1. No.
   2023Y007

2. Title
   The Effect of Tobacco on Cellular Metabolism of Embryonic Neural Cells

3. Period
   2023-2025

4. Summary
   In this study, we analyzed the effects of nicotine administration during pregnancy on fetal developmental mechanisms, focusing specifically on the glycogen metabolic pathway, which is one of the intracellular metabolic pathways. We found that treating neural stem cells with nicotine reduced intracellular glycogen levels. However, at the concentration of approximately 10μM used in this analysis, no effects on cell proliferation or differentiation were observed. It has been reported that oral administration of nicotine *in vivo* results in changes in the number of neural stem/progenitor cells during development (Aoyama et al. 2016). Similarly, we administered nicotine orally to pregnant mothers and analyzed its effects on the fetus. Notably, no significant differences were observed in Glycogenin (Gyg)-deficient mice, which exhibit abnormalities in glycogen metabolism. We analyzed the effects of nicotine administration at the *in vivo* level. Nicotine exposure between embryonic days 13.5 and 18.5 resulted in a significant increase in Iba1-positive microglia in Gyg-deficient mice. Furthermore, since no effects on proliferation or other parameters were observed in cultured microglial cell lines lacking Gys1, it is considered that the *in vivo* effects of nicotine during pregnancy influence microglia not directly, but rather by acting on neural stem cells. It was considered necessary to prepare neural stem cells from Gyg-deficient mice, prepare culture medium treated with chronic nicotine, and clarify the response when this was added to microglial cells. Furthermore, it was considered possible that nicotine treatment leads to changes in stress sensitivity by affecting not only neural stem cells but also the intracellular metabolism of microglia. Since glycogen has been reported to be used as an energy source to counteract various stress conditions, such as low energy or hypoxia, the findings obtained in this study are considered useful for elucidating the effects of nicotine on microglia.