Expression of Proteins Linked to Poor Outcome in Women with Ovarian Cancer

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(PhysOrg.com) -- Scientists have established the presence of certain proteins in ovarian cancer tissues and have linked these proteins to poor survival rates in women with advanced stages of the disease. The study, led by scientists at the National Cancer Institute (NCI), part of the National Institutes of Health, appears in *Cancer* online, April 19, 2010.

The proteins in question belong to the nuclear factor kappa Beta (NF-kB) family. NF-kB controls many processes within the cell including cell survival and proliferation, inflammation, immune responses, and cellular responses to stress.

"This study sheds light on the distinctive genetic features of the NF-kB pathway and may provide targets for the development of novel therapies for ovarian cancer," said lead investigator, Christina M. Annunziata, M.D., Ph.D., associate clinical investigator, Medical Oncology Branch.

Abnormalities in NF-kB signaling have been found in several types of cancer, including ovarian cancer, but the mechanism and importance of such alterations in ovarian cancer was not defined. To address these knowledge gaps, the research team investigated the expression of NF-kB-related proteins in the cells of tumor tissue obtained at surgery from 33 previously untreated women who were newly diagnosed with advanced epithelial ovarian cancer. The patients had similar stage (all late stage), grade, and type of disease. All patients were treated with a three-drug regimen of standard chemotherapy agents in an NCI clinical trial that was conducted at the NIH Clinical Research Center.

To assess NF-kB family members and associated proteins in ovarian tumor cells, the scientists used immunohistochemistry, a method that uses antibodies — a type of protein that the body's immune system produces when it detects harmful substances — to identify specific molecules in tissue specimens. Subsequently, they looked for associations between the percentage of tumor cells in individual proteins and patient outcomes.

The data revealed that the presence of one NF-kB family member—p50—in more than one-quarter of the cells was associated with poor survival. Low-frequency or nonexpression of a target gene, matrix metallopeptidase 9 (MMP9), was also associated with poor prognosis. Further, the team identified two NF-kB family members—p65 and RelB—and a protein called IKKa that plays a role in promoting inflammation, that were frequently expressed in the same cells, providing more evidence that NF-kB is active in some ovarian cancers. It is possible that the NF-kB activity in these cancers could increase their growth and/or resistance to treatment.

"This work continues to define and characterize the biological relevance of NF-kB activity in ovarian cancer by translating research findings with ovarian cancer cells in the laboratory to ovarian cancer in women at the time of initial diagnosis," said Annunziata.

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