**Serotonergic regulation of hepatic energy metabolism**

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 Serotonin is a biogenic amine synthesized from the essential amino acid tryptophan. Because serotonin cannot cross the blood-brain barrier, it functions differently in central nervous system and peripheral tissues. Although most serotonin in the body is synthesized at the periphery, its biological roles have not been well elucidated. Older studies using chemical agonists and antagonists yielded conflicting results, because the complexity of serotonin receptors and the low selectivity of agonists and antagonists were not known. My lab has been performing a number of studies using tissue specific knock out of serotonin receptors to assess the role of peripheral serotonin in regulating energy metabolism.

In this presentation, I will discuss recent progress in my lab regarding the mechanism how gut derived serotonin can interact with hepatic insulin signaling and regulates hepatic energy metabolism. Insulin signaling is known to induce lipogenesis and suppress gluconeogenesis in the liver, so during insulin resistance, hepatic lipogenesis is expected to decrease and gluconeogenesis to increase. However, while hepatic gluconeogenesis increases as expected, hepatic lipogenesis unexpectedly increases during insulin resistance. The mechanism of this selective hepatic insulin resistance remains yet to be elucidated. Serotonin (5-HT) has been reported to induce lipogenesis and gluconeogenesis in the liver through HTR2A and HTR2B, respectively. Herein, we investigated molecular mechanism how 5-HT activates both lipogenesis and gluconeogenesis and its contribution to selective hepatic insulin resistance.