

# HPV mRNA AND p16INK4a AS TRIAGE MARKERS IN CERVICAL CYTOLOGY

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**Background:** Cervical cancer screening is hampered by the low sensitivity of Pap cytology for the detection of cervical precancer. While HR-HPV DNA detection has a higher sensitivity to detect precancer, it cannot discriminate between transient and transforming HPV infections and therefore has limited specificity. Therefore, research on novel biomarkers is warranted to improve current screening algorithms.

**Objectives:** We evaluated two novel biomarkers for transforming HPV infections, HPV E6/E7 mRNA detection and p16 immunocytology in patients with abnormal cervical cytology.

**Methods:** 277 liquid based cytology specimens (PreservCyt, Cytoc) were collected from patients referred to colposcopy due to abnormal cytology and from patients during follow-up after previous treatment for cervical dysplasia. The APTIMA HPV E6/E7 mRNA test (Gen-Probe) was performed and Thinprep slides were stained with the CINtec p16 cytology test (mtm Laboratories). p16 staining was assessed according to a previously described nuclear scoring algorithm. In addition HR-HPV DNA was detected by the Hybrid Capture 2 assay (HC2) (Qiagen) from the same PreservCyt vial. 35% of the patients had CIN3 or worse in a punch biopsy or cone tissue, 23.9% had CIN2, 12.2% CIN1 and the remaining were disease negative. We compared assay performance to detect histology proven CIN2 or greater (CIN2+) and CIN3 or greater (CIN3+).

**Results:** All assays yielded a comparable sensitivity for the detection of CIN3+ (96.9% for APTIMA, 96.7% for CINtec, 96.8% for HC2). Clinical specificity for CIN3+ was 50.6% for APTIMA, 57.6% for CINtec and 40.4% for HC2. Sensitivity/specificity for the detection of CIN2+ was 89.6%/67.5% for APTIMA, 85.5%/74.2% for CINtec and 93.5%/55.9% for HC2.

**Conclusions:** Our results suggest that HPV mRNA detection and p16 cytology can increase the specificity for the detection of high risk lesions in a cervical disease enriched population with similar sensitivity that is achieved by HR-HPV DNA detection.