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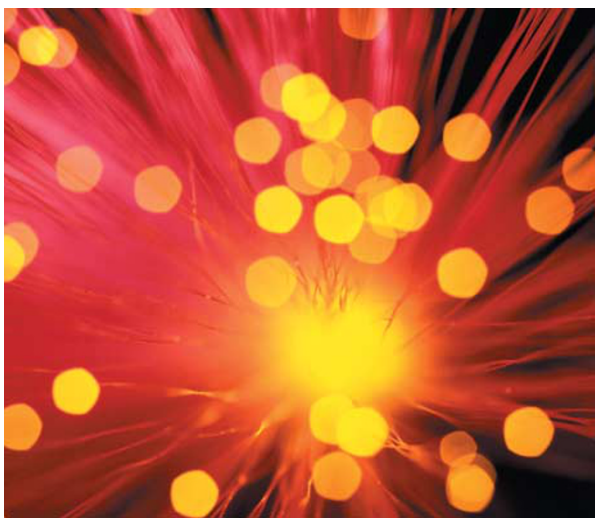
SENSORY TRANSDUCTION

Seeing the light

Three studies have shown that melanopsin — a pigment that is found in the type of retinal ganglion cell that allows light to entrain the circadian clock — can function as a photopigment in other types of cell. As well as confirming that melanopsin is photosensitive, the studies reveal that it is closer in some ways to invertebrate photopigments than to other photopigments in vertebrates.

Circadian entrainment in mammals relies on a set of intrinsically photoreceptive retinal ganglion cells (ipRGCs). Although these contain melanopsin, and lose their photoreceptive properties if melanopsin is removed, it has not previously been shown that melanopsin itself is the photopigment in these cells. To show that melanopsin is not only necessary, but also sufficient, for photosensitivity, three groups expressed the pigment in different types of cell — *Xenopus* oocytes, human embryonic kidney (HEK293) cells and a mouse neuronal cell line called neuro-2a. In each case, the expression of melanopsin caused the cells to become photosensitive.



The three groups also investigated the signalling pathways that mediated phototransduction in the transfected cells. Molyan *et al.* found that, in neuro-2a cells, melanopsin signals through a G-protein signalling pathway to regulate the opening of an intrinsic ion channel. In *Xenopus* oocytes and HEK293 cells, according to Panda *et al.* and Qiu *et al.*, the activation of melanopsin by light can trigger the opening of TRPC3 calcium channels — a mammalian homologue of the TRP and TRPL channels, which are involved in phototransduction in *Drosophila*. The activation of TRPC3 channels in these cells also involves signalling through a G-protein pathway, and the signalling pathway is similar to that found in invertebrate photoreceptors.

Photosensitive opsins, such as melanopsin, use 11-*cis*-retinaldehyde as a chromophore. When light converts 11-*cis*-retinaldehyde to all-*trans*-retinaldehyde, it creates a conformational change in the opsin that triggers G-protein activation. In vertebrate photoreceptors, the chromophore is converted back to 11-*cis*-retinaldehyde through a complex pathway in the retinal pigment epithelium, but in invertebrates the opsins themselves can carry out the photoisomerase activity that is needed to regenerate the chromophore. Both Melyan *et al.* and Panda *et al.* provide evidence that melanopsin resembles invertebrate opsins in that it has an intrinsic photoisomerase activity that can convert all-*trans*-retinaldehyde into 11-*cis*-retinaldehyde.

Although further studies are needed to pin down the exact mechanism by which melanopsin mediates phototransduction in ipRGCs, these three studies provide proof that melanopsin can function as a photopigment, and also point towards an invertebrate-like signalling mechanism. In a fourth study that investigated the melanopsin-driven dispersal of melanosomes in cultured *Xenopus* melanophores, Isoldi *et al.* also found evidence for a signalling pathway that resembled those in invertebrate photoreceptors. This similarity between ipRGCs and invertebrate photoreceptors could give valuable insights into the biology and evolution of the circadian light-entrainment system in vertebrates.

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References and links

ORIGINAL RESEARCH PAPERS Melyan, Z. *et al.* Addition of human melanopsin renders mammalian cells photoresponsive. *Nature* 26 January 2005 (10.1038/nature03344) | Qiu, X. *et al.* Induction of photosensitivity by heterologous expression of melanopsin. *Nature* 26 January 2005 (10.1038/nature03345) | Panda, S. *et al.* Illumination of the melanopsin signaling pathway. *Science* **307**, 600–604 (2005) | Isoldi, M. C. *et al.* Rhabdomeric phototransduction initiated by the vertebrate photopigment melanopsin. *Proc. Natl Acad. Sci. USA* **102**, 1217–1221 (2004)