

Inicio > Methylation of twelve CpGs in human papillomavirus type 16 (HPV16) as an informative biomarker for the triage of women positive for HPV16 infection.

Methylation of twelve CpGs in human papillomavirus type 16 (HPV16) as an informative biomarker for the triage of women positive for HPV16 infection. ^[1]

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Abstract

An accurate biomarker for the follow-up of women positive for human papillomavirus type 16 (HPV16) DNA may improve the efficiency of cervical cancer prevention. Previously, we analyzed all 113 HPV16 CpGs in cervical cytology samples and discovered differential methylation at different stages of premalignancy. In the current study, we identified a methylation biomarker consisting of a panel of 12 HPV16 CpG sites in the E5, L2, and L1 open reading frames, and tested whether it fulfilled three necessary conditions of a prospective biomarker. A total of 33 cytology samples from North American and West African women with all grades of cervical intraepithelial neoplasia (CIN) and invasive cervical cancer (ICC) were analyzed by using DNA bisulfite sequencing. The results showed (i) a highly significant trend for increasing HPV16 biomarker methylation with increasing histologic severity ($P < 0.0001$), (ii) 100% sensitivity for ICC over a wide range of methylation cutoff scores; 80% detection of CIN3 at cutoff scores up to 39% methylation, and (iii) substantially lower detection of CIN2, from 0% to 71%, depending on the cutoff score. Our results support the prognostic potential of the HPV16 methylation biomarker for the triage to colposcopy of women with HPV16-positive screening tests and, eventually, for the management of women with HPV16-positive CIN2.

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