Supporting information for

Photosensitizer-Conjugated Hyaluronic Acid-Shielded Polydopamine Nanoparticles for Targeted Photo-mediated Tumor Therapy

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Experimental methods for supporting information

**Biodegradation of PHPD-NPs:** The PHPD-NPs (0.5 mg/mL) were suspended in PBS buffer (150 mM) solution. After treatment of hydroxyl peroxide (5 mM) for 24 h, the color change was observed and taken by digital camera.

**Flow cytometry quantification of the CD44 receptor expression level:** NIH3T3 and MDA-MB-231 cells were washed twice with DPBS and incubated with FITC labeled anti-CD44 antibody (clone IM7, LSBio, Seattle, Washington) at 4 °C for 30 min followed by washing with DPBS and subjecting to flow cytometry. The flow cytometry was performed using a BD FACS Canto II flow cytometry analyzer and FACS Diva software (BD Biosciences).

**Energy-dependent endocytosis behavior of PHPD-NPs:** MDA-MB-213 cells were incubated with PHPD-NPs (0.1 mg/mL) in a SF culture medium for 4 h at 4 °C or 37 °C under 5 % CO₂. After incubation, the cells were analyzed by flow cytometry and CLSM imaging system.
Figure S1. Chemical synthetic route for PS-HA conjugates.
Figure S2. $^1$H-NMR analysis of Ac-HA and PS-HA conjugates in DMSO-$d_6$. 
Figure S3. Schematic illustration of iron-mediated coordination in preparation of PHPD-NPs.
Figure S4. FT-IR analysis of i) PD-NPs and ii) PHPD-NPs.
Figure S5. Photo-activity measurement of PHPD-NPs in the present of HAase. (a) Fluorescent images and (b) quantitative fluorescent intensity analysis of the PHPD-NPs incubated with different concentration of HAase over time.
Figure S6. Biodegradation of PHPD-NPs. Photograph of non-treated PHPD-NPs dispersion (0.5 mg/mL) and after addition of H$_2$O$_2$ (5 mM). The color (dark brown) of PHPD-NPs faded after treatment of H$_2$O$_2$. 
Figure S7. *In vitro* cellular internalization of PHPD-NPs at different concentrations of PD-NPs: (a) Flow cytometry quantification of the cellular internalization of PHPD-NPs against MDA-MB-231 cells at different concentrations of PD-NPs. (b) Confocal laser scanning microscopy image of MDA-MB-231 cells treated with PHPD-NPs as different concentration. (Incubation time: 4 h, scale bar: 20 µm).
Figure S8. Flow cytometry quantification of the CD44 receptor expression level in NIH3T3 and MDA-MB-231 cells.
Figure S9. Energy-dependent endocytosis behavior of PHPD-NPs. (a) Flow cytometry quantification of the cellular internalization of PHPD-NPs against MDA-MB-231 cells at different temperatures (4 and 37 °C). (b) Confocal laser scanning microscopy images of MDA-MB-231 cells treated with PHPD-NPs at different temperatures (4 and 37 °C).
**Figure S10.** Cell viability of MDA-MB-231 cells treated with PD-NPs, PS-HAs and PHPD-NPs under laser irradiation at 3.0 J/cm² power.
Figure S11. Cell viability of MDA-MB-231 cells treated with free pheo-a (2.4 µg/mL) in the hypoxic and normoxic conditions under different laser irradiation power. The photo-mediated cytotoxicity of free pheo-a was significantly decreased in hypoxic conditions when compared with that of normoxic conditions.
Table S1. Chemical characterization of PS-HA conjugates

<table>
<thead>
<tr>
<th>Code</th>
<th>DS of acetyl groups(^{(a)})</th>
<th>DS of PS molecules(^{(b)})</th>
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<tbody>
<tr>
<td>PS-HA</td>
<td>0.40 ±0.02</td>
<td>0.10 ±0.03</td>
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\(^{(a)}\) Degree of substitution of acetyl groups per HA unit (2 glucose rings), determined by \(^1\)H-NMR (n=3).
\(^{(b)}\) Degree of substitution of pheo-a molecules per HA unit (2 glucose rings), determined by UV-Vis spectrophotometer (n=3).