significantly protected CA1 hippocampal neurons against 20 min transient forebrain ischemia. Also, baicalein, the main components of Scutellaria baicalensis showed a similar neuroprotective effects. We further examined in vitro antioxidative effects of methanol extracts of Scutellaria baicalensis and its fraction, and baicalein using LDH and MTT assay in PC 12 cells. Thus, the neuroprotective effects of methanol extracts of Scutellaria baicalensis and baicalein in vivo was explained in part by its inhibitory effects on oxidative stress of significantly protected PC 12 cells after hydrogen peroxide treatment.

[PB3-3] [04/21/2000 (Fri) 10:30 - 11:30 / [1st Fl, Bldg 3]]

Comparison of pharmacokinetic profiles and brain uptakes of antibody-transferrin fusion proteins specific for the rat transferrin receptor

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The antibody(Ab)-transferrin fusion protein has been constructed to deliver drugs across the blood-brain barrier. This fusion molecules consist of the end of hinge and heavy chain constant region 3 (C_H3) of antibody specific for the trasnsferrin receptor genetically fused to transferrin.

Ab-transferrin fusion proteins was iodinated by chloramine T method and pharmacokinetic parameters and brain uptake of iodinated Ab-transferrin fusion proteins was measured by intravenous injection technique.

In results, brain uptakes of Ab specific for the rat transferrin receptor (TAIQ) is similar to mouse monoclonal antibody, OX26 specific for the rat transferrin receptor. But, brain uptakes of Ab-transferrin fusion proteins specific for the rat transferrin receptor are very low comparison with OX26.

Our results show that only TAIQ may be used to target to the brain for delivery of neuropharmaceutical drug.

[PB3-4] [04/21/2000 (Fri) 10:30 - 11:30 / [1st Fl, Bldg 3]]

Mutations of Walker type ATP-binding motifs of vanilloid receptor 1(VR1) abolish the augmenting effect of intracellular ATP

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Activity of ion channel is modulated by intracellular factors such as ATP. Previously, we reported that the addition of ATP to the bath of along with CAP caused a two-fold increase in the activity (NPo) of capsaicin (CAP)-activated channel. The augmenting effect of ATP is Mg2+-independent and induced by non-hydrolyzable analogs of ATP, AMPPNP and ATPgS. These results suggest the possible presence of the ATP-binding sites in the channel. We, therefore, mutated VR1, cloned CAP channel, on each putative Walker A- or B-type ATP-binding motif to clarify the implication of ATP binding. CAP evoked single-channel currents (icap) in inside-out excised membrane patches isolated from Xenopus oocytes expressing wild-type VR1. In these patches, the addition of 2 mM ATP greatly augmented icap by 232 ± 19% (n = 7). In oocytes injected with RNA of the mutant (VR1-K735R) at the Walker A-type motif, CAP activated icap as normally observed in oocytes expressing wild-type VR1. The VR1-K735R mutant, however, completely blocked the augmenting effect of ATP. In addition, the mutant (VR1-D178N) at the Walker B-type motif also blocked the

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.
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[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$₩beta$ 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.

[PB4-2] [04/21/2000 (Fri) 10:30 - 11:30 / [1st Fl, Bldg 3]]

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 sudy. 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.