PRESS RELEASE

Epigenetic Factors in Fruit Flies May Provide Insights into Human Psychiatric Disorders

21 October 2011, Singapore - Temasek Life Sciences Laboratory (TLL) is pleased to announce the major discovery of specific epigenetic factors[1] and their roles in the remodeling of the nervous system in *Drosophila*, more commonly known as fruit fly, which could provide insights into understanding the neurological events leading to human psychiatric disorder.

The peak age of onset for human psychiatric disorders is adolescence, a transition stage between childhood and adulthood, during which remarkable physical and behavioral changes take place. At adolescent stage, human brains undergo a dramatic decrease in neuronal connections, a process known as neuronal pruning, in response to a robust increase in levels of steroid hormones such as thyroid and sex hormones. Perturbation of the neuronal network maturation may trigger some psychiatric disorders including schizophrenia, a mental disorder associated with excessive pruning occurring in the brain cortex.

Working with fruit flies, a powerful model genetic organism, Principal Investigator Dr. Yu Fengwei and his team at Temasek Life Sciences Laboratory have demonstrated that specific epigenetic factors control the initiation of neuronal pruning in some sensory neurons during fly metamorphosis, the transition stage between larval and adult forms.

Similar to the remarkable changes in human brains during adolescence, unnecessary larval neuronal processes of the fly nervous system are selectively removed through retraction or degeneration.

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1. Epigentic factors are heritable factors affecting the development or function of an organism that are not associated with its DNA sequence.

Dr. Yu and his team have systematically analyzed almost all fly epigenetic factors, from which a Brahma-containing chromatin remodeling complex and a histone acetyltransferase CREB-binding protein (CBP) were identified for their critical roles in neuronal pruning.

The onset of fly metamorphosis is triggered by a pulse of systemic steroid hormone ecdysone. Dr. Yu's previous work had identified two key ecdysone response factors: a transcription factor Sox14 and a cytoskeletal protein Mical, which was published in another well-known Neuroscience journal *Nature Neuroscience* in 2009. Interestingly, both Brahma and CBP specifically activate the expression of Sox14 by enhancing the levels of histone modifications, such as acetylation in the vicinity of the *sox14* gene area. Thus, the scientists indicated that specific epigenetic factors cooperate with systemic steroid hormones to alter chromatin states and selectively activate critical downstream programs that are required for the maturation of the nervous system.

"Given that there are several Brahma and CBP-related proteins in humans, their functions remain to be analyzed. Our findings have therefore opened the door for new studies of epigenetic regulation in the maturation of the nervous systems in mammals during adolescence." said Dr. Yu.

Professor Chan Soh Ha, Executive Director of TLL, says, "Fruit fly is one of the many model organisms which TLL utilizes to study genetics and molecular cell biology. The discovery made from fruit fly provides insights into the working of other organisms such as human. I would like to congratulate Dr. Yu for his publication in the high impact journal Neuron and look forward to future developments from his research."

"We will continue to use fruit flies to uncover critical players in neuronal pruning and systematically understand the network involved in this regulation," Dr. Yu said. "Our studies will pave the way for future study of these human proteins in the context of psychiatric disorders, including schizophrenia, a common mental disorder with a lifetime prevalence of approximately 1 in every 100 individuals in the population."

Dr. Yu also added that it may be possible to manipulate the levels of histone modification which can ameliorate the pathogenesis in humans. Encouragingly, it had been reported that the administration of antipsychotic drugs, that regulate histone modification levels, could attenuate schizophrenia-like behavioral abnormalities in mice.

“Next, we will also investigate the pruning process occurring in the mammalian nervous systems with our collaborators,” Dr. Yu said. “We would like to apply what we knew from the small simple insect to more complex mammals, which may also lead to new therapeutic avenues for human psychiatric disorders.”

This study has recently been published in Neuron, a highly regarded international scientific journal and a sister journal to Cell, and this is one of the few scientific articles from Singapore that is published in Neuron.

About Temasek Life Sciences Laboratory (TLL)

TLL is a non-profit organisation established in 2002 to undertake cutting-edge research in molecular biology and genetics utilising a broad range of model organisms. TLL is affiliated to the National University of Singapore and Nanyang Technological University. Our vision is to create an environment which can attract the brightest young minds worldwide, support their research and challenge them to be leaders in their own fields.

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