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Researchers find that protein believed to protect against cancer has a Mr. Hyde side

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In a biological rendition of fiction's Strange Case of Dr. Jekyll and Mr. Hyde, researchers from the Mayo Clinic campus in Florida and Harvard Medical School have found that a protein thought to protect against cancer development can actually spur the spread of tumors.

The scientists, reporting in the Sept. 3 issue of Molecular and Cellular Biology, found that FOXO3a, a transcription factor that regulates gene expression, becomes active when growing cancer cells begin to starve. Their research suggests that this protein then turns on molecular switches that allow the cancer cells to invade surrounding tissues.

"This is a complete reversal of what everyone thought about FOXO3a — that we should find a way to activate this transcription factor so as to fight cancer growth," says cancer biologist Peter Storz, Ph.D., the study's lead investigator from Mayo Clinic in Florida.

Findings from the study, which was funded in part by the Florida Department of Health, illustrate the growing recognition in the research community that proteins can play multiple roles with respect to tumor progression, he says.

"More and more we see that, when it comes to cancer, proteins can have split personalities," Dr. Storz says. "Proteins once firmly believed to be tumor suppressors that protect against cancer development have recently been found to act as oncogenes, or cancer promoters, in certain cancers and in some biological circumstances. We now understand that proteins

behave in different ways, depending on the cellular context."

Dr. Storz and his laboratory colleagues focus on understanding how cancer cells spread. This study builds upon a recent finding by collaborating author Alex Toker, Ph.D., associate professor, Department of Pathology, Harvard Medical School. Dr. Toker had found that Akt, a protein that protects tumor cells from programmed cell death and induces proliferation of cancer, in some circumstances also inhibits tumor cell invasion. "This is an important protein that dogma said acts as an oncogene but which Dr. Toker demonstrated could also inhibit cancer spread, and thus may act as a suppressor for metastasis," Dr. Storz says.

Because Akt is an important negative-regulator of FOXO3a, the team looked at whether FOXO3a was actually the player with the Jekyll and Hyde split personality. They found that the transcription factor does indeed revert to its dangerous persona when a cancer cell becomes starved. "Our hypothesis is that if a cancer cell doesn't get the nutrients it needs, it turns on FOXO3a, which leads to the migration and invasion of tumor cells into areas with better growth conditions," Dr. Storz says. "This data fits neatly with Dr. Toker's findings about Akt, because Akt targets FOXO3a."

Source: Mayo Clinic (news : web)