Fasting cycles increase Fdft1 to inhibit colorectal cancer growth in mouse model

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Conclusions:
We use gene expression profiles to understand fasting cycles inhibits the progression of colorectal cancer in mice model. Fasting cycles is likely to be an optional treatment for colorectal cancer. Fdft1 is likely to be a new target for the diagnosis and treatment of patients with colorectal cancer.

Introduction
Colorectal cancer is one of the most common cancers in the world. Although there are many treatments for colorectal cancer, its prognosis is not significantly improved. Some studies suggest that fasting can improve the efficacy of antitumor therapy and delay the recurrence of cancer, but the mechanisms behind it are still unclear. Our study was aimed to assess the inhibitory effect of fasting cycles on colorectal cancer in mouse models and try to explore the mechanism behind it.

Methods
We detected the differentially expressed genes in mice subcutaneous colorectal cancer tissues (3 in normal diet group and 3 in fasting mimic diet group) by microarray. Using bioinformatics analysis to explore the function of differential genes, we finally choose Fdft1 as our hub gene. We first observed the clinical significance of Fdft1 in patients with colorectal cancer through IHC staining and qPCR. The lentivirus-based RNA interference was utilized to knockdown and over-expression Fdft1 in mouse CT26 cells. The effect of Fdft1 on cell proliferation was detected by CCK8, colony formation assays, cell cycle and apoptosis detection. Finally, we observed the effects of Fdft1 on colorectal cancer mouse xenograft model under normal diet and fasting mimic diet.

Results
The mice subjected to fasting mimic diet displayed a significant retarded progression of colon cancer tumor compared to those in normal diet. Microarray data showed that the most differential expression genes were predominantly enriched in cholesterol synthesis pathway. We finally choose Fdft1 as our hub gene. Our research suggested that the expression level of Fdft1 was significantly decreased in colorectal cancer tissue compared to their matched non-tumor tissues. The decreased expression of Fdft1 was significantly associated with tumor size, lymph node metastasis, distant metastasis, pathological stage, clinical stage and a worse 5 year survival. Over-expression of Fdft1 in CT26 cells suppressed cell growth via induction cell cycle arrest. Knockdown of Fdft1 in CT26 cells promoted cell growth via inhibition cell apoptosis. Our study suggested that CT26 over-expression of Fdft1 can inhibit the growth of colorectal cancer in mice model. When combined with fasting mimic diet, the inhibitory effect of CT26 over-expression of Fdft1 would be better.