E6 Based Rapid Diagnostic Test for Cervical Pre-Cancer and Cancer

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AVantage HPV E6 Test

Test Workflow

Test Principle

Funding for this work was provided by:

The START project was supported by PATH through a grant from the Bill & Melinda Gates Foundation.

NH SBR 1 R41 CA103384-01 "A Novel Diagnostics for Oncogenic HPV".
NH SBR 1 R43 AI068193-01 "Rapid Strip Test for Cervical Cancer via HPV-E6 Detection"

Collaborations and consultants:

Arbor Vita Corporation maintains a collaboration with Drs. G. Orfanoudaki, G. Trave and E. Weiss of the University Louis Pasteur of Strasbourg. Two of the anti-E6 mAbs used for this work were kindly provided by Dr. E. Weiss (Grosann, C. et al., J. Mol. Recogn. 1995 8:121-125).

Arbor Vita Corporation gratefully acknowledges Dr. Paul Lambert and Dr. Karl Munger for discussions and advice.

INTRODUCTION:

In developing countries, cervical cancer is a leading cause of cancer-related death of women, due to the lack of implementation of screening tests for cervical pre-cancer and cancer. A screening test for low resource settings should be simple, rapid, and cost effective. Ideally, such a test would be informative regarding HPV oncogenic activity (Table 1).

Expression of both HPV E6 and E7 oncoproteins is essential for cervical cell transformation to occur. Results from a collaborative clinical study conducted previously by Arbor Vita Corporation, PATH, and the Chinese Academy of Sciences demonstrated a correlation of E6 oncoprotein positivity with both severity of cervical histopathology and risk for progression. Hence, E6 oncoprotein promises to be an appropriate biomarker of HPV-mediated oncocytic activity. (Figure 1).

AVC, in collaboration with PATH, has developed a rapid diagnostic test, AVantage HPV E6 Test, that detects E6 oncoprotein from cervical swabs. The final test will enable detection of E6 of seven most prevalent HPV types in cervical cancer. The AVantage HPV E6 Test uses high affinity mAb for the specific capture and detection of high-risk HPV-E6 oncoproteins in a lateral flow based format (Figure 2+3).

RESULTS:

Analytical sensitivity:

In the background of pathologic negative cervical swab samples, the analytical assay sensitivity is below 2,000 cervical cancer cells per test for the HPV types 16, 18 and 45 and < 10,000 cervical cancer cells per test for the HPV types 33, 58 and 52 (Figure 4).

Performance on clinical specimens:

Hundreds of pathology-negative cervical swab samples have been tested by AVantage HPV E6 Test strip 1. Figure 5 shows a representative experiment for 60 pathology-negative cervical swab samples where all test results were negative for E6, suggesting a very low false positive rate.

In a pilot clinical study, 44 cervical swab samples of confirmed pathology (normal, CIN1, CIN3 and cancer) were tested on AVantage HPV E6 Test - Strip 1 (16, 18 and 45). HPV typing was performed via PCR linear array. All 19 pathology-negative or CIN1 samples were negative for E6 protein, as expected. 5 out of 7 CIN3 samples and 8 out of 9 cervical cancer samples were positive for E6 protein expression (Figure 6).

CONCLUSION:

Arbor Vita Corporation in collaboration with PATH has developed a novel E6 oncoprotein-based rapid diagnostic assay for cervical pre-cancer and cancer to implement in low-resource regions: AVantage HPV E6 Test.

The results of a pilot clinical study suggest that E6 is an appropriate biomarker for diagnosis of cervical pre-cancer and cancer.

AVantage HPV E6 Test

Table 1

Test Specifications

- Point of care test
- Sample type: cervical swabs
- Simple, inexpensive, robust (no cold chain required)
- Marker: HPV-E6 protein of “top 7 prevalent” HPV types (HPV-16; -18; -45; -31; -33; -52; -58)
- Additional typing information for HPV-16;18-45
- Target sensitivity: ~ 50 pg E6 per cervical swab (corresponds to ~50,000 CxCa cells)

Table 2

Avantage HPV E6 Test Performance:

- 9/9 CxCa samples
- 5/7 CIN3 samples
- 0/16 CIN1 or Pathology-negative samples

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