[課程－２]

審 査 の 結 果 の 要 旨

氏名　　李　軍

In this study, the applicant aims to reveal the molecular mechanisms which modulate dendritic morphogenesis, including dendrite growth and dendritic spine development. Particularly, this study is focused on the function of CYLD, a novel and uncharacterized postsynaptic density component protein, which was initially identified as a tumor suppressor in familial cylindromatosis patients. The results obtained from this study are as follows:

1. The applicant generated an anti-CYLD polyclonal antibody. Using this antibody, the applicant detected the expression level and cellular localization of endogenous CYLD in developing hippocampal neurons, and found that CYLD expression increased during development and was gradually enriched in postsynaptic spines, where intact F-actin is essential for its localization.

2. 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.

3. Overexpression and knockdown of CYLD demonstrated that CYLD positively

regulated both dendritic growth and formation of postsynaptic spines in a NF-κB signaling-independent manner.

4. Phenotypes in dendrite growth 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.

In the present study, the applicant provided evidences that CYDL played important roles in sequential promotion of dendritic growth and postsynaptic spine maturation. This research extended our knowledge about CYLD function, and shed light on the further understanding of molecular mechanism during the neuronal development. Therefore, it is worth to grant a PhD degree.