Biologists use Sinatra-named fly to show how to see the blues -- and the greens

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New York University biologists have identified a new mechanism for regulating color vision by studying a mutant fly named after Frank ('Ol Blue Eyes) Sinatra. Their findings, which appear in the journal *Nature*, focus on how the visual system functions in order to preserve the fidelity of color discrimination throughout the life of an organism. They also offer new insights into how genes controlling color detection are turned on and off.

Many biologists study how different cells develop to acquire their fate. The NYU research team, headed by Claude Desplan, a professor of biology, examined how they stay the same. Cells have complex functions that must be maintained through extensive coordination, and failure to do so could lead to "confused" cells whose function is not clear. This is particularly important for cells, such as neurons, which live for a long time—usually the entire lifetime of an animal.

The NYU researchers focused on the photoreceptor neurons in the retina of the fruit fly *Drosophila*. *Drosophila* is a powerful model for studying eye development as it is amenable to very precise genetic manipulations. This allows researchers to analyze how the visual system functions when its different elements are affected.

The work builds upon a previous finding from Desplan's laboratory. In a 2005 study, published in *Cell*, Desplan and his colleagues identified a molecular pathway by which one photoreceptor cell type controls its choice to be sensitive to one color of light vs. another—in this instance, green vs. blue. This sensitivity is due to the presence of light-sensing proteins, Rhodopsins: each photoreceptor makes a decision to express either blue light-sensitive Rhodopsin5 or green light-sensitive Rhodopsin6, but not both. This exclusive expression of different Rhodopsins underlies the fly's ability to discriminate colors.

In the Nature study, the researchers explored a phenomenon that occurs over the lifetime of an organism. Because Rhodopsins are continually produced in the eye, the researchers wanted to know what keeps each photoreceptor from starting to make the wrong Rhodopsin later in life. Their findings showed that, in fact, the Rhodopsin itself can prevent the gene encoding another Rhodopsin from turning on incorrectly.

The researchers observed that, in mutant flies that have a non-functioning Rhodopsin6 (green-sensitive) gene, the photoreceptors that would have normally produced this Rhodopsin instead slowly start to make the blue-sensitive Rhodopsin5. After two weeks, essentially all of these photoreceptors were observed making the blue Rhodopsin. The authors named one of the mutations in Rhodopsin6 gene "Frank Sinatra" because presumably it makes old eyes more sensitive to blue light—they don't actually become blue in color.

These findings showed, then, that in normal flies, green Rhodopsin6 maintains repression of the blue Rhodopsin5 gene. This result is surprising—previously, it had not been known that Rhodopsins could control how other Rhodopsins are made.

The neurons governing our sense of smell are organized in a similar fashion. Once each olfactory neuron, which is responsible for this sense, makes a functional olfactory receptor protein, that receptor can prevent other genes encoding different olfactory receptors from being turned on in the same cell.

While the researchers did not investigate what brings about this change in Rhodopsins, they think of this as a maintenance mechanism that prevents cells from having blue and green Rhodopsins together.

"The two types of photoreceptors could be connected to different neuronal circuits in the brain which interpret the information they receive from photoreceptors as being about blue or green light," noted Daniel Vasiliauskas, the leading author of the paper and a post-doctoral fellow at NYU. "Thus changing the Rhodopsin that a photoreceptor makes could lead to sensory confusion and reduce the fly's ability to tell apart different colors."

"An alternative possibility is that our findings point to a mechanism that allows a fly to adapt to changing circumstances," he added. "If we keep flies in the dark for extended periods of time, we start seeing the same thing happening: blue Rhodopsin5 is made in the green Rhodopsin6-producing photoreceptors, leading to cells that have both. This change could be associated with changes in the downstream circuits that must now adapt to correctly interpret the information they receive."

Provided by New York University

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