Researchers identify genes that may help in ovarian cancer diagnosis and prognosis

9 April 2012

Scientists from Duke University Medical Center have determined that genes acting as molecular "on/off" switches can define clinically relevant molecular subtypes of ovarian cancer, providing ideal potential targets for use in clinical prognostic and diagnostic testing. These bimodal genes can define tumor subtypes that have different overall prognoses and respond to different therapeutic regimens. The researchers' results are published in the May issue of *The Journal of Molecular Diagnostics*.

"We identified a very small set of genes that have the potential to be robust prognostic markers in epithelial ovarian cancer," explains lead investigator Michael B. Datto, MD, PhD. "We also demonstrated the utility of a novel approach, bimodal gene discovery, in identifying clinically relevant expression targets."

Ovarian carcinoma has the highest mortality rate among gynecologic malignancies and is the fifth most common cause of cancer death in women. Prognostic methods for serous carcinomas, the most common type of epithelial ovarian malignancy, remain relatively inaccurate. The majority of patients present with high-grade, late-stage tumors and have an overall poor prognosis. Within this group, however, there is a subset with durable response to chemotherapy, resulting in better survival. There are currently no tests in general use that can distinguish tumors that may be more effectively treated.

Based on early work in breast cancer, Dr. Datto and his colleagues hypothesized that clinically relevant bimodal genes exist in epithelial ovarian cancer. Using a large, publically available ovarian cancer microarray dataset, they applied a previously described biomodal index discovery algorithm to evaluate the expression of all genes across 285 samples. They identified many genes with robust patterns of bimodal expression. They also found that a number of genes with bimodal expression patterns are significantly associated with tumor type and/or overall patient survival. When combined into a single sum survival score, the top survival-significant genes identify a clinically distinct molecular subtype of malignant serous ovarian carcinoma.

"From a clinical testing perspective, genes with a continuous pattern of expression can make difficult testing targets. However, the distinction between 'on' or 'off' expression for a particular bimodal gene is relatively straightforward," says Dr. Datto. "This allows clear-cut decision making boundaries and development of precise, reliable testing methods. Bimodal genes may also be candidates for testing by less quantitative methods such as immunohistochemistry."

Several of the bimodal genes that the researchers identified have known roles in tumorigenesis. "This raises the possibility that we have described molecular switch genes that will not only be relevant in the context of ovarian carcinoma, but across multiple tumor types," Dr. Datto concludes.

More information: "Genes with Bimodal Expression Are Robust Diagnostic Targets that Define Distinct Subtypes of Epithelial Ovarian Cancer with Different Overall Survival," by D.N. Kernagis, A.H.S. Hall, and M.B. Datto. DOI: 10.1016/j.jmoldx.2012.01.007. *The Journal of Molecular Diagnostics*, Volume 14, Issue 3 (May 2012)

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