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·专题报告·

Prominent Roles of the Renin Angiotensin System in Atherosclerosis

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The renin angiotensin system (RAS) is emerging as a prominent factor in the development of experimental atherosclerosis. We have previously demonstrated that the RAS is profoundly activated in hypercholesterolemia. This was demonstrated in LDLR$^{-/-}$ mice fed a saturated fat enriched diet and manifested as increased plasma concentrations of angiotensinogen and angiotensin peptides, especially angiotensin Ⅱ (AngⅡ). Many of the functions of AngII are via activation of AT1a receptors. Deletion of AT1a receptors in LDL receptoR$^{-/-}$ resulted in a profound decrease in atherosclerosis without any change in systolic blood pressure. To determine whether the beneficial effects of AT1a receptor deletion was attributable to the production of other angiotensin peptides, we prevented the production of all angiotensin peptides by the administration of the renin inhibitor, aliskiren, to LDLR$^{-/-}$ mice. The drug promoted a dose- related decrease in atherosclerosis that was unrelated to changes in blood pressure. To further confirm the effect of the RAS on atherosclerosis we generated mice that were hypomorphic for angiotensinogen, the only known precursor of all angiotensin peptides. The reduction of angiotensinogen to barely detectable concentrations in plasma led to an almost complete ablation of atherosclerosis. Current evidence indicates that AngⅡ primarily exerts its effects on atherosclerosis through cells of the vascular wall.

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