

## **Abstract**

A quick PubMed search for articles containing the keyword “Sirtuins” generates more than 4,000 papers, and the number has rapidly increased in recent years. The role of sirtuins in biochemistry, physiology and clinical medicine has been noticed as a key factor for metabolic and age-related diseases. However, there is little information about sirtuins in veterinary medicine. On the other hand, increasing in metabolic and age-related disease is also a major problem in veterinary medicine in recent years, and development of the early diagnosis and prevention method for the above diseases is urgent subject for veterinary medicine. The aim of this study was to reveal the molecular mechanisms of sirtuins in inflammation of animal tissues. We successfully cloned the cat SIRT1 and SIRT3 cDNAs. Cat sirtuin1 (SIRT1) and sirtuin3 (SIRT3) showed high sequence homology with other vertebrate SIRT1 (>61.3%) and SIRT3 (>65.9%), respectively. Cat SIRT1 and SIRT3 were highly conserved, and they showed especially high homology in the catalytic core domain, functional sites with Sirtuin2 family. Obesity was induced by feeding on high-fat diet (HFD) for 8 weeks in cats. In the obese cats, ALT, ALP and AST activities, hepatic injury markers, increased significantly. Although peripheral leukocyte inflammatory cytokine mRNA expression level did not increase, SIRT1 mRNA expression significantly increased in the obese cats. Cat p65 subunit of nuclear factor kappa beta (p65) was successfully cloned from a cat cDNA library. The deduced amino acid sequence was highly conserved in mammal p65 (>87.5%), in particular the functional domains were conserved very well. With luciferase reporter assay, it was proved that isolated cat p65 cDNA sequence encodes a functionally active cat p65 protein. In addition, transiently expressed cat p65 significantly up-regulated expression of pro-inflammatory cytokines in cat fibroblast cells.

We analyzed the relationship between SIRT1 and cat p65 in inflammation of cat tissues. Transiently expression of SIRT1 suppressed the NF- $\kappa$ B transcriptional activity and pro-inflammatory cytokine expression by cat p65 and LPS in fibroblast cells.

In conclusion, cat SIRT1 has anti-inflammatory function via NF- $\kappa$ B in fibroblast cells. We consider that SIRT1 involving in the occurrence of chronic inflammation relate to onset of metabolic and age-related diseases.