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Poster presentation

P11-15. Induction of a mucosal immune response to HIV after systemic immunization with poly(lactic acid) nanoparticles formulated with gag antigen and polyI:C

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Background

To efficiently neutralize HIV at portals of entry, strong humoral responses are needed, associated to efficient cellular responses to avoid the dissemination of HIV in organism. If poly(lactic acid) (PLA) nanoparticles carrying HIV proteins have shown to induce a high systemic humoral immune response in mice, rabbit or macaque following sub-cutaneous administration, cellular and mucosal responses are still faint. Thus, to increase potency and specificity of mucosal immune responses, additional immunostimulatory signals, such as TLR ligands could be delivered with HIV antigens. The aim of this study was to compare the effect of co-administration of polyI:C, a TLR3 agonist, with PLA p24 nanoparticles on the mucosal and cellular responses in two animal models.

Methods

We compared the effect on immune responses of PLA-p24 administrations (10 μg in mice and 200 μg in macaque) adjuvanted or not with polyI:C (0.05 μg in mice and 125 μg in macaque) co-administered with nanoparticles. Systemic (humoral and cellular) immune responses were monitored in sera, and mucosal response was followed by measuring anti-p24 antibodies IgA and IgG in vaginal washes and faeces.

Results

Sub-cutaneous administration of PLA-p24 induced a high systemic humoral response that was not modified by the addition of polyI:C. Nevertheless, while no cellular response was observed in macaque after two administrations of PLA-p24 alone, a high gag-specific IFN-gamma T cellular response was induced after boosting with the co-administration of polyI:C with PLA-p24. In mice, the co-administration of polyI:C with PLA-p24 increased significantly the mucosal humoral response as shown by high level of anti-p24 IgG and IgA in faeces, and high level of anti-p24 IgG in vaginal washes.

Conclusion

Our findings suggest that co-delivery of TLR3 ligand with HIV antigens when using PLA nanoparticles could potentiate immune responses, both at the cellular and humoral level. Moreover, addition of TLR agonist improves mucosal immune responses.