Abstract

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Title of diploma thesis:

Anti-inflammatory effects of ursodeoxycholyl lysophosphatidylethanolamide on THP-1 human macrophages via Toll-like receptor 4

Nonalcoholic steatohepatitis (NASH) became the most common liver disease in developed countries. It is well-known that the level of protectant phosphatidylcholine (PC) is decreased in NASH. The bile acid-phospholipid conjugate ursodeoxycholyl lysophosphatidylethanolamide (UDCA-LPE) was designed in order to specifically deliver PC to hepatocytes. However, previous studies have proved that UDCA-LPE possesses its proper hepatoprotectant capacity and exhibits anti-apoptotic, anti-inflammatory, anti-fibrotic properties and also improved steatosis and hyperlipidaemia in various models *in vivo*. These effects may be mediated secondary through modulation of immune system. Therefore, in order to dissect if UDCA-LPE directly influences immune cells *in vitro*, release of pro-inflammatory cytokines TNFα, IL-6 and IL-1β in LPS-induced THP-1-derived human macrophages was measured by ELISA. Moreover, effects of UDCA-LPE on MAPK signalling pathways and nuclear translocation of NFκB were determined by Western blot analysis and immunofluorescence. For deeper investigation, lipid rafts were isolated using Optiprep gradient and recruitment of adaptor proteins TRAF6 and MyD88 into the lipid rafts was assessed by Western blot analysis. UDCA-LPE was able to significantly inhibit release of all measured pro-inflammatory cytokines, nuclear translocation of NFκB and activation of MAPK members JNK1/2 and p38. We therefore may anticipate that UDCA-LPE can exhibit its hepatoprotective properties via modulation of immune system in LPS-induced inflammatory response. Due to its versatility, UDCA-LPE has a potential to become a novel therapeutic approach for treatment of NASH.