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 **Acute Coronary Syndromes****SUBCUTANEOUS IMMUNIZATION WITH RECOMBINANT HEAT SHOCK PROTEIN 65 IMPAIRS THE PROPERTIES OF HIGH DENSITY LIPOPROTEIN IN APOLIPOPROTEIN E KNOCKOUT MICE**

Poster Contributions

Hall C

Saturday, March 29, 2014, 3:45 p.m.-4:30 p.m.

Session Title: Acute Coronary Syndromes: Basic I

Abstract Category: 2. Acute Coronary Syndromes: Basic

Presentation Number: 1150-221

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Background: Heat shock protein 65 (HSP65), as a major autoantigen, contributes to the development of atherosclerosis through immunoinflammatory reactions. Whether the functions of high density lipoprotein (HDL) are impaired in atherosclerosis mice by subcutaneous immunization with HSP65 remains unclear.

Methods: Apolipoprotein E knockout (ApoE^{-/-}) mice were randomly divided into three groups and immunized with phosphate-buffered saline (PBS) as control or different concentrations of HSP65 (5 μ g or 25 μ g). Sixteen weeks after the first immunization, paraoxonase1 (PON1) activity, myeloperoxidase (MPO) activity, High-density lipoprotein inflammatory index (HII) and the levels of cytokines were assessed. Additionally, [³H] labeled cholesterol efflux rate was evaluated by liquid scintillation spectrometry. Hepatocytes and peritoneal macrophages were isolated to examine the expression of cholesterol transport regulating proteins, including PPAR- γ , LXR- α , and ABCA1.

Results: In the HSP65-immunized mice, PON1 activity and the expression of IL-10 were reduced, whereas, HII, MPO activity, and the expression of IFN- γ were elevated gradually. Cholesterol efflux rate was significantly decreased by 15.65% and 30.36% compared with control at concentration of 5 μ g (P=0.001) and 25 μ g HSP65 (P<0.001), respectively. In addition, HSP65 markedly attenuated the expression of regulating proteins in mRNA and protein levels in a dose-dependent manner. The mice immunized with HSP65 developed significantly larger aorta atherosclerotic plaques when compared with control group.

Conclusions: The reverse cholesterol transport, anti-inflammatory and anti-oxidant capacities of HDL were suppressed in HSP65-immunized mice. Further results revealed that HSP65 decreased the expression of cholesterol transport proteins in macrophages and hepatocytes, which hindered the process of reverse cholesterol transport and accelerated the progression of atherosclerosis.

Keywords: heat shock protein 65; atherosclerosis; high density lipoprotein; reverse cholesterol efflux