Animal Bioresource in Japan

A New Enpp1 allele, Enpp1ttw-Ham, Identified in an ICR Closed Colony

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Abstarc :

We recently have reported on a novel ankylosis gene that is closely linked to the *Enpp1* (ectonucleotide pyrophosphatase/phosphodiesterase 1) gene on chromosome 10. Here, we have discovered novel mutant mice in a Jcl:ICR closed colony with ankylosis in the toes of the forelimbs at about 3 weeks of age. The mutant mice exhibited rigidity in almost all joints, including the vertebral column, which increased with age. These mice also showed hypogrowth with age after 16 weeks due to a loss of visceral fat, which may have been caused by poor nutrition. Histological examination and soft X-ray imaging demonstrated the ectopic ossification of various joints in the mutant mice. In particular, increased calcium deposits were observed in the joints of the toes, the carpal bones and the vertebral column. We sequenced all exons and exon/intron boundaries of *Enpp1* in the normal and mutant mice, and identified a G-to-T substitution (c.259+1G>T) in the 5? splice donor site of intron 2 in the *Enpp1* gene of the mutant mice. This substitution led to the skipping of exon 2 (73 bp), which generated a stop codon at position 354 bp (amino acid 62) of the cDNA (p.V63Xfs). Nucleotide pyrophosphohydrolase (NPPH) activity of ENPP1 in the mutant mice was also decreased, suggesting that *Enpp1* gene function is disrupted in this novel mutant. The mutant mice reported in this study will be a valuable animal model for future studies of human osteochondral diseases and malnutrition.

Key Word :
Enpp1, pontaneous mutation, tiptoe walking (ttw)

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