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"Use of DNA Methylation Markers to Predict Cervical Dysplasia Outcomes"

OBJECTIVES: This study aims to use established DNA methylation markers that have been shown to be dysregulated in cervical cancer for the purpose of creating an at home test meant to identify the necessity of treatment in patients with human papillomavirus (HPV)-associated cervical dysplasia, reducing overtreatment.

BACKGROUND: Each year, approximately 3 million U.S women are diagnosed with HPV-associated low grade cervical dysplasia. Most individuals with this diagnosis will resolve it naturally; however, a few women will progress to high-grade dysplasia which increases their risk of developing cervical cancer. There is currently no diagnostic test to predict which women will progress and which will clear the HPV infection and resolve dysplasia on their own. A panel of 6 DNA methylation markers has been shown to differentially detect high grade dysplasia and cervical cancer from low-grade dysplasia. We hypothesize this methylation panel will be able to predict patients' prognosis and distinguish patients who require early intervention treatment among women who test positive for HPV.

METHODS: Archived cytology specimens (Pap tests) from 26 women attending the cervical colposcopy clinic at University Medical Center were included in this pilot study. For HPV genotyping, DNA was extracted using the Qiamp DNA Blood Mini Kit. A dual human β-Globin/HPV PCR was performed to determine sample quality (amplification of human DNA) and detect HPV infection. Samples positive for HPV were genotyped by Roche Linear Array. A second DNA extraction was performed following bisulfite treatment of the cytology specimens. DNA methylation detection was performed by qPCR using the GynTect assay and scored according to GynTect diagnostic criteria. Data was analyzed to determine the relation between GynTect positives, HPV detection, and severity of dysplasia.

RESULTS: All 26 specimens were adequate for HPV testing. 13 of these samples (50%) were positive for HPV. High-risk HPV (hr-HPV) was identified in 9 samples (69%). The most common hr-HPV detected were types 16, 58, and 66. Cytology data shows no association between hr-HPV, low-risk HPV, and LSIL. HSIL diagnosis was associated with hr-HPV. Of the 26 samples tested, 9 (35%) were scored as GynTect positive. The majority (44%) of patients who scored positive also had hr-HPV. DNA methylation had 100% detection for patients with HSIL.

CONCLUSIONS: The Gyntect DNA methylation panel is a promising diagnostic tool that can detect high grade dysplasia and cervical cancer. Its ability to predict outcomes of low-grade cervical dysplasia has yet to be examined. We expect that patients who tested positive for DNA methylation will have progressive cervical dysplasia.