



Athero-protective effects of a human apoB-100 related peptide vaccine in apoE-/- mice are modulated by peptide dose and time of initiation of high fat diet



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PRESENTER DISCLOSURE INFORMATION

Preiman K Shah Research Grant CardioVax Modest
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BACKGROUND

LDL immunization reduces development of atherosclerosis in rabbits (Palinski 1995, Ameli 1996) and in apoE knockout mice (George 1998, Freigang 1998, Chyu 2004, Zhou 2001, 2005)

More than 100 human apoB-100 related peptides were screened for their potential as possible immunogens to be used in vaccine strategy to modulate atherosclerosis (Fredrikson,2003).

PURPOSE AND HYPOTHESIS

In this study, we tested if different doses of apoB-100 related peptide p210 (KTTKQ SFDLs VKAQY KKNKH) and timing of high fat (HF) diet exposure modulate its athero-protective effects.

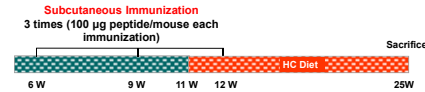
We also studied the effect of p210 in vitro on dendritic cells to explore the mechanism of p210 athero-protective effect.

MATERIALS AND METHODS

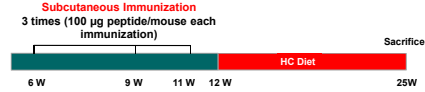
Methods I

Male apoE-/- mice were immunized at 6, 9, and 11 wks of age with p210 at doses of 25, 50 or 100 µg conjugated to cBSA with alum as adjuvant. Mice receiving cBSA/alum served as control.

HC was started 1 week before last booster (Group 1)



HC was started 1 week after last booster (Group 2)

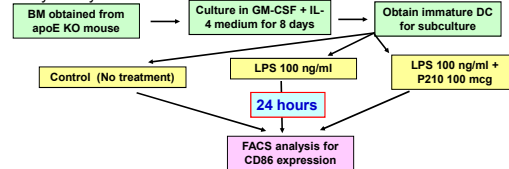


Atherosclerosis was assessed by en face analysis of lipid-stained aorta at 25 wks.

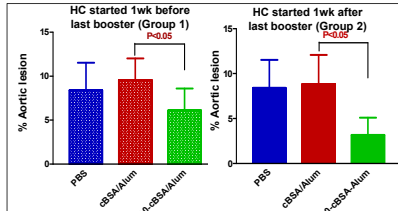
Methods II

Dendritic cells (DCs) were generated from apo E knock-out mice bone marrow by stimulating with GM-CSF and IL-4.

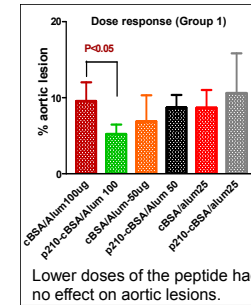
At day 8, DCs were treated with LPS(100ng/ml) with or without p210. Peptide for 24 hours, cells were stained with CD11c and CD86, then analyzed by FACS



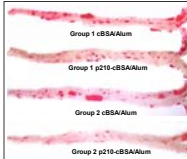
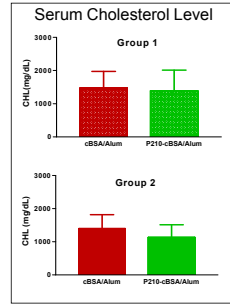
RESULTS



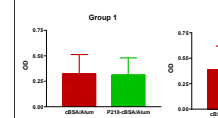
p210 immunization at 100 µg reduced atherosclerosis in both groups with greater reduction in Group 2 (61%) versus Group 1 (36%).



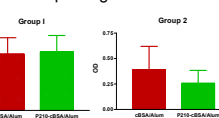
Lower doses of the peptide had no effect on aortic lesions.



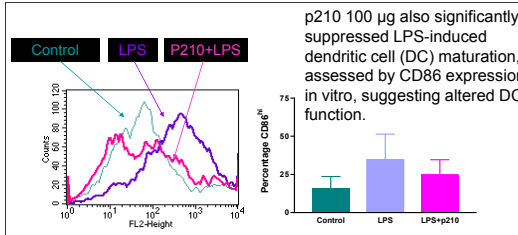
Anti-p210 IgG Titer



Anti-p210 IgM Titer



Among mice immunized with 100 µg p210, Group 2 mice had lower p210 IgG compared with its control group



p210 100 µg also significantly suppressed LPS-induced dendritic cell (DC) maturation, assessed by CD86 expression in vitro, suggesting altered DC function.

CONCLUSIONS

p210 immunization at a dose of 100 µg reduces atherosclerosis whereas lower doses are ineffective.

Delayed initiation of HF diet until after completion of immunization produced greater athero-protective effects. Peptide dose and timing of HF diet modulate athero-protective effects of p210 immunization in apoE-/- mice.

The mechanism of action by p210 in reducing atherosclerosis may involve altered CD86 signaling on dendritic cells.