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Poster presentation

P02-12. Bupivacaine, a local anaesthetic, enhances immunogenicity of a multiepitopic DNA vaccine containing HIV promiscuous CD4 T cell epitopes

DS Rosa*, SP Ribeiro, EC Mairena, J Kalil and E Cunha-Neto

Address: Division of Clinical Immunology and Allergy, Dept. of Internal Medicine, University of São Paulo School of Medicine, Sao Paulo, Brazil
* Corresponding author

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Background

DNA vaccines offer several advantages over other vaccine concepts, but poor immunogenicity in clinical use is still a general concern. Therefore, strategies to optimize the immunogenicity of DNA vaccines are urgently needed. Here, we explored the efficacy of Bupivacaine on augmenting the immunogenicity of a DNA vaccine encoding multiple HIV epitopes designed by our group.

Methods

The nucleotide sequence encoding 18 CD4/CD8 HIV-1 T cell epitopes was subcloned in pVAX-1. The DNA vaccine (pVAX-HIVBr18) or empty pVAX were used to immunize BALB/c mice, alone or in the presence of Bupivacaine (a local anaesthetic with adjuvant properties). T cell responses were assessed by IFN-gamma and IL-2 ELISPOT, polyfunctional flow cytometry, Cytometric bead array on culture supernatants, and CFSE proliferation. Breadth of immune response was evaluated using ELISPOT assay against individual peptides.

Results

Coadministration of pVAXHIVBr18 with Bupivacaine was able to induce higher numbers of IFN-gamma secreting cells (ELISPOT) as well as a marked increase in IFN-gamma and TNF-α secretion against pooled HIV peptides when compared to pVAXHIVBr18 alone. Additionally, coadministration with Bupivacaine induced an increase of trifunctional ($IFN^+/IL\text{-}2^+/TNF^+$) CD4 T cells compared to the DNA vaccine alone. Also, coadministration of DNA vaccine with Bupivacaine increased IFN-gamma$^+$/IL-2$^+$ effector memory CD4 T cells and IFN-gamma producing effector memory CD8 T cells. Proliferative capacity of antigen-specific CD8 T cells was improved by Bupivacaine coadministration, as compared to DNA vaccine alone. This adjuvanted formulation induced multiepitopic responses with similar breadth as DNA alone.

Conclusion

Our data suggest that Bupivacaine can increase the magnitude of cytokine-producing effector memory $CD4^+$ and $CD8^+$ T cells, as well as increasing polyfunctional cytokine production of $CD4^+$ T cells, and increase proliferation of $CD8^+$ T cells. This may have an impact in the clinical use of DNA vaccines.