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Enzyme-Triggeredsheddablemicelles as an intelligent vehicle for promoted Cell uptake and anticancer siRNA delivery

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RNA interference (RNAi) mediated by small interfering RNA (siRNA) has been reported as a potential therapeutic tool for cancer and other diseases. Due to its instability in vivo, poor cellular uptake and no targeting ability, delivery is the major obstacle to its application. siRNA delivery systems for cancer therapy usually have a poly (ethylene glycol) (PEG) layer on the particles surface to stabilize nanoparticles, minimize the nonspecific interaction in vivo, and thus prolong the circulation time. However, PEGylation significantly reduces cellular uptake of the nanoparticles after they reached at the tumor site, which go against the in vivo antitumor efficiency. Herein, we develop an intelligent micelles which have a matrix metalloprotease 2 (MMP-2)-sensitive peptide between PEG shell and poly (ε-caprolactone) core and can shed the PEG layer when triggered by tumor overexpressed MMP-2. We show clear evidences that the PEGylated micelles are stable in serum and capable of deshielding the PEG layer at the environment contains MMP-2 to facilitate the delivery of siRNA to the tumor cells in vitro and in vivo. Finally, we systemically administrate this micelle loading siRNA targeting Polo-like kinase 1 and efficiently inhibite breast tumor growth.

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