MedicalXpress

Researchers identify potential new target for ovarian cancer

August 16 2010

For the first time, Salt Inducible Kinase 2 (SIK2) has been found to play a critical role in cell division and to regulate the response of some ovarian cancers to chemotherapy.

Findings were reported by researchers from The University of Texas MD Anderson Cancer Center in the August issue of *Cancer Cell*. The study adds to growing evidence that combination therapies targeting different phases of the cell division cycle are vital for optimal cancer treatment.

Researchers found that depleting SIK2 from ovarian cancers sensitized the cancer cells to paclitaxel, a commonly prescribed chemotherapeutic agent that inhibits cell division, making the drug more effective in stopping the cancer's growth. Levels of the SIK2 protein are increased in approximately 30 percent of ovarian cancers and are associated with poorer survival in women with the disease.

"There is a large window of opportunity to improve the effectiveness of existing chemotherapies by modifying the sensitivity of cancer cells to the drugs," said study senior author Robert C. Bast, Jr., M.D., vice president for translational research at MD Anderson. "In our search for proteins that are responsible for that sensitivity, we found that SIK2 was required for cell division and that its inhibition offers a novel approach to improving chemotherapy for ovarian cancer that deserves further study."

Although mitosis-inhibiting drugs are used successfully to treat a range of cancers, only about 50 percent of ovarian cancer patients respond to taxanes and it is not yet possible to identify in advance which patients will benefit. As a result, many patients receive taxanes arbitrarily as part of a combination of chemotherapy drugs.

SIK2 role in regulating cell division previously unknown

Bast and first author Ahmed Ashour Ahmed, M.D., Ph.D., a former postdoctoral fellow in Bast's lab who is now a member of the faculty at Oxford University, analyzed nearly 780 pools of siRNAs to identify proteins that alter sensitivity to paclitaxel. SIK2, a previously described member of the "AMPK" family of kinases that are active in resting cells, was found to regulate sensitivity to paclitaxel and to prevent division after doubling of DNA during proliferation of cancer cells. SIK2 was found in the cell centrosomes, which must split in order to direct distribution of chromosomes into each daughter cell.

"The discovery that SIK2 plays a role in cell cycle regulation is groundbreaking since to date it has been linked to cellular metabolism and energy balance," Ahmed said. "In addition to improving the response of some cancer to taxane, our findings add support to emerging evidence that cancer cell metabolism and mitosis functions are coupled."

According to researchers, drugs that inhibit SIK2 are needed to permit future clinical studies. Such drugs do not yet exist but knowing the right target is an important first step.

Provided by University of Texas M. D. Anderson Cancer Center