論　文　要　旨

Chorein, the protein responsible for chorea-acanthocytosis, interacts with β-adducin and β-actin

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Abstract

Chorea-acanthocytosis (ChAc) is an autosomal, recessive hereditary disease characterized by striatal neurodegeneration and acanthocytosis, and caused by loss of function mutations in the vacuolar protein sorting 13 homolog A (*VPS13A*) gene. *VPS13A* encodes chorein whose physiological function at the molecular level is poorly understood. In this study, we show that chorein interacts with β-adducin and β-actin. We first compare protein expression in human erythrocyte membranes using proteomic analysis. Protein levels of β-adducin isoform 1 and β-actin are markedly decreased in erythrocyte membranes from a ChAc patient. Subsequent co-immunoprecipitation (co-IP) and reverse co-IP assays using extracts from chorein-overexpressing human embryonic kidney 293 (HEK293) cells, shows that β-adducin (isoforms 1 and 2) and β-actin interact with chorein. Immunocytochemical analysis using chorein-overexpressing HEK293 cells demonstrates co-localization of chorein with β-adducin and β-actin. In addition, immunoreactivity of β-adducin isoform 1 is significantly decreased in the striatum of gene-targeted ChAc-model mice. Adducin and actin are membrane cytoskeletal proteins, involved in synaptic function.

Expression of β-adducin is restricted to the brain and hematopoietic tissues, corresponding to the main pathological lesions of ChAc, and thereby implicating β-adducin and β-actin in ChAc pathogenesis.

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