Fajun Yang, J Obes Wt Loss Ther 2012, 2:9
http://dx.doi.org/10.4172/2165-7904.S1.008

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference and Exhibition on
Obesity & Weight Management

December 3-5, 2012 DoubleTree by Hilton Philadelphia, USA

CDK8 regulation of lipid metabolism

Fajun Yang
Albert Einstein College of Medicine, USA

Transcriptional cofactors play pivotal roles in the precise control of gene expression, and thus are involved in human health problems, including obesity. The multi-subunit protein complex named Mediator is a transcriptional cofactor, which can bridge transcription factors to the basal transcription apparatus. Cyclin-dependent kinase-8 (CDK8) is a subunit of the Mediator complex. However, the biological functions of CDK8 remain poorly understood. Here, we identify CDK8 as a negative regulator of lipogenic gene expression by suppressing the SREBP-1c transcription factor, which is a key activator of rate-limiting enzymes in the *de novo* lipogenesis pathway. CDK8 knockdown in hepatocytes results in SREBP-dependent up-regulation of lipogenic genes and an increase of lipid accumulation. Transient knockdown of CDK8 in mouse liver *in vivo* leads to increased expression of SREBP-target genes. As a result, hepatic CDK8 knockdown causes acceleration of *de novo* lipogenesis and accumulation of neutral lipids in mouse liver. In addition, hepatic CDK8 knockdown in mice results in an increase of plasma triglycerides. Consistent with the inhibitory role of CDK8 in *de novo* lipogenesis, hepatic CDK8 proteins in mouse models of obesity are significantly lower than normal. Dysregulation of lipid metabolism in obesity causes fatty liver and dyslipidemia, which are prevalent health problems in the developed countries and are closely associated with type II diabetes and cardiovascular disease. Thus, CDK8 may play a role in the development of fatty liver and dyslipidemia in obesity.

Fajun.Yang@einstein.yu.edu