MICE DEFICIENT IN SFRP1 EXHIBIT INCREASED ADIPOSY, DYSREGULATED GLUCOSE METABOLISM.
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The molecular mechanisms involved in the development of obesity and related complications remain unclear. Wnt signaling plays an important role in preadipocyte differentiation and adipogenesis. The expression of a Wnt antagonist, secreted frizzled related protein 1 (SFRP1), is increased in response to initial weight gain, then levels are reduced under conditions of extreme obesity in both humans and animals. Here we report that loss of Sfrp1 exacerbates weight gain and glucose homeostasis in mice in response to diet induced obesity (DIO). Sfrp1<sup>-/-</sup> mice fed a high fat diet (HFD) exhibited an increase in body mass accompanied by increases in body fat percentage, visceral WAT mass, and adipocyte size. Fasting glucose levels are elevated, glucose clearance is impaired, hepatic gluconeogenesis regulators are aberrantly upregulated, and glucose transporters are repressed in Sfrp1<sup>+/+</sup> mice fed a HFD. Additionally, we observed increased steatosis in the livers of Sfrp1<sup>+/+</sup> mice. Our findings demonstrate that the expression of Sfrp1 is a critical factor required for maintaining appropriate cellular signaling in response to the onset of obesity.