1. No.
   2021G032

2. Title
   Nicotine addiction and its therapeutics targeting for dopamine receptor modulator

3. Period
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4. Summary
   In this study, we focused on the type 3 fatty acid-binding protein (FABP3), which binds to dopamine D2 receptors, and analyzed its physiological significance in the development of nicotine dependence and its usefulness as a therapeutic target. First, pharmacological experiments using FABP3-deficient mice showed that the formation of nicotine dependence was completely abolished, indicating that FABP3 is essential for the development of nicotine addiction. In addition, decreased expression of D1 receptors and increased expression of D2 receptors were suggested to be involved in the formation of nicotine dependence. Next, we developed the FABP3 inhibitor MF1 and examined the effects of the compound on nicotine dependence formation, dependence after nicotine withdrawal, and relapse; MF1 completely inhibited nicotine dependence formation and suppressed activation of CaMKII and ERK in D1 and D2 receptor-expressing cells in the nucleus accumbens. Furthermore, we analyzed the effect of the FABP3 inhibitor MF1 on the formation of nicotine dependence in more detail and found that D2 receptor/FABP3 signaling-mediated activation of CaMKII and ERK is critical for the formation of nicotine dependence. These results reveal a novel molecular mechanism of nicotine dependence and suggest that FABP3 inhibitor may be useful as a novel therapeutic agent to suppress nicotine dependence.