Lipid nanoparticles as delivery vehicle for bio-macromolecules

Jessica Morlieras[1,2], Alan Hibbitts[1,2], Thomas Courant[1,2], Emilie Bayon[1,2], Hei Lanne Reynaud[3] Christian Villiers[3], Mathilde Menneteau[1,2], Patrice Marche[3] and Fabrice Navarro[1,2]

[1]Univ. Grenoble Alpes, Grenoble, F-38000, France; [2]CEA, LETI MINATEC, Technologies for Healthcare and Biology Division, 17 rue des martyrs, 38054 Grenoble Cedex 9, France; [3]Institut Albert Bonniot - UJF/INSERM U823, Rond-point de la Chantourne, 38042 Grenoble Cedex 9, France.

Corresponding author: fabrice.navarro@cea.fr

Abstract

Nanomedicine, the application of nanotechnology to medicine, is a growing field for decades. Several nanoparticles are already on the market, especially for tumour diagnosis or therapy. Their applications are based on their ability to reach the tumour tissue due to the well-known “enhanced permeability and retention” (EPR) effect where they can accumulate locally in the tumour and increase thus the efficiency of their contents. Most of these drugs are hydrophobic small molecule compounds whereas new therapeutic strategies in development are based on larger molecules from biological origin such as peptides, proteins or nucleic acids. Novel nanoparticle formulations are now highly anticipated for delivery of these bio-macromolecules, in particular for applications beyond cancer therapy. We designed lipid nanoparticles able to deliver either nucleic acids, or antigen proteins. A panel of chemical strategies have been explored for loading the bio-macromolecules into/onto the particles, ranging from simple electrostatic interaction to covalent grafting by using modified polymers. The resulting particles presented not only a high colloidal stability, but also a good safety profile. Moreover, their efficacy for the concerned applications were improved either to transfect nucleic acids into cells or to elicit immune responses in mice whenever the protein antigens are coupled to the nanoparticles. Further preclinical evaluation of these particles containing bio-macromolecules in different animal models is now ongoing and will contribute to their successful clinical translation.