LEPTIN EFFECTS ON MACROPHAGES AND NEUTROPHILS IN LEAN AND OBESE MICE.

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Introduction and objective: Leptin is an adipokine that regulates metabolism and immunity. Since neutrophils lack the main functional receptor, ObRb, their response to leptin need further investigation. In this study, we investigate leptin signaling involved in neutrophil migration in lean and obese mice. Materials and Methods: This study was approved by FIOCRUZ Animal Welfare Committee. Bone marrow isolated neutrophils and peritoneal cells from C57Bl/6 male mice were incubated in vitro with leptin. C57BL/6, TNFR1 -/-, MIP-1 α-/-, 5-LO-/-, PI3Kγ-/- male mice were stimulated with leptin 1 mg/kg ip; mice were pre-treated with rapamycin, Zileuton and U-75302 and anti-KC antibodies. Mice were fed with high-fat (HF) diet for obesity induction, or normal-fat diet; after 15 weeks, HF fed mice showed hyperglycemia and hyperleptinemia. Results and Conclusions: Peritoneal cells incubated in vitro with 20 nM leptin produce KC and TNF-α. In vivo, neutrophil migration is detected after 1h, 6h and 24h of leptin i.p. injection; recruitment at 24h is dependent on TNF-α, KC and PI3Kγ, and independent on LTB₄, MIP-1α and mTOR. HF diet activates peritoneal macrophages, with increased lipid bodies formation. Obese and lean animals present neutrophil recruitment at similar levels, despite higher level of TNF-α in peritoneal fluid from obese animals. In vitro, isolated neutrophils did not show adhesion or spreading on immobilized fibrinogen 20 min after stimulation with leptin 20 nM. These data suggest the occurrence of obesity inflammatory background, which, however, did not affect the ability of leptin to induce neutrophil recruitment in vivo; still, leptin promoted indirect neutrophils recruitment through the activation of macrophages and production of mediators. Furthermore, HF fed mice show activation-prone peritoneal macrophages, without modifying the recruitment of neutrophils. These findings contribute to a better understanding of leptin role in innate immunity. Acknowledgements: CNPq, Faperj, Capes, Capes-Sus for financial support.

Keywords: leptin; neutrophil migration; obesity