Magnetic and Acoustically Active Lipospheres for Magnetically Targeted Nucleic Acid Delivery

With the aim of obtaining a carrier for combined magnetic-field-and ultrasound-targeted nucleic acid delivery, acoustically active lipospheres are prepared that comprise magnetic nanoparticles and plasmid DNA or synthetic siRNA. The lipospheres, with average diameters of 5 μm and smaller, are obtained upon shaking a mixture of soybean oil, a cationic lipid, magnetic nanoparticles, a nucleic acid, and aqueous buffer in a perfluoropropane atmosphere in a sealed vial. These lipospheres create contrast in ultrasound imaging and display greatly increased magnetophoretic mobility and in consequence greatly improved magnetic retention in a flow model when compared with free magnetic nanoparticles. In cell culture, the lipospheres are sedimented within minutes to the surface of cells using a gradient magnetic field. This sedimentation results in the association of about 50% of the applied plasmid DNA with the cells and in functional DNA and siRNA delivery in vitro. Under these conditions, ultrasound does not have an enhancing effect on nucleic acid delivery. When magnetic, acoustically active lipospheres carrying 125iodine-labeled plasmid DNA are injected into the tail veins of mice, the application of a gradient magnetic field to the chests of the mice results in a two-to threefold enrichment of both lung lobes with the plasmid. A similar
enrichment is obtained when ultrasound alone (1 MHz, 10 min) is applied. The combined application of magnetic field and ultrasound has no synergistic effect in terms of liposphere capture in the lungs. Histological analysis reveals intact lipospheres in lung capillaries. A synergistic effect of magnetic field and ultrasound is observed in site-specific plasmid deposition in a dorsal skinfold chamber model in mice after injection into the carotis. These conditions also result in functional plasmid delivery to the vasculature after intrajugular injection.