Stealth properties of poly(ethylene oxide)-based triblock copolymer micelles: A prerequisite for a pH-triggered targeting system

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Résumé en anglais	Evaluation of the biocompatibility of pH-triggered targeting micelles was performed with the goal of studying the effect of a poly(ethylene oxide) (PEO) coating on micelle stealth properties. Upon protonation under acidic conditions, pH-sensitive poly(2-vinylpyridine) (P2VP) blocks were stretched, exhibiting positive charges at the periphery of the micelles as well as being a model targeting unit. The polymer micelles were based on two different macromolecular architectures, an ABC miktoarm star terpolymer and an ABC linear triblock copolymer, which combined three different polymer blocks, *i.e.* hydrophobic poly(ε-caprolactone), PEO and P2VP. Neutral polymer micelles were formed at physiological pH. These systems were tested for their ability to avoid macrophage uptake, their complement activation and their pharmacological behavior after systemic injection in mice, as a function of their conformation (neutral or protonated). After protonation, complement activation and macrophage uptake were up to twofold higher than for neutral systems. By contrast, when P2VP blocks and the targeting unit were buried by the PEO shell at physiological pH, micelle stealth properties were improved, allowing their future systemic injection with an expected long circulation in blood. Smart systems responsive to pH were thus developed which therefore hold great promise for targeted drug delivery to an acidic tumoral environment.
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