**457f Novel Alternating Copolymer Structures for Targeted in Vivo Imaging and Therapy in Cancer**

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The biggest single problem that prevents a dramatic reduction in the mortality due to cancer is the limitation on current medical imaging techniques, computed tomography (CT) and magnetic resonance imaging (MRI), that provide detailed anatomical snapshots of the body but fail to provide accurate, basic information necessary to manage the patient's disease optimally. The limitations are manifested in several ways: (1) Small primary tumors go undetected. (2) Metastatic disease is grossly underdiagnosed. (3) Treatment response to therapy is poorly measured. A related problem in cancer therapy is the lack of selectivity of chemotherapeutic agents that are toxic to proliferating cells. The resulting side effects limit dosing and prevent use altogether. A solution to this problem is to selectively carry contrast agents and drugs into cancer cells so as to enhance uptake and selectivity. Versatile, amphiphilic, polyethylene glycol-based alternating copolymer structures have been developed that self-assemble into micelle nanoparticles, carry imaging and/or therapeutic agents, penetrate cells, and can be linked to a ligand for specific tumor cell targeting. These unique alternating copolymer micelle nanoparticles were used in this study as delivery vehicles targeted to human cancer cells expressing the underglycosylated mucin-1 antigen, which is found on almost all epithelial cell adenocarcinomas. These nanoparticles have a number of advantages including the following: (1) The probes are small (10-35 nm in diameter), which increases uptake into tumors by the enhanced permeability and retention effect of tumor vasculature. (2) Uptake is further selectively enhanced by the targeting probe. (3) The probes have high carrying capacity for bound and encapsulated imaging and therapeutic agents. (4) The chemistry is very flexible and versatile and is amenable to diverse imaging and therapeutic applications. (5) The main polymer is synthesized by an enzymatic route, which is much faster and more convenient than an entirely chemical synthesis. In this study, the nanoparticle size and shape were characterized by dynamic and static light scattering and cryo-transmission electron microscopy (cryo-TEM). Coupling of perfluorocarbons to the polymer backbone was verified with 1H- and 19F-NMR spectroscopy. The in vitro cytotoxicity of the base polymer, with and without perfluorocarbons attached and/or encapsulated, was very low. The in vitro cellular uptake of these nanoparticles was quantified by measuring fluorescence intensity and visually verified by confocal microscopy. In addition, 19F-MRI was used to image and quantify the uptake of these micelles in vitro. The solubility of a chemotherapy drug, doxorubicin, increased by encapsulation in these nanoparticles, and cellular uptake, and hence cell death, was enhanced as compared to that of free drug.