BMAL1, a master regulator of circadian rhythm, controls lipid metabolism and obesity

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BMAL1 is a transcription factor known to regulate circadian rhythm. Recent SNP analysis of human Bmal1 gene revealed that two Bmal1 haplotypes are associated with type 2 diabetes and hypertension. Also, BMAL1 functions are disregulated in visceral fat in metabolic syndrome patients. These results suggest that lack of BMAL1 functions may lead to onset of metabolic syndrome. To confirm this hypothesis, we analyzed the BMAL1 KO mice subjected to high fat diet challenges. With normal diet, the BMAL1 KO mice exhibit less food intake and smaller body weight. After only 2 days of high fat feeding, severe excretion of sebum was observed in the BMAL1 KO mice. Interestingly, after 4 weeks of feeding with high fat diet, the body weight of the BMAL1 KO mice is heavier than that of the control mice. Also, adipose tissue in the BMAL KO mice was smaller than that in the control mice. In contrast, liver in the BMAL1 KO mice accumulated more lipids and was enlarged compared to that in the control mice. The glucose disposal rate of the KO mice is significantly slower than that of control mice. These results indicate that BMAL1 regulates lipid storage and the lack of this function may result in glucose intolerance. Consequently, we are led to conclude that lack of BMAL1 functions is a risk factor of the onset of metabolic syndrome.