Shell Cross-linked Stimuli-Responsive Micelles as Vehicles for Biomedical Applications

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In the past few years, polymer micelles have been suggested as promising vehicles for drug delivery due to their outstanding advantages in drug loading capacity and cellular uptake efficiency, as well as the enhanced permeability and retention (EPR) effect resulting from the nano-scaled dimension. However, the physically assembled micelles are always too fragile to protect the encapsulated cargos during the *in-vivo* delivery, and also inefficient in achieving a controlled release. Thus, cross-linking, especially reversible cross-linking structure, should definitely bring a breakthrough to the application of polymer micelles in biomedical applications.

Herein, we reported self-assembled polymer micelles based on poly(vinyl alcohol)-*b*-poly(*N*-vinylcaprolactam) (PVOH-*b*-PNVCL) block copolymers above the LCST. Different cross-linking strategies were attempted to obtain reversible shell cross-linking (SCL) micelles bearing stimuli-responsive properties. These micelles were utilized as reservoirs for guest molecules, such as drugs, inorganic nanoparticles, *etc*. The reversible cross-linking structures endow them a possibility to achieve controlled drug release, in responsive to external environmental triggers. Biological assays, such as cytotoxicity, cellular internalization, as well as *in-vivo* drug release behaviors were carried out with cancer cell MEL-5. The results indicated that these SCL micelles can be envisaged as drug delivery vehicles for specifically physiological needs, such as cancer treatment, diabetes treatment, magnetic resonance imaging (MRI), as well as treatment of tumors via hyperthermia effect, *etc*.