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OX40-OX40L INTERACTION TARGETS NFATC1 IN APOE−/− MICE DURING ATHEROGENESIS

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Objectives We investigated the effect of OX40-OX40L interaction on the nuclear factor of activated T cells c1 (NFATc1) in ApoE−/− mice.

Methods Atherosclerotic plaque was induced by rapid perivascular carotid collar placement in ApoE−/− mice. The expression of OX40, OX40L and NFATc1 in lymphocytes was measured by Real Time PCR (RT-PCR) and flow cytometry (FCM), respectively. The presence of NFATc1 in the atherosclerotic plaque was detected by immunohistochemistry. The level of IL-4 was measured by ELISA.

Results We found that the expression of NFATc1 was significantly elevated both in atherosclerotic lesion and in leukocytes from ApoE−/− mice. In vitro, after stimulating OX40-OX40L interaction by anti-OX40L mAb, NFATc1 mRNA expression and protein concentration increased by RT-PCR and FCM, respectively in lymphocytes, while anti-OX40L mAb suppressed expression of NFATc1 in lymphocytes. Moreover substantially elevated level of IL-4 was induced by anti-OX40 mAb, while NFATc1 inhibitor markedly suppressed production of IL-4.

Conclusions This study suggests that OX40-OX40L interaction regulates the expression of NFATc1, which may play a critical role in atherosclerotic plaque formation, which might also have implications with pathophysiology of atherosclerosis.