Defining Women at High Risk of Ovarian Cancer

To the Editor:

We read with interest the article by Dr. Pejovic et al. (1) on cytogenetic instability in cultured ovarian epithelial cells from a small number of women at high risk of ovarian cancer. In studies of this sort, the definition of high risk is critical, but risk details for each of the five “high-risk” women in this study were not provided, including pedigree and genetic testing information. The authors state that “mutation screening for BRCA1 and BRCA2 cannot accurately identify at-risk patients who are members of ovarian cancer families.” We dispute that statement; although a significant proportion of families affected only with breast cancer are not explained by BRCA1 or BRCA2 mutations, the presence of ovarian cancer is highly predictive of linkage to BRCA1 and BRCA2 (2) and of the presence of cryptic mutations in BRCA1 and BRCA2 when DNA sequencing has failed to identify mutations (3). Moreover, the risk of ovarian cancer is not significantly elevated in breast cancer–only families with negative BRCA1 and BRCA2 testing (4). Thus, a woman with breast cancer, one relative with breast cancer, and negative BRCA1 and BRCA2 testing would meet the definition of “high risk” in this study but would actually be at low future risk of ovarian cancer. The fact that four of the five “high-risk” patients were negative for BRCA1 and BRCA2 mutations is more suggestive of lack of risk than confirmation of the infrequency of BRCA1 and BRCA2 mutations in high-risk women.

Importantly, normal ovarian epithelial cells are not vigorous in culture, tolerating few passages before senescence. How soon after establishment of cultures were the assays done and did cytogenetic assessment vary based on length of time in culture? How was epithelial purity documented and mycoplasma contamination excluded? The authors provide some provocative findings, but it is premature to suggest that the assay could be a screening tool to define ovarian cancer risk. To verify that their assay is in fact predictive of ovarian cancer risk, the authors should test the assay on ovarian cultures from women with the highest known ovarian cancer risk, those with inherited BRCA1 mutations. In the meantime, we should continue to encourage women from high-risk families to seek genetic counseling and risk assessment from specialists in cancer genetics (5).

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References
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