論 文 要 旨

Phenotypic abnormalities in a chorea-acanthocytosis mouse model are modulated by strain background

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Chorea-acanthocytosis (ChAc) is an autosomal recessive hereditary disease characterized by neurodegeneration in the striatum and acanthocytosis that is caused by mutations in the *VPS13A* gene. We previously produced a ChAc model mice encoding a human disease mutation with deletion of exons 60–61 in the *VPS13A* gene . The behavioral and pathological phenotypes of the model mice varied a good deal from individual to individual, indicating that differences between individuals may be caused by the content of a genetic hybrid 129/Sv and C57BL/6J strain background. To establish the effect of the genetic background on phenotype, we backcrossed the ChAc-model mice to different inbred strains: C57BL/6J and 129S6/Sv. Although no significant difference between ChAc-mutant mice and wild-type mice on the C57BL/6J background was observed, the ChAc-mutant mice on the 129S6/Sv showed abnormal motor function and behavior. Furthermore, we produced ChAc-mutant mice on two different inbred strains: BALB/c and FVB. Significant reduction in weight was observed in ChAc mutant mice on the FVB and 129S6 backgrounds. We found a marked increase in the osmotic fragility of red blood cells in the ChAc mutant mice backcrossed to 129S6/Sv and FVB. The phenotypes varied according to strain, with ChAc mutant mice on the FVB and 129S6 backgrounds showing remarkably abnormal motor function and behavior. These results indicate that there are modifying genetic factors of ChAc symptoms.