O3F5-1 M3 muscarinic receptor mediates carbachol-induced contraction of mouse uterine smooth muscle

Takio Kitazawa[1], Ryuichi Hirama[1], Kozue Masunaga[1], Tatsuro Nakamura[1], Koichi Asakawa[1], Jinshan Cao[1], Hiroki Teraoka[2], Toshihiro Unno[3], Sei-ichi Komori[3], Masahisa Yamada[4], Jurgen Wess[5], Tetsuro Taneike[1]

[1]Dept. Pharmacol. Sch. Vet. Med. Rakuno Gakuen Univ., Ebetsu, Hokkaido 069-8501, Japan, [2]Dept. Toxicol. Sch. Vet. Med. Rakuno Gakuen Univ., Ebetsu, Hokkaido 069-8501, Japan, [3]Lab. Pharmacol. Fac. Applied Biol. Sci. Gifu Univ., Gifu 501-1193, Japan, [4]Yamada Research Unit. RIKEN Brain Sci. Inst., Saitama 351-0198, Japan, [5]Lab. Bioorganic Chem. National Institute of Diabetes, Digestive and Kidney Diseases, Bethesda MD 20892, USA

Functional muscarinic receptor (mAChR) in the mouse uterus was characterized. Carbachol (CCh) increased muscle tonus and phasic contractile activity of mouse uterine strips. 4-DAMP, AF-DX116, AF-DX384, p-F-HHSiD, himbacine, methoctramine, pirenzepine and tropicamide inhibited CCh-induced contraction competitively. The pKb values correlated well with the known pKi of these antagonists for M3 mAChR. In uterine strips from mice treated with pertussis toxin, Emax for CCh was decreased but EC50 remained unchanged. In uterine strips treated with 4-DAMP mustard and AF-DX116, followed by washout of AF-DX116, CCh did not cause contraction. Both M2 and M3 mAChR mRNAs were detected in the mouse uterus via RT-PCR. CCh also caused contraction of uterine strips isolated from M2 mAChR deficient mice but the concentration-response curve was shifted to the right compared with wild type mice. However uterine strips from M3 and M2/M3 mAChR deficient mice were insensitive to CCh. In conclusion, although both M2 and M3 mAChRs were expressed in the mouse uterus, CCh-induced contractile responses were predominantly mediated by M3 mAChR. Activation of M2 mAChR alone did not cause contraction; however, M2 mAChR activation enhanced M3 mAChR-mediated contraction.