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Nanoparticle transport in a tumor-like environment

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Recent progress in the usage of nanotechnology for biomedical research has led to the rapid development of novel materials known as "nanoparticles" (NPs) for improved therapeutics and imaging in cancer therapy. Among other nanoparticle systems, gold nanoparticles (GNPs) are emerging as promising novel agents for cancer therapy. However, most of these studies were performed with properly oxygenated (normoxic) cells. The oxygen concentration in human tumors is highly heterogeneous, and there are many regions with very low levels of oxygen (hypoxia). We have investigated the NP uptake and transport under hypoxic conditions for the first time. Our results showed that the hypoxic cells with prolonged exposure (eighteen hours) to hypoxia had a higher NP uptake at both 6- and 24-hour NP incubation time points. No significant toxicity was introduced by NPs under hypoxic and normoxic conditions. Proper understanding of NP behavior and the therapeutic response in a tumor-like environment (hypoxic) can be used to improve the outcome of future cancer care. The biocompatibility of GNPs would accelerate the application of such innovations to clinics in the near future.

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The role of apolipoprotein E in uptake of atovaquone into the brain in murine acute and reactivated toxoplasmosis

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We investigated whether coating of atovaquone nanosuspensions (ANSs) with apolipoprotein E (apoE) peptides improves the uptake of atovaquone into the brain. The passage across the blood-brain barrier (BBB) of ANSs stabilized by polysorbate 80 (Tween*V* 80), poloxamer 184 (P184), or poloxamer 338 (P338) and the same formulations coated with apoE peptides were analyzed in vitro and *in vivo*. Passage through a rat co-culture model of the BBB did not differ between individual atovaquone formulations, and the addition of apoE peptides did not enhance the transport. Following the induction of toxoplasmic encephalitis (TE) in mice, treatment with all atovaquone formulations reduced the number of parasites and inflammatory foci compared with untreated mice. Uptake of atovaquone into the brain did not depend on coating with apoE. Finally, incubation of apoE peptide–coated ANSs with brain endothelial cells for 30 min did result in the accumulation of nanoparticles on the cell surface but not in their uptake into the cells. In conclusion, ANSs coated with Tween*V* 80 or poloxamers showed therapeutic efficacy in murine toxoplasmosis. ApoE- and apoE-derived peptides do not induce the uptake of ANSs into the brain. Alternative mechanisms seem to be in operation, thereby mediating the passage of atovaquone across the BBB.

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