RECONSTRUCTING THE RETINA

The ways in which lost vision might be restored are coming into focus as researchers move closer to recreating the eye’s most complex structure — the retina — in the laboratory.

By David Holmes; illustration by Alisdair Macdonald

WEIRD WIRING

The retina comprises a thin layer of light-sensitive tissue at the back of the eye. This intricate structure is essential for vision.

CELL CIRCUITRY

In the retina, five types of neuron — photoreceptors, bipolar cells, retinal ganglion cells, horizontal cells and amacrine cells — are wired together to form one of nature’s most complex circuit boards. When light hits the retina, it stimulates photoreceptors, creating an electrical signal that is conveyed through other neurons of the retina to the optic nerve, and then on to the brain.

Photoreceptors

There are two main types of light-sensitive cell in the eye: rods and cones. Rods enable vision in poor light, whereas cones are responsible for colour vision. Photoreceptors convert light into electrical signals that travel through other retinal neurons to reach the optic nerve.

Bipolar cell

Responsible for transmitting signals from photoreceptors to a retinal ganglion cell.

Retinal ganglion cell

Relays signals from bipolar and amacrine cells to the brain through long projections called axons that form the optic nerve.

Horizontal cell

Regulates the signal that emerges from several rods and cones.

Amacrine cell

Reaches across several bipolar cells to regulate signals directed at retinal ganglion cells. So far, around 30 subtypes have been identified.

A COMMON FAILING

Degenerative diseases of the retina affect hundreds of millions of people worldwide. The most common such condition is age-related macular degeneration (AMD).

- AMD is caused by a build-up of fatty deposits, known as drusen, between the RPE and the choroid. The cause is unclear, but by-products from photoreceptors are thought to contribute.
- These deposits gradually grow in size and number, leading to increasingly distorted vision.
- In advanced AMD, the RPE is disrupted, resulting in the death of photoreceptors and the loss of central vision. 10–15% of cases progress to a form known as wet AMD, in which blood vessels penetrate the retina and leak fluid that causes vision to deteriorate rapidly.

DAMAGE CONTROL

No treatments have been approved for early-stage AMD, but drugs that inhibit blood-vessel formation can slow the progression of wet AMD.

~9% of blindness is caused by AMD.

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FRESH EYES
In the past decade, refinements to techniques for culturing or differentiating stem cells have increased the possibility of using stem-cell therapies to tackle retinal-degenerative diseases such as AMD.

In advanced AMD, dysfunction of the RPE is the main cause of failing vision. Clinical trials are under way to replace damaged RPE with healthy retinal pigment epithelial cells grown from stem cells.

A suspension of retinal pigment epithelial cells derived from stem cells is injected into the distorted space above the choroid. Initial trials in people have shown this approach to be safe.

However, it is unclear whether cells delivered in suspension will survive in great-enough numbers for the RPE to regenerate and function correctly.

Implanting the cells as a sheet removes the need for them to adhere to Bruch’s membrane. Clinical trials have shown the procedure to be safe, and some recipients have reported improvements in vision.