# Mammals can be stimulated to regrow damaged inner retina nerve cells

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Researchers at the University of Washington (UW) have reported for the first time that mammals can be stimulated to regrow inner nerve cells in their damaged retinas. Located in the back of the eye, the retina's role in vision is to convert light into nerve impulses to the brain.

The findings on retina self-repair in mammals will be published this week in the Early Edition of the *Proceedings of the National Academy of Sciences*. Other scientists have shown before that certain retina nerve cells from mice can proliferate in a laboratory dish. Today's report gives evidence that retina cells can be encouraged to regenerate in living mice.

The UW researchers in the laboratory of Dr. Tom Reh, professor of biological structure, studied a particular retinal cell called the Müller glia.

"This type of cell exists in all the retinas of all vertebrates," Reh said, "so the cellular source for regeneration is present in the human retina." He added that further studies of the potential of these cells to regenerate and of methods to re-generate them may lead to new treatments for vision loss from retina-damaging diseases, like macular degeneration.

The researchers pointed out the remarkable ability of cold-blooded vertebrates like fish to regenerate their retinas after damage. Birds, which are warm-blooded, have some limited ability to regenerate retinal nerve cells after exposure to nerve toxins. Fish can generate all types of retinal nerve cells, the researcher said, but chicks produce only a few

types of retinal nerve cell replacements, and few, if any, receptors for detecting light.

Müller glia cells generally stop dividing after a baby's eyes pass a certain developmental stage. In both fish and birds, the researchers explained, damage to retinal cells prompts the specialized Müller glia cells to start dividing again and to increase their options by becoming a more general type of cell called a progenitor cell. These progenitor cells can then turn into any of several types of specialized nerve cells.

Compared to birds, the scientist said, mammals have an even more limited Müller glia cell response to injury. In an injured mouse or rat retina, the cells may react and become larger, but few start dividing again.

Because the Müller glia cells appeared to have the potential to regrow but won't do so spontaneously after an injury, several groups of researchers have tried to stimulate them to grow in lab dishes and in lab animals by injecting cell growth factors or factors that re-activate certain genes that were silenced after embryonic development. These studies showed that the Müller glia cells could be artificially stimulated to start dividing again, and some began to show light-detecting receptors. However, these studies, the researchers noted, weren't able to detect any regenerated inner retina nerve cells, except when the Müller glia cells were genetically modified with genes that specifically promote the formation of amacrine cells, which act as intermediaries in transmitting nerve signals.

"This was puzzling," Reh said, "because in chicks amacrine cells are the primary retinal cells that are regenerated after injury." To resolve the discrepancy between what was detected in chicks and not detected in rodents, the Reh laboratory conducted a systematic analysis of the response to injury in the mouse retina, and the effects of specific growth

factor stimulation on the proliferation of Müller glia cells.

The researchers injected a substance into the retina to eliminate ganglion cells (a type of nerve cell found near the surface of the retina) and amacrine cells. Then by injecting the eye with epidermal growth factor (EGF), fibroblast growth factor 1 (FGF1) or a combination of FGF1 and insulin, they were able to stimulate the Müller glia cells to re-start their dividing engines and begin to proliferate across the retina.

The proliferating Müller glia cells first transformed into unspecialized cells. The researchers were able to detect this transformation by checking for chemical markers that indicate progenitor cells. Soon some of these general cells changed into amacrine cells. The researchers detected their presence by checking for chemicals produced only by amacrine cells.

Many of the progenitor cells arising from the dividing Müller glia cells, the researchers observed, died within the first week after their production. However, those that managed to turn into amacrine cells survived for at least 30 days.

"It's not clear why this occurs," the researchers wrote, "but some speculate that nerve cells have to make stable connections with other cells to survive."

Source: University of Washington