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INTRODUCTION

Spotlight on the evolution of vision

Since the 1980s our understanding of the evolution of visual systems has undergone an explosion with the advent of technologies for molecular and genomic analyses. The revolutionary finding that put the evolution of vision into the spotlight was the demonstration that homeodomain-containing transcription factors controlling pattern formation and development in the fly eye could also do so in mice and humans (Ton et al., 1991; Glaser et al., 1992; Quiring et al., 1994; Halder et al., 1995; Gehring & Ikeo, 1999). These landmark discoveries revealed that organisms with anatomically and morphologically different visual systems contain remarkably similar genes. This stimulated a proliferation of exciting work, prompting a reassessment of the evolution of eyes (Gehring & Ikeo, 1999; Arendt, 2003; Plachetzki et al., 2005; Nilsson & Arendt, 2008; Collin et al., 2009; Lamb et al., 2009; Nilsson, 2009; Yau & Hardie, 2009; Fain et al., 2010; Jacobs, 2010; Feuda et al., 2012; Porter et al., 2012).

These similarities among organisms are not only limited to developmentally controlled genes. Studies in invertebrates have contributed to uncovering signal transduction mechanisms in our eyes. For example, an invertebrate-related r-opsin, melanopsin, was discovered in intrinsically photoreceptive ganglion cells (ipRGC) in the vertebrate eye (Provencio et al., 2000; Graham et al., 2008). Further reminiscent of the invertebrate signaling cascade, the transient receptor potential channels 6 and 7 (TRPC6 and TRPC7) function in the ipRGCs through a phospholipase C (PLC) signaling cascade, demonstrating that ipRGCs use an invertebrate-type phototransduction cascade. The discovery of additional invertebrate-related TRP channels (TRPM1) in ON-bipolar cells (Morgans et al., 2009; Shen et al., 2009) has lent further support to the recognition that studies on the visual systems of invertebrates offer powerful information about human eyes. TRP channels were first discovered in *Drosophila* and mutations in the *trp* gene lead to retinal degeneration in fruit flies (Minke, 2010; Hardie, 2011; Montell, 2011). Likewise, mutations in *TRPM1* are linked to autosomal-recessive congenital stationary night blindness in humans (Audo et al., 2009). Interestingly, it is estimated that 90% of the disease-causing genes in humans have counterparts in organisms that emerged very early in evolution, prior to the bilaterian radiation (about 520–540 million years ago during the Cambrian explosion) (Domazet-Loso & Tautz, 2008).

Investigators continue to capitalize on a host of versatile genetic, electrophysiological, molecular, cell biological and biochemical techniques to dissect fundamental processes in a variety of experimental organisms. These studies are aimed at not only for understanding the evolution of vision and visual function but also for developing treatments and potential cures for human eye diseases (Fadool et al., 1997; Wang & Montell, 2007; Nilsson, 2009; Yau & Hardie, 2009; Colley, 2010; Fain et al., 2010; Jacobs, 2010; Hardie, 2011; Montell, 2012). For example, even the light-activated protein pumps used by microbes, channelrhodopsin and halorhodopsin, are providing a way to restore light sensitivity to retinas whose photoreceptors have degenerated. They have also proved useful in optogenetics technologies aimed at uncovering neural circuits (Deisseroth, 2011; Greenberg et al., 2011; Polosukhina et al., 2012). These examples underscore the importance of investigating all light-sensitive systems independent of their shedding light on the evolution of vision.

A sequence of stages has been envisioned to explain how a primitive eyespot evolved to become a complex camera-type eye (Nilsson & Arendt, 2008; Nilsson, 2009). In multicellular organisms, these flat eyespots can be simple single-cell photoreceptors, scattered on the surface. Some eyespots have no associated pigment cells and are unable to detect the direction of a light source. It is thought that the eyespot dimpled inward to form a pit or cup eye. This provides higher visual acuity by allowing the eye to sense the direction of light. Flatworms are an example of an organism with this type of eye, which can do little more than to detect movement. It is proposed that the eye then became constricted at the eye opening, forming a narrower aperture. This advance enabled sharper imaging abilities, and the chambered nautilus has such an eye. However, in order to further increase visual acuity, the aperture would need to be so small that it would shut out much light. So a lens was needed, and, subsequently, the image became sharper and sharper as eye evolution proceeded to produce the complex camera-type human eye (Nilsson & Arendt, 2008; Nilsson, 2009). Despite the perceived simplicity of microbes, jellyfish, worms, fruit flies and fish, they are remarkably complex creatures with genetic make-ups that are surprisingly similar to our own.

In this issue, three articles are focused on our current knowledge of the evolution of vision from the earliest of known visual systems, consisting of simple eyespots, to pit eyes and cup eyes, to low-resolution eyes and finally to the complex high-resolution camera-type eye. In studying evolution, it is often found that molecular data point in one direction and morphological findings in another (Nilsson & Arendt, 2008; Nilsson, 2009). First, **Nilsson** provides new details on how eye evolution is directed by the demands of visually guided behavior. He discusses how in evolution the progression of gradually more complex behaviors made demands for increasing the performance of photoreceptor organs. Nilsson proposes a sequence of four sensory tasks, beginning with nondirectional photoreception, followed by directional photoreception, low-resolution vision and culminating in high-resolution vision. To understand why certain morphological features, physiology and molecular make-up have evolved, he points out that it is important to understand the selection

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pressures on visually guided behavior that favored one path at the expense of another (Nilsson & Arendt, 2008; Nilsson, 2009).

Next, **Goldsmith** provides an overview of the types of photoreceptors and photosensitivity spanning unicellular organisms to humans. He discusses the photochemistry of vision and visual pigments of all eyes. Every visual pigment molecule consists of a protein (opsin) that is covalently bound to its chromophore, 11-*cis* vitamin A aldehyde (retinal) or a closely related retinoid, and in the light, the retinal is isomerized from the 11-*cis* to the all-trans configuration. In contrast, there is much more evolutionary variation in the processes that regenerate the 11-*cis* isomer from the all-*trans* photoproduct. The opsins associate with distinct G-proteins, usually resulting in either hyperpolarizing (vertebrate) or depolarizing (invertebrate) conductance changes at the photoreceptor cell membrane.

Goldsmith discusses the story of evolution as one of tinkering (Jacob, 1977). Natural selection acts on chance mutations to produce an enormous variety of morphological forms and variation within functional themes in eyes. For example, the rhabdomeric and ciliary photoreceptors express rhodopsin visual pigments with maximal absorption from 340 nm in the near UV to 620 nm in the red. Visual pigments are frequently matched to the color spectrum of the available light. For example, the rhodopsins in deep-sea fish are blue-shifted to be better suited for the spectral composition of light at depth since long-wavelength light is absorbed in the water column. On the other hand, Mantis shrimp express 16 different visual pigments and use colored filters to tune long-wavelength receptors to shallow- or deep-water habitats (Cronin et al., 2001).

Finally, **Jacobs** discusses the evolution of color vision with a specific emphasis on the discovery that the short-wavelength-sensitive opsin genes (SWS1) from widely divergent eutherian (placental) mammals have accumulated mutations that cause them to lose full function or to be completely nonfunctional. Complete loss limits these species to a single type of functioning cone, thus resulting in a lack of color vision and important consequences for visual behavior. Several dozen species from five mammalian orders have lost short-wavelength cones, and Jacobs estimates that as many as 10% of all species may be affected. To explain this widespread cone loss, Jacobs points out that there is a single consistent finding: most of these species are nocturnal, marine or have retinal adaptations consistent with those found in nocturnal animals.

Jacobs emphasizes that the overall pattern in the evolution of cone pigments has been one of loss. Vertebrate cone pigments are specified by opsin genes from four families: SWS1 and SWS2 (short wavelength-sensitive opsin, type 1 and type 2), LWS (long wavelength-sensitive opsin) and Rh2 (rod-like cone opsin). Jacobs points out that all four families were present early in vertebrate history, at least 540 million years ago, when jawed and jawless vertebrates diverged (Collin et al., 2009). Through evolution, there is a trend for the loss of cone pigments. He also discusses *why* some SWS1 genes become pseudogenes. The loss of the SWS1-specified cone photopigments represents a significant trend in the evolution of mammalian vision. He predicts that in the future, additional nocturnal species will join those in abandoning their short-wavelength cones. He does not, however, predict this loss in diurnal animals, projecting that the SWS1 opsin gene family will not follow the disappearance of the Rh2 and SWS2 gene families from eutherian mammals.

Forty years ago, the Russian evolutionary biologist, Theodosius Dobzhansky, famously wrote: "Nothing in biology makes sense except in the light of evolution." The three papers that follow in this issue illustrate this notion very well. Other mysteries in vision will undoubtedly be explained as we unravel various aspects of the evolution of visual systems across species. Why, for example, are cone, ganglion and horizontal cells the first to be generated during development of the vertebrate retina in many animals? Were these the cells that made up the earliest retinas, which consisted, perhaps, of a photoreceptor, output neuron and glial cell? Cones clearly evolved before rods, in some species, there are ganglion cells that receive direct input from cones, and horizontal cells, especially in fish, have many glial-like characteristics (Dowling, 2012). Rods, bipolar and Muller glial cells are generated later in development and perhaps arose later during evolution. Study of retinas and retinal development in a wide variety of species may well provide insights on these matters.

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