# Supplementary Materials <br> Photo Irradiation-Induced Core Crosslinked <br> Poly(ethylene glycol)-block-poly(aspartic acid) Micelles: <br> Optimization of Block Copolymer Synthesis and Characterization of Core <br> Crosslinked Micelles 

Kouichi Shiraishi ${ }^{1}$, Shin-ichi Yusa ${ }^{2}$, Masanori Ito ${ }^{2}$, Keita Nakai ${ }^{2}$, Masayuki Yokoyama ${ }^{1}$<br>${ }^{1}$ Medical Engineering Laboratory, Research Center for Medical Sciences, The Jikei University School of Medicine, 163-1, Kashiwashita, Kashiwa, Chiba, 277-0004, Japan<br>${ }^{2}$ Department of Applied Chemistry, Graduate School of Engineering, University of Hyogo, 2167<br>Shosha, Himeji, Hyogo 671-2280, Japan

## Corresponding Author

*E-mail address: masajun2093ryo@jiikei.ac.jp, Tel: +81-4-7164-1111 (ext. 6710)

Alkylated chalcone derivatives


Scheme S1 synthesis of alkylated chalcone derivative

Figure $\mathrm{S} 1(\mathrm{a}) .{ }^{1} \mathrm{H}$ NMR of Chal- $\mathrm{C}_{8}-\mathrm{Br}$ in $\mathrm{CDCl}_{3}$


Figure $\mathrm{S} 1(\mathrm{~b}) .{ }^{1} \mathrm{H}$ NMR of Chal-C5-Br in $\mathrm{CDCl}_{3}$


Figure $\mathrm{S} 1(\mathrm{c}) .{ }^{1} \mathrm{H}$ NMR of Chal- $\mathrm{C}_{2}-\mathrm{Br}$ in $\mathrm{CDCl}_{3}$


Alkaline hydrolysis of PEG-PBLA


Scheme S2
Figure $\mathrm{S} 1(\mathrm{~d}) .{ }^{1} \mathrm{H}$ NMR of PEG-P(Asp) in $\mathrm{D}_{2} \mathrm{O}+\mathrm{NaOD}(\mathrm{pH}>10)$


Esterification of PEG-P(Asp) with 3-bromo-N-butyl-propanamide(3-BNBPA)





Table S1 Reaction condition of $N$-butyl-propanamide (NBPA) introduction

| Polymer <br> $\mathrm{mg} /$ Asp mmol | DBU <br> $\mathrm{mg} / \mathrm{mmol}$ | $3-\mathrm{BNBPA}$ <br> $\mathrm{mg} / \mathrm{mmol}$ | Yield <br> $/ \mathrm{mg}$ | Esterification <br> yield/ / * |
| :---: | :---: | :---: | :---: | :---: |
| 100.9 | 58.5 | 131.5 | 78.3 | 24 |
| $/ 0.32$ | $/ 0.38$ | $/ 0.63$ |  |  |

*Esterification yield was calculated by ratio between $-\mathrm{CH}_{2}$ - (propanamide) and $-\mathrm{OC}_{2} \mathrm{H}_{4}$ - $(\mathrm{PEG})$ in ${ }^{1} \mathrm{H}-\mathrm{NMR}$.

Figure $\mathrm{S} 1(\mathrm{e}) .{ }^{1} \mathrm{H}$ NMR of PEG-P(Asp-NBPA) in DMSO+TFA


Esterification of PEG-P(Asp) with 1-iodoalkyl


Figure S1(f). ${ }^{1} \mathrm{H}$ NMR of PEG-P(Asp-pentyl) in DMSO+TFA


Figure S2. GPC peak area of the CCL micelle, the non-CCL micelle, and medium (saline) without the column. We used averages of peak areas of three different batches of media for estimation. Peak areas of the CCL micelle and the non-CCL micelle were estimated by the use of sample concentration and the medium volume. For example, we obtained that the non-CCL micelle's peak area was $1.59 \times 10^{6}$ at $1.0 \mathrm{mg} / \mathrm{mL}$. Therefore, $88 \%$ of the non-CCL micelle was observed, whereas $12 \%$ of the non-CCL micelle was adsorbed. In contrast, the CCL micelle's peak area was $1.76 \times 10^{6}$ at $1.0 \mathrm{mg} / \mathrm{mL}$ (98\%).


Figure S3. UV-vis spectrum of PEG-P(Asp-chal-C2) in DMSO


Absorption spectrum of (left) chalcone- $\mathrm{C}_{2}-\mathrm{Br}$ and (right) PEG-P(Asp-chal- $\mathrm{C}_{2}$ ) in DMSO. Absorption peak intensity at 352 nm was decrease after the reaction.

Figure S4. DLS and TEM images of aggregation form of PEG-P(Asp-nonyl-chal-C8) (shown in run 1 in Table 3). DLS charts indicate radius of PEG-P(Asp-nonyl-chal-C8) micelles (a) before and (b) after photo irradiation.


Figure S5 GPC trace of (a) non-CCL micelles and (b) CCL micelles in MeOH (containing 0.1M $\mathrm{LiClO}_{4}$ ).


Figure S6 Fluorescence spectra of pyrene encapsulated (a) non-CCL micelles and (b) CCL micelles. (a)

(b)


Table S2 Results of esterification in PEG-P(Asp)

| Run | Chal-C $\mathrm{C}_{\mathrm{x}}-\mathrm{Br}$ <br> leq $^{*}$ | X | DBU <br> leq | Chal <br> $/ \mathrm{N}$ | Yield <br> $1 \%$ |
| :---: | :---: | :---: | :---: | :---: | :---: |
| 1 | 0.1 | 2 | 0.1 | 0.4 | 15.4 |
| 2 | 0.3 | 2 | 0.3 | 0.2 | 2.6 |
| 3 | 0.3 | 2 | 0.3 | 1.2 | 15.4 |
| 4 | 1.0 | 2 | 0.3 | 0.8 | 10.3 |
| 5 | 0.3 | 2 | 0.3 | 0.4 | 5.1 |
| 6 | 0.3 | 5 | 0.3 | 1.7 | 21.8 |

[^0]Scheme S1 Reaction mechanism of chalcone derivative



[^0]:    * Equivalent vs Asp residue.

