Targeting nanoparticles to M cells with non-peptidic ligands for oral vaccination

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Over the last decade, polymer micelles and nanoparticles attracted an increasing interest in drug research because they can be used as efficient drug delivery systems[1]. Nanoparticles are submicron-sized polymeric colloidal particles with a therapeutic agent of interest encapsulated within their polymeric matrix[2]. The addition of an amphiphilic block copolymer made up of poly(ethylene oxide) and an aliphatic polyester, such as poly(ε-caprolactone) (PCL) or polylactide (PLA), to the formulation permits to take advantage of the protein repellent properties of PEO to increase the time live of the nanoparticles in the vascular residence.

The use of polymeric nanoparticles for the delivery of complex antigens, the combination of antigens, and genetic vaccines makes them one of the most promising strategies for oral vaccination[3]. Polymeric carriers protect antigens against degradation and inactivation in the harsh gastro-intestinal environment and have the ability to enhance their transmucosal transport. When these copolymers have a targeting agent, the biodistribution of polymeric micelles can be modulated and can induce specific cellular uptake by receptor-mediated endocytosis.

The presence of RGD allows the targeting of β1 integrins at the apical surface of human M cells and the enhancement of an immune response after oral immunization. Is it possible that RGD peptide partial degraded during its transport in the gastrointestinal tract.

To check the hypothesis that a non-peptidic ligand could exhibit a higher stability in the gastrointestinal tract, new non-peptidic ligands targeting intestinal M cells or APCs for oral immunisation were grafted onto the PEG chain of PCL-b-PEG copolymer and incorporated in PLGA-based nanoparticles. The presence of GRGDS and RGDp in the formulation significantly increased the transport of nanoparticles across an in vitro model of human M cells compared to enterocytes, due to interactions between those ligands and the β1 integrins detected at the M cell apical surface. In vivo, an immune response was induced after intragastric and intraduodenal administration of ovalbumin loaded-nanoparticles. Targeted formulations were also able to induce a cellular immune response. In conclusion, the *in vitro* transport of nanoparticles and the immune response were positively influenced by the presence of ligands at the surface of nanoparticles. These targeted-nanoparticles could thus be a promising delivery system for oral immunization.

References

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