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Autotaxin (ATX) is an exo-nucleotide pyrophosphatase and phosphodiesterase (NPP) which stimulates tumor cell motility at low nanomolar concentration. Cellular ATX mRNA expression was most abundant in breast tumor cells in several tumor cells, and breast cancer cells with high invasive and/or metastatic capacity such as MDA-MB-435S and MDA-157 showed relatively higher ATX expression. The pretreatment of cells with pertussis toxin abolished the cell migration response to ATX as a chemoattractant. Taken together, these data strongly suggest that cellular expression of ATX is correlated with an invasive phenotype of breast tumor cells.

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

### **Effects of acute cocaine administration on the basal ganglial nervous systems : Immunohistochemical studies**

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Cocaine is a potent psychomotor stimulant which has become a popular drug of abuse. The purpose of the study was to examine time-course effects of acute cocaine exposure on dopaminergic, GABAergic and enkephalinergic nervous systems in the basal ganglia using immunohistochemical techniques. Sprague-Dawley rats were sacrificed 0.5, 2, 4 and 24 hr after administration of cocaine (1 mg/kg, i.v.). Immunohistochemical staining was performed using antibodies against tyrosine hydroxylase (TH), dopamine transporter (DAT), glutamic acid decarboxylase (GAD), parvalbumin (PV), and Met- and Leu-enkephalin (Enk). TH-immunoreactivity (IR) was gradually decreased, but DAT-IR was increased, in both the striatum (ST) and the nucleus accumbens (NA) until 4 hr after cocaine administration and then returned to the basal level at 24 hr compared with the saline-treated control. Similar patterns of changes in TH- and DAT-IR were also observed in the substantia nigra (SN). Met-Enk-IR was increased at 2-hr time point and then returned to the control level in the ST without any clear changes in the SN. Leu-Enk-IR was increased until 2-hr time point and then returned to the control level in the globus pallidus whereas no changes were observed in the ST and SN. GAD-IR appeared to be increased until 4 hr and then return to the control level in the SN. PV-IR was not altered in the ST and cerebral cortex compared with the control. The results suggest that immunohistochemical techniques can be used as a useful tool to study neurochemical effects of cocaine on the basal ganglial nervous systems.

[PB3-2] [ 04/21/2000 (Fri) 10:30 - 11:30 / [1st Fl, Bldg 3] ]

### **Scutellaria baicalensis protects CA1 hippocampal neurons after global cerebral ischemia in rats**

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Scutellaria baicalensis is one of the most widely used oriental herbal medicines against bacterial infections of the respiratory and the gastrointestinal tract. Current study was carried out to evaluate neuroprotective effects of Scutellaria baicalensis after transient global ischemia using 4-vessel occlusion model in rats. Methanol extracts of Scutellaria baicalensis administered intraperitoneally

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<sub>H</sub>3) of antibody specific for the transferrin 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 Mg<sup>2+</sup>-independent and induced by non-hydrolyzable analogs of ATP, AMPPNP and ATPγS. 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