

# Circulation

(Circulation. 2009;120:S1018.)

© 2009 American Heart Association, Inc.

## Mechanisms of Atherosclerosis: Lipid Biology

### Abstract 4908: Athero-protective Effects of Immunization With apoB-100 Related Peptide Vaccine in apoE<sup>-/-</sup> Mice is Associated With Enhanced CD8 Regulatory T Cell Response

Xiaoning Zhao; Kuang-Yuh Chyu; Paul C Dimayuga; Juliana Yano; Xiaojun Li; Portia Trinidad; Jianchang Zhou; Wai Man Lio; Jonathan Kirzner; Lai F Chan; Bojan Cercek; Prediman K Shah.

Cedars Sinai Med Cntr, Los Angeles, CA

**Background:** We previously reported that immunization of apoE<sup>-/-</sup> mice with human apoB-100 related peptide P210 (KTTKQ SFDLS VKAQY KKNKH) resulted in a 60% reduction in atherosclerosis by a regulatory T-cell (Treg) response elicited by the vaccine. In this study, we investigated the mechanisms involved in this regulatory response.

**Methods and Results:** Male apoE<sup>-/-</sup> mice were immunized at 6, 9 and 11 weeks of age with P210 conjugated to cBSA, and alum as adjuvant, at a dose of 0.1 mg/mouse and euthanized at 13 weeks of age, or fed atherogenic diet until euthanasia at 25 weeks of age. At 13 weeks, FACS analysis of regional LN showed significantly reduced CD11c + CD86 + dendritic cells (DC) in the p210 group (Table), suggesting an immune-regulatory response. Treg profiling showed significantly increased CD8 + CD25 + Treg in the peripheral blood (PBMC) of P210 group (Table) without changes in the CD4+CD25+ and CD8+CD28- Treg. CD11c+ DCs in atherosclerotic lesions at 25 weeks were reduced in P210 (2.9± 1.7%, n = 12; p<0.05) compared with cBSA or PBS group (3.9± 1.6%, n = 7 and 4.5± 1.2%, n = 18; respectively) with concomitant reduction of macrophages in P210 group compared with cBSA and PBS (12.4± 2.5% vs. 15.4± 3.1% and 16.1± 2.9%, respectively; p<0.05).

**Conclusion:** Our results indicate that P210 vaccination resulted in a CD8+CD25+ Treg response mediated by decreased DC co-stimulatory signaling, leading to a reduction of plaque DC and macrophage content, and attenuated plaque growth, suggesting a novel role of CD8+ Treg in reducing atherosclerosis.

	Lymph Nodes (N≥3)		PBMC (N≥9)	Spleen (N≥4)
	CD11c+CD86+	CD8+CD25+	CD8+CD25+	CD8+CD25+
PBS	1.40±0.17	6.28±1.17	4.39±0.78	8.24±0.67
cBSA	1.86±0.56	6.00±1.10	3.97±1.20	8.23±1.51
P210	1.07±0.34*	7.14±1.22	5.74±1.77*	10.74±3.26

All values are expressed as percent of gated cells. \*P<0.05 vs PBS and cBSA, ANOVA.