HCl. The organic layer was collected and then evaporated *in vacuo* to yield **COOH-dye@SiNP** (25 mg).

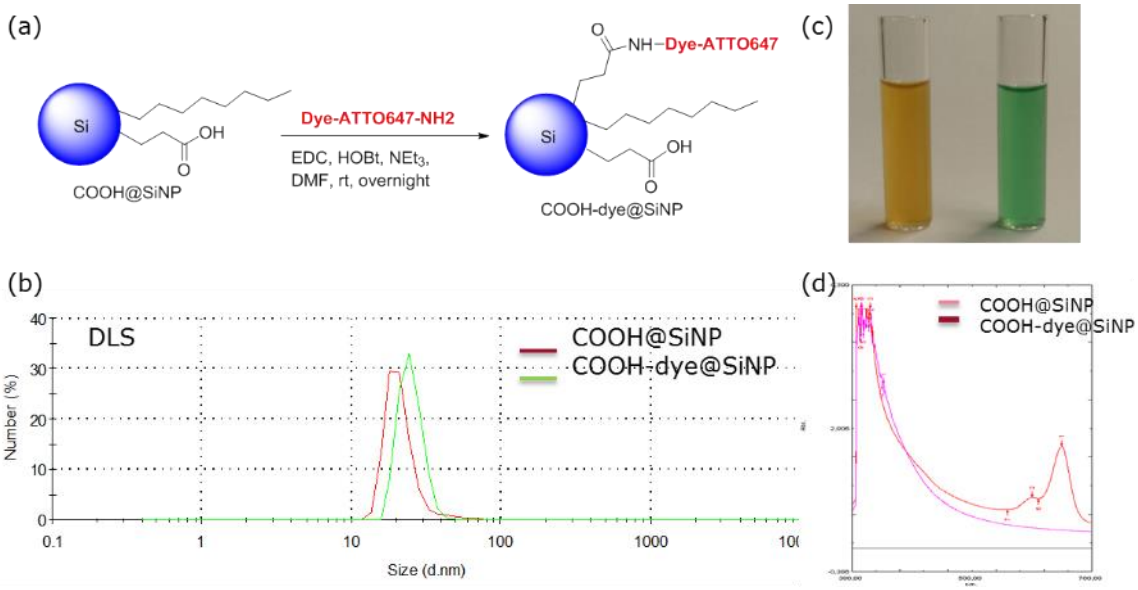


Figure S4. (a) Synthetic scheme of the preparation of **COOH-dye@SiNP**s; (b) dynamic light scattering (DLS) spectrum of **COOH@SiNP**s and **COOH-dye@SiNP**s in methanol; (c) a representative photograph of **COOH@SiNP**s (left) and **COOH-dye@SiNP**s (right) in DMF; (d) the UV absorption spectrum of **COOH@SiNP**s and **COOH-dye@SiNP**s in DMF.

Proton NMR spectra of amino sugar ligands: Glc 1, Lac 2 and Gg3 3.

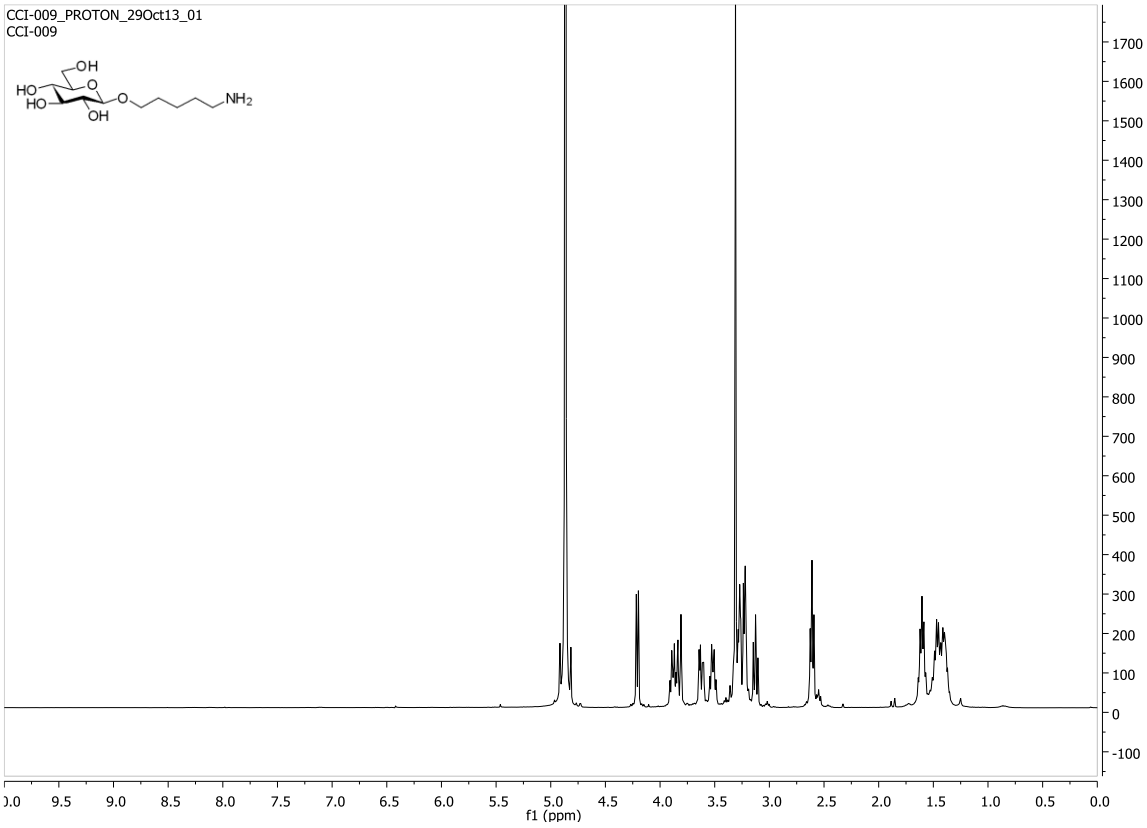


Figure S5. NMR spectrum of amino Glc-ligand **1**.

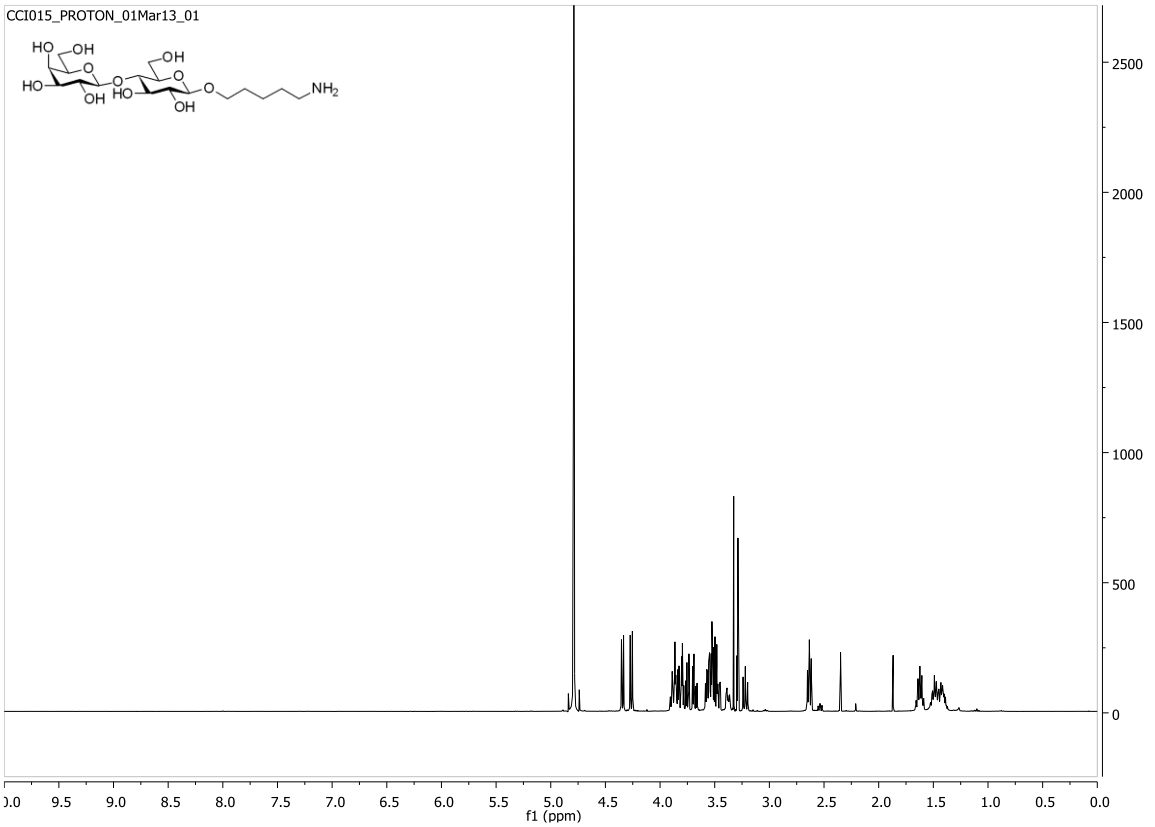


Figure S6. NMR spectrum of amino Lac-ligand **2**.

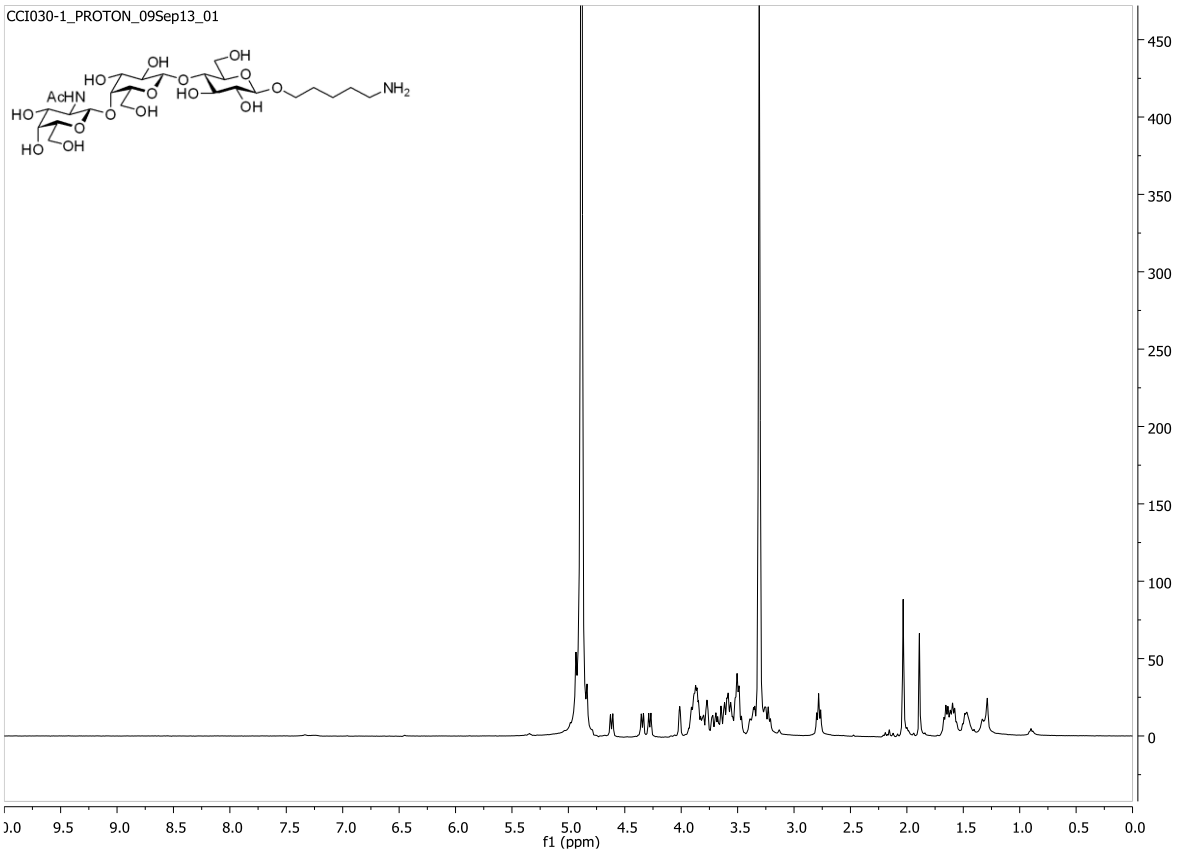


Figure S7. NMR spectrum of amino Gg3-ligand **3**.

Synthesis of Glc-dye@SiNPs, Lac-dye@SiNPs and Gg3-dye@SiNPs.

To a serious solution of **COOH-dye@SiNP**s (5.0 mg) in dried DMF (1.5 mL), amino carbohydrate ligands Glc **1**, Lac **2** and Gg3 **3** (0.58 mL of stock 10 mM solution, 5.85 µmol) were added under Ar, respectively. EDC (2.3 mg, 11.7 µmol), HOBT (1.8 mg, 11.7 µmol) and Et_3N (10 µL, 71.7 µmol) were added to each reaction mixture and stirred at room temperature for 48 h in the dark under Ar. After 48 h, ethanolamine (10 µL, 165.0 µmol) was added to each reaction mixture for capping the unreacted carboxyl acid group for another 18 h in the dark under Ar. After the reaction, DMF was removed by *vacuum* and all three samples were purified by size exclusion chromatography (LH-20) and dialyzed with Float-A-Lyzer G2 (in size of 0.5 kD to 1.0 kD) to get **Glc-dye@SiNP**s, **Lac-dye@SiNP**s and **Gg3-dye@SiNP**s, respectively.

Dynamic light scattering (DLS) and surface charge determination (zeta-potential) measurements

Dynamic light scattering (DLS) for hydrodynamic diameter determination

DLS measurements were carried out at a scattering angle of 173° with a Malvern Zeta Nanosizer working at 4-mW He–Ne laser (633 nm). The **COOH@SiNP**s and **COOH-dye@SiNP**s were measured in methanol (Figure S4b) and sugar-dye@SiNP (**Glc-dye@SiNP**s, **Lac-dye@SiNP**s and **Gg3-dye@SiNP**s) were measured in PBS (Figure S8).

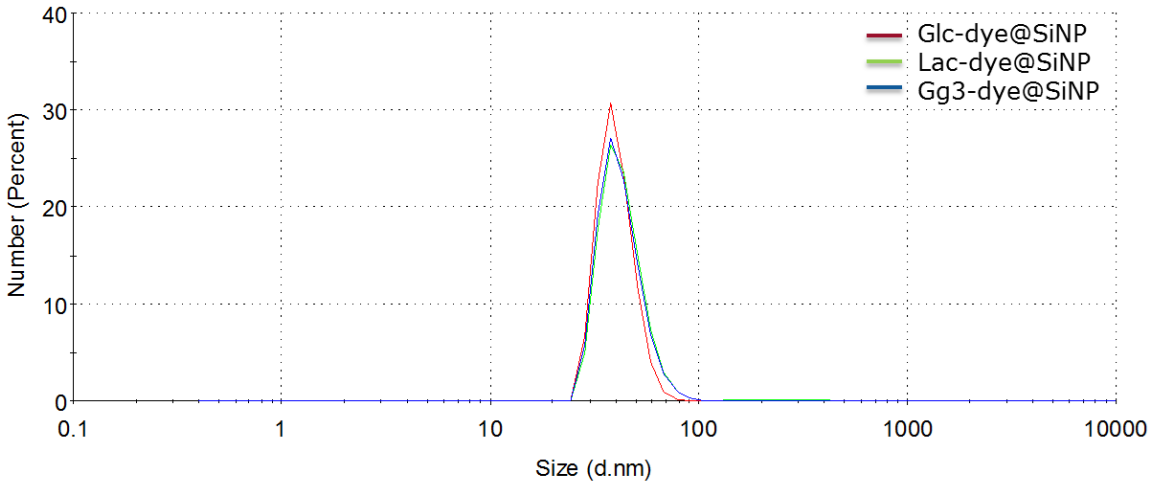


Figure S8. DLS hydrodynamic diameter spectrum of **sugar-dye@SiNP**s in double distilled-water.

Zeta potential

A Malvern Zetasizer instrument was used to measure the electrophoretic mobility of nanoparticles. The Helmholtz-Smoluchowski equation was used to correlate the measured electrophoretic mobilities to the zeta potentials. Three replicates of each sample were measured six times at 25°C in double distilled water (Figure 1b).

Infrared spectroscopy spectra

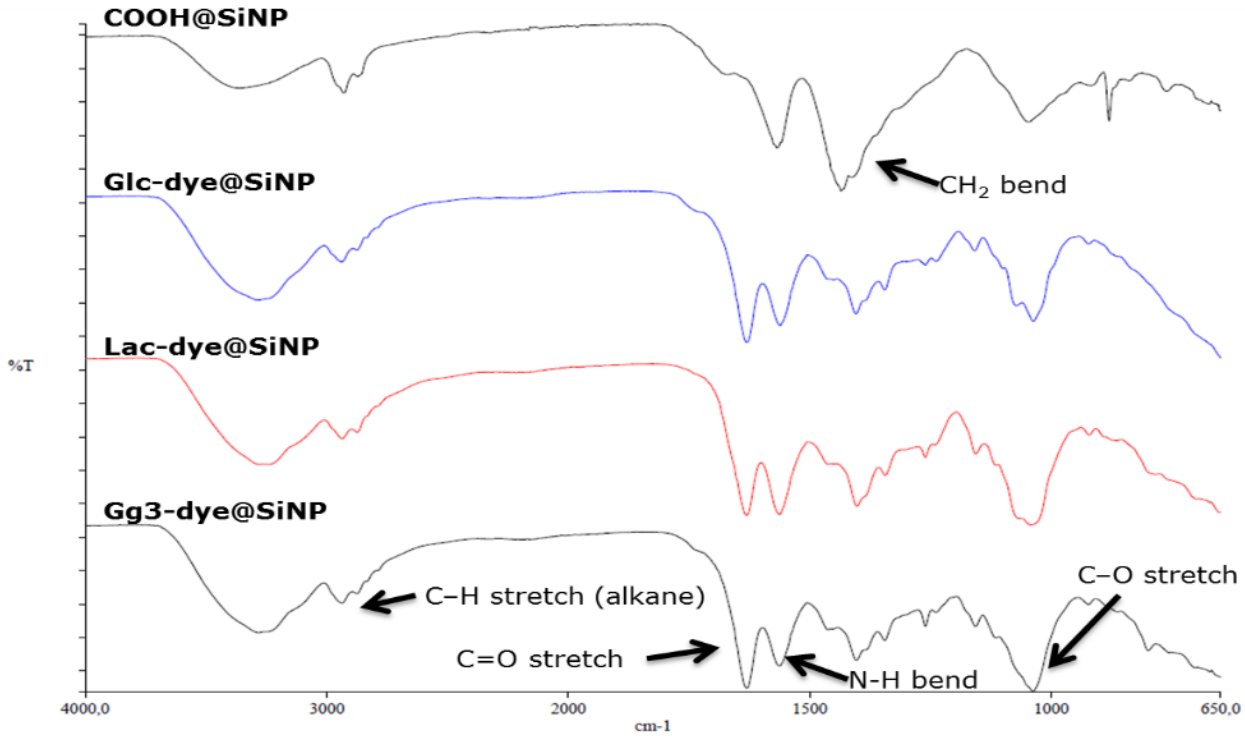


Figure S9. IR spectra of **sugar-dye@SiNP**s.

Proton- and carbon-NMR spectra of sugar-dye@SiNP and molecular weight estimation.

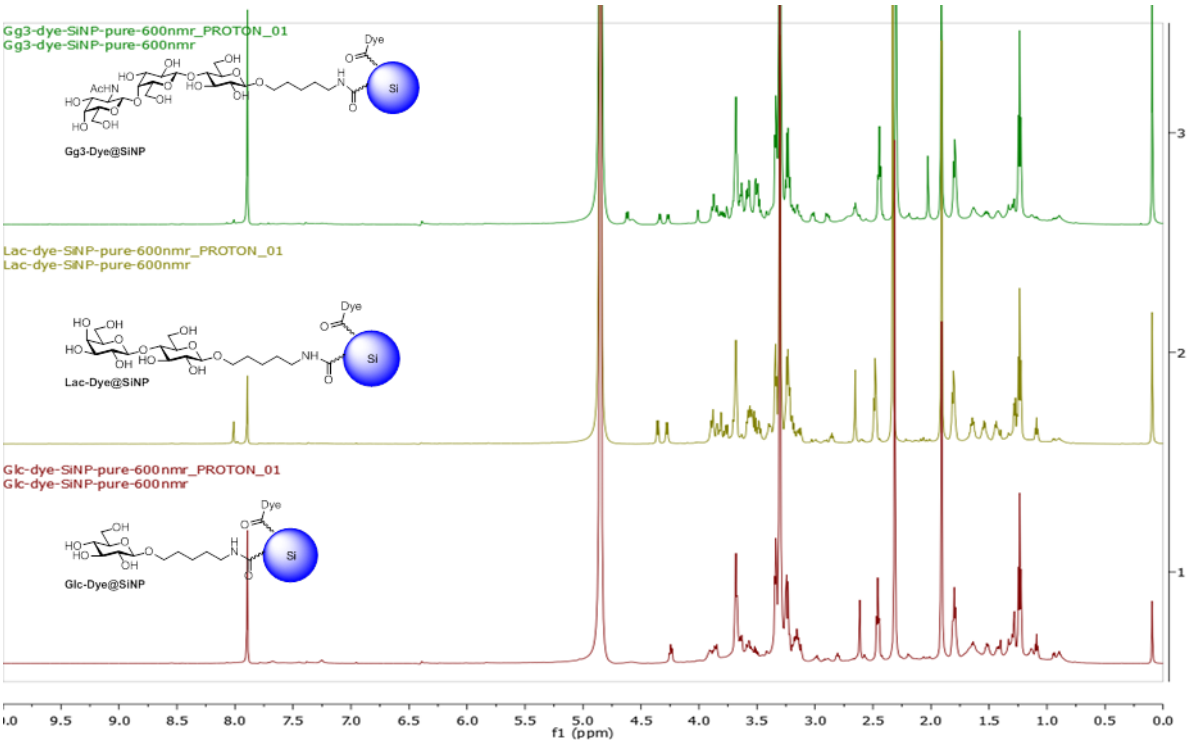
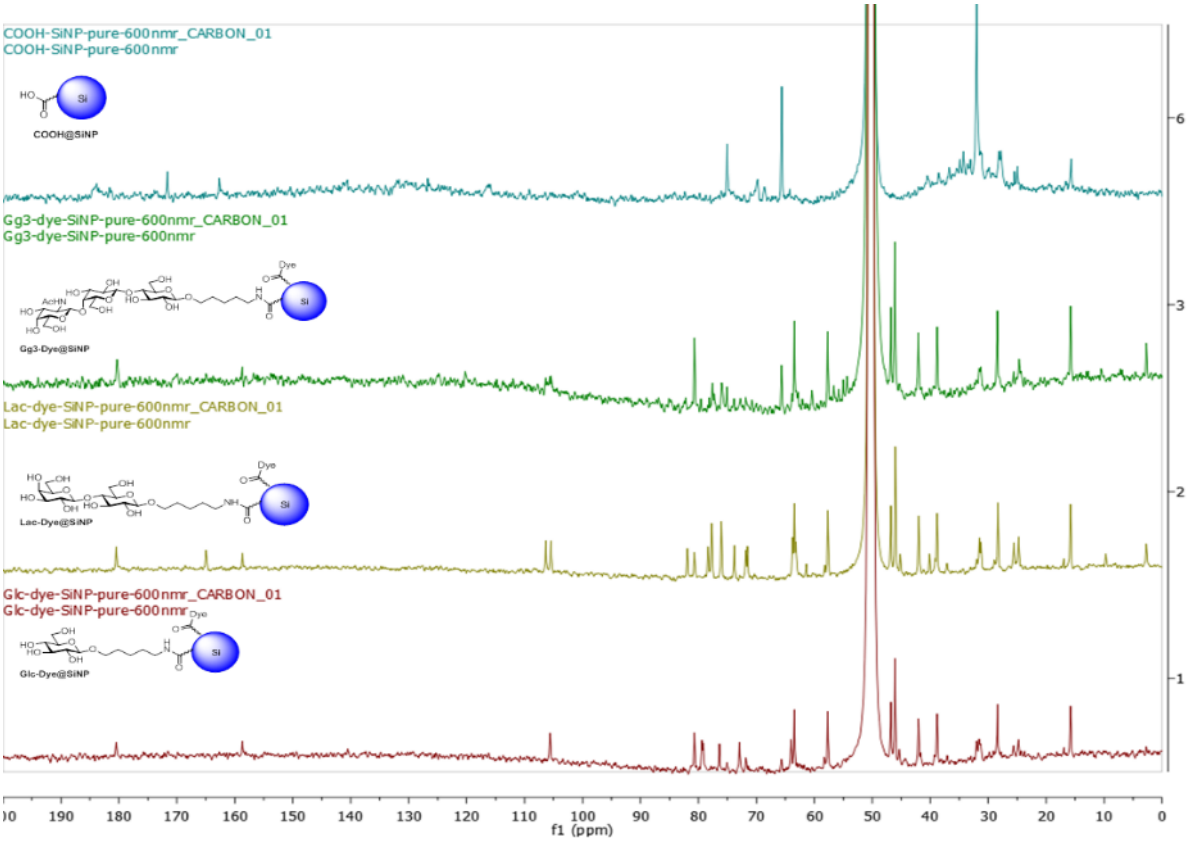


Figure S10. Proton-NMR of **sugar-dye@SiNP**s. In addition, $CHCl_3$ (6.5 μmol) was added to CD_3OD as internal standard for sugar quantification on **sugar-dye@SiNP**s.

Table S2. Sugar determination on the nanoparticles and its corresponding molecular weight calculation.

	Glc-dye@SiNP	**Lac-dye@SiNP**	**Gg3-dye@SiNP**
mg (in NMR tube)	3.00	5.50	2.00
$CHCl_3$ (intenal standard, 6.5 μmol)	1.00	1.00	1.00
NMR integral, H1 ratio	0.44	0.80	0.20
ligands umol in total	2.86	5.20	1.30
ligands umol per mg	0.95	0.95	0.65
coupling yield	81.5%	80.8%	55.6%
sugar per nanoparticle	12.2	12.1	8.3
molecular weight of each SiNP	13.7 kD	15.7 kD	15.7 kD

(a)


COOH-SiNP-pure-600nmr_CARBON_01
COOH-SiNP-pure-600nmr
COOH@SiNP
Gg3-dye-SiNP-pure-600nmr_CARBON_01
Gg3-dye-SiNP-pure-600nmr
Gg3-Dye@SiNP
Lac-dye-SiNP-pure-600nmr_CARBON_01
Lac-dye-SiNP-pure-600nmr
Lac-Dye@SiNP
Glc-dye-SiNP-pure-600nmr_CARBON_01
Glc-dye-SiNP-pure-600nmr
Glc-Dye@SiNP
f1 (ppm)

(b)

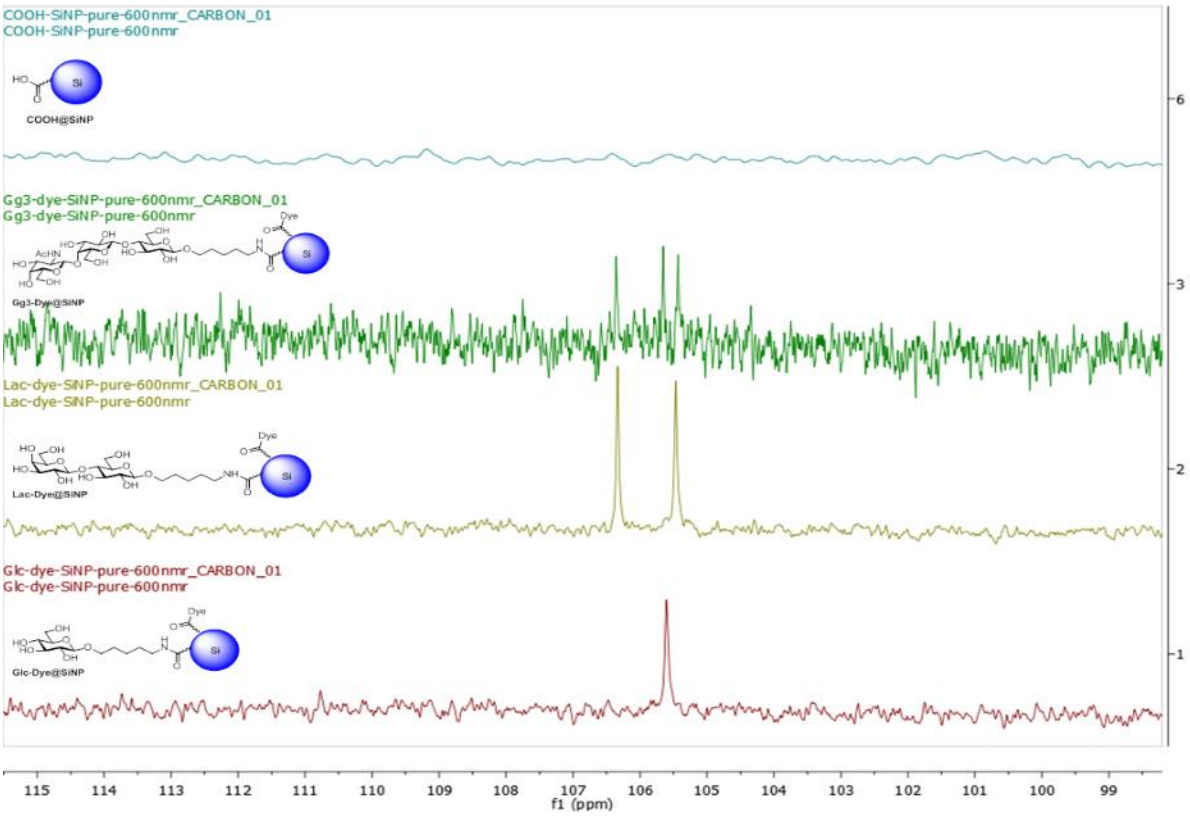

COOH-SiNP-pure-600nmr_CARBON_01
COOH-SiNP-pure-600nmr
COOH@SiNP
Gg3-dye-SiNP-pure-600nmr_CARBON_01
Gg3-dye-SiNP-pure-600nmr
Gg3-Dye@SiNP
Lac-dye-SiNP-pure-600nmr_CARBON_01
Lac-dye-SiNP-pure-600nmr
Lac-Dye@SiNP
Glc-dye-SiNP-pure-600nmr_CARBON_01
Glc-dye-SiNP-pure-600nmr
Glc-Dye@SiNP
f1 (ppm)

Figure S11. (a) Carbon NMR spectra of **sugar-dye@SiNP**s. (b) The enlarged carbon NMR spectra in the sugar anomeric carbon section.

Photoluminescence excitation spectrum of COOH-dye@SiNPs and sugar-dye@SiNPs.

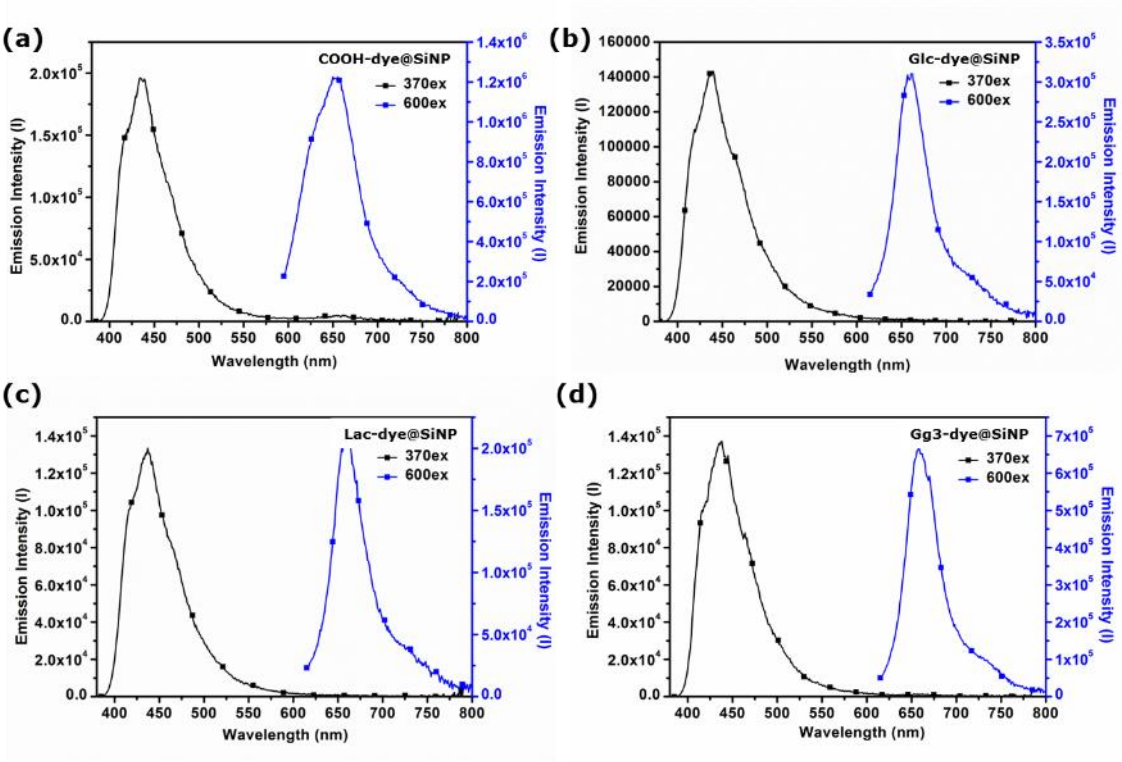


Figure S12. Emission spectra were excited at 370 and 600 nm.

XPS of COOH-dye@SiNPs and sugar-dye@SiNPs

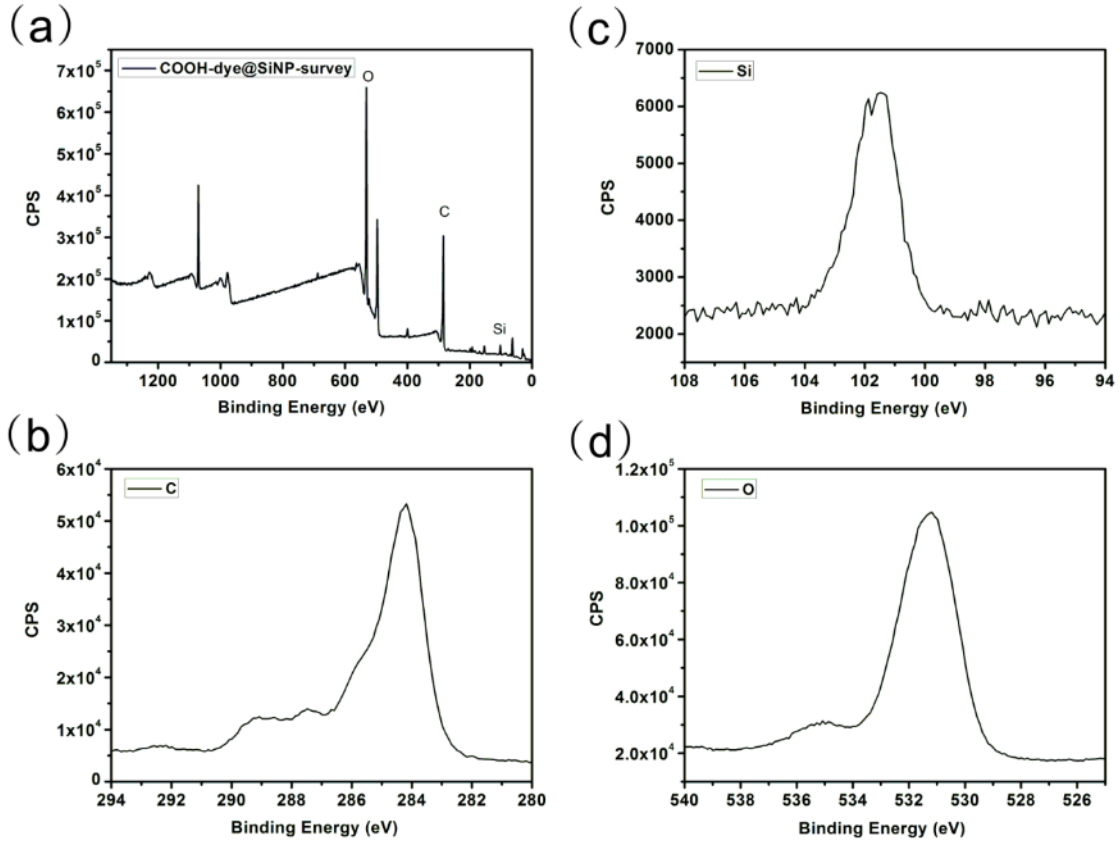


Figure S13. XPS data of **COOH-dye@SiNP**s. (a) survey scan of **COOH-dye@SiNP**s. (b), (c), (d) Si, C, O elemental scan of **COOH-dye@SiNP**s.

Table S3. XPS data of **COOH-dye@SiNP**s

Element	Peak BE	FWHM eV	Area (P) CPS.eV	Atomic %
C1s	284.80	3.04	912666.1	47.66
O1s	531.65	3.08	1661913	35.91
N1s	399.83	4.19	82390.6	2.77
Si2p	101.85	2.65	65753.01	3.42

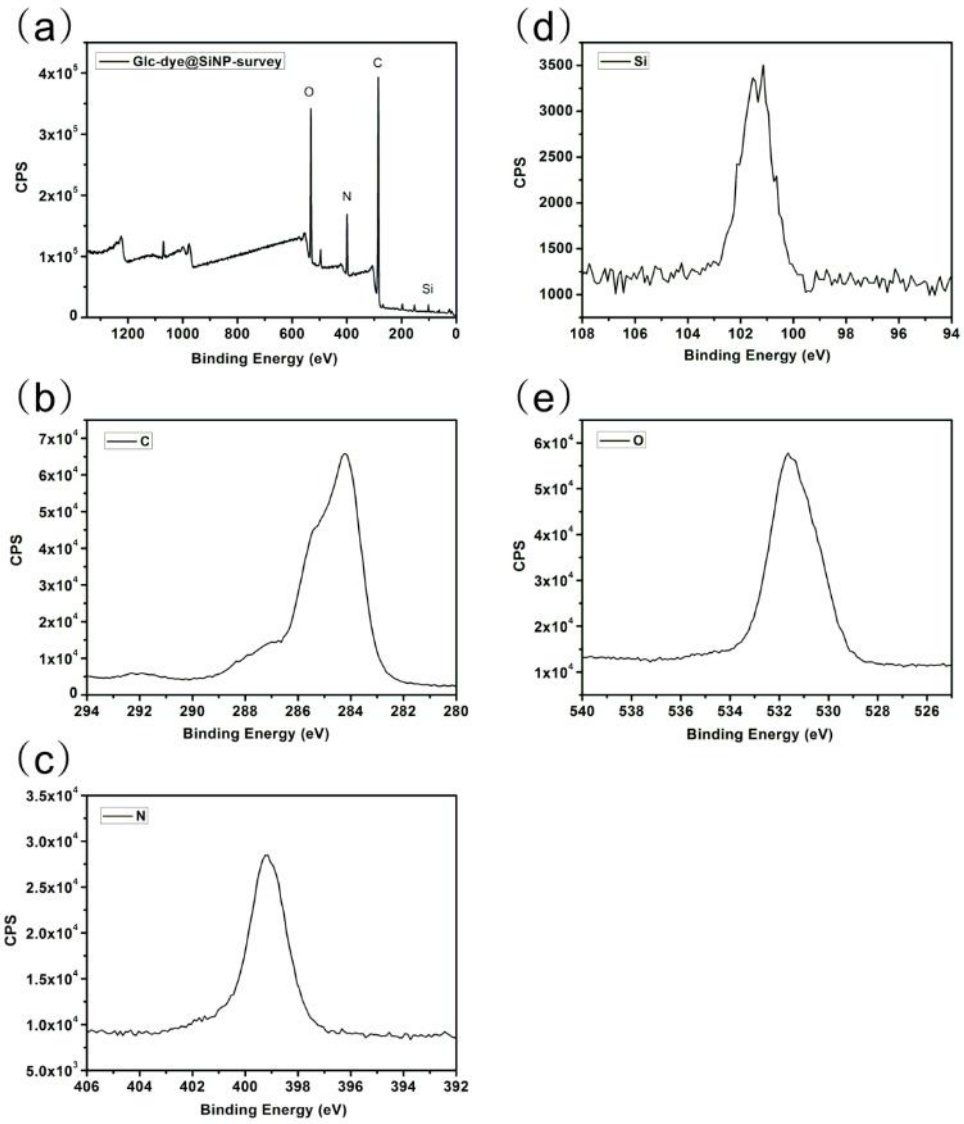


Figure S14. XPS data of **Glc-dye@SiNP**s. (a) survey scan of **Glc-dye@SiNP**s. (b), (c), (d), (e) Si, C, O, N elemental scan of **Glc-dye@SiNP**s.

Table S4. XPS data of **Glc-dye@SiNP**s.

Element	Peak BE	FWHM eV	Area (P) CPS.eV	Atomic %
C1s	284.80	3.09	1181356	66.82
O1s	531.50	3.06	813437.7	19.03
N1s	399.11	2.68	288407	10.51
Si2p	101.65	2.56	31820.55	1.79

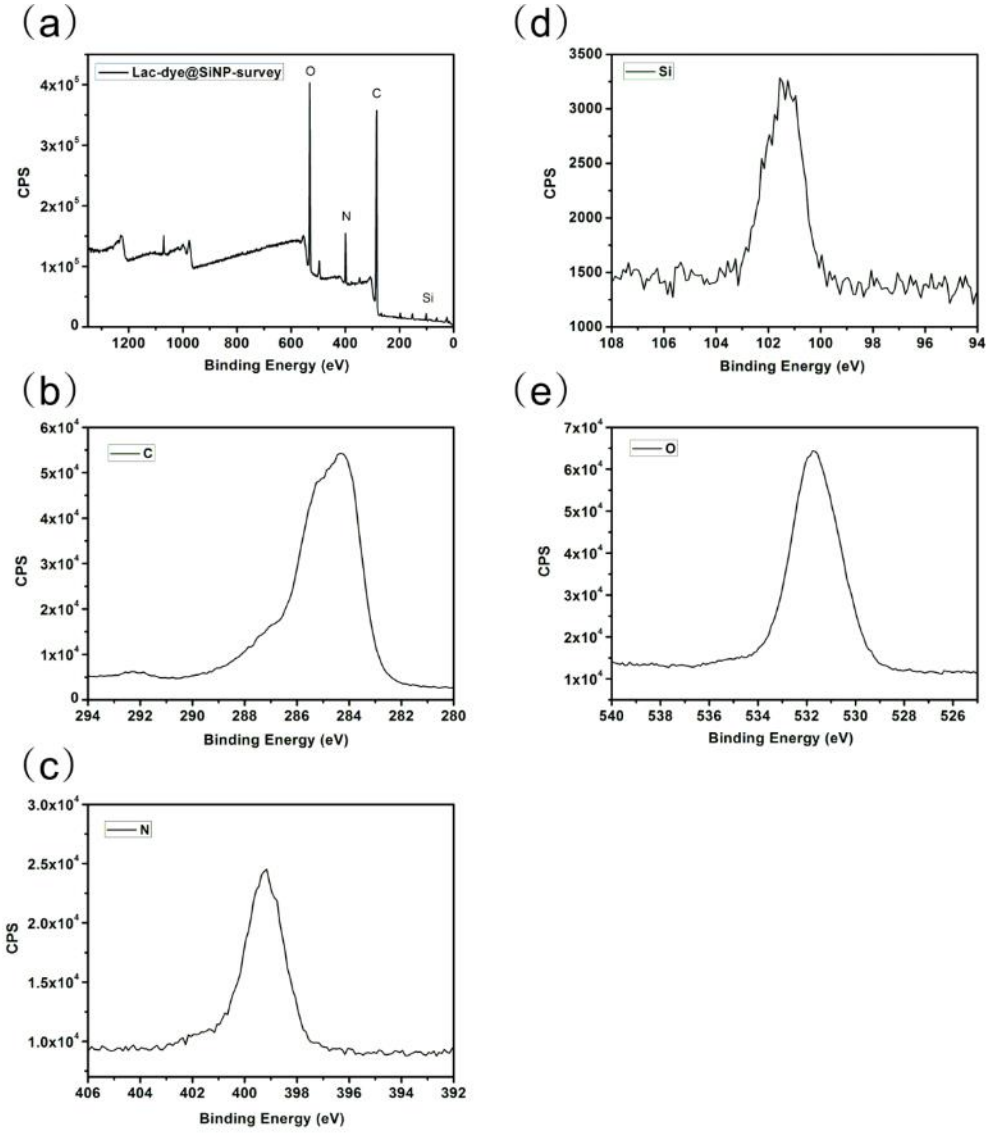


Figure S15. XPS data of **Lac-dye@SiNP**s. (a) survey scan of **Lac-dye@SiNP**s. (b), (c), (d), (e) Si, C, O, N elemental scan of **Lac-dye@SiNP**s.

Table S5. XPS data of **Lac-dye@SiNP**s.

Element	Peak BE	FWHM eV	Area (P) CPS.eV	Atomic %
C1s	284.80	3.22	1111220	64.50
O1s	531.58	3.06	948267.9	22.77
N1s	399.43	2.75	239710.7	8.97
Si2p	101.59	2.72	31995.13	1.14

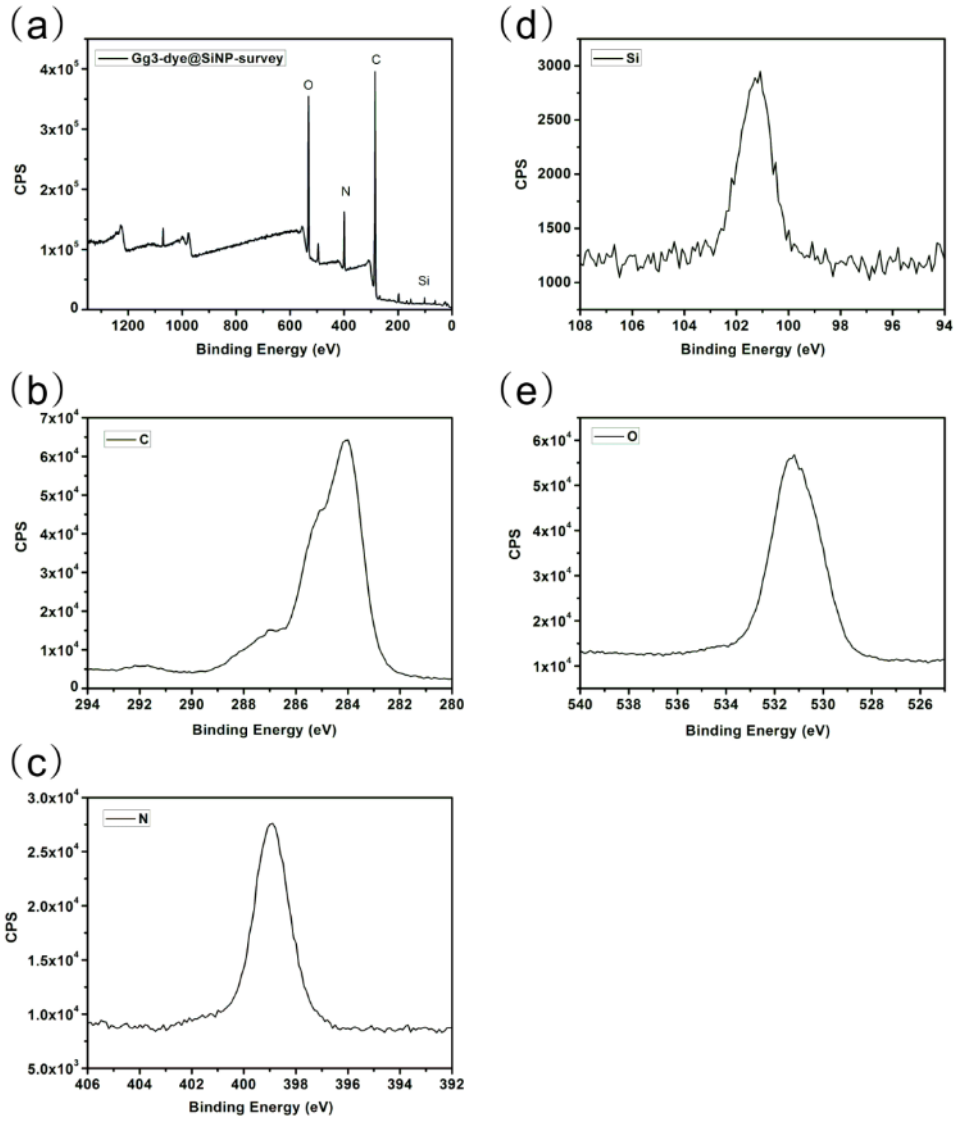


Figure S16. XPS data of **Gg3-dye@SiNP**s. (a) survey scan of **Gg3-dye@SiNP**s. (b), (c), (d), (e) Si, C, O, N elemental scan of **Gg3-dye@SiNP**s.

Table S6. XPS data of **Gg3-dye@SiNP**s.

Element	Peak BE	FWHM eV	Area (P) CPS.eV	Atomic %
C1s	284.80	3.07	1168631	67.13
O1s	531.55	3.06	816307.9	19.40
N1s	399.43	2.61	266307	9.86
Si2p	101.74	2.40	25846.21	1.48

TEM of sugar-dye@SiNPs

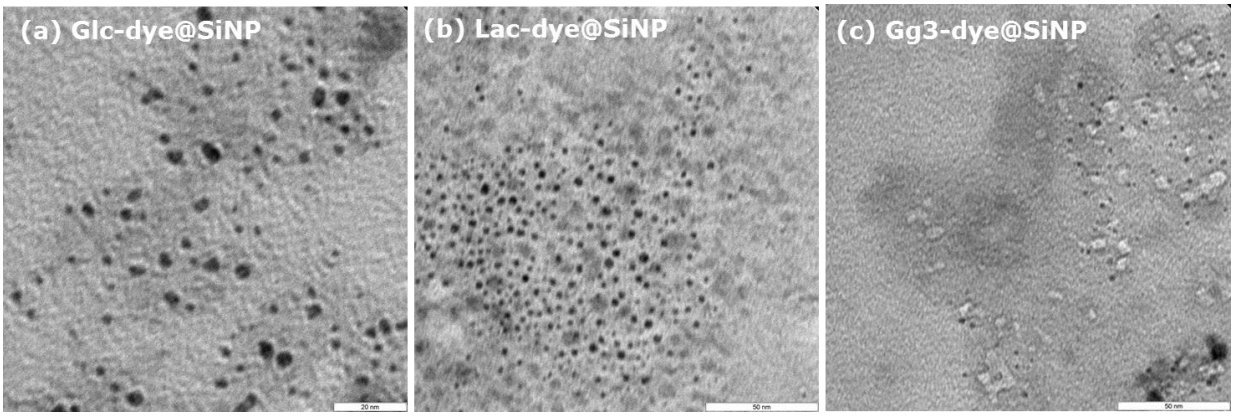


Figure S17. TEM images of different **sugar-dye@SiNP**s. (a) **Glc-dye@SiNP**s. Scale bar: 20 nm; (b) **Lac-dye@SiNP**s. Scale bar: 50 nm; (c) **Gg3-dye@SiNP**s. Scale bar: 50 nm.

Surface plasmon resonance (SPR) measurements

For binding studies, GM3-functionalized and biotinylated poly[N-(2-hydroxyethyl)acrylamide] polymers (GM3-biotin-PAA; Lectinity Holdings, Moscow, Russia) were immobilized on a streptavidin-coated SA sensor chip (GE Healthcare, Waukesha, WI, USA). SPR measurements were performed using a Biacore T100 instrument (GE Healthcare). As control, Lactose (Lac)-biotin-PAA was immobilized on the reference flow cell. The chip surface was first conditioned with three consecutive injections of 1 M NaCl in 50 mM NaOH (one minute each). A stock solution of Lac- or GM3-biotin-PAAs in MilliQ (1 mg/mL) was used for preparation of a working solution (15 µg/mL) in HBS buffer (10 mM Hepes, 150 mM NaCl, 2 mM $CaCl_2$, 2 mM $MgCl_2$, 0.005% Tween 20, pH 7.4). For immobilization, each working solution was injected at a flow rate of 5 µL/min for 420 s. After injection of the ligand, an extra wash using 50% isopropanol in 1 M NaCl and 50 mM NaOH was included according to the manufacturer's instructions. The HBS buffer was also used as running buffer. For binding studies, different concentrations of the **sugar-dye@SiNP**s (20, 40, 60, and 80 µg/mL) were prepared in HBS buffer using a stock solution of 10 mg/mL in MilliQ. The **sugar-dye@SiNP**s were injected at a flow rate of 30 µL/min for 120 s followed by a dissociation phase of 180 s. To regenerate the chip after each run, two consecutive 30 s injections of EDTA (20 mM) in HBS buffer were performed at a flow rate of 100 µL/min followed by a stabilization time of 30 s. Data were analyzed using the Biacore Evaluation software (GE Healthcare). For analysis, the response units measured in the reference flow cell were subtracted from the ones detected in the flow cell with immobilized GM3-biotin-PAA. Additionally, the response units of a blank sample (running buffer alone) were subtracted from the binding curve of each analyte. Final

SPR sensorgrams were generated using the Prism software (GraphPad Software, La Jolla, CA, USA). Steady-state affinity analysis was performed using the Biacore T100 Evaluation Software (GE Healthcare).

For interaction studies with the asialoglycoprotein receptor (ASGPR), recombinant human ASGPR H1 (R&D Systems, Minneapolis, MN, USA) was immobilized on a CM5 sensor chip (GE Healthcare) using the amine coupling kit (GE Healthcare). The chip surface was first activated by injection of the EDC/NHS mixture according to the manufacturer's instructions. The ASGPR H1 was dissolved in a 10 mM sodium acetate buffer, pH 4.0, to adjust a concentration of 50 µg/mL and was injected for 480 s in a flow rate of 10 µL/min. Potential free reactive sites were subsequently quenched using ethanolamine (1 M, pH 8.5). A reference flow cell was only activated and quenched without ligand immobilization. The carbohydrate-functionalized Si-NPs were injected at different concentrations (5, 20, and 40 µg/mL) for 120 s followed by a dissociation phase of 180 s. To regenerate the chip after each run, EDTA (20 mM) in HBS buffer was injected at a flow rate of 100 µL/min for 30 s followed by a stabilization time of 30 s. Data were analyzed using the Biacore Evaluation software as described earlier.

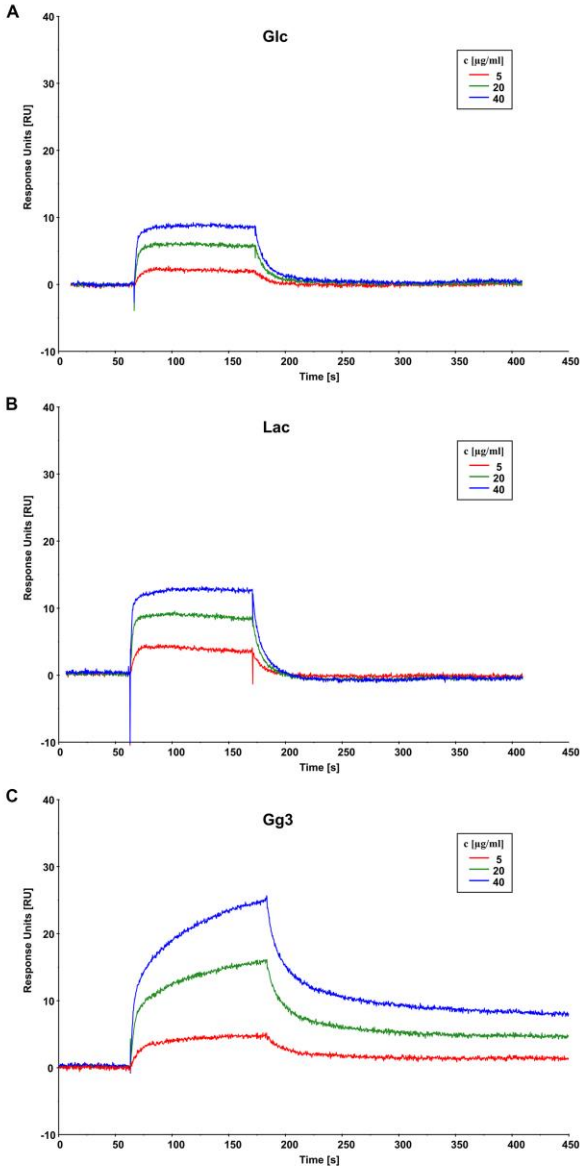


Figure S18. SPR analysis of the interaction of immobilized asialoglycoprotein receptor with the **sugar-dye@SiNPs**. For initial SPR binding studies, the recombinant human ASGPR H1 was immobilized on a CM5 sensor chip. Various concentrations (5, 20, or 40 µg/mL) of (A) **Glc-dye@SiNP**s, (B) **Lac-dye@SiNP**s, or (C) **Gg3-dye@SiNP**s were flowed over the chip surface as analytes to detect binding to the immobilized ASGPR. The SPR sensorgrams were generated by subtraction of the reference flow cell as well as of the signals obtained by injection of the running buffer alone. As expected, specific binding was most prominent for the **Gg3-dye@SiNP**s. Steady-state affinity analysis revealed an apparent k_D value in the micromolar range using a theoretical molecular weight of the **Gg3-dye@SiNP**s of 15.7 kDa.

Biological Studies

Flow cytometry

For cell binding studies, B16F10 cells (ATCC® CRL-6475) were used as a murine melanoma cell line exhibiting high levels of the GM3 ganglioside[2]. Cells were seeded in a 48-well plate using complete DMEM (supplemented with 10% fetal calf serum, 100 U/mL penicillin, 100 µg/mL streptomycin, 2 mM L-glutamine) and were cultivated overnight. The next day, cells were washed once with PBS and 100 µL of fresh FCS-free DMEM containing various concentrations (2 or 5 µg/mL) of the respective **sugar-dye@SiNP**s were added. After one or two hours of incubation at 37°C, cells were washed three times with ice-cold PBS. Subsequently, cells were measured by flow cytometry using a FACSCanto II flow cytometer (BD Biosciences, San Jose, CA, USA). Data were analyzed with the FlowJo analysis software (Tree Star Inc., Ashland, OR).

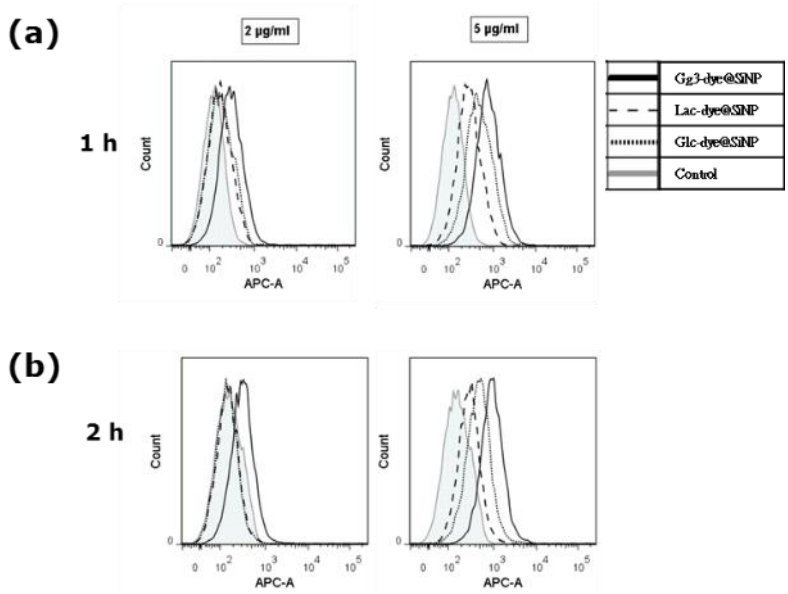


Figure S19. The B16F10 melanoma cells were incubated with 2 or 5 µg/mL of the different **sugar-dye@SiNP**s for 1 or 2 h, respectively. Binding/uptake of the carbohydrate-functionalized SiNPs was analyzed by flow cytometry and was compared to untreated cells (shaded curve).

Confocal microscopy studies

For cell binding/uptake studies, the GM95 cell line (RIKEN BioResource Center) was used as control since it represents a B16F10-derived mutant cell line that does not express the GM3 ganglioside[3] which was confirmed by thin layer chromatography (data not shown). For

fluorescence microscopy studies, 6 x 10^4 B16F10 cells in 1 mL complete DMEM were seeded onto 12-mm coverslips (Menzel, Braunschweig, Germany) in 24-well plates and were incubated at 37 °C overnight. The next day, cells were washed with PBS and the **sugar-dye@SiNP**s in 200 µL of FCS-free DMEM with 20 µg/mL were added, respectively. After 2 h incubation at 37 °C, cells were washed three times with PBS supplemented with 3% BSA and were fixed by incubation in 4% paraformaldehyde in PBS in the dark for 15 min. Cells were again washed twice followed by permeabilization of the cells using 0.1% Triton in PBS and blocking with 5% FCS in PBS to exclude unspecific binding for 30 minutes at room temperature. Subsequently, a rabbit anti-EEA1 (early endosome antigen 1) antibody (Thermo Fisher Scientific, Waltham, MA, USA) was diluted 1:200 in the blocking buffer, added to the cells and incubated for one hour. Cells were washed three times and a FITC-labeled anti-rabbit IgG antibody (Fisher Scientific, Schwerte, Germany) was added 1:800 in the blocking buffer. In the same step, 190 nM of Alexa 555-labeled phalloidin (tebu-bio, Offenbach, Germany) was added to the cells in order to stain the actin cytoskeleton. After one hour incubation, cells were washed three times with a PBS solution containing 3% BSA. Cells were finally washed and mounted in 2,2'-Thiodiethanol mounting media (Sigma-Aldrich). Cells were then analyzed using a LSM 700 confocal scanning microscope (Zeiss, Oberkochen, Germany).

The colors of the confocal microscopy images correspond to the following signals:

1) The blue color derives from the inherent fluorescence of the SiNPs.
2) The B16F10 and GM95 cell morphology was shown by differential interference contrast microscopy.
3) The green color is associated with EEA-1 on early endosomes.
4) The red color corresponds to the actin cytoskeleton.
5) The purple color derives from the additional ATTO-647N dye coupled to the Si-NPs.

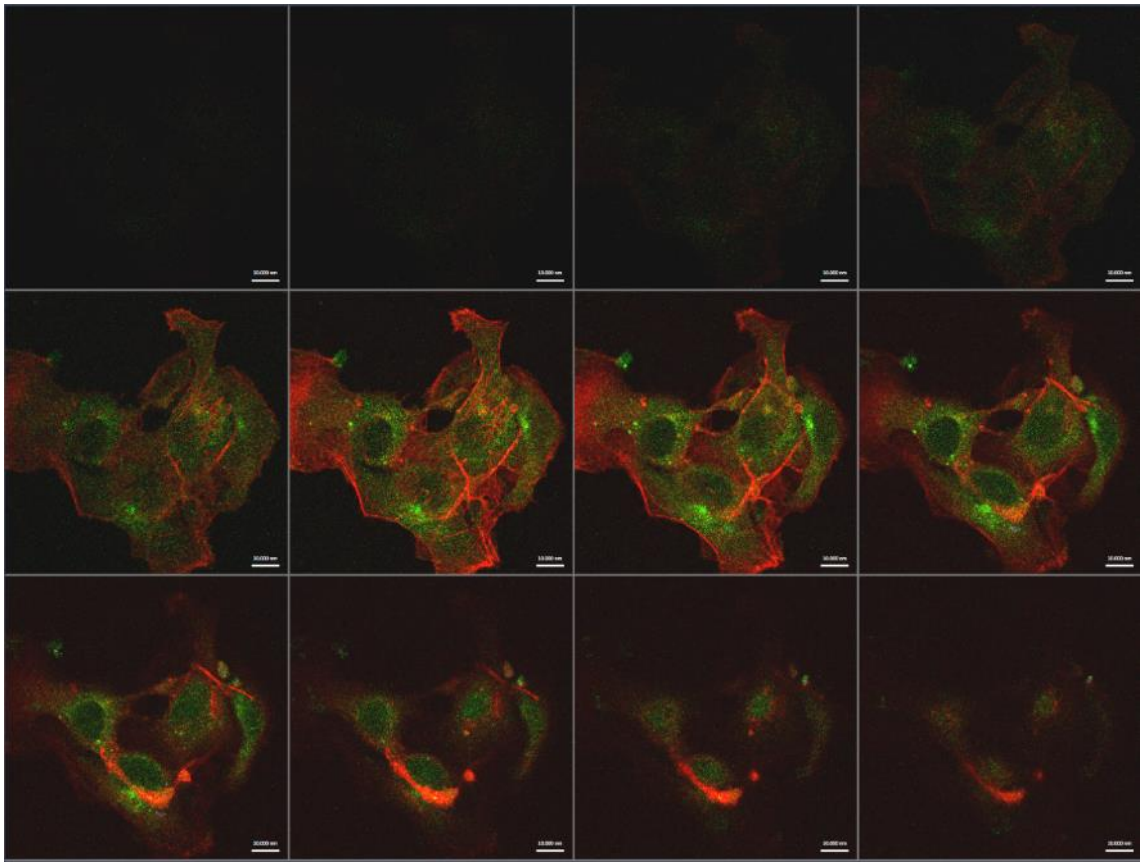


Figure S20. Z-stack of B16F10 cells stained for the actin cytoskeleton (red) and early endosomes but no incubation with SiNPs (as blank control).

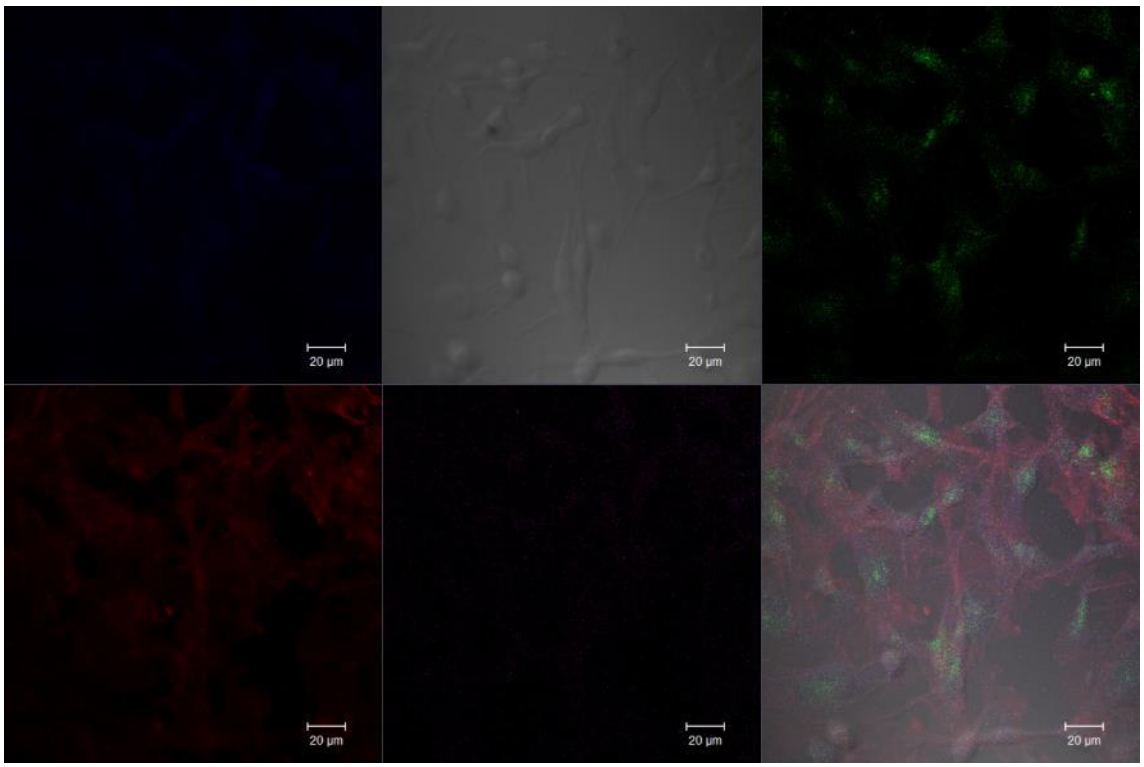


Figure S21-1. First image of the Z-stack of B16F10 cells treated with 20 µg/mL of **Gg3-dye@SiNP**s for 2 hours.

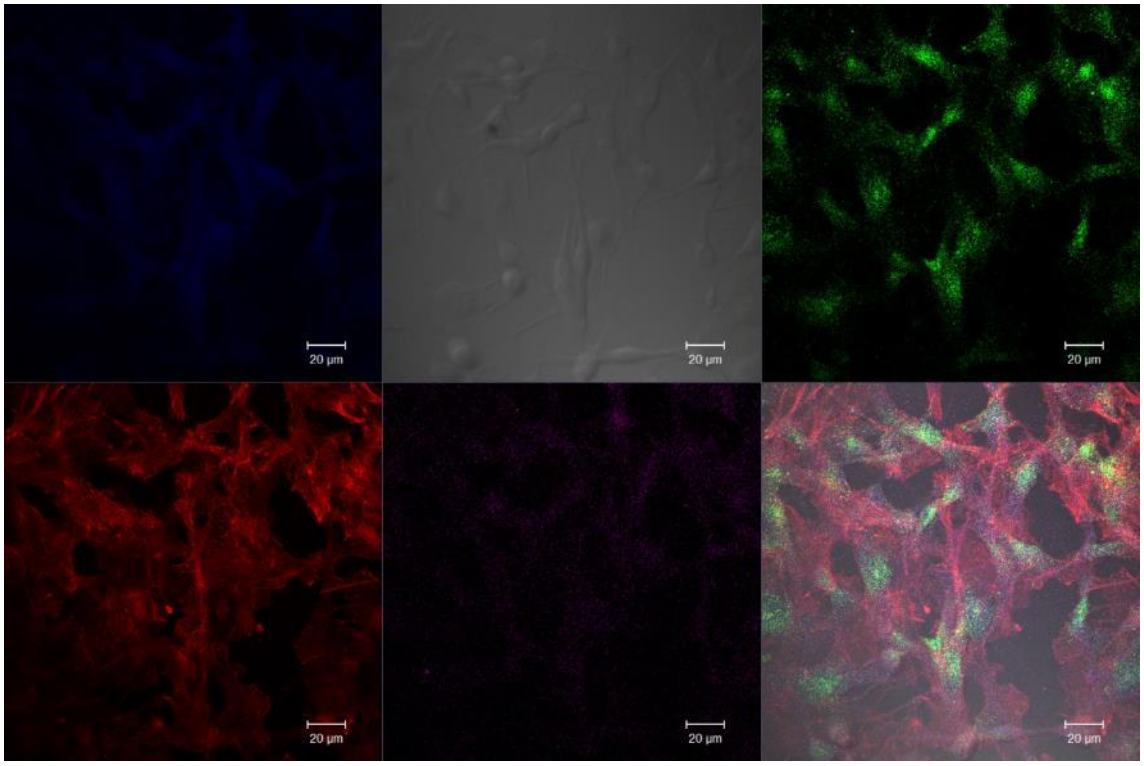


Figure S21-2. Second image of the Z-stack of B16F10 cells treated with 20 µg/mL of **Gg3-dye@SiNP**s for 2 hours.

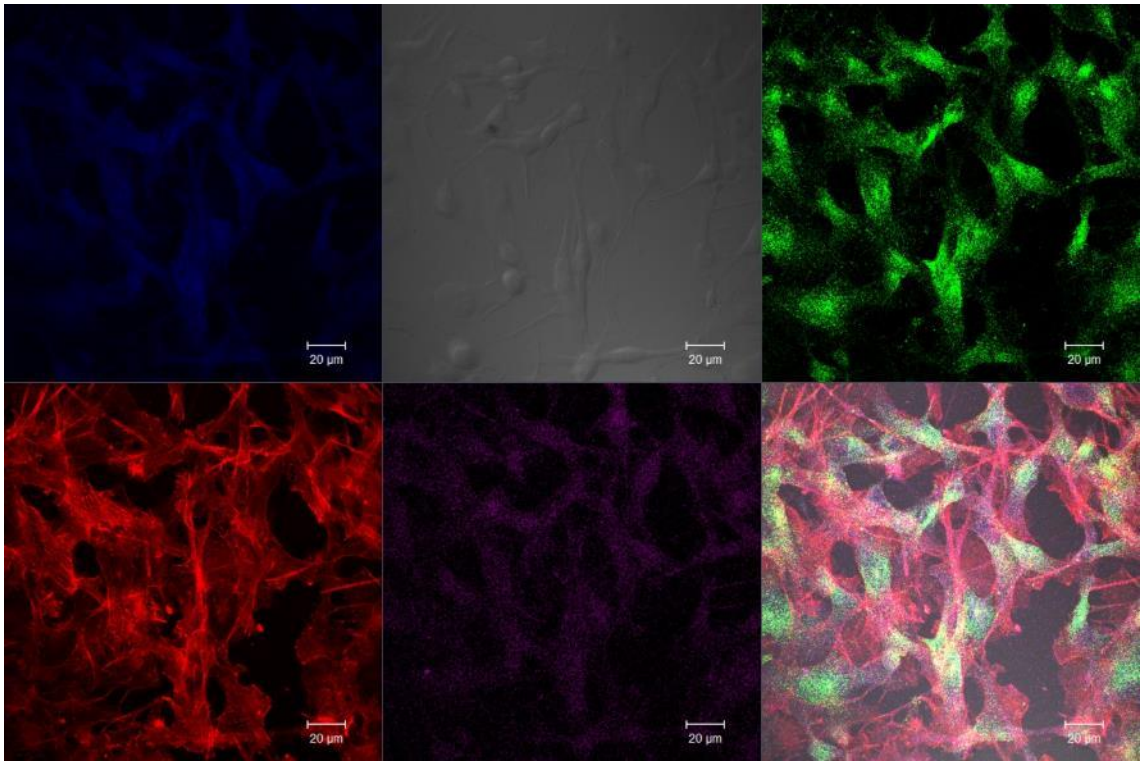


Figure S21-3. Third image of the Z-stack of B16F10 cells treated with 20 µg/mL of **Gg3-dye@SiNP**s for 2 hours.

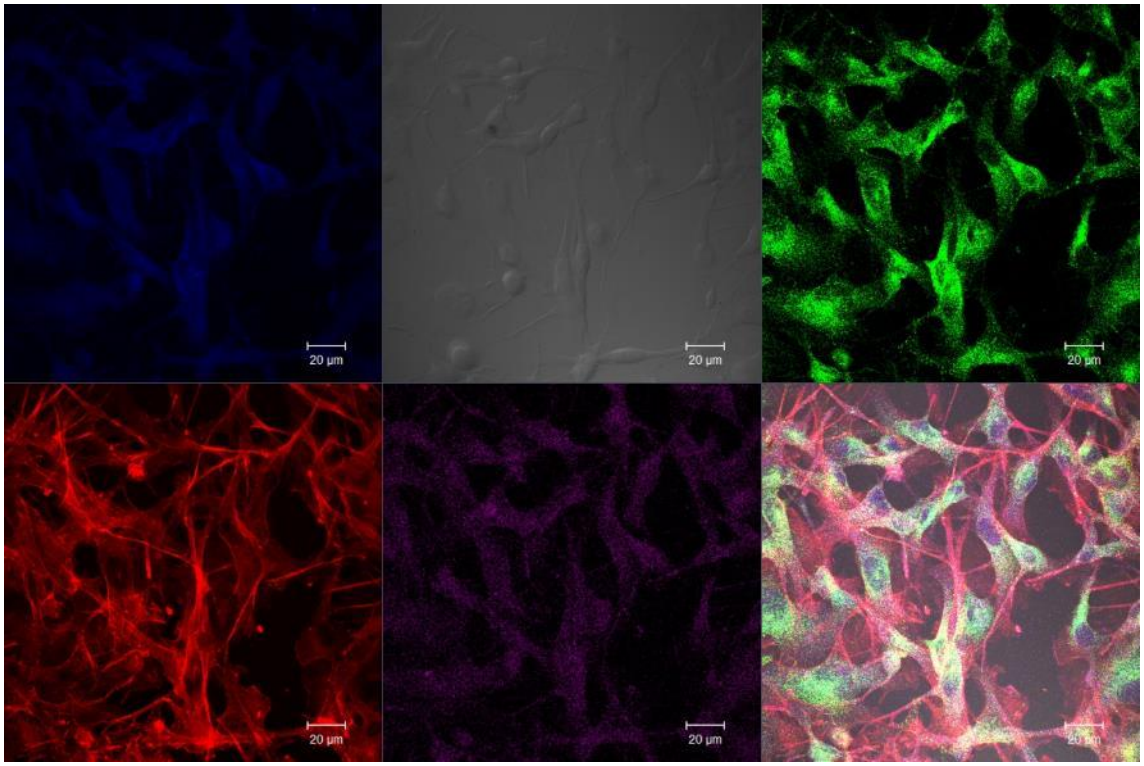


Figure S21-4. Forth image of the Z-stack of B16F10 cells treated with 20 µg/mL of **Gg3-dye@SiNP**s for 2 hours.

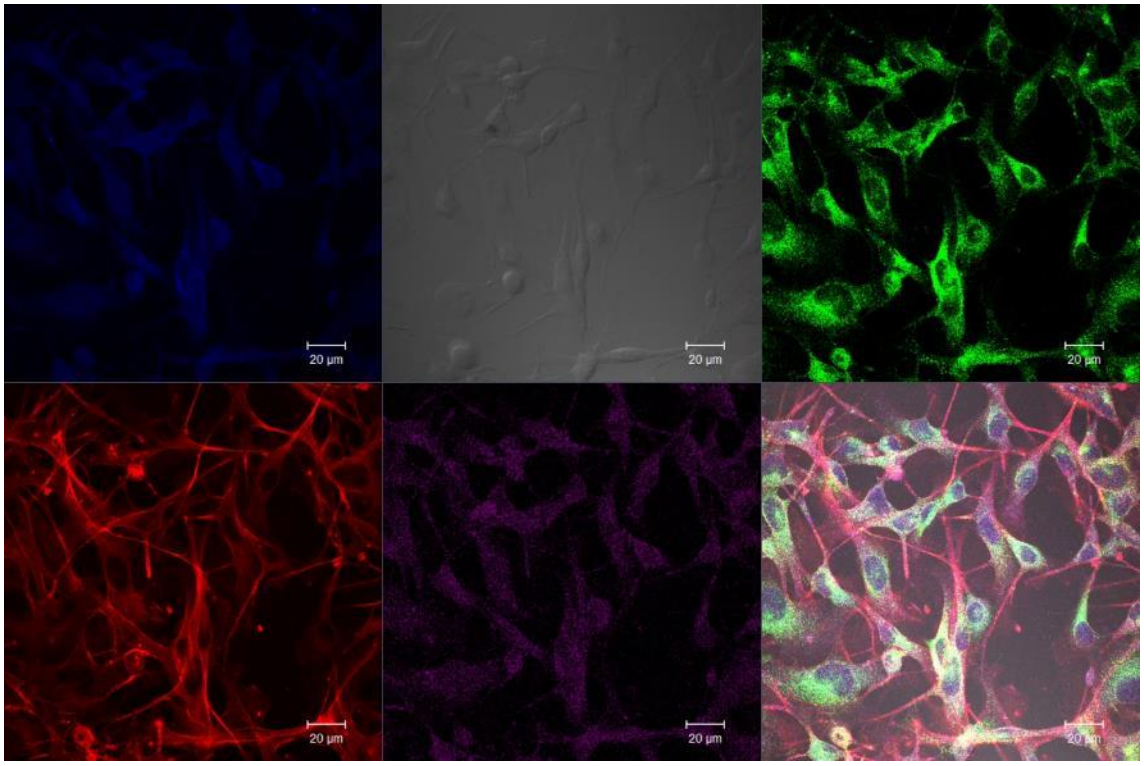


Figure S21-5. Fifth image of the Z-stack of B16F10 cells treated with 20 µg/mL of **Gg3-dye@SiNP**s for 2 hours.

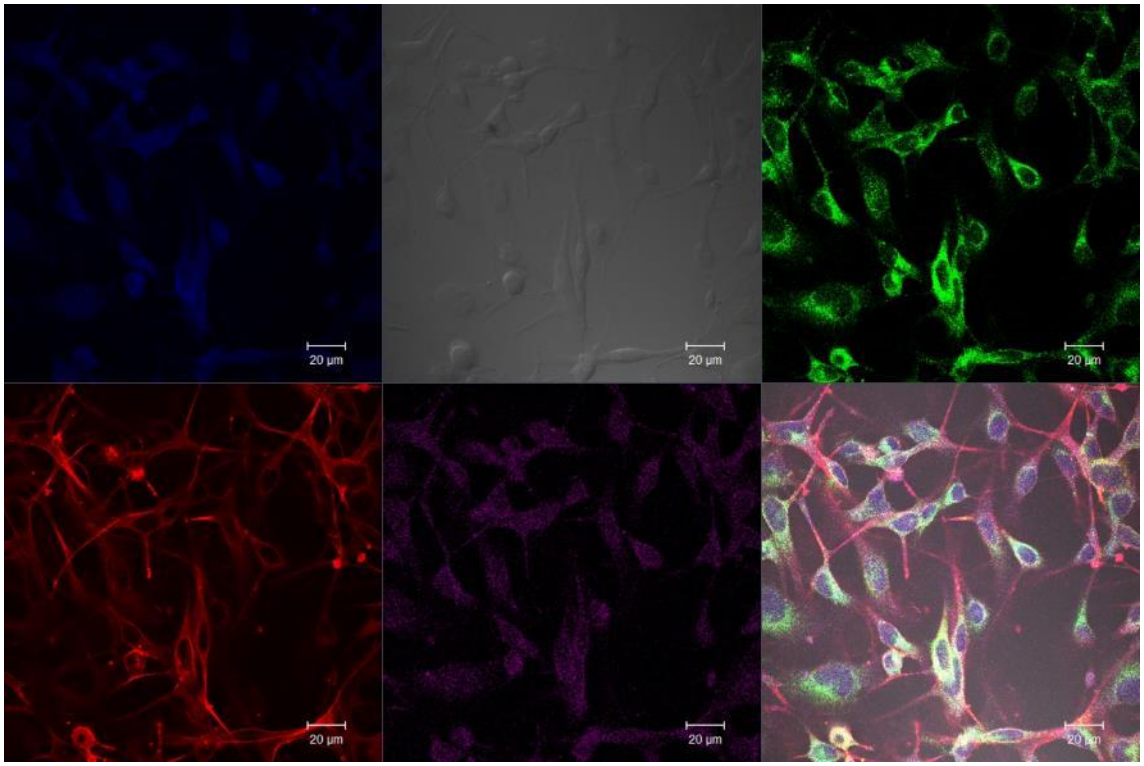


Figure S21-6. Sixth image of the Z-stack of B16F10 cells treated with 20 µg/mL of **Gg3-dye@SiNP**s for 2 hours.

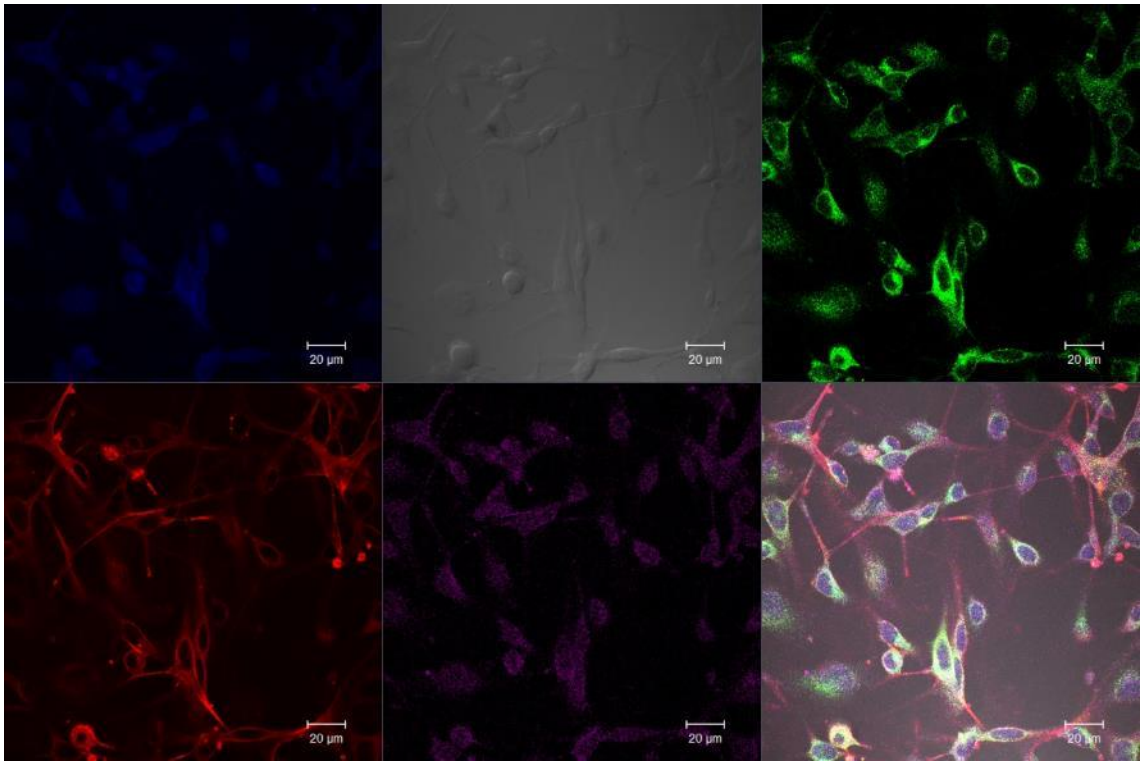


Figure S21-7. Seventh image of the Z-stack of B16F10 cells treated with 20 µg/mL of **Gg3-dye@SiNP**s for 2 hours.

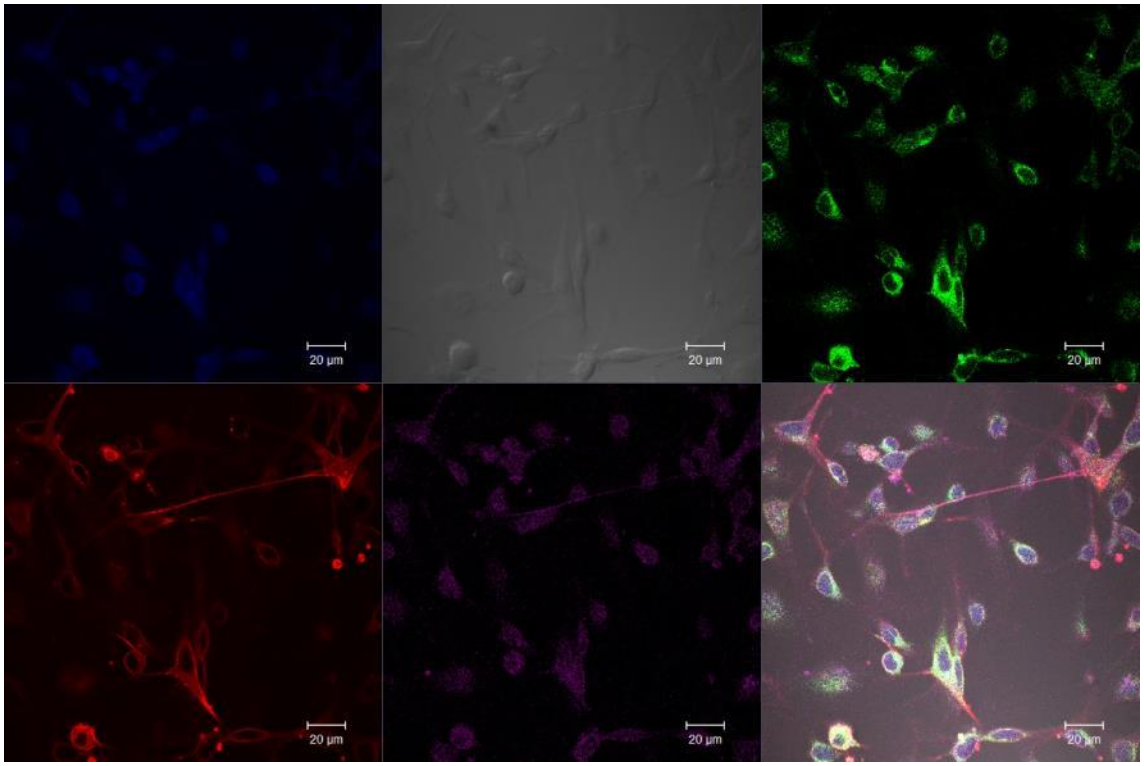


Figure S21-8. Eighth image of the Z-stack of B16F10 cells treated with 20 µg/mL of **Gg3-dye@SiNP**s for 2 hours.

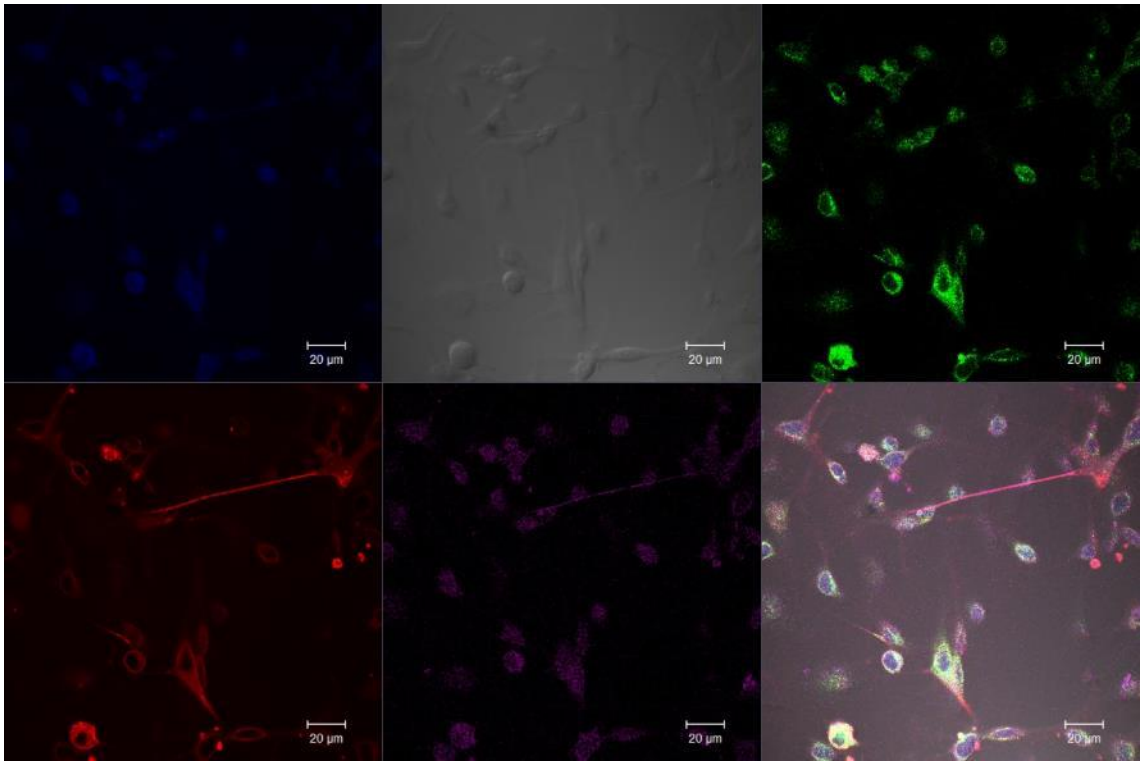


Figure S21-9. Ninth image of the Z-stack of B16F10 cells treated with 20 µg/mL of **Gg3-dye@SiNP**s for 2 hours.

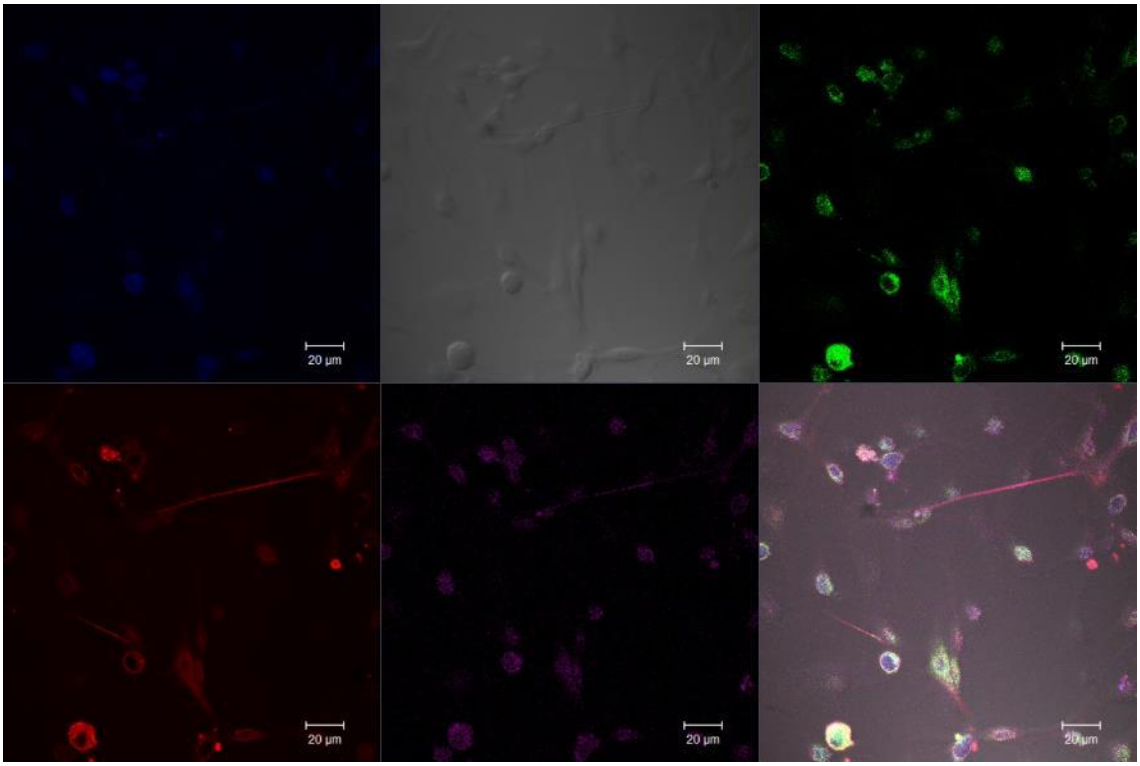


Figure S21-10. Tenth image of the Z-stack of B16F10 cells treated with 20 µg/mL of **Gg3-dye@SiNP**s for 2 hours.

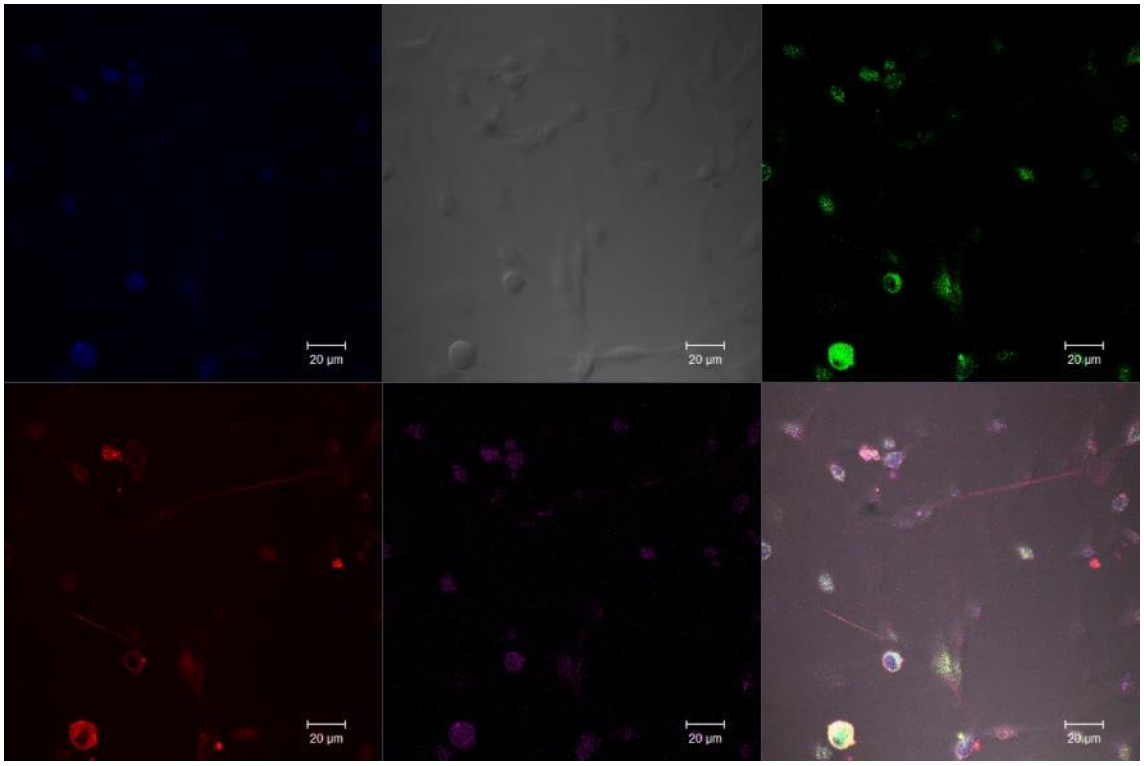


Figure S21-11. Eleventh image of the Z-stack of B16F10 cells treated with 20 µg/mL of **Gg3-dye@SiNP**s for 2 hours.

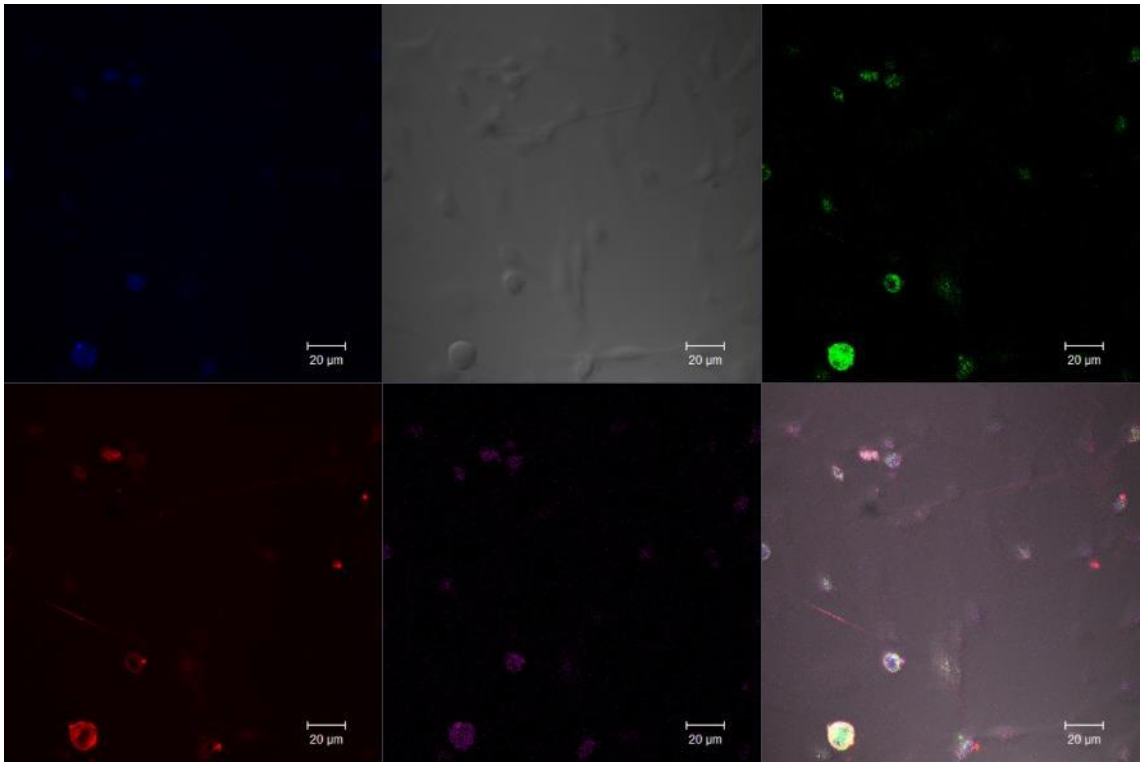


Figure S21-12. Twelfth image of the Z-stack of B16F10 cells treated with 20 µg/mL of **Gg3-dye@SiNP**s for 2 hours.

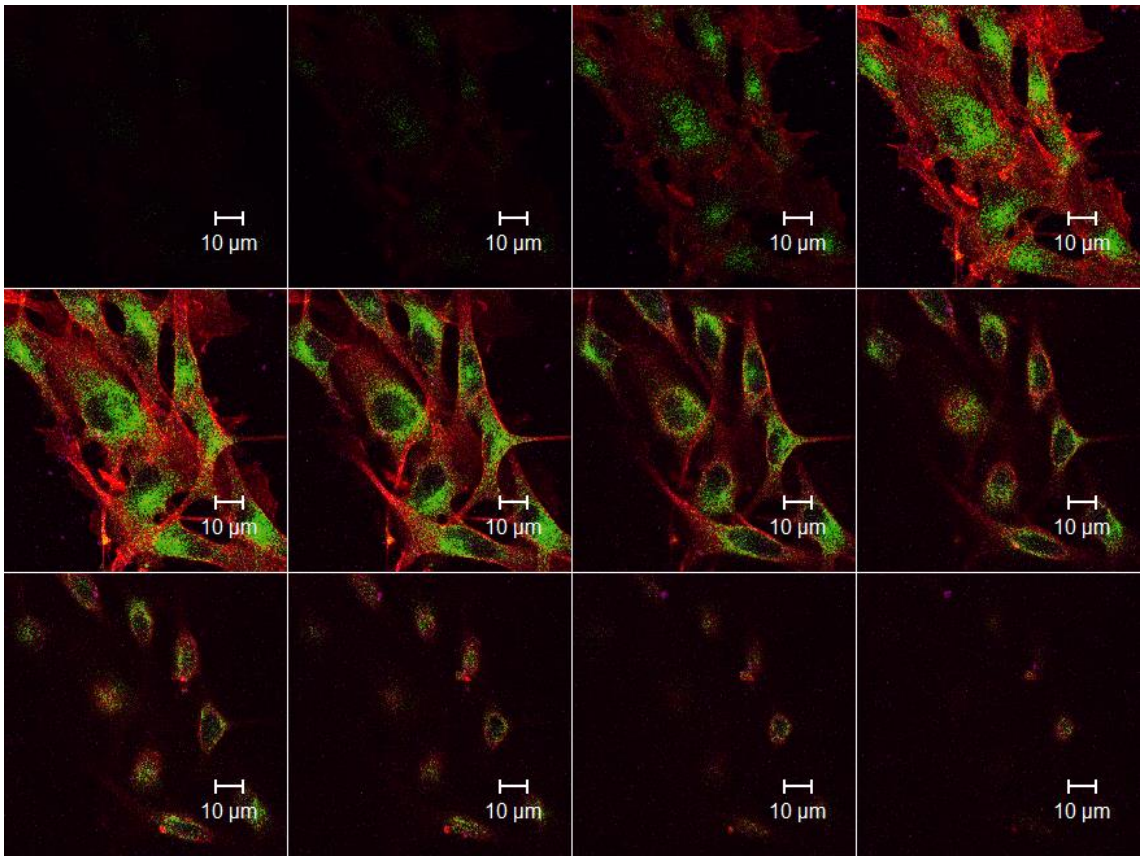


Figure S22. Z-stack of B16F10 cells treated with 20 µg/mL of **Glc-dye@SiNP**s for 2 hours.

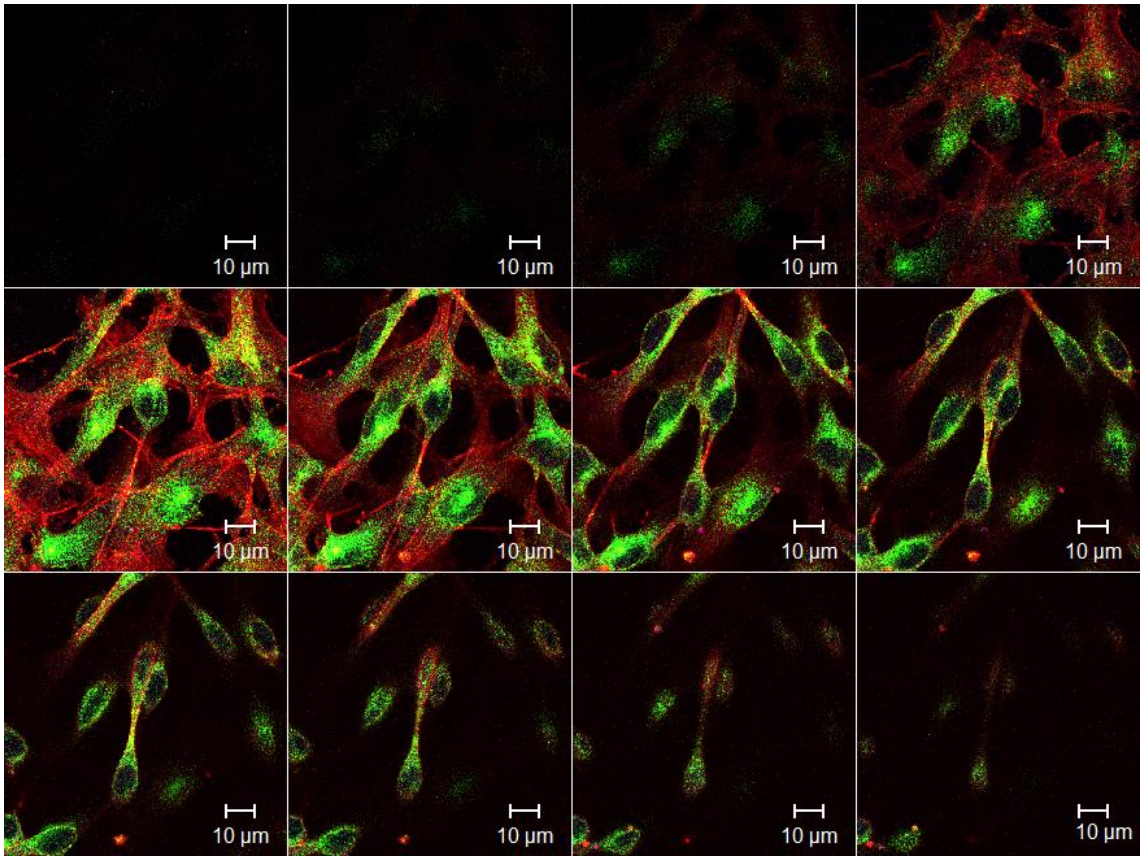


Figure S23. Z-stack of B16F10 cells treated with 20 µg/mL of **Lac-dye@SiNP**s for 2 hours.

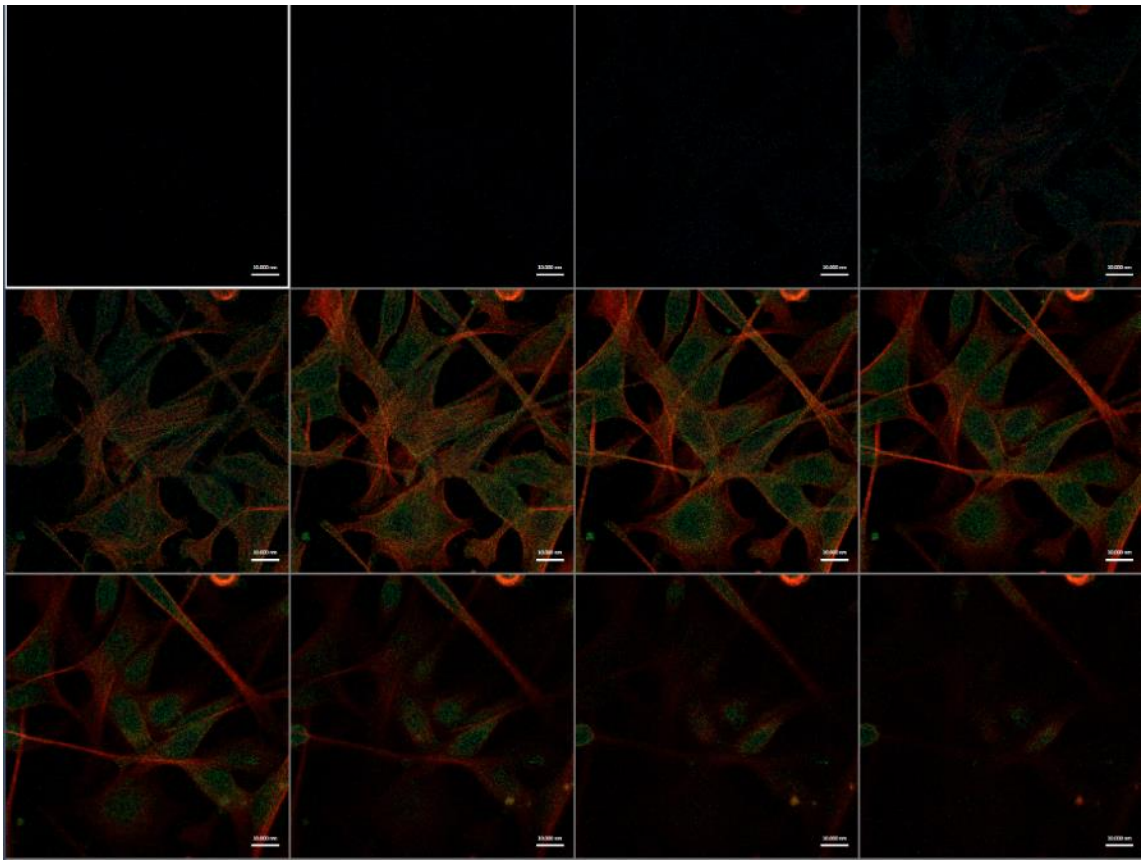


Figure S24. Z-stack of GM95 cells (as blank control) stained for the actin cytoskeleton (red) and early endosomes (green). Scale bar 10 µm.

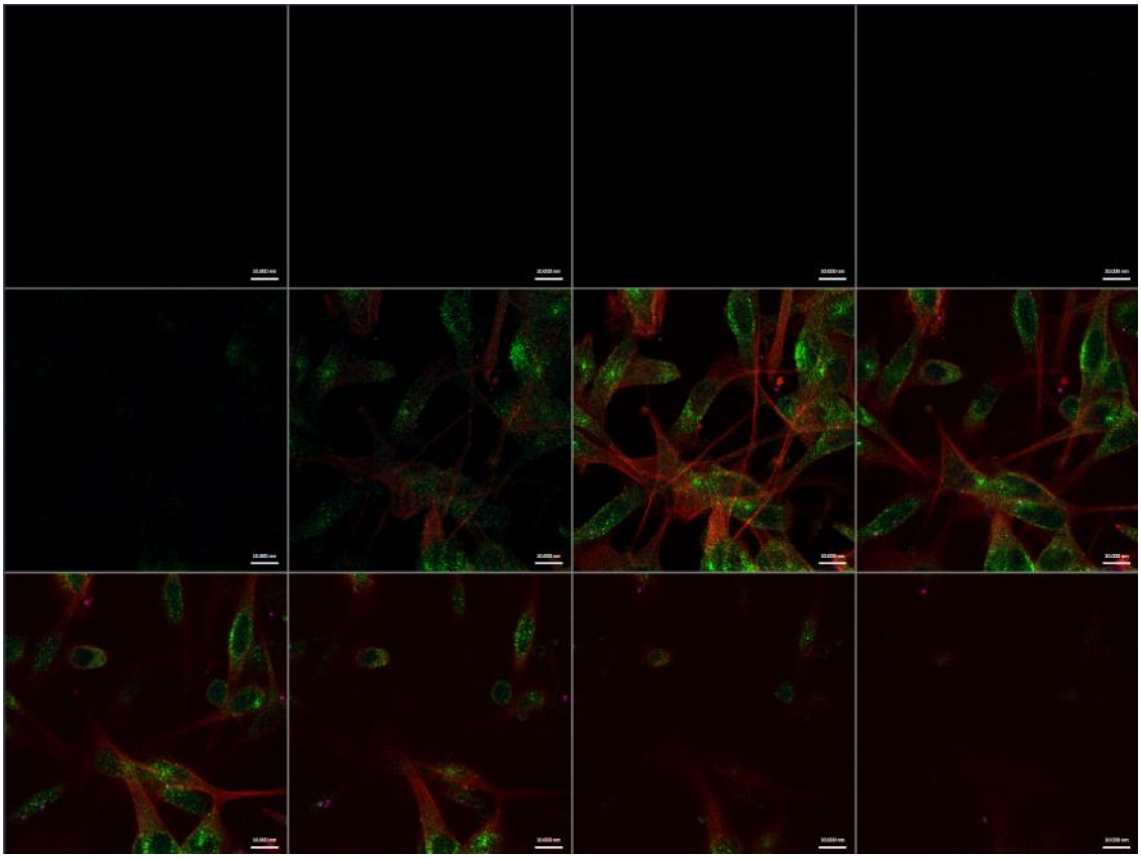


Figure S25. Z-stack of GM95 cells treated with 20 μg/mL of **Gg3-dye@SiNP** for 2 hours. Scale bar 10 μm.

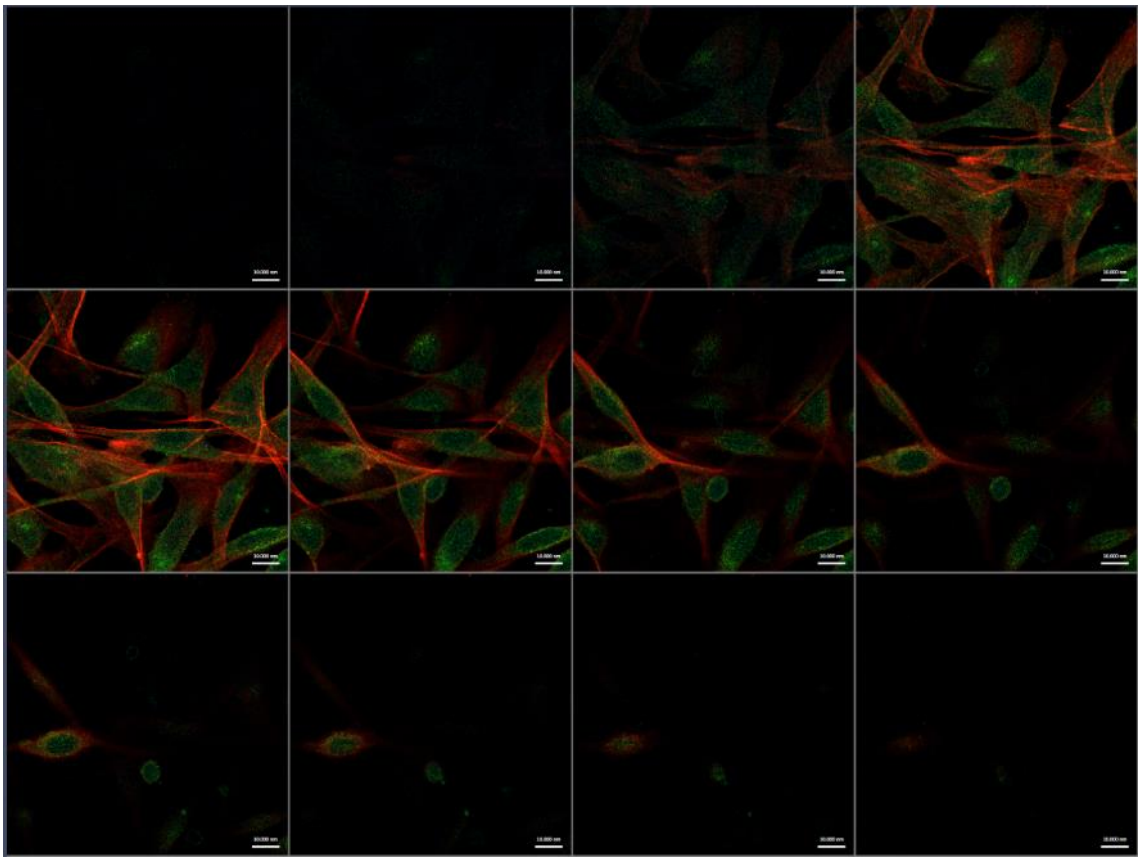


Figure S26. Z-stack of GM95 cells treated with 20 μg/mL of **Glc-dye@SiNP** for 2 hours. Scale bar 10 μm.

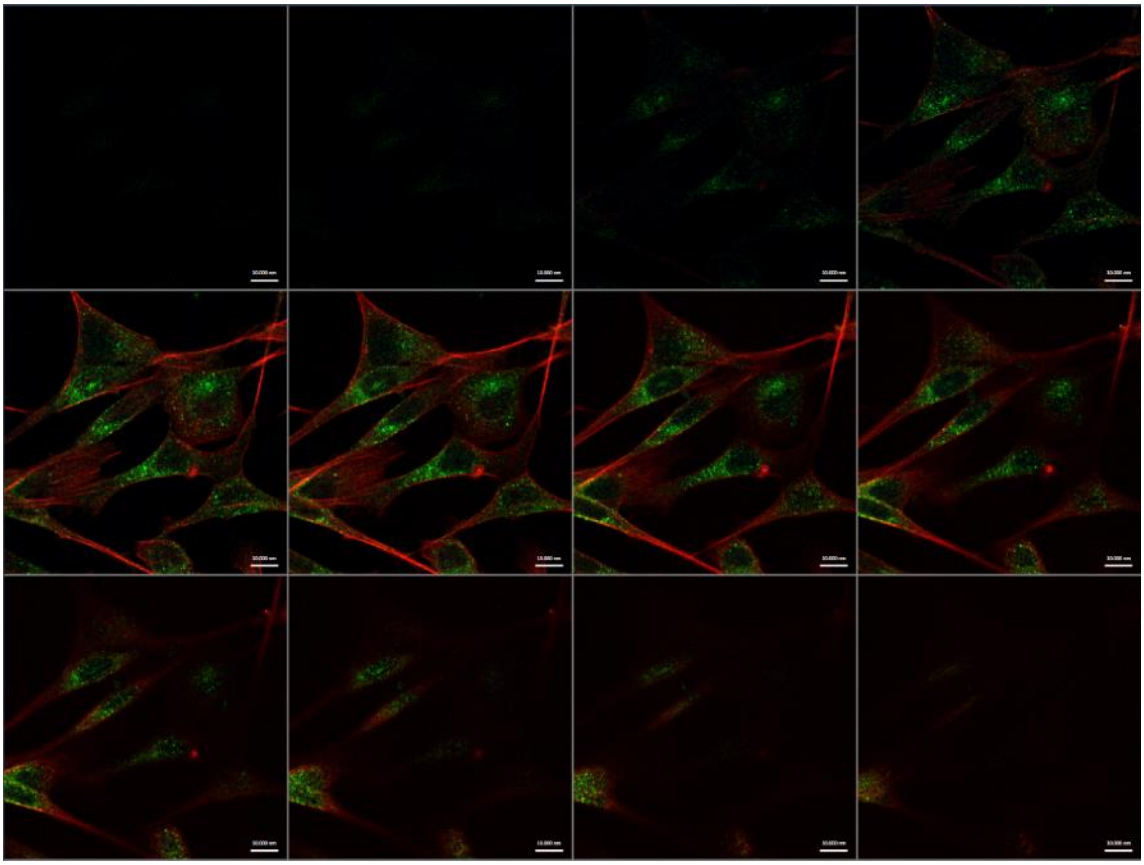


Figure S27. Z-stack of GM95 cells treated with 20 μg/mL of **Lac-dye@SiNP** for 2 hours. Scale bar 10 μm.

References

(1) Carney, R. P.; Kim, J. Y.; Qian, H.; Jin, R.; Mehenni, H.; Stellacci, F.; Bakr, O. M. *Nature communications* **2011**, *2*, 335.

(2) Azuma, Y.; Ishikawa, Y.; Kawai, S.; Tsunenari, T.; Tsunoda, H.; Igawa, T.; Iida, S.-i.; Nanami, M.; Suzuki, M.; Irie, R. F.; Tsuchiya, M.; Yamada-Okabe, H. *Clinical Cancer Research* **2007**, *13*, 2745.

(3) Ichikawa, S.; Nakajo, N.; Sakiyama, H.; Hirabayashi, Y. *Proceedings of the National Academy of Sciences of the United States of America* **1994**, *91*, 2703.