

PAIR OF CANCER GENES FOUND TO DRIVE BOTH CELL MIGRATION AND DIVISION

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Link suggests news ways of thinking about tumor growth and inflammation

Johns Hopkins researchers have found that two genes already known to control cell movement are also needed for proper cell division. They report their findings in the April issue of [*Developmental Cell*](#).

The researchers discovered that the two genes are required for a dividing cell's halves to separate, raising the possibility that interfering with them could be helpful in stopping the uncontrolled cell division found in cancers. Mutations in the genes, called PTEN and PI3K, already had been found in over half of all human cancers.

"In cancer, you sometimes see cells failing to divide or undergoing unequal divisions. In addition, cell migration can lead to tumors spreading and developing in different places in the body," says [Peter Devreotes](#), Ph.D., professor and director of [Cell Biology](#) at the Johns Hopkins School of Medicine's Institute for Basic Biomedical Sciences. "Now that we know that PTEN and PI3K are involved in both of these processes, it should stimulate new avenues of research in cancer."

Medicines that target PI3K or PTEN and prevent cell migration could also potentially help with inflammatory disorders, such as arthritis, since inflammation is caused when lots of immune cells move to one part of the body and cause it to swell painfully, he says.

The researchers also hope their findings will provide a bridge between two scientific fields that have traditionally kept to themselves.

"Scientists studying cell migration have focused on the front of the cell and what drives it, while cell division researchers have concentrated on the furrow within the dividing cell," says Devreotes. "But we've found that when you look at the whole cell, there are a lot of similarities between division and movement."

In normal cells, the two genes work in tandem to regulate a molecule called PIP3, which helps the cell decide where to push outward - PI3K makes PIP3 on the membrane on one side of a cell

while PTEN breaks it down on the other side. But when both enzymes are missing, levels of PIP3 remain constant throughout the membrane, and the cell can't migrate properly.

In experiments with single-celled amoebae, Devreotes and his team learned that PTEN and PI3K do the same thing to PIP3 in dividing cells. When a normal cell prepares to divide, it first doubles its genetic material, and then creates a "furrow" down the middle, cutting the cell in half. The research team noticed that the two halves of a normal dividing cell looked and acted like two cells moving away from each other.

"Essentially, the two halves are like migrating cells - PIP3 levels are high on the sides that represent the 'fronts' of what will be two new cells, and they are low at the furrow, or what amounts to the back of the new cells," says Devreotes.

In their experiments, cells without PTEN and PI3K couldn't regulate levels of PIP3, and they divided much slower than normal cells. These cells became "stuck" and accumulated many copies of their genetic material because they could do everything required for cell division except complete the split, the researchers found.

"There are ways the cell can make PIP3 even when PI3K is missing, but the major way to break it down is by using PTEN. So if PTEN isn't there to destroy PIP3 at the furrow, the halves can't pull apart," says Chris Janetopoulos, Ph.D., a research associate in Devreotes's lab and first author on the paper.

The cells' problems were eliminated when the researchers added the human PTEN gene to the mutated amoebae. Like the amoeba's own PTEN, the human version cleaned up PIP3, restoring its normal distribution within the cell. This indicates that human cells likely use the new mechanism to divide as well.

The next steps are to study the roles of the two genes in dividing cells by seeing if controlling the location of the PTEN and PI3K proteins can determine the direction in which cells divide, Devreotes says.

The research was funded by grants from the National Institutes of Health. The authors on the paper were Janetopoulos, Jane Borleis, Francisca Vazquez, Miho Iijima, and Devreotes.

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