S10-1 **Anti-aging research using klotho mouse**

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The *klotho* mouse shows multiple phenotypes resembling human aging caused by the mutation of a single gene. This mutation is caused by the insertion of ectopic DNA into the regulatory region of the α-*klotho* gene. The α-*klotho* gene encodes a type I membrane protein that is expressed predominantly in the kidney and brain. As a result of a defect in α-*klotho* gene expression, the *klotho* mouse exhibits multiple age-associated disorders, such as arteriosclerosis, osteoporosis, pulmonary emphysema and short life span. However, the mechanism by which the α-*klotho* gene product suppresses the aging phenomena has not been identified. Analysis of the pathophysiology of *klotho* mice is expected to give clues not only to understanding the mechanisms of individual diseases associated with aging but also the molecular mechanisms during human aging. We previously reported that the aberrant activation of μ-calpain is caused by the α-*klotho* mutation, and such change leads to degradation of cytoskeletal elements. Similar phenomena were observed in normal aged mice. Such deterioration may trigger tissue abnormalities in *klotho* mice and aged mice, but klotho protein may suppress these processes. We will summarize the function of α-klotho protein based on our research on the relationship between proteolysis and age-related disorders and the resent advanced researches.