

# New insights into the evolutionary history of photoreceptor cells

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**Although the common descent of all life has been widely accepted since Darwin's time, new research occasionally provides us with arresting reminders of the unity of evolutionary history. Recent papers by Arendt *et al.* and Panda *et al.* provide one such reminder. They illustrate that the two classes of animal photoreceptors, ciliary and rhabdomeric photoreceptors, are likely to share an ancient common ancestor and have been evolving in parallel since their duplication over 600 million years ago.**

## Photoreceptor evolution

Metazoan photoreceptors can be divided into ciliary and rhabdomeric classes. Ciliary photoreceptors are commonly associated with vertebrates, whereas rhabdomeric photoreceptors are usually considered to be an invertebrate characteristic. Both cell types are neurons that are specialized for photoreception, but they differ in their morphology. Ciliary photoreceptors use cellular projections consisting of microtubules called cilia, whereas rhabdomeric photoreceptors use membranous tubes called microvilli. Both of these morphologies serve to increase the surface area of the cell that is exposed to light. Traditionally, the distinctions between ciliary and rhabdomeric photoreceptors were based on morphology, a situation that has led to ambiguity and conflicting treatments of photoreceptor evolution. One traditional view is that these two photoreceptor classes have different evolutionary origins. However, several recent articles, notably those by Arendt *et al.* [1] and Panda *et al.* [2], show how molecular markers can aid in identifying photoreceptors of each class.

This enhanced understanding of ciliary and rhabdomeric cell types has motivated new ways of viewing the evolutionary history of photoreceptors (Figure 1). First, shared gene expression patterns, such as that of the transcription factor *Pax6*, indicate that the two cell types might be homologous, meaning they can be traced back to a common ancestral cell that probably existed early in the history of animals [3]. Second, molecular markers, such as opsin proteins and other members of the phototransduction cascade, can be used to distinguish rhabdomeric versus ciliary cell types [3]. Ciliary cells express genes from one sub-family of opsin, whereas rhabdomeric cells express genes from another subfamily. At least one other gene family (transducin) involved in the photo-

transduction cascade shows a similar pattern [3]. As well as enabling identification, these separate clades of opsin and accessory proteins indicate that the encoding genes were probably duplicated at the time that the two cell types first differentiated (Figure 1).

Here, we briefly review support for a new view of photoreceptor evolution that treats ciliary and rhabdomeric photoreceptors as sister cell lineages with parallel evolutionary histories. Because these cell types arose before the diversification of bilaterian animals (i.e. animals showing bilateral symmetry in either their adult or larval stage), both should still be present in many groups. This prediction contradicts most traditional accounts of photoreceptor evolution.

## Support for a new view of photoreceptor evolution

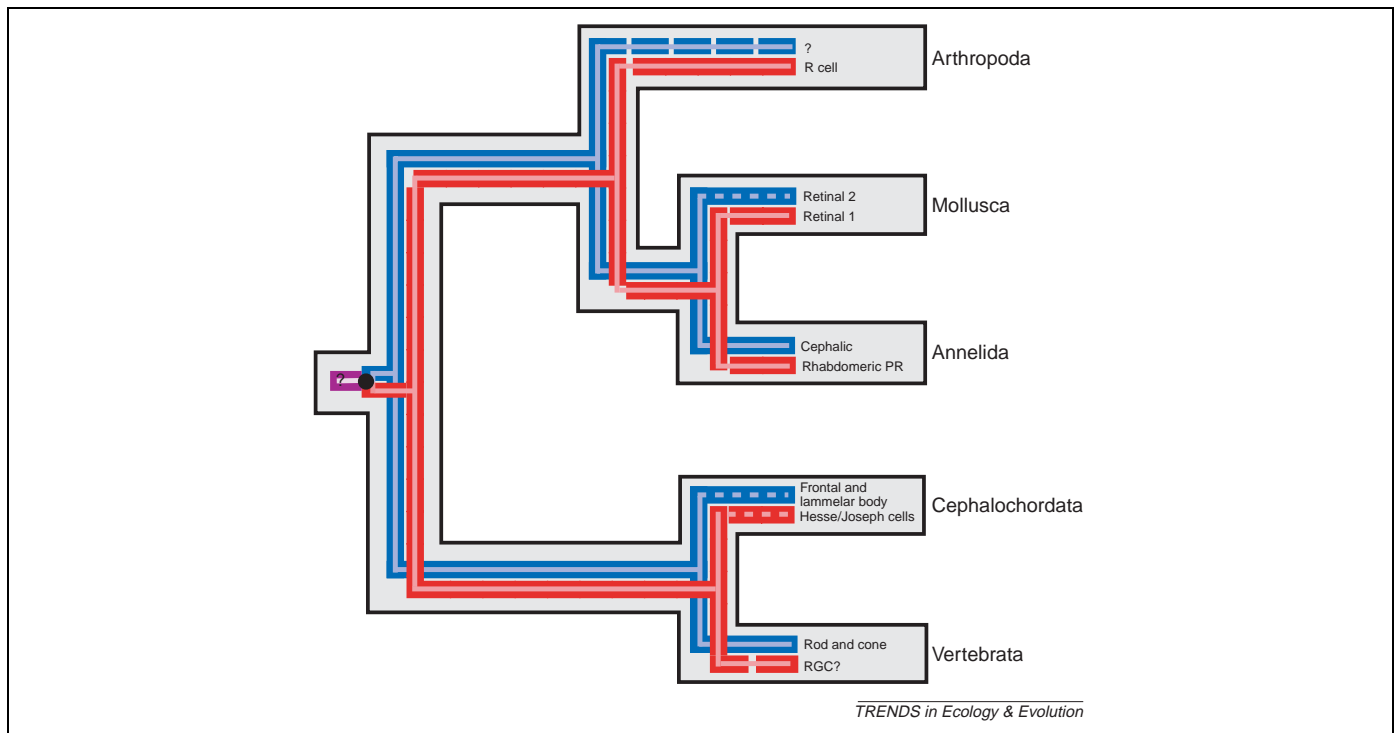
If photoreceptor evolution proceeded by duplication and subsequent diversification, ciliary and rhabdomeric photoreceptors would have been evolving as separate cell types in the same animal lineages. Although loss of one or both cell types is possible during evolution, the phylogenetic hypothesis is supported if most species have both photoreceptor cell types. The new molecular markers provide tools for testing this hypothesis, which has recently been supported by studies in invertebrate and vertebrate models.

New evidence has identified ciliary photoreceptors of an invertebrate. Arendt *et al.* [1] describe a ciliary receptor in the brain of the rag worm *Platynereis* (Annelida). First, they found that these photoreceptors utilize an opsin protein that is a member of the ciliary opsin sub-family. Analyses of the amino-acid motifs of this opsin further suggest a role in eliciting a ciliary-type phototransduction cascade. Second, these brain photoreceptors are also under the control of a developmental regulatory gene, *rx*, which is homologous to the gene that regulates vertebrate ciliary photoreceptors in development [1]. Finally, morphological data are consistent with the idea that these cells in *Platynereis* represent true ciliary photoreceptors. Together, these findings provide conclusive evidence that ciliary photoreceptors are present in this lineage. In other words, exceptions to the phylogenetic rule of thumb (rhabdomeric for invertebrate and ciliary for vertebrate) might not in fact be exceptional.

Another obstacle to the idea of photoreceptor evolution by ancient duplication and divergence is that vertebrates were thought to have only ciliary photoreceptor cells. New findings in neurophysiology by Panda *et al.* [2], and other

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**Figure 1.** Phylogeny depicting the evolutionary history of photoreceptors at three levels of biological organization [13]. Ciliary (blue) and rhabdomeric (red) photoreceptors and their respective opsin sub family, c-opsin (light blue) and r-opsin (pink), share a common evolutionary history that began in an ancient duplication event, although the characteristics of the prototypical photoreceptor remain unclear. Within each animal clade, there is evidence for the existence of both ciliary and rhabdomeric photoreceptors. Dashed lines indicate instances where one line of evidence might be incomplete, or at variance with the cell-type distinction. In arthropods a c-opsin is known from mosquito, but the cell type has not been characterized fully. Scallops have dual retinas, each housing either ciliary or rhabdomeric photoreceptors, but the c-opsin from their ciliary photoreceptors falls outside of the orthology subgroup in question. It is unclear whether this cell type is truly ciliary or represents another offshoot of the main ciliary–rhabdomeric photoreceptor lineage. In the cephalochordate *Branchiostoma*, six different opsins have been described, but the photoreceptors that express these opsins have yet to be determined. Finally, RGCs lack morphology that is consistent with their membership in the rhabdomeric photoreceptor lineage, but the other markers supporting the distinction are present. Dashed lines highlight areas for future study.

parallel studies [4–7], provide evidence that is consistent with the hypothesis that rhabdomeric photoreceptors exist in the vertebrate lineage in the form of retinal ganglion cells (RGCs). RGCs coordinate neuronal impulses in the vertebrate retina and traffic this information to the optic chiasm (Figure 2). These recent studies show that RGCs utilize melanopsin, a member of the rhabdomeric opsin sub-family [8]. Furthermore, the phototransduction cascade elicited by melanopsin in cultured cells might be homologous to that utilized by rhabdomeric photoreceptors. In addition to the recent studies of the RGC phototransduction cascade, previous studies provide evidence of additional similarities between RGCs and rhabdomeric photoreceptor cells. Homologues of the atonal gene (*ato*) are required for rhabdomeric photoreceptor [9] and RGC differentiation [10] in the development of flies and mice, respectively. The expression of other genes in the *ato* pathway has also been described in both rhabdomeric and RGC cells [9]. Although an alternative hypothesis exists (RGCs might have independently recruited genes that are utilized in rhabdomeric photoreceptors), the similarity of molecular markers, including both structural genes and genes involved in specification, provides strong support for RGCs as true homologs of rhabdomeric photoreceptor cells.

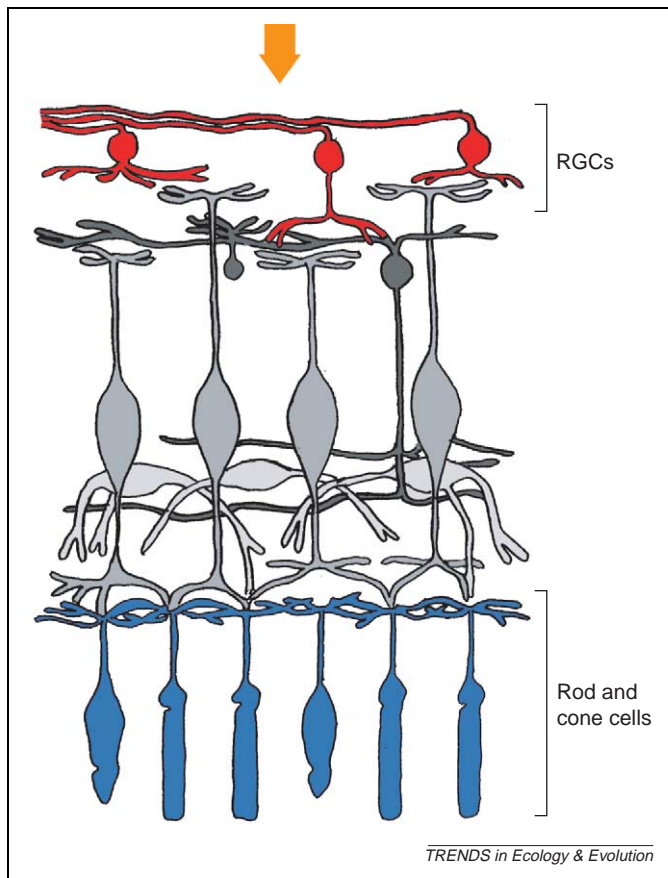
How could it be that no one had previously suspected vertebrate RGCs to be rhabdomeric photoreceptor cells? One answer is that RGC morphology is quite different

from that of other photoreceptor cells. RGCs lack microvilli or any specialized morphology designed to increase light absorption. Furthermore, RGC photosensitivity is involved in circadian and pupillary adjustments and has no role in visual perception. One non-molecular clue to homology is a topological similarity that is shared by the two cell types: they both send axonal projections to the brain. However, this is not strong enough evidence by itself to homologize rhabdomeric photoreceptors and RGCs.

In summary, many morphological characteristics of RGCs have diverged substantially from rhabdomeric cells, but molecular markers have maintained clear signals, which suggest that the RGCs are the ‘missing’ vertebrate rhabdomeric photoreceptor cells. One obstacle to the idea of an ancient and singular origin for both photoreceptor cell types appears to have fallen.

#### Implications and future directions

In light of the fascinating story that has recently unfolded regarding photoreceptors, it is clear that the evolutionary histories of complex structures, such as eyes, can be viewed from different levels of organization, which include, but are not limited to, developmental control, structure, constituent cell types and, in the case of photoreceptors, cell signaling machinery. Common descent is a biological truism that unifies these levels. The concepts of duplication and subfunctionalization [11], which are important theoretical tools in molecular evolution and



**Figure 2.** Architecture of the vertebrate retina. The vertebrate retina is a complex laminar structure consisting of numerous neuronal cell types, at least some of which are evolutionarily derived from either ciliary or rhabdomeric photoreceptor cells. The rod and cone cells (in blue) receive light information from the photic environment (arrow) and encode it into nervous excitations. Owing to the inverse orientation of the vertebrate retina, light must pass through the retina before being absorbed by the photoreceptors. Rod and cone cells are ciliary photoreceptors. RGCs (in red) coordinate both visual and non-visual neuronal impulses and send this information to the brain. RGC axonal projections help comprise the optic nerve. Based on new evidence, RGCs might be derived rhabdomeric photoreceptors [2].

genomics, mirror the processes of speciation and divergence that occur at higher levels of biological organization. It appears that our new understanding of the evolutionary history of photoreceptors underlines the fact that duplication and divergence are important processes in evolution at the level of the cell type [3].

The origin of the ciliary and rhabdomeric cell types appears to have occurred concomitantly with a duplication of genes. As such, the cell types represent discrete evolutionary lineages that share a common ancestor. Molecular markers, including opsin and signaling genes that form separate sub-families, support the discrete nature of each cell-type lineage. However, molecular data exist for

only a few taxa. Sequence data from opsin and phototransduction signaling proteins from basal bilaterian taxa and bilaterian outgroups will provide interesting additional tests of the new view of photoreceptor evolution. For example, morphological data indicate that both photoreceptor types exist in the cubozoan jellyfish [12]. Sequence data from opsins and phototransduction proteins from a cubozoan could help confirm the identity of these photoreceptors and provide valuable outgroup data for phylogenetic analyses. Comprehensive taxon sampling using the new molecular tools, coupled with a robust metazoan phylogeny will be key to completing the story of photoreceptor cell evolution and is likely to uncover additional surprises along the way.

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