FRET imaging approaches for in vitro and in vivo characterization of synthetic lipid nanoparticles

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Résumé en anglais	DiI and DiD, two fluorophores able to interact by FRET (Förster resonance energy transfer), were coencapsulated in the core of lipid nanocapsules (LNCs) and nanoemulsions (LNEs), lipophilic reservoirs for the delivery of drugs. The ability of FRET imaging to provide information on the kinetics of dissociation of the nanoparticles in the presence of bovine serum albumin (BSA) or whole serum, or after incubation with cancer cells, and after systemic administration in tumor-bearing mice, was studied. Both microscopic and macroscopic imaging was performed to determine the behavior of the nanostructures in a biological environment. When 2 mg/mL FRET LNEs or LNCs were dispersed in buffer, in the presence of unloaded nanoparticles, BSA, or in whole serum, the presence of serum was the most active in destroying the particles. This occurred immediately with a diminution of 20% of FRET, then slowly, ending up with still 30% intact nanoparticles at 24 h. LNCs were internalized rapidly in cultured cells with the FRET signal decreasing within the first minutes of incubation, and then a plateau was reached and LNCs remained intact during 3 h. In contrast, LNEs were poorly internalized and were rapidly dissociated after internalization. Following their iv injection, LNCs appeared very stable in subcutaneous tumors implanted in mice. Intact particles were found using microscopic FRET determination on tumor sections 24 h after injection, that correlated well with the 8% calculated noninvasively on live animals. FRET investigations showed the potential to determine valid and reliable information about in vitro and in vivo behavior of nanoparticles.
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