Press Release from National Tsing Hua University
For information, please contact
Sabrina Li, Division of Public Affairs
yhl@mx.nthu.edu.tw
+886-3-516-2372

Taiwanese scientists find "memory cells" in the brain

腦科學重大突破—清華大學發現儲存長期記憶的腦細胞

February 9, 2012　Hsinchu, Taiwan, Republic of China.

After 7 years of diligent research, a team of multi-disciplinary Taiwan scientists led by Professor Ann-Shyn Chiang of National Tsing Hua University have found that the formation of long-term memory requires the manufacture of new proteins in only a few cells in the brain.

The discovery is reported as a full article in the February 10, 2012 edition of *Science* magazine.

According to Professor Chiang, "*A long-standing goal in the field of neuroscience is to understand how learning and memory register in the brain.　Where in the brain does a new experience first reside?　How does a labile, fresh memory become stable and long-lasting?*"

In humans, neuroscientists have known for a long time that the storage of memories of facts and events requires a neuroanatomical structure called the hippocampus.　Once activated by an experience, the hippocampus then facilitates long-term memory formation in the cortex. With approximately 100 billion neurons in the human brain, however, it is extremely difficult to identify exactly which cells and circuits participate in any particular memory.

Surprisingly, fruit flies and humans show many similar behaviors required for the basic demands of daily life (learning, memory, attention, sleep, exploration, etc), using many similar genes and proteins. Yet, their brain circuitries are enormously less complex than those of humans. Fruit flies also have an impressive armamentarium of genetic tools, which have been used quite successfully to study the molecular mechanisms of many diseases, including Alzheimer's, Parkinson's and Huntington's diseases.

One experimental observation seen widely among animal species is that the formation of long-term memory requires protein synthesis. To discover where in the fruit fly brain protein synthesis was required, we engineered a genetic tool to block the production of new proteins in individual neurons and then systematically screened neurons in the brain to identify those few in which protein synthesis was necessary during long-term memory formation. Unexpectedly, long-term memory was impaired after inhibiting protein synthesis in just two cells, called the "dorsal-anterior-lateral (DAL) neurons"! Moreover, long-term memory remained normal when protein synthesis was inhibited in that part of the fruit fly brain, "the mushroom body," which previously was thought to be the insect's "learning/memory center."

The formation of long-term memory depends on repetitive learning with spaced rest intervals, whether in fruit flies or humans. Using this spaced training procedure to identify mutant strains of the fruit fly with impaired long-term memory, this group of Taiwan scientists, in collaboration with Dr. Tim Tully at Dart Neuroscience in San Diego, were able to previously identify many mutants required for long–term memory. When this team of scientists looked to see where the corresponding genes were expressed in the brain, many did so in the DAL neurons. Using genetic engineering to prevent the activation of these genes selectively in the DAL neurons, Chunchao Chen, the lead author of the Science publication, discovered that protein synthesis in DAL neurons was required for the formation of long-term memory.

Together with Tsai-Feng Fu at National Chi Nan University in Taiwan, another new genetically engineered tool was also developed to visualize new protein synthesis in a single neuron in real time. It was

found that at least two genes, *calcium/calmodulin-dependent protein kinase II* and *period*, were synthesized in the DAL neurons specifically in response to spaced training.

How could the two DAL neurons encode complex memories? Chen and his colleagues showed that memory retrieval was impaired when the electrical activity of DAL neurons was blocked. They also showed that DAL neurons connect directly to neurons of the mushroom body, which is a structure consisting of thousands of neurons.

These findings suggest a simple model for the formation and retrieval of long-term memory formation. During memory formation sustained electrical activity in the mushroom body initiates electrical activity in DAL neurons. This electrical activity then initiates the synthesis of new proteins in DAL neurons, which then alters the function (and/or structure) of DAL neurons. During memory retrieval, DAL neurons facilitate electrical activity in the mushroom body after re-exposure to the original stimulus. Thus, by changing the activities (via new protein synthesis) in only a few nodes (DAL neurons) in a complex network, a previous experience (memory) can change a fly's behavioral choices.

"*The identification of individual "memory neurons" also will enable the identification of additional "memory proteins", thereby contributing to a more complete understanding of the molecular mechanisms of learning and memory and diseases thereof. We will also use our new genetic tools to make a more complete map of the brain circuits involved in learning and memory. It waits to be confirmed whether human brains also store long-term memories via the manufacture of new proteins in only a few nodes in complex circuits.*" concluded Professor Chiang.