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COMMENTARY
Two are better than one: unraveling the functions of cone arrestin in zebrafish (Commentary on Renninger, Gesemann and Neuhauss)

Cheryl M. Craft[1,2]
[1]Mary D. Allen Laboratory in Vision Research, Doheny Eye Institute, Los Angeles, CA, USA
[2]Departments of Ophthalmology and Cell & Neurobiology, Keck School of Medicine of the University of Southern California, Los Angeles, CA, USA

Since the surprising discovery of a second visual arrestin in mammalian pinealocytes and cone photoreceptors, numerous studies have examined cone arrestin's structural and functional similarities to and differences from rod arrestin (Craft *et al.*, 1994; Nikonov *et al.*, 2008). The rod arrestin or Arrestin1 binds to and terminates the light-activated, phosphorylated G-protein-coupled rhodopsin (Xu *et al.*, 1997), whereas both visual arrestins work in concert in cone photoreceptors to shut off the light-activated photoreceptor signal transduction cascade, as shown for mouse S- and M-opsin (Nikonov *et al.*, 2008).

In this issue of *EJN*, Renninger and colleagues add a new dimension to understanding the visual arrestin saga by introducing two rod arrestins (*arrS*), three *β*-arrestins, and focusing on two paralogs of cone arrestin (*arr3a* and *arr3b*) in the zebrafish (*Danio rerio*). The Arr3a is exclusively expressed in M- and L-wavelength sensitive cones, whereas Arr3b is found in S- and UV-wavelength-sensitive cones. Their comprehensive study provides the first clear evidence of Arr3a's involvement in the high temporal contrast sensitivity of cone vision.

As zebrafish exhibit light responses after 3 days of development, they are an ideal animal to study visual behavior (Brockerhoff *et al.*, 1995). They are tetrachromatic with ultraviolet-sensitive cones as well as red-, green- and blue-sensitive cones, and their retinas continue to grow throughout their life. Using this cone-dominated visual system as a model system for their analysis, Renninger *et al.* (2011) examined the cellular expression of the distinct isoforms of arrestin in the visual system using a combination of *in-situ* hybridization and cone arrestin paralog-specific antibodies to examine cellular distribution at different developmental stages. These straightforward morphological experiments were followed by a set of elegant physiological experiments using targeted gene knockdown of the two cone arrestins in zebrafish larvae to unravel their visual responses with electroretinography. The functional knockdown of *arr3a* led to an electroretinography photo-response recovery delay. Additional experiments with the functional inactivation of *arr3a* were used to dissect out the psychophysical responses with optokinetics, a stereotypic ocular movement that is probably mediated by the modulation of M- and L-cone input (Orger & Baier, 2005). These latter experiments distinguished behavioral differences between low-contrast (dark-adapted) conditions that affected high temporal frequency patterns, and high-contrast (light-adapted) conditions that showed a deceleration of the temporal transfer function in the *arr3a* morphant larvae.

Because of the lower abundance of the S- and UV-wavelength-sensitive cones in zebrafish, the function of *arr3b* remains undetermined; however, this work provides conclusive evidence that *arr3a* regulates high temporal resolution in high acuity color vision with experiments that are not possible in the rod-dominant mammalian retina. This work illustrates the use of the zebrafish as a vertebrate model to address the basic cellular function of cone arrestin and contributes to our broader understanding of visual processing and the complex physiology of high acuity color vision.

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