Principal Investigator: Keisuke Kamimura
Grant Title: Roles of heparan sulfate proteoglycans in *Drosophila* synaptic plasticity

Abstract

1. Objectives

Heparan sulfate proteoglycan (HSPG), a glycoprotein bearing heparan sulfate (HS) as a side chain, is a major component of cell surface and extracellular matrix. HSPGs interact with various ligand proteins, possibly through the myriad of distinct HS fine structures, which were generated by various HS modifying enzymes. In this study, we attempted to clarify the roles of HSPGs and the HS fine structures in synaptic plasticity using the fruit fly *Drosophila* neuromuscular junction (NMJ), a model system of excitatory glutamatergic synapses.

2. Methods

In larval *Drosophila*, food deprivation induces higher locomotor activity, which leads to an increase in the number of synaptic boutons at NMJ. Increase in locomotor speed and bouton production by food deprivation depends on octopamine, the invertebrate counterpart of adrenalin and noradrenalin. We examined the possibility that HSPG regulates this octopamine-mediated synaptic plasticity.

3. Results

We found that Dally-like (Dlp), a GPI-anchored form of HSPG glypican, is involved in this octopamine mediated synaptic plasticity. RNAi-mediated knockdown of *dlp* did not impair normal crawling activity, but the locomotor speed was not increased by food deprivation. Consistent with this result, *dlp* RNAi prevented food deprivation-dependent bouton proliferation. We also found that postsynaptic levels of Dlp was decreased by food deprivation and this change was not induced in octopamine deficient animals. These results suggested that octopaminergic signaling inhibits postsynaptic Dlp localization and Dlp is required for octopamine mediated synaptic plasticity. We also found that food deprivation-dependent bouton proliferation was prevented by RNAi for *brother of tout-velu* (*botv*) and *Sulf1*, which encode HS polymerase, Ext-like, and HS modification enzyme, 6-*O*-endosulfatase, respectively. Several studies have shown that neuronal activity affects the presynaptic BMP signaling and postsynaptic levels of glutamate receptor. We found that *dlp* is required for the activity dependent alteration of BMP signaling activity and glutamate receptor localization. Thus, our study shows that HSPG and the HS fine structure play critical roles in octopamine mediated synaptic plasticity.