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# Research points to new target for stopping colon cancer

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New research led by scientists at the University of North Carolina at Chapel Hill School of Medicine have found a drug target that suggests a potent way to kill colon cancers that resist current drugs aimed at blocking a molecule found on the surface of cells.

Drugs that target the epidermal growth factor receptor, or EGFR, have been used for a number of cancers. But these drugs called EGFR inhibitors, such as cetuximab, have not been very effective against colon cancer.

The new study, however, shows that drugs that target the closely related receptor ERBB3 would probably be much more effective than EGFR inhibitors at treating most colorectal cancers, said David Threadgill, Ph.D., adjunct professor in the department of genetics at UNC and lead author of the study. He also is a member of the UNC Lineberger Comprehensive Cancer Center and a professor in the genetics department at North Carolina State University.

The study is published online August 17 in the Journal of Clinical Investigation.

The researchers genetically blocked ERBB3 in a mouse model of colon cancer and in human colon cancer cell lines. "If you genetically remove ERBB3, as you would if you were pharmacologically targeting it, then the mice rarely develop colon cancer," Threadgill said.

In the human colon cancer cell lines that are resistant to EGFR inhibitors, cell death increased dramatically when ERBB3 was genetically removed. "So ERBB3 is essential for preventing colon cancer cells from dying," Threadgill said. Now Threadgill is testing a pharmacologic inhibitor to get the same anti-ERBB3 effect they achieved with genetics. "If we can use an inhibitor to block ERBB3, then it should be a very potent anti-cancer therapeutic," he said.

More broadly, the study suggests a new path for developing anti-cancer drugs.

Many cancer therapeutics, such as EGFR inhibitors, target proteins that are kinases—enzymes that initiate a cascade of signals that tell cells to reproduce. But ERBB3 is a pseudo-kinase; it functions only by binding with other proteins that have kinase activity.

"This study shows that targets that historically hadn't been considered because they don't have the typical activities of a kinase can be equally if not more important in supporting cancer cells," Threadgill said.

Source: University of North Carolina School of Medicine (news : web)