How our vision dims: Chemists crack the code of cataract creation

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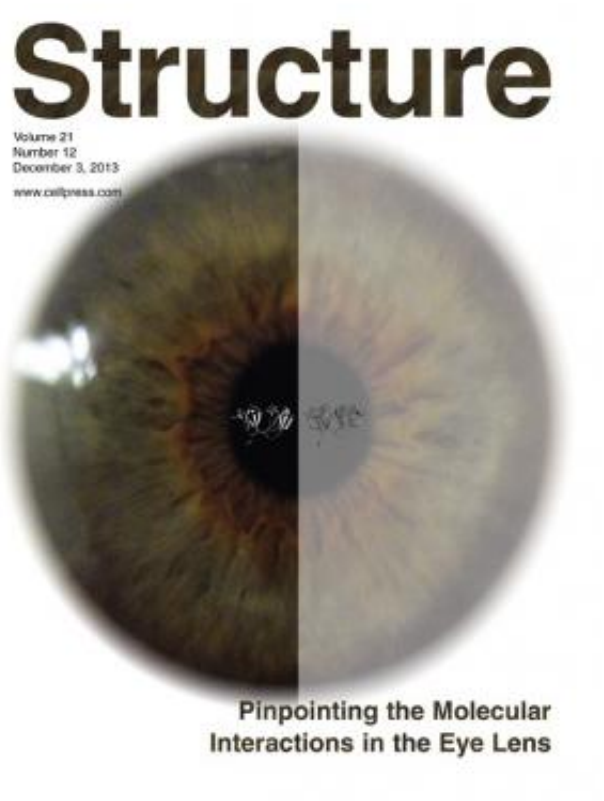

The December cover of Structure magazine. UC Irvine scientists have painstakingly identified and compared the molecular make-up and reactions of normal crystallin proteins in an eye lenses (left) and in a genetic mutation known to cause cataracts in young children (right). The work could lead to development of new treatments for the world's leading cause of blindness. Credit: Courtesy of Structure magazine

Groundbreaking new findings by UC Irvine and German chemists about how cataracts form could be used to help prevent the world's leading cause of blindness, which currently affects nearly 20 million people worldwide.

"That's the dream, and this is a big step," said Rachel Martin, UC Irvine associate professor of chemistry and co-author of a paper featured on the December cover of the journal *Structure*. "Understanding the molecular mechanism of what goes wrong in the eye that leads to a cataract could lead to the development of better treatment options, including more sophisticated artificial lenses and drugs."

It has long been known that human eyes have a powerful ability to focus because of three kinds of crystallin proteins in their lenses, maintaining transparency via a delicate balance of both repelling and attracting light. Two types of crystallin are structural, but the third – dubbed a "chaperone" – keeps the others from clumping into cataracts if they're modified by genetic mutation, ultraviolet light or chemical damage.

The UC Irvine team painstakingly explored and identified the structures of the normal proteins and a genetic mutation known to cause cataracts in young children. They found that the chaperone proteins bind far more strongly to the mutated proteins in an effort to keep the lens clear. One major problem: Every human eye contains a finite number of the helpful proteins. Once they're used up, the researchers learned, weakened ones quickly begin to aggregate and form blinding cataracts.

Now that this mechanism has been mapped at the molecular level, the team is hopeful that organic chemists can create sight-saving treatments to prevent such aggregation.

While people with adequate medical care can have corrective surgery for cataracts, the World Health Organization has found that millions suffer

major vision loss because they do not have access to laser surgery or other options. By 2019, the number of people older than 50 with impaired sight is expected to grow even higher, particularly in China, India, Southeast Asia and Eastern Mediterranean nations.

More information: www.cell.com/structure/abstrac … 0969-2126(13)00368-7

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