THE ROLE OF MACROPHAGE NF-κB INDUCING KINASE (NIK) IN HEPATIC INSULIN SIGNALING

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INTRODUCTION AND OBJECTIVES: The obesity has acquired epidemic characteristics and the same numbers that indicate the increase in obesity also showed a significant increase in individuals with diabetes mellitus type 2. It is that both diseases exhibit a metabolic response characteristic, which leads to changes in intracellular signaling pathways and glucose homeostasis. High fat diet (HFD) consumption is responsible for the increased fat mass leading to an increased production of pro-inflammatory cytokines. Several studies indicate the involvement of macrophages in this process. The non-canonical NF-κB pathway contributes to the pro-inflammatory signaling activation, and may represent a key metabolic pathway in response to obesity, especially in insulin resistance. The aim of this study is to evaluating the impact of modulation of NIK protein in monocytes and / or macrophages induced by LPS or palmitate on insulin resistance in hepatocytes.

MATERIAL AND METHODS: We employed culture of macrophages cells (RAW267.4 and BMDMs) treated with palmitic acid or LPS and used conditioned medium for culturing hepatocytes. Total RNA were extracted from macrophage cells and used to evaluate the expression of pro-inflammatory cytokines genes (TNFα, IL-1β e IL-6) using qRT-PCR. Immunoblotting was used to determine the expression and/or phosphorylation of protein that would indicate the development of insulin resistance (AKT, pAKT) in hepatocytes.

RESULTS AND CONCLUSIONS: The results of the present study showed that the macrophages (RAW 267.4) that were treated with palmitic acid increased TNF-α and IL-1β gene expression, whereas treatment with LPS increased IL-1B compared to control. BMDMs cells exhibited increase in IL-1β e IL-6 expression. No difference was found in AKT phosphorylation in hepatocytes treated with LPS compared to control. For the moment, it wasn’t possible to observe a crosstalk between hepatocytes and liver macrophages in the development of insulin resistance.

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Key Words: fatty acid; NF-kB Inducing Kinase; inflammation