Investigating cholesterol and tryptophan metabolism in inflammatory macrophages

Nagashree Bhat, Prarthana Guha, Ashcharya Rishi, Pavan Gondrala and Subhrangsu Mandal*

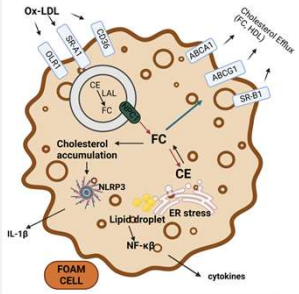
Department of Chemistry and Biochemistry, University of Texas at Arlington, TX-76019

ABSTRACT

Inflammation alters macrophage metabolism, increasing tryptophan catabolism and disrupting cholesterol homeostasis. In macrophages, cholesterol is internalized via LDL receptors and esterified by ACAT1(Acetyl-CoA acetyltransferase). Excessive esterification can lead to atherosclerosis. Our study shows that LPS-treated THP1-derived macrophages (THP1-Mφ) exhibit reduced SR-B1 expression and cholesterol uptake, indicating impaired HDL-mediated transport. We also observed elevated ACAT1 expression and peroxidized lipid levels, suggesting increased esterification and oxidative stress during inflammation. We aim to investigate the roles of modified-LDL receptors and de-esterification enzymes in inflamed macrophages and explore the connection between tryptophan catabolism and cholesterol transport to identify potential cardiovascular disease biomarkers.

INTRODUCTION

- Inflammation is a type of immune response against pathogens, damaged tissue, in which macrophages are activated to clear the cellular debris and mediate immune response.
- Chronic inflammation leads to diabetes, Alzheimer's, Cardio-vascular Diseases (CVD).
- Cholesterol is taken up and esterified by ACAT1 enzyme in macrophages.
- Hyper-activity of ACAT1 may lead to cholesterol accumulation followed by cytokine expression.



- Modified cholesterol (oxidation/ acetylation) can activate macrophages and foam cell formation.
- Our recent studies have demonstrated that, one of the High-Density Lipoprotein(HDL) transporter, Scavenger Receptor B1(SR-B1) along with cholesterol uptake was downregulated under LPS treatment in THP1-Mφ.
- Tryptophan catabolizing enzyme, IDO1, is significantly upregulated under LPS induced macrophages.

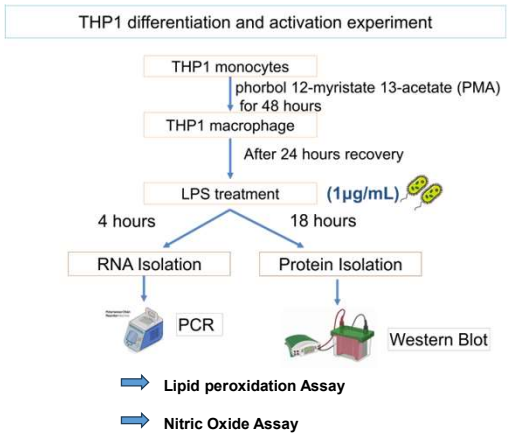
OBJECTIVES

•To investigate changes in modified-LDL receptors and de-esterification enzymes under inflammation.

•To understand how tryptophan catabolism affects cholesterol transport.

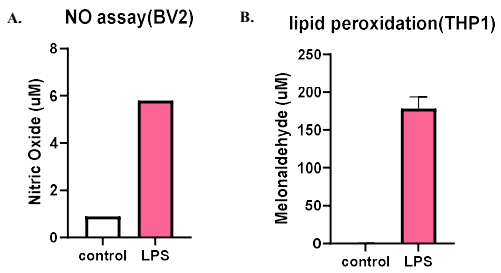
•To identify potential biomarkers for inflammation-driven cardiovascular risk.

MATERIALS AND METHODS

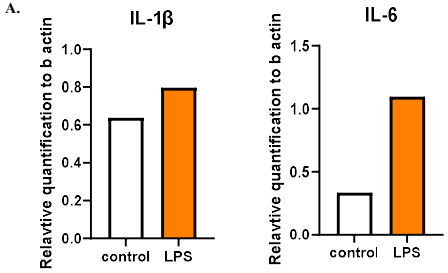


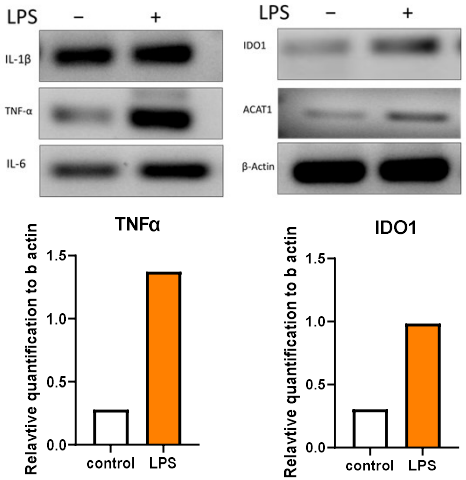
RESULTS

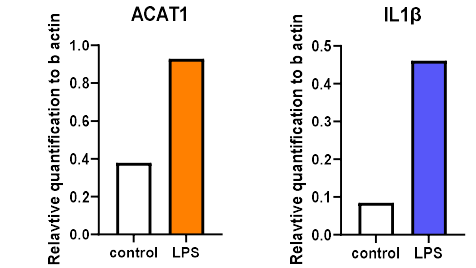
1. Nitric Oxide production and Lipid peroxidation are elevated under LPS induction in macrophages

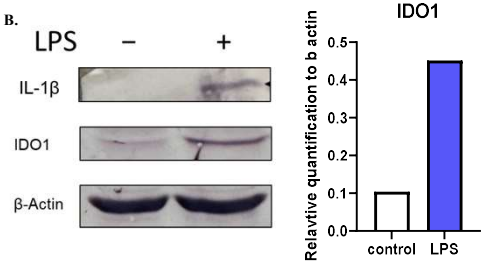


2. Cytokine and inflammatory genes are upregulated upon LPS stimulation in macrophages



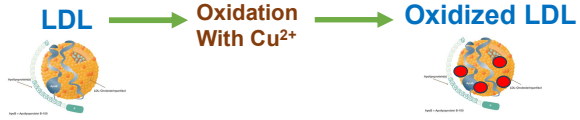


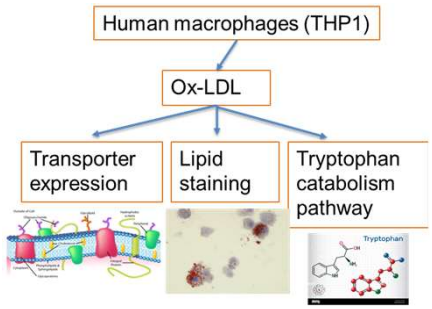




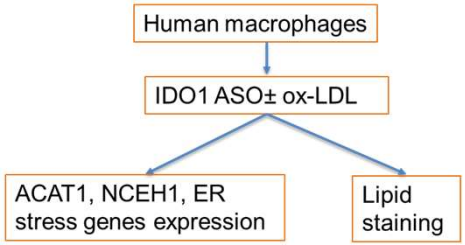
FUTURE DIRECTION

Elucidate mechanisms of modified-LDL receptors and de-esterification enzymes in cholesterol homeostasis under inflammation.





Investigate the link between tryptophan catabolism and cholesterol transport.



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