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## Gene Identification of the Myotonia Mouse Derived from ENU Mutagenesis

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Myotonia mutant mice were first discovered in 3rd generation in ENU (N-ethyl-N-nitrosourea) mutagenesis. For the genetic mapping, the male BALB/c myotonia carrier was mated with normal female C57BL/6. The segregation ratio of normal and mutant mice in F2 (F1XF1) was close to 3:1 (178:50) without sex differences. Therefore, it was supposed that the mutant gene was autosomal single recessive. The causative gene was mapped using microsatellite markers on central region (about 25cM from centromere, between D6MIT223 and D6MIT268) of chromosome 6. On the basis of phenotype and map position, we selected clc1 as a candidate gene. For the mutation analysis, total RNA from the femoral muscle of mutant was used as template for RT-PCR and the PCR products were sequenced directly. Sequence comparison between mutant and normal mice revealed the single nucleotide change T1919C resulting in amino acid change from valine to alanine in CLCN1 protein. This is a new mutation causing a congenital myotonia, which will provide new insight in function of CLCN1.

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## Genetic approaches to studying cognition in mammals: analysis of NCX2 knockout mice

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The plasma membrane Na+/Ca2+ exchanger (NCX) plays an important role in Ca2+ homeostasis by extruding Ca2+ out of the cell. To define the physiological function of the exchanger in vivo, we generated mice deficient for NCX2 which is the major isoform in the brain. Hippocampal neurons of the mutant mice exhibited a significantly delayed clearance of elevated Ca2+ following depolarization. Electrophysiological analysis revealed an enhancement of both STP and LTP, but the absence of LTD in the hippocampal Schaffer collateral-CA1 synapses of the mutant mice. Behaviorally, the mutant mice exhibited enhanced performance in hippocampus-dependent learning and memory tasks. These studies demonstrate that NCX2-mediated Ca2+ homeostasis is critical for the control of synaptic plasticity and hippocampus-dependent learning and memory.