GW23-e2220 **THE SERA FROM COLLAGEN-INDUCED ARTHRITIS MICE ACCELERATE MACROPHAGE-DERIVED FOAM CELLS FORMATION**

doi:10.1136/heartjnl-2012-302920a.9

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Objectives Rheumatoid arthritis (RA) is associated with excess of cardiovascular mortality and atherogenesis is accelerated in RA patients, but the exact mechanism remains unclear. Current findings support that the initiation and development of both RA and atherosclerosis (AS) can be induced by common circulating inflammatory cytokines and proinflammatory process. The chronic systemic inflammation in RA is considered as an independent risk factor for the aggravation of AS. The formation of foam cells in the arterial intimal layer is the characteristic of atherosclerotic lesions. However, little is known about the effect of systemic inflammatory state and circulating inflammatory mediators of RA on foam cells transformation of macrophages. We explored the effect of RA on macrophage-derived foam cells formation, and possible mechanisms.

Methods The sera from collagen-induced arthritis (CIA) and control mice were harvested at 8 weeks after immunisation (type II collagen or acetic acid, respectively) and blood lipid levels were measured. Murine macrophage cell line (RAW264.7 cells) were treated with 3% sera of CIA mice or control mice for 24 h in the presence or absence of NF-κB inhibitor (Bay11-7082). The mRNA and protein expressions of CD36, ABCA1 and ABCG1 were determined by Realtime-PCR and western blot. Fluorometric method was used to examine the cholesterol content in cells and cholesterol efflux to apoA-I, HDL and mice sera. Intracellular lipid was analyzsd by oil red O staining. The mRNA expressions of p50, p65 and IκB-α were determined by Realtime-PCR and NF-κB binding activity was examined by electrophoretic mobility shift assay.

Results Compared to control mice sera, CIA mice sera increased CD36 mRNA and protein expressions (7.10±2.28fold and 1.58 ±0.04fold, $p<0.05$) and ABCA1 mRNA expression in RAW264.7 cells. The cholesterol efflux to CIA mice sera (2.98±1.06%) decreased significantly when compared with control sera (5.54 ±1.32%), which probably was related to the lower HDL level of CIA mice sera. In accord with ABCA1 and ABCG1 protein expressions, there were no significant differences in apoA-I-mediated and HDL-mediated intracellular cholesterol efflux in lipid-load RAW264.7 cells treated with CIA and control mice sera. Compared to control mice sera, intracellular lipids and cholesterol ester (CE), free cholesterol (FC) contents increased in RAW264.7 cells treated with CIA mice sera for 24 h (CE:2.07±0.0202 μg/mg protein to 2.82±0.04 μg/mg protein, FC:6.30±0.28 μg/mg protein to7.28 ±0.22 μg/mg protein, $p<0.05$),which indicated the CIA mice sera had the effect on acceleration macrophage-derived foam cells formation. Additionally, CIA mice sera up-regulated p50, p65 and IκB-α mRNA expressions and increased NF-κB binding activity. NF-κB inhibitor Bay11-7082 suppressed ABCA1 mRNA expression which was induced by CIA mice sera, but there were no significant differences in CD36 and ABCG1 mRNA expressions.

Conclusions Our results suggest that the sera from CIA mice accelerate the macrophage-derived foam cells formation. The mechanism is possibly involved in the impaired balance between influx and efflux of cholesterol in macrophages by increasing lipid uptake via CD36 up-regulation and reducing cholesterol efflux to CIA sera. NF-κB pathway activated by CIA may involve in the process.