

Magnetic-Fluid-Loaded Liposomes (MFLs) for Selective Imaging and Treatment of Brain Tumors: example of combination of multi-scale approaches to validate *in vivo* magnetic targeting.

Hélène Marie¹, Laurent Lemaire², Florence Franconi³, Sonia Lajnef⁴, Yves-Michel Frapart⁴, Valérie Nicolas⁵, Ghislaine Frébourg⁶, Michaël Trichet⁶, Christine Ménager⁷, Sylviane Lesieur¹

¹ *Laboratoire Physico-Chimie des Systèmes Polyphasés, Institut Galien Paris-Sud, UMR CNRS 8612, Faculté de Pharmacie, Université Paris-Sud, LabEx LERMIT, Châtenay-Malabry, France*¹

² *INSERM UMR-S 1066, Micro et nanomédecines Biomimétiques – MINT, Université d'Angers, LUNAM Université, Angers, France*

³ *PRIMEX-CIFAB, LUNAM Université, Université d'Angers, IRIS/IBS, CHU d'Angers, Angers, France*

⁴ *UMR CNRS 8601, FR3443 Université Paris Descartes – Sorbonne Paris Cité, Paris, France*

⁵ *Plateforme Imagerie cellulaire, IFR 141-IPSIT, Faculté de Pharmacie, Université Paris-Sud, Châtenay-Malabry, France*

⁶ *Sorbonne universités, UPMC Univ Paris 06, Institut de Biologie Paris-Seine (IBPS), FR 3631 UPMC-CNRS, Service de microscopie électronique, Paris, France*

⁷ *Equipe Colloïdes Inorganiques, Phenix, UMR CNRS 8234, Université Pierre et Marie Curie - Paris 6, Paris, France*

Hybrid devices based on the association of iron oxides with lipid nanoscale particles play an increasing role for targeted delivery of chemotherapeutics, mainly due to their biocompatibility and intrinsic efficacy as contrast agents for *in-vivo* Magnetic Resonance Imaging (MRI). In this study, we aimed at demonstrating the targeting of glioblastoma, into the striatum of mice, using magnetic-fluid-loaded liposomes (MFLs). MFLs targeting was achieved with a magnetic field gradient, from a magnet placed onto the head of the mice.

In vivo MRI showed that MFLs were successfully delivered to glioblastoma cells via the vasculature. Brains were then processed for Transmission Electron Microscopy (TEM) and Chemical mapping using Energy-Filtered TEM (EFTEM). MFLs were identified as electron dense clusters of iron nanoparticles inside cells lining the vascular lumen or in the adjacent extracellular matrix space.

Challenge here was to localize 200 nm diameter particles randomly dispersed into a complex tissue (glioblastoma). To avoid looking for a needle in a haystack, we exploited the internal rhodamine labeling of MFLs to localize magnetic-fluid-enriched regions on 70 μm thick sections, prior to TEM or EFTEM preparation.

The results revealed MFLs as potent tools for selective targeting of malignant brain tumors, especially promising for therapeutic issue as it can be expected that healthy brain tissue will be spared upon treatments by deleterious anticancer drugs carried by MFLs.

Reference

Marie H. et al. 2015. *Superparamagnetic Liposomes for MRI Monitoring and External Magnetic Field-Induced Selective Targeting of Malignant Brain Tumors*. Adv. Funct. Mater. 25, 1258–1269. DOI: 10.1002/adfm.201402289.