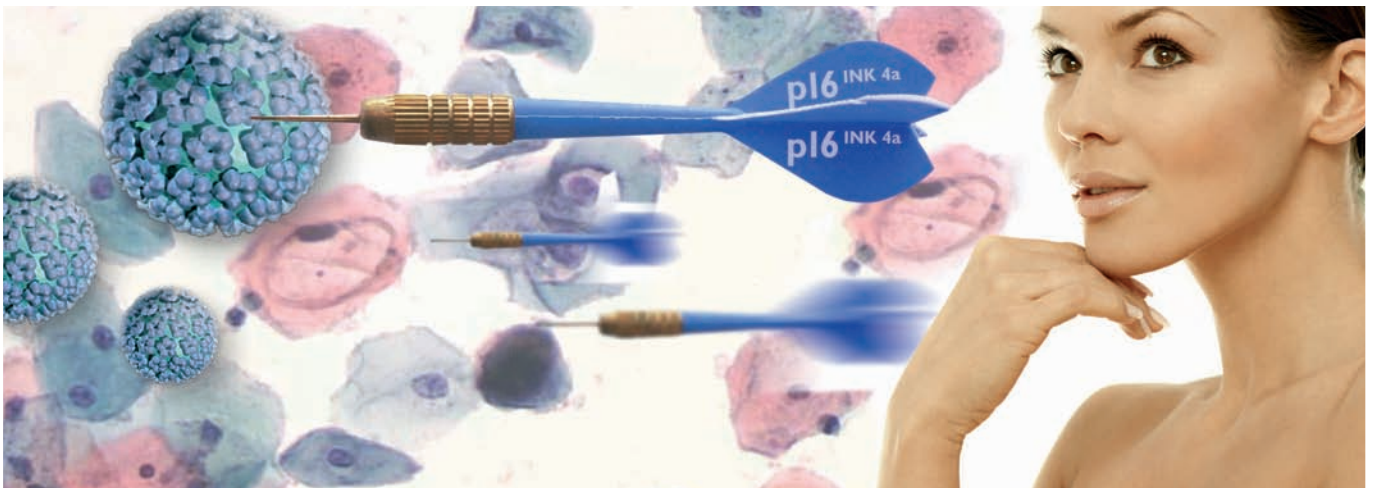


p16 INK4a

New molecular marker for improved detection of cancer of the uterine cervix



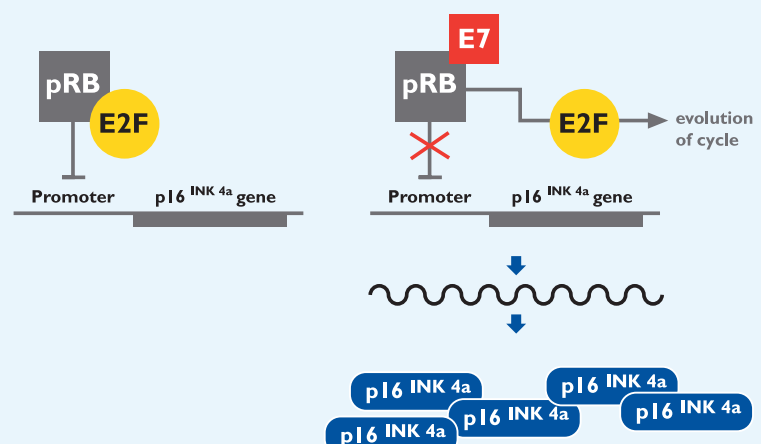
It is known that between 10 and 20% of all cytological studies diagnosed as ASC-US/L-SIL underlie a high-grade lesion. In addition, most high-grade dysplasias come from patients with ASC-US/L-SIL cytology. This, together with the low specificity and low positive predictive value of cytology, makes additional tests necessary in screening for cancer of the uterine cervix.

Protein p16 is encoded by the suppressor gene CDKN2 located on chromosome 9p21. It is an inhibitor of the cycline dependent kinases (cdk) that participate in the transition from the G1 to S phase of the cell cycle.

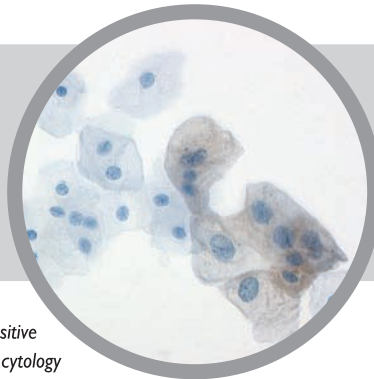
Numerous clinical studies indicate that protein p16 show intense overexpression in cells with cervical intraepithelial lesions, where high risk HPV oncoproteins (HPV-AR) begin their process of cellular transformation. For this reason it has been proposed as a biological marker for the unequivocal identification of cells with HPV-induce dysplastic changes, indicating oncogenic activation of these cells.

Mechanism of p16 INK 4a overexpression

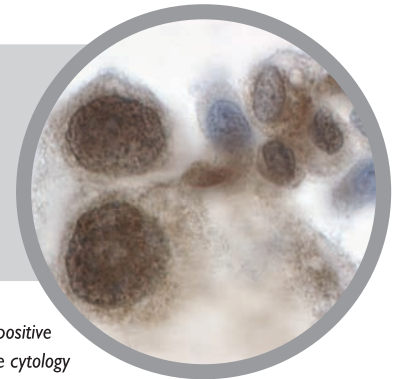
In carcinogenic and pre-carcinogenic cells



p16 overexpression is easy to detect by a simple immunochemical stain of material from the uterine cervix obtained in liquid-phase cytology.



L-SIL, p16 positive
Liquid phase cytology



H-SIL, p16 positive
Liquid phase cytology

In the supplement of November 2006 of the journal *Progresos de la Sociedad Española de Ginecología y Obstetricia*, which reviews the latest consensus on the prevention of cancer of the uterine cervix, p16 protein is listed in the section of new molecular markers for screening cancer of the uterine cervix.

p16 INK 4a cytology for classifying ASC-US and L-SIL

Wentzensen et al. Abstract. EUROGIN April 2006

	Sensitivity	Specificity
ASC-US	90,0 %	86,3 %
L-SIL	100,0 %	83,5 %

Study design using 225 consecutive cases of ASC-US and L-SIL pap cytology (from LBC) with a follow-up biopsy.

High sensitivity and specificity of cytologic results of p16 INK 4a for high grade CIN confirmed by biopsy.

The principal benefits of using p16 in cytology are:

- Enhanced diagnostic precision.
- Improved sensitivity to H-SIL.
- Clarification of difficult cases: ASC-US, L-SIL, ASC-H and glandular lesions.

In contrast with other tests that detect HPV and, therefore, only the presence of infection, p16 is a marker of viral integration and oncogenic activation, meaning that it is not just a marker of infection, but of disease.

By use of p16 can help to confirm the cytologic diagnosis and increase reproducibility. It is a tool that improves the patient's diagnosis and can save time in effective treatment of the disease.



System Quality Certificate.
Setting: Laboratory Tests,
Histopathology and Industrial
Testing, Water Speciality.
Reg. No.: 12 100 23729 TMS

Plaza Ramon Llull, 7-10
08203 SABADELL (Barcelona) - SPAIN
Tel. +34 93 727 22 33 (8h - 20h)
Fax +34 93 727 78 16

www.keynova.com / www.cerba.com
E-mail: cerba@cerba.com
International Dep.: it@keynova.com
Commercial Dep.: comercial@cerba.com
Customer service: atcl@cerba.com