Discovery of retinal cell type ends 4-decade search

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A research team combining high-energy physicists from the University of California, Santa Cruz, and neuroscientists from the Salk Institute in La Jolla, Calif., has discovered a type of retinal cell that may help monkeys, apes, and humans see motion. The team's work appears in the October 10 issue of *Journal of Neuroscience*.

The cell type has very similar properties to so-called Y retinal ganglion cells, which were first described in cats in 1966. Upon the Y-cell's discovery, scientists began a decades-long search for its counterpart in primates. The UCSC–Salk Institute team named the new cell type the upsilon cell, after the Greek uppercase letter written as "Y."

This week's discovery puts scientists one step closer to understanding how primates transform the chaos of light bombarding their eyes into a clear, steady, color picture of the world around them.

"This has been a fantastic journey through high-energy physics, neurobiology, technology, and human health," said senior author Alan Litke, adjunct professor of physics at UCSC's Santa Cruz Institute for Particle Physics (SCIPP). "We started out developing instruments to look for fundamental particles such as the top quark and the Higgs boson. Then we realized we could apply some of those technological concepts to studying neural systems. Now we are using the new technology for experiments that will help guide the design of future retinal prosthetic devices."

The retina is the paper-thin coating on the back of the eye that turns light into coded messages headed to the brain. The first step in the process is handled by rod and cone cells that transform arriving photons of light into electrical signals. Another three cell layers process those signals and then pass them on to ganglion cells like the Y and upsilon, which are middlemen that collate the signals and send them up the optic nerve to the brain. The eye has only about one retinal ganglion cell for every 100 rod and cone cells. Although biologists have identified at least 22 distinct types of primate retinal ganglion cells, the functions of only about a half-dozen of them are known.

"People have looked at cell morphology, but that can't tell us in any detail how the cell responds to light," Litke said. "If we're interested in how the retina is processing visual information, we really want to focus a movie on it and see what it reacts to--to find out if it's seeing color, responding to motion, or whatever it might be doing."

The upsilon cells went undetected for so long, Litke suggested, mainly because they are only a tiny fraction of all the ganglion cells. This small number makes the cells very difficult to detect with traditional physiological techniques, which typically monitor only one cell or a tiny patch of retina at any one time.

So Litke and his colleagues developed a new detection system inspired by their research detecting particles in high-energy-physics collisions. The device crammed 512 electrodes into an area of 1.7 square millimeters (about the size of a pinhead). Each of the team's experiments, conducted in the Salk Institute lab of neurobiologist E. J. Chichilnisky, recorded the electrical activity of more than 250 cells simultaneously, five to 10 of which were upsilon cells.

"The high density and large number of the electrodes gave us the ability to pick out individual neurons and at the same time examine a whole

collection of cells," Litke said. "If you had only a few electrodes, you might detect a single cell with unusual properties, but you wouldn't know what to do with it--it might just be a sick cell. Now we can identify a significant number of these cells in a single preparation, all with the same properties. That gives us confidence in our results."

To figure out how the upsilon cells handle information, the researchers projected simple movies through a microscope lens and onto a patch of retina. As rod and cone cells picked up the images, they sent electrical signals to a wide variety of retinal nerve cells. After picking up the signals on the electrode array, SCIPP postgraduate researcher Dumitru Petrusca matched them with the movie, allowing him to map out the light-sensitive regions of each cell. The team found that the collection of upsilon cells forms a mosaic across the retina, with nearly continuous coverage and very little overlap.

The sensitive regions of upsilon cells measured 300 to 500 microns across, considerably larger than most other retinal ganglion cells (a micron is one-millionth of a meter; 300 microns is about three times the width of a human hair). Upsilon cells showed particular sensitivity to oscillating fields of stripes, the sort of input they might receive when a textured surface moves across their field of view.

Together, these qualities suggest an ability to sense motion. Amid a flood of information heading to the brain, sensitivity to changing patterns would emphasize the parts of the picture that are moving. And the large size of the cell's sensitive region would be better suited to sensing motion than providing pinpoint resolution on a stationary object.

If the upsilon cells prove to be connected to the brain the way cat Y-cells are, then they likely feed their information to two separate processing centers. One, called the lateral geniculate nucleus, is a waystation to the visual cortex. The other, the superior colliculus, helps turn the eyes and

the head toward a stimulus. Litke said this would strengthen the suggestion that the upsilon cells help detect motion.

"You see something coming in your peripheral vision, and you turn your head because maybe it's a lion coming to attack you," he said.

With their 512-electrode array, Litke and his colleagues are planning to keep on filling in the blanks of other unknowns. "We're working on many other cell types," Litke said. "This is just the tip of the iceberg."

Source: University of California - Santa Cruz