Palmitic acid enhances TLR4 expression and promotes resistin/TLR4 signaling

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Introduction / Aim

Toll-like receptor 4 (TLR4) has a critical role in innate immunity, and the activation of inflammatory pathways plays an important role in the induction of insulin resistance. Indeed, we have recently reported that TLR4 is implicated in resistin-induced inflammation and insulin resistance in the hypothalamus (1). We also show that TLR4 is up-regulated in the hypothalamus of mice fed a high-saturated fat diet. Here, we explore the molecular mechanism implicated in the regulation of TLR4 expression. For this purpose, human neuroblastoma cells (SHSY-5Y) were exposed during 4h to either the saturated fatty acid palmitic acid or the omega-3 polyunsaturated fatty acid docosahexaenoic acid (DHA), and then challenged for resistin.

Results

Resistin treatment increases NFkB activation

Resistin induces phosphorylation of Akt and P38 MAPK

DHA suppresses palmitic acid and resistin induced up-regulation of IL-6 and TNF-α

We analyzed the effect of resistin, palmitic acid and DHA on inflammation markers. We show that resistin was able to activate NF-κB and to increase Akt and p38 MAPK phosphorylation. In addition, resistin and palmitic acid upregulate both IL-6 and TNF-α. Interestingly, this effect is completely abolished by DHA treatment.

Palmitic acid pretreatment increases TLR4 expression

Palmitic acid potentiates resistin effects and promotes resistin/TLR4/Myd88 signaling

We studied the possible synergistic interaction between resistin and palmitic acid. Our results show that palmitic acid but not DHA pretreatment increases TLR4 expression, at the protein and mRNA levels. Importantly, palmitic acid pretreatment potentiates resistin effects and promotes resistin/TLR4/Myd88 signaling.

Conclusion

In conclusion, we show in neurons that: 1) palmitic acid increases TLR4 expression, 2) palmitic acid amplifies resistin pro-inflammatory effects, 3) DHA treatment overcomes both resistin and palmitic acid pro-inflammatory effects.

Reference