We investigated what the high expression of Nramp2 influence pH dependent lead uptake in Astrocytes. The treatment of Deferoxamine increases mRNA level of Nramp2 in astrocytes. It was time- and concentration-dependent, and saturable. Lead uptake in astrocytes increased time-, pH-, and concentartion-dependently, and was saturable. At pH 7.5 it was the highest level. It was proportional to the amount of Nramp2 expression in pH 5.5, but not proportional to it at pH 6.5 and 7.5. We may suggest that Nramp2 in astrocytes functions at a low pH.

[PA1-68] [10/18/2001 (Thr) 14:00 - 17:00 / Hall D]

Study of diabetic animal model

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To compare the characteristics of diabetic animal models, several mice strains aged 6 week, KKAy, NZO, C57BL/6J obese(ob/ob) mice with long-lasting genetic diabesity and C57BL/6J mice with high-fat diet induced diabesity were studied for 20 weeks. We determined plasma glucose, body weight biweekly and serum insulin, creatinine, urine albumin, plasma HbA1c, total cholesterol, triglyceride levels at 10, 20 week. We also examined PPAR gamma, GLUT4, TGF beta 1, fibronectin protein expressions by immunoblotting and glucokinase, glucose-6-phosphatase enzyme activities. Ob/ob mice exhibited marked obesity, hyperglycemia, hyperinsulinemia and glucokinase activities were decreased, glucose-6-phosphatase activities increased at 20 week when compared to those of 10 week. High-fat diet induced diabetic mice showed remarkable weight gain rate and KKAy mice showed increased triglyceride, total cholesterol, HbA1c levels at 20 week. At 20 week, renal TGF beta 1 and fibronectin protein expressions increased, skeletal muscluar GLUT4 decreased in all strains, whereas adipose PPAR gamma decreased in only high-fat diet induced diabetic mice when compared to those of 10 week.

[PA1-69] [10/18/2001 (Thr) 14:00 - 17:00 / Hall D]

Increase in the Expression of Fibrinogen B β Chain, B Cell Translocation Gene1 and Thyroid Hormone Responsive Protein Genes in the Liver of Rats with Protein-Calorie Malnutrition by DD-PCR

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Protein-calorie malnutrition (PCM), as one of global health problems, arises during protein and/or energy deficit due to disease and nutritional inadequacy. Previously, we showed that PCM elicited oxidative stress with activation of the phase II detoxifying gene expression, which was reversed by cysteine supplementation. As part of the attempts to identify the cellular adaptive responses and the associated gene expression during PCM, the current study was initiated to analyze the genes differentially expressed in the rat during PCM. Among 1,916 bands amplified, 85 putative differentially amplified bands were enhanced by PCM in the liver, while the expression of 64 bands was suppressed. Northern and/or reverse transcription-polymerase chain reaction (RT-PCR) analyses revealed that PCM increased the expression of fibrinogen B β chain, B cell translocation gene1 (BTG1) and thyroid hormone responsive protein (THRP) mRNAs. The increase in the hepatic fibrinogen B β chain mRNA was not prevented by cysteine supplementation. Cysteine was also active in reversing the increase in BTG1 mRNA during PCM. Northern blot analysis revealed that THRP, highly expressed in the brain in a tissue-specific manner, was induced by PCM and that cysteine supplementation abolished the THRP induction. Conversely, the level of hepatic albumin mRNA was markedly decreased by PCM, which was partially restored by cysteine supplementation. Differential display RT-PCR analysis allowed us to identify the genes that are responsive to oxidative stress during PCM and to characterize the differential role of

cysteine on the expression of the fibrinogen B β chain, BTG1 and THRP genes as a homeostatic adaptive response during protein deficiency.

Poster Presentations - Field A2. Therapeutics

[PA2-1] [10/18/2001 (Thr) 14:00 - 17:00 / Hall D]

Antiproteinuric Effect of Enalapril in Children with Nephrotic Syndrome

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Enalapril, an angiotensin converting enzyme inhibitor, was used to treat pediatric patients with nephrotic syndrome. The objective is to study the antiproteinuric effect of enalapril in children with nephrotic syndrome.
Patients were eligible when the children with nephrotic syndrome were treated with enalapril and corticosteroid at Seoul National
University Children's Hospital. The exclusion criteria were the secondary nephrotic syndrome. Dosage of enalapril started with 0.1mg/kg/d. The primary variables evaluating efficacy of enalapril to nephrotic syndrome were time-dependent changes in serum total protein, albumin, total cholesterol and serum creatinine, BUN and urinary protein/creatinine ratio. Adverse drug events associated with enalapril and corticosteroid were evaluated. There were total 35 patients with 26 boys and 9 girls, age ranging from 3 to 22years. Ten patients had hypertension at baseline.
Histological lesions were focal and segmental glomerulosclerosis in 18, minimal change nephrotic syndrome in 7, membranoproliferative glomerulonephritis in 2, membranous glomerulonephritis in 1 and 7 patients not done kidney biopsy.
Serum total protein and albumin levels increased simultaneously. Total protein increased from 5.1(±1.1) g/dL to 5.7(±1.0)g/dL (p=0.029) and 6.1(±1.1)g/dL (p=0.009) at 6 months and 3 years after treatment, respectively. Serum albumin increased from 2.4(±0.9)g/dL to 2.9(±0.9)g/dL (p=0.009) and 3.3(±1.2) g/dL (p=0.005) at 6 months and 3 years after treatment, respectively. Total cholesterol level decreased from 384.7(±156.5)mg/dL to 293.4(±160.5)mg/dL (p=0.081) at 3 years after treatment. Serum creatinine level showed statistically significant change and BUN level showed no statistically significant change. Enalapril
treatment was associated with significant and persistent reduction of urinary protein/creatinine ratio from 16.3(±20.6) to 6.0(±8.9) (p=0.011) and 3.7(±7.0) (p=0.003) at 6 months and 3 years after treatment, respectively.
Side effects of enalapril were observed for cough in one patient and elevated BUN and Scr in one patient.
We conclude that enalapril treatment was effective in reducing proteinuria with preserved renal funtion.

[PA2-2] [10/18/2001 (Thr) 14:00 - 17:00 / Hall D]

Cyclosporin Induced Hyperuricemia and the Uricosuric Efficacy of Benzbromarone in Kidney Transplant Patients

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