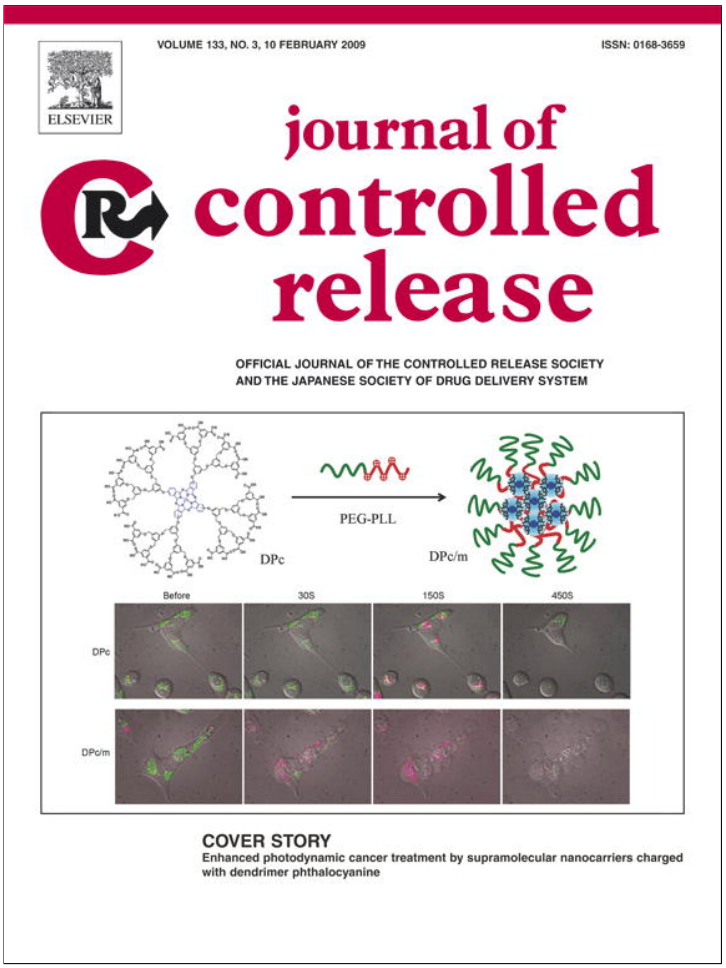

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Cover Story

Dendrimer polymeric micelles for enhanced photodynamic cancer treatment

Polymeric micelles have been used extensively for targeted delivery of drugs to solid tumors. Polymeric micelles are known to cumulate at the tumor site by enhanced permeation and retention effect. Thus, it is natural to consider utilizing polymeric micelles for targeted delivery of photosensitizers to the tumor site for photodynamic therapy (PDT). PDT is based on production of highly reactive oxygen species by irradiating a photosensitizer with laser light. Because of its localized treatment, PDT became a promising approach for treatment of localized solid cancers. Conventional photosensitizers such as porphyrin and phthalocyanine derivatives, however, have a few limitations. They easily form aggregates, which have a significantly lower ability to form reactive oxygen species. For this reason, it has been difficult to encapsulate photosensitizers into liposomes or polymeric micelles. Conventional photosensitizers also cause skin hyperphotosensitivity, forcing patients to be isolated in a dark room for weeks.

An article in this issue by Professor Kataoka's group describes preparation of a novel polymeric micelle with the core consisting of dendrimer phthalocyanine (DPc) [1]. In their clever approach, anionic DPc was electrostatically interacted with poly(ethylene glycol)-poly(L-lysine) (PEG-PLL) to prepare DPc-encapsulated polymeric micelle (DPc/m). The study showed that DPc/m was effective in inducing efficient and exceptionally rapid cell death accompanied by characteristic morphological changes. The result obtained with DPc/m was drastically better than that by DPc alone. The fluorescent microscopic observation revealed that DPc/m was initially present in endosomes/lysosomes, and subsequently translocated to the cytoplasm during photoirradiation, resulting in photo-damage to mitochondria followed by cell death. DPc/m significantly enhanced *in vivo* antitumor efficacy, but at the same time reduced skin phototoxicity in comparison with clinically used porfimer sodium.

The study by Professor Kataoka's group is expected to open a new avenue of designing more effective and less toxic photosensitizer formulations for clinical PDT. The study is also important for its applicability to gene delivery in general. PEG-PLL can be easily used for interaction with DNA or RNA to form the polymeric micelles similar to DPc/m. The fact that DPc/m was effective in the *in vivo* studies indicates that dendrimer polymeric micelles can be an effective nanocarrier for drug delivery in general.

Reference

[1] N. Nishiyama, Y. Nakagishi, Y. Morimoto, P.-S. Lai, K. Miyazaki, K. Urano, S. Horie, M. Kumagai, S. Fukushima, Y. Cheng, W.-D. Jang, M. Kikuchi, K. Kataoka, Enhanced photodynamic cancer treatment by supramolecular nanocarriers charged with dendrimer phthalocyanine, J. Control. Release 133 (2009) 245–251, doi:10.1016/j.jconrel.2008.01.010.

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