Enzyme key to learning in fruit flies

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Fruit fly. Credit: John Tann/Wikipedia

An animal's reaction to an odor or food or other stimuli depends largely on past experiences and how they have been entered into memory.

While it is known that the connections between neurons in the brain, called synapses, are altered during learning many mysteries remain about how memories are formed. It is particularly important to study how individual proteins and genes act on this process because loss of learning

and memory due to aging or diseases can reduce our well-being.

In a just-published paper in the journal *Cell Reports*, a team of scientists, led by Anandasankar Ray, an associate professor at the University of California, Riverside, have begun to unravel some of these mysteries.

They showed that a specific enzyme called Histone Deacetylase Inhibitor 6 (HDAC6) plays an important role in learning in fruit flies (*Drosophila melanogaster*), a common model organism. More detailed analysis showed that the enzyme is likely to act like a "dimmer switch," or regulator, that can increase or decrease the signal across synapses (neuronal connections) as an animal learns something new.

Histone deacetylases (HDACs) have been extensively studied as drug targets in neurodegenerative diseases, such as Lou Gehrig's (amyotrophic lateral sclerosis), Parkinson's, Alzheimer's, and Huntington's, but less is known about their role in healthy neurons. Research by others has shown that HDAC6 could have diverse roles depending on the neurodegenerative diseases.

But, knowing that the HDAC6 enzyme has a role in learning in the fruit fly model may help in the future if it works the same way in humans, Ray said. He said small molecule drugs that are already known to block the activity of the enzyme could potentially be used to treat post-traumatic stress disorder. Or drugs that enhance activity of the enzyme could be used to improve memory as a person ages or is inflicted with a disease that causes memory loss.

The *Cell Reports* paper is called, "The Role of Histone Deacetylase 6 in Synaptic Plasticity and Memory." In addition to Ray, who is also director of the Center for Disease Vector Research at UC Riverside, the authors are: Sarah Perry, (an ex-graduate student of the UC Riverside Genetics, Genomics & Bioinformatics program UCR in the Ray lab), and Beril

Kiragasi and Dion Dickman, both of the University of Southern California.

The study will be featured on cover of the Feb. 7, 2017 issue of *Cell Reports* with a drawing from the first author Sarah Perry.

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