Journal of Neuroscience and Cognitive Studies

Clinical Image
Published: 03 Nov, 2017

A Drosophila Model for Alzheimer's Disease with Amyloid Plagues and Neurofibrillary Tangles

*Wei Zhang[1], Yu-Han Huang[1], Tzu-Kang Sang[2,3] and Hui-Yun Chang[1,3]**

[1]Department of Medical Science, National TsingHua University, Taiwan

[2]Department of Life Science, National TsingHua University, Taiwan

[3]Brain Research Center, National TsingHua University, Taiwan

Clinical Image

The study of cognition is one of the most challenging subjects of neuroscience in this century. Memory is the most vital cognitive faculty of the human mind and much of the information we have obtained has been drawn from studying disorders, such as the cognitive symptom of memory loss in Alzheimer's disease. About 100 years ago, Alois Alzheimer described this cognitive disease as a mental illness of dementia with neuropathological hallmarks of neurofibrillary tangles and senile plagues in 1907 [1]; and "Alzheimer's disease" was historically termed by Emil Kraepelinin 1910. Currently, Alzheimer's disease is still a medical and social challenge without cure.

A complete understanding of the molecular and neuronal mechanism of brain diseases will be valuable for constructing effective strategies to optimize clinical prevention or diagnosis and therapeutic treatments of these specific cognitive diseases such as Alzheimer's disease. The human genome projects and genome-wide association studies [2] have identified numerous genes for hereditable Alzheimer's disease. However, our understanding of how these diverse functions of AD genes conjoin to maintain healthy post mitotic neuronal function in memory of brains remains incomplete. In order to maximize the advantageous accessibility of fly genetics and fly brains, we along with many other researchers have established fly models for Alzheimer's disease [3,4]. Here, we attempt to describe a fly model for AD which could fill the gap between fly genetic models and mouse models for AD that give a strong neuropathology which recapitulates the plague and neurofibrillary tangle like phenotypes in the animal model of *Drosophila*.

Our first effort was to co-express Aβ42 and GFP in glutamatergic neurons and several other types of neurons and observe Aβ42's effect on these neurons over time. As shown in Figure 1, it appears that the expression of Aβ42 formed "AD plague-like" protein accumulations by whole mount fly brain staining with monoclonal antibody, 6E10 against Aβ amino acid 1-16 where it located to outside of neuron surface labeled with membrane CD8-GFP using confocal microscopy. We notably observed that the formation of AD plague like neuropathology is a risk combination of neuronal vulnerability and time-dependent process (not shown).

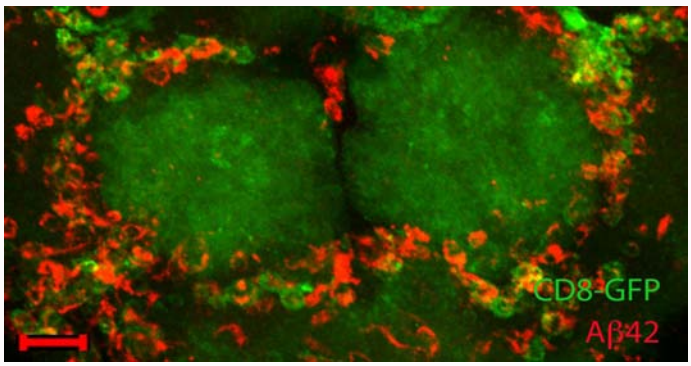

Figure 1: Expression of Aβ42 recapitulated plague-like pathology in fly brains. A confocal micrograph of a fly brain with co-expression of CD8-GFP and Aβ42 in glutamatergic neurons stained using anti- Aβ42 antibody. Scale bar, 20 μm. Note Aβ plague-like pathology, the 6E10-staining pattern (red) is abnormal extracellular protein accumulation that is not co-localization to the glutamatergic neuronal expression pattern of CD8-GFP (green) as an age-dependent process.

OPEN ACCESS

Correspondence:
Hui-Yun Chang, Institute of Systems Neuroscience, Department of Medical Science, National TsingHua University, 101, Section 2, Kuang-Fu Road, Hsinchu 30013, Taiwan, Tel: 886-3-574-2778;
E-mail: huiyun@life.nthu.edu.tw

Received Date: *07 Jul 2017*
Accepted Date: *26 Oct 2017*
Published Date: *03 Nov 2017*

Citation:
Zhang W, Huang Y-H, Sang T-K, Chang H-Y. A Drosophila Model for Alzheimer's Disease with Amyloid Plagues and Neurofibrillary Tangles. J Neurosci Cogn Stud. 2017; 1(1): 1005.

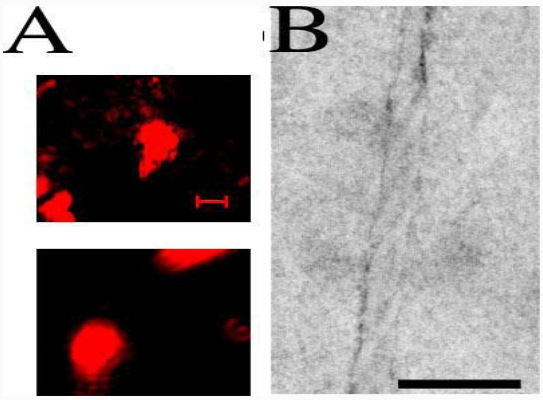

Figure 2: Tau neuropathology in fly brains. (A) A confocal micrograph of a fly brain using Congo red staining. The AD-like tangle pathologyis prominent which was produced by expression of tau in dopaminergic neuron. Scale bar, 10 μm. (B) An electron micrograph of abnormal PHF similar to those extracted from AD brain was observed as shown here by sarkosyl extraction from tau expression fly brains. Scale bar, 100 nm.

The second neuropathological hallmark of AD is the neurofibrillary tangle. Many groups have modeled tau pathologyin fly brains; this previous paper [5] specifically described expression of tau caused neurofibrillary tangle-like pathology by Congo red staining and its filament ultrastructure shown in Figure 2. We anticipate that this fly model for AD with amyloid plagues and neurofibrillary tangles is clinically and pathologically similar to AD patient brains. This will be suitable for the study of how the diverse function of AD genes can cooperate to maintain a healthy neuron in aging brains and to understand how their dysfunction contributes to age-dependent cognitive diseases, such as AD, the first step toward to find the potential neuron repair genes for this cognitive brain disease.

Acknowledgements

We are grateful to Ming-Tsan Su, Chun-Hong Chen, Hsiu-Mei Hsieh and Kathy J. Sang for their critical information and suggestion on this project. This work is supported by National Science Council Grant B007-003 (H.-Y. C).

References

1. Alzheimer A. On a peculiar, severe process of the cerebral cortex. Neurol Central. 1906;25:1134.
2. Van Cauwenberghe C, Van Broeckhoven C, Sleegers K. The genetic landscape of Alzheimer disease: clinical implications and perspectives. Genet Med. 2016;18(5):421-30.
3. Moloney A, Sattelle DB, Lomas DA, Crowther DC. Alzheimer's disease: insights from Drosophila melanogaster models. Trends Biochem Sci. 2010;35(4):228-35.
4. Prussing K, Voigt A, Schulz JB. Drosophila melanogaster as a model organism for Alzheimer's disease. Mol Neurodegener. 2013;8:35.
5. Wu TH, Lu YN, Chuang CL, Wu CL, Chiang AS, Krantz DE, et al. Loss of vesicular dopamine release precedes tauopathy in degenerative dopaminergic neurons in a Drosophila model expressing human tau. Acta Neuropathol. 2013;125(5):711-25.