1. No.

   2019T001

2. Title

   Unravelling the mechanism of epigenetic regulation in the onset and development of lifestyle-related diseases focused on smoking and immunometabolism

3. Period

   2019-2023

4. Summary

   It has been suggested that DNA methylation is essential for the functional maturation of the liver as a metabolic organ in postnatal period, but the detailed mechanism is not clear. It is also important to elucidate the molecular mechanisms by which maternal smoking affects the risk of lifestyle-related diseases in the offspring via DNA methylation.

   In this study, we found that 1) DNA demethylation in the mouse liver occurs in postnatal period in concert with increased expression of genes related to lipid metabolism, cholesterol metabolism, and glucose metabolism, and dramatic DNA methylation changes are observed especially during lactation period, 2) DNA methylation changes during lactation period are strongly associated with changes in gene expression compared to other periods, 3) Several transcription factors related to glycolipid metabolism, such as HNF4α, CEBPα, and PPARα, have been identified as genes involved in DNA methylation changes, and the interaction of these transcription factors leads to the formation of DNA methylation state, and 4) The components of smoking (nicotine and benzo(a)pyrene) are involved in the dramatic changes in DNA methylation.

   In the future, it will be important to clarify the *in vivo* significance of DNA methylation in the functional maturation of the liver in the postnatal period and we have identified the important molecular basis and molecular targets in this study.