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Scientists eye secrets of retinal regeneration

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Peering at microscopic changes within the retina, scientists in the Department of Ophthalmology at Weill Cornell Medical College in New York City, have discovered a key mechanism driving eye health and eye disease.

Reporting in the cover article of a recent edition of *Cell*, the team says they have discovered just how light-sensing discs in the retina's rod cells regenerate themselves.

The retina uses two cell types -- rods and cones -- to sense incoming light.

"Rod cells make up the majority of photoreceptors in the human eye, and disruptions in these discs' ability to grow and capture light may be at the root of a host of disabling or blinding eye diseases such as retinitis pigmentosa," explains senior author Dr. Ching-Hwa Sung, professor of cell biology in ophthalmology and professor of cell and developmental biology at Weill Cornell Medical College.

"Rod cells contain tiny organelles called the 'outer segment,' which contain about 1,000 flattened discs containing rhodopsin -- a visual pigment that absorbs light," Dr. Sung explains. "Each day, our eyes shed the top 10 percent of these discs, but until now, no one really knew how the retina generated new discs. We believe we have solved that riddle."

According to the researchers, the rod cell's outer segment is constantly pushing up and forming new discs in a bottom-up process as older discs

get shed at the segment's tip.

"There were theories as to how this might occur, but no hard evidence to back any of them up," explains lead researcher Dr. Jen-Zen Chuang, assistant professor of cell biology in ophthalmology at Weill Cornell.

In the study, the researchers used a variety of state-of-the-art techniques, including a gene-based method called "retinal transfection," to gain a more accurate picture of outer segment growth in rat retinas.

"Basically, retinal transfection means introducing different genes into the eye to switch particular cellular functions on or off," Dr. Chuang explains.

After a variety of these and other types of experiments, the team discovered that the new light-sensing discs are formed by the fusion, at the base of the outer segment, of rhodopsin vesicles.

"This fusion makes a kind of preliminary disc, and then this disc matures and grows until it joins the hundreds of other discs on the rod cell's outer segment," Dr. Sung says. "All of this happens with the help of a regulating protein called the 'Smad Anchor for Receptor Activation' (SARA)," she adds. "It's a central player in the disc-fusion process, allowing new growth to occur."

Besides rewriting the ophthalmology textbooks on retinal growth, the discovery should greatly enhance research into eye disease, the experts say.

"There are currently more than 100 retinal eye diseases in human populations, and problems with rhodopsin trafficking or outer segment development are thought to play a role in many of these potentially blinding conditions," Dr. Sung notes. "In fact, we got interested in this

type of research because we knew that breakdowns in rhodopsin trafficking were crucial to a common eye disease, retinitis pigmentosa."

Retinitis pigmentosa, a genetic disorder affecting about 100,000 Americans, is caused by the gradual death of rods and cones, triggering a progressive loss of vision.

Until now, however, little was known about rod cell regeneration, especially when it came to replacing rhodopsin-bearing discs.

"Our discovery now lays the groundwork for people to study just how many of these retinal diseases occur," Dr. Sung says. "That's why it's so important from a clinical point of view."

Source: Weill Cornell Medical Center

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