Biologists uncover regulatory mechanism for gene expression in the visual system

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Biologists have uncovered a key regulatory mechanism used for gene expression in the visual system. Their findings, which appear in the latest issue of the journal *Cell*, offer new insights into the complexity behind the genetic make-up of biological systems.

The study, which included researchers from New York University's Department of Biology, Japan's Okayama University, Cincinnati Children's Hospital, and Germany's University of Würzburg, examined the photoreceptor cells in the retina of the fruit fly Drosophila. Drosophila is a powerful model for studying eye development as it is amenable to very specific genetic manipulations, allowing researchers to analyze how its visual system functions when its different elements are affected.

Though scientists have identified specific roles for many genes in various biological contexts, the ways in which these genes interact are poorly understood. This is especially the case with the eye, an extraordinarily complex system. For example, in the Drosophila eye, expression patterns of Rhodopsins—the light detectors of the retina—determine at least 13 distinct types of photoreceptors.

Among their goals, the researchers sought to address how genes interact in distinct ways in different cells. In other words, how do genes work in networks to control the exquisite and precise patterns of rhodopsin gene expression?

In the *Cell* study, the researchers identified a gene that is a critical node in this network—one that regulates the expression of several rhodopsin genes in the visual system. They specifically looked at how this network figured in Rhodopsin expression in several types of photoreceptors that are normally used for motion detection or color vision.

In their comparison between normal and mutant visual systems, the researchers found that the transcription factor gene defective proventriculus (dve) is a critical node in the network regulating Rhodopsin expression. In dve mutants, the Rhodopsins normally found in the color vision photoreceptors are expressed in the motion detecting photoreceptors. This mutation causes defects in light detection especially when flies are presented with subtle differences in light levels.

The dve gene is a shared component of two opposing, interlocked feed-forward loops (FFLs), which serve as critical network motifs controlling gene expression. Specifically, in one FFL, Dve acts to repress Rhodopsin expression in the motion detecting photoreceptors. Moreover, in the color vision photoreceptors, a second FFL relieves repression by Dve while activating Rhodopsin expression. Therefore, this network serves to both restrict and induce cell type-specific expression. This interlocked FFL motif may be a general mechanism to control gene expression, the researchers concluded.

"We know that genes work in combinations, but the coherence of interactions across cell types is not well understood," said Robert Johnston, a post-doctoral fellow in the laboratory of NYU biologist Claude Desplan, two of the study's co-authors. "We show how these networks function across several different cell types—this mechanism makes sure that Rhodopsins are in the right cells."

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