

Supporting Information

- 1 Water-soluble multidentate polymers compactly coating Ag₂S quantum dots
2 with minimized hydrodynamic size and bright emission tunable from red to
3 second near-infrared region

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13 Materials.

Abbreviation	Full name	Abbreviation	Full name
PAA	poly(acrylic acid), M _w =1750	NHS	N-hydroxysuccinimide
Fmoc-EDA	N-Fmoc-ethylenediamine	DIC	N,N'-diisopropylcarbodiimide
BME	β-mercaptoethanol	DMF	dimethylformamide
		DMSO	dimethylsulfoxide

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15 Part S1. The preparation of multidentate polymers

16 Preparation

17 Briefly, 1 g of PAA (~14 mmol of carboxylic acids) was dissolved with 25 mL DMSO, and placed in a 100 mL
18 three-necked flask. After 24 h stirring at 35 °C, cysteamine (0.18 g, 2.4 mmol) and Fmoc-EDA (0.68 g, 2.4 mmol)
19 were dissolved in 10 mL DMSO, and the resultant mixed solution was added to the above flask. The mixture in this
20 flask was protected from light and bubbled with N₂ flow for 30 min at 35 °C. Then, NHS (1 mg, 9 mmol) dissolved
21 in 5 mL DMSO was added. After that, DIC (0.74 g, 5.8 mmol) was added slowly over the course of 40 min under
22 vigorous stirring. The reaction mixture was bubbled with N₂ flow for additional 30 min, and then the reaction was
23 allowed to proceed for 7 days at 40 °C in the dark. Afterward, 15 mL of piperidine was added, the reaction solution
24 was stirred for 4 h to deprotect the primary amines. BME (0.5 g, 6.4 mmol) was added to quench the reaction, and
25 the solution was stirred for additional 2 h at 40 °C, followed by cooling it to room temperature and filtering.

26 The resultant solution was condensed to 4 mL at 45 °C using a rotary evaporator, and the products (multidentate
27 polymers) were precipitated with the mixture of ice-cold acetone/chloroform (v/v, 2/1), and then were isolated *via*
28 centrifugation. The polymers were dissolved in 5 mL DMF, filtered and precipitated with acetone/chloroform again.
29 The polymers were treated repeated three times, and finally were washed with acetone, dried in vacuum, and stored
30 under N₂ atmosphere.

31 Determination of Reactive Thiols and Amines

32 Using fluorescamine and Ellman's reagent, the reactive amines and thiols of the freshly prepared polymers were
33 analyzed. For the determination of amines, fluorescamine dissolved in DMSO (10 mg/mL) and glycine standards
34 dissolved in deionized water (0.1 μm-1.0 mM) were freshly prepared, respectively. In detail, 0.4 mL water, 25 μL
35 of sodium borate buffer (1 M, pH 8.5), 50 μL samples or standards, and 14 μL of fluorescamine solution were
36 mixed together. After stirring for 20 min in the dark, fluorescence intensity (at 470 nm) of mixture solution was

Supporting Information

1 measured (excited at 380 nm). The polymers (10 $\mu\text{g/mL}$) were analyzed immediately after dissolution in sodium
 2 hydroxide (20 mM). For the determination of thiols, Ellman's reagent (as a 2 mM stock solution) dissolved in
 3 sodium acetate buffer (50 mM, pH 4.7), L-cysteine standards (10 μM -0.1 M) dissolved in deionized water were
 4 freshly prepared at 4 $^{\circ}\text{C}$. After mixing 0.85 mL of water, 10 μL samples or standards, 100 μL of Tris buffer (1 M,
 5 pH 8.5), and 50 μL of Ellman's reagent together, the polymers (0.5 mg/mL) were analyzed immediately after
 6 dissolution with 20 mM of sodium hydroxide. By drawing standard curves, the determination of the molar amount
 7 of thiol or amine per gram of polymers was conducted. The determined values were converted to moles of
 8 functional group per polymer chain using the molecular weight of the polymers, which was calculated to be ~ 2.2
 9 kDa *via* gel filtration chromatography. As a result, for freshly prepared multidentate polymers, each polymer
 10 molecule contains approximately ~ 3.5 active thiols and ~ 3.0 active amines, according to detected results from
 11 Ellman's reagent and fluorescamine assays.

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13 **Table S1. Comparison of Synthetic Conditions for Preparing Ag_2S QDs with Different Reaction**
 14 **Temperature (Temp.), Precursors, Solvents, Capping Reagents, Emission Wavelengths, Diameters and**
 15 **PLQYs.**

Precursors	Solvents	Capping reagents	Temp. ($^{\circ}\text{C}$)	Emission (nm)	Diameter TEM (nm)	PLQY (%)	^b Ref.
$(\text{C}_2\text{H}_5)_2\text{NCS}_2\text{Ag}$	1-octadecene, octadecylamine	Oleic acid	200	1058	10.2	---	(14)
$(\text{C}_2\text{H}_5)_2\text{NCS}_2\text{Ag}$	1-dodecanethiol, cyclohexane, ethanol	DHLA	230	1150-1200	5.4-7	5.8	(15)
$(\text{C}_2\text{H}_5)_2\text{NCS}_2\text{Ag}$,	1-dodecanethiol, cyclohexane, ethanol	DHLA, 6-PEG	210	1200	5.4, ^a 26.8	15.5	(16)
AgAc, $(\text{TMS})_2\text{S}$, S powder, AgNO ₃	1-octadecene, myristic acid, toluene	1-octylamine	110	690-1227	1.5-4.6	0.18	(17)
AgNO ₃ , 3-MPA	Ethylene glycol	3-MPA	145	510-1221	1.5-6.3	2.1	(20)
AgAc, GSH	Ethylene glycol	GSH	150	1106	7.6	3.3	(21)
AgNO ₃ , GSH	Water	GSH	95	960-1015	5.5	1.97	(22)
AgNO ₃ , S-N ₂ H ₄ ·H ₂ O	Water	GSH	Room temp.	624-727	1.7-3.7	1.2	(23)
AgNO ₃ , Na ₂ S	Water	BSA	Room temp.	1050-1294	3.3, ^b 10	1.8	(6)
AgNO ₃ , Na ₂ S	Water	BSA, antiVEGF	Room temp.	840	2.1	---	(24)
AgNO ₃ , Na ₂ S	Water	2-MPA	90	780-950	2.3-3.1, ^a 3.0-4.7	7-39	(25)

16 Note: ^a The diameters of Ag_2S QDs determined by DLS. ^b The referred references (Ref.) listed in the “References”
 17 as below. Abbreviations of precursors and capping reagents have been provided in the following auxiliary table.

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19 Auxiliary Table

Abbreviation	Full name	Abbreviation	Full name
$(\text{TMS})_2\text{S}$	hexamethyldisilathiane	DHLA	dihydrolipoic acid
3-MPA	3-mercaptopropionic acid	6-PEG	six-armed poly(ethylene glycol)
GSH	glutathione	BSA	bovine serum albumin
AgAc	silver acetate	antiVEGF	vascular endothelia growth factor

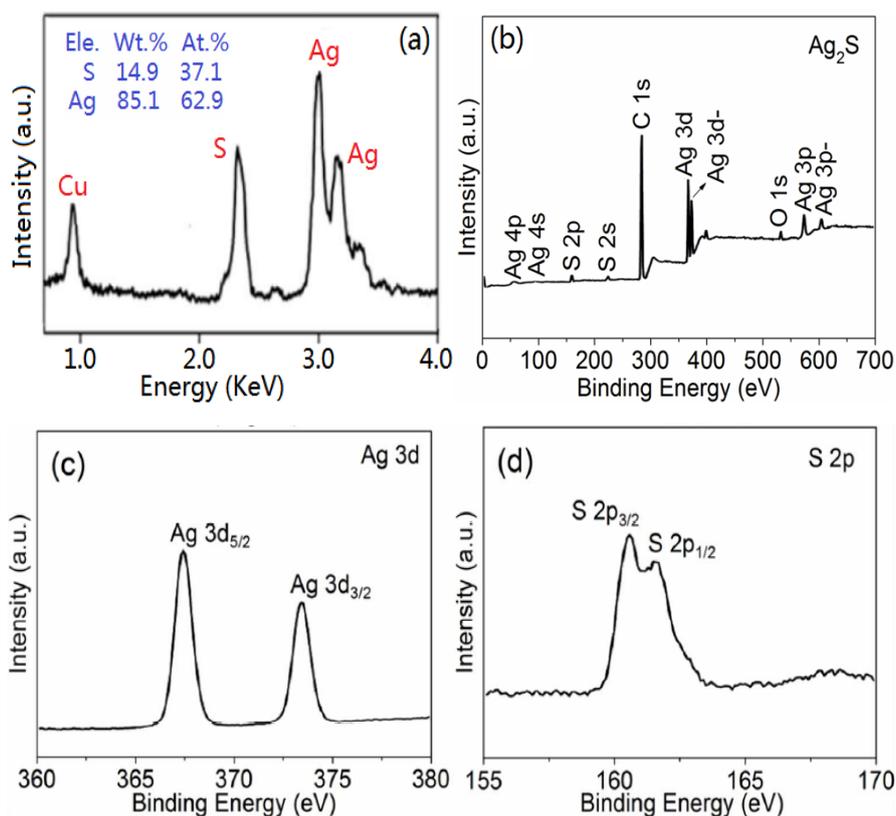
Supporting Information

			antibody
S-N ₂ H ₄ ·H ₂ O	sulfur-hydrazine hydrate complex	2-MPA	2-mercaptopropionic acid

1 References (based on the order of manuscript)

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18 **Fig. S1.** (a) EDX and (b) XPS spectra of Ag₂S QDs. (c) Ag 3d and (d) S 2p signals in XPS spectra of Ag₂S QDs.

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20 Part S2. The calculation of the molar capping ratio for Ag₂S QDs

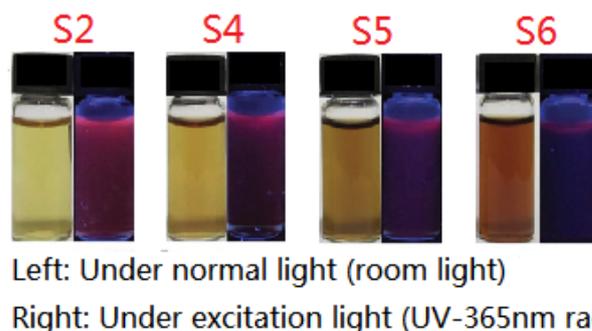
21 The molar capping ratio (MCR) was defined as the number of thiol and amine groups per surface atom of Ag₂S
 22 QDs, $MCR = (N_{SH} + N_{NH_2}) / (N_{Ag} + N_S)$. For instance, a 3.7 nm of Ag₂S QD has ~250 total surface atoms, obtained
 23 from theoretical calculations and empirical data (*Chem. Mater.* **2003**, *15*, 4300-4308.; *J. Am. Chem. Soc.* **2005**, *127*,
 24 2524-2532.; *Nano Lett.* **2005**, *5*, 331-338.; *J. Phys. Chem.* **1994**, *98*, 4109-4117.; *J. Phys. Chem. C* **2007**, *111*, 75-

Supporting Information

1 79.; *Nano Lett.* **2004**, *4*, 2361-2365.; *J. Phys. Chem. B* **2005**, *109*, 19320-19328). One polymer chain contains 3.5
2 thiols and 3.0 amines. So, the optimal MCR of 1.8 (in manuscript) indicates the addition of ~70 polymer chains per
3 QDs, or ~150 mg of polymer per μmol of QDs. At an elevated temperature, the polymers bind to the QD. This
4 binding is highly efficient because no free amine could be detected in dialysate during purification.

5 The polydispersity index (PDI) was calculated from chromatograms using conventional techniques for polymer
6 characterization, with the formula: $\text{PDI} = M_w / M_n$. The PDI for pure protein solutions typically was 1.25-1.35.

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9 **Fig. S2.** A series of photographs of the as-prepared Ag_2S QDs in aqueous solution for different samples under
10 normal (room) light and UV (365 nm) light illumination.

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12 **Table S2. Concentration Analysis of Ag^+ Ions Leaked from Ag_2S QDs in Cell Culture Media.**

^a C_0 (mg/mL)	^b $C_{24\text{h}}$ (mg/mL)	^c LR (%)	^d RSD	^e $C_{48\text{h}}$ (mg/mL)	LR (%)	RSD
0.01	7.00×10^{-6}	0.07	3.85	1.40×10^{-5}	0.14	2.05
0.05	1.45×10^{-4}	0.29	1.69	1.50×10^{-4}	0.30	3.59
0.1	3.20×10^{-4}	0.32	2.46	4.90×10^{-4}	0.49	0.92
0.5	3.95×10^{-3}	0.79	3.09	4.20×10^{-3}	0.84	2.84
1.0	8.60×10^{-3}	0.86	3.65	9.10×10^{-3}	0.91	1.46

13 ^a The concentration of Ag_2S QDs before incubation.

14 ^b The concentration of Ag^+ ions leaked from Ag_2S QDs when incubating in cell culture media for 24 h.

15 ^c The leakage ratio (LR) of Ag^+ ions: $\text{LR} (\%) = 100 \times (C_{24\text{h or }48\text{h}}) / C_0$.

16 ^d The relative standard deviation (RSD, %) of LR was defined as $100 \times (\text{relative standard} / \text{mean})$.

17 ^e The concentration of Ag^+ ions leaked from Ag_2S QDs when incubating in cell culture media for 48 h.

18 All concentrations were measured by ICP-MS, and expressed as mean of six repeated measurements.

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Supporting Information

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