Abstract

Objectives
It has been shown that cytologic nuclear atypia can be a predictor of poor prognosis in endometrial cancers. Endometrial cancers with high-grade nuclei, such as endometrial serous adenocarcinomas, clear cell carcinoma, uterine carcinosarcoma, have been shown to have a worse prognosis compared to tumors with low nuclear grade, such as FIGO grade I endometrioid endometrial carcinoma. In this study, we investigated whether we could find markers associated with nuclear atypia in endometrial cancers.

Methods
A total 29 cases of endometrial cancer were extracted. The slides were reviewed by a pathologist, and the tumor nuclei were graded from 1 to 3 based on the degree of atypia present. The slides were stained with TOP2a (3F6, 1:20 dilution, Abnova) antibodies. Staining of more than 10% of cells with +1 intensity was considered positive for TOP2a. TP53 mutation status was determined by a next generation sequencing panel. The association of the results with nuclear grade was determined using χ² test and multinomial logistic regression.

Results
Of 29 cases, 18 had grade 3 nuclei, six had grade 2 nuclei, and five had grade 1 nuclei. The cases consisted of seven serous carcinomas, seven carcinosarcomas, 10 endometrioid carcinomas, two clear cell carcinomas, and one mixed serous and endometrioid carcinoma. Ten of 29 cases had TP53 mutation, and 22/29 cases were positive for TOP2a. Both univariate and multivariate analysis showed that TP53 mutation and TOP2a expression are significantly associated with high-grade nuclear atypia (P values .006 and .004 respectively).

Conclusion
TP53 mutation is more common in endometrial cancers known to have worse prognosis and high nuclear grade (uterine serous carcinoma and uterine carcinosarcoma). TOP2a expression is known to be a predictor of poor prognosis in tumors such as breast cancer. We have shown that these two markers are associated with high nuclear grade in endometrial cancers (irrespective of tumor subtype). More work is needed to elucidate whether tumor markers and nuclear cytomorphology can be better predictors of outcome than tumor subtype.