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References

1 Roh MH, Lassin Y, Miron A, *et al.* High-grade fimbrial-ovarian carcinomas are unified by p53, PTEN and PAX2 expression. Mod Pathol 2010;23:1316–1324.
2 Hernandez E, Bhagavan BS, Parmley TH, *et al.* Interobserver variability in the interpretation of epithelial ovarian cancer. Gynecol Oncol 1984;17:117–123.
3 Lund B, Thomsen HK, Olsen J. Reproducibility of histopathological evaluation in epithelial ovarian carcinoma. Clinical implications. APMIS 1991;99: 353–358.
4 Stalsberg H, Abeler V, Blom GP, *et al.* Observer variation in histologic classification of malignant and borderline ovarian tumors. Hum Pathol 1988;19: 1030–1035.
5 Sakamoto A, Sasaki H, Furusato M, *et al.* Observer disagreement in histological classification of ovarian tumors in Japan. Gynecol Oncol 1994;54:54–58.
6 Madore J, Ren F, Filali-Mouhim A, *et al.* Characterization of the molecular differences between ovarian endometrioid carcinoma and ovarian serous carcinoma. J Pathol 2010;220:392–400.
7 Schwartz DR, Kardia SL, Shedden KA, *et al.* Gene expression in ovarian cancer reflects both morphology and biological behavior, distinguishing clear cell from other poor-prognosis ovarian carcinomas. Cancer Res 2002;62:4722–4729.
8 Al-Hussaini M, Stockman A, Foster H, *et al.* WT-1 assists in distinguishing ovarian from uterine serous carcinoma and in distinguishing between serous and endometrioid ovarian carcinoma. Histopathology 2004;44:109–115.
9 Gilks CB, Ionescu DN, Kalloger SE, *et al.* Tumor cell type can be reproducibly diagnosed and is of independent prognostic significance in patients with maximally debulked ovarian carcinoma. Hum Pathol 2008;39:1239–1251.
10 Soslow RA. Histologic subtypes of ovarian carcinoma: an overview. Int J Gynecol Pathol 2008;27:161–174.
11 McCluggage WG. My approach to and thoughts on the typing of ovarian carcinomas. J Clin Pathol 2008;61: 152–163.
12 Gilks CB, Prat J. Ovarian carcinoma pathology and genetics: recent advances. Hum Pathol 2009;40:1213–1223.
13 Tavassoli FA, Devilee P. (eds). World Health Organization Classification of Tumours: Pathology and Genetics of Tumours of the Breast and Female Genital Tract. IARC Press: Lyon, France,, 2003.
14 Köbel M, Kalloger SE, Baker PM, *et al.* Diagnosis of ovarian surface epithelial carcinoma cell type is highly reproducible: a transcanadian study. Am J Surg Pathol 2010;34:984–993.
15 Press JZ, De Luca A, Boyd N, *et al.* Ovarian carcinomas with genetic and epigenetic BRCA1 loss have distinct molecular abnormalities. BMC Cancer 2008;8:17.
16 Gelmon K. Serous Ovarian Cancer, But Not Triple-negative Breast Cancer, Responds to Monotherapy with the PARP Inhibitor Olaparib. American Society of Clinical Oncology Annual Meeting: Chicago, 2010.

Response to Gilks *et al*

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To the Editor: The crux of this letter is a disagreement with the term 'high-grade endometrioid carcinoma'. First, the authors point out that the diagnosis is not easily reproduced between pathologists. Second, they state that the molecular data indicate very little difference between high-grade endometrioid and high-grade serous carcinomas.[1] Third, they perceive that continued use of the term 'high-grade endometrioid' will create confusion that will be detrimental to patient care. Fourth, they imply that the differences in the frequencies of two parameters—tubal intraepithelial carcinoma and dominant ovarian mass—in cases of high-grade serous and endometrioid carcinomas are insufficient reason to separate them.

We agree with the first two statements and anyone who properly reads the paper by Roh *et al*[2] should arrive at the same conclusion. Each case of high-grade muellerian carcinoma analyzed in our study was re-reviewed and re-classified into three categories in recognition of the problem of subclassifying these tumors. It should be obvious that we performed this study to determine whether differences existed between the histological groups. In fact, the summary statement in the abstract applies the term 'high-grade muellerian carcinoma' to this group of tumors. Using this term in practice addresses the third argument by making it clear to the oncologist that the tumor is not a low-grade endometrioid adenocarcinoma. Because these high-grade malignancies are typically high-stage when diagnosed, patients will not be harmed by this terminology.

But women who must deal with this disease, either directly or indirectly, and the field of ovarian cancer research in general, would be ill served by premature efforts to increase reproducibility by ignoring histological variation. In our study, we found only one tubal intraepithelial carcinoma in 12 cases of high-grade endometrioid carcinoma, which

does not endorse a common origin for both high-grade serous and endometrioid carcinomas.[2] However, some authors imply that all serous carcinomas come from the fimbria and a recent report suggests that fimbriectomy alone will eliminate the risk of pelvic serous cancer.[3,4] Do they know for certain that this protection will extend to all of the tumors in this proposed amalgam of high-grade serous cancer? We also disagree with the notion that ovarian involvement by a high-grade serous tumor confers 'endometrioid' histology. Endometrioid histology can be seen at any tumor site. Parenthetically, in our experience, about 15% of carcinomas in women with *BRCA1* or *BRCA2* mutations are high-grade endometrioid carcinomas. Some can even be traced to the fallopian tube, yet have distinctly different p53 expression patterns relative to their serous counterparts.[5] Having progressively developed this concept of tubal carcinogenesis, we would like nothing more than to see all high-grade muellerian carcinomas traced to the fimbria.[6] However, the data, even from studies that carefully evaluate the fallopian tubes, leave significant gaps.[3,7,8]

The transcriptomes, immunophenotypes, stages at presentation, and responses to therapy of high-grade muellerian carcinomas underscore their similarities in an era of imperfect prevention, detection and therapy.[1,2] Going forward, the success of efforts to prevent a given malignancy could hinge on where it originates from and its differentiation pattern. Call them all high-grade muellerian carcinomas if you wish to be consistent in clinical practice, but be ever mindful of nuances in pathology. Nuances can have powerful implications, and their recognition and translation define our discipline.

Disclosure/conflict of interest

The authors declare no conflict of interest.

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References

1 Madore J, Ren F, Filali-Mouhim A, *et al.* Characterization of the molecular differences between ovarian endometrioid carcinoma and ovarian serous carcinoma. J Pathol 2010;220:392–400.
2 Roh MH, Yassin Y, Miron A, *et al.* High-grade fimbrial-ovarian carcinomas are unified by altered p53, PTEN and PAX2 expression. Mod Pathol 2010;23: 1316–1324.
3 Przybycin CG, Kurman RJ, Ronnett BM, *et al.* Are all pelvic (nonuterine) serous carcinomas of tubal origin? Am J Surg Pathol 2010;34:1407–1416. [Published erratum appears in Am J Surg Pathol. 2010;34:1891].
4 Leblanc E, Narducci F, Farre I, *et al.* Radical fimbriectomy: A reasonable temporary risk-reducing surgery for selected women with a germ line mutation of BRCA 1 or 2 genes? Rationale and preliminary development. Gynecol Oncol 2011 (in press).
5 Medeiros F, Muto MG, Lee Y, *et al.* The tubal fimbria is a preferred site for early adenocarcinoma in women with familial ovarian cancer syndrome. Am J Surg Pathol 2006;30:230–236.
6 Mehra K, Mehrad M, Ning G, *et al.* STICS, SCOUTs and p53 signatures; a new language for pelvic serous carcinogenesis. Front Biosci (Elite Ed) 2011;3:625–634.
7 Kindelberger DW, Lee Y, Miron A, *et al.* Intraepithelial carcinoma of the fimbria and pelvic serous carcinoma: evidence for a causal relationship. Am J Surg Pathol 2007;31:161–169.
8 Carlson JW, Miron A, Jarboe EA, *et al.* Serous tubal intraepithelial carcinoma: its potential role in primary peritoneal serous carcinoma and serous cancer prevention. J Clin Oncol 2008;26:4160–4165.