

Regulatory T cells have an atheroprotective effect in apolipoprotein B peptide immunization

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Introduction:

Immunization with apo B-100 derived peptides has been shown to inhibit atherosclerosis development in mice (1). The immune mechanism mediating the protection is, however, not yet fully understood. The aim of the present study was to elucidate the role of CD25 positive T cells in the athero-protective effect of a vaccine based on the apo B peptide p210.

Experimental set up:

- Apo E^{-/-} mice
- apo B-100 peptide p210 immunizations
- mice fed a high fat diet from 10 weeks
- weekly injections of blocking CD25 antibodies
- at sacrifice atherosclerosis was determined by Oil Red O staining of the descending aorta and T cells analysed with flow cytometry

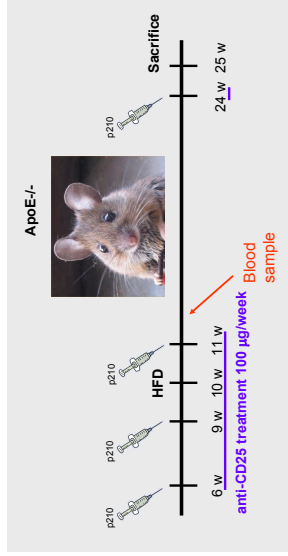


Figure 1. Experimental design

Results:

- The presence of CD4+CD25+ T cells in blood are increased after p210 immunizations and decreased after CD25 blocking antibody treatment (Figure 2)
- Atherosclerosis in aorta is decreased by p210 immunizations. CD25 blocking antibodies inhibited the atheroprotective effect of p210 (Figure 3)
- The presence of regulatory T cells in the spleen are increased after p210 immunizations.
- Treatment with CD25 blocking antibodies completely blocks p210 immunization-induced increase in regulatory T cells (Figure 4)
- Splenic T cells in immunized mice have reduced proliferation in response to CD3/CD28 bead stimulation (Figure 5)

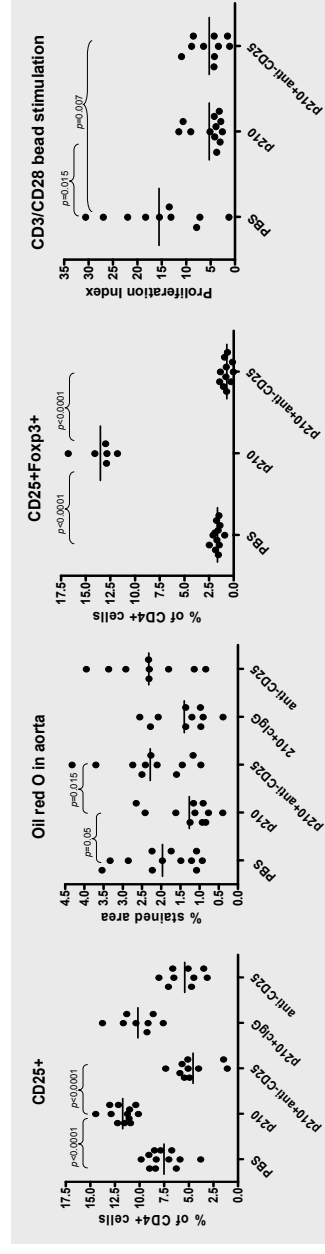


Figure 2. Flow cytometric analysis of CD25+ CD4 T cells in blood at 12 weeks of age

Figure 3. Oil red O staining of aortic plaques at 25 weeks of age

Figure 4. Flow cytometric analysis of regulatory T cells in spleen at 25 weeks of age

Figure 5. Splenic T cell proliferation after CD3/CD28 bead stimulation for 96 hours

Conclusions:

- Immunization with an apo B-100 peptide induced an atheroprotective immune response.
- By neutralizing CD25 in p210 immunized mice the protection was blocked, indicating that regulatory T cells play an important role in the atheroprotection induced with p210 immunizations.
- The reduced proliferation rate in splenic T cells from p210 immunized mice is also an indication of activated regulatory T cells.

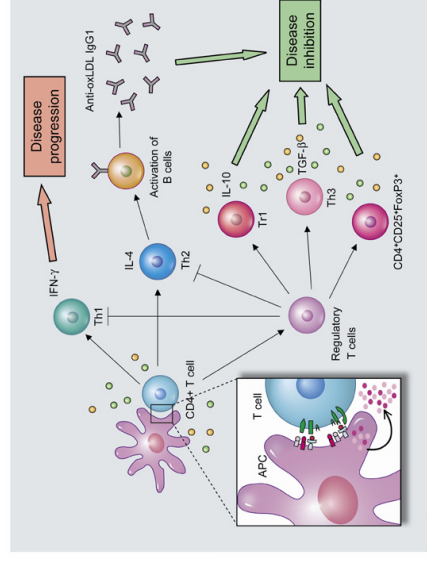


Figure 6. Summary

References:

1. Fredrikson GN, Soderberg I, Lindholm M, Dimayuga P, Chyu KY, Shah PK, Nilsson J. Inhibition of Atherosclerosis in ApoE-Null Mice by Immunization with ApoB-100 Peptide Sequences. *Arterioscler Thromb Vasc Biol.* 2003;23(5):879-884.

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