Title

Deletions of Fstl3 and/or Fst Isoforms 303 and 315 Results in Hepatic Steatosis

Authors

Nathan A. Ungerleider, *University of Massachusetts Amherst* Follow

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Abstract

TGFβ ligands, activin and myostatin have been shown to stimulate insulin production and secretion. Antagonists, Follistatin (FST) and Follistatin like 3 (FSTL3) were partially and fully ablated, respectively, creating hyperinsulinemic mice with fatty liver. Much research has surfaced on the connection between hepatic steatosis and hepatic insulin resistance. We present two different models, each with a different mechanism behind the development of fatty liver. FST288-only mice have increased synthesis of mRNA and proteins responsible for hepatic triglyceride (TG) uptake, while our double mutants have increased synthesis of mRNA and proteins responsible for TG synthesis. This alteration was likely independent of hepatic insulin resistance as livers from both mouse lines were insulin sensitive. Experiments conducted in this study to realize the causal factor of hepatic steatosis can be performed on adipose and muscle tissues in the future to better characterize the phenotype.

First Advisor

Alan L Schneyer