論文の内容の要旨

論文題目　The role of CYLD in neuronal morphology

（神経細胞形態における CYLD の役割）

氏名　李 軍

Abstract

CYLD was initially identified as a tumor suppressor deubiquitylating protein in familial cylindromatosis patients. Recently, proteomic analysis using rodent brain samples revealed enrichment of CYLD in purified postsynaptic density (PSD) fractions. Here we report that CYLD regulates dendritic growth and postsynaptic differentiation in hippocampal neurons. CYLD shows diffuse localization in rapidly growing dendrites, but is gradually concentrated in spines, where intact F-actin is essential for its localization. Overexpression and knockdown of CYLD demonstrate that CYLD positively regulates both dendritic growth and formation of postsynaptic spines. Overexpression of CYLD and pharmacological manipulation in non-neuronal cells suggested enhancement of α-tubulin acetylation by CYLD and its preferential association with stable microtubules. Phenotypes in dendritic morphogenesis induced by CYLD overexpression and knockdown can be reversed by manipulation of the critical acetylation site of α-tubulin, suggesting tubulin acetylation is a downstream pathway of CYLD-dependent dendritic growth. These results suggest important roles of CYLD in sequential promotion of dendritic growth and postsynaptic spine maturation.