$3.3 million grant awarded to UCSD Neurobiologists

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UCSD NEUROBIOLOGISTS AWARDED $3.3 MILLION GRANT

Six University of California, San Diego biologists have been awarded a $3.3 million National Institutes of Health grant to investigate the molecular basis of nerve cell signaling that underlies all thought and behavior.

The three-year award, called a Program Project grant, will support coordinated studies in each of six Department of Biology laboratories and provide centralized facilities for computer analysis, instrumentation and other services.

Each study will focus on a different nervous system, from those of leeches and lobsters to frogs and fruit flies.

"Invertebrates have traditionally been studied because their nerve cells are very large and identifiable, and the nerve circuits underlying their simple behaviors can provide models for more complex patterns of neural activity such as thought," according to Allen I. Selverston, professor of biology and director of the Neurobiology Program Project. "This is very fundamental research aimed at revealing the way neurons process information at a cellular and molecular level."

The other five project leaders are biology professors Darwin K. Berg, William B. Kristan Jr. and Nicholas C. Spitzer; associate professor William A. Harris; and assistant professor Charles Zuker.

Selverston's lab is studying a small nerve circuit in the lobster as a model for the way larger neural circuits are affected by neurotransmitters (chemical messengers). Specifically, he is focusing on a circuit which controls three teeth within the lobster stomach, studying how chewing behavior is altered by exposure to the signal chemicals CCK and proctolin.

To deliver a signal, neurotransmitters must fit in lock-and-key style into receptors on the surface of the receiving nerve cell. One of the best-studied receptors in mammals is the receptor for acetylcholine, which the brain uses to tell muscles to move. Nerve cells also use acetylcholine to talk to one another, and Berg's lab has pioneered work in this area. He is investigating factors that determine the number of these receptors on individual nerve cells.

Zuker is focusing on the molecular and biochemical process in the eye that translates incoming light into electrical signals that are then transmitted to the brain. Using genetic engineering techniques, he has cloned the genes for several photopigments (rhodopsins) from the eyes of fruit flies, then introduced each gene into the embryos of otherwise blind flies. The goal is to learn the function of each gene by studying the visual activity it restores in these transgenic flies.

When neurotransmitters bind with receptors, the result is the opening of tiny passages--called ion channels--into the interior of the nerve cell. Ions flowing through these openings can change the electrical potential of the neuron. Spitzer is studying changes that occur in the protein structure of potassium ion channels as an organism grows and develops. He does this by injecting channel-forming substances into frogs' eggs, then examining the opening and closing of channels in the egg membrane.

The factors that cause nerve cells to specialize and change their identity during development are being studied in Kristan's lab. In all but two body segments of the leech, a pair of specialized neurons (Retzius cells) send threadlike projections called axons out to transmit signals from peripheral tissues. In the remaining two segments, those cells innervate reproductive tissues. Kristan is studying how contact with these different target tissues alters the properties of nerve cells.

Harris is interested in how nerve cells find their proper targets during development, especially the hypothesis that glial or support cells in the nervous system lay out a pathway that growing nerve fibers follow. Using antibodies, Harris will block substances normally produced by glial cells to see if this affects the growth of cells cultured from the retina of a frog.

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