論 文 要 旨

Novel pathogenic *XK* mutations in McLeod syndrome and interaction between XK protein and chorein

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Neuroacanthocytosis syndromes are rare neurodegenerative disorders mainly comprising chorea-acanthocytosis (ChAc) and McLeod syndrome (MLS). Both diseases share symptoms characterized by acanthocytosis and chorea-including Huntington's disease-like neuropsychiatric symptoms. However, little has been reported on the common molecular pathophysiology. In this study, we report the results of genetic analysis of six suspected MLS patients, including novel mutations and the results of molecular analysis which indicate an interaction between the ChAc- and MLS-responsible proteins: chorein and XK protein.

Erythrocyte membrane proteins from suspected MLS patients and ChAc patients, ChAc mutant carriers, and normal controls were analyzed by XK- and chorein-immunoblotting. We performed mutation analysis and XK-immunoblotting to molecularly diagnose the suspected MLS patients. Lysates of cultured cells were co-immunoprecipitated with anti-XK and anti-chorein antibodies.

All suspected MLS cases were molecularly diagnosed with MLS and novel mutations were identified. The average onset age was 46.8 ± 8 years, which was older than that of the ChAc patients. The immunoblot analysis revealed remarkably reduced chorein immunoreactivity in all MLS patients. The immunoprecipitation analysis indicated a chorein-XK interaction.

In this study, *XK* pathogenic mutations were identified in all six MLS cases, including novel mutations. Chorein immunoreactions were significantly reduced in MLS erythrocyte membranes. In addition, we demonstrated a possible direct or indirect interaction between the chorein and XK protein via molecular analysis. Our results suggest that reduced chorein levels following lack of XK protein in unknown molecular pathway are possibly associated with molecular pathogenesis in MLS.