Possible ovarian cancer treatment target identified

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A multi-institutional study has identified a potential personalized treatment target for the most common form of ovarian cancer. In the December 8 issue of *Cancer Cell*, the research team describes finding that a gene called MAGP2 - not previously associated with any type of cancer - was overexpressed in papillary serous ovarian tumors of patients who died more quickly. They also found evidence suggesting possible mechanisms by which MAGP2 may promote tumor growth.

"Ovarian cancer is typically diagnosed at an advanced stage when it is incurable, and the same treatments have been used for virtually all patients," says Michael Birrer, MD, PhD, director of medical gynecologic oncology in the Massachusetts General Hospital (MGH) Cancer Center, the study's corresponding author. "Previous research from my lab indicated that different types and grades of ovarian tumors should be treated differently, and this paper now shows that even papillary serous tumors have differences that impact patient prognosis." Birrer was with the National Institutes of Health when this study began and joined the MGH Cancer Center in 200?.

The fifth most common malignancy among U.S. women, ovarian cancer is expected to cause close to 15,000 deaths during 2009. Accounting for 60 percent of ovarian cancers, papillary serous tumors are typically diagnosed after spreading beyond the ovaries. The tumors typically return after initial treatment with surgery and chemotherapy, but while some patients die a few months after diagnosis, others may survive five years or longer while receiving treatment.

To search for genes expressed at different levels in patients with different survival histories, which could be targets for new treatments, the researchers conducted whole-genome profiling of tissue samples that had been microdissected - reducing the presence of non-tumor cells - from 53 advanced papillary serous ovarian tumors. Of 16 genes that appeared to have tumor-associated expression levels (is there a better way to describe the other genes in figure 1B?), only expression of theThe gene for microfibril-associated glycoprotein 2 (MAGP2) had the strongest correlation with was clearly correlated with reduced patient survival.

Further analysis confirmed that MAGP2 expression was elevated in another group of malignant ovarian tumors but not in normal tissue. The gene's expression was also reduced in patients whose tumors responded to chemotherapy. Recombinant expression of MAGP2 in samples of the endothelial cells that line blood vessels caused the cells to migrate and invade other tissues, which combined with the observation that MAGP2-rich tumors have increased microvessel density suggests a potential role for the protein in the growth of a tumor's blood supply.

"By confirming that different ovarian tumors have distinctive gene signatures that can predict patient prognosis, this study marks the beginning of individualized care for ovarian cancer," says Birrer, a professor of Medicine at Harvard Medical School. "MAGP2 and the biochemical pathways it contributes to are definitely targets for new types of therapies, and we plan to pursue several strategies to interfere with tumor-associated pathways. But first we need to validate these findings in samples from patients treated in clinical trials."

Source: Massachusetts General Hospital (news : web)