atherosclerosis lesion area in a lipid-independent manner. In parallel, it was observed that decreased expression of vascular HMGB1, RAGE, VCAM-1, MCP-1 and TF in apoE deficient mice treated with simvastatin versus vehicle or SM. Furthermore, increased sRAGE in serum were observed in simvastatin-treated apoE deficient mice, and the level of sRAGE was negatively correlated with the serum HMGB1 level and atherosclerosis lesion area. More interestingly, consistent with the premise that addition of HMGB1 to HUVECs resulted in increased expression of HMGB1, RAGE and VCAM-1, and simvastatin reverted the effects of HMGB1. The roles of simvastatin were similar to RAGE blockade by anti-RAGE antibody in vitro.

Conclusion Simvastatin suppressed HMGB1-RAGE axis and atherosclerosis via mevalonate pathway.

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SIMVASTATIN SUPPRESSED HMGB1-RAGE AXIS AND ATHEROSCLEROSIS VIA MEVALONATE PATHWAY

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Objective Recent studies suggested that high mobility group box 1 (HMGB1) and receptor for advanced glycation end products (RAGE) contribute to atherosclerosis, and statin may inhibit tissue RAGE or increase serum sRAGE. However, it remains unclear whether statin suppress HMGB1-RAGE axis in atherosclerosis models. Thus, in this study, we tested the hypothesis that simvastatin suppresses HMGB1-RAGE axis and atherosclerosis in apoE deficient mice.

Methods Male apoE deficient mice, age five weeks, were offered western diet. At the age of eight weeks, mice were treated with once-daily simvastatin (50 mg/kg/day), simvastatin (50 mg/kg/day)+mevalonic acid (30 mg/kg/day) (SM) or vehicle; all mice were killed at age 11 weeks.

Results Compared with apoE deficient mice treated with vehicle or SM, simvastatin-treated mice displayed decreased