[課程−２]

審査の結果の要旨

氏名　戴　暁　婧

This study aims to reveal the basic mechanisms which regulate unique dendritic morphology of interneurons. This study particularly focused on Dlx1, a member of transcriptional factors with homeobox domain expressed in a subset of interneurons. The results obtained from this study are as follows:

1. Exogenous expression of Dlx1 in hippocampal pyramidal neurons, which are excitatory neurons and lack endogenous Dlx expression, caused reduction of complexity of dendritic arborization, suppression of axonal growth and decrease of PSD-95 density.

2. Exogenous expression of truncated Dlx1 mutants in hippocampal pyramidal neurons revealed that the DNA binding motif of Dlx1 is essential for its suppressive effect on dendritic growth.

3. To investigate the potential downstream genes of Dlx1 on regulation of dendrite morphology, the effects of Npn-2 and PAK3 on dendrite morphology were analyzed. Knockdown of Npn-2 or PAK3 induced prominent suppression of dendritic and axonal growth, whereas overexpression of Npn-2 or PAK3 induced slight increase of dendritic branching. Importantly, the inhibitory effect of Dlx1 on dendritic branch and spine development of pyramidal neurons could be rescued by expression of neuropilin-2 and PAK3, suggesting their roles as downstream effectors of Dlx1.

4. To confirm the roles of endogenous Dlx1 in development of interneuron dendrites, Dlx1 was knocked down in cultured hippocampal interneurons, which caused enhancement of dendritic arborization and increase of immature protrusion. This result suggests that the reduction of Dlx1 can induce enhancement of dendritic growth and the

amounts of Npn-2 and PAK3 are not saturated in interneurons with respect to their functions in dendritic growth.

By using hippocampal dissociated culture, this paper revealed the role of Dlx1 in interneurons to regulate both the morphology of dendrite and density of dendritic spine and clarified that both Npn-2 and PAK3 are the possible downstream genes of Dlx1. This study shed light on the understanding of the molecular mechanism to regulate unique morphology of inhibitory neurons and, therefore, it is worth granting a degree.