

INTERPRETATION GUIDELINES

HPV-16 Status by Real-Time PCR

METHODOLOGY/RESULT INTERPRETATION:

Quantitative Real-Time PCR is used to measure the number of copies of HPV-16 E2, HPV-16 E6, and human GAPDH genes within a cervical specimen. The quantities of the two HPV-16 genes are compared in the E2/E6 Ratio, which is an estimate of the Viral Status (See Table 1). The quantities of the E6 and GAPDH genes are compared in a copy number ratio (CNR), which is reported as Viral Load (viral genome copies/human genome).

Table 1. How the E2/E6 Ratio Relates to HPV-16 Integration Status

E2/E6 Ratio	Viral Status
≥ 0.8	Episomal
≥ 0.2 and < 0.8	Mixed
< 0.2	Integrated

CLINICAL SIGNIFICANCE:

Viral Status is an estimate of the HPV-16 virus integration state. As illustrated in Figure 1, the HPV-16 virus contains a circular DNA genome. When HPV-16 infects a host cell, the viral DNA genome remains circular and distinct from the host genome, a form called an “episome”. In this episomal form, the HPV-16 virus has complete copies of two viral genes, E6 and E2. As an HPV-16 infection persists, the viral episome may become integrated into the host DNA genome. In the process of integration, the viral genome is disrupted and the E2 gene may be completely or partially deleted. This integrated form of HPV-16 can be found in up to 80% of HPV-16 positive cervical cancers [1-3].

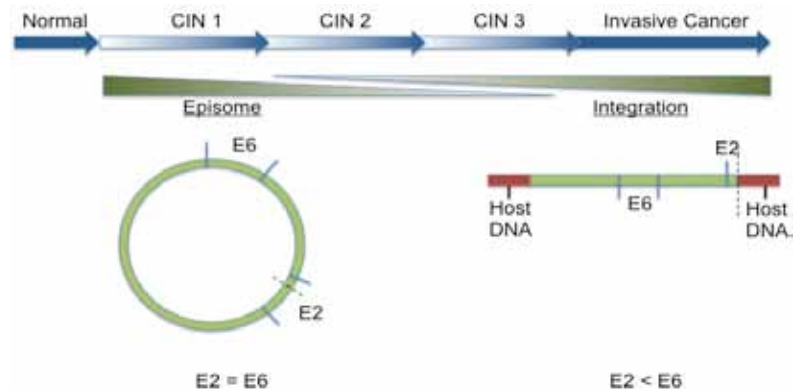


Figure 1. The HPV-16 Viral Genome Status in Cervical Cancer.

Multiple clinical studies have shown that the episomal form was mostly found in non-progression of preinvasive lesions, whereas the integrated form was found mostly in progression of preinvasive lesions. Thus, a decrease in the episomal form was associated with poorer outcome [4-6].

Viral Load is a measurement of the copies of the HPV-16 viral genome per copy of the host genome. Multiple clinical studies have shown that HPV viral load can be a predictor of development of high-grade cervical lesions or cervical cancer [4, 6-10]. However, a consensus threshold value to evaluate the risk of cervical cancer progression has not been determined.

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This test was developed and its performance characteristics determined by this laboratory. It has not been cleared or approved by the Food and Drug Administration (FDA). The FDA has determined that such clearance or approval is not necessary. This test is used for clinical purposes. It should not be regarded as investigational or for research. The laboratory is regulated by the Clinical Laboratory Improvement Act of 1988.