The Blood-Brain-Barrier Crossing *in vivo* using Magnetic Nanocapsules

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For treatment of variety of central nervous system (CNS) diseases, one of the major issues is the inability for effective penetration of CNS drugs, even small molecule drugs, into the brain parenchyma through blood brain barrier (BBB). Currently no practical method seems to efficiently overcome such a limitation. Thus, a new technique that allows better drug penetration into the brain is highly desirable. We have successfully created magnetic nanocapsules (MNCs) of 100 nm size, which provide powerful magnetic vector for BBB crossing. These nanocapsules containing a fluorophore within have been engineered for direct tracking and measurement of the position of MNCs, which also allow cellular-level high-resolution imaging analysis such as confocal microscopy. Applied magnetic field facilitated the extravasation and/or accumulation of these magnetic nanocapsules in the brain parenchyma.

Unlike other targeted delivery methods, (i.e., mediated by antibodies to specific cell surface receptors), magnetically forced translocation of MNCs do not mediate un-favored signal transduction events triggered by interaction between the delivery vehicle and its targeted receptor, and can also avoid undesirable accumulation of particles (nanocapsules) in other organs that express the targeted receptor. Moreover, it is easy to fine-tune the accumulation of particles by longer exposure to the magnetic force with relatively less toxicity observed. Together, the enhanced magnetic properties of iron oxide particles in the nanocapsule configuration and the capacity to use magnet to alter

their distribution allow minimally invasive translocation of the particles to the brain parenchyma and therefore have great potential for usage in the treatment of CNS diseases.

(a) (b)

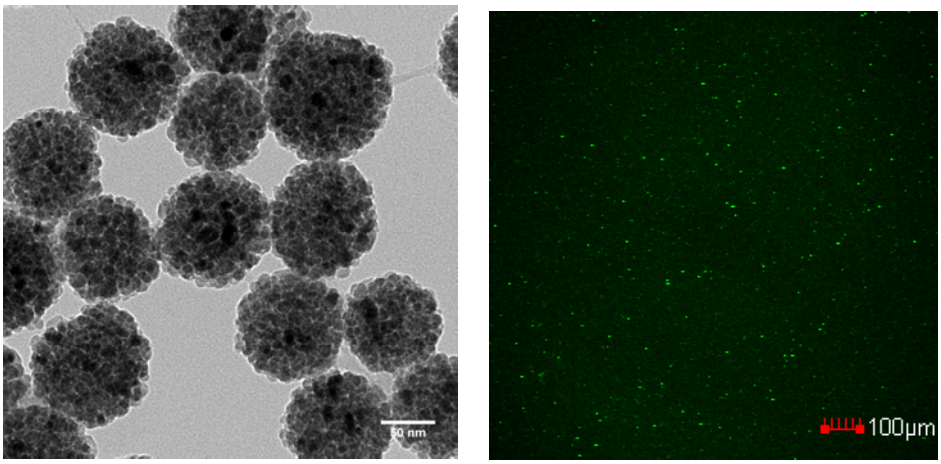

Figure 1: Synthesis of fluorophore labeled magnetic nanoparticles (MNPs). (a) TEM showing trapped magnetic nanoparticles. (b) Confocal microscopy image showing green colored MNPs.

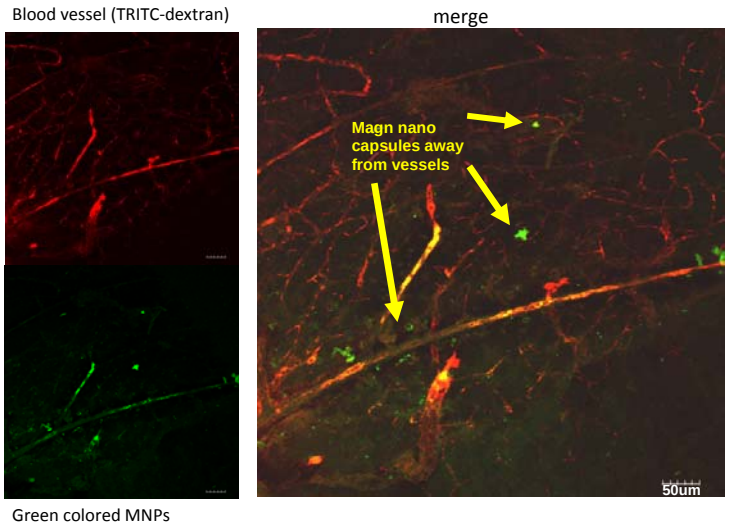

Figure 2: Confocal microscopy image of vessel (perfused with TRITC-dextran, red) and MNCs (labeled with fluorophore, green) demonstrates extravasation of MNCs.