

augmenting effect of ATP. VR1 mutant having mutations at both Walker-type A and B motifs (VR1-D178N/K735R) also blocked the ATP augmenting effect (n = 12). These results clearly indicate that the augmenting effect of ATP requires allosteric binding of ATP to the channel at these loci. Supported by National Creative Research Initiatives organized by KISTEP.

[PB4-1] [04/21/2000 (Fri) 10:30 - 11:30 / [1st Fl, Bldg 3]]

A Broad-Spectrum Caspase Inhibitor Blocks Concanavalin A-Induced Hepatitis in Mice

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Fulminant hepatic failure (FHF) is a clinical syndrome resulting from massive death of liver cells or sudden and severe impairment of liver function. The causes of FHF are diverse and the overall mortality is very high. Recently, it became clear that apoptosis of hepatocytes is the critical cause of acute hepatic failure in FHF. It is well-known that a family of cysteine proteases called caspase is one of key mediators of the apoptotic pathway. Thus, caspases are attractive potential targets for the treatment of disorders resulted from excessive apoptosis. In this report, we examined the activity of a new caspase inhibitor Xyz 033 mp. This non-peptide inhibitor showed broad-spectrum caspase-inhibiting activity and protected primary rat hepatocytes from apoptotic death. In mice model of FHF induced by Con A, Xyz 033mp suppressed the elevated AST and ALT, and specifically reduced IL-1 β concentration. In Addition, histological examinations indicated that Xyz 033mp protected hepatocytes from the fatal apoptogenic effect of Con A. Finally, Xyz 033mp inhibited PARP cleavage caused by apoptotic death of hepatocytes. These results suggest that Xyz 033mp could be a candidate of therapeutic agent for FHF caused by massive apoptotic death of hepatocytes.

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Identification of allergenic potential components of pork meat

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Any food may cause an allergic reaction, but most reactions are accounted for by 7 foods (pork, chicken, beef, milk, eggs, wheat, and soy) in Korea in contrast to 6 foods (milk, tree nut, eggs, wheat, peanuts, and soy) in USA. Sensitization to pork meat seems to be predominantly prevalent in Korea. To detect allergenic components of pork meat, sera of twenty-five patients with allergy syndrome, a positive skin prick test response, and a positive open food challenge test reaction to pork were used in this study. A crude extract of pork was prepared by blending raw meat in phosphate buffered saline (pH 7.0), and some of this extract was heated and/or incubated with SGF (simulated gastric fluid) preparations in order to characterize as a heat-stable or digestion-resistant allergens. ELISA assay performed to determine specific IgE antibody levels in sera of the patients showed that the mean values in these sera was twofold higher than those in sera of milk-sensitive patients. The different polypeptide components of these extracts were separated by sodium dodecylsulfate-polyacrylamide gel electrophoresis and analyzed by IgE immunoblotting with sera from pork-sensitive patients as compared with non-allergic sera. Most IgE binding components were identified with molecular weights ranging from 25 to 75 kDa in crude extracts of pork meat. In case of heat-treated pork preparations, four proteins (111, 66, 50, 40 kDa) were predominant, and the three putative allergens (66, 60, 50 kDa) were still present in SGF-treated preparations. These results suggest that three components (66, 60, and 50 kDa) would be major allergens even though they presented weak affinity.