Commentary

Cervix endometrial cancer human papilloma virus

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ABSTRACT

The decreasing costs of next generation sequencing technologies and greater acceptance of molecular and biologic findings into the pathology domain, have shifted our paradigms of classification for many gynecologic tumors.

Introduction

The decreasing costs of next generation sequencing technologies and greater acceptance of molecular and biologic findings into the pathology domain, have shifted our paradigms of classification for many gynecologic tumors.

Molecular information is increasingly used for typing of neoplasms, risk assessment and directing cancer treatment. This review highlights recent developments in the molecular stratification of endometrial carcinoma, endocervical adenocarcinoma, vulvar carcinoma and selected uterine sarcomas.

Uterine sarcomas

The incorporation of RNA-sequencing technologies in advanced clinical laboratories have resulted in a fusillade of findings in the realm of uterine sarcomas.

Endometrial carcinoma

Endometrial carcinoma (EC) is the most common gynecological malignancy in the developed world with increasing annual incidence and mortality rates in North America. Similar to the progress made in breast cancer, where subtyping integrates molecular information for stratification, molecular subtyping of EC has emerged as a priority in the gynecological oncology sphere.

The Cancer Genome Atlas (TCGA): in 2013, the Cancer Genome Atlas (TGCA) published a comprehensive genomic analysis of EC (endometrioid, serous and mixed histotypes, n = 373). The TCGA described four prognostically distinct groups, characterized by tumour mutational burden and somatic copy number alterations: i) ultra-mutated EC with DNA polymerase epsilon (POLE) mutations in the exonuclease domain (POLE EDM), ii) Hypermutated EC with microsatellite instability (MSI), iii) low mutation rate EC with low frequency of DNA copy-number alterations (CN-L), and iv) low mutation rate EC but with high-frequency of DNA copy-number alterations (CN–H). In terms of somatic mutations, ultramutated EC were enriched in ARID1A (>70%), FBXW7 (>80%), KRAS (>50%), and PI3K pathway (>70%) mutations, hypermutated EC had the highest RPL22 (>40%), CN-L EC had the highest CTNNB1 (>50%) and CN–H EC had the highest TP53 (>90%) and lowest frequency of PTEN (<10%) mutations.1 The TCGA also revealed that molecularly distinct ECs exhibited overlapping histologic features, as well as vice versa, that biologically similar EC can have varied morphologic appearances.

In a review of the major molecular findings in gynecologic pathology, we would be remiss not to mention the recent molecular findings in UTROSCT, at least briefly.