Location, location, location important for genes, too

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Cells become cancerous mainly because they lose control of their growth. To better understand how this happens, a new study at Ohio State University's Comprehensive Cancer Center looks at four genes that help regulate cell growth in embryos and that contribute to cancer in adults.

The genes – E2f1, E2f2, and E2f3a and E2f3b – are generally believed to work together to help control cell proliferation, a belief that comes from experiments using only cells. Cancer researchers at The Ohio State University carried out several studies in an animal model to learn if it is also true in the body during development.

The scientists also hoped to learn why many organisms, including humans, have multiple E2F genes of this type, while other animals have just one copy.

Their study, published in the Aug. 28 issue of the journal *Nature*, shows that mice need just one of the four genes to develop from fertilized eggs through adulthood.

"We found that if E2f3a is present, the animals can develop normally through adulthood, even when all the other genes are absent," says study leader Gustavo Leone, an associate professor of molecular virology, immunology and medical genetics at Ohio State's Comprehensive Cancer Center.

Then came the real surprise. To learn if the E2f3a gene was doing something truly critical and different from the other three E2Fs, the scientists swapped it with one of the others – they replaced it first with E2f3 gene, then with the E2f1. Neither change made any difference; these "swapped" mice developed quite normally.

"If the E2F3a gene was doing something unique, replacing it with one of the others should prevent development," Leone says. "But the animals still developed just fine.

"We conclude from this that it is the gene's location in the genome, plus the timing and level of its activity, that makes it so important during development," he says.

But if just one of the genes is sufficient for development, why are the others needed?

"Organisms above insects have multiple E2Fs, and these findings don't tell us what the others are doing," Leone says. "We surmise that the other genes are required for adult survival under the stressful conditions in the wild. We are investigating that now."

Source: Ohio State University