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ABERRANT EXPRESSION OF Fc γ RIIIA CONTRIBUTES TO DEVELOPMENT OF ATHEROSCLEROSIS

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Purpose Previous studies have shown that Fc receptor III A of immunoglobulin G (Fc γ RIIIA, also named CD16) was involved in the development of coronary heart disease (CHD). However, the mechanism of CD16 in contribution to CHD development remains largely unclear. Here, we focused on the signaling pathway it stimulates in the initiation and progression of CHD.

Methods We investigated Fc γ RIIIA mRNA expression in the leukocytes, serum protein level of soluble CD16 (sCD16) and membrane CD16 on monocytes in 100 diagnosed CHD patients and 40 healthy people at similar ages. We determined soluble CD14 (sCD14) to analyse whether monocytes are activated or not. Macrophage colony stimulating factor (M-CSF), TNF α and IL-1 in sera were determined as well. Furthermore, the role of Fc γ RIIIA in the initiation and progression of CHD was analysed by monocytes adherence to human umbilical vein endothelial cells (HUVECs) in vitro and aortic atherosclerotic formation in ApoE^{-/-} mouse model in vivo.

Results There was a significant increase of Fc γ RIIIA at the mRNA level in leukocytes (1.372 ± 0.454), the protein level of both serum sCD16 (3.237 ± 0.988) and membrane CD16 on monocytes ($4.8 \pm 2.2\%$) in CHD patients when compared to the healthy control. High level of sCD14 in sera (3.744 ± 0.896 μ g/ml) was found in CHD patients. Similar to sCD14, the levels of M-CSF (120.144 ± 32.123 pg/ml), TNF α (48.297 ± 11.545 pg/ml) and IL-1 (75.842 ± 20.682 pg/ml) in sera were also higher in CHD patients. Further experiments showed that the elevated level of Fc γ RIIIA on monocytes dramatically correlated with the adhesive efficiency of HUVECs ($10.5 \pm 5.5\%$) in vitro, and also aortic atherosclerotic formation in ApoE^{-/-} mouse model, along with increased levels of TNF α (41.758 ± 9.776 pg/ml), IL-1 (71.752 ± 13.201 pg/ml;) and soluble E-selectin (sE-selectin) (2.977 ± 0.560 μ g/ml) in sera and both the mRNA level (3.968 ± 0.284) and the protein level (0.455 ± 0.018) of MMP-9 in aorta. Additionally, similar to Simvastatin, IVIG pretreatment inhibited this response in ApoE^{-/-} mice.

Conclusion Taken together, these results demonstrate that FcγRIIIA plays a crucial role in the development of atherosclerotic formation by targeting inflammatory cytokines and MMPs, and inhibition of FcγRIIIA or its signaling may represent a promising approach for the prevention and treatment of CHD.