Moderated Poster
11:45 PM – 1:05 PM
Wednesday, April 13, 2016

MP1 **CORRECTING ATHEROGENIC EFFECTS OF LUPUS PLASMA ON MACROPHAGES WITH RESVERATROL AND MYCOPHENOLATE**

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10.1136/jim-2016-000080.13

Purpose of Study Premature atherosclerosis with coronary artery disease is a major cause of morbidity in Systemic Lupus Erythematosus (SLE). SLE patient plasma induces a pro-atherogenic profile of cholesterol transport genes in macrophages. A common immunosuppressive treatment for SLE, mycophenolate (MMF) reduces scavenger receptors thus reducing lipid influx. We have demonstrated athero-protective properties of the polyphenol resveratrol on cholesterol efflux. This study determines whether MMF and resveratrol work synergistically to regulate cholesterol transport in macrophages exposed to pro-atherogenic SLE plasma.

Methods Used THP-1 human macrophages ($10^6/\text{ml}$) were incubated in 10% SLE plasma with: media (control); MMF ($1 \mu\text{g}/\text{ml}$); resveratrol ($50 \mu\text{M}$); and MMF+resveratrol. After 24 h incubation, total RNA and protein were isolated. Message level of scavenger receptors CD36, LOX1, and SRA1; and efflux proteins 27-hydroxylase, ATP binding cassette transporter (ABC)A1, and ABCG1 were evaluated by QRT-PCR and confirmed by immunoblot. Cholesterol efflux was measured by Amplex Red Cholesterol Assay kit run $\pm$ cholesterol esterase.

Summary of Results In 10% SLE plasma, MMF suppressed efflux genes ABCA1 and ABCG1 ($58.38 \pm 3.5\%$ and $72.98 \pm 3.3\%$) vs. SLE plasma alone ($p < 0.0001$) while MMF+resveratrol corrected this suppression. In SLE plasma, MMF+resveratrol decreased SRA1 and LOX-1 by $15 \pm 2.5\%$ and $47 \pm 1.0\%$, respectively vs. resveratrol alone ($p < 0.0001$). SLE plasma promoted cholesterol accumulation in THP-1 macrophages and prevented efflux into medium. It increased the ratio of cholesterol esters to free cholesterol (ChE/FC). Resveratrol decreased intracellular cholesterol and restored ChE/FC ratios to that of cells in healthy control plasma.

Conclusions MMF and resveratrol exhibit complimentary effects on macrophages exposed to SLE plasma. Both agents combined restore cholesterol influx and efflux gene expression to that of cells treated with control plasma.

Resveratrol additionally reverses cholesterol accumulation caused by SLE plasma. Further evaluation of resveratrol +MMF in atherosclerosis in SLE may lead to improved treatment.