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seeing through the murk

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We need light to see. There are times, though, when things are so gloomy it is difficult for light to shine through. So, to beat the darkness, either we create our own light or adapt to the lack of it. In Nature, the natural habitat of many vertebrates is water – sea water or fresh water. Unlike sea water, lakes or streams can be very turbid and, thus, less easy to move around in. Over a century ago, scientists had already observed that the eyes of freshwater fish have a visual pigment system that is not the same as those of marine fish or, for that matter, land animals. Freshwater fish, for instance, are able to navigate through hazy waters the way a bird would fly across a cloudless sky. This is because they can perceive wavelengths of light that humans, for instance, cannot. For us, everything would remain blurry. More surprising, perhaps, are certain vertebrates such as bullfrogs and salmon that have both visual pigment systems, and switch from one to the other depending on the environment. How can they do this? Thanks to an enzyme, known as cytochrome P450 27C1.

"Twilighted Walk", by Charles Hollinger

Graphite on watercolour paper

(7.5" x 10.5")

Courtesy of the artist

Since the close of the 19th century, we have known that the visual pigments of freshwater fish are different from their seawater counterparts. Visual pigments consist of a protein component known as rhodopsin, and a small molecule – or chromophore – that is bound to it. Rhodopsin is itself a photopigment. Under the microscope, it produces a deep-red colour when extracted from marine fish, while it produces something closer to purple when extracted from freshwater fish. This change in colour – from deep red to purple – is known as a red-shift. In the 1930s, the American biologist George Wald believed that the red-shift in the eyes of fish influenced the way they could see. He turned out to be right, and subsequently demonstrated that the shift was due to a simple chemical modification in the chromophore, which makes it prefer the longer wavelengths of light. In the world of optics, this means that freshwater fish are able to discern better in a gloomy environment than marine fish are. In other words, they can see deeper. This makes sense for freshwater fish that swim in waters that are usually murky because of the presence of mud and algae for example.

What is vision? Vision begins when a photon of light alters the structure of a chromophore, which in turn alters the structure of rhodopsin, thus activating the cascade in which light is converted into electrical signals. These signals are then processed by our brain, and the result is what we see. For humans, visible light is made up of wavelengths that range from 400 to 700nm, i.e. between the ultraviolet (shorter wavelengths) and the infrared (longer wavelengths). Visual acuity depends on both the rhodopsin and the chromophore it carries. So how does this apply to freshwater fish? Because of turbidity, fresh water tends to filter shorter wavelengths of light – i.e. the blues, greens and yellows that you would see in the sea – leaving behind the longer wavelengths, i.e. the reds and infrareds. If an eye can deal with longer wavelengths then it can see through murky waters.

As Wald had suggested, the chromophore is at the heart of the red-shift, and he called it vitamin A. He then went on to demonstrate that there were two kinds of vitamin A in fish retinas: freshwater fish had vitamin A2 while marine fish had vitamin A1. The difference between the two is a double bond in vitamin A2, causing it to prefer to absorb light with longer wavelengths. As the 20th century unfolded, studies revealed that the visual system of a wide range of freshwater fish – but also amphibians and reptiles – were indeed red-shifted. In fact, in amphibians, the immature tadpole has vitamin A2, while the adult frog that spends more time out of the water has vitamin A1. Bullfrogs actually have both types of vitamin A in their retinas! This is probably because they sit for long hours in ponds with their eyes barely out of the water, and they need to see both above the water level and beneath it. Salmon have an even more intricate system: in seawater, their visual pigments contain vitamin A1. They then switch to vitamin A2 when they enter rivers to reproduce.

Though a lot had been understood by the end of the 1930s, how fish are able to switch from one vitamin A to another remained a mystery – until only a few years ago when scientists uncovered an enzyme in the retinal pigment epithelium of zebrafish: Cyp27c1. Cyp27c1 belongs to the family of cytochromes P450 – a very large family of proteins involved in electron transfer, as would be expected in the process of phototransduction – and has proved to be not only necessary but essential in the vitamin A1 to vitamin A2 shift. In effect, Cyp27c1 tunes the entire visual system by controlling the balance of both vitamins in the retina. However, to date, the chemical pathway involved is still unknown.

Understanding the molecular detail of chromophores, their role in fine-tuning vision and how Nature has evolved ways of switching from one visual system to another is a fascinating field of research. The fact that the same enzyme – Cyp27c1 – is used both by fish and amphibians suggests that this particular system has existed for hundreds of millions of years, and so has had plenty of time to be refined. In fact, besides the nature of the water, other environmental factors such as changes in temperature or season can also influence the vitamin A1/A2 balance. What about birds and mammals? Despite the fact that Cyp27c1 homologs are found in their genomes and that they share a visual pigment system that is similar to those of fish and amphibians, so far vitamin A has not been shown to adjust their vision. Cyp27c1 function in birds and mammals is in fact currently unknown, though studies suggest roles outside the eye.

If Nature can devise different ways of enhancing vision, could they be mimicked to help the visually impaired see better? Perhaps. Today, an enzyme such as Cyp27c1 has major implications in the novel field of optogenetics – a body of techniques that use light to control the activities of cells, such as neurons, in living tissue. Currently, optogenetics is limited to visible light and can only be used for the superficial layers of the brain. Because of its ability to red-shift the visual system, Cyp27c1 could help in the design of optogenetic experiments to penetrate the deeper layers of a tissue. So, just as Cyp27c1 helps fish peer into the dark, in the future it could also help scientists shed light on the more obscure parts of the brain.

Cross-references to UniProt

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Cytochrome P450 27C1, *Lithobates catesbeiana (American bullfrog)* : P0DOX0
Cytochrome P450 27C1, *Homo sapiens (Human)* : Q4G0S4

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