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Unsymmetric Vesicles with a Different Design on Each Side for Near-Infrared Fluorescence Imaging of Tumor Tissues

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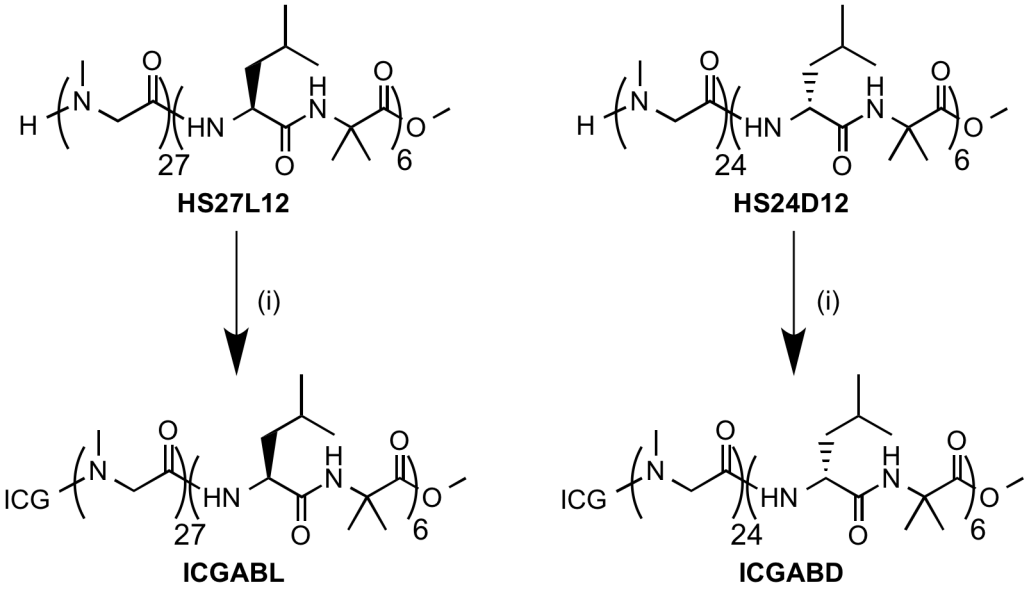
CONTENTS

1. Synthesis of amphiphilic peptides

The synthesis route of the amphiphilic peptides modified with ICG, **ICGABL** and **ICGABD** were illustrated in Scheme 1. Other amphiphilic peptides, **A_3BL**, **ABD**, **lipoABL** and **lipoABD** were synthesized as previously reported.



Scheme 1. Reagents and conditions: (i) ICG-sulfo-OSu, DCC, DMF, rt, 24 h.

ICGABL

To a solution of **HS27L12** (2.0 mg, 637 nmol) in DMF (100 μL), a solution of ICG-sulfo-OSu (1.0 mg, 1.08 μmol) and DCC (444 μg, 2.15 μmol) in DMF (120 μL) was added at 0 °C. The reaction mixture was stirred at 0 °C for 0.5 h and then at room temperature for 23 h. The solution was concentrated under reduced pressure and the crude product was purified with Sephadex LH20 column (eluent : methanol). The product was obtained as a green solid (2.4 mg, 98%).

MALDI-TOF mass spectrum supported the degree of polymerization to be 27.

MALDI-TOF-MS (matrix: α-cyano-4-hydroxycinnamic acid (CHCA)): calcd. for $C_{187}H_{295}N_{41}O_{44}S$ [$(M + H)^+$], 3852.190; found, 3852.192.

ICGABD

To a solution of **HS24D12** (2.0 mg, 683 nmol) in DMF (100 μL), a solution of ICG-sulfo-OSu (1.0 mg, 1.08 μmol) and DCC (444 μg, 2.15 μmol) in DMF (120 μL) was added at 0 °C. The reaction mixture was stirred at 0 °C for 0.5 h and then at room temperature for 23 h. The solution was concentrated under reduced pressure and the crude

product was purified with Sephadex LH20 column (eluent : methanol). The product was obtained as a green solid (2.2 mg, 88%).

MALDI-TOF mass spectrum supported the degree of polymerization to be 24.

MALDI-TOF-MS (matrix: CHCA): calcd. for $C_{178}H_{280}N_{38}O_{41}S$ $[(M + H)^+]$, 3677.035; found, 3677.018.

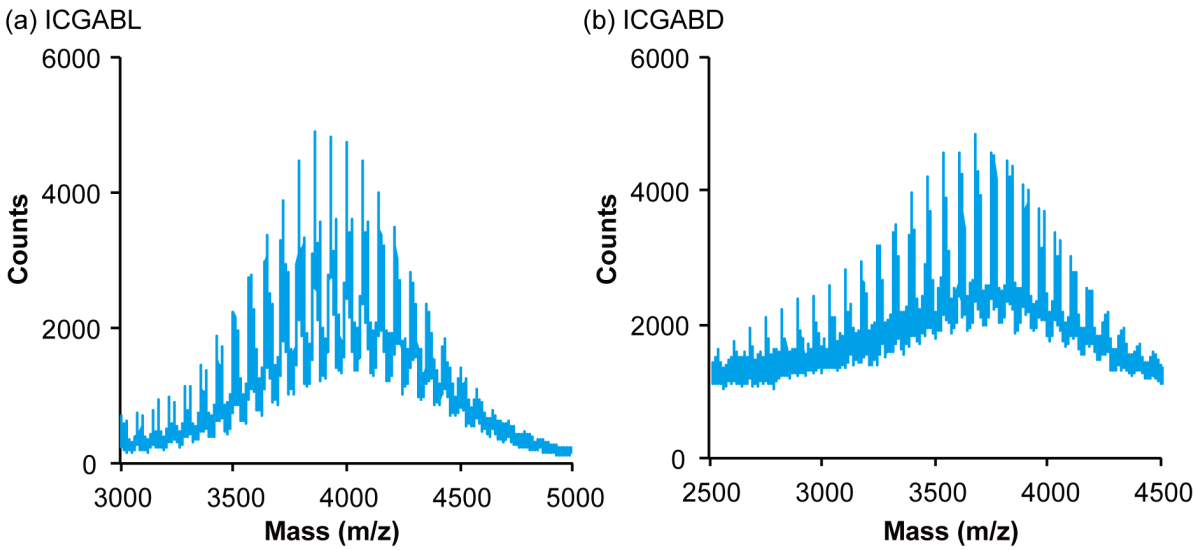


Fig. S1 MALDI-TOF mass data of (a) **ICGABL** and (b) **ICGABD**.

2. wide-area TEM images of vesicles containing lipoic acid

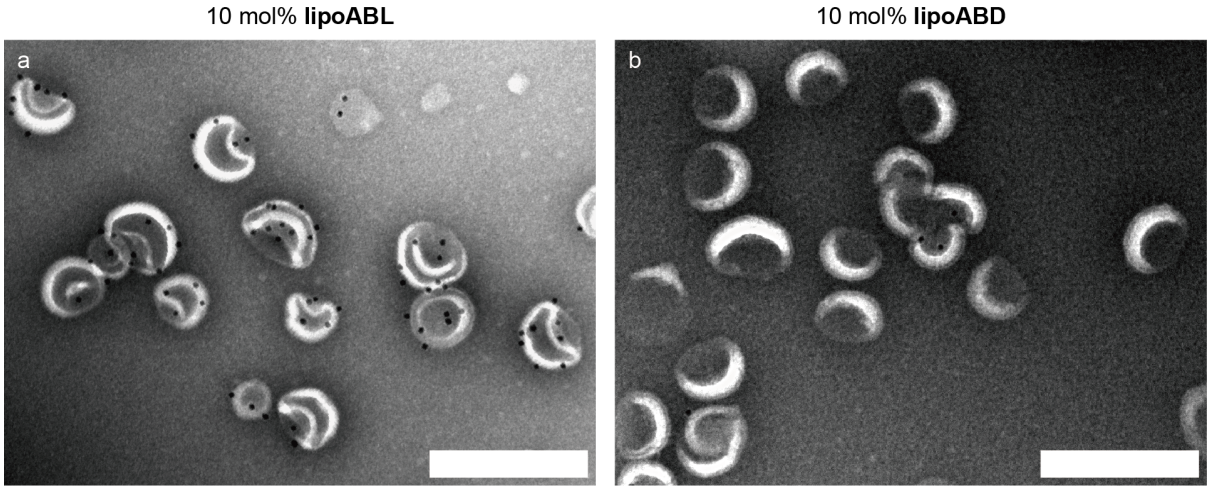


Fig. S2 TEM images (negative stained with 2% uranyl acetate) of vesicles prepared from (a) **A_3BL** + **ABD** + **lipoABL** (0.4/0.5/0.1) and (b) **A_3BL** + **ABD** + **lipoABD** (0.5/0.4/0.1) in milliQ upon a heat treatment at 90 °C for 1 h. An aliquot of a 10 nm AuNP suspension was added to the vesicles on the TEM grid. Bars indicate 200 nm.

3. TEM images of vesicles attached AuNPs

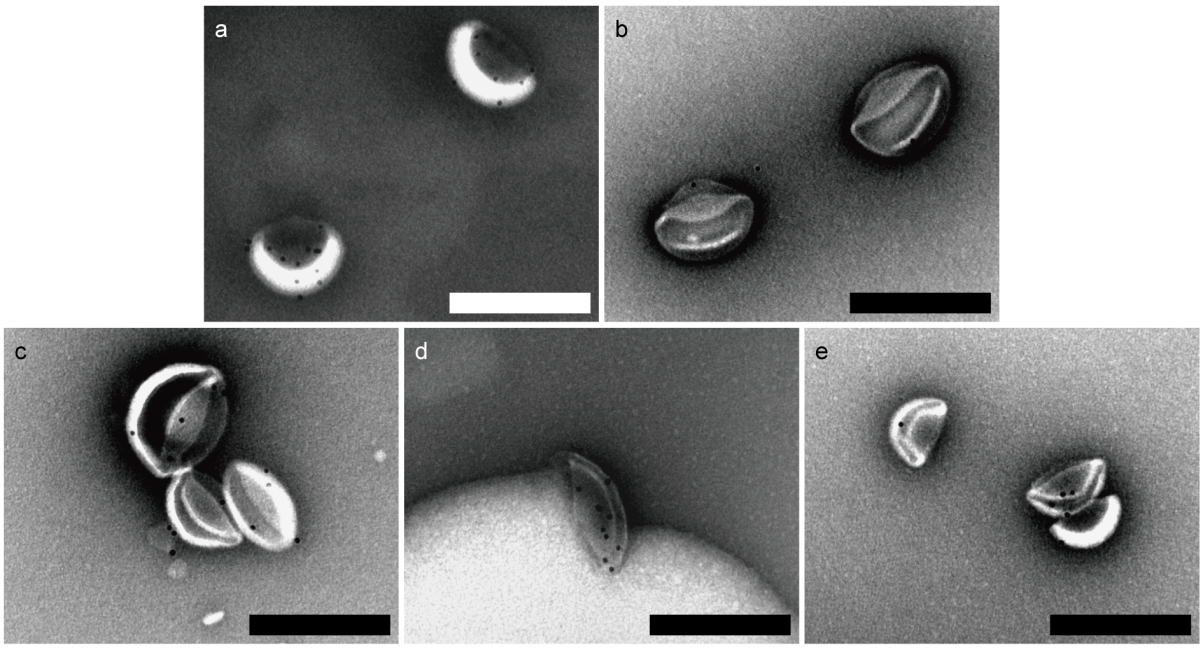


Fig. S3 TEM images (negative stained with 2% uranyl acetate) of vesicles prepared from (a) **A_3BL** + **ABL** + **ABD** + **lipoABL** (0.3/0.1/0.5/0.1), (b) **A_3BL** + **ABL** + **ABD** + **lipoABD** (0.3/0.2/0.4/0.1), (c) **A_3BL** + **ABL** + **ABD** + **lipoABL** (0.25/0.15/0.5/0.1), (d) **A_3BL** + **ABL** + **ABD** + **lipoABD** (0.25/0.25/0.4/0.1) and (e) **A_3BL** + **ABL** + **ABD** (0.3/0.2/0.5) in milliQ upon a heat treatment at 90 °C for 1 h. An aliquot of a 10 nm AuNP suspension was added to the vesicles on the TEM grid. Bars indicate 200 nm.

4. The hydrodynamic diameters of vesicles

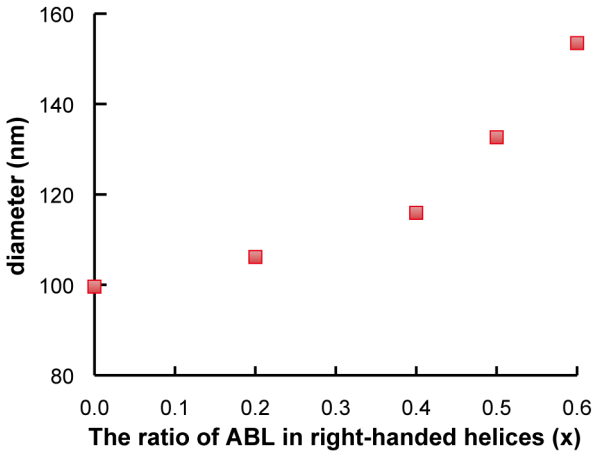


Fig. S4 The hydrodynamic diameter of vesicles at each proportion of **ABL** in constituent right-handed helices. **A_3BL**/**ABL**/**ABD** = 1-x/x/1 (mol/mol/mol).

5. Histogram of the diameters of ICGABL vesicle and ICGABD vesicle

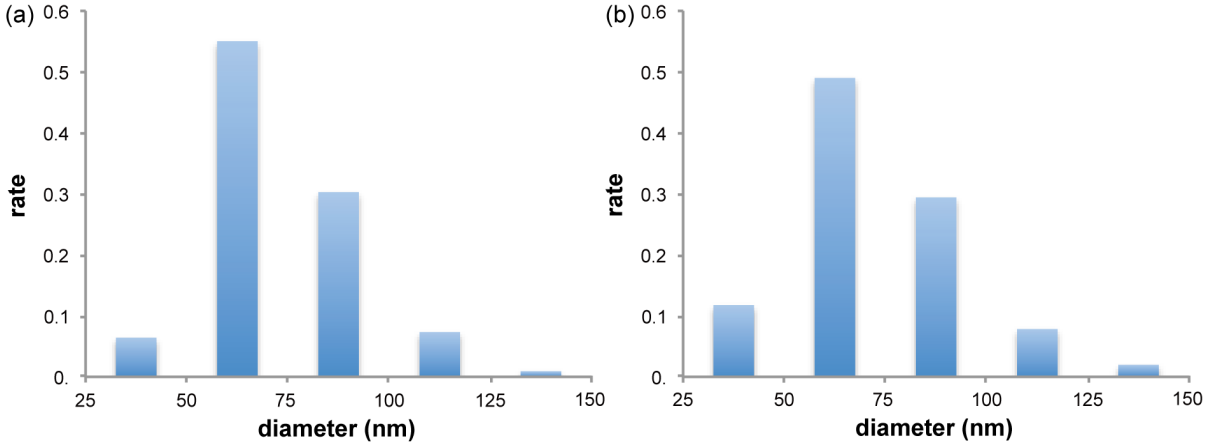


Fig. S5 Histograms of the diameter of the vesicles containing (a) **ICGABL** and (b) **ICGABD** observed by Cryo-TEM.