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Protein is involved with colon cancer cell's ability to invade other cells

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Understanding how the protein km23-1 enables in the spread of colon cancer may lead to new treatments for the disease, according to researchers at Penn State College of Medicine.

Previous research shows that km23-1 is involved in the movement of cancer cells and in the control of specific proteins at the leading edge of moving cells. Kathleen Mulder, professor of biochemistry and molecular biology, who discovered the protein, now says km23-1 is used in the cancer cell's ability to move out of a tumor in the early stages of invasion.

"km23-1 may be able to help in this process due to its role in the assembly of large groups of proteins favorable to cancer invasion," Mulder said.

Colorectal cancer is the third most common cancer in the United States. Tumors spreading to other parts of the body are the greatest threat to a patient's survival.

The researchers limited the amount of km23-1 available in the cells they studied, which allowed them to see how it affects cell behavior.

A reduction in km23-1 caused a decrease in the production of transforming growth factor beta (TGF-beta). In healthy cells, TGF-beta helps prevent cancer growth.

However, in cancer cells, the protein actually aids in the spread of tumors. Limiting km23-1 also blocks the activity of proteins previously shown to lead to TGF-beta production. Researchers reported their results in *PLOS ONE*.

The researchers also find that cells with less km23-1 have reduced amounts of a protein that forms a framework structure associated with the spread of cancer. This scaffolding holds together key factors that help the cancer cells move and invade to form secondary tumors.

Mulder and colleagues say that by decreasing km23-1, colon cancer cells do not spread as much. This also affects several proteins known to make a cancer cell invasive, demonstrating that km23-1 is an important potential target for cancer therapies.

The researchers also looked at another protein that influences cell survival, migration and invasion, called ERK, which has higher activity in cancer cells. Lowering the levels of km23-1, reduced ERK activation. Decreased ERK activity relates to the production of TGF-beta and cell movement.

"If we can block km23-1, we can stop the spread of colon cancer earlier," Mulder said. "But we would also affect other important functions of the protein. In order to address this issue, we are now trying to find the specific partners of km23-1 that contribute to the invasion of the cancer cells. Then we can design more precise therapeutic agents that target critical regions of km23-1 rather than eliminating the entire protein."

Researchers used a cell model that represents a unique class of colon cancer that needs further study. This model features cells that move as groups, and not singularly.

"The type of cell movement, or migration, has important implications with respect to the detection of tumor cells in the blood of cancer patients, as well as for the development of new treatments," Mulder said.

Provided by Pennsylvania State University