1. **No.**

   FP01812200

2. **Title**

   Influence of Nicotine in Milk Producing Abilities of Mammary Epithelial Cells

3. **Period**

   2016-2018

4. **Summary**

Breast milk contains appropriate and abundant nutrition for suckling infants and is secreted by mammary epithelial cells (MECs) in lactation. The milk production ability and of MECs is regulated via activation/inactivation of specific pathway such as STAT5, GR, STAT3, NFκB signaling. Exogenous substances such as lipopolysaccharide and isoflavones activate or inactivate such signal pathway and influence in milk production in MECs. In this study, we investigated the influences of nicotine in milk production in MECs. High concentration of nicotine exposure (10-100 μM) caused the decrease in intracellular and secreted β-casein in cultured MECs in time- and dose-dependent manners. MECs treated with nicotine showed the increase in claudin-4. Nicotine treatment also affected the expression of STAT5 and activation of STAT3. Low concentration of nicotine exposure (0.1-1.0 μM) also caused the decrease in secreted α- and β-casein without affecting the amount of intracellular caseins, claoudin-3, and claudin-4. STAT5 and NFκB were inactivated by low concentration of nicotine treatment concurrently with inactivated p38/MAPK and Akt. In addition, cicotine was administered to lactating mouse. Excessive activation of STAT5 was caused in the lactating mammary glands concurrently with up-regulation of α-lactalbumin. Tight junction proteins (claudin-3, -4, occludin) were abnormally localized in the basolateral membrane. These results indicate that nicotine adversely affects milk production ability of MECs.