1. **No.**

   FP01812198

2. **Title**

   The Effect of Nicotine on Non-alcoholic Steatohepatitis Progression in Rat Models for Fatty Liver

3. **Period**

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4. **Summary**

   Fatty liver is noted as a complication of obesity. A part of fatty liver is accompanied by inflammation and fibrosis, and it develops into non-alcoholic steatohepatitis (NASH), complicated with liver cirrhosis or cancer. The mechanism from fatty liver to NASH progression remains unclear, and their treatment has not been established. Using a Seipin-deficient rat, a model of lipodystrophy, we examined the effect of nicotine on NASH progression of fatty liver. No influence was observed on food intake and body weight, when nicotine was subcutaneously administered for 4 weeks in Seipin-deficient rats fed with a high fat diet. However, deterioration of glucose metabolism (increase in ad-lib fed glucose and insulin levels) and lipid metabolism (increase in serum total-cholesterol and triglyceride levels and lipid accumulation in the skeletal muscle) were observed. In addition, liver enlargement and increase in hepatic enzyme levels were observed associated with increase in lipid accumulation in the liver. The expression of inflammation-related genes (IL-6 and TNFα) and fibrosis-related gene (Col1A1) were increased in the liver, and histological progression of fibrosis was also observed. From the above, it has been shown that nicotine can promote fatty liver to NASH.

   In the future, we would like to contribute to the elucidation of the molecular mechanism from fatty liver to NASH progression and the development of new therapeutic methods through the analysis of this animal model.