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Magnetic Micelles for a Targeted,

Magnetically Triggered Drug Delivery System

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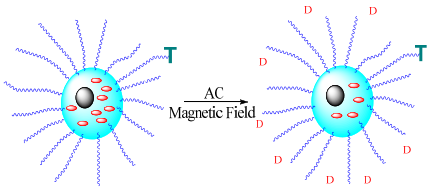
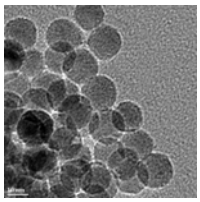
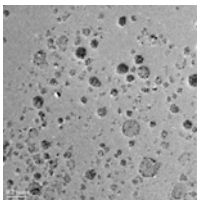
We are building a targeted, nanoscale drug delivery device consisting of magnetite nanoparticles and cancer drug trapped in the crystalline core of a polymer micelle made from poly(ethylene glycol)-*b*-caprolactone diblock copolymers. The drug delivery vehicle will be injected into the body to travel through the blood stream until it encounters cancerous tissue and bind to the surface of the cancer cell through the targeting moiety on the terminus one of the poly(ethylene glycol) blocks. Application of an external radio frequency magnetic field heats the magnetite particle by induction, which melts the polycaprolactone core, thereby allowing the cancer drug to leave the micelle and attack the cancer cells. When the magnetic field is discontinued, the core will crystallize, This targeted, magnetically triggered drug delivery system will provide the oncologist unprecedented control of chemotherapy. The chemotherapy can be localized at the cancer site through both the targeting function and the selective, localized application of the magnetic field. Furthermore, pulsing the magnetic field gives the oncologist temporal control of the chemotherapy.



To realize this magnetically triggered drug delivery system we must design the materials package and assemble the pieces into a polymer micelle delivery system. A series of diblock copolymers were prepared by the tin-catalyzed, ring opening polymerization of ε-caprolactone from the alcohol terminus of poly(ethylene glycol) monomethylether (M_n ~ 2,000 or 5,000). Magnetite particles were prepared by the thermal decomposition of iron(III) oleate in refluxing octadecene. The particles and diblock copolymers were dissolved in tetrahydrofuran and the solution was dropped into ultrapure water with ultrasonication to make magnetic micelles. The micelles consisted of many magnetite particles trapped in the polycaprolactone core. A maleimide terminated poly(ethylene glycol) was reacted with ε-caprolactone to give a diblock copolymer with maleimide at the terminus of the poly(ethylene glycol block. The maleimide group reacted with the thiol group that was part of the RGD peptide targeting group. The cyclic RGD peptide was cyclic pentamer consisting of arginine, glycine, aspirate, phenylalanine and cysteine. The cysteine has a thiol group that allowed us to conjugate the peptide to the diblock copolymer. The cyclic RGD peptide will bind to integrin receptors expressed on the surface of certain cancer cell lines and flow cytometry studies confirmed our targeted micelles will bind to the cancer cells.



TEM image of the magnetite nanoparticles



TEM image of the magnetic micelles

Our remaining tasks are to demonstrate magnetically triggered release of cancer drugs and to show the release will kill cancer cells *in vitro*. Beyond this project we will demonstrate this device will work *in vivo* using animal models.