The Role of Hepatic Glucose Metabolism in LPS-mediated Glucose Clearance

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Toll-like receptor 4 (TLR4) is integral to an innate immune response and is the receptor for the endotoxin, lipopolysaccharide (LPS) produced from the death of gram-negative bacteria in the gut. Data from the Hulver lab shows low dose treatment with LPS in skeletal muscle cell culture increases glucose oxidation. Additionally, low dose LPS, delivered via intraperitoneal injections, acutely enhances whole-body glucose tolerance in C57Bl/6 mice. The liver plays an essential role in glucose homeostasis by regulating glucose uptake and release when blood glucose is high or low, respectively. There is evidence to suggest the liver is one of the first tissues affected by LPS treatment. The purpose of this study was to evaluate the role of hepatic glucose metabolism in LPS-mediated glucose clearance. The predicted outcomes were that acute LPS exposure, relative to saline controls would more potently 1) suppress transcription and activity of proteins important for hepatic glucose production, and 2) increase transcription and activity of proteins important for glucose uptake and glycogen synthesis. Methods: wild-type (WT) and over-expressing TLR4 C57B1/6 mice were injected with saline or LPS (0.1 μL/mL) and glucose (1g/kg BW) four hours post LPS/saline treatment. Mice were euthanized 30 minutes following the injection of glucose and tissues were collected in order to study rate-limiting steps in hepatic glycolysis, glycogen synthesis and gluconeogenesis using rt-PCR and Western Blotting techniques. These studies will provide insight into the role of gut-derived endotoxin on glucose metabolism in the liver.