Researchers use fruit flies to study proto-oncogenes

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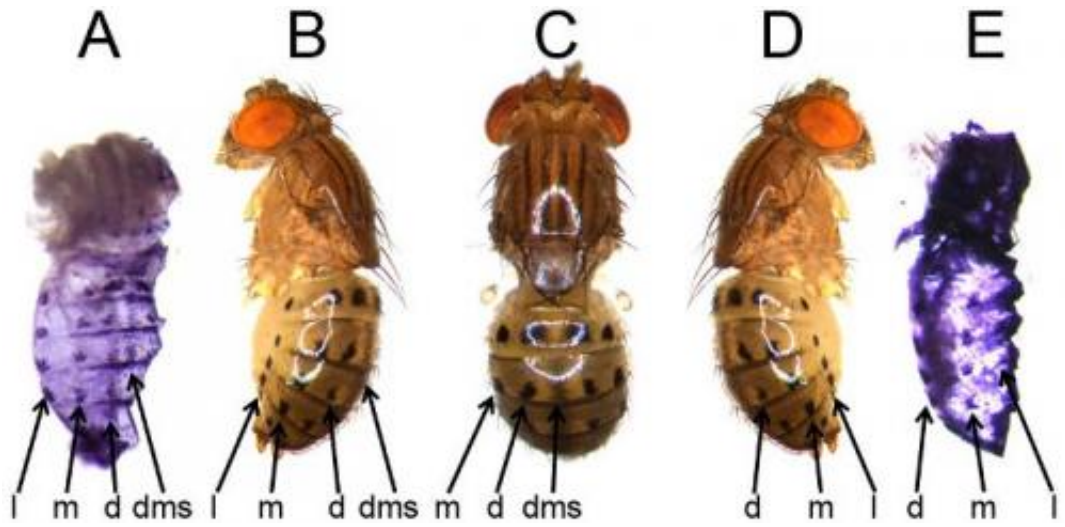

Pupae (A and E) and adult (B, C, and D) fruit flies showing lateral (l), median (m), dorsal (d), and dorsal midline shade (dms) spots.

(Phys.org)—Spots on the butts of fruit flies are really, really small. But what a researcher and his graduate student are discovering about them could be gigantic.

Thomas Werner, assistant professor of biological sciences at Michigan Technological University, and his PhD student, Komal Kumar Bollepogu Raja, have discovered that three genes that cause cancer and disease in humans also "paint" the spots on the fly's body. This discovery could enable researchers to study how those genes work in fruit flies and apply

that knowledge to treating cancer in people.

"The last common ancestor of man and fruit flies lived about 600 million years ago," says Werner. "All the genes needed to build a body were already present in that ancestor, and today we still share virtually all of our body-building genes with fruit flies. This is why we are able to study human diseases like cancer in fruit flies."

Werner and Raja are interested in how DNA encodes body forms and patterns in animals. They use color patterns as a model.

They've made strong connections between developed spots and three genes, all of which have cancer- and disease-causing counterparts in humans. Thus, the abdominal spots of this tiny fruit fly could be a great model for understanding genetic pathways that cause cancer.

"We are looking here at proto-oncogenes, which are cancer genes that cause disease when they are active in an uncontrolled manner," Werner explains. "Both humans and flies have them, and in flies they learned to paint black spots on the abdomen."

This reveals that old genes can learn new tricks; they just need to become part of a new genetic pathway, like, in this case, adding designer patterns to a boring garment. "And you get your evolutionary novelty without having to invent new genes," Werner says.

Werner's been down this research road before. He introduced stripes onto the spotted wings of fruit flies ("from a leopard to a zebra"), showing that a certain cancer gene is sufficient to induce pigment patterns on Drosophila wings, and landed on the cover of *Nature*, one of the leading scientific journals in the world.

"Now we want to use our new methods to find out how the abdominal

pigment pattern is generated, and how it is encoded in DNA," says Raja."

The genes that seem to paint the pigment spots on the abdomen are important for other reasons, Werner says. Some of them have additional roles in defining the head-to-tail axis in animals and are crucial for the proper development of the vertebrae in humans. If these genes misbehave during the development of the human embryo, gross disabilities or embryonic death will occur.

"Many diseases like cancer and vertebra-related disabilities are caused by the 'misbehavior' of genes, when they are expressed at times and places or in amounts they are not supposed to be," Werner says. "Our work focuses on understanding how the cancer- and disease-causing genes in the fruit fly are regulated, and how they regulate their downstream target genes."

The biggest promise for the future, however, involves those three "bad" genes. By studying them, Werner and Raja believe they can identify targets for gene therapies against cancer and genetically inherited developmental defects.

Targeting these genes when they start misbehaving could lead to happier and healthier tomorrows for many people: a grand result from research on miniscule flies.

Provided by Michigan Technological University