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calization of DBI and FABPs suggests that they work together for various intracellular fundamental activities or metabolism. For example, in enterocytes, DBI and I-FABP seem to play an important role in the absorption and transportation of lipids derived from food. DBI and B-FABP may be involved in the en-

ergy metabolism in astrocytes and related cells, which are thought to support neuronal development and functions. In addition, the patterns of DBI/FABP colocalization indicate that the specialization of their cooperative functions is decided by the tissue-specific expression of FABP subtypes.

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Novel methods for diagnosis and treatment of obesity in dogs

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Obesity is the most common nutritional disorder and the risk factor for a number of diseases in small animal practice. During the last decade, there has been a great advance in our understanding on human obesity, especially on some obesity-related molecules. For example, an adipocyte-derived peptide, leptin, was discovered as a key blood hormone for the regulation of food intake and energy expenditure. Alternatively, mitochondrial uncoupling protein (UCP) has been expected as a target for prevention and treatment of obesity, because this molecule has been proved in rodents to dissipate excess fat energy as heat. On the basis of such recent knowledge, in the present study, I have tried to develop novel and reliable methods for diagnosis and treatment of obesity in the dog.

1. Serum leptin was assayed in beagles under various physiological and pathological conditions using an enzyme-linked immunosorbent assay specific to canine leptin. The serum leptin concentration was decreased during starvation, but increased after food intake and administration of insulin or dexametha-

sone. The serum leptin concentration was positively correlated with body fat content, and was higher in experimentally developed obese beagles. Elevated serum leptin concentration was also confirmed in clinically obese dogs with higher body condition scores regardless of their breed, age and sex. These results indicate that serum leptin is a good biochemical index of adiposity and useful for diagnosis of obesity in the dog.

2. To evaluate visceral and subcutaneous fat contents separately in beagles, computed tomographic analysis (CT) was applied under standard scanning conditions of 120 kV, 200 mAs and 5 mm in slice thickness. Fat area measured at 3rd lumbar vertebra using level detection analysis at -105/-135 HU correlated well with total body fat content. In experimentally developed obese beagles, the total fat area increased as expected, but the ratio of the visceral to subcutaneous fat area tended to decrease.

3. Three isoforms of canine UCP cDNA were cloned by reverse-transcription polymerase chain reaction. Nucleotide and deduced

amino acid sequences were highly homologous to those of other species. The tissue distribution of each isoform mRNA was also similar to those of other species. Sympathetic stimulation increased UCP 1 mRNA expression in adipose tissue of beagles. These results suggest that UCP may be involved in the regulation of energy expenditure in the dog, as in rodents.

4. On the basis of the above results, serum leptin analysis and CT were performed in obese beagles before and after treatment with a low calorie diet containing either fish oil or tallow. Body weight decreased on both

diets, slightly but significantly more on the fish oil diet. Serum leptin and total fat area in CT also decreased similarly on the two diets. The decrease of subcutaneous fat seemed more strikingly than that of visceral fat. Analysis of UCP mRNA revealed that the UCP 3 mRNA level in skeletal muscle increased on the fish oil diet. These results further support the usefulness of serum leptin assay and CT for diagnosis of obesity in the dog, and suggest that fish oil has an anti-obesity effect probably due to the increase of UCP expression and energy expenditure.

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Up-regulation of mitochondrial uncoupling proteins by stimulation of nuclear and β -adrenergic receptors in L6 myotubes

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Obesity is the most common nutritional disorder in humans and also in companion animals. The principal causes of obesity have been thought to be increased energy intake and decreased exercise or both. Recent studies have shown a significant involvement of metabolic heat production in the regulation of energy balance and its impairment as a possible cause of obesity. The most likely mechanism of metabolic heat production is thought to be uncoupling of mitochondrial oxidative phosphorylation, which is accelerated by an uncoupling protein (UCP) family. UCP 1 is present only in brown adipose tissue, a specific site of cold-induced heat production in small rodents. Other isoforms of UCP are

widely expressed, and particularly UCP 2 and UCP 3 in skeletal muscle are expected to be important in metabolic heat production in larger mammals. There have been many literatures that the gene expression of UCP 2 and UCP 3 in skeletal muscle is changed by physiological and pharmacological conditions affecting energy balance, but these in vivo studies are not suitable to clarify the cellular and molecular mechanisms regulating UCP gene expression in skeletal muscle. To this end, in the present study, I investigated the mRNA expression of UCP 2 and UCP 3 in vitro using a widely used muscle cell line, L6, particularly focusing on the possible involvement of nuclear and β -adrenergic receptors.