



ADVANCES IN CERVICAL SCREENING: SELF-COLLECTION AND MOLECULAR TESTING

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Cytology-based cervical screening programmes have proven to be effective in decreasing the incidence of and mortality from cervical cancer, however the effects have levelled off. Main reasons are incomplete participation to screening and suboptimal performance of the screening assay. Therefore, over the last decades, efforts to improve screening have focused on increasing the attendance rate and the development of alternative screening assays to replace cytology tests.

Since a persistent infection with human papillomavirus (HPV) is a prerequisite for development of cervical cancer, HPV DNA testing has been introduced as screening tool. The HPV test has proven to be a more objective and more sensitive screening test, and protects better against cervical cancer and its high-grade precursor lesions than cytology. Furthermore, HPV testing allows self-collection of (cervico-)vaginal specimens for screening, which increases coverage. However, since HPV tests also detect transient HPV infections in addition to disease-related HPV infections, triage testing of HPV-positive women is necessary to identify those with clinically relevant disease in need of treatment.

Candidate disease markers for triage testing involve the host cell (epi)genetic changes, such as DNA hypermethylation, that following a transforming HPV infection drive progression to cancer. DNA methylation can be easily detected by methylation-specific PCR (MSP) on cervical exfoliated cell specimens. We identified a series of methylation target genes, of which the methylation levels showed a significant increase with severity of cervical disease ($p < 0.005$). Analysis of HPV-positive cervical scrapes and self-collected (cervico-)vaginal specimens showed that these methylation markers enable the detection of all cervical cancers and advanced CIN2/3 lesions, characterized by a persistent HPV infection with a duration of >5 years, in both sample types.

In conclusion, DNA methylation analysis provides an attractive triage tool for HPV-positive women, which specifically detects cervical lesions in need of treatment and can prevent overtreatment. DNA methylation analysis supports full molecular self-screening in HPV-based cervical screening programs.

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