“The Role of Toll-like Receptor Signalling as a potential underlying mechanism in Metabolic Syndrome”

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The toll-like receptor (TLR) signalling is the most implicated mechanism during inflammation. All components of metabolic syndrome (MetS) share an underlying chronic inflammatory aetiology, manifested by increased levels of pro-inflammatory cytokines. This study aimed to investigate the role of tocotrienol in modulating TLR signalling during the pathogenesis of MetS. Male Wistar rats (n=42) were divided into seven groups. The baseline group was sacrifice upon acclimatization. The normal group was given standard rat pellet and tap water. The remaining five groups were fed with high-carbohydrate high-fat (HCHF) diet and 25% fructose drinking water to induce MetS. At week 8, these animals were assigned with five different treatments [tocopherol-stripped corn oil (vehicle), 60 mg/kg annatto tocotrienol (AnT3), 100 mg/kg AnT3, 60 mg/kg palm tocotrienol (pT3) or 100 mg/kg pT3]. The rats were sacrificed at week 20. Blood was drawn and immediately processed into serum. Liver was harvested, homogenised in protein extraction buffer and supernatant was collected. The measurements of TLR2, TLR4, downstream targets [total nuclear factor-kappa B (NF-κB) and phosphorylated NF-κB (pNF-κB)] as well as inflammatory cytokines [C-reactive protein (CRP) and interleukin-10 (IL-10)] were performed. Our data revealed that HCHF diet increased the levels of TLR2, TLR4 and caused NF-κB phosphorylation in liver. In serum, HCHF diet increased TLR2, TLR4, NF-κB and CRP levels in animals. Treatment with AnT3 or pT3 lowered TLR2, TLR4, causing NF-κB dephosphorylation and increased level of IL-10 in the liver of the HCHF rats. The elevations of TLR2 and CRP in serum were prevented following AnT3 or pT3 supplementation. In summary, tocotrienol potentially reduced inflammatory response during the occurrence of MetS. The postulated mechanism of action may be in part mediated through the inhibition of TLR signalling, thus favouring the balanced profile between pro- and anti-inflammatory cytokines.

The above final report has not been presented at the annual “MTSF Grant Research Symposiums” as the scheduled Years 2020 & 2021 Grant Research Symposiums were cancelled due to the Covid-19 pandemic.