Fundamental Research on Suncus (*Suncus murinus*) as an Animal Model of Lipodystrophy

Abstract of Doctoral Thesis

Sayaka Saga

Graduate School of Veterinary Medicine and Life Science

Nippon Veterinary and Life Science University

Lipodystrophy syndromes characterized by loss of whole or partial body fat are associated with insulin resistance, diabetes and lipid metabolism abnormalities including fatty liver. Leptin is an adipocyte-derived hormone thought to play an important role in the pathophysiology of lipodystrophy. House musk shrew (*Suncus murinus*), a small experimental animal with low body fat, may be a possible model for human lipodystrophy. The objectives of this study were to clarify the structure and distribution of suncus leptin.

To determine the primary structure of suncus leptin, we cloned the suncus *Lep* cDNA using the RACE method. The obtained amino acid residues (aa) sequence was compared with other mammals, and the protein structure was predicted by homology modeling.

The suncus *Lep* cDNA encodes 170 aa of the putative suncus leptin precursor containing a predicted signal peptide of 21 aa, and the mature leptin is consisted of 149 aa. The mature leptin is 75%–82% homologous to that of other mammal species. Insertion of the 3 aa, VPQ, not seen in other mammals was found in the CD-loop. This VPQ insertion is thought to be due to a nucleotide insertion of nine bases by slippage-like microindels. The predicted 3D structure of suncus leptin exhibited a typical four alpha-helix structure, however, the VPQ region protruded compared with human leptin. *Lep* mRNA expression was observed only in white and brown adipose tissues.

This study revealed the structure and distribution of suncus leptin. Because the addition of VPQ, which is not found in other mammals, was observed, suncus leptin attracts

attention to its physiological action. It is thought that suncus is useful as a model animal for lipodystrophy in humans, particularly as a model animal without complications.