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Haptoglobin in the brown bear (*Ursus arctos*): Molecular structure and hibernation-related seasonal variations

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Haptoglobin (Hp), a hemoglobin-binding protein in plasma, is known as an acute phase protein (APP), increasing during acute phase of inflammation in most mammals. Hp of dog, a Carnivora species, was purified and found to have a unique molecular structure compared with those of human and rodents. Furthermore, serum concentration of several APPs, such as α_2-macroglobulin (α_2M) and α_1-antitrypsin (α_1-AT)-homologous protein showed seasonal variations related with hibernation in some squirrels. In this study, to characterize Hp of the Carnivora and to determine whether the seasonal variations of APPs are common in hibernation, I focused on Hp of the brown bear (*Ursus arctos*), the largest hibernating Carnivora, and analyzed the molecular structure and seasonal variations.

Dog Hp consists of α and β chains, the former being glycosylated, and the two $\alpha\beta$ units are joined by a noncovalent interaction rather than a disulfide bridge. Hp was purified from sera of Hokkaido brown bear, and the subunit structure and N-terminal amino acid sequences were analyzed. The analyses by gel-filtration and sodium dodecyl sulfate-polyacrylamide gel electrophoresis revealed that bear Hp has a similar subunit arrangement to dog Hp, lacking a disulfide bridge between two α chains. This was confirmed by N-terminal amino acid sequence analysis of the α chains. A similar subunit structure was also found in cat Hp. Thus, the unique subunit arrangement of Hp reported in dog may be common in the Carnivora. In contrast to dog Hp, however, α chains of bear and cat Hps were found not to be glycosylated.

A specific antibody against the purified bear Hp was obtained from a rabbit, and an immunological assay was developed using this antibody. Hp concentration was measured in sera collected from 101 reared and 27 wild Hokkaido brown bears. The mean serum Hp concentration was 0.94 ± 0.25 mg/ml in wild bears, which was nearly equal to those reported in other species. In reared bears, the mean Hp concentration was apparently higher (3.82 ± 0.29 mg/ml), although total protein and albumin concentrations were nearly equal in the two groups.

The blood samples of the reared adult bears were divided retrospectively into four groups depending on the month of sample collection. Although none of the reared bears hibernated even in winter, serum Hp concentration showed a significant seasonal change: that is, it was the lowest in spring (2.29 ± 0.25 mg/ml), increased in autumn, and was the highest in winter (4.53 ± 0.72 mg/ml). Total protein and albumin concentrations also showed slight but significant seasonal variations, whose patterns were apparently different from that of Hp.

To clarify the seasonal variation of serum Hp concentration, blood samples were serially obtained 5 or 6 times, including at the time of hibernation, during a 1-year period from 7 European brown bears kept in the Zoological Garden, University of Oulu, Finland. Mean serum Hp concentration was low in non-hibernating seasons and increased 3.5-10 folds during hibernation. The mean level of α_2M also showed a similar but

much smaller (1.5-1.6 folds) rise during hibernation, but those of α_1-AT and C-reactive protein, the other APPs, did not show any seasonal variations. It was concluded that the increase in serum Hp concentration during hibernation in the brown bear is independent of acute phase response, but associated with a hibernation-specific mechanism.

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Pharmacological profiles of TAK-029, a novel antagonist to platelet GPIIb/IIIa, and its antithrombotic effects

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Responses and pharmacological classification of purinoceptors — Studies in guinea-pig adrenal chromaffin cells and rat gastric circular smooth muscle

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The effects of extracellular ATP on voltage-dependent Ca^{2+} channels were examined using guinea-pig isolated adrenal chromaffin cells, and those of ATP on contractile responses were studied using rat gastric circular smooth muscle.

In the chromaffin cells, ATP evoked an inward current (I_{ATP}) and a rise of intracellular Ca^{2+} concentration. ATP also showed the inhibition of Ca^{2+} current (I_{Ca}) dependently on the amplitude of I_{ATP}. However, when a high concentration of EGTA was used in the intracellular solution, the inhibitory effect became independent of the amplitude of I_{ATP}. This reduction was decreased by dialysis of cells with GDPβS or GTPγS, or by the application of a depolarizing prepulse. ADP, AMP and adenosine also reduced I_{Ca} and the effect of adenosine was the most potent. These results suggest that Ca^{2+} entry through ATP-activated channels results in the inactivation of Ca^{2+} channels, in addition, that