# Cell death in retina helps tune our internal clocks

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(Medical Xpress)—With every sunrise and sunset, our eyes make note of the light as it waxes and wanes, a process that is critical to aligning our circadian rhythms to match the solar day so we are alert during the day and restful at night. Watching the sun come and go sounds like a peaceful process, but Johns Hopkins scientists have discovered that behind the scenes, millions of specialized cells in our eyes are fighting for their lives to help the retina set the stage to keep our internal clocks ticking.

In a study that appeared in a recent issue of *Neuron*, a team led by biologist Samer Hattar has found that there is a kind of turf war going on behind our eyeballs, where intrinsically photosensitive retinal ganglion cells (ipRGCs) are jockeying for the best position to receive information from rod and cone cells about light levels. By studying these specialized cells in mice, Hattar and his team found that the cells actually kill each other to seize more space and find the best position to do their job.

Understanding this fight could one day lead to victories against several conditions, including autism and some psychiatric disorders, where neural circuits influence our behavior. The results could help scientists have a better idea about how the circuits behind our eyes assemble to influence our physiological functions, said Hattar, an associate professor of biology in the Krieger School of Arts and Sciences.

"In a nutshell, death in our retina plays a vital role in assembling the retinal circuits that influence crucial physiological functions such as

circadian rhythms and sleep-wake cycles," Hattar said. "Once we have a greater understanding of the circuit formation underlying all of our neuronal abilities, this could be applied to any neurological function."

Hattar and his team determined that the killing among rival ipRGCs is justifiable homicide: Without this cell death, circadian blindness overcame the mice, who could no longer distinguish day from night. Hattar's team studied mice that were genetically modified to prevent cell death by removing the Bax protein, an essential factor for cell death to occur. They discovered that if cell death is prevented, ipRGCs distribution is highly affected, leading the surplus cells to bunch up and form ineffectual, ugly clumps incapable of receiving light information from rods and cones for the alignment of circadian rhythms. To detect this, the researchers used wheel running activity measurements in mice that lacked the Bax protein as well as the melanopsin protein which allows ipRGCs to respond only through rods and cones and compared it to animals where only the Bax gene was deleted.

What the authors uncovered was exciting: When death is prevented, the ability of rods and cones to signal light to our internal clocks is highly impaired. This shows that cell death plays an essential role in setting the circuitry that allows the retinal rods and cones to influence our circadian rhythms and sleep.

Hattar's study was funded by the National Institute of General Medical Sciences and the National Institute of Neurological Disorders and Stroke and was carried out in close collaboration with Rejji Kuruvilla, an associate professor who is another member of the mouse tri-lab community in the Department of Biology at Johns Hopkins.

**More information:**
www.cell.com/neuron/abstract/S0896-6273(12)01105-1

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