Controlled Synthesis of Peptide-Based Amphiphilic Copolymers

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Supporting Information

1. Characterization of methoxypoly(oxyethylene) α-naphthylmaleamate (**IIa-2**):

Yield: 86 %. ^{1}H NMR ($CDCl_3$): δ 3.37 (C*H*$_3$-O); δ 3.64 (O-C*H*$_2$-C*H*$_2$-O); δ 4.33 (C*H*$_2$-O-C=O); δ 6.64-6.85 (C*H*=C*H* + C*H*^{1}-Naphthyl); δ 7.27-8.15 (C*H*$^{2-7}$-Naphthyl); δ 8.95 (*H*N-C=O).

2. Characterization of PEO-based macroinitiators.

2.1. Macroinitiator **IIIa-2** (Michael addition of AET.HCl to methoxypoly(oxyethylene) α-naphthylmaleamate):

Yield: 75 %. GPC in *N,N*-dimethylacetamide (vs. PEO standards): M_w/M_n = 1.26. ^{1}H NMR ($CDCl_3$): δ 2.85 (S-C*H*$_2$); δ 3.00-3.15 (C*H*$_2$-N$^+$ + O=C-C*H*$_2$-CH); δ 3.37 (C*H*$_3$-O); δ 3.64 (O-C*H*$_2$-C*H*$_2$-O); δ 4.33 (C*H*$_2$-O-C=O); δ 4.45 (O=C-C*H*-S); δ 4.45 (O=C-C*H*-S); δ 6.65 (C*H*^{1}-Naphthyl); δ 7.27-8.15 (C*H*$^{2-7}$-Naphthyl); δ 8.95 (*H*N-C=O).

2.2. Macroinitiator **IIIa-3** (Michael addition of Cys-OEt.HCl to methoxypoly(oxyethylene) dodecylmaleamate):

Yield: 72 %. GPC in *N,N*-dimethylacetamide (vs. PEO standards): M_w/M_n = 1.34. ^{1}H NMR ($CDCl_3$): δ 0.87 (CH_3); δ 1.15-1.40 (CH_3-$(CH_2)_9$) + CH_3-CH_2-O); δ 1.50 (($CH_2)_9$-CH_2); δ 2.90-3.25 (O=C-CH_2-CH + CH_2-NH + S-CH_2-CH); δ 3.37 (CH_3-O); δ 3.65 (O-CH_2-CH_2-O); δ 3.95 (O=C-C*H*-S); δ 4.16-4.35 (CH_2-O-C=O + O-CH_2-CH_3); δ 4.45 (*CH*-N^+); δ 8.25 (*H*N-C=O).

3. Amphiphilic PEO-peptide block copolymers.

In a typical polymerization procedure, 0.4081 g (0.17 mmol) of the macroinitiator (**IIIa-1**) were dissolved in 10 mL of DMF and degassed. Separately, a solution of ZLLys-NCA (1.561 g, 5.1 mmol) in 10 mL of DMF was prepared and degassed. The two solutions were combined via transfer needle under dry argon and the polymerization was performed at 70 ^{o}C for 5 days. The polymer solution was concentrated and the product was precipitated in diethyl ether. Then it was extracted with methanol.

3.1. Block copolymer **IVa-1.1** (obtained from macroinitiator **IIIa-1**):

Yield: 68 %. GPC in *N,N*-dimethylacetamide (vs. PEO standards): M_w/M_n = 1.38. ^{1}H NMR (DMSO-d_6): δ 0.81 (CH_3-$(CH_2)_{10}$); δ 1.10-2.00 (CH_3-$(CH_2)_{10}$ + αCH-$(CH_2)_3$); δ 2.80-3.10 (S-CH_2 + αCH-$(CH_2)_3CH_2$ + O=C-CH_2-CH + $(CH_2)_{10}$-CH_2-NH + S-CH_2-CH_2-NH); δ 3.22 (CH_3-O); δ 3.50 (O-CH_2-CH_2-O + O=C-C*H*-S); δ 3.75-4.36 (α*CH*-NH + CH_2-O-C=O); δ 4.97 (Z-CH_2); δ 7.05-7.35 (C_6H_5 + αCH-$(CH_2)_4$-N*H* + S-$(CH_2)_2$-N*H*); δ 7.69-8.27 (αCH-N*H* + CH_2-N*H*-(C=O)-CH-S).

3.2. Block copolymer **IVa-2.1** (obtained from macroinitiator **IIIa-2**):

Yield: 73 %. GPC in *N,N*-dimethylacetamide (vs. PEO standards): M_w/M_n = 1.33. ^{1}H NMR (DMSO-d_6): δ 1.00-2.15 (αCH-$(CH_2)_3$); δ 2.74-3.11 (S-CH_2 + αCH-$(CH_2)_3CH_2$ + O=C-CH_2-CH + S-CH_2-CH_2-NH); δ 3.23 (CH_3-O); δ 3.50 (O-CH_2-CH_2-O); δ 3.64-4.43 (α*CH*-NH + CH_2-O-C=O + O=C-C*H*-S); δ 4.94 (Z-CH_2); δ 6.65-8.93 (C_6H_5 + αCH-$(CH_2)_4$-N*H* + S-(CH_2-CH-N*H* +$C_{10}H_7$ + αCH-N*H* + $C_{10}H_7$-N*H*-C=O).

3.3. Block copolymer **IVa-3.1** (obtained from macroinitiator **IIIa-3**):

Yield: 67 %. GPC in *N,N*-dimethylacetamide (vs. PEO standards): M_w/M_n = 1.36. ^{1}H NMR (DMSO-d_6): δ 0.81 (C*H*$_3$-(CH$_2$)$_{10}$); δ 1.00-2.10 (CH$_3$-(C*H*$_2$)$_{10}$ + C*H*$_3$-CH$_2$-O + αCH-(C*H*$_2$)$_3$); δ 2.75-3.12 (S-C*H*$_2$ + αCH-(CH$_2$)$_3$C*H*$_2$ + O=C-C*H*$_2$-CH + (CH$_2$)$_{10}$-C*H*$_2$-NH); δ 3.22 (C*H*$_3$-O); δ 3.50 (O-C*H*$_2$-C*H*$_2$-O); δ 3.62-4.33 (αC*H*-NH + C*H*$_2$-O-C=O + S-CH$_2$-C*H*-NH + O=C-C*H*-S + CH$_3$-C*H*$_2$-O); δ 4.96 (Z-C*H*$_2$); δ 7.05-7.40 (C$_6$*H*$_5$ + αCH-(CH$_2$)$_4$-N*H* + S-(CH$_2$-CH-N*H*); δ 7.67-8.34 (αCH-N*H* + CH$_2$-N*H*-(C=O)-CH-S).

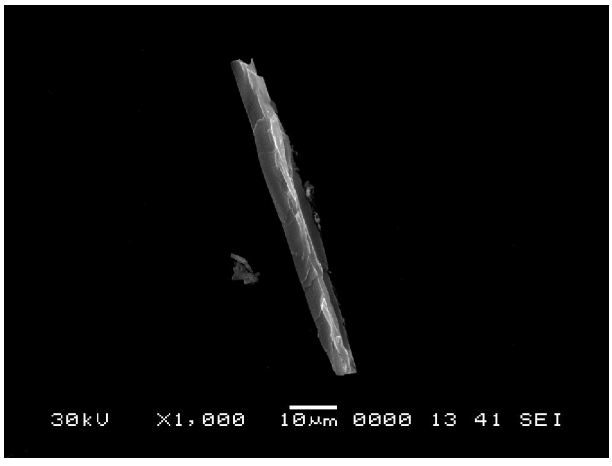

Figure S1. Scanning electron micrograph of deprotected lipopolypeptide **IV-2**.