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Scientists take next step in understanding potential target for Ovarian cancer treatment

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A traffic cop protein in the cell may have an even more important role: transporting a messenger protein that tells components in the nucleus to stop cell growth. The discovery of this additional role may lead to diagnostic tools and earlier treatments for ovarian cancer.

A Penn State College of Medicine research team, led by Kathleen M. Mulder, Ph.D., professor of pharmacology, is studying the normal function of a protein called “km23”, the traffice cop protein, because the team previously found altered forms of the protein in 42 percent of tumor tissue samples taken from women with ovarian cancer.

No similar alterations were found in normal human tissues, suggesting that the km23 alterations may be a possible diagnostic indicator for development of ovarian cancer and that the km23 protein itself may be a possible target for cancer therapies.

km23 is part of the signaling system for a growth factor called “TGF,” which attaches to TGFß receptors at the cell membrane. It activates km23 into action.

km23 acts like a traffic cop for specific proteins as they move in the cell on a highway called a “microtubule.” It is responsible for helping to match the right cellular “cargo” with the right “motor” complex to get the cargo to the correct destination when it’s needed. One of those precious cargoes is a TGF-signaling component that must get to the cell nucleus to turn on specific genes that help stop cell growth.

“Alterations in the TGFß signaling system are known to contribute to cancer,” Mulder said. “We have been searching for new components of this signaling system to determine whether they are also altered in cancer and contribute to its development. These components can then be used to design new treatment strategies for cancer once we understand how they normally function.”

In the current study, Mulder’s team found that blocking km23 from doing its job in the TGF- signaling system disrupted the transport of the signaling component to the nucleus. Ultimately, this resulted in degradation of the signaling component and reduced gene expression in the nucleus.

The study findings were published recently in The Journal of Biological Chemistry http://www.jbc.org/cgi/reprint/282/26/19122.

The team can use the results of this kind of disruption of normal km23 function for clues about what might happen to the protein in ovarian cancer cells. Then, drug development, targeting the irregular function of the protein, can begin.

“Our studies provide a better understanding of how the protein works, what it does, and how its functions may be altered in cancer cells. This leads us to the critical next step -- the design of drugs that can repair the defect in the cancer cells without interrupting the processes of the normal cell,” Mulder said. “When you find something that isn’t working right in the cancer cells, it suggests possibilities as to how to intervene to fix the problem.”

Epithelial ovarian cancer is often diagnosed at an advanced stage and accounts for about 15,000 deaths each year. Despite advances in surgical techniques and chemotherapy, overall survival rates have not improved significantly because of late detection, often after the disease has already

spread to remote organs. Identification of an early warning signal and a new therapeutic agent for the disease should lead to improved survival rates.

Source: Penn State