Abnormal properties of cancer protein revealed in fly eyes

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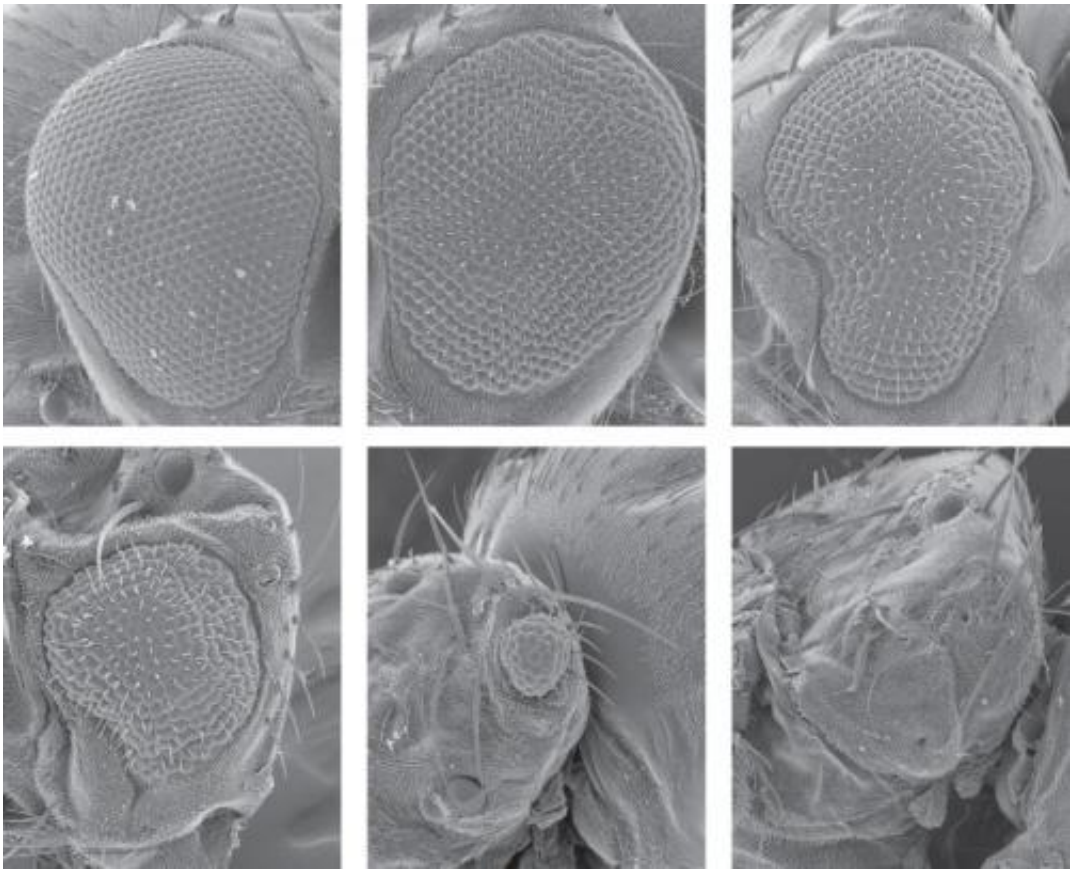

Michigan State University scientists look at fruit fly eyes to unlock the secrets of an important cancer gene. Credit: MSU

Mutations in the human retinoblastoma protein gene are a leading cause of eye cancer. Now, Michigan State University scientists have turned to fruit fly eyes to unlock the secrets of this important cancer gene.

In a paper featured on the cover of the current issue of the *Journal of Biological Chemistry*, Michigan State University researchers provide the first detailed examination of a set of mutations similar to those present in the human cancer gene, said Irina Pushel, MSU undergraduate and co-author.

"By systematically evaluating mutations of increasing severity, we now have a model to better predict how we think the protein will react with each mutation," said Pushel, who co-authored the paper with Liang Zhang, lead author and MSU graduate student, and Bill Henry and David Arnosti, MSU molecular biologists. "We're trying to understand the protein, not even in the specific context of cancer, but rather studying how it interacts within the cell, how it interacts with DNA."

The protein, retinoblastoma, would appear to play a key role in everything. When it's healthy, it helps control cell growth and development. If absent, the organism would die. In its abnormal state cells can overgrow, as seen in cancer, or undergo premature death, as in other human diseases.

Since fruit flies are essentially tiny people with wings, in terms of genetics, these model organisms can play a key role in advancing human medicine.

"If we find one of these mutations in a human, then we can predict what will happen with the protein, such as folding incorrectly," Pushel said. "This isn't going to immediately lead to a new drug to treat cancer. However, we have to know how the protein works before we can develop a drug to fix it. Future medicines will be built upon models such as this, though that is years away."

Previous work has shown that a specific part of this protein plays a role in regulating other genes. In this study, the team modified some of the

known important parts of this region of retinoblastoma.

Boosting levels of even standard, or wild-type, protein altered fruit flies eyes and wings. However, when levels of the mutated protein began to climb, deformations were consistent and dramatic.

While a cancer treatment based on this finding may be years away, the insight and understanding into cell development and gene regulation is immediate, Pushel said.

"That's the cool thing about basic research; it may not lead directly to the creation of a new drug, but it helps decipher the genetic code, which for each person controls the unique pattern of how they grow and how they develop – that's amazing," she said. "It will have many impacts, from understanding development to personalized medicine."

Provided by Michigan State University

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