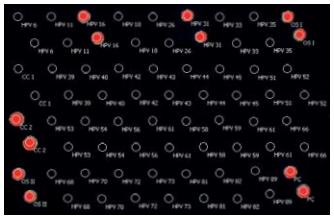
EUROArray HPV



- **Simultaneous detection and typing of all 30 relevant anogenital HPV subtypes in one reaction**
- **Differentiation between high- and low-risk HPV subtypes**
- **Fully automated evaluation using the EUROArrayScan system**

Technical data

Substrate	Single-stranded DNA probes, length: 15 to 50 nucleotides
Test procedure	PCR (approx. 60 min) / hybridisation (60 min) / fully automated evaluation; total working time approx. 1.5 min per sample (with 40 samples per run)
Reagents	Ready for use
Controls	DNA-negative control and further integrated controls
CE IVD certificate	Complete process incl. DNA extraction validated
Test kit format	5, 10 or 20 slides, each with 5 reaction fields or 8 slides, each with 3 reaction fields
Order no.	**MN 2540-0505, -1005, -2005, -0803**

Clinical significance

The EUROArray HPV is designed for the molecular diagnostic determination and typing of human papillomavirus (HPV), associated with the development of dysplasia, particularly of cervix carcinoma (cervical cancer).

HPV direct detection tests play a particularly important part in the early detection of cervix carcinoma, alongside cytology (pap smear). While a pap smear detects cells of the cervical mucosa which are already changed, PCR (polymerase chain reaction)-based tests enable detection of HPV infections before they cause morphological changes in the cells. To date, 30 genital HPV types have been described which are divided into two groups according to their oncogenic potential, namely high-risk and low-risk HPV. While high-risk HPV can cause carcinoma and are detected in over 99 % of cervix carcinoma, low-risk HPV alone only occur in non-malign tissue changes. The WHO officially classified the genotypes 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59 and 66 as carcinogenic and therefore high-risk HPV. HPV 16 is detectable in 50 to 60 % and HPV 18 in 10 to 20 % of cervix carcinoma. Despite this, also further HPV, like 26, 53, 68, 73 and 82 were detected in cervical carcinoma and therefore need to be considered high-risk HPV. The low-risk viruses encompass HPV 6 and 11 as main cause of genital warts (Condylomata acuminata). Further low-risk types are 40, 42, 43, 44, 54, 61, 70, 72, 81 and 89 (CP6108).

To evaluate the course and risk of an HPV infection, it is helpful to determine the subtype in addition to discriminating between high- and low-risk HPV. This usually allows the differentiation between a new and a persisting infection and thus improves the individual risk assessment of a carcinoma.

Diagnostic application

The EUROArray HPV contributes essentially to the early detection of cervix carcinoma. The test enables the simultaneous detection and typing of all 30 relevant anogenital high-and low-risk HPV subtypes in a single reaction. The test system is based on the detection of viral oncogenes E6/E7, whose expression constitutes the basis for malign transformation of dysplasia.

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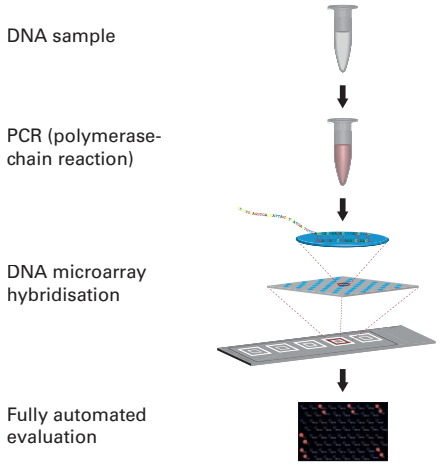
Test principle

This test system is based on the multiplication of defined gene sections of human papilloma virus and the subsequent determination through a hybridisation reaction with immobilised DNA probes in a microarray system. A DNA preparation of cervical smears from the patients is used as sample material. In the first reaction step, sections of the viral oncogenes E6 and E7 of human papilloma virus present in the sample are amplified by polymerase chain reaction (PCR) using a multiplex primer system and, at the same time, labelled with a fluorescent dye. In a second step, the products are detected using an oligonucleotide microarray. The specific binding (hybridisation) of the fluorescence-labelled PCR product to the corresponding oligonucleotide probe is detected using a special microarray scanner (EUROArrayScanner). The EUROArrayScan software evaluates all spot signals automatically and deduces the test result.



Test performance

The PCRs are incubated in the thermocycler and then, using the TITERPLANE technique, on EUROArray slides containing microarray BIOCHIPs. Scanning and evaluation are performed using the EUROArrayScanner (incl. EUROArrayScan software). This provides fully automated evaluation of EUROArray analyses and detailed documentation of results.

Analytical sensitivity

The lower detection limit (limit of detection, LOD) of this test system depends on the HPV subtype and lies between 50–200 DNA copies/reaction, in some cases beyond that. The LOD is the minimum detection limit. Therefore, a reduced number of DNA copies of the pathogen is usually detected.

Analytical specificity

The specificity of the test system is also ensured by the use of specific primer and probe systems for every HPV subtype to be detected. The PCR products of the different HPV subtypes do not show any cross reactivities on the probe of another HPV subtype when template DNA in a concentration range between the LOD and 2 million DNA copies is used.

Furthermore, cross reactions to the following microorganisms found in the anogenital region were experimentally ruled out: Bacteroides fragilis, Bifidobacterium longum, Candida albicans, Chlamydia trachomatis, Clostridium perfringens, Corynebacterium amycolatum, Enterobacter cloacae, Enterococcus aerogenes, Enterococcus agglomerans, Enterococcus faecalis, Enterococcus faecium, Epstein-Barr virus, Fusobacterium equinum, Fusobacterium nucleatum, Herpes simplex virus 1 and 2, Lactobacillus acidophilius, Neisseria gonorrhoeae, Peptoniphilus harei, Streptococcus agalactiae, Trichomonas vaginalis.

Evaluation

A total of 188 clinical samples from two panels were investigated. Panel 1 (n=115) had been stored in PreservCyt® Solution and was pre-characterised with 5 different CE/IVD labelled HPV reference tests. For 114 samples (99.2 %) the EUROArray HPV yielded results which were 100 % in agreement with the results of one or several reference tests.

Panel 2 had been stored on Whatman FTA Elute Cards (n=57) or unprocessed on cotton swabs (n=16) and was pre-characterised with an HPV subtyping test. In total, the share of determinations which yielded a complete agreement of results or detected additional subtypes with the EUROArray only amounted to 92.5 %.

Literature reference

1. Dickson EL, Vogel RI, Geller MA, Downs LS Jr. Cervical cytology and multiple type HPV infection: a study of 8182 women ages 31-65. Gynecol Oncol. (2014) Jun;133(3):405-8.
2. Clifford GM, Smith JS, Plummer M, Munoz N, Franceschi S. Human papillomavirus types in invasive cervical cancer worldwide: a meta-analysis. Br. J Cancer 88 (2003) 63-73.
3. Cogliano V, Baan R, Straif K, Grosse Y, Secretan B, El GF. Carcinogenicity of human papillomaviruses. Lancet Oncol. 6 (2005) 204.

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MN_2540_D_UK_A04, 02/2020