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Cancer applications of multistage nanovector systems based on microfabricated porous silicon particles

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The administration of carriers tailoring therapeutic agents specifically to the disease loci has emerged as a striking, higher therapeutic index treatment modality aimed at personalization of cancer therapy. We developed a multistage nanocarrier system that integrates several rationally designed nanovectors acting in a synergistic fashion. This multistage porous silicon nanovector (MSV) is based on the biodegradable nanoparticles rationally designed to tailor the diseased vasculature through optimized margination towards the walls of the tumor blood vessels. The first stage porous silicon particles target tumor-associated endothelium or macrophages. Once the particles arrested in the close proximity to the tumor, second-stage nanoparticles/macromolecules carrying the therapeutic agents are released into the tumor microenvironment by time-dependent degradation of the silicon carrier. Particles-cell interactions and degradation of MSV can be controlled by means of particle surface modifications. In this talk, the importance of MSV design in terms of nanovector geometry and covalent/non-covalent attachment of tumor microenvironment targeting moieties to the surface of MSV, aiming therapeutics preferentially accumulating in the tumor site, will be discussed. In particular, we demonstrate that in orthotopic models of liver metastases of breast and lung cancers, albumin-bound paclitaxel (ABX)-loaded within MSV (MSV-ABX) enables therapeutic and survival benefits as compared to ABX.