Sodium Chloride Regulation of COX-2 gene expression is independent of aldosterone activated mineralocorticoid receptor

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Production of prostaglandins involved in renal salt and water homeostasis is modulated by regulated expression of the inducible form of cyclooxygenase-2 (COX-2) at restricted sites in the rat kidney. COX-2 expression in the kidney is regulated by dietary salt intake, but the mechanism of its action is not fully understood. We have previously that high salt regulates COX-2 expression in rat kidney. The aim of the present study was to examine the role of mineralocorticoid receptor (MR) in regulation of COX-2 in kidney cell line (COS). In COS cells, TPA and hypertonicity induced a marked increase in COX-2 promoter activity. Spironolactone antagonized the aldosterone-induced trans-activation activity of the rMR transiently expressed in COS cells lacking steroid receptors. But stimulation of COX-2 promoter activity by hypertonicity was not reduced by inhibition of MR (spironolactone, 100 nM) in COS cells transiently transfected with COX-2 and rMR. We conclude that COX-2 is regulated by hypertonicity and this regulation is not occurred through MR. Currently, we are searching for regulatory region responsible for salt-induced COX-2 gene expression using several luciferase constructs containing COX-2 promoter. This work was supported in part by grants from the Korean Ministry of Health and Welfare (01-PJ1-Pg1-01CH06-0003; YJL).

[PB1-3] [04/18/2003 (Fri) 09:30 - 12:30 / Hall P]

Anti-inflammatory activity of organic germanium

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Germanium is present in all living plant and animal matter in micro-trace quantities. Clinical trials and use in private practices for more than a decade have demonstrated germanium's efficacy in treating a wide range of serious afflications, including cancer, arthritis and senile osteoporosis. To investigate anti-inflammatory activity of organic germanium, we measured the effect of organic germanium on histamine release, ROS generation, arachidonic acid release in RBL 2H3 cells, and caragennin-induced paw edema in rats. Organic germanium inhibited caragennin-induced paw edema in a dose-dependent manner, suggesting that organic germanium has anti-inflammatory activity. Although organic germanium alone slightly increased ROS and peroxynitirte generation in RBL 2H3 cells, it dose-dependently inhibited mellitin-induced arachidonic acid release in RBL 2H3 mast cells. These results suggest that anti-inflammatory effect of organic germanium may be due to the inhibition of phospholipase A2 activity and organic germanium may be used as anti-inflammatory agent.

[PB1-4] [04/18/2003 (Fri) 09:30 - 12:30 / Hall P]

Effects of aloesin on physiological changes in rats after multiple oral administration

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This study was conducted to examine the effect of subchronic oral administration of aloesin on

changes in the body weight and blood biochemistry in rats. Aloesin were given orally at a rate of 100 mg/kg every 12 hours for 15 days. The rats in the control group received isotonic saline. The body weight and food consumption were measured every 12 hrs immediately prior to each treatment throughout the study period. At the end of treatment, blood biochemistry was measured. The final mean body weight was not altered at the end of the aloesin treatment as compared with control. Subchronic administration of a relatively high dose of aloesin did not appear to cause adverse effects as the biochemical parameter values including AST, ALT, albumin, glucose, BUN and creatinine levels were not altered as compared with the control values. (This work was supported by a grant from the Ministry of Health & Welfare 02-PJ1-PG4-PT04-0002)

[PB1-5] [04/18/2003 (Fri) 09:30 - 12:30 / Hall P]

Histamine Signaling Pathway in Sensory Neurons is Similar to Bradykinin

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Histamine is found in most tissues of the body and activates polymodal nociceptors via unmyelinated afferent C-fibres. We have demonstrated that bradykinin, acting at B2 bradykinin receptors, excites sensory nerve endings by activating capsaicin receptors via production of 12-lipoxygenase metabolites of arachidonic acid in dorsal root ganglion. Histamine is known to the activator of phospholipase A2- arachidonic acid pathway via a G-protein- coupled H1 receptor. We, therefore, hypothesized that histamine activates capsaicin receptors by inducing the production of fatty acid agonists of capsaicin receptors in dorsal root ganglion neurons. This study shows that histamine evokes transient increases of intracellular Ca2+ concentration ([Ca2+]i) in a dose-dependent manner by stimulating H1 histamine receptor in dorsal root ganglion neurons. Histamine-induced [Ca2+]i increase was dependent on extracellular Ca2+ and was reversibly inhibited both by the capsazepine and by the SC0030, competitive antagonists of capsaicin receptor. The quinacrine and the nordihydroguaiaretic acid blocked histamine-induced Ca2+ influx in dorsal root ganglion neurons, but not the indomethacin. These results suggest that histamine increases Ca2+ influx by activating capsaicin channel via phospholipase A2- lipoxygenase pathway in neuronal cells, like bradykinin.

[PB1-6] [04/18/2003 (Fri) 09:30 - 12:30 / Hall P]

Cloning of a novel ion channel candidate by in silico gene mining

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Capsaicin, a pungent ingredient in chili pepper, is known to excite sensory neurons that mediate pain sensation. This effect of capsaicin is determined by unique receptors and the capsaicin receptor (transient receptor potential subfamily V, member 1 (TRPV1)) was cloned recently. TRPV1 contains six transmembrane domains and three ankyrin repeats at N-terminal. This characteristic architecture is common in other ion channels in TRPV families. Taking notice of these structural similarities, seeking of novel ion channel candidates residing in genome