Electronic Supplementary Material (ESI) for Soft Matter.

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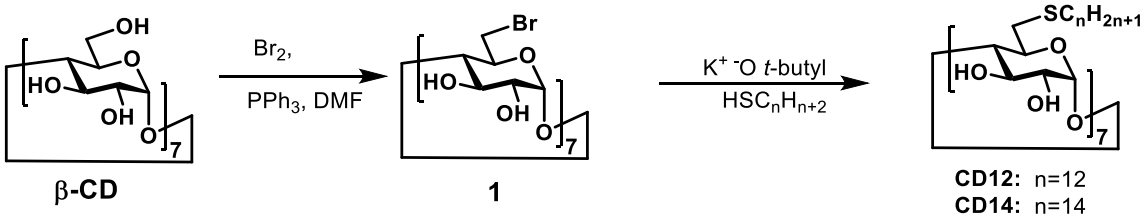
1. Materials and Methods

Briefly, reagents were purchased from Fluka, Sigma-Aldrich, Alfa Aesar, Fisher Chemicals, TCI Chemicals and Acros Chemicals. Fluorescence measurements were performed with a FluoroMax-3 spectrofluorometer (Horiba Jobin Yvon GmbH) or a FluoroMax-4 spectrofluorometer (Horiba Scientific) equipped with a stirrer and a temperature controller (25.0 ± 0.1 ºC). Vesicles were prepared with a Mini-Extruder from Avanti Polar Lipids (pore size 200 nm). A Labconco, FreeZone 4.5 lyophilizer was used. Samples were sonicated with a Ultrasonic Cleaner, GB-928 sonicator bath or a Q-Sonic sonicator probe. Dynamic light scattering measurements were taken with a Wyatt Tech, DynaPro NanoStar

Abbreviations. βCD: β-Cyclodextrin; CF: 5(6)-Carboxyfluorescein; DCC: *N*,*N*-Dicyclohexylcarbodiimide; DCM: Dichloromethane; DI water: deionized water; DMAP: 4-dimethylaminopyridine; DMF: *N*,*N*-Dimethylformamide; DTDP: 3,3-dithiopropionic acid; GSH: Glutathione; HCL: hydrochloric adic; PEG: poly(ethylene glycol); PEGOMe: poly(ethylene glycol)-methyl ether; PPh_3: triphenylphosphine; TEA: triethylamine; THF: tetrahydrofuran; Tris: Tris(hydroxymethyl)aminomethane; TsCl: p-toluenesulfonyl chloride.

2. Synthesis

2.1 Synthesis of Hosts.



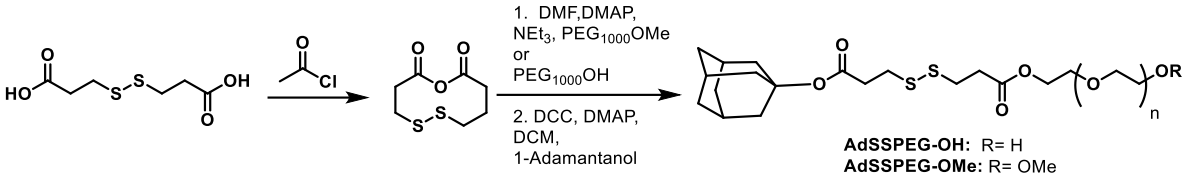
Synthesis of Compound 1: To a round bottom flask containing PPh_3 (18.36 g, 70 mmol) in DMF (≈20 mL) and purged under nitrogen, $Br_{2\,(l)}$ (3.59 mL, 70 mmol) was added dropwise and stirred at 60 ℃ for 30 min. β-CD (4.0 g, 3.5 mmol) in anhydrous DMF (≈10 mL) was added to the

reaction mixture dropwise and stirred overnight (≈18 h) at 80 ℃. Approximately half the solvent volume was removed under reduced pressure and the resulting reaction mixture was added to methanol (≈100 mL). The pH was adjusted to 10-12 with K-*t*-butoxide and stirred at room temperature for 30 min. This reaction mixture was then precipitated in rapidly stirring ice-cold deionized water (DI water). The precipitate was isolated via vacuum filtration, transferred to a falcon tube, and then dissolved in methanol. The resulting solution was centrifuged (Eppendorf, Centrifuge 5810) three times in 5 min intervals at 7500 RPM. Methanol was decanted and the precipitate was transferred to a round bottom flask and dissolved in a minimal amount of DMF. The solvent was then removed under reduced pressure. Product was dried under high vacuum pump overnight (≈18 h) to obtain a white powder **(1)**.

Brominated β-CD **(1)** (350 mg, 0.22 mmol), either 1-dodecanethiol (for **CD12**) or 1-tetradecanethiol (**CD14**) (0.89 g/1.01 g, 4.4 mmol), and K-*t*-butoxide (0.49 g, 4.4 mmol) in anhydrous DMF (20 mL) were stirred for 72 h at 80 ℃. The reaction mixture was then precipitated in rapidly stirring ice cold DI water. The precipitate was isolated via vacuum filtration and transferred to a round bottom flask. The precipitate was then refluxed (65 ℃) in methanol (≈20 mL) for 1 h. The resulting precipitate was isolated by vacuum filtration and washed with hot methanol. The product was dried under high vacuum pump overnight (≈18 h) to obtain a white powder (n = 12) **(CD12)** ^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.74 (s, 1H), 5.26 (s, 1H), 4.99 (d, *J* = 3.6 Hz, 1H), 4.01 (t, *J* = 9.1 Hz, 1H), 3.94 (s, 1H), 3.74 (dd, *J* = 9.6, 3.5 Hz, 1H), 3.51 (t, *J* = 9.1 Hz, 1H), 3.08 (d, *J* = 13.4 Hz, 1H), 2.89 (dd, *J* = 13.9, 6.7 Hz, 1H), 2.62 (t, *J* = 7.4 Hz, 2H), 1.45 – 1.21 28 (m, 20H), 0.90 (t, *J* = 6.8 Hz, 3H). **(CD14)** ^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.74 (s, 1H), δ 5.26 (s, 1H), 4.99 (d, *J* = 3.6 Hz, 1H), 4.01 (t, *J* = 9.1 Hz, 1H), 3.98 – 3.89 (m, 1H),

3.74 (dd, *J* = 9.8, 3.5 Hz, 1H), 3.70 – 3.63 (m, 3H), 3.08 (d, *J* = 13.4 Hz, 1H), 2.89 (dd, *J* = 13.6, 6.6 Hz, 1H), 2.62 (t, *J* = 7.4 Hz, 3H), 1.47 – 1.16 (m, 24H), 0.90 (t, *J* = 6.7 Hz, 3H).

2.2 Synthesis of Guests.



3,3′-Dithiodipropionic acid (2.10 g, 10 mmol) was added to a round bottom flask and refluxed (65 ℃) in acetyl chloride (7.14 mL, 100 mmol) for 2 h. The reaction mixture was cooled to room temperature, and acetyl chloride was removed under reduced pressure. The resulting residue was precipitated in rapidly stirring ice-cold diethyl ether. The precipitate was then isolated via vacuum filtration and washed with ice cold diethyl ether. The product was dried under high vacuum pump overnight (≈18 h) to obtain an off-white powder.

6.5 mmol of dried r PEG MW_{ave}1000 or PEG MW=1000 methyl ether OMe (6.5 mmol), dithiopropionic anhydride (2.68 g, 13 mmol) and DMAP (0.79 g, 6.5 mmol) were dissolved in anhydrous DMF (20 mL). TEA (1.82 mL, 13 mmol) was added dropwise. The resulting solution was purged under nitrogen three times and allowed to stir at 35 ℃ for 36 h. The reaction mixture was precipitated in rapidly stirring ice-cold diethyl ether. The precipitate was isolated via vacuum filtration and washed with ice cold diethyl ether. The product was then dried under high vacuum pump overnight (≈18 h) to obtain a brown powder.

Dithiopropionic acid-PEG or dithiopropionic acid-PEG-OMe (5.87 mmol) and 1-adamantanol (1.79 g, 11.74 mmol) was dissolved in anhydrous DCM (20 mL) at 0 ℃. DCC (2.42 g, 11.47 mmol) dissolved in anhydrous DCM (5 mL) and added to the first solution at dropwise at 0 ℃ and stirred for 2 h at 0 ℃. The reaction mixture was then allowed to stir for 22 h at room temperature

and the precipitate was filtered off. The filtrate was washed three times with 10% HCl. The aqueous layer was extracted with DCM until the organic layer appeared clear (x 6). The organic layer was washed three times with brine and dried over $MgSO_4$. The solvent was then removed under reduced pressure. The resulting residue was precipitated in rapidly stirring ice-cold heptane, isolated via vacuum filtration, and washed with ice cold diethyl ether. The product was further purified in DI water via dialysis (Float-A-Lyzer G2) with a 0.1-0.5 kDa pore membrane and the solution was flash-frozen with liquid nitrogen and left on the lyophilizer overnight (≈18 h) to remove water and obtain a yellow-orange powder **AdSSPEG-OH:** ^{1}H NMR (400 MHz, DMSO-d_6) δ 5.62 –5.58 (m, 3H) 3.49–3.25 1 (m, 86H), 2.88 (t, *J* = 6.9 Hz, 4H), 2.62 (t, *J* = 6.9 Hz, 4H), 1.77 – 1.68 (m, 8H), 1.68 – 1.46 (m, 8H), **AdSSPEG-OMe:** ^{1}H NMR (400 MHz, Chloroform-*d*) δ 4.29 – 4.19 (m, 2H), 3.83 – 3.44 (m, , 86H), 3.37 (s, 3H), 2.95 – 2.88 (m, 4H), 2.76 (t, *J* = 6.9 Hz, 4H), 2.21 – 2.04 (m, 8H), 1.77 – 1.49 (m, 8H).

3. Inclusion Complex Formation.

Host (CD12 or CD14) and guest (AdSSPEG-OH or AdSSPEG-OMe) were combined in equimolar amounts (1.5 μmol) in a round bottom flask with DI water (≈ 2 mL) and sonicated (Ultrasonic Cleaner, GB-928) at 40 kHz for 30 min. The solvent was removed under reduced pressure and the supramolecular amphiphile was used for further experiments.

4. Critical Aggregation Concentration (CMC) via Fluorimetry.

Fluorimeter (Horiba Scientific, Fluorolog-QM) was set to spectra acquisition with λ_{ex} = 515 nm with a slit width of 7 nm and λ_{em} = 530 – 670 nm with a slit width of 7 nm for fluorescent probe nile red. Samples were prepared at a broad range of supramolecular amphiphile concentrations (0

– 500 μM) with nile red concentration held constant at 0.156 μg/mL. Samples were sonicated (Ultrasonic Cleaner, GB-928) at 40 kHz for 10 minutes and was then stored in vials for a few hours allow for equilibration. Fluorimeter measurements were taken in triplicate for each sample, and λ_{max} and the Fluorescence Intensity (CPS) at λ_{max} were recorded. Fluorescence intensity (CPS) at λ_{max} was plotted against amphiphile concentration (μM), the slope approaches 0 at the critical micelle concentration (CMC). Two linear fits were found before (0) and after (f) the CMC. Finding the intersection of these lines via Equation 1 will give CMC (x).

$$(mx + b)_f = (mx + b)_0 \qquad \textbf{Eq. 1}$$

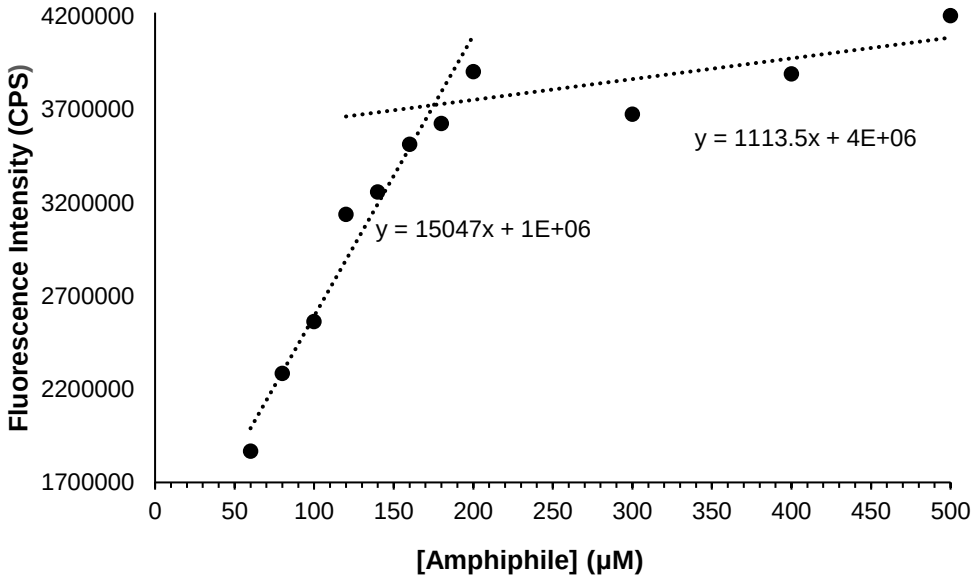


Figure S1: AdSSPEG-OMe guest CMC measured via fluorescence emission spectroscopy at approximately 638 nm at various concentrations of amphiphile and nile red held constant at 0.156 μg/mL. CMC was found to be 200.54 μM

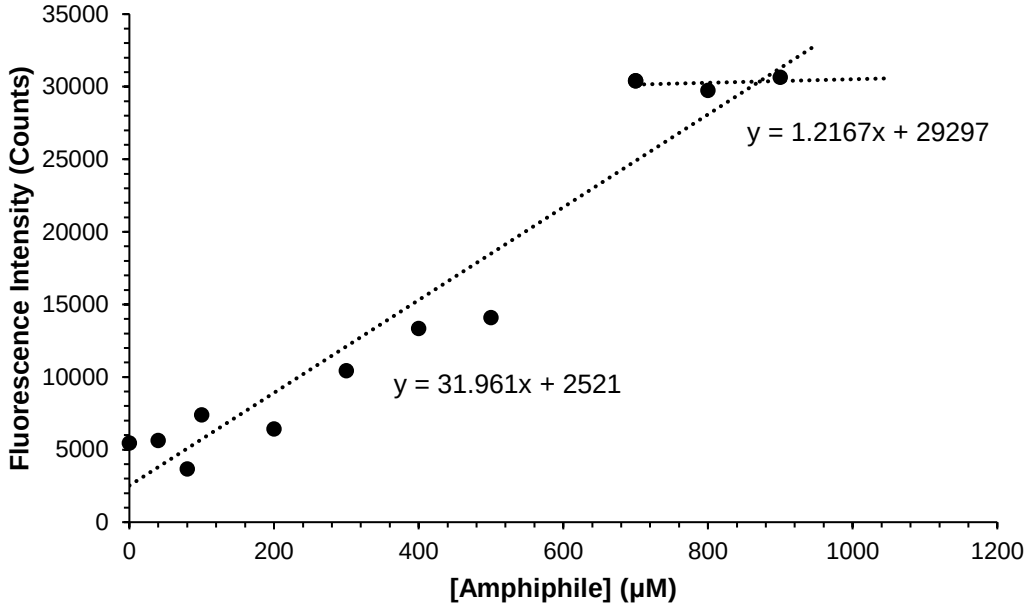


Figure S2: AdSSPEG-OH guest CMC measured via fluorescence emission spectroscopy at approximately 638 nm and various concentrations of amphiphile and nile red held constant at 0.156 μg/mL. CMC was found to be 870.9 μM.

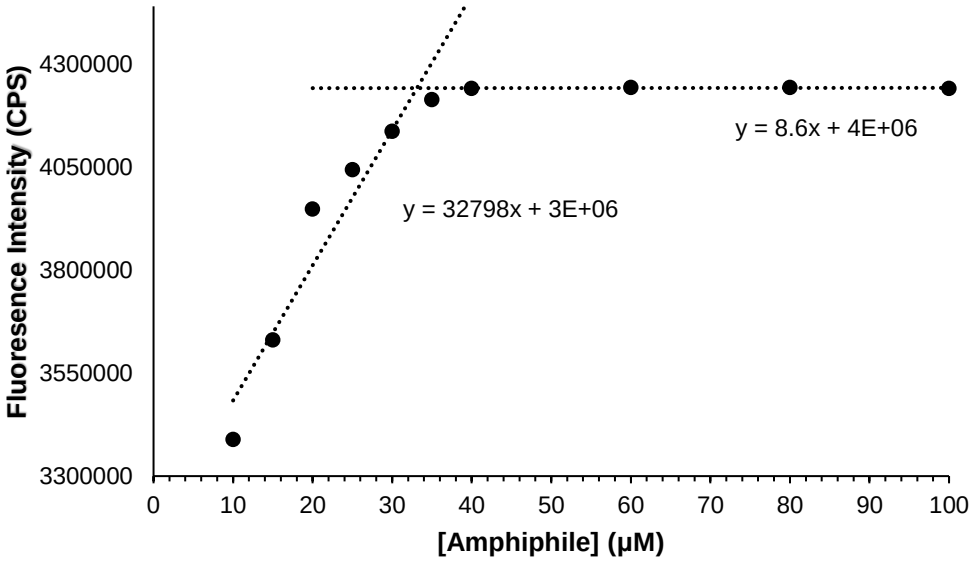


Figure S3: AdSSPEG-OMe:βCD-C12 inclusion complex CMC measured via fluorescence emission spectroscopy at approximately 638 nm and various concentrations of amphiphile and nile red held constant at 0.156 $\boldsymbol{\mu}$g/mL. CMC was found to be 30.50 $\boldsymbol{\mu}$M

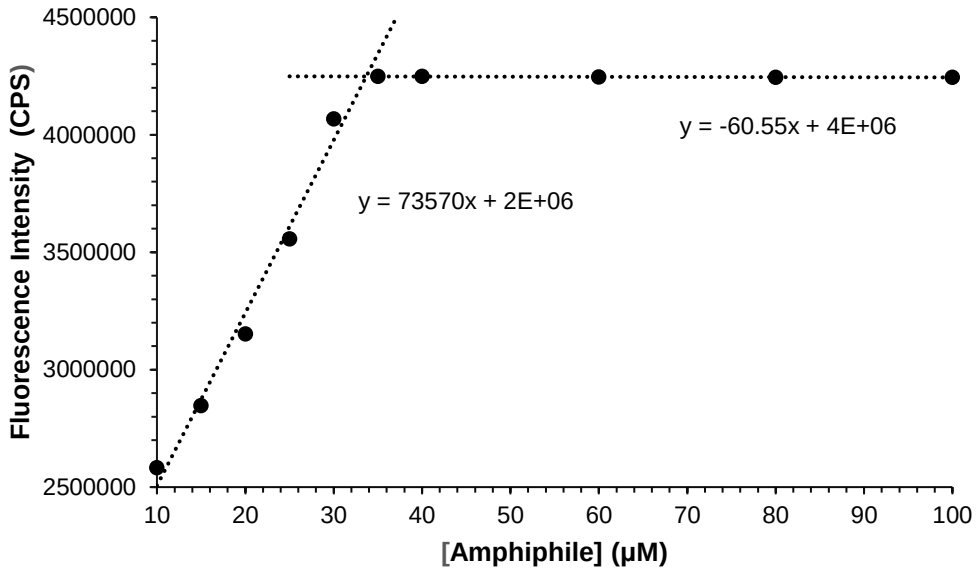


Figure S4: AdSSPEG-OMe:βCD-C14 inclusion complex CMC measured via fluorescence emission spectroscopy at approximately 638 nm and various concentrations of amphiphile and nile red held constant at 0.156 $\boldsymbol{\mu}$g/mL. CMC was found to be 27.16 $\boldsymbol{\mu}$M

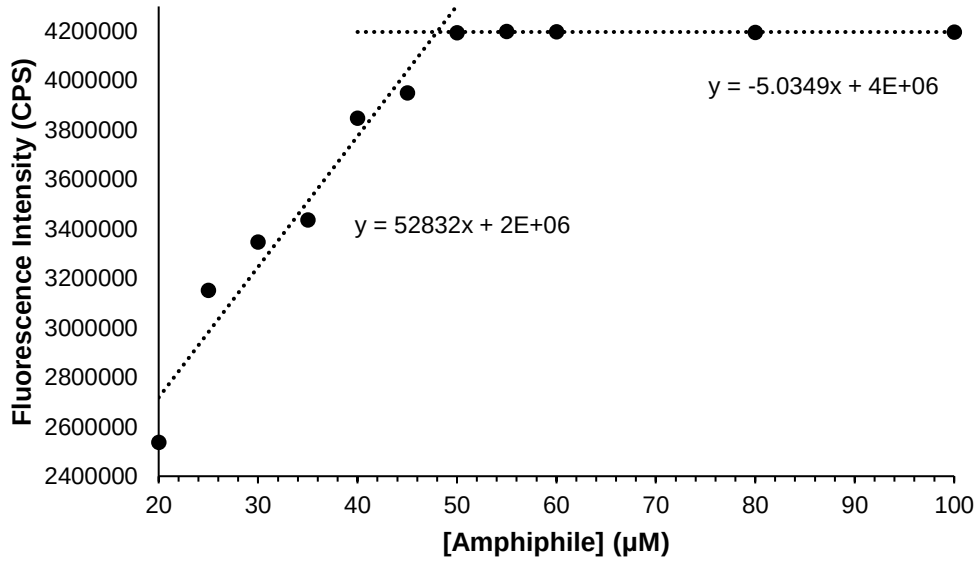


Figure S5: AdSSPEG-OH:βCD-C12 inclusion complex CMC measured via fluorescence emission spectroscopy at approximately 638 nm and various concentrations of amphiphile and nile red held constant at 0.156 μg/mL. CMC was found to be 37.85 μM

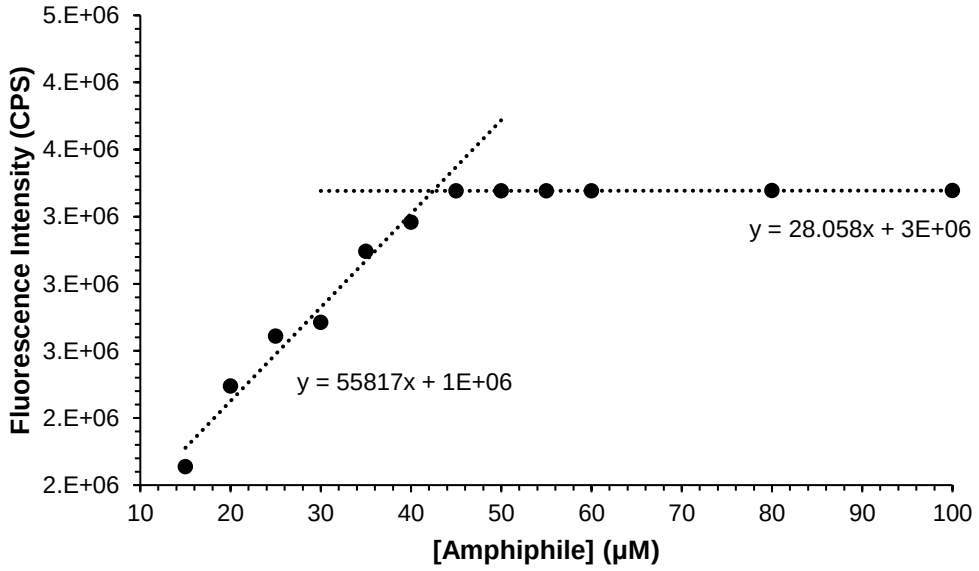


Figure S6: AdSSPEG-OH:βCD-C14 inclusion complex CMC measured via fluorescence emission spectroscopy at approximately 638 nm and various concentrations of amphiphile and nile red held constant at 0.156 μg/mL. CMC was found to be 35.97 μM

5. Vesicle Formation.

5.1 Vesicles in Tris Buffer.

Supramolecular amphiphile (1.5 μmol) was dissolved in 1:1 chloroform: DI water (≈ 2 mL total) and sonicated (Ultrasonic Cleaner, GB-928) at 40 kHz for 30 min. The solvent was removed under reduced pressure to afford the thin film inclusion complex. The thin film was rehydrated with Tris buffer (10 mM Tris base, 10 mM NaCl, pH 7.40, ≈ 1 mL) and allowed to sit for 30 min at room temperature. This buffer solution was subjected to five freeze-thaw (liquid nitrogen- 55 ℃ water bath), and was then probe sonicated (QSonica Sonicators, Ultrasonic Processor) at 20 kHz for 2 min. The solution was filtered through a 450 nm filter and then extruded (Avanti Polar Lipids, Inc.) ten times with a 200 nm pore size polycarbonate membrane.Purified vesicles were stable for up to 8 months, stored in the fridge.

5.2 Fluorescent Vesicle Formation.

Supramolecular amphiphile (1.5 μmol) was dissolved in 1:1 chloroform: DI water (≈ 2 mL total) and sonicated (Ultrasonic Cleaner, GB-928) at 40 kHz for 30 min. The solvent was removed under reduced pressure to afford the thin film inclusion complex. The thin film was rehydrated with 5,6-carboxyfluorescin (CF) buffer (50 mM CF, 10 mM Tris base, 10 mM NaCl, pH 7.40, ≈ 1 mL) and allowed to sit for 30 minutes at room temperature, subjected to freeze-thaw cycles (5×), probe sonicated (20 kHz, 2 min) and extruded (15×) through a polycarbonate membrane (pore size, 200 nm). Extravesicular components were removed by gel filtration (Sephadex G-50) with 10 mM Tris, 107 mM NaCl, pH 7.4 buffer as eluent

6. Vesicle Characterization.

6.1 Dynamic Light Scattering (DLS) Measurement.

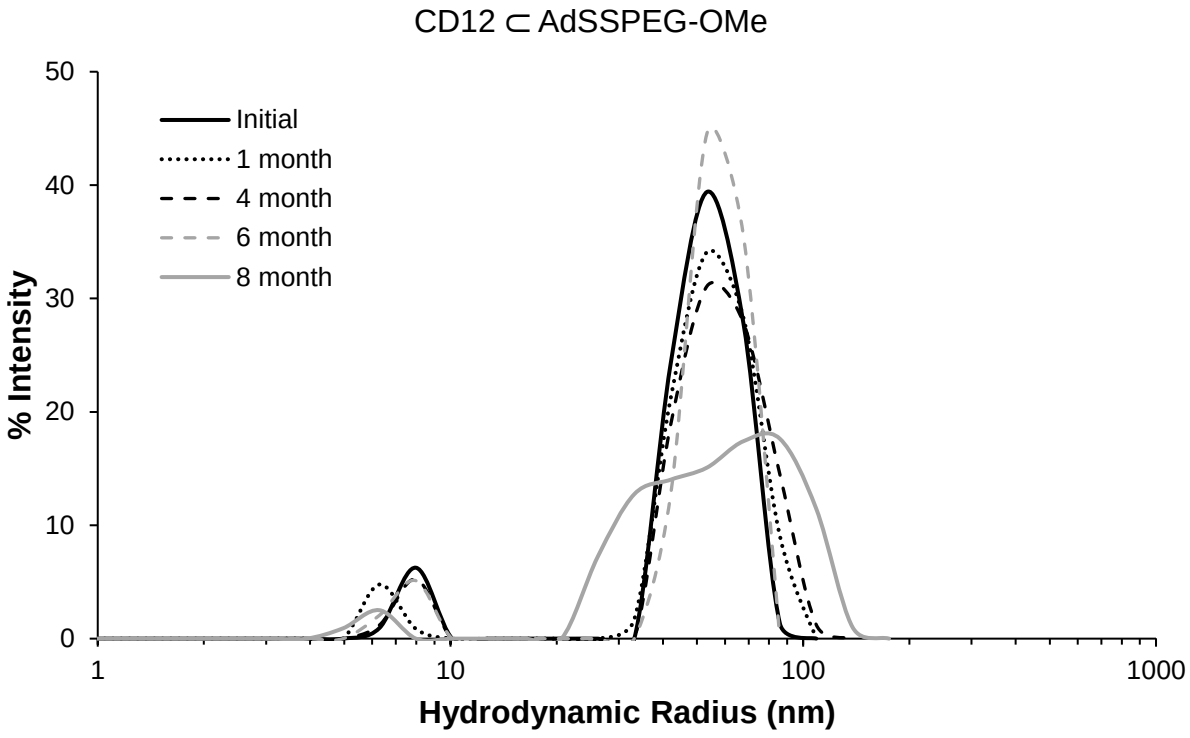


Figure S7: Hydrodynamic radius of CD12 ⊂ AdSSPEG-OMe vesicles over time.

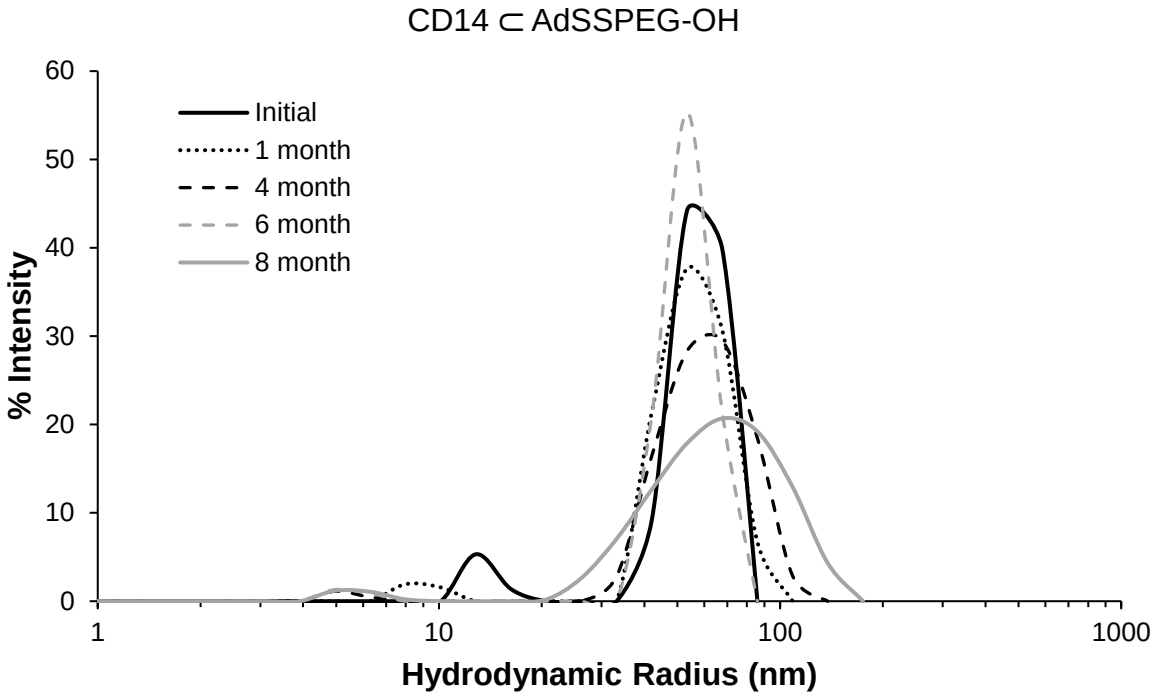


Figure S8: Hydrodynamic radius of CD14 ⊂ AdSSPEG-OH vesicles over time.

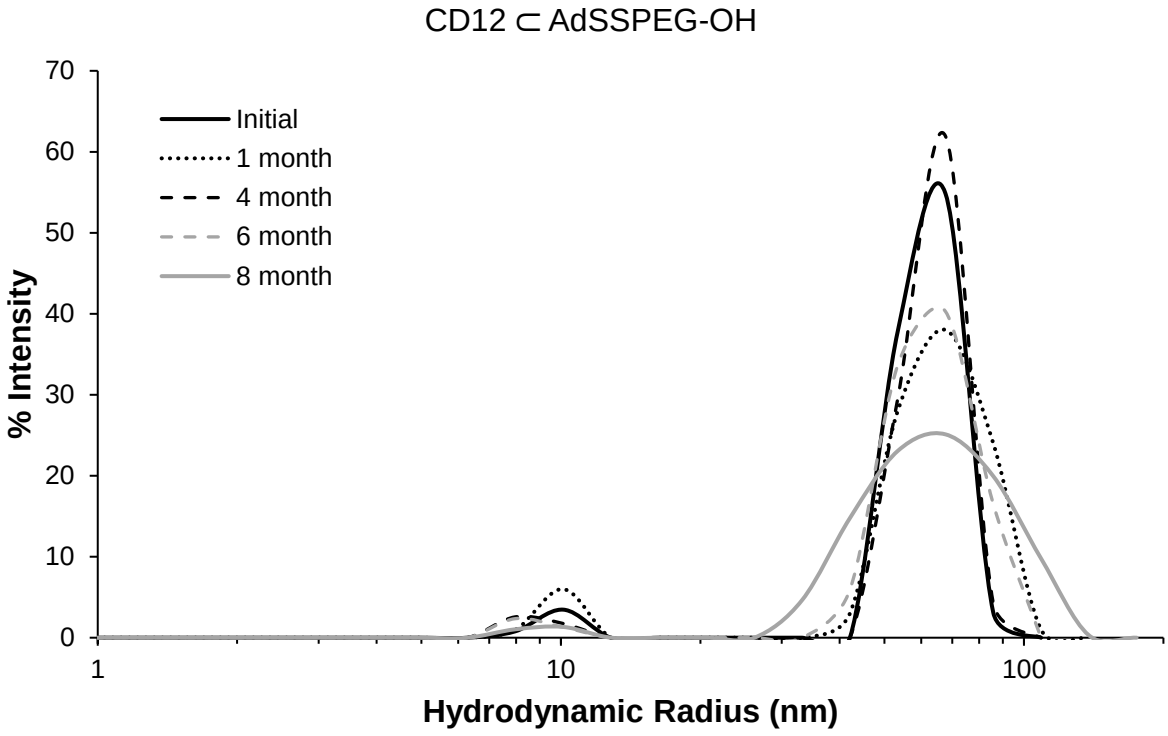


Figure S9: Hydrodynamic radius of CD12 ⊂ AdSSPEG-OH vesicles over time.

6.2 Fluorescent Vesicle Encapsulation and Lysing via Fluorimetry.

Fluorimeter (Horiba Scientific, Fluorolog-QM) was set to kinetics acquisition with λ_{em} = 517 nm with a slight width of 1 nm, and λ_{ex} = 492 nm with a slit width of 1 nm for fluorescent probe CF. Total run time was 90 sec with data collection every 0.1 sec. Fluorescent vesicles were diluted with Tris buffer (25 μL vesicles, 2000 μL Tris buffer) and allowed to equilibrate for 30 sec before measurements were taken. The kinetics acquisition was initiated, and a baseline was established for 30-40 sec before adding 250 μL of 10% Triton X-100 detergent to lyse the vesicles. The percent change in fluorescence intensity (%ΔFluorescence Intensity) was calculated using Equation 2, where I_f = Fluorescence Intensity (CPS) after lysing with Triton-X, and I_i = Fluorescence Intensity (CPS) at before lysing with Trition-X

$$\%\,\Delta Fluorescence\ Intensity = \frac{(I_f - I_i)}{I_i} * 100 \qquad \textbf{Eq. 2}$$

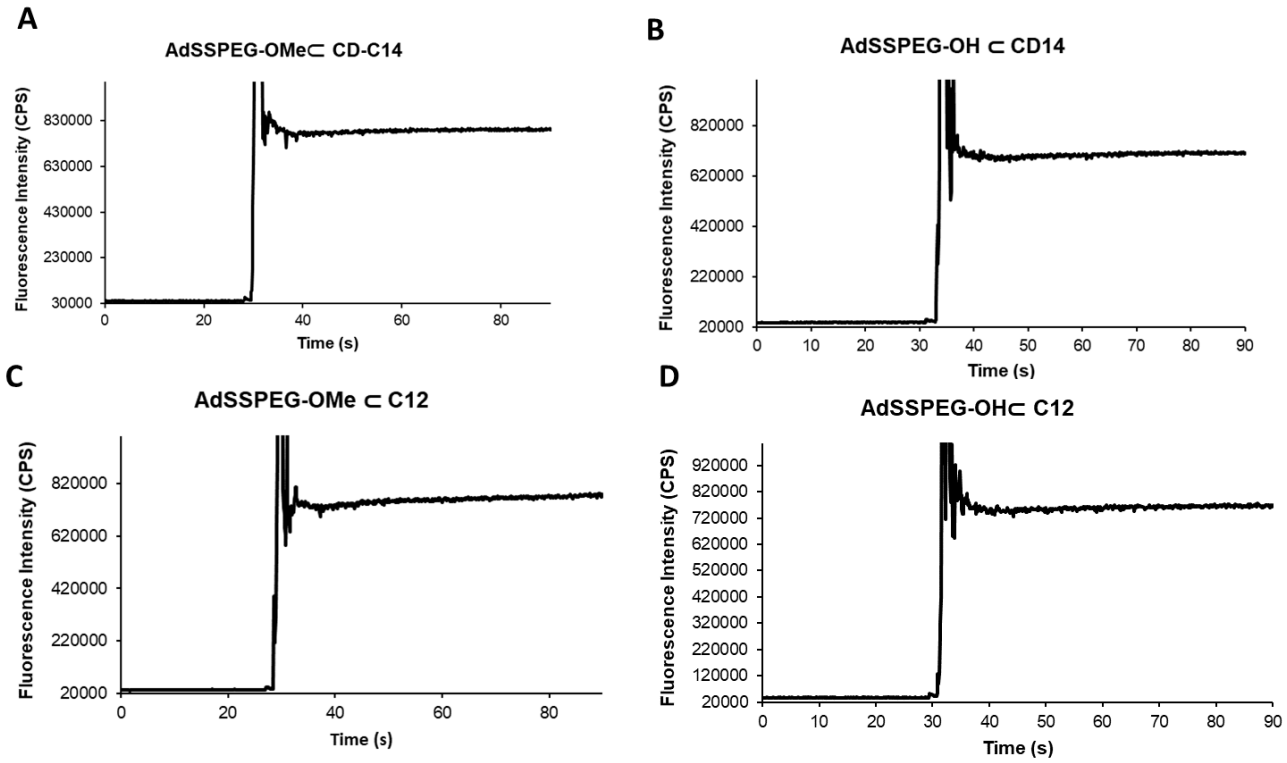


Figure S10: Lysing of 50 mM CF filled vesicles measured via fluorescence spectroscopy. At 30s, 250 µL 10% Triton X-100 was injected and the fluorescence intensity increased by A) 1875 % for **AdSSPEG-OMe ⊂ CD14**, B) 1758 % for **AdSSPEG-OH ⊂ CD14** C) 2203 % **AdSSPEG-OMe ⊂ CD12** and D) 2071% for **AdSSPEG-OH ⊂ CD12**.

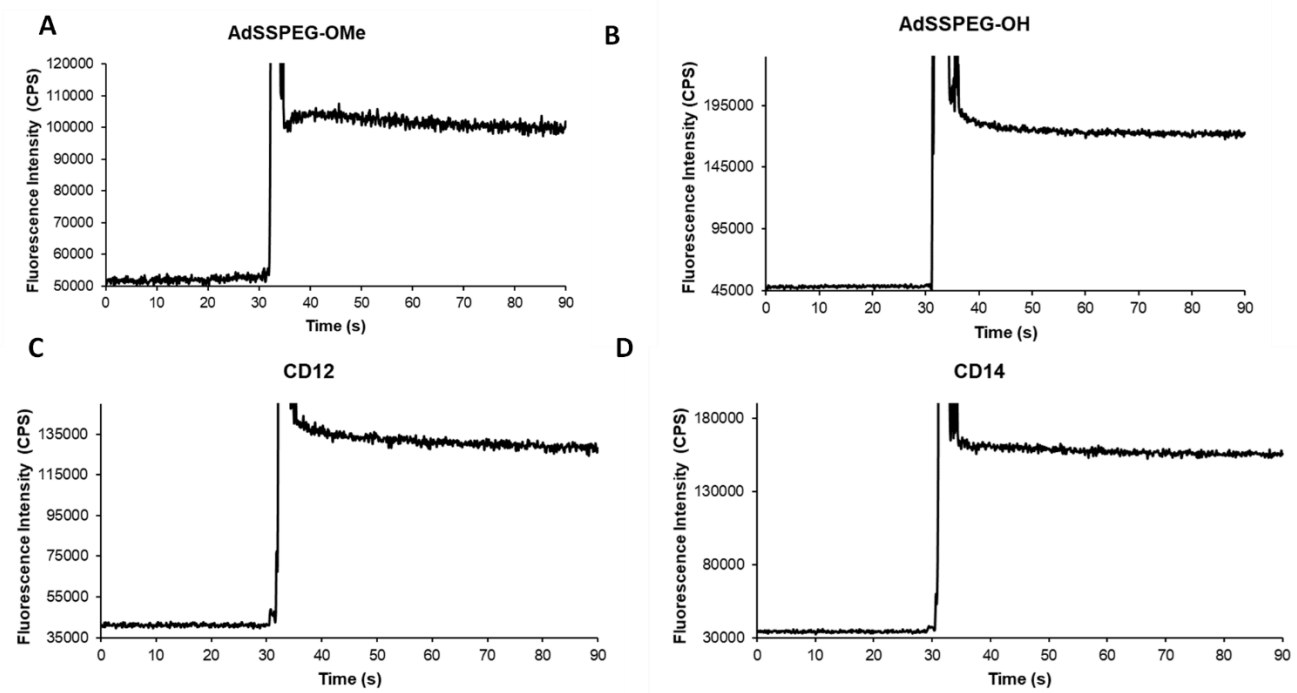


Figure S11: Lysing of **host** and guest components prepared in 50 mM CF, measured via fluorescence spectroscopy. At 30s, 250 µL 10% Triton X-100 was injected and the fluorescence intensity increased by **A)** 96% for **AdSSPEG-OMe, B)** 328 % for **AdSSPEG-OH, C) 204**% for CD12, and **D)** 370% for **CD14**

7. Vesicle Glutathione (GSH) Degradation via DLS.

Vesicles prepared according to section 4.1 (with the modification of Tris buffer pH = 8.5) were measured on DLS (Wyatt Tech, DynaPro NanoStar). Initial measurements were recorded, and then vesicle particle size stability was tested with intracellular and extracellular concentrations of glutathione (GSH). For intracellular [GSH] degradation experiments, a GSH buffer (500 mM GSH, 10 mM Tris base, 10 mM NaCl, pH 8.5) was prepared. A 25 μL aliquot of vesicles was added to a vial with 2000 μL of Tris buffer and 50 μL of GSH buffer to give a final [GSH] = 12 mM,.[57, 58] Samples were orbit mixed for 1 h, and then overnight (≈18 h), and measurements were taken at each time increment. For extracellular [GSH] degradation experiments, a GSH buffer (1 mM GSH, 10 mM Tris base, 10 mM NaCl, pH 8.5) was prepared. A 25 μL aliquot of vesicles was added to a vial with 2000 μL of Tris buffer and 40 μL of GSH buffer to give a final [GSH] = 20

μM.[57, 58] Samples were orbit mixed for 1 h, and then overnight (≈18 h), and measurements were taken at each time increment.

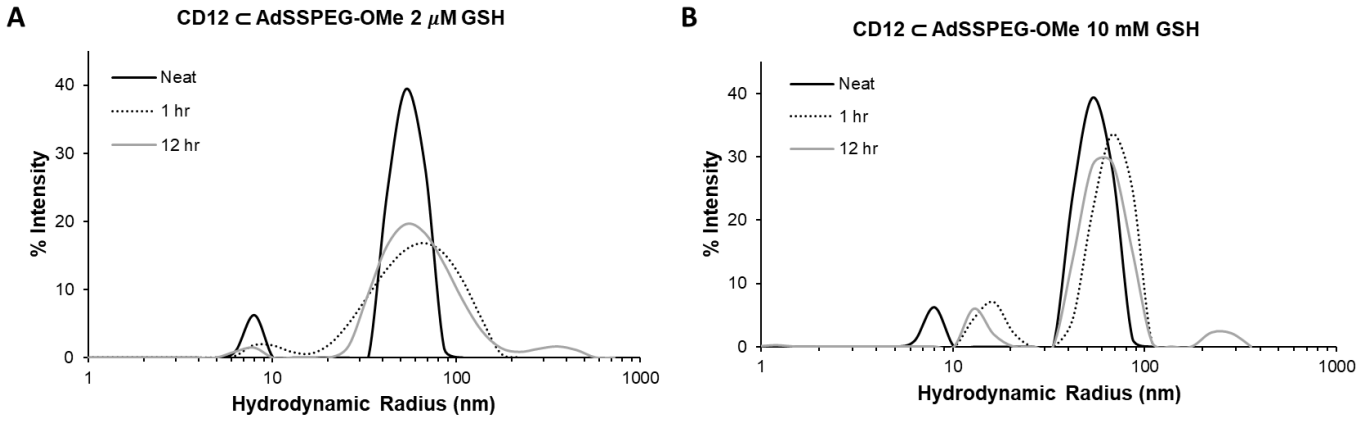


Figure S12: DLS monitoring of CD12 ⊂ AdSSPEG-OMe vesicles treated with A) extracellular and B) intracellular [GSH].

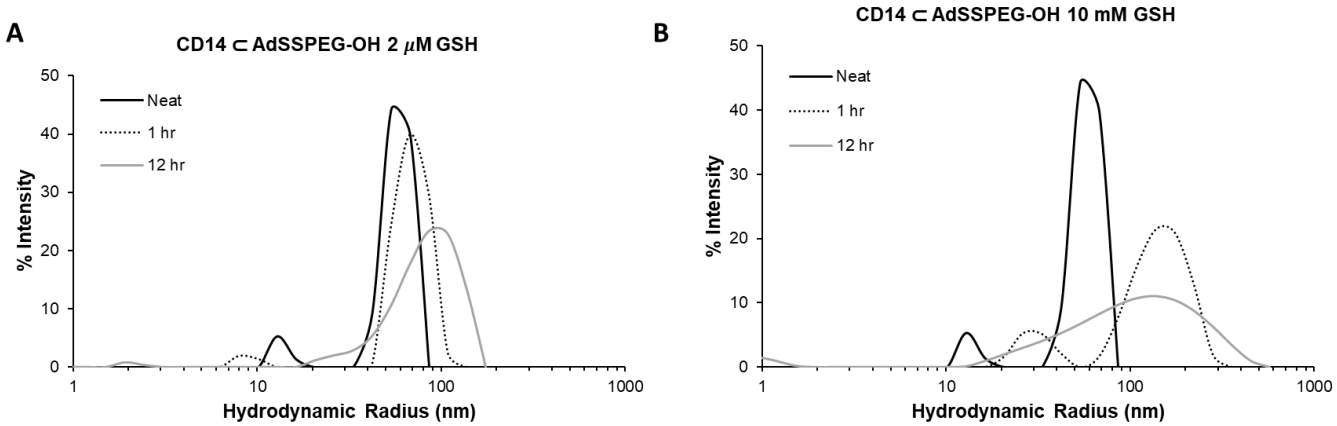


Figure S13: DLS monitoring of CD14 ⊂ AdSSPEG-OH vesicles treated with A) extracellular and B) intracellular [GSH].

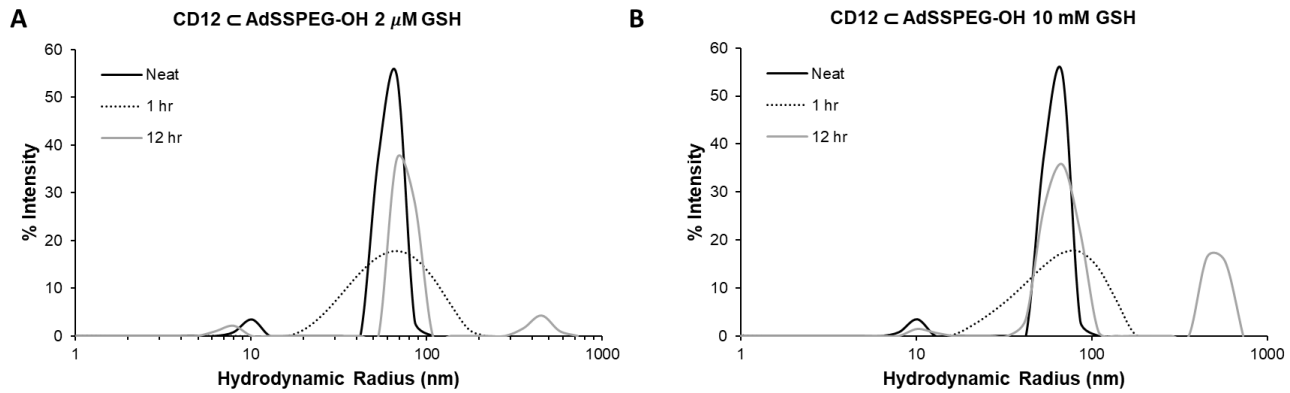


Figure S14: DLS monitoring of CD12 ⊂ AdSSPEG-OH vesicles treated with A) extracellular and B) intracellular [GSH].

8. Vesicle Glutathione (GSH) Degradation via Fluorescence Emission Spectroscopy

Fluorescent vesicles were prepared with 5,6-carboxyfluorescein (CF) according to section 5.2, with the modification of 3.75 μmol supramolecular amphiphile used. The percent change in fluorescence intensity of the vesicles was measured via fluorescence emission spectroscopy according to section 6.2. For intracellular [GSH] degradation experiments, a GSH buffer (500 mM GSH, 10 mM Tris base, 10 mM NaCl, pH 8.5) was prepared. A 921 μL aliquot of vesicles and 19 μL of 500 mM GSH buffer was added to a small glass container to give a final [GSH] = 10 mM. For extracellular [GSH] degradation experiments, a GSH buffer (1 mM GSH, 10 mM Tris base, 10 mM NaCl, pH 7.9 was prepared. A 938 μL aliquot of vesicles and 2 μL of 1 mM GSH buffer was added to a small glass container to give a final [GSH] = 2 μM. These two vesicle solutions were stirred at room temperature, for thirteen days. The percent change in fluorescence intensity of the vesicles was measured approximately daily.