Supporting Information to Accompany:

Peptoid-Directed Assembly of CdSe Nanoparticles

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Experimental Methods.

Materials.

All reactions and manipulations were conducted in ambient air in a well-ventilated fume hood using or on a benchtop as appropriate unless otherwise indicated. Acetonitrile (99.8%), cadmium sulfate 8/3-hydrate (>99%), L-cysteine (97%), ethyl alcohol (≥99.5%), hydrochloric acid (37%), 3-mercaptopropionic acid (≥99%), S-methyl-L-cysteine (>97%), selenium powder (99.5%), sodium hydroxide (98%), sodium sulfite (>98%) were purchased from Sigma-Aldrich Chemical Co. and used without further purification. 6-maleimidohexanoic acid (>98%) was purchased from Fisher Scientific and used without further purification. Deuterated chloroform (99.8%) and deuterium oxide (99.96%) were purchased from Cambridge Isotope Labs and used without further purification. 18.2 MΩ water was collected from an EMD Millipore purification system. All peptoids were synthesized and assembled by Bin Cai and Tengyue Jian at PNNL. UV−vis spectra were collected on a Cary 5000 spectrophotometer from Agilent.

Synthesis of Cysteine CdSe Magic-Sized Clusters.

The synthesis of CdSe MSCs is adapted from Park et al[1]. In a reflux setup, 12 mL water, 0.239 g Na_sSO_3, and 0.05 g Se powder were heated to 90 °C with stirring. The reaction was allowed to proceed in the dark overnight at a constant temperature at 90°C. The resulting Se^{2-} solution must be kept at 90 °C until use and must be used within two days for best results. In a separate Erlenmeyer flask, 10 mL of water and 1.754 g of L-cysteine (7.3 mmol) were mixed and then NaOH (1 M) was added until the solution reached pH 12 (~15 mL). This was necessary to ensure complete deprotonation of the cysteine. It is important to add NaOH to the cysteine suspension to limit disulfide bond formation. The solution was stirred for 30 min until clear and colorless. A 5 mL Cd^{2+} solution (0.15 M, 0.75 mmol) was added dropwise and stirred for an additional 30 min until clear. The resulting solution was then adjusted to a total volume of 46.25 mL. After the solutions were prepared, 3.75 mL of Se^{2-} solution (0.188 mmol) was rapidly injected into the flask containing Cd-cys. The solution was stirred in the dark for 1 h and then was heated to 40 °C for 20 min. The reaction progress was monitored via UV-Vis absorption spectroscopy. After cluster growth was complete, the clusters were precipitated using acetonitrile (2:1, acetonitrile: cluster solution) and the clusters were allowed to settle out of solution

overnight. This was done to avoid cluster aggregation induced by centrifugation. The colorless supernatant was then decanted and the pellet containing the clusters was resuspended in 10 mL of water. The clusters were stored in the dark. The purified clusters showed an absorption maximum at 420 nm and had a diameter of 2.23±0.32 nm by TEM analysis.

Synthesis of Cysteine CdSe Quantum Dots.

In a 3-neck 50 mL round bottom flask equipped with a condenser, thermowell, and rubber septum, 25 mL of crude CdSe MSCs are added without further dilution or ligand addition. The solution was heated to reflux (100 °C) and the reaction was monitored via UV-Vis spectroscopy. The reaction was allowed to proceed for 4 h until the spectra no longer changed and a final peak maximum around 540 nm was achieved. The resulting material was purified via precipitation using acetonitrile (2:1 acetonitrile:QD solution), followed by centrifugation for 10 min at 7600 rpm. The resulting QD pellet was suspended in minimal water (10 mL) and the precipitation process was repeated. The material was centrifuged for a total of 5 cycles and the final pellet was suspended in water and stored in the dark at room temperature. The resulting QDs showed an absorption maximum at 540 nm with a diameter of 2.90±0.62 nm by TEM analysis.

Synthesis of Mercaptopropionic Acid CdSe Nanoparticles.

Mercaptopropionic acid (MPA) capped CdSe particles were synthesized using the same conditions as above. In the synthesis of the starting MSCs MPA was substituted for cysteine. The resulting MSCs were purified using 5 cycles of precipitation and redissolution cycles with ethanol. The resulting MPA-capped MSCs showed a broad absorption at 420 nm with TEM showing a large amount of aggregation upon drying. MPA QDs were synthesized as detailed above and purified using ethanol as the precipitant. The resulting QDs showed two broad absorption features at 445 and 475 nm with a diameter of 2.77±0.70 nm by TEM analysis.

Synthesis of S-methyl-L-cysteine CdSe Nanoparticles.

The procedure was the same as described above but substituting S-methyl-L-cysteine (SMLC) for cysteine in the synthesis of the starting MSCs. Instead of isolating MSCs after 4 h, the reaction was continued overnight. The resulting particles were QDs with no MCSs isolated. The SMLC particles were purified using both ethanol and acetonitrile for a total of 10 cycles of precipitation and redissolution. The final material showed an absorption maximum at 592 nm and diameter of 2.96±0.86 nm by TEM analysis.

General procedure for peptoid-CdSe conjugation.

The peptoids were made and assembled following the procedure by Jin et al[2,3]. Conjugation was performed at room temperature by diluting the peptoid stock solution (10 μL, 1 mM) in 45 μL of water (pH 6) followed by the addition of 5 μL of CdSe QDs (2.5×10^{14} particles/mL, pH 6). The sample was allowed to incubate for at least 1 h. Imaging was then performed with no further purification or dilution.

TEM sample preparation and analysis.

TEM images were collected on a FEI Tecnai G2 F20 microscope operated at 200 keV for bright field and STEM. Samples were prepared by drop-casting 5 μL of sample onto a suspended ultrathin carbon film on lacey carbon support film, 400 mesh, copper grids purchased from Ted

Pella Inc. The samples were allowed to dry in air for 20 min on the grids before dabbing excess water off and drying completely on a Kimwipe. Before imaging, the grids were placed in a desiccator for at least 2 h. TEM analysis was performed using manual analysis with the help of ImageJ. Histograms, average sizes, and standard deviations for CdSe QDs and MSCs were obtained by manual analysis of over 200 particles per sample. EDX analysis was performed at PNNL by Guomin Zhu on an aberration-corrected Titan 80-300™ scanning/transmission electron microscope (S/TEM).

AFM analysis.

AMF images were collected on an Asylum Research Cypher in non-contact mode with SNL-10 probes purchased from Bruker AFM Probes. AFM was performed on fixed TEM grids prepared as detailed above.

NMR analysis.

^{1}H NMR spectra were recorded on 300 and 500 MHz Bruker Advance spectrometers. All samples were run with 10 scans and a delay time of 30 s. $Cd(MPA)_2$ was prepared following the standard CdSe procedure detailed above, stopping prior to the addition of the Se^{2-} solution. The $Cd(MPA)_2$ complex was isolated via precipitation and redissolution with EtOH (3:1, EtOH : Cd-MPA solution) and centrifugation. The complex was resuspended in water and lightly purified with two additional precipitation and redissolution cycles and the resulting pellet was then fully dried. The complex was resuspended in minimal D_2O and purity was confirmed via ^{1}H NMR spectroscopy. 6-maliemidohexanoic (EMCA) was used as a maleimide source for binding with MPA. 0.25 equivalents of EMCA relative to $Cd(MPA)_2$ was added via solid addition to avoid solubility issues with EMCA in water. After every addition the tube was shaken well for 30 s prior to analysis. Up to about 4 equiv. of EMCA was added to solution before the saturation point of EMCA in water was reached.

Supplemental Data.

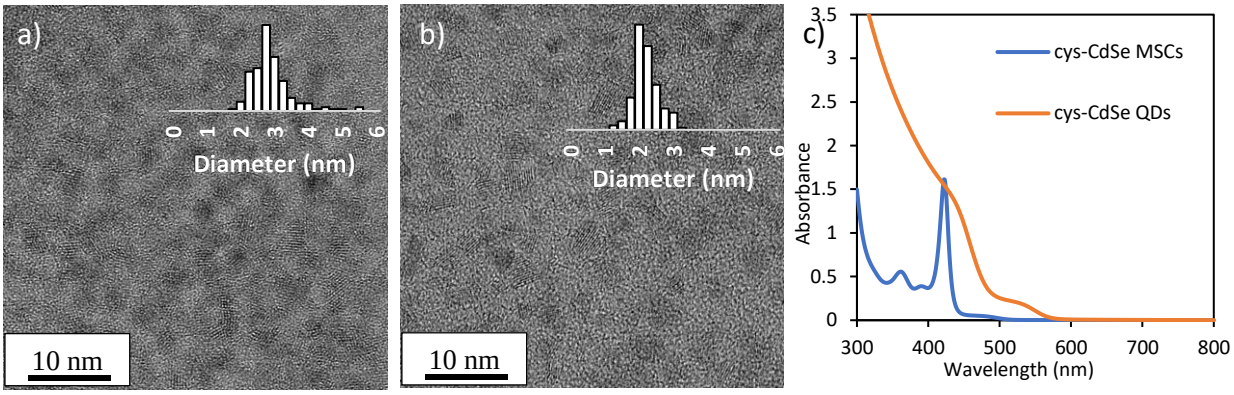

Figure S1. Representative TEM images with size distributions of cysteine-capped CdSe QDs, 2.90 ± 0.62 nm (a) and clusters 2.23 ± 0.36 nm (b). Representative UV-Vis absorption spectra of CdSe QDs and clusters (c).

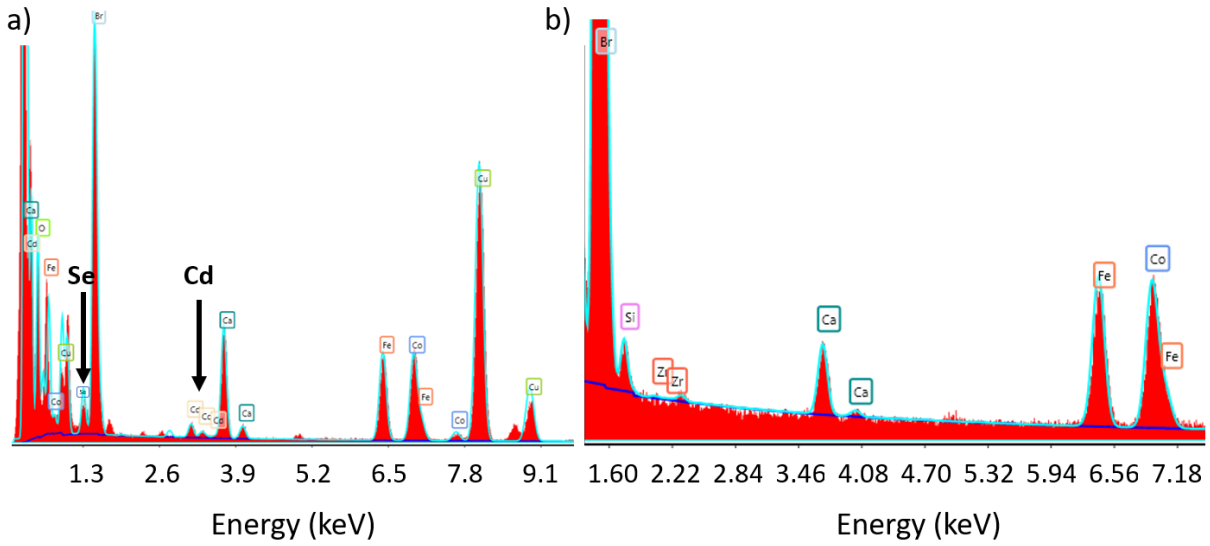

Figure S2. (a) EDX point scans of peptoid-CdSe QD conjugates showing Cd, Se peaks from QDs and Br peak from the peptoid. (b) Peptoid nanostructures alone with no Cd or Se peaks. Fe, Co, and Ca peaks are from impurities in the column. Cu peak from the TEM grid.

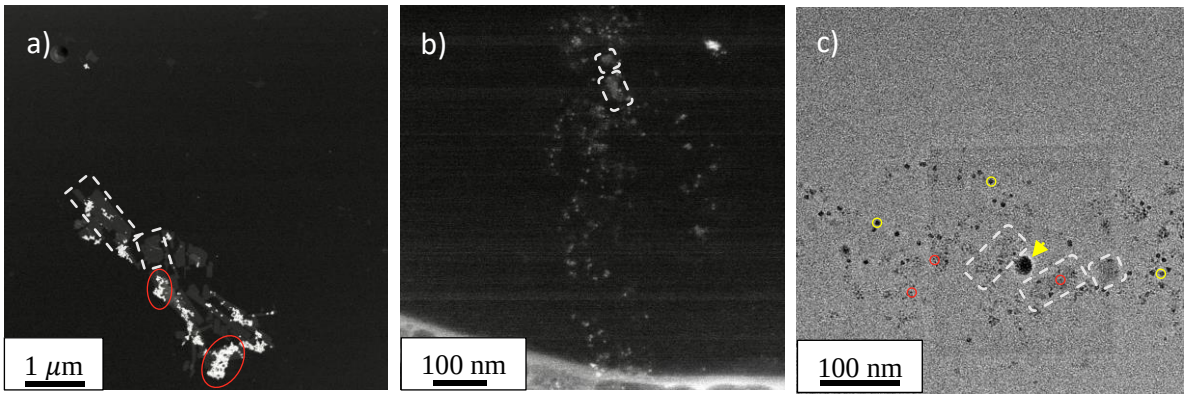

Figure S3. Peptoid sheets with cys-CdSe QDs with peptoids at pH 6 (a) and at pH 7 (b,c). Peptoid sheets maintain stability at pH 6 with large rectangular shape (white) but QDs become aggregated (red). At pH 7 peptoid sheets become rounded and shrunk (white) but QDs are dispersed and unaggregated (red). Larger QDs seen are an impurity from TEM sample prep (yellow) and some beam damage from STEM (yellow arrow).

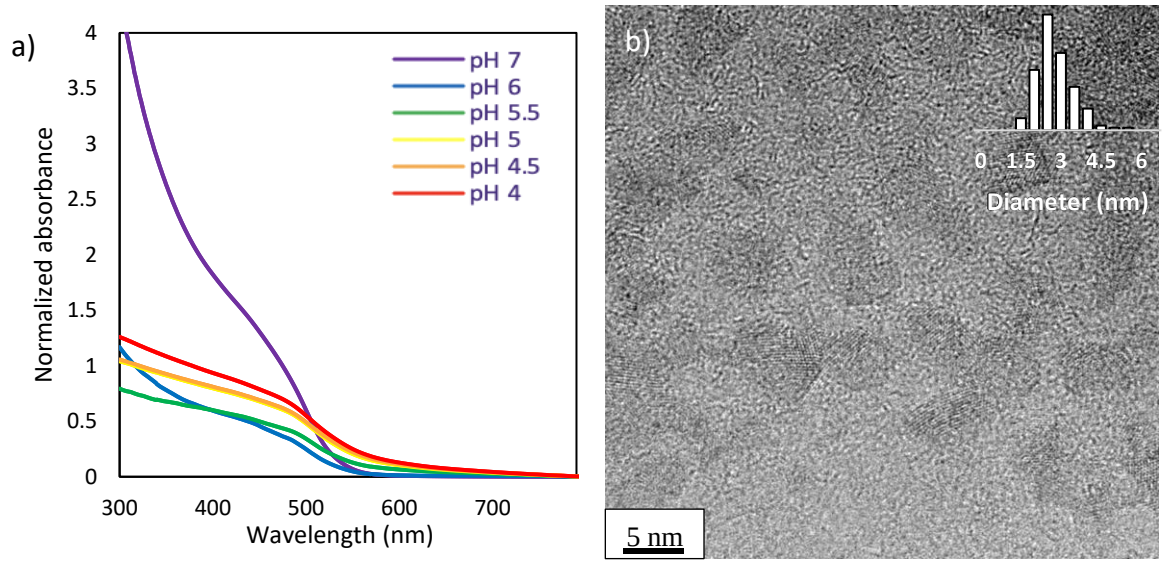

Figure S4. MPA-capped CdSe QDs titrated from pH 7 to 4 monitored by UV-Vis with absorption features at 444 and 494 nm maintained down to pH 5.5 (a). TEM shows further stability with minimal size change after incubation at pH 6 overnight, 2.77±0.70 nm (b). The particles show more facets than seen with cys-CdSe, likely due to the less dense particle coverage on the TEM grid for MPA-CdSe allowing for HRTEM of the particles.

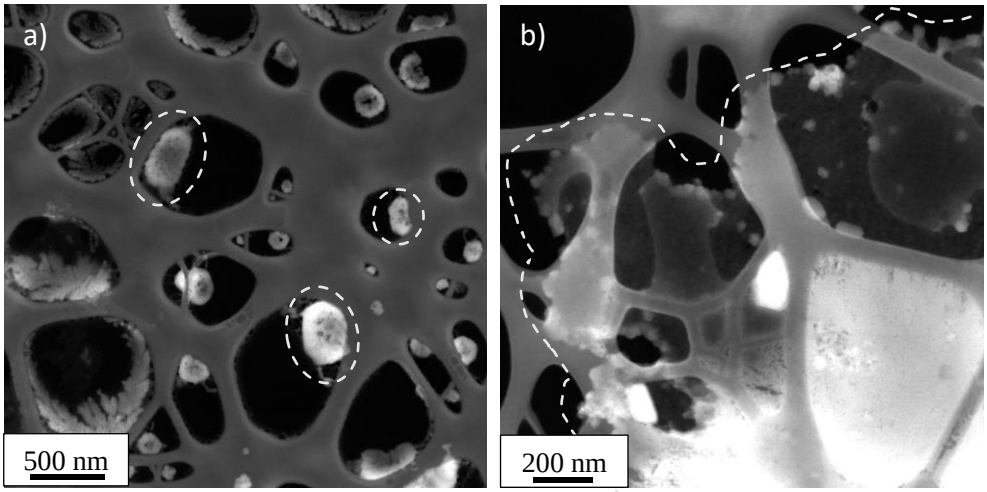

Figure S5. Peptoid sheets (10% MA) incubated at pH 7 overnight. Sheets (white) show shrunken size and rounded shape (a) and large amorphous areas of organic material with rounded edges (b).

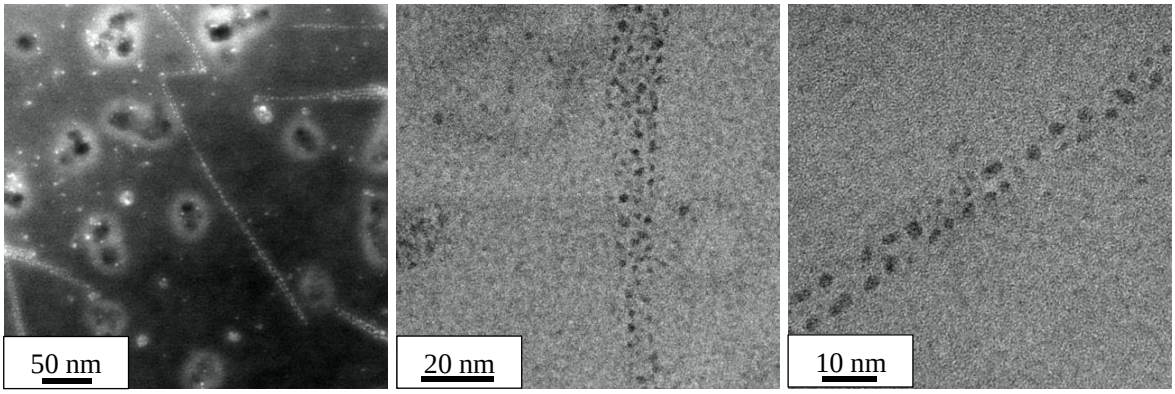

Figure S6. Conjugation under basic conditions between QDs and peptoid sheets leading to fibril peptoid morphologies.

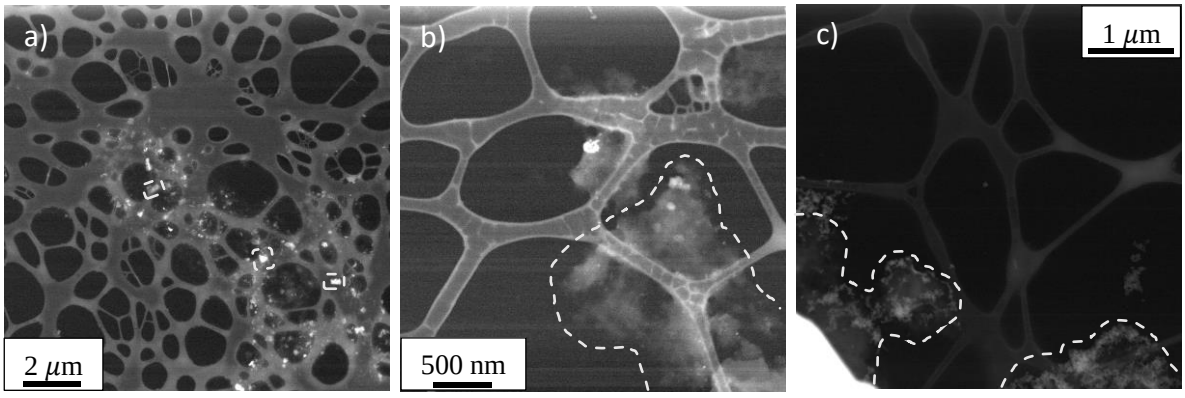

Figure S7. Destabilization of conjugated peptoid sheets with increasing maleimide content at 20 (a), 50 (b), and 80% MA (c). 20% MA keeps the rectangular peptoid shape but at 50 and 80% MA the sheets lose definition and become amorphous. Sheet edges are highlighted with dashed-white lines.

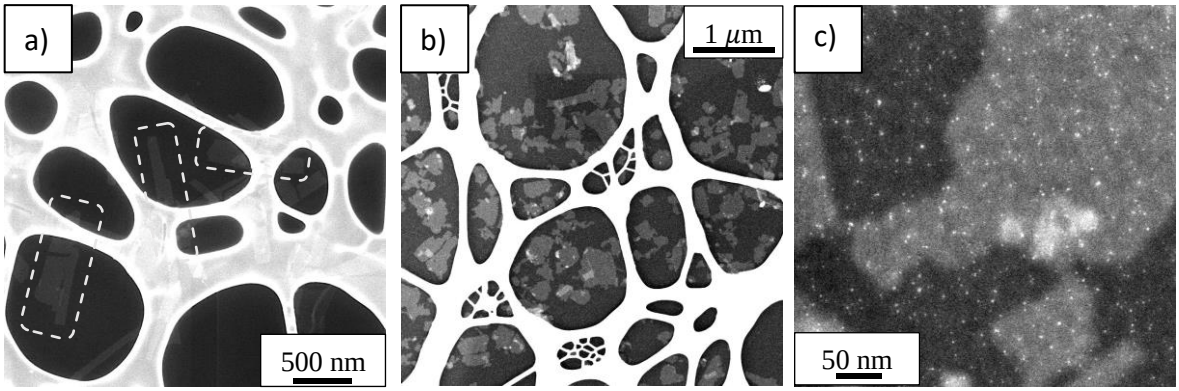

Figure S8. Unstained peptoid sheets (white dashed line) without QDs present showing well defined edges and no destabilization from the electron beam or vacuum (a). Peptoid sheets with unbound QDs present showing maintained sheet integrity under the electron beam and vacuum (b,c).

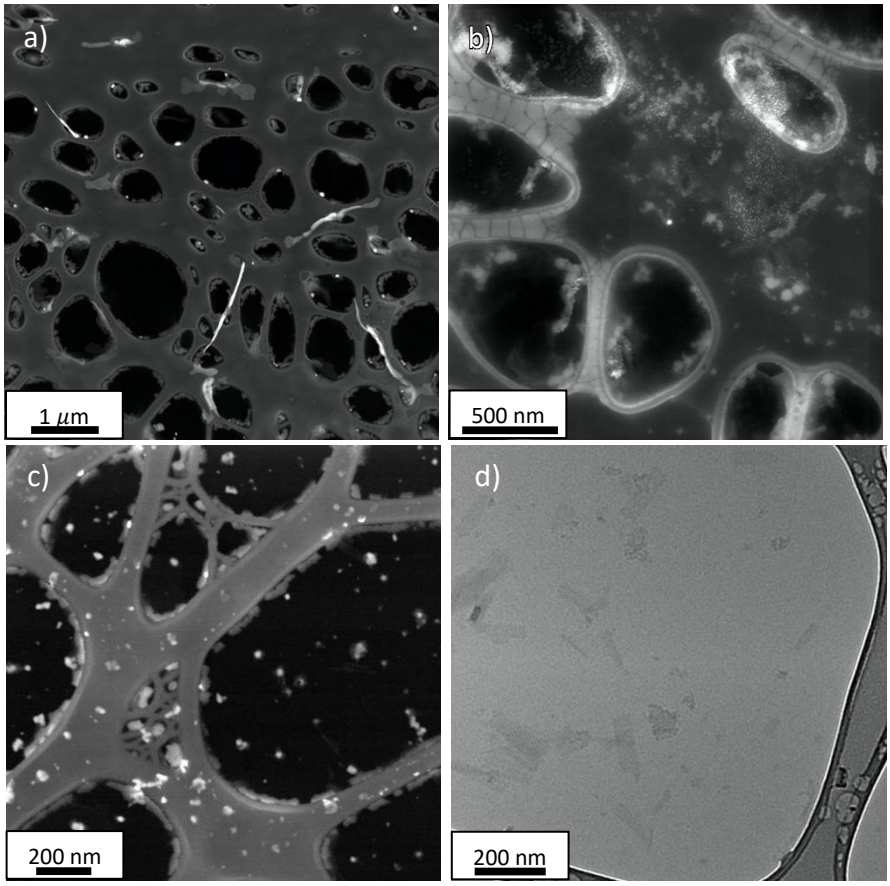

Figure S9. Representative TEM imgaes of CdSe-peptoid conjugates after conjugation with varying degrrees of destabilization observed from sample to sample. For each sample, CdSe QDs capped with MPA (a-c) or cysteine (d) were conjugated with a maleimide content of 10% (a,b), 20% (c), and 50% (d).

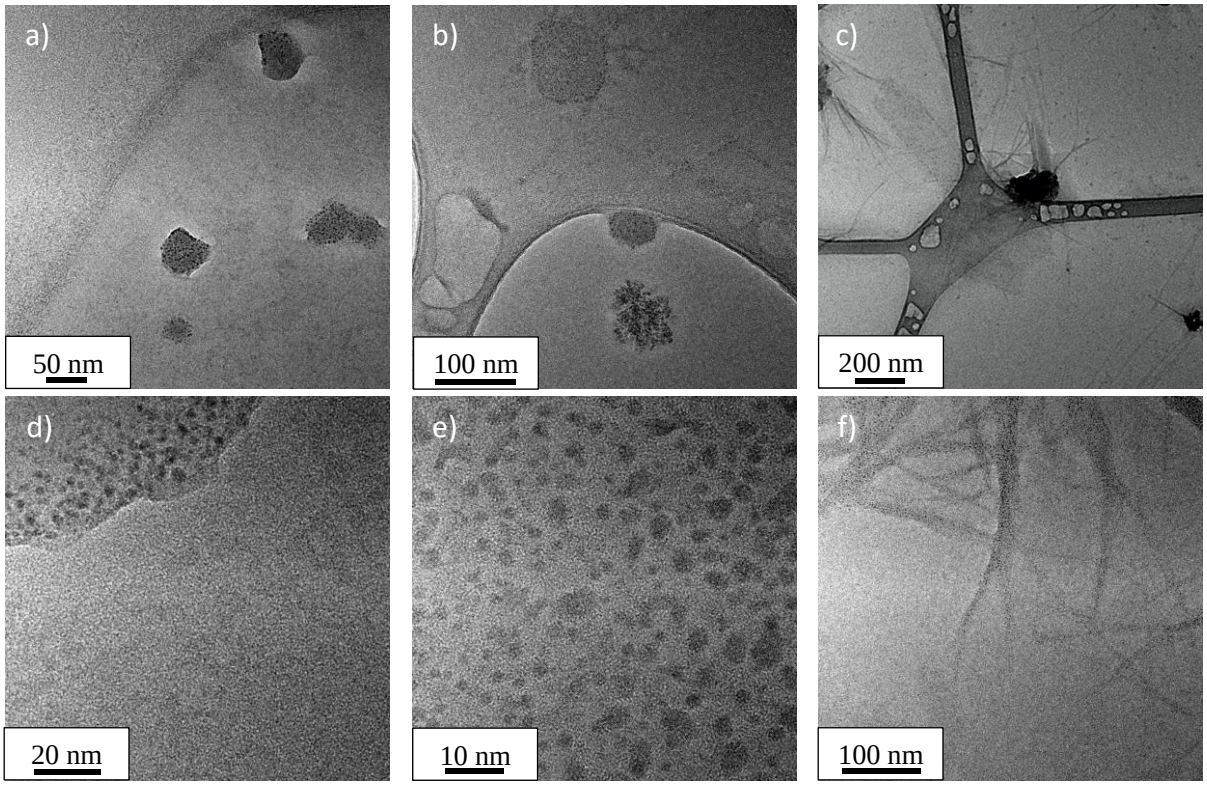

Figure S10. Peptoid sheets conjugated with cys-CdSe at 20 (a,d), 50 (b,e) and 80% MA (c,f). No difference in particle coverage is seen between 20-80% MA. Conjugation was performed at pH 7 leading to peptoid shrinkage and rounding (a,b) and fibril like morphology (c,f). High preference for QD attachment to the peptoid was observed.

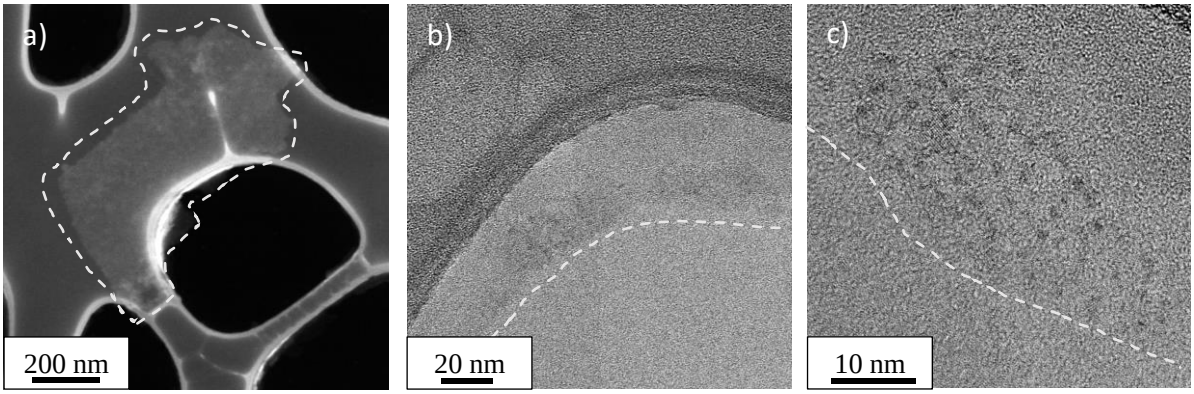

Figure S11. 2.5% MA peptoid sheets with MPA-CdSe QDs showing localization of QDs at the peptoid edges. The peptoid sheet maintained the large rectangular size (a) but QDs only appeared at the edge of the peptoid sheets (b,c). Peptoid edges are highlighted by white dashed lines.

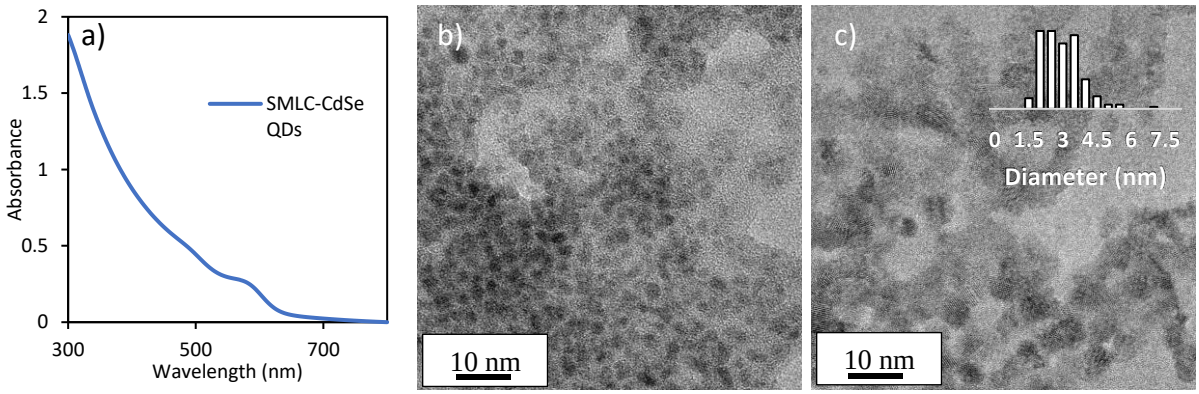

Figure S12. Purified CdSe QDs capped with S-methyl-L-cysteine with one broad absorption feature (a) and two populations via TEM with average size of 2.96 $\pm$ 0.86 nm (b,c).

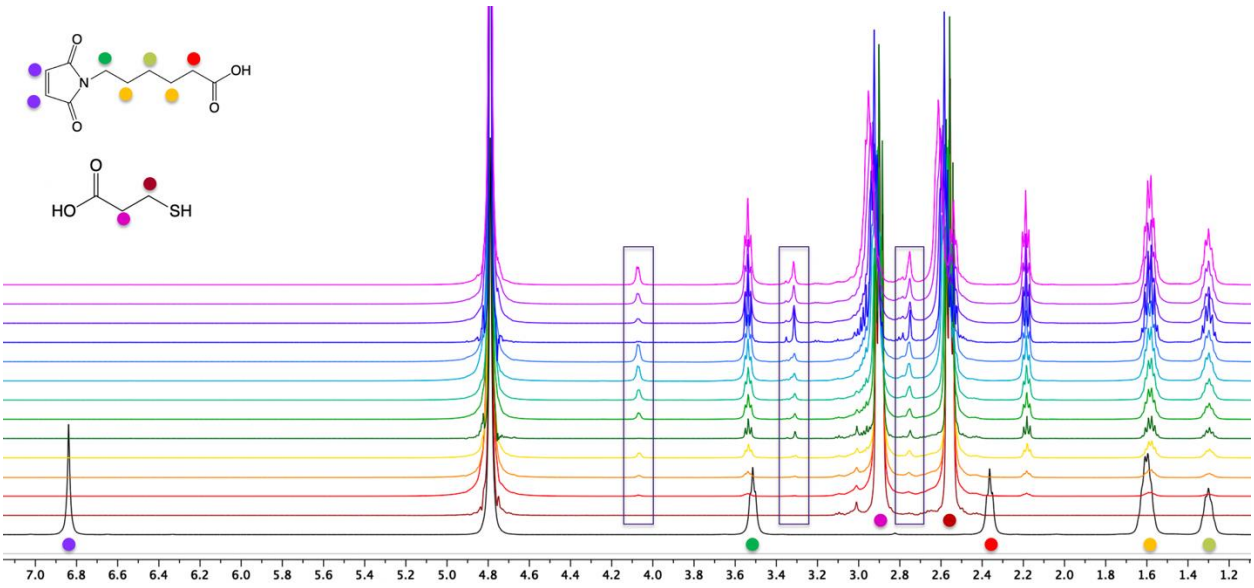

Figure S13. Full NMR spectra of Cd-MPA with EMCA additions showing no unbound maleimide. Growth of peaks associated with successful conjugation highlighted in black.

Table S1. Integrations of Cd-MPA complex with EMCA additions. Integrations are normalized to the EMCA backbone peak at 2.18 ppm with an integration of 2.

Equiv. EMCA added	MPA peak 1 (2.56 ppm)	MPA peak 2 (2.90 ppm)	New peak (2.54 ppm)
0	2.03	2	
0.24	352.37	353.07	
0.59	180.79	181.47	
1.06	169.75	169.97	
1.53	68.41	68.54	
2.00	55.23	55.75	
2.52	19.22	19.53	
2.77	14.55	14.68	
3.02	12.89	12.85	
3.27	8.12	10.82	2.94
3.56	6.82	9.06	2.33
3.85	5.89	7.88	2.22

References.

1. Y.-S. Park, A. Dmytruk, I. Dmitruk, A. Kasuya, Y. Okamoto, N. Kaji, M. Tokeshi and Y. Baba, *J. Phys. Chem. C*, 2010, **114**, 18834–18840.
2. H. Jin, F. Jiao, M. D. Daily, Y. Chen, F. Yan, Y.-H. Ding, X. Zhang, E. J. Robertson, M. D. Baer and C.-L. Chen, *Nature Commun.*, 2016, **7**, 12252.
3. H. Jin, Y.-H. Ding, M. Wang, Y. Song, Z. Liao, C. J. Newcomb, X. Wu, X.-Q. Tang, Z. Li, Y. Lin, F. Yan, T. Jian, P. Mu and C.-L. Chen, *Nature Commun.*, 2018, **9**, 270.