Motor protein may offer promise in ovarian cancer treatment

26 April 2011

(Medical Xpress) -- A motor regulatory protein can block human ovarian tumor growth, leading to eventual cancer cell death and possible new therapies to treat the disease, according to Penn State College of Medicine researchers.

Among U.S. women, an estimated 21,880 new cases and 13,850 deaths occurred in 2010 from epithelial ovarian cancer, one of the most common forms of ovarian cancer and the most lethal gynecologic cancer in women.

Previously, Kathleen M. Mulder, Ph.D., professor, biochemistry and molecular biology, along with members of her laboratory, learned that km23-1 -- a protein -- is defective in nearly half of all ovarian cancer patients. In the current study, researchers induced over-expression of km23-1 in human ovarian cancer cells placed in mice, causing the cells to produce large amounts of the normal protein.

km23-1 is a subunit of dynein, a motor protein that transports cargo along paths in the cell called microtubules. The dynein motor has many jobs in the cell, including major roles in cell division.

"Although microtubule-binding agents, such as the drug paclitaxel, are being used in the treatment of ovarian cancer, drug resistance has significantly limited their efficacy," Mulder said. "It is critical to develop novel, targeted therapeutics for ovarian cancer. Motor protein regulatory agents may offer promise for providing improved efficacies with reduced side effects in the treatment of ovarian cancer and other human malignancies."

Nageswara Pulipati, Ph.D., postdoctoral fellow in Mulder's lab, said, "We used a method to cause the tumors to express high levels of normal km23-1, but only in the experimental group of mice. Compared to the control group, the tumors were much smaller when km23-1 was over-expressed."

Findings were reported online and will appear in an upcoming edition of The International Journal of Cancer.

"The dynein motor protein is needed to transport checkpoint proteins along the microtubules during mitosis. However, when km23-1 levels are high, at least one checkpoint protein, BubR1, is not transferred properly," said Qunyan Jin, M.D., research associate in Mulder's lab.

During the cell division process, several checkpoints exist where specific proteins put a hold on cell division until proper completion of a specific step can be verified. When km23-1 is over-expressed, a checkpoint is stalled during mitosis -- the stage in the cell division process that normally facilitates equal splitting of the chromosomes into two identical groups before the mother cell splits into two daughter cells.

"Normally, if everything is correct at this checkpoint, the cell then goes on to divide," Mulder said. "However, with the over-expression of km23-1, the checkpoint stays on and cell division does not proceed normally, which leads to a slow cell death."

Mulder and her lab team will now look at how the over-expression of km23-1 may be mimicked to target km23-1, using nanotechnology to deliver a drug to the cancer cells, and how this approach may possibly be used in humans.

Provided by Pennsylvania State University