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'Clickable' Polymer-Caged Nanobins as a Modular Drug Delivery Platform

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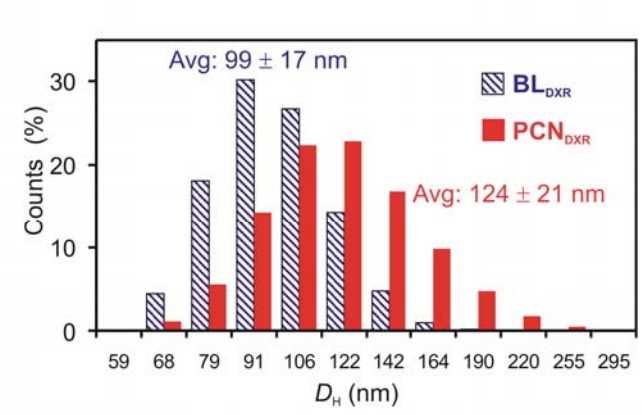

Figure S1. Hydrodynamic diameters (D_H) of BL_{DXR} and PCN_{DXR} measured by dynamic light scattering (DLS).

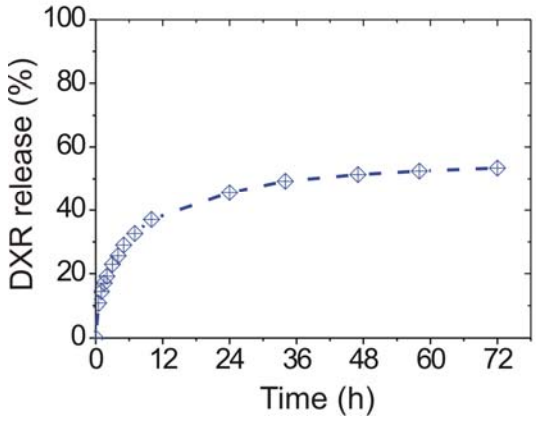

Figure S2. Time-dependent DXR-releasing profile for bare liposomes (BL_{DXR}) at pH 5.0, 37 °C.

Table S1. pH-dependent apparent DXR-release rates ($k_{release}^{apr}$). These rates were obtained by fitting the release profiles of Figures 1a and S2, assuming that the drug-releasing kinetics is a pseudo-first-order process.

pH (°C)	Sample Formulation	$k_{release}^{apr}$
5.0 (37)	PCN_{DXR}	26.76
6.0 (37)	PCN_{DXR}	15.48
7.4 (37)	PCN_{DXR}	4.95
7.4 (25)	PCN_{DXR}	1
5.0 (37)	BL_{DXR}	15.19

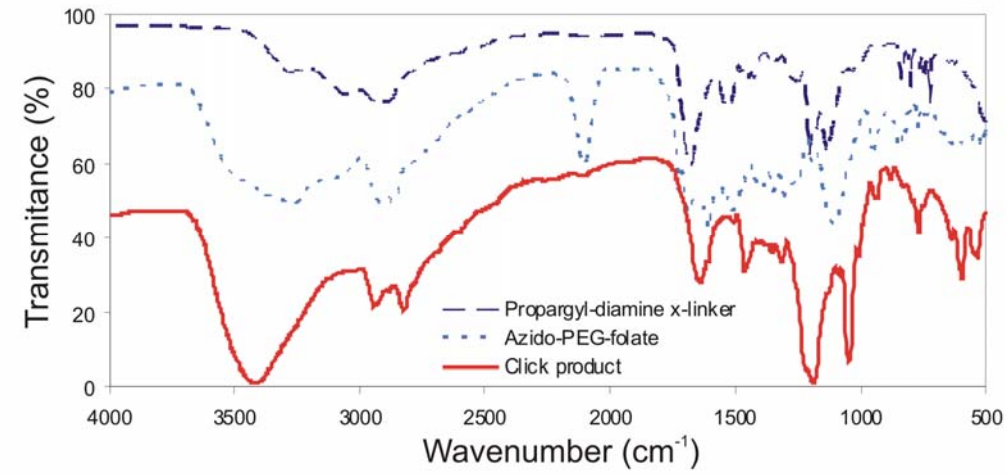

Figure S3. The FTIR spectra of the azido-PEG-folate, the propargyl diamine cross-linker, and the click product.

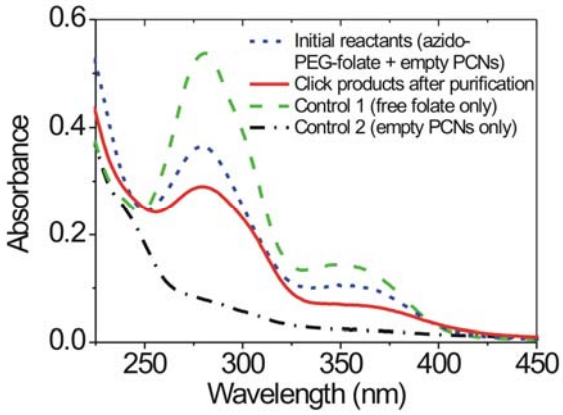

Figure S4. The UV-vis spectra of click reactants (azido-PEG-folate + empty PCNs), click products after purification, free folic acid only (Control 1), and empty PCNs only (Control 2).

To demonstrate the modular versatility of the alkyne groups on the surface of PCNs, we also click-conjugate an azido-ethidium dye to empty PCNs (Figure S5). The reactions were performed in the dark either with or without Cu catalyst and the respective products were isolated by gel-filtration. Both excitation and emission spectra from ethidium-conjugated PCNs (e-PCNs) are highly intense (solid lines in Figure S5), indicating successful attachment of the dye on the surfaces of PCNs with Cu catalyst. In contrast, only low-intensity excitation and emission spectra (dashed lines in Figure S5) were observed from the controlled PCN sample that was treated with azido-ethidium in the absence of the Cu catalyst. The little intensities that was observed in the controlled PCN sample can be attributed to the physical entrapment of dye molecules inside liposomal core given the well known membrane permeability of ethidium dye.[1,2]

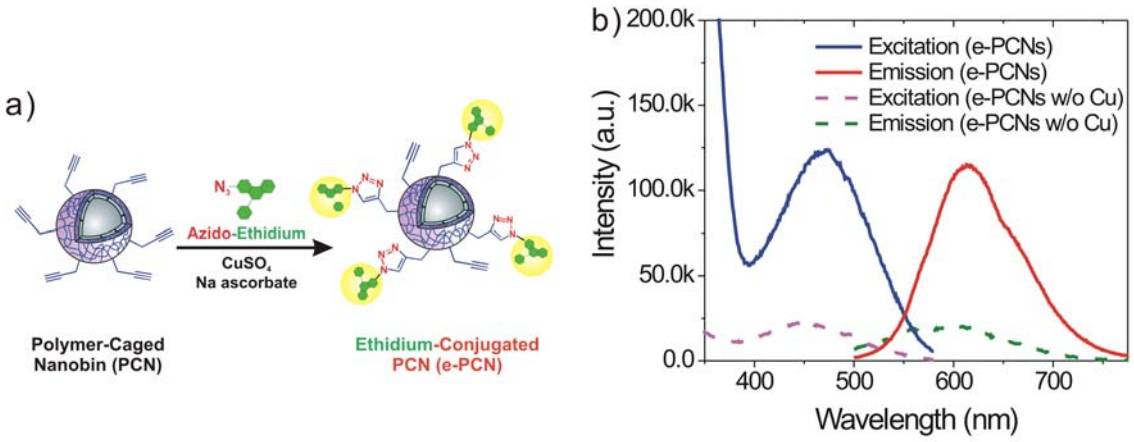

Figure S5. a) Scheme of click-conjugation reaction of azido-ethidium dye to empty PCNs. b) Excitation and emission spectra of ethidium-conjugated PCNs (e-PCNs, solid lines), prepared via click reaction in the presence of a Cu catalyst, and controlled PCNs (dashed lines) reacted with the azido-ethidium dye without the Cu catalyst. The low intensities observed in the controlled PCN samples can be attributed to the physical entrapment of dye molecules inside liposomal core given the well-known membrane permeability of ethidium dye.[1,2]

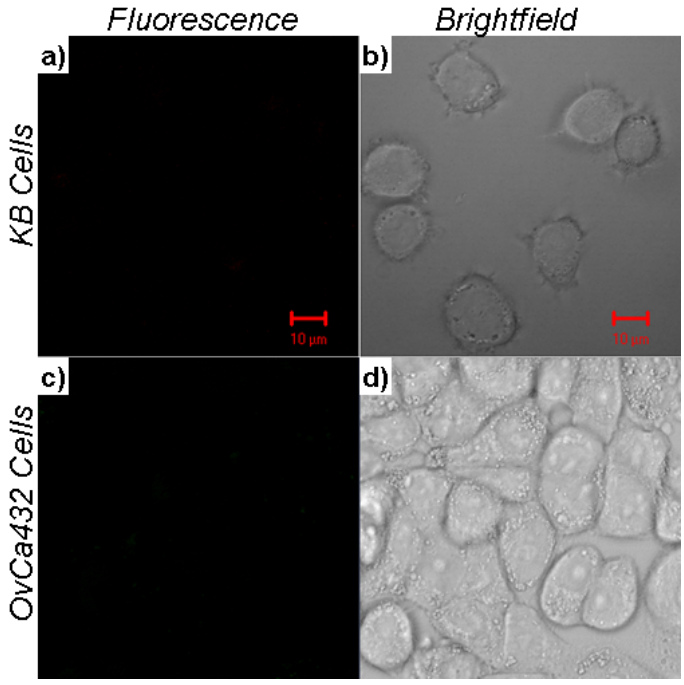

Figure S6. Confocal laser-scanning fluorescence microscopy images (a and c) and bright-field transmission microscopy images (b and d) of KB (a and b) and OvCa432 (c and d) cells that have not been exposed to any DXR formulations.

Reference:

(1) Aeschbacher, M.; Reinhardt, C. A.; Zbinden, G. *Cell Biol. Toxicol.* **1986**, *2*, 247-255.
(2) Berns, M. W.; Wang, Z.; Dunn, A.; Wallace, V.; Venugopalan, V. *Proc. Natl. Acad. Sci. U.S.A.* **2000**, *97*, 9504-9507.