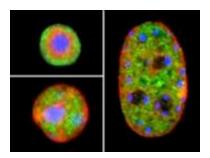
SCIENCE NEWS

Seemingly misplaced DNA acts as lenses Nocturnal mammals orient nucleic material in retinal cells to focus light By <u>Tina Hesman Saey</u> Web edition : Thursday, April 16th, 2009

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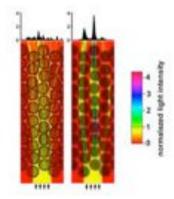
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DNA stains reveal that the nuclei of rod cells (top left) from a mouse's retina have a different arrangement of DNA than ganglion cells (bottom left) or skin cells (right). Blue and red colors show where densely-packed inactive DNA called heterochromatin is located; green shows where active DNA is located. In most cells, heterochromatin is pushed to the outer edges of the nucleus. But rod cells in nocturnal mammals have heterochromatin concentrated in the center, where it acts like a lens to focus light, perhaps enhancing night vision, a new study reports.Solovei, I. et al. Cell April 17, 2009

Mice and cats don't usually agree, but both animals have the same bright idea about night vision. Cats, rats, mice and other nocturnal mammals arrange DNA in some eye cells to form miniature lenses that help focus light, a new study shows.

Scientists at the Ludwig-Maximilians University Munich in Germany and colleagues discovered the unusual DNA arrangement while investigating the function of several genes in the rod cells of mouse eyes, says Boris Joffe, one of the authors of the new study, which appears in the April 17 *Cell*. Rod cells are light-gathering cells in the retina of the eye. They operate under low-light conditions, while cone cells perform the light-gathering duty when it is bright.

Usually active genes are located in the part of the DNA that is at the center of a cell's nucleus. There, the genes have easy access to the cellular machinery that rewrites instructions encoded in the DNA into RNA. Inactive DNA is pushed to the periphery of the nucleus, where it is out of the way.

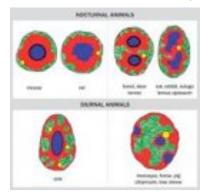


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A computer simulation shows that light would scatter in rod cells with a conventional DNA arrangement (left). But rod cells with an inverted configuration recently discovered by scientists could channel light more effectively (right).Solovei, I. et al. Cell April 17, 2009 But rod cells in the mouse retina shove active genes to the outside of the nucleus, the researchers found. The center of the nucleus is instead occupied by densely-packed inactive DNA called heterochromatin. Mice put this type of DNA front and center in their rod cells.

"Everything that must be inside is outside, and everything that should be outside is inside," Joffe says. "It was an absolutely heretic finding."

Why the cells take on the unusual conformation was at first a mystery. "We checked one explanation after another and none of them worked, so we were forced to think of something completely unusual," Joffe says.



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Scientists recently discovered that nocturnal mammals concentrate inactive DNA, called heterochromatin (blue and red), in one or two spots in the center of the nucleus in rod cells. In animals that are active during the day, rod cells have a DNA arrangement like that of other cells in the body, with active DNA (green) at the center of the nucleus.Solovei, I. et al. Cell April 17, 2009

The team decided to examine retinas from other species to see if mice are the only creatures with the unusual DNA conformation in rod cells. After examining a dozen different species of mammals, the researchers noticed a pattern. Nocturnal animals, including cats, rats, deer, opossum, rabbits and ferrets, had the inside-out arrangement in rod cells, but animals that are active during the day had the conventional DNA arrangement with heterochromatin to the outside of the nucleus.

But the researchers still did not know why a nocturnal lifestyle would be associated with the inverted DNA arrangement in the rod cells. The team consulted Jochen Guck, a biophysicist at the University of Cambridge in England, to find the answer.

"It was very obvious to me that the nuclei could only be lenses," Guck says.

Placing dense heterochromatin in the center of the nucleus raises the refractivity index — the degree to which the material decreases the speed of light traveling through it. The photons travel faster through the loosely packed DNA containing active genes, called euchromatin, and slower through the dense heterochromatin. Slowing down the photons creates a lens to focus light in the center of the cell.

Rod cells form columns in the retina of nocturnal animals, so that many little lenses are stacked on top of each other. The DNA lenses form a chain that acts a bit like fiber-optic cables, Guck suggests. He performed a computer simulation that shows that light would be channeled along the columns of rod cells with the inverted configuration, but cells with the conventional DNA arrangement would scatter light instead.

This is the first time scientists have discovered DNA acting as a lens in photoreceptor cells, says Gregory Acland, a veterinary ophthalmologist at Cornell University. "It's one of those things that once someone has pointed it out, you think, 'oh, that's interesting,' " he says. But arranging components of retina cells to reduce light scattering certainly isn't new, Acland says. For instance, birds, lizards and fish use oil droplets in cone photoreceptor cells to funnel light, he says.

Photoreceptors do channel light, but until now that function was known to occur mostly in cone cells. This may be the first evidence for light-funneling in rods, says Trevor Lamb, a vision scientist at the Australian National University in Canberra. But nocturnal animals have so many rod cells, and so few photons hit the retina at night that it isn't clear whether funneling light through the cells would actually improve night vision, he says.

Inverted nuclei may be a remnant from mammals' ancestors, which were likely nocturnal animals. The inverted configuration of the nucleus may make it harder for the cell to transcribe DNA into RNA because the

transcription machinery must be spread around to mom-and-pop shops located on the outskirts of the nucleus instead of concentrated in factories in the center, Joffe speculates. Species that are active in the daytime have jettisoned the inverted structure; for them, the light-focusing advantages don't outweigh the disadvantage of inefficient transcription, he says.

"As soon as it is not necessary, good-bye inverted pattern," Joffe says.