A non-visual opsin could help future studies of the brain and central nervous system

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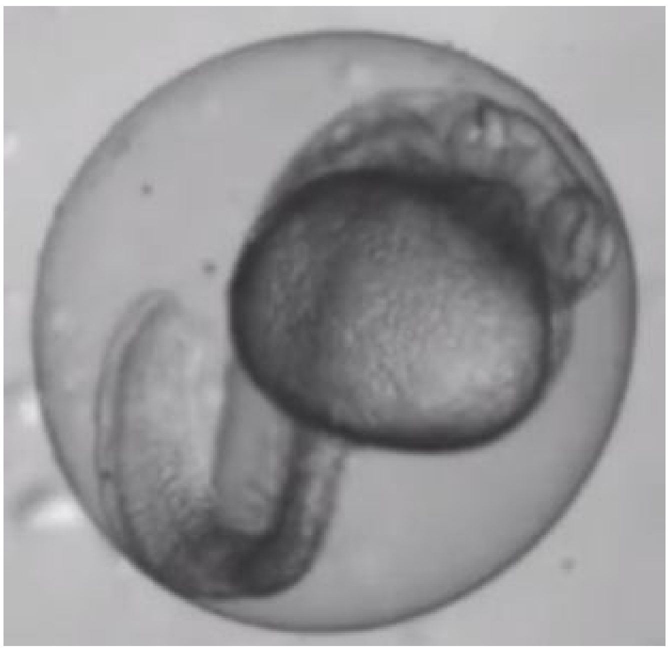

In the on-going search for a better understanding of how the brain and central nervous system develop, a potentially powerful new tool could soon be available. Researchers at Lawrence Berkeley National Laboratory (Berkeley Lab) have discovered a light-sensitive opsin protein that plays a surprising and possibly critical role in neuron maturation and circuit formation.

Ehud Isacoff, a neurobiophysicist who holds joint appointments with

Berkeley Lab's Physical Biosciences and Materials Sciences Divisions, as well as UC Berkeley's Department of Molecular and Cell Biology, and who directs the Helen Wills Neuroscience Institute, led a study of translucent zebrafish embryos in which it was shown that an extra-retinal opsin, called VALopA, which is expressed in the spinal network, responds to light by dramatically inhibiting the spontaneous motor activity of neurons in their early stages of development.

"VALopA may be one of the most effective ways we've ever found to silence neurons with light, a technique that can tell us which neurons must be active to carry out a specific computation or behavior," Isacoff says. "Our results have uncovered a novel role for a non-visual opsin and a mechanism for environmental regulation of spontaneous activity in a circuit previously thought to be governed only by intrinsic developmental programs."

Isacoff is the corresponding author of a paper in Current Biology describing this work, on which the experiments were designed and performed by graduate student Drew Friedmann, technician Adam Hoagland and postdoctoral fellow Shai Berlin. The paper is titled "A Spinal Opsin Controls Early Neural Activity and Drives a Behavioral Light Response."

Light has been an exceptionally powerful tool for the scientific study of neurons – the nerve cells that process information throughout the body. However, neuronal cell differentiation and the formation of neural networks take place prior to the advent of sensory experience and are largely guided by spontaneously generated motor activity. When Isacoff and his co-authors studied this motor activity in embryonic zebrafish during the formation of a synchronized neuronal circuit common to all vertebrates known as the "spinal central pattern generator," they were surprised to discover that the activity was being heavily regulated by light.

"We looked at coiling behavior, a pre-locomotory behavior that is driven by spontaneous central pattern generator activity, and found it could be dramatically suppressed by illumination with green light," says lead author Friedmann, a member of Isacoff's research group. "In dark-adapted fish, coiling ceased within two seconds of the start of illumination, and the suppression persisted for many minutes, even after the light was extinguished. A systematic examination of early zebrafish development revealed that photo-inhibition is present as soon as motor activity begins."

By inducing delays in neuronal motor activities, VALopA serves as a mechanism for controlling the rate of development of the locomotory circuit in the spinal cord of zebrafish. This opens up the possibility for scientists in the future to use VALopA in combination with light to silence select neurons.

"Researchers used to silence neurons by killing them and more recently deployed opsins from microbes to temporarily silence them with light" Friedmann says. "But these microbial opsins alter the acid or chloride balance of cells in non-physiological ways. We now can gain the same power of selective suppression of activity, but with the vertebrate VALopA opsin which we showed acts through the normal inhibitory mechanism of the neuron. The long-lasting inhibition by VALopA after a brief light pulse makes it particularly powerful."

Isacoff and his colleagues are now investigating whether VALopA is also involved with circadian rhythms and seasonal behaviors. Non-visual detection of light by the vertebrate hypothalamus, pineal, and retina is known to govern these phenomena.

"Mammals, birds and fish all use non-visual opsins for controlling their daily clocks but these activities are regulated in the brain," Isacoff says. "Whether VALopA, which is active in the spinal cord, also plays a role remains to be seen but it is an interesting question."

More information: "A Spinal Opsin Controls Early Neural Activity and Drives a Behavioral Light Response," *Current Biology*, Volume 25, Issue 1, 5 January 2015, Pages 69-74, ISSN 0960-9822, dx.doi.org/10.1016/j.cub.2014.10.055

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