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lots of commercial fetal bovine sera, the Ft levels ranged between 800 and 6,000 ng/ml. The serum Ft iron concentration ranged from 0.16 to 0.96 μg/ml, and the iron content of Ft was about 20% regardless of serum Ft concentration. The percentage of Ft iron to total serum iron ranged from 8.8 to 28.5%, and correlated significantly with Ft concentration. There was a significant correlation between serum Ft concentration and transferrin saturation. These findings demonstrate that bovine fetuses have the elevated iron stores.

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Adrenergic Regulation of Glucose Utilization and Glucose Transporter in Rat Brown Adipose Tissue

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Brown adipose tissue (BAT) is known to be the major site of nonshivering heat production during cold acclimation and spontaneous overfeeding. The metabolic activation and subsequent heat production in BAT are primarily controlled by sympathetic nerves distributed abundantly to this tissue. Although the main substrate for BAT thermogenesis is fatty acids derived from intracellular triglyceride, glucose metabolism in BAT is also activated by the sympathetic nerves. In order to clarify the regulatory mechanism of BAT glucose metabolism, in this study, I examined the effects of cold exposure and adrenergic stimulation on tissue glucose utilization and glucose transporter both *in vivo* and *in vitro*.

Exposure of rats to a cold environment at 4°C for 10 days increased the glucose uptake remarkably in BAT. In parallel with tissue glucose utilization, the protein and mRNA levels of an insulin-responsive glucose transporter GLUT4, which is the major glucose transporter in rat adipose tissues, were also increased. These stimulative effects of cold exposure were completely abolished when sympathetic nerves into BAT had been surgically severed, but were mimicked when noradrenaline was administered continuously for 10 days at 24°C. Continuous administration of a β-adrenergic agonist (isoproterenol) was as effective as noradrenaline, whereas an α-adrenergic agonist (phenylephrine) showed no effect. In contrast to BAT, in other insulin-sensitive tissues neither cold exposure nor adrenergic agonist-treatment showed noticeable effects on tissue glucose utilization and GLUT4. From these results, it was concluded that the stimulative effect of cold exposure on glucose utilization in BAT is based on the increased synthesis of GLUT4 protein evoked by the β-adrenergic action of noradrenaline released

from sympathetic nerve entering to this tissue.

To confirm the above results obtained from the *in vivo* experiments and to investigate the molecular mechanism of the β-adrenergic action on BAT glucose utilization, next, some *in vitro* experiments were performed using a primary culture system of brown adipocytes. When confluent precursor cells of cultured brown adipocytes were treated with dexamethasone (DEX), mRNAs for GLUT4, hormone-sensitive lipase, and C/EBP α were increased remarkably, indicating a predominant effect of DEX on the terminal differentiation of the cultured cell. BAT has an adipocyte-specific β-adrenoceptor (β3) in addition to β1- and β2-adrenoceptors. In the cells, β1- and β2-adrenoceptor mRNA remained constant regardless of DEX-treatment, while β3-adrenoceptor mRNA was present only in DEX-treated differentiated cells. To assess the metabolic response mediated by β3- adrenoceptor, glucose transport into the cells was estimated. Noradrenaline enhanced glucose transport in DEX-treated differentiated cells, but not in undifferentiated cells. β3-adrenergic agonists mimicked completely the stimulatory effect of noradrenaline at lower concentrations. These results suggest that the β3-adrenoceptor plays a significant role in the response of glucose transport to adrenergic stimulation.

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Anti-obesity effects of selective agonists to the β3-adrenergic receptor in dogs

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Obesity is the most common nutritional disorder in small animal practices, as in humans. Current treatment of obesity in dogs mostly relies on reducing energy intake by low calorie diet or fasting. It is known that in rodents and humans that the β3-adrenergic receptor (β3-AR) is present primarily in adipocytes and plays a significant role in the adrenergic stimulation of lipolysis and heat production. The aim of this study was to evaluate the effectiveness of β3-AR agonists for the treatment and prevention of obesity in the dog without any side effects.

1) The acute lipomobilizing effects of β3-AR-selective agonists were examined in the dog *in vivo*. When a selective β3-AR agonist, CL316,243 (CL), was infused intravenously into dogs, the plasma level of free fatty acid increased in 30 min and persisted at higher levels for several hours. ICI D7114, another β3-AR agonist, also showed a similar lipomobilizing effect, but with two order of lower potency. β3-AR agonist infusion also increased the plasma insulin level, and heart rate. Thus, the lipomobilization effect of the β3-AR agonist may be due to a direct action on the β3-AR in adipocytes. These results suggested that functional β3-AR is present in adipose tissues of the dog and that it is effective for in vivo lipomobilization.