Biomedical Applications of Size-optimized Silica Nanoparticles

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Rapid sequestration and prolonged retention of intravenously injected nanoparticles by the liver and spleen (reticuloendothelial system (RES)) presents a major barrier to effective delivery to the target site and hampers clinical translation of nanomedicine. On the other hand, although the rapid clearance of ultrasmall NPs (< 8 nm, the renal clearance threshold) via the renal pathway reduces toxicity concerns, it also impedes sufficient accumulation at the tumor site for effective therapeutic efficacy. Here we describe the development of size-optimized ultrasmall (diameter ~12 −15 nm) porous silica nanoparticles (UPSNs) that maximize tumor accumulation without prolonged retention in the RES organs. We integrate whole-body imaging and physiologically-based pharmacokinetic computational modeling to dissect the pharmacokinetics and nano-bio interactions of UPSNs in vivo. Our results demonstrate prolonged plasma half-life, attenuated RES sequestration, and accelerated hepatobiliary clearance of UPSNs, that results in rapid, enhanced and prolonged tumor accumulation via passive means in primary and metastatic models in a tumor-agnostic manner. Finally, we discuss exemplary applications of our versatile platform in radiotheranostics, image-guided surgery and immunomodulation in mouse models of primary and metastatic cancers.