Cancer vaccine based on hybrid lipid-polymeric nanoparticles

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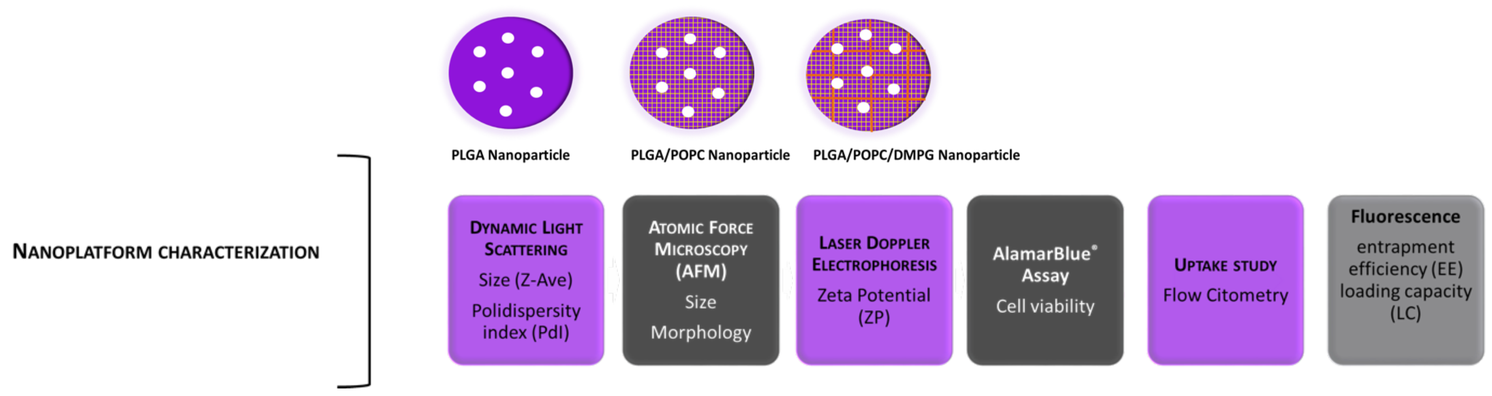
Introduction

Hybrid lipid-polymeric nanoparticles stand out as potential candidates for the development of biocompatible and biodegradable delivery systems, combining advantages of polymeric nanoparticles and lipid systems. These hybrid nanoplatforms have been revealed advantageous for *in vivo* delivery of different active entities.

Aim: The present study was focused on the design of a hybrid lipid-polymeric nanoplatform for the delivery of multiple antigens and immune modulators to dendritic cells (DCs) to foster the induction of extensive and coordinated host immune responses.

Methods

OVA Alexa Fluor® 647 conjugate, a model antigen, was entrapped in PLGA-lipid hybrid nanoparticles by the double emulsion-solvent evaporation method. Two different lipids, 1-Palmitoyl-2-oleoyl-sn-glycero-3-phosphorylcholine (POPC) and 1,2-Dimyristoyl-sn-glycero-3-phosphorylglycerol (DMPG), were used to modify nanoparticle matrix.

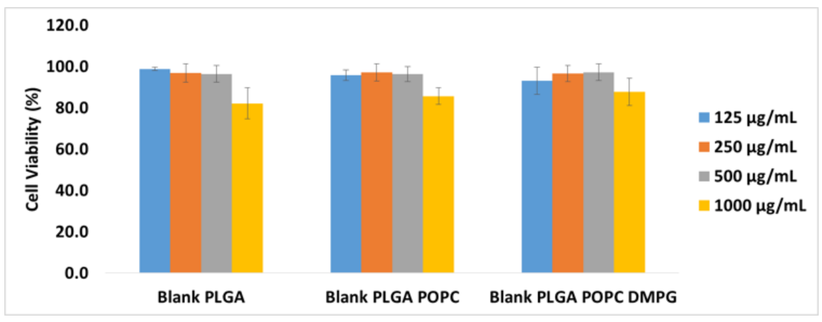


Results

NANOPARTICLE PHYSICOCHEMICAL PROPERTIES

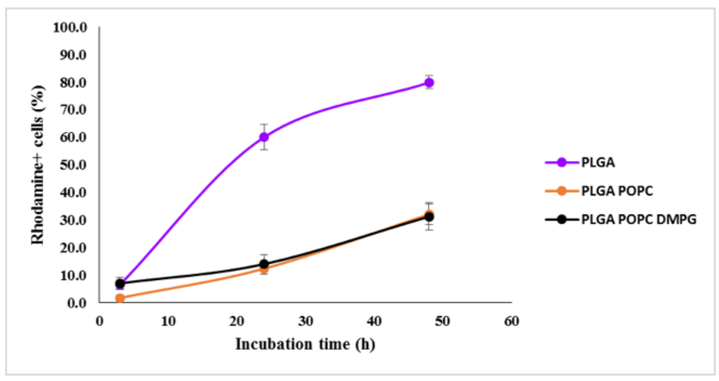
Formulations	Z-Ave (nm)	PdI	ZP (mV)	EE (w/v)	LC (µg/mg)
Blank PLGA	198.6± 11.00	0.100 ± 0.029	-3.89 ±1.72	0.0 ± 0.0	0.0 ± 0.0
OVA-PLGA	190.7 ± 3.66	0.063 ± 0.005	-3.80 ± 1.11	69.9 ± 4.6	3.5 ± 0.2
Blank PLGA/POPC	167.3 ± 4.21	0.085 ± 0.010	-3.12 ± 0.34	0.0 ± 0.0	0.0 ± 0.0
OVA-PLGA/POPC	175.2 ± 12.94	0.100 ± 0.059	-2.42 ± 0.29	60.6 ± 4.9	3.0 ± 0.2
Blank PLGA/POPC/DMPG	143.9 ± 15.29	0.088 ± 0.009	-7.83 ± 1.04	0.0 ± 0.0	0.0 ± 0.0
OVA-PLGA/POPC/DMPG	136.6 ± 0.59	0.078 ± 0.015	-5.26 ± 0.48	84.1 ± 1.4	4.2 ± 0.1

CELL VIABILITY (Alamar Blue®) – JAW SII ((N= 3, n=6), 24h)



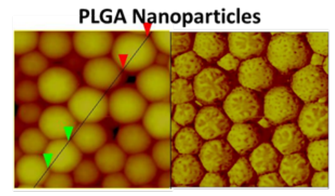
Controls: 0.5 % (w/v) Triton X-100 (11.8 % ± 1.40 %), PBS (100.0 % ± 3.92 %)

UPTAKE STUDY – JAW SII – PLGA-Rhodamine (N=3, n=3)

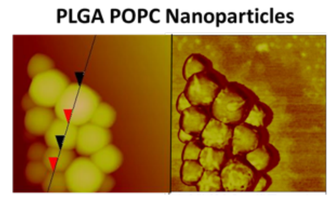


SURFACE MORPHOLOGY EVALUATION
AFM - 715x715 nm²

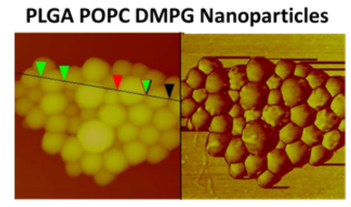
PLGA Nanoparticles



PLGA POPC Nanoparticles



PLGA POPC DMPG Nanoparticles



The mean diameter of hybrid lipid-polymeric nanoparticles was lower than the one presented by the polymeric ones. All formulations presented a monodispersed population, ZP close to neutrality and high EE and LC values. AFM analysis evidenced that the addition of lipids to the PLGA matrix resulted in smoother nanoparticle surfaces. The viability of nanoparticle-treated cells was close to 100 %, and nanoparticle internalization levels by DCs increased with the incubation time. Hybrid nanoparticles were taken up by DCs at lower extent than the polymeric-based carriers. However, additional studies focused on the characterization of nanoparticle-cell interaction and intracellular trafficking may clarify the potential of these novel hybrid lipid-polymer nanoparticles for immune modulation.

Conclusions & Perspectives

A promising hybrid nanoplatform for antigen delivery and DC activation and maturation was developed. *In vivo* studies are ongoing to evaluate if the hybrid lipid-polymeric nanoparticles are able to induce a selective and extensive immune response capable of eliciting a reduction of melanoma tumor growth or even its eradication.

Acknowledgements

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