Adjuvant choice modulates self antigen specific CD4 responses generated by peptide vaccination

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Introduction:

- CD4 cells are potent effectors but CD4 responses to self antigens are attenuated.
- Cellular stress induces autophagy which leads to modification of proteins recognised by the immune system.
- In the absence of inflammation, immune is regulated, whereas in its presence CD4 responses to modified self-antigens are stimulated.
- T cells targeting modified self-antigens play a role in the pathophysiology of several autoimmune diseases.
- Cancer cells citrullinate proteins and present modified peptides as targets for CD4 T cells.
- Responses can be induced by peptide vaccination.
- Selection of an appropriate adjuvant is necessary in order to induce immunity with peptide vaccines.
- In this study we investigate the effect of adjuvant on the induction and cytokine profile of self antigen specific CD4 responses.

Results:

Modified peptides induce strong Th1 responses that mediate tumour therapy

Methods:

- HLA-DRA4 or C57Bl/6 mice were immunised with a single dose of 25μg citrullinated vimentin (Vim), enolase (Eno), myelin oligodendrocyte glycoprotein (MOG) or ovalbumin (Ova) peptide in combination with adjuvant.
- Splenocytes were monitored at indicated time points by cytokine elispot assays or ELISA for peptide specific immune responses.
- HLA-DRA4 transgenic were challenged with B16F1 tumour expressing HLA-DRA4 either prior to or post vaccination with citrullinated peptide in adjuvant.

Citrullination. A modification that occurs within stressed cells. Peptidylarginine deiminases (PADs) enzymes are activated and convert arginine to citrulline by altering the positively charge aldimine group to neutral charged betaine group of citrulline.

Adjuvant choice polarises the cytokine response of modified epitopes

References:


Conclusion

These results demonstrate the stimulation of memory responses to self antigens that recognise and target tumour cells using modified peptide epitopes. Furthermore the cytokine phenotype of these self antigen specific responses can be dramatically polarised when combined with different adjuvant combinations and costimulation resulting in a change in tumour targeting ability.