Poster | Disorders of Nervous Systems and Treatment

[3P]Neurodegenerative Disorders

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*Videos are available throughout the meeting period.

[3P-217]Semi-automated quantitative system for neurodegeneration reveals the axonal degeneration by the Impaired PtdIns(4,5)P2 synthesis in *Drosophila* photoreceptor axons.

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Drosophila, as a simple in vivo model, has provided valuable and novel insights into the pathological mechanism of the neurogenerative diseases such as Alzheimer's disease, Parkinson's disease, Amyotrophic lateral sclerosis, and Huntingon's disease. In these studies, eye structure was used an indicator of the degeneration and genetic interactions. However, this method is rather qualitative but not quantitative. In addition, the disruption of eye structure is not always consistent with axonal degeneration of photoreceptor when knockdown or overexpression experiments were performed even using the same eye-specific *GMR-Gal4* driver. It suggests that the eye structure sometimes may not reflect the retrograde neurodegeneration. Here we developed a semi-automated quantitative system for the axonal number of photoreceptor neurons using a machine learning algorithm. The system makes layer masks covering the axonal terminals from confocal images. By using the layer in image analysis software such as IMARIS, it can count the number of axonal terminals. Using this method, we found the disruption of lipid homeostasis caused axonal degeneration. Mutations of *CdsA*, CDP- diacylglycerol (CDP-DAG) synthase, caused axonal degeneration in photoreceptor. We assume that the alteration of the composition of specific phospholipids causes the axonal degeneration because the reduction of CDP-DAG affects the amount of various phospholipids, such as phosphatidic acid, cardiolipin and phosphatidylinositol. To identify the phospholipids that are involved in this phenotype, we performed RNAi screening for genes that synthesize each phospholipid. As a result, we have identified *Phosphatidylinositol synthetase* (*Pis*) and *Phosphatidylinositol 4-phosphate 5-kinase at 59B* (*PI4P5K*), which synthesizes PtdIns(4,5)P2, as a candidate. Taken together, the reduction of PtdIns(4,5)P2 results in the neurodegeneration. Importantly, the reduction of PtdIns(4,5)P2 had often reported in various neurodegenerative diseases such as Alzheimer's disease. In this poster, we will discuss how the reduction of PtdIns(4,5)P2 causes the neurodegeneration.