Preparation and in vitro evaluation of imiquimod loaded polylactide-based micelles as potential vaccine adjuvants

Thomas Trimaille[1], Gloria Jiménez-Sánchez[2], Didier Gigmes[1] and Bernard Verrier[2]

[1] Aix-Marseille Université, CNRS, ICR UMR 7273, Marseille, France
[2] Université Lyon 1, CNRS, LBTI UMR 5305, Lyon, France

Contact : thomas.trimaille@univ-amu.fr

In the vaccine research against infectious diseases and cancer, subunit vaccines represent a safe approach, but weak immunogenicity of the antigens requires use of adjuvants, not often innocuous. To this regard, biocompatible and biodegradable nanoparticles (NPs) based on polylactide (PLA) are interesting candidates and have shown good potential as adjuvants, using either encapsulated or surface-adsorbed antigens [1]. Additionally, these NPs can serve as a versatile platform to further introduce immunostimulatory molecules such as toll-like receptor (TLR) ligands, able to efficiently target and stimulate/activate dendritic cells (DCs), which play a crucial role in the development of immune responses.
In recent works, we have designed a versatile PLA-based micellar NP platform which allows core/corona functionalization with hydrophobic/hydrophilic molecules, through the hydrophobic PLA core and the presence of N-succinimidyl (NS) ester reactive groups in the poly(N-vinylpyrrolidone) (PNVP)-based corona, and showed its potential interest for drug/vaccine delivery [2]. In a vaccine delivery purpose, these micelles were (i) core-loaded with imiquimod, a hydrophobic TLR7 ligand, and (ii) surface functionalized with an antigenic protein (HIV-1 Gag p24) through reaction of p24 lysines and N-terminal amine with the NS ester pendant groups of the micelle corona. The impact of imiquimod encapsulation in the micelles on its immunostimulatory properties was investigated in vitro, by monitoring: (i) the NF-κB and mitogen-activated protein kinases (MAPK) pathways through experiments with RAW-Blue™ cells, a mouse macrophage cell line encoding an NF-κB/AP-1-inducible reporter construct; (ii) human dendritic cells (DCs) maturation markers by flow cytometry. RAW-Blue™ cell based experiments showed that imiquimod encapsulated in the micelles was much more efficient to activate the NF-κB and MAPK pathways than free imiquimod. Furthermore, encapsulated imiquimod was found to induce much higher maturation of DCs than the free analog. Finally, these immunostimulatory properties of the loaded imiquimod were shown to be conserved when the p24 antigen was coupled at the micelle surface [3].
Taken together, these data regarding improved immunostimulatory efficiency suggest the strong potential of our micelle-based nano-system for vaccine delivery.

References.

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