LEPTIN REGULATION OF MACROPHAGE LIPID METABOLISM: ROLE OF PI3K AND MTOR

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Leptin is an adipocyte-derived hormone/cytokine that links nutritional status with neuroendocrine and immune functions. Mechanisms of leukocyte activation induced by leptin were investigated.

Leptin is related to both lipid metabolism and inflammation, so we investigated its action on leukocyte lipid bodies (LBs) - cytoplasmic depots of esterified arachidonate and eicosanoid-forming enzymes, with function in signaling and production of inflammatory mediators. Leptin injected in mice peritoneal cavity, induced macrophage lipid body formation (leptin: 14.29 ± 0.73 LBs/cell; control: 6.89 ± 0.60 LB/cell). Leptin-induced macrophage lipid bodies that correlated with priming for leukotriene B_4 production (control: 0.28 ± 0.33 ng/Ml; leptin: 2.92 ± 0.54 ng/mL). Leptin induced i*n vivo* neutrophil recruitment and macrophage activation were requisitely dependent of PI3K, as both were inhibited in the PI3K knockout mice. Lipid body formation and LTB_4 synthesis were inhibited by the mTOR inhibitor, rapamycin. The enhancement of ADRP, associated with lipid accumulation, was also determined by immunoblotting of the peritoneal cells after Leptin injection.

Our results establish PI3K/mTOR as an important signaling pathway for leptin induced macrophage activation and lipid metabolism, and provide a link between intracellular (mTOR) and systemic (leptin) nutrient sensors in leukocyte function. Moreover, we established an important connection between the lipid metabolism and inflammation.