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Researcher's fish-eye view could offer insights for human vision

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A Purdue University student's research project related to zebrafish eye development could lead to a better understanding of vision problems that affect billions of people worldwide.

Zeran Li, as an undergraduate student in biological sciences, led a research team that uncovered an enzyme's role in the regulation of eye size in the fish. If the enzyme's role is similar in human eyes, it could be relevant to human vision problems, such as nearsightedness and farsightedness.

"New insights into the process of eye-size control in zebrafish may help our understanding of the regulation of eye size in humans," said Li, who has since graduated and is pursuing a doctorate in neuroscience at Washington University. "Vision problems occur when the size or shape of the eye changes, and what causes this is unclear. Perhaps this research will lead to a better understanding of this mechanism and the discovery of a new treatment for these problems."

These vision problems, called refractive errors, occur because the physical length of the eye from the cornea to the retina is different from the optical length. If an eye is too long or too short, light is focused in front of or behind the retina and vision is blurred, she said.

Refractive errors affect 3.8 billion people worldwide, according to the International Center for Eye Education.

Li worked in the laboratory of Yuk Fai Leung, a Purdue assistant professor of biological sciences. Leung oversaw the research and guided the team, but credits the two undergraduate students in his lab for the idea.

"The inspiration for this study came from the undergraduate students," he said. "Their observations and interpretations helped shape our current focus and allowed us to make this discovery. I'm very proud of the scientists they are becoming."

The findings are detailed in a paper in PLoS ONE. In addition to Li and Leung, paper co-authors include Purdue undergraduate student Devon Ptak, postdoctoral researchers Liyun Zhang and Wenxuan Zhong, and continuing lecturer Elwood Walls.

Zebrafish are used as a model to study development and growth problems. The zebrafish, which are named for their naturally occurring black stripes, must be made transparent to enable the careful observation and imaging necessary for the research. The most common way to achieve this transparency is to treat zebrafish embryos with a chemical called phenylthiourea that blocks the formation of black pigment, he said.

Li had previously observed that zebrafish embryos treated with the chemical have smaller eyes than untreated fish, and found that in addition to blocking pigmentation, the chemical inhibits thyroid activity.

The thyroid produces hormones that regulate metabolism and influence growth, and it was thought that a general suppression of the thyroid hormone could be causing the reduction in eye size. Li theorized that phenylthiourea might suppress thyroid hormone production because it shares the same structure as a known thyroid hormone inhibitor. She tested the effects of several different inhibitors and found that not all

had the same effect on eye growth. Only those that halted production of the enzyme thyroid peroxidase resulted in smaller eye size.

"If thyroid peroxidase has a specific role in the regulation of eye growth, it would be logical for it to express in the eye," Leung said. "Perhaps a localized manipulation of its activity in the eye could be used as a strategy to correct some vision problems. Of course, first we must learn much more about how it regulates eye size."

The findings also serve as a warning of the potential changes phenylthiourea may have on zebrafish - a widely used animal model - that could affect research results, he said.

"Our findings and others have shown that phenylthiourea can affect various aspects of physiology, so the results obtained from fish treated with it may not truly reflect what is going on inside the embryo," Leung said. "One should be cautious in interpreting their findings after phenylthiourea treatment. This discovery highlights the need to find a new way to remove pigmentation."

Leung's group attempted to find an alternative inhibitor for pigmentation, but all caused physiological problems and none were as efficient as phenylthiourea, he said.

The team plans to further investigate the relationship of thyroid peroxidase and thyroid hormone on eye growth and development.

Leung said the team also is analyzing the effects of traditional Chinese medicines considered good for vision using fish models of human retinal degeneration.

"Hopefully our efforts will expedite the discovery of novel treatments for human eye diseases," he said.

More information: www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0040132