New generation of nanocarrier-loaded hydrogels: from conception to in vivo applications

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À l'invitation de la professeure Gaëlle Roullin

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The combination of pharmaceutical technologies can be a wise choice for developing innovative therapeutic strategies. The association of nanocarriers and gels provides new therapeutic possibilities due to the combined properties of the two technologies. Gels support the nanocarriers, localize their administration to the target tissue, and sustain their release. In addition to the properties afforded by the gel, nanocarriers can provide additional drug sustained release or different pharmacokinetic and biodistribution profiles than those from nanocarriers administered by the conventional route to improve the drug therapeutic index. An innovative free-polymer hydrogel platform was obtained by the association of lipid nanocapsules (LNCs). The hydrogel network was allowed by H-bond interactions between cross-linking agents exposed at the oil/water interfaces of LNCs. The viscoelastic properties of the hydrogels were correlated to the concentrations of both LNCs and cross-linking agent, and these mechanical properties forced the profiles of the sustained release of LNCs. Once all the LNCs are released, the main advantage of this platform compared to the conventional nanocarrier-loaded hydrogels is the absence of implant (polymer network) located at the administration site, which can lead to additional toxicities. These hydrogels are injectable using syringes and showed a good biocompatibility after an *in vivo* subcutaneous injection, with a local inflammatory response similar to that of induced by an approved excipient. Two preclinical applications of the hydrogels have been successfully explored: one to target metastasis from lung carcinoma and the other to delay the recurrences of glioblastoma after primary tumor resection.