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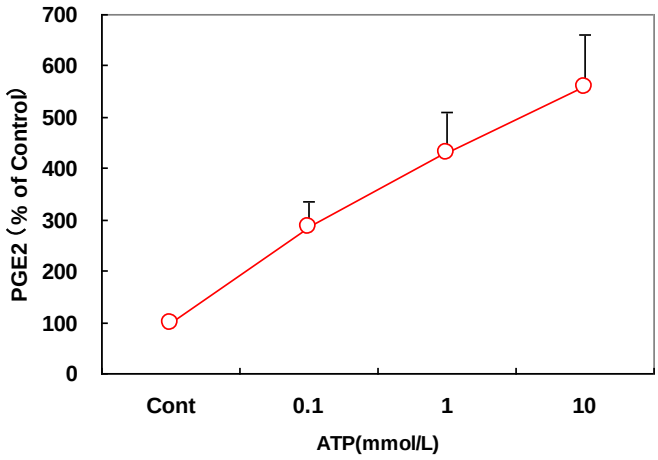
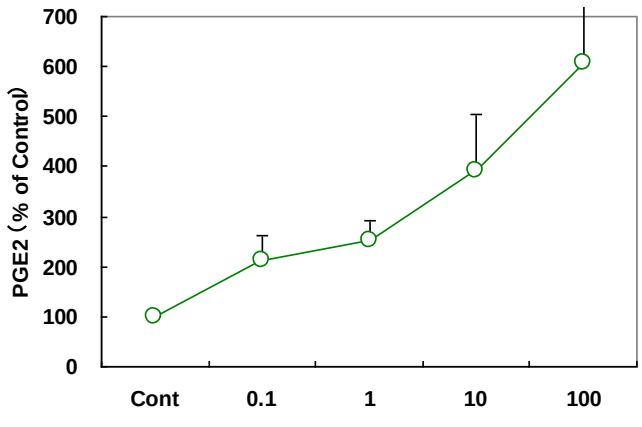
STIMULATIONS OF AUTONOMIC RECEPTORS CAUSE RELEASE OF PROSTAGLANDIN E2 (PGE2) FROM RAT BLADDER

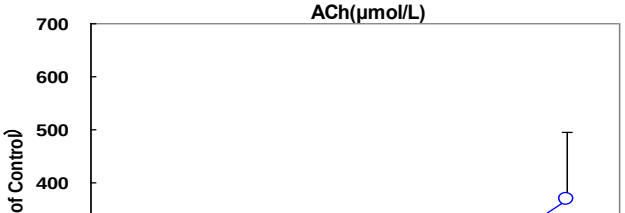
aims of study
Recently, it has been shown that various neurotransmitters or factors contribute to the increased excitability to the C-fiber bladder afferent nerves, and that prostaglandins E_2 (PGE_2) act as one of such neuromodulators for increased micturition reflex and detrusor overactivity. PGE_2 are synthesized locally in both bladder smooth muscle and urothelium, and synthesis is initiated by various physiologic stimuli, such as stretching of the detrusor muscle, injury to the bladder urothelium, stimulation of the nerves and by agents such as adenosine triphosphate (ATP) and mediators of inflammation.
However, little information exists regarding the mechanism of PGE_2 releases from bladder. Therefore, this study has investigated the interaction between PGE_2 release and autonomic receptors stimulation in rat bladder strips.

Study design, materials and methods
Paired longitudinal strips with urothelium were isolated from female rat bladders, and were mounted in a 20-ml organ bath filled with Krebs-Henseleit solution. Microdialysis probe was inserted into the strip, and Ringer solution was perfused into the probe at a constant flow rate of 2 μl/min. And, dialysate was collected after incubation with adenosine triphosphate (ATP: 10^{-4} - 10^{-2} M; n=12), acetylcholine (ACh: 10^{-7} - 10^{-4} M; n=8), or noradrenaline (NA: 10^{-7} - 10^{-4} M; n=8). In the separate experiments, inhibitory effects of indomethacin (cyclooxygenase (COX) inhibitor, 10^{-6} M) for PGE_2 releases from bladder strips were also performed after incubation with ATP (10^{-4} - 10^{-2} M; n=8). The amount of PGE_2 was measured by EIA assay. Results are mean±SEM % when the values without ATP, ACh, or NA incubation are 100 %.

Results
Treatments with ATP, ACh and NA showed concentration-dependent increases in PGE_2 release from rat bladder strips. The % maximum increases were 558±103 % (ATP), 607±200 % (ACh), and 369±127 % (NA), respectively. The % maximum increases in ATP and ACh were significantly higher than that in NA., Pretreatment with indomethacin almost completely inhibited ATP-induced PGE_2 releases, suggesting that COX was involved in PGE_2 releases via purinergic receptor's stimulation in rat bladder.







Interpretation of results

These data demonstrates that PGE_2 is released from bladder via stimulations of purinergic, muscarinic, or adrenergic receptors.

Concluding message

The contributions of purinergic and muscarinic receptors to PGE_2 releases from bladder are greater than that of adrenergic receptors. The interaction between PGE_2 release and various autonomic receptors stimulations might be related to regulation of bladder function.

Specify source of funding or grant	**none**
Is this a clinical trial?	**No**
What were the subjects in the study?	**ANIMAL**
Were guidelines for care and use of laboratory animals followed or ethical committee approval obtained?	**Yes**
Name of ethics committee	**Kumamoto University Graduate School of Medical Sciences ethics committee**