The E3 ubiquitin ligase MDM2 acts as a key determinant of hepatic VLDL-triglycerides and ketone body production in obesity.

Zhuohao Liu¹, Karen SL Lam¹, Aimin Xu¹,², Kenneth KY Cheng¹
¹Dept of Medicine, State Key Laboratory of Pharmaceutical Biotechnology, ²Dept of Pharmacology & Pharmacy, The University of Hong Kong

Introduction
Obesity is a major risk factor for the development of hyperlipidemia and its related cardiovascular complications. Apart from its well-established role in cancer biology, the MDM2-p53 axis has been recently shown to regulate glucose and lipid metabolism. Our preliminary data indicated that MDM2 is dramatically induced in the liver of obese mice. In this study, we aimed to investigate the potential role of hepatic MDM2 in controlling systemic lipid homeostasis using a hepatocyte-specific MDM2 knock out (H-MDM2KO) mouse model.

Mouse Model

Figure 1. MDM2 is induced in liver of obese mice.

Figure 2. Genetic deletion of hepatic MDM2 has no impact on glucose and energy metabolism.

Results

Figure 3. Hypertriglyceridemia of H-MDM2KO mice is caused by increased VLDL-TG secretion.

Figure 4. H-MDM2KO mice exhibit impaired fasting-induced ketogenesis.