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発表題目（※学会発表の場合のみ記載）	*Wdr6* gene deletion suppresses fat accumulation in the *Lep*$^{ob/ob}$ mouse model of obesity and type 2 diabetes

発表の概要と成果（抄録を公開している URL がある場合、「概要・成果」を記載した上で、URL を末尾に記してください。また、抄録 PDF は別途ご提出ください。なお、抄録 PDF は Web 上には公開されません。）

[Introduction] We recently found that knockdown of a novel metabolism-related molecule, WD repeat domain 6 (WDR6), in 3T3-L1 adipose progenitor cells inhibited chemically induced differentiation into adipose-like cells and suppressed lipid accumulation. However, the effect of Wdr6 deficiency on in vivo fat accumulation remains unclear. In this study, we generated *Lep*$^{ob/ob}$ mice, a model of bulimic obesity deficient in Wdr6, and performed in vivo phenotypic analysis.

[Materials and Methods] Male *Wdr6*$^{+/+}$*Lep*$^{ob/ob}$, *Wdr6*$^{+/-}$*Lep*$^{ob/ob}$, and *Wdr6*$^{-/-}$*Lep*$^{ob/ob}$ mice were generated by mating the *Wdr6*$^{-/-}$ and *Lep*$^{ob/ob}$ mice. They were reared on a normal diet and their body weight and food intake were measured weekly. Whole-body CT images were obtained at 16 weeks of age using micro-CT to quantify fat in the 4th to 5th lumbar vertebrae. The animals were dissected after one night of fasting, each organ was harvested, and the organ weights were determined. The liver function indices AST, ALT, triglycerides, and total cholesterol in the plasma were also measured using a kit. To determine the adipocyte size, the diameter of the isolated cells was measured using an automatic cell counting device. Statistical analysis was performed using Repeated measure ANOVA and Tukey's HSD test.

[Results] The body and subcutaneous fat weights of *Wdr6*$^{-/-}$*Lep*$^{ob/ob}$ mice were lower than those of *Wdr6*$^{+/+}$*Lep* $^{ob/ob}$ mice, although there was no difference in cumulative food intake. In addition, the plasma ALT levels were significantly lower in *Wdr6*$^{-/-}$*Lep*$^{ob/ob}$ mice than in *Wdr6*$^{+/+}$*Lep*$^{ob/ob}$ mice. In contrast, the plasma AST, triglyceride, and total cholesterol concentrations were not significantly different between the groups. In terms of organ weights, peri-testicular, brown fat, and liver weights were not significantly different between the groups. Furthermore, neither the diameter size of cells in peritesticular epididymal fat and subcutaneous fat varied between groups, and in fat quantification by CT, *Wdr6*$^{-/-}$ *Lep*$^{ob/ob}$ mice had significantly lower volumes of visceral and subcutaneous fat than *Wdr6*$^{+/+}$*Lep*$^{ob/ob}$ mice.

[Discussion] These results suggest that deletion of *Wdr6* in *Lep*$^{ob/ob}$ mice may suppress body weight gain due to fat accumulation and prevent hepatic dysfunction. In addition, although the fat mass

in *Wdr6*$^{-/-}$*Lep*$^{ob/ob}$ was lower than that in *Wdr6*$^{+/+}$*Lep*$^{ob/ob}$, the diameter of adipocytes did not change, suggesting that there may be more undifferentiated cells in *Wdr6*$^{-/-}$ *Lep*$^{ob/ob}$ mice. To obtain more detailed qualitative and quantitative changes in the adipose tissue in these mice, we will perform histological analysis by using various kinds of antibodies.