

with different concentrations (5, 25, 50, 100 µg/ml) and different exposure time (50 µg/ml CRP cocubated for 6, 12, 24 and 48 h). The protein expression of TLR4 was measured by flow cytometry and mRNA expression of TLR4 and MD-2 were tested by quantitative PCR. Measurements of TNFα, IL-6 and MMP-9 in the supernatants of cultured monocytes were performed by ELISA.

**Results** CRP (5, 25, 50 and 100 µg/ml) increased dose-dependently the expression of TLR4 protein ( $32.22 \pm 2.80\%$ ,  $49.94 \pm 5.58\%$ ,  $74.82 \pm 3.24\%$  and  $90.82 \pm 2.88\%$ ;  $p < 0.005$  vs control, respectively). 50 µg/ml CRP stimulated CD14<sup>+</sup> monocytes for various times (6, 12, 24 and 48 h) and also increased time-dependently the expression of TLR4 protein ( $29.80 \pm 2.70\%$ ,  $47.44 \pm 4.41\%$ ,  $81.71 \pm 2.92\%$  and  $50.57 \pm 3.34\%$ ;  $p < 0.005$  vs control, respectively). CRP (5, 25, 50 and 100 µg/ml) increased dose-dependently the expression of TLR4 mRNA (159%, 211%, 320% and 390%;  $p < 0.005$  vs control, respectively) and MD2 mRNA (146%, 236%, 311% and 416%;  $p < 0.005$  vs control, respectively). 50 µg/ml CRP stimulated CD14<sup>+</sup> monocytes for various times (6, 12, 24 and 48 h) and increased time-dependently the expression of TLR4 mRNA (162%, 264%, 354% and 208%;  $p < 0.005$  vs control, respectively) and MD2 mRNA (147%, 241%, 311% and 190%;  $p < 0.005$  vs control, respectively). The release of TNFα, IL-6 and MMP-9 in the supernatants of monocytes treated with CRP increased dose-dependently. TLR4 inhibitor of high dose (30 µg/ml) could block the release of TNFα, IL-6 and MMP-9 mediated by TLR4 and MD2 upregulated by CRP completely.

**Conclusion** CRP can active the signal transduction of TLR4 on CD14<sup>+</sup> monocyte, and induced the production of TNFα, IL-6 and MMP-9. Our finding illustrates that CRP, as pathogen associated molecular (PAMP), may induce innate immune response in vitro by monocyte Toll-like receptor signalling.

#### e0110 THE EFFECTS OF ATORVASTATIN ON C-REACTIVE PROTEIN INDUCED TOLL-LIKE RECEPTOR 4 EXPRESSION ON CD14<sup>+</sup> MONOCYTE

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**Objective** To observe the effects of atorvastatin on C-reactive protein (CRP) induced Toll-like receptor 4 expression on CD14<sup>+</sup> monocyte in human, and anti-inflammatory effect of atorvastatin.

**Methods** CD14<sup>+</sup> monocytes were isolated from blood in healthy volunteers by the Ficoll density gradient and stimulated by CRP with different concentrations (5, 25, 50, 100 µg/ml) and different exposure time (50 µg/ml CRP cocubated for 6, 12, 24 and 48 h). The protein expression of TLR4 was measured by flow cytometry and mRNA expression of TLR4 and MD-2 were tested by quantitative PCR. Measurements of TNFα, IL-6 and MMP-9 in the supernatants of cultured monocytes were performed by ELISA.

**Results** CRP (5, 25, 50 and 100 µg/ml) increased dose-dependently the expression of TLR4 protein ( $32.22 \pm 2.80\%$ ,  $49.94 \pm 5.58\%$ ,  $74.82 \pm 3.24\%$  and  $90.82 \pm 2.88\%$ ;  $p < 0.005$  vs control, respectively). CRP 50 µg/ml stimulated CD14<sup>+</sup> monocytes for various times (6, 12, 24 and 48 h) and also increased time-dependently the expression of TLR4 protein ( $29.80 \pm 2.70\%$ ,  $47.44 \pm 4.41\%$ ,  $81.71 \pm 2.92\%$  and  $50.57 \pm 3.34\%$ ;  $p < 0.005$  vs control, respectively). Atorvastatin (1.0, 2.5, 5.0, 7.5 and 10 µmol/l) inhibited dose-dependently the expression of TLR4 protein induced by CRP 50 µg/ml for 24 h [68.17%, 52.43%, 27.72%, 17.46% and 9.99%;  $p < 0.005$  vs control (80.39%), respectively], and restrained dose-dependently the expression of TLR4 mRNA ( $p < 0.005$  vs control, respectively) and MD2 mRNA ( $p < 0.005$  vs control, respectively). The release of TNFα, IL-6 and MMP-9 in the supernatants of monocytes treated with CRP 50 µg/ml was inhibited dose-dependently by atorvastatin. Atorvastatin 10 µmol/l inhibited mostly the release of TNFα, IL-6 and MMP-9 in

the supernatants of monocytes treated with CRP 50 µg/ml (24%, 22.6% and 15.6%,  $p < 0.005$  vs baseline, respectively).

**Conclusion** CRP can increase dose-dependently and time-dependently the expression of TLR4 on CD14<sup>+</sup> monocyte in human, and the production of TNFα, IL-6 and MMP-9 in CD14<sup>+</sup> monocyte. Atorvastatin can inhibit dose-dependently the expression of TLR4 mRNA and protein induced by CRP and the release of TNFα, IL-6 and MMP-9 in CD14<sup>+</sup> monocytes in human. Atorvastatin has anti-inflammatory effects and may restrain innate immune response in vitro by inhibition of monocyte Toll-like receptor signalling.

#### e0111 ASSOCIATION BETWEEN MYELOPEROXIDASE -463 G/A GENE POLYMORPHISM AND ITS PLASMA LEVELS WITH RISK OF CORONARY ARTERY DISEASE IN CHINESE POPULATION

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**Objective** The aim of this study was to investigate whether myeloperoxidase gene polymorphism and its plasma levels were associated with risk of coronary artery disease (CAD) in Chinese population.

**Methods** A case-control study was conducted in Fujian provincial hospital, 157 patients with established CAD (cases) and 78 individuals without angiographically significant CAD (controls) were enrolled. Blood samples were collected to identify the MPO polymorphism and its plasma levels.

**Results** Genotypes were determined in all individuals. The frequencies of three genotypes were significantly different in both group ( $p < 0.05$ ). Plasma MPO levels were significantly greater in patients with CAD than in controls ( $332.05 \pm 167.56$  pg/ml vs  $277.81 \pm 142.68$  pg/ml,  $p < 0.05$ ). In the case group, 7(4.5%) were homozygous for AA, 101(64.3%) for GG and 49(31.2%) were heterozygous. Mean MPO plasma levels were  $200.10 \pm 31.47$  pg/ml for AA,  $297.43 \pm 125.28$  pg/ml for AG and  $367.66 \pm 177.14$  pg/ml for GG genotypes. In the case group, the MPO levels with GG were significantly higher than that in individuals with GA ( $p < 0.05$ ) and AA ( $p < 0.05$ ), but with no difference between GA and AA genotype ( $p > 0.05$ ). Plasma MPO levels correlated with its genotype.

**Conclusion** We found association between MPO polymerase and its plasma levels with CAD risk in Chinese population. These findings provide new sights for atherosclerosis diagnosis and risk assessment.

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#### e0112 STUDY OF MYELOPEROXIDASE LEVEL AND CD11B/CD18 EXPRESSIONS ON LEUKOCYTES IN PATIENTS WITH CORONARY HEART DISEASE

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**Objective** Myeloperoxidase (MPO) and CD11b/CD18, markers of leukocyte activation, are involved in the pathogenesis of atherosclerosis. The aim of the study was to investigate the plasma MPO level and CD11b/CD18 expressions on leukocytes in patients with coronary heart disease (CHD).

**Methods** This case-control study included 157 patients with angiographically proven CHD (cases). Controls included 78 subjects with normal coronary angiograms. MPO was measured using an