MULTIFUNCTIONAL NANOPARTICLES FOR SPECIFIC NEUROBLASTOMA TARGETING

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Neuroblastoma is a solid extracranial cancer of the nervous system. Besides leukemia, brain tumors, and central nervous system tumors, neuroblastoma is the most common cancer in children.[1] It mainly affects children under 15 years old and accounts for 15% of childhood cancer deaths.[2] There is a wide variety of treatment options for neuroblastomas; ranging from surgery or chemotherapy in children with low-risk to medium-risk forms of the disease, to aggressive multimodal therapies in patients with high-risk forms.[3] A treatment used in certain high-risk patients is iodine-131 meta-iodobenzylguanidine (I-131 MIBG) radiotherapy. MIBG is a norepinephrine analogue that localizes to adrenergic cells. Neuroblastoma cells overexpress adrenergic receptors, and thus take up MIBG at higher rates than other tissues.[4] Because of this, when modified with I-131, MIBG is used as a radiotherapy agent.[5] I-131 MIBG treatment, as a highly specific therapy, avoids many of the heavy side effects seen in other cancer treatments, but its radioactivity causes a need for highly specialized facilities. Additionally, all patients undergoing I-131 MIBG treatment must remain in isolation for several days while radiation in their system is reduced to safe levels, which is especially difficult for children. As an alternative to I-131 MIBG treatment, a nanoparticle (NP) system that uses MIBG to home to neuroblastoma cells and then releases chemotherapy agents in their immediate vicinity may result in a better treatment for the disease. It would be more patient friendly in that, in addition to the above stated advantages of MIBG, it would contain no radioactive properties and therefore avoid the need for patient isolation and specialized facilities, which would increase patient compliance and reduce costs. Similar NPs were previously shown to be useful for drug loading purposes and therapeutic release rates can be controlled in NP systems, as opposed to the traditional therapy.[6] Through electrohydrodynamic (EHD) co-jetting, our group has fabricated surface modifiable, biodegradable nanoparticles that can be used for predictable, controlled, and distinct delivery of therapeutics.[7] In this work we present the fabrication poly-lactic-glycolic acid NPs chemically modified to display MIBG on their surface that were manufactured using our EDH methodology. We characterized the system using proton nuclear magnetic resonance, scanning electron microscopy, dynamic light scattering, and nanoparticle tracking analysis. Increased particle uptake for MIBG modified NPs vs controls in a neuroblastoma line was observed using confocal microscopy and flow cytometry. Future work will investigate the efficacy of these particles for delivering chemotherapeutics in in-vitro and in-vivo systems based on previously published work on drug loading studies in our group.[8]

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