Adiponectin regulates expression of hepatic genes critical for glucose and lipid metabolism.

Abstract:
The effects of adiponectin on hepatic glucose and lipid metabolism at transcriptional level are largely unknown. We profiled hepatic gene expression in adiponectin knockout (KO) and wild-type (WT) mice by RNA sequencing. Compared with WT mice, adiponectin KO mice fed a chow diet exhibited decreased mRNA expression of rate-limiting enzymes in several important glucose and lipid metabolic pathways, including glycolysis, tricarboxylic acid cycle, fatty-acid activation and synthesis, triglyceride synthesis, and cholesterol synthesis. In addition, binding of the transcription factor Hnf4a to DNAs encoding several key metabolic enzymes was reduced in KO mice, suggesting that adiponectin might regulate hepatic gene expression via Hnf4a. Phenotypically, adiponectin KO mice possessed smaller epididymal fat pads and showed reduced body weight compared with WT mice. When fed a high-fat diet, adiponectin KO mice showed significantly reduced lipid accumulation in the liver. These lipogenic defects are consistent with the down-regulation of lipogenic genes in the KO mice.