IPVS
Belgian branch

Abstract template IPVS Belgian branch

Oral presentation [X] / Poster [X]

Biomimetic polyelectrolyte microparticles facilitate antigen presentation by porcine dendritic cells

Bert DEVRIENDT[1,*], Kim BAERT[1], Marijke DIERENDONCK[2], Herman FAVOREEL[1], Jean Paul REMON[2], Bruno G. DE GEEST[2], Eric COX[1]

[1]Laboratory of Immunology, Faculty of Veterinary Medicine, Ghent University, Merelbeke; [2]Laboratory of Pharmaceutical Technology, Department of Pharmaceutics, Faculty of Pharmaceutical Sciences, Ghent University, Ghent.

Introduction

Vaccination is regarded as the most efficient and cost-effective way to prevent infectious diseases. Vaccine design nowadays focuses on the implementation of safer recombinant subunit vaccines. However, these recombinant subunit antigens are often poor immunogens and several strategies are currently under investigation to enhance their immunogenicity. The encapsulation of the antigens in biodegradable microparticulate delivery systems seems a promising strategy to boost their immunogenicity[1]. Here, we evaluate the capacity of polyelectrolyte microparticles (PECMs), fabricated by single step spray-drying, to deliver antigens to porcine dendritic cells (DCs) and how these particles affect their functional maturation (DCs). As clinically relevant model antigen F4 fimbriae, a bacterial adhesin purified from a porcine-specific enterotoxigenic *E. coli* (ETEC) strain, was chosen.

Materials and methods

PECMs were loaded with either BSA-FITC or the F4 fimbriae by co-spray-drying these antigens with the PECM constituents: the polyelectrolytes dextran-sulphate and poly-L-arginine and the sacrificial template mannitol. PBMCs were isolated from blood by density gradient centrifugation. $CD172a^+$ monocytes were further enriched by positive immunomagnetic bead selection (MACS) and cultured for 4 days with recombinant porcine (rp) IL-4 and rpGM-CSF to generate porcine monocyte-derived DCs (MoDCs). These *in vitro* generated immature MoDCs were incubated for 24 h with LPS (1 µg), F4 fimbriae (1.0 and 0.1 µg) and F4-fimbriae-loaded polyelectrolyte microparticles (F4-PECM; 1.0 and 0.1 µg encapsulated antigen) and the phenotypical and functional DC maturation was assessed by confocal and live cell imaging, flow cytometry, T-cell proliferation assays and porcine-specific cytokine ELISAs.

Results

In confocal images we detected multiple particles per cell in >80% of the examined DCs, indicating that the resulting antigen-loaded PECMs were efficiently internalised by porcine MoDCs. F4-PECMs enhanced CD40 and CD25 surface expression by DCs and this phenotypical maturation correlated with an increased secretion of IL-6 and IL-1β. More importantly, F4-PECMs enhanced both the T-cell stimulatory ability and antigen presentation capacity to $CD6^+$ T-cells of MoDCs. Moreover, PECMs efficiently promoted the $CD8^+$ T-cell stimulatory activity of dendritic cells, indicating an enhanced ability of the DCs to cross-present the encapsulated antigens via MHCI.

Discussion and conclusions

In conclusion, single step spray-dried antigen-loaded polyelectrolyte microparticles efficiently enhanced the functional maturation and increased the cross-presentation ability of porcine DCs. Interestingly, the elevated IL-6 and IL-1β secretion could hint at the capacity of PECM-stimulated DCs to drive T-cell polarisation towards a Th17 phenotype, while higher IL-1β levels could also indicate inflammasome activation. Our results confirm recent data obtained in rodent models that these PECMs boost the immunogenicity of vaccine antigens[2]. In addition, this antigen delivery system allows not only the co-encapsulation of immune potentiators, such as PRR ligands, but also the functionalisation of the microparticles' surface with targeting ligands to enhance the delivery of these carrier systems to the immune system. Our results could accelerate the development of veterinary and human subunit vaccines based on polyelectrolyte microparticulate delivery systems to combat a variety of extra- and intracellular pathogens.

References

[1]De Koker et al., 2011, Chem Soc Rev 40:320-39
[2]Dierendonck et al., 2011, ASC Nano, 5:6886-93

Abstract template IPVS Belgian branch