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2. Title
   Regulatory mechanism of the milk-producing ability of mammary epithelial cells by acetylcholine in the lactating mammary gland

3. Period
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4. Summary
Smoking during lactation negatively affects maternal milk production. Nicotine also decreases secreted casein and tight junction (TJ) proteins in mammary epithelial cell (MECs) concurrently with inactivating STAT5 and Akt, which are signaling molecules to regulate milk production. Nicotine is a ligand for the nicotinic acetylcholine receptors (nAChRs). However, it remains unclear whether nicotine affects milk production via nAChRs in MECs. In this study, we investigated whether AChRs in MECs regulate milk secretion and TJs. The results showed that mouse MECs express five nAChR subunits, five mAChRs, and molecules involved in ACh metabolism. In the lactating culture model using MECs, nAChR agonist (NS3861) decreased α-casein secretion and inactivated STAT5 and Akt. The allosteric modifier of nAChRα2 (Br-PDTC) caused decreased secretion of α- and β-casein and inactivation of STAT5 and Akt, and increased expression levels of the TJ component protein CLDN4. Furthermore, the mAChR-M1 agonist McN-A-343 inactivated STAT5, Akt, and STAT3, activated p38, decreased β-casein secretion, and altered the localization of TJ proteins. These results suggest that MECs have a regulatory mechanism for milk secretion mediated by mAChRs and nAChRs. Nicotine would disrupt milk secretion by interfering with this mechanism.