

TLR4 is Necessary for LPS Mediated Liver Inflammation in NASH

Arul Mehta, Touhid Islam, Arun P Palanisamy, Kenneth D Chavin

Saint Ignatius High School/ Case Western Reserve University, School of Medicine

Introduction: Non-alcoholic fatty liver disease (NAFLD), the most common liver disorder in Western countries with an estimated overall prevalence of 20-30%, is expected to increase in prevalence to 50% by 2030. NAFLD, considered a relatively benign condition, can progress to the more insidious non-alcoholic steatohepatitis (NASH). NASH has all the hallmarks of NAFLD with the added component of hepatic inflammation. Animal studies have shown that gut flora and chronic liver disease are closely interrelated. There exists a relationship between feeding mice a diet high in saturated fat (MD) and increased liver steatosis, increased inflammation, and neutrophil infiltration consistent with NASH, compared to a control diet (CD) fed mice. LPS is increased in NASH and obesity and adding extraneous LPS results in weight and adipose gain.

Goals: In this study we take a closer look at inflammatory molecules TNF- α , IL-1 β , CCL-1 and TGF- β , and anti-oxidative molecule, catalase in this TLR4KO model to better understand LPS-TLR-4 pathway in dietary fat mediated hepatic steatosis.

Methods: Samples from WT and TLR4 KO mice fed CD or MD and treated LPS, were used for Western blot and RT-PCR analysis. Graph Pad Prism was used for statistical analysis.

Results: TLR-4 KO mice fed MD exhibited reduced levels of expression of TNF- α , IL-1 β , CCL-1 and TGF- β . Addition of LPS in fat fed TLR4 KO mice did not alter the levels of inflammatory cytokines. Protein levels of catalase were increases both in TLR4KO CD and MD fed mice.

Conclusion: The results show that TLR4 is a necessary intermediate in the microbiome/LPS mediated inflammatory changes and also in the modulation of anti-oxidative function of catalase during NASH progression.