

Liver insulin resistance and ceramides

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Hepatic lipid accumulation is an early manifestation of insulin resistance. The precise mechanisms that lead to this lipid accumulation and the downstream consequences on hepatic and whole body insulin action are yet to be fully understood. Plasma ceramide concentrations are elevated in models of acute and chronic fatty acid availability and insulin resistance. Furthermore, liver cells are sensitive to fatty acid levels and secrete ceramide in both a dose and time dependent manner. Finally, ceramide contained within LDL is sufficient to induce both whole body and skeletal muscle insulin resistance. Collectively, liver-derived plasma ceramide are mediators in the pathogenesis of insulin resistance.