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Laboratory of Biochemistry

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Teaching staff of the laboratory is composed of a professor and an associate professor. An instructor is expected to join in very near future. In addition, seven postgraduate, three undergraduate, and one research students are enrolled. The staff teach undergraduate students biochemistry and its practice at the second grade, and research works at the fifth and sixth grades. The staff also direct the postgraduate students to perform research works for a thesis of Doctor of Veterinary Medical Science.

The main research projects in this laboratory are as follows :

1. Neural regulation of adipose tissue metabolism and obesity : Excessive acumulation of triglyceride in adipose tissue is defined as obesity, which is one of the most important nutritional and metabolic disorders leading to diabetes mellitus, hypertension and atheroscrelosis not only in humans but also in companion animals. Brown adipose tissues (BAT) is the major site of metabolic thermogenesis. We have demonstrated that the metabolic and thermogenic functions of BAT are controlled directly by the sympathetic nervous system, and that any dysfunction of the sympatho-BAT system results in a reduced energy expenditure and obesity. To extend this view and to examine how to activate the sympatho-BAT system, we are now investigating the molecular and cellular mechanims for the sympathetic control of BAT, particularly focusing on the beta3-adrenoceptor specifically expressed in adipocytes and the mitochondrial uncoupling protein, a BAT-specific thermogenic protein[1]. The major methods used are cell culture, DNA and RNA manipulation, and immunological analysis of protein, in addition to the conventional biochemical techniques. On the basis of these in vitro studies, in vivo experiments using rats, mice and dogs are carried out to explore more appropriate and effective ways for prevention and treatment of obesity.

2. Interaction between the immune system and tbe brain : The brain and the peripheral immune systems closely interact each other to maintain whole body homeostasis during inflammation and stress situations. We have demonstrated that peripherally and/or centrally given interleukin-1 (IL-1), a typical cytokine produced in response to inflammatory stimuli, activates the peripheral stress-pathways, i.e., the adrenocortical and sympathetic nervous systems. On the other hand, splenic lymphocyte activities are under the influence of sympathetic nerves[2]. Thus, IL-1 is one of the key molecules in the crosstalk between the brain and the immune system. To clarify the neurochemical mechanism of the IL-1 actions in the brain, we are investigating sympathetic nerve and lymphocyte activities of the spleen after administrating intracranially various IL-1-related molecules and their antagonists such as prostaglandins, corticotropin-releasing hormone, calcitonin gene-related peptide, and urocortin. In addition to these neuropeptides, using the RNA subtraction method, we are also screening some novel molecules in the brain which response to IL-1, and inflammatory and/or stress stimuli. These studies contribute to understanding the pathophysiological features of stress-induced immunomodulation in humans and also in domestic animals.

3. Regulation of dopamine receptor signaling : Dopamine, a catecholamine neurotransmitter, exerts physiological effects linked to motor and motivated behaviors through its specific receptors. Among these receptors, D1 and D5 dopamine receptors stimulate cyclic-AMP formation by activating stimulatory GTP-binding protein (Gs) and adenylyl cyclase. We have demonstrated that 1) D1 receptors could couple to Go

protein in addition to Gs[3], and 2) D5 receptors could couple to Gz protein. These results suggest that D1 and D5 receptors can activate other effector signaling. We have also shown that 1) ascorbic acid inhibited D1 antagonist binding, but increased the affinity of binding of dopamine for D1 receptors, and 2) long-term exposure of the neuroblastoma to dopamine reduced expression of Gsa mRNA. The latter results might be related to several neurological disorders, such as schizophrenia and Parkinson's diseases. To explore this signaling more in detail, we are investigating changes in the adenylyl cyclase system after long-term exposure to dopamine.

4. Comparative studies of haptoglobin : Haptoglobin is a hemoglobin-binding protein synthesized in and secreted from the liver. We have demonstrated that serum haptoglobin in the bovine has a unique molecular structure of a polymeric form and a marker of inflammation and stress. Furthermore, a series of comparative studies of haptoglobin revealed that serum haptoglobin of brown bears shows marked seasonal variations, being high during hibernation[4]. The reasons and physiological significance of such apparent species differences in the serum haptoglobin profile are now investigated in relation to the molecular structure of this molecule.

References

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