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Oseltamivir-conjugated polymeric micelles engineered as active smart drug delivery platforms for effective tumor targeting

Traditional chemotherapy cancer agents are typically highly hydrophobic small molecules designed to work intracellularly, targeting rapidly dividing cells. Administration of these drugs alone, complicated by insolubility in biological fluids and tissues, and an incapacity to effectively localize in metastasized tumors, results in adverse toxic side effects and prevents potent selective targeting. Functionalized drug delivery systems using polymeric nanostructures are at the forefront of cancer research, engineered for safer, more efficient and effective use of chemotherapy. Here, we designed and engineered a new polymeric micelle delivery system for active tumor targeting followed by micelle–drug internalization via receptor-induced endocytosis. By decorating micelles with oseltamivir, we investigated whether they actively targeted human pancreatic PANC1 cancer cells. Amphiphilic block copolymers with oseltamivir conjugated at the hydrophilic end (oseltamivir-poly(polyethylene glycol methyl ether methacrylate)-block-poly(methyl methacrylate) were synthesized using reversible addition–fragmentation chain transfer (RAFT) living radical polymerization with self-assembling properties. Oseltamivir-micelles targeted pancreatic PANC1 cancer cells, reduced Neu1 sialidase activity and tumor cell viability with subsequent internalization of the micelles loaded with a fluorescent hydrophobic drug. Neu1 binding was shown to be a prerequisite step toward micelle internalization. The ability to both target and halt the growth of a tumor cell using a newly designed nanocarrier system, combined with the internalization of the micelle loaded with a cytotoxic chemotherapeutic represents the novel aspect of this work.

Biography

Szewczuk is Full Professor of Immunology and Medicine, Queen's University, Kingston, Ontario Canada. Dr. Szewczuk's current research has focused on the role of glycosylation in receptor activation with a particular focus on alternate new active tumor targeting drug delivery systems.

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