¹Fangfang Jiao, ²Yue Wu, ³Maixia Wen, ³Mao Ma, ²Zuyi Yuan. ¹*Xi'an Jiaotong University;*
²*Department of Cardiovascular Medicine, First Affiliated Hospital of Medical College;*
³*Department of Health Center, First Affiliated Hospital of Medical College, Xi'an Jiaotong University*

Objectives JUPITER trial demonstrated that administering Rosuvastatin to 'apparently healthy people' (with normal lipid levels, but hsCRP³ 2 mg/L) could decrease the incidences of cardiovascular diseases significantly. Whereas, little is known about the inflammatory state of 'apparently healthy people.' NF-κB is a major inflammatory pathway enlarging the effects of CRP and could be suppressed by statins. The aim of this study was to figure out whether NF-κB is in active status in the circulating mononuclear cells in 'apparently healthy people'.

Methods We collected fasting venous blood samples from 'apparently healthy people' (n=14) and control group (n=14). The recruit and exclusion criteria referred Jupiter trial in the context of Chinese Han people. We recruit men age 55 years and older and women age 65 years and older, who have hsCRP³ 2 mg/L, LDL-C <3.4 mmol/l, and cholesterol <5.5 mmol/l, and who have no history of myocardial infarction, stroke, arterial revascularisation, or coronary risk equivalent as defined by current NCEP guidelines. Control group have hsCRP <2 mg/L, and other criteria were the same with apparently healthy group. Additional exclusion criteria were as follows: current use of statins or other lipid-lowering therapies; current use of postmenopausal oral hormone therapy; current use of immunosuppressants; uncontrolled hypertension; history of cancer; chronic inflammatory conditions; history of alcohol or drug abuse within the past year. MNC was isolated by Ficoll standard density gradient centrifugation, and nuclear and cytoplasmic protein were extracted separately. NF-κB DNA binding activity was measured by electrophoretic mobility shift assay (EMSA). Detect and compare the expression of p65, p50, IκB-α and IκB-β by western blotting. Densitometry was performed with the use of Odyssey infrared imaging system, and all values were corrected for loading with GAPDH. Levels of IL-6 and TNF-α in serum were assessed by ELISA.

Results The baseline characteristics of the apparently healthy people and control group were equivalent. The average hs-CRP in apparently healthy group and the control group were 4.89 mg/l (3.54–10.03 mg/l), and 0.53 mg/l (0.31–0.98 mg/l) respectively. The NF-κB binding activity in nuclear extracts increased markedly compared to that of control group (fluorescent intensity 6.19 ± 1.76 vs 3.02 ± 1.18 , $p < 0.001$), and the NF-κB activation had a positive correlation with levels of hsCRP ($r = 0.683$, $p < 0.001$). The expression of p50 in 'apparently healthy people' was significantly higher ($p < 0.001$) and the level of IκB-β was lower ($p < 0.001$) than that of control group in protein level, whereas the expression of p65 was a little higher in 'apparently healthy people' group ($p > 0.05$) and level of IκB-α showed no significant difference between the two groups. The TNFα expression in serum of 'apparently healthy people' group is significantly higher than that of control group (22.32 ± 0.89 pg/ml vs 17.91 ± 1.35 pg/ml, $p < 0.05$), but the expression of IL-6 between the two groups showed no significant differences (81.37 ± 23.56 pg/ml vs 61.40 ± 29.91 pg/ml, $p = 0.46$).

Conclusions These data showed for the first time that NF-κB binding activity and expression of P50 were higher in 'apparent healthy people' than that of healthy control, and the activity of NF-κB is positively correlated with the levels of hsCRP in serum, all of which might call on attentions on the 'apparently healthy status', and build the base for revealing the mechanisms underlying the Jupiter Trial in further research.

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ACTIVATION AND EXPRESSION OF NF-κB IN CIRCULATING MONONUCLEAR CELLS IN APPARENTLY HEALTHY PEOPLE

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