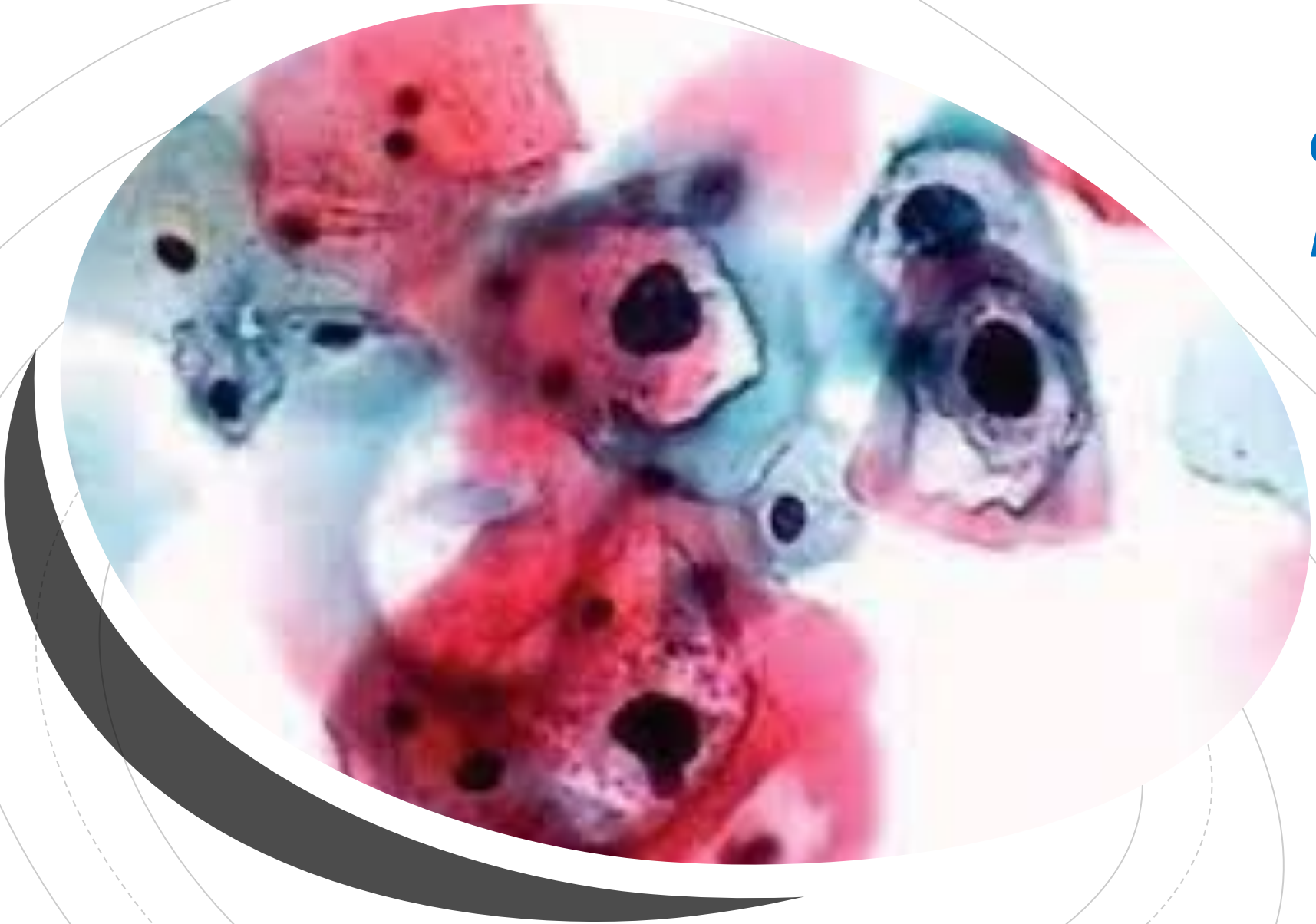
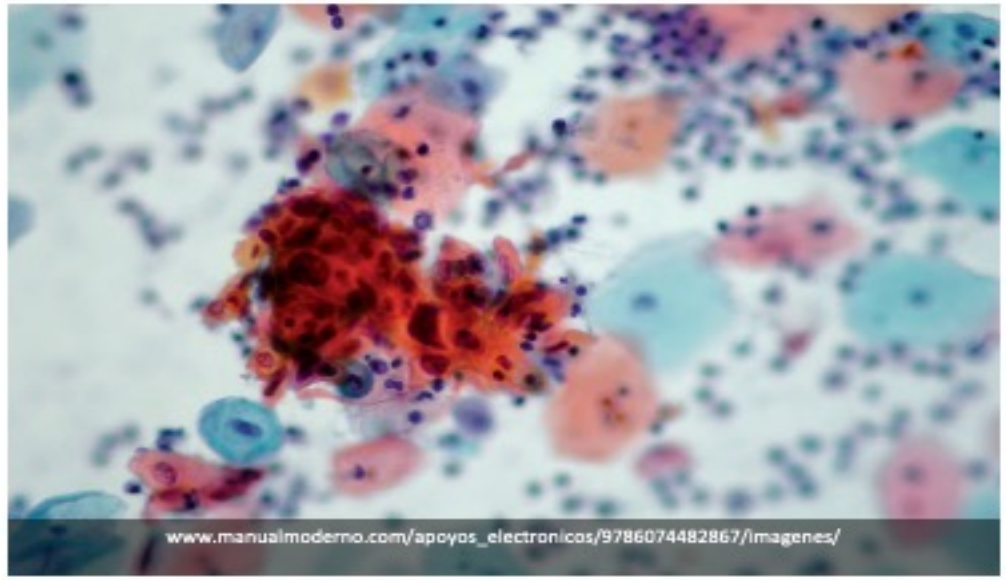


CITOLOGIA EN BASE LIQUIDA Y DETERMINACION DE VPH

CONTENIDO

- VPH (Definición y clasificación)
- Tumores asociados al VPH
- Oncogénesis
- Pruebas de tamización
- Pruebas ADN-VPH
- Otras técnicas
- Casos clínicos
- Conclusión



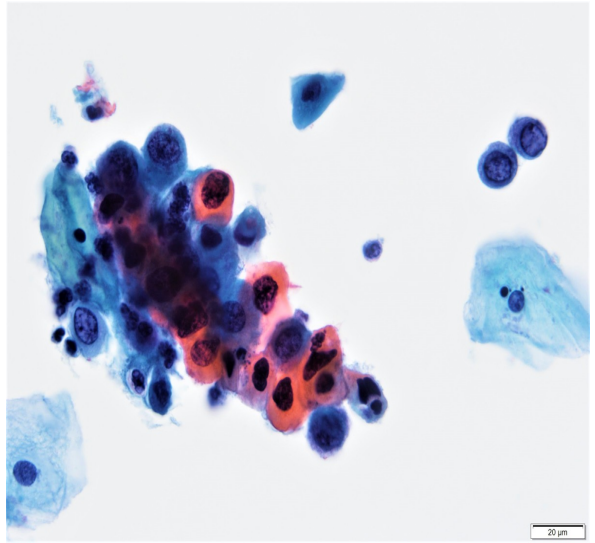
www.manualmoderno.com/apoyos_electronicos/9786074482867/imagenes/

- ***La infección por VPH es la enfermedad de transmisión sexual más frecuente en el mundo***

cristinasandoval1394.blogspot.es/1435631449/cancer-de-mama-y-cervico-uterino-es-posible-prevenirlos-/

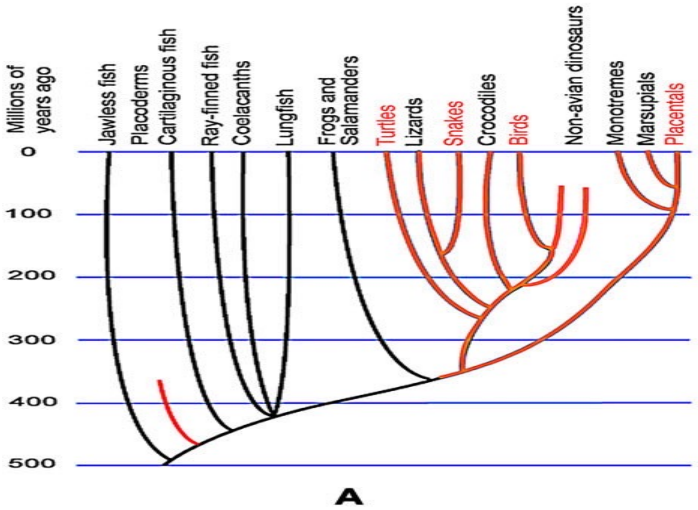
- *Esta infección se adquiere como cualquier enfermedad de transmisión sexual, pero hasta 20 años más tarde se puede desarrollar el cáncer por persistencia de la infección e integración viral.*

CERVIX

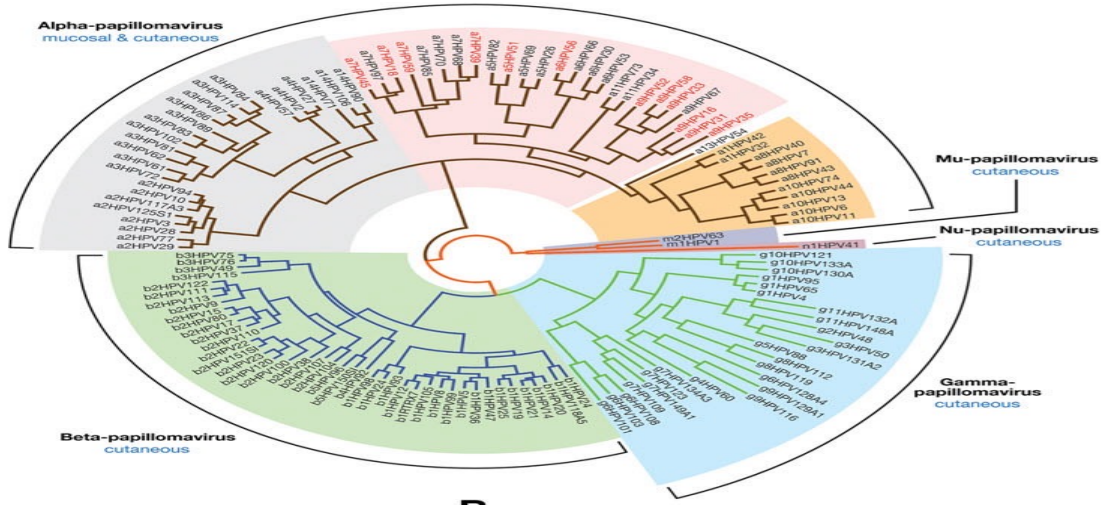


- *90%: Eliminación a los dos años*
- *10: Persistentes*
- *1% Cáncer*

ETIOLOGIA



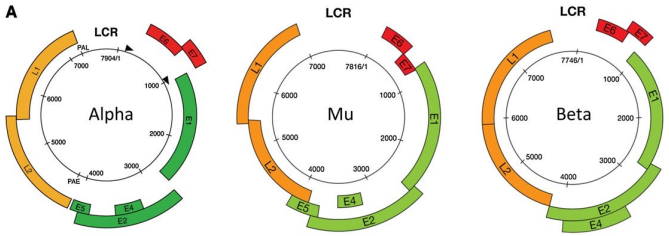
A



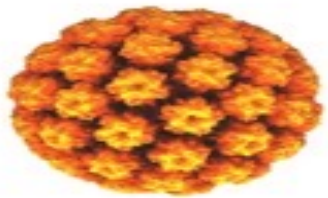
B

Genus + Species	Type Species	Invasive Cervical Cancer	IARC Category	Squamous Cell Carcinoma	Adeno Carcinoma	Tropism
Alpha 1	HPV32		3			mucosal
	HPV42					
Alpha 2	HPV3					cutaneous
	HPV10					
	HPV28		3			
	HPV29		3			
	HPV77		3			
	HPV94					
	HPV117					
	HPV125					
Alpha 3	HPV16	0.01				mucosal
	HPV52		3			
	HPV58		3			
	HPV72		3			
	HPV81		3	0.4		
	HPV83		3	0.4		
	HPV84		3			
	HPV86		3			
	HPV87		3			
	HPV89		3			
	HPV102					
	HPV114					
Alpha 4	HPV2		3			cutaneous
	HPV27		3			
	HPV57		3			
Alpha 5	HPV26	0.37	2B	0.22		mucosal
	HPV51	1.25	1	0.75	0.54	
	HPV69	0.08	2B			
	HPV82	0.07	2B	0.26		
Alpha 6	HPV30	0.37	2B			
	HPV53	0.26	2B	0.04		
	HPV56	0.84	1	1.09		
	HPV66	0.08	2B	0.19		
Alpha 7	HPV18	10.28	1	11.27	37.3	
	HPV39	1.67	1	0.82	0.54	
	HPV45	5.68	1	5.21	5.95	
	HPV59	1.08	1	1.05	2.16	
	HPV68	1.04	2A	0.37		
	HPV70	0.11	2B			
	HPV85		2B			
	HPV97					
Alpha 8	HPV7		3		41.62	cutaneous (mucosal)
	HPV40		3		1.08	
	HPV43				0.54	
	HPV91	0.01	3		1.08	
Alpha 9	HPV16	61.35	1	54.38		mucosal
	HPV31	3.65	1	3.82	0.54	
	HPV33	3.83	1	2.05		
	HPV35	1.94	1	1.57		
	HPV52	2.71	1	2.25		
	HPV58	2.22	1	1.72		
	HPV67	0.31	2B			
Alpha 10	HPV6	0.11	3	0.07		mucosal
	HPV11	0.02	3	0.07		
	HPV13		3			
	HPV44	0.01	3			
	HPV74	0.01	3			
Alpha 11	HPV34	0.07	2B	0.49		mucosal
	HPV73	0.52				
Alpha 12						
Alpha 13	HPV54					mucosal
Alpha 14	HPV71					
	HPV90		3			
	HPV106		3			

C



Rev. Med. Virol. 2015; 25: 2–23.



> 150 tipos

16

18 26

31 33 35

39 45 51 52

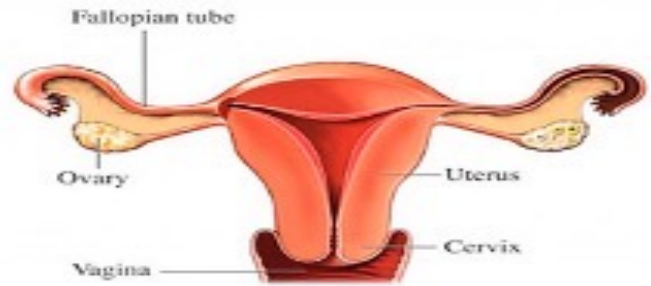
53 56 58 59 66

68 70 73 82 85

6 11 40 42 43 44 54

61 62 71 72 81 83 84 89

Isabel Cristina Almonacid U



Alto riesgo — ***CANCER***

- 42 Genitales
- 16: Tipo más frecuente a nivel mundial

Bajo riesgo — ***VERRUGAS VIRALES***

Otros órganos: ?

Patogenicidad de los Virus del Papiloma Humano

VPH de alto riesgo (AR)

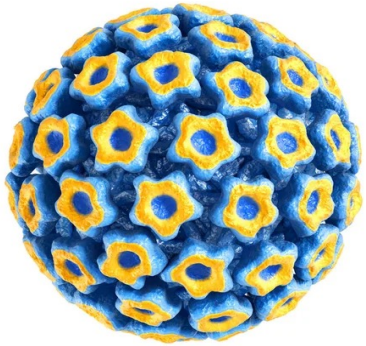
Patogenicidad	Subtipo de VPH
Muy alto riesgo	**16,18,31,33,35,45 y 58** Lesiones intraepiteliales de alto grado, carcinomas (cérvix, endocérvix, recto, ano, glándula mamaria, pulmón, estómago, amígdala, laringe, sinusoides, lengua)
Alto riesgo	**39,51, 52,56,59,66 y 68** Lesiones intraepiteliales de alto grado y carcinomas
Probable alto riesgo	**26,53, 67, 69 y 82** Lesiones malignas en mucosas

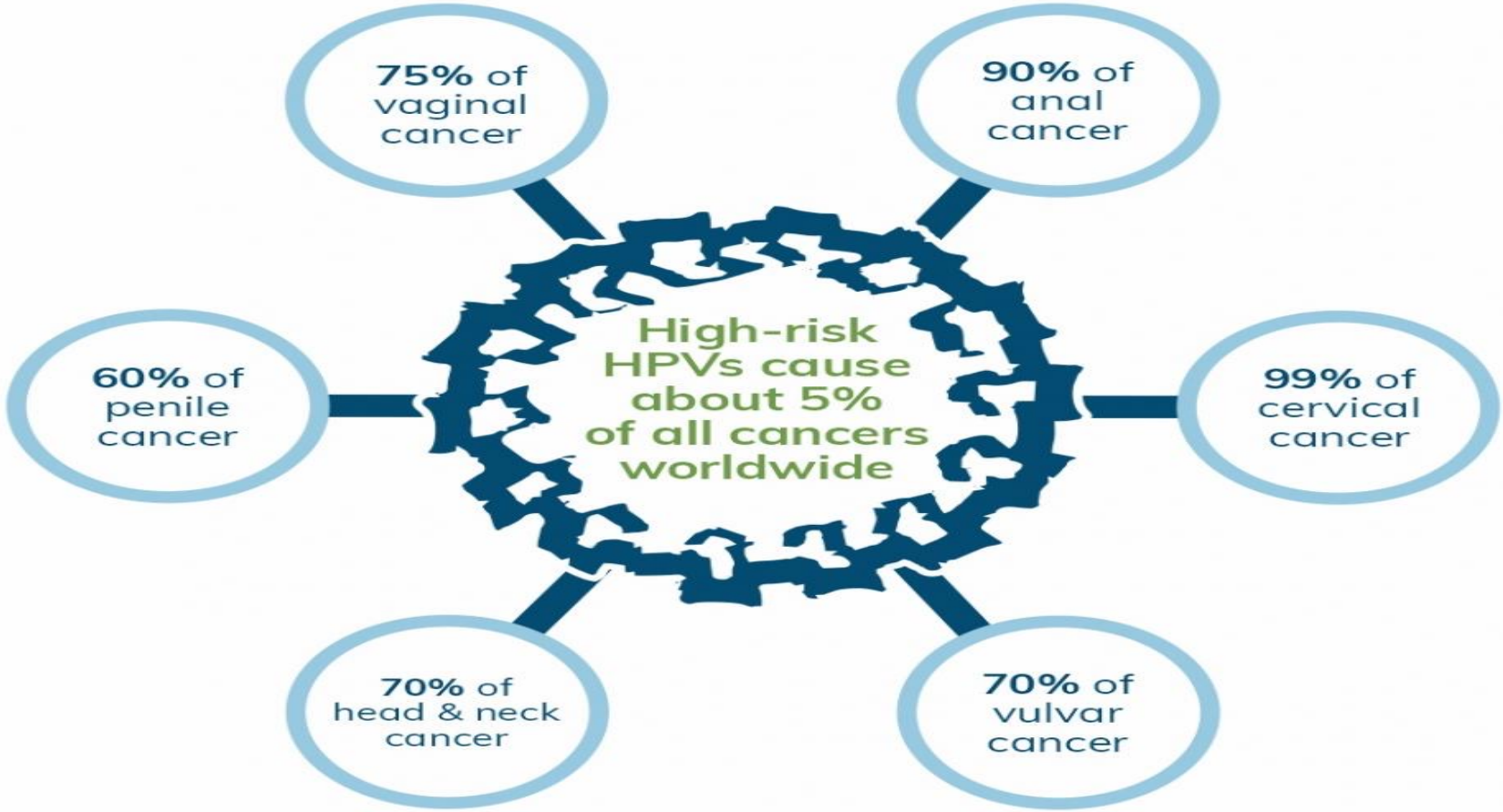
VPH de bajo riesgo (BR)

Patogenicidad	Subtipo de VPH
Bajo riesgo	**6 y 11** Papilomatosis recurrentes respiratoria, condilomas acuminados, papilomas en vías respiratoria altas, Lesiones intraepiteliales de bajo grado, carcinomas verrucosos, carcinomas de esófago
Probable bajo. Riesgo	**13, 32 y 34** Lesiones benignas en mucosa, carcinomas verrucosos
Muy bajo riesgo.	**40, 42, 44,54, 55, 57, 61,62 y 64** Lesiones de bajo riesgo en mucosa oral y genital

Isabel Cristina Almonacid Urrego

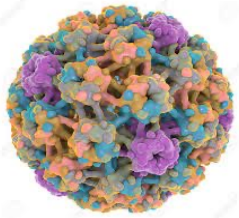
Cancers caused by HPV infection



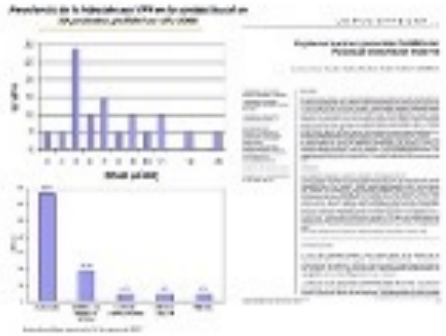


https://www.cancer.gov/about-cancer/causes-prevention/risk/infectious-agents/hpv-and-cancer

Otros tumores



Placenta



Cavidad oral

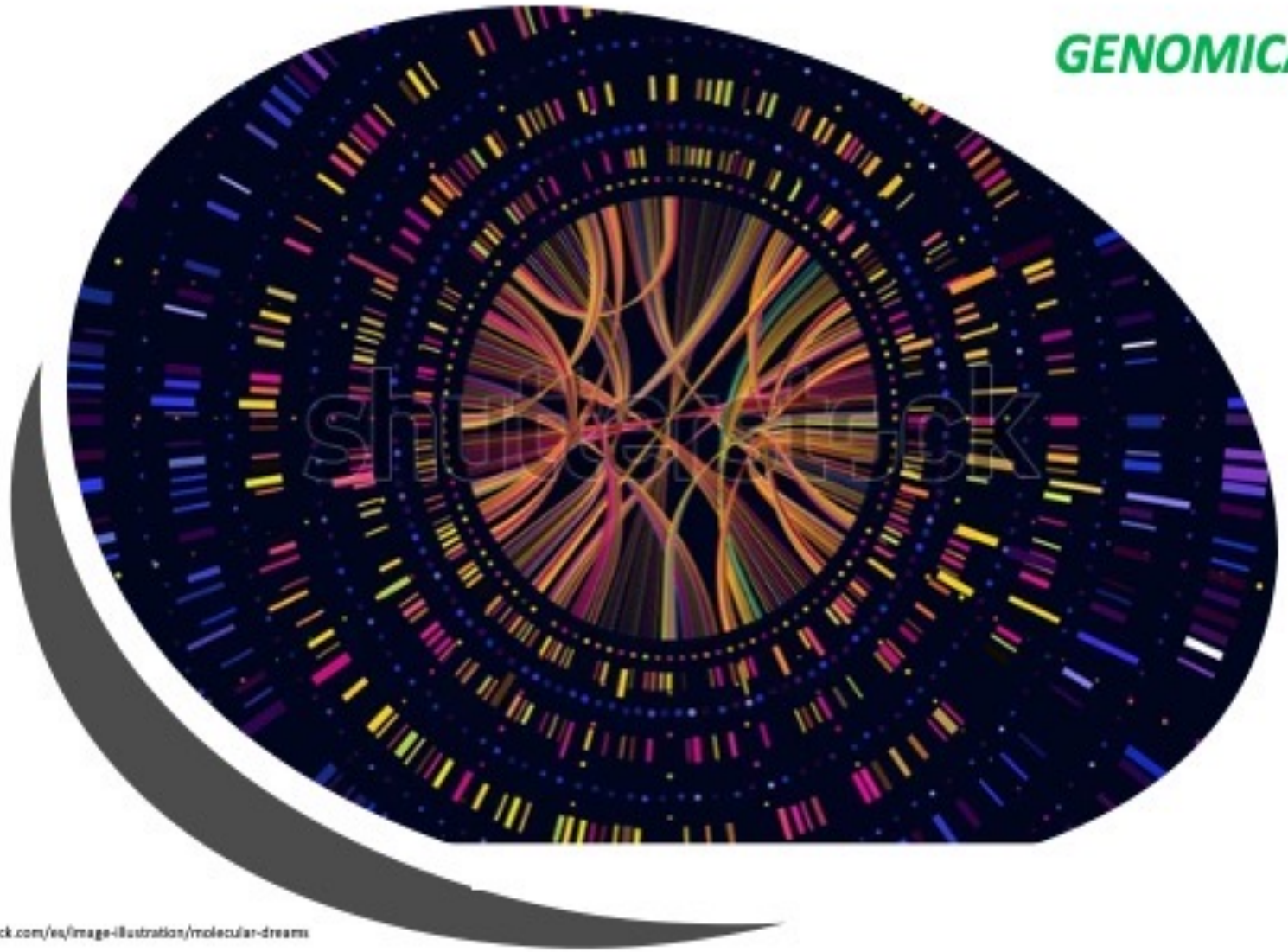
TGI

Glándula mamaria

Pulmón

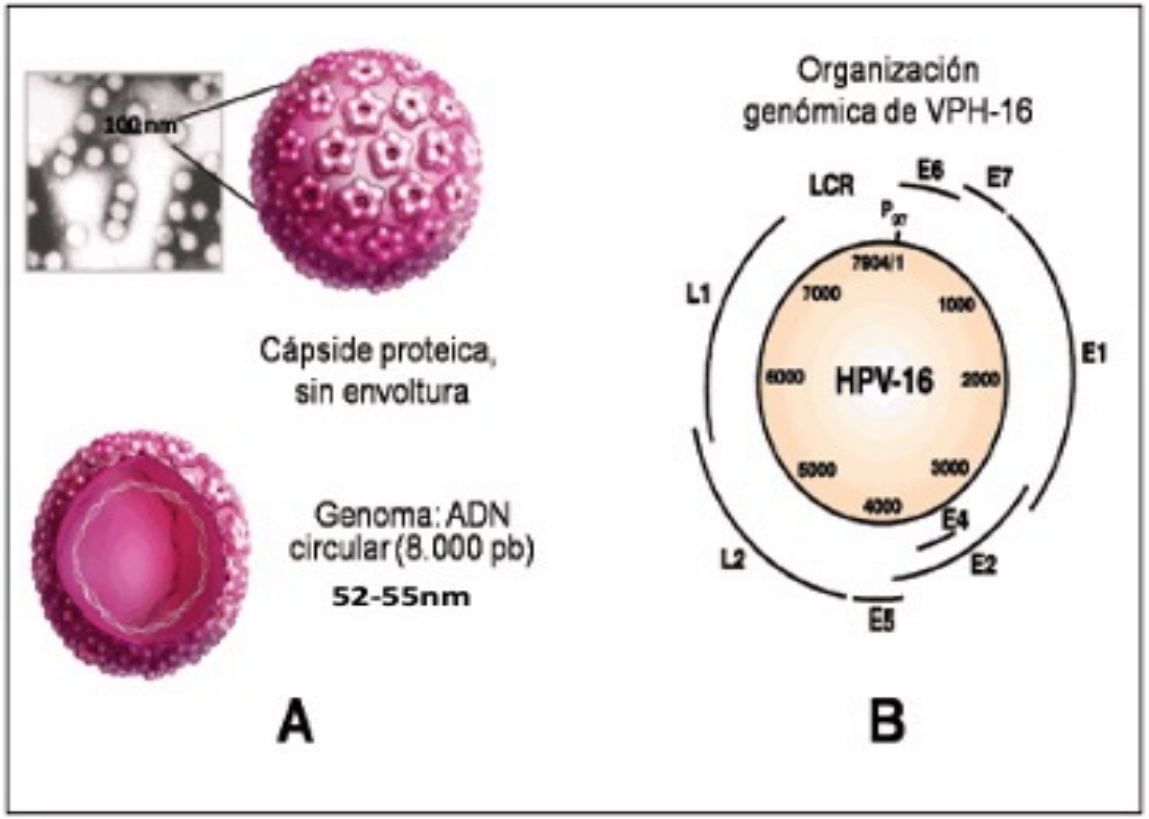
Vejiga

GENOMICA



https://www.shutterstock.com/es/image-illustration/molecular-dreams

Organización genómica



www.eurocytology.eu/es/course/771

9-10 marcos de lectura abierta localizados en una sola cadena

Región codificante

- ***Genes tempranos (No estructurales)***

E6, E7, E1, E2, E4, E5: Control de la replicación del DNA e inducen la transformación maligna en la célula del huesped

- ***Genes tardíos (Estructurales)***

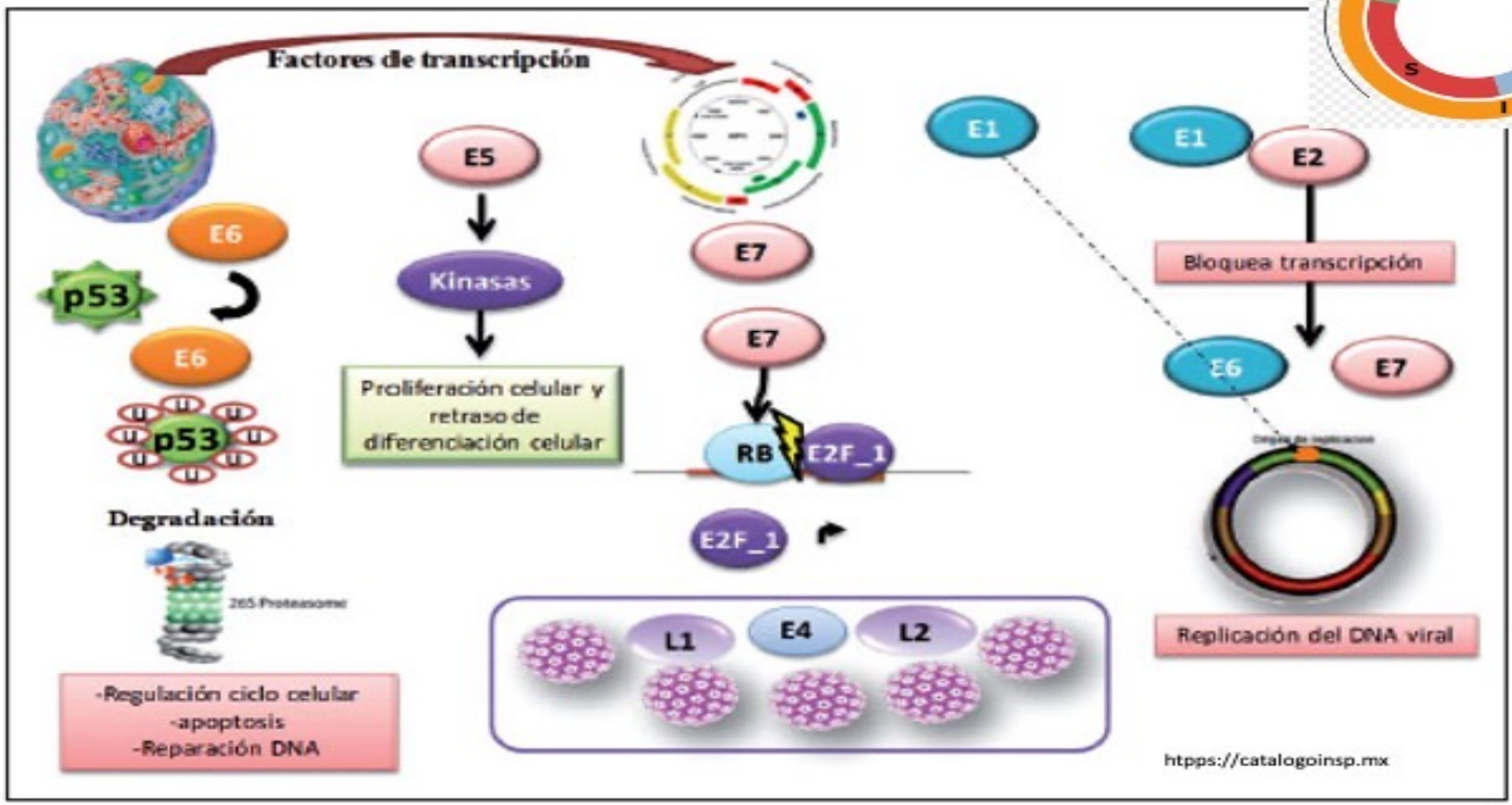
L1,L2: Proteínas mayor y menor de la cápside

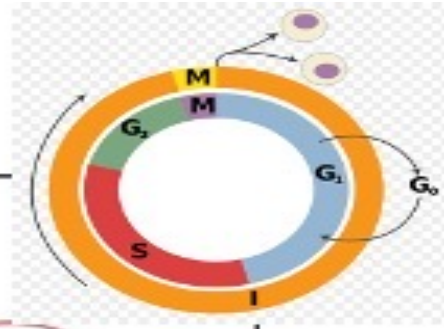
Región no codificante

- ***LCR***: Región no codificante: contiene los promotores que inician la replicación y controlan transcripción

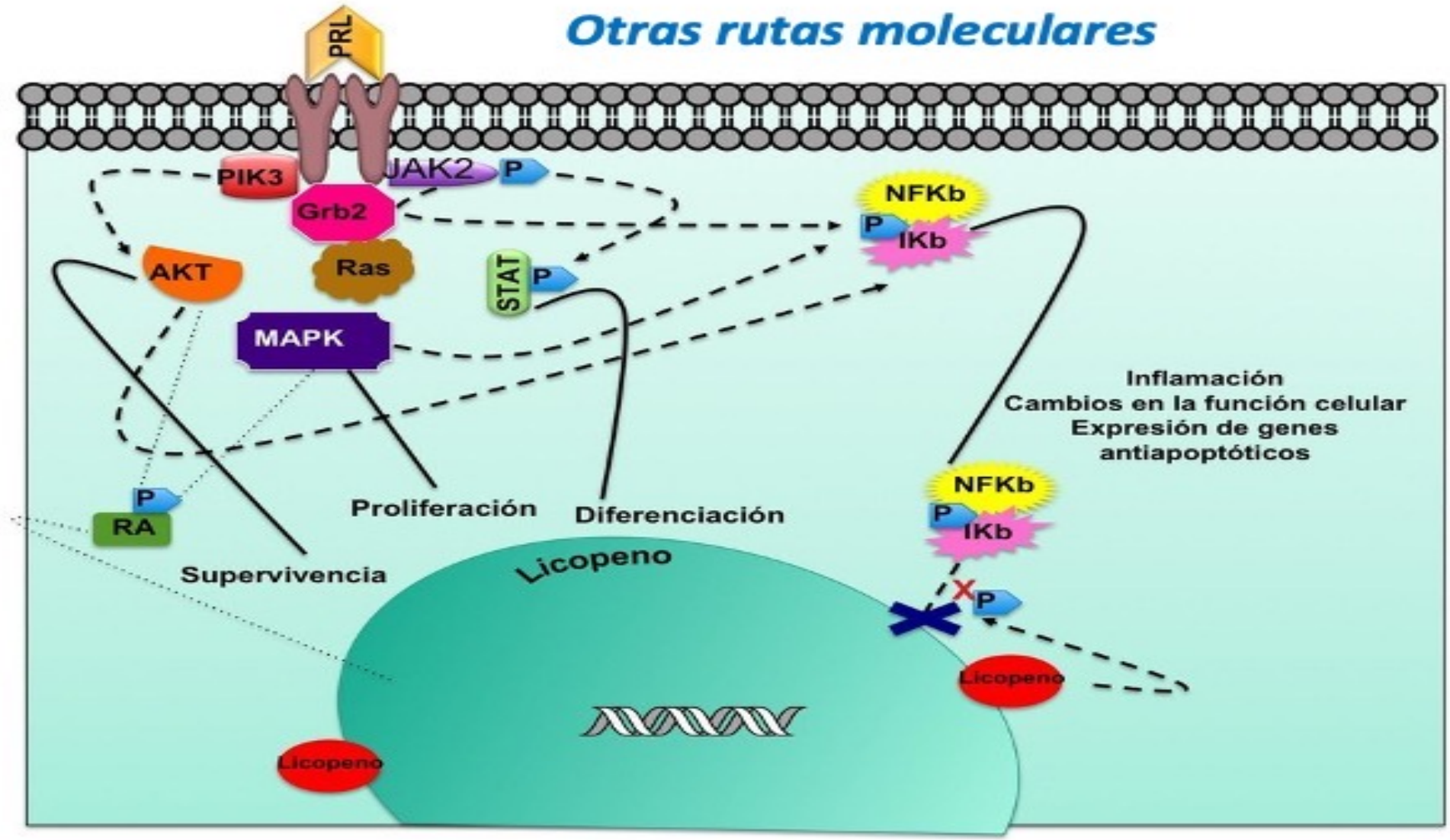
Capacidad de transformar células epiteliales

Rutas Moleculares



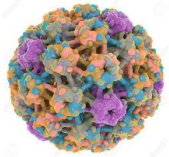


Otras rutas moleculares

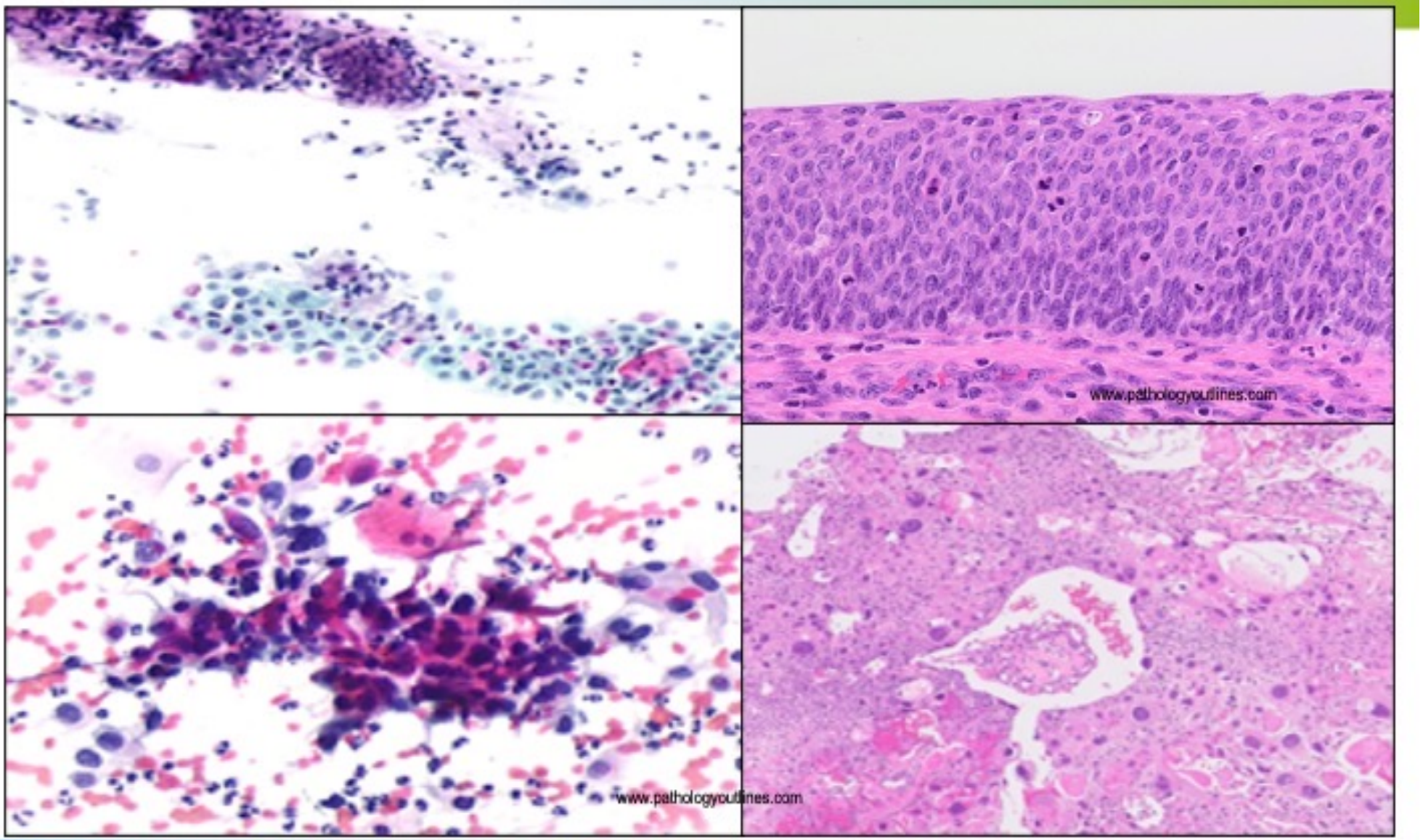


https://www.researchgate.net/figure/Figura-4-Rutas-de-senalizacion

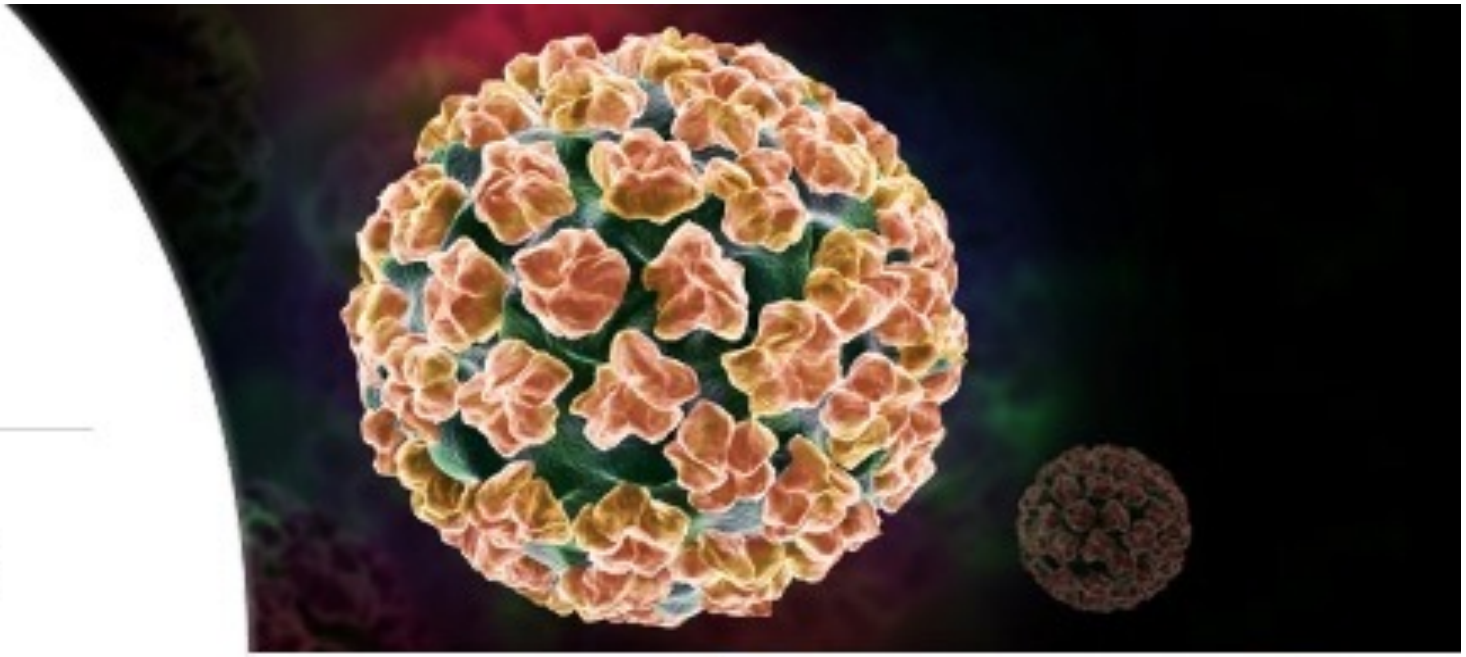
LESIONES PRENEOPLASICAS

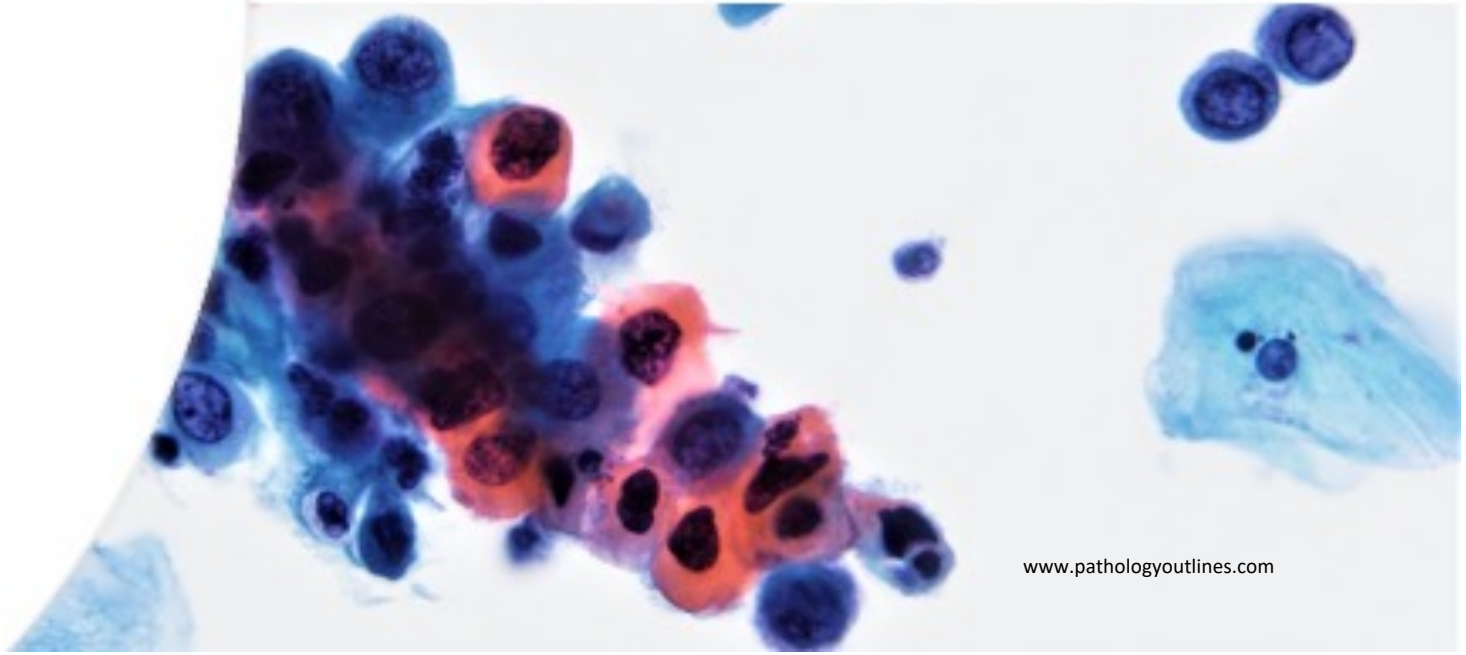


CANCER



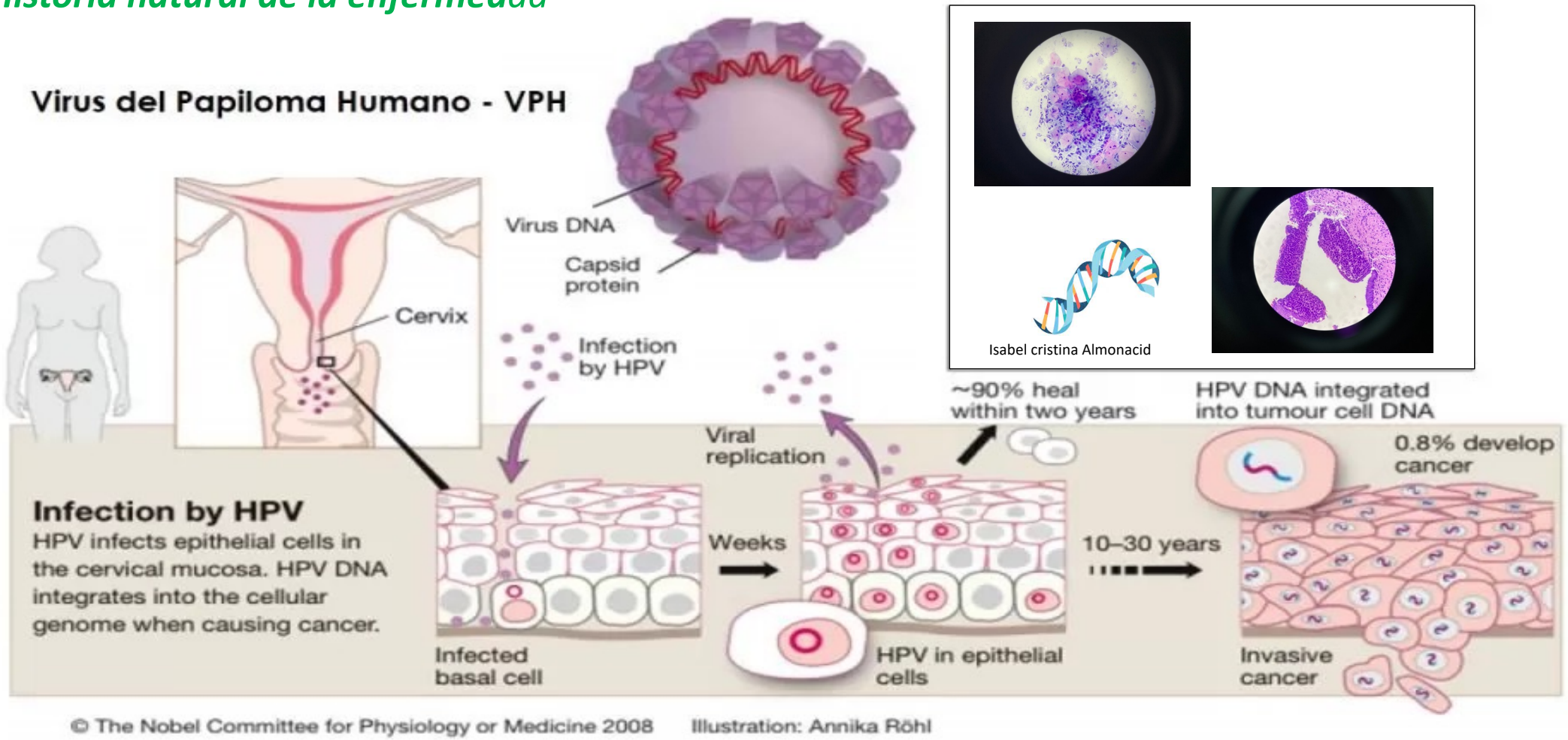
- *Cancer de cuello uterino una enfermedad molecular*





www.pathologyoutlines.com

Historia natural de la enfermedad

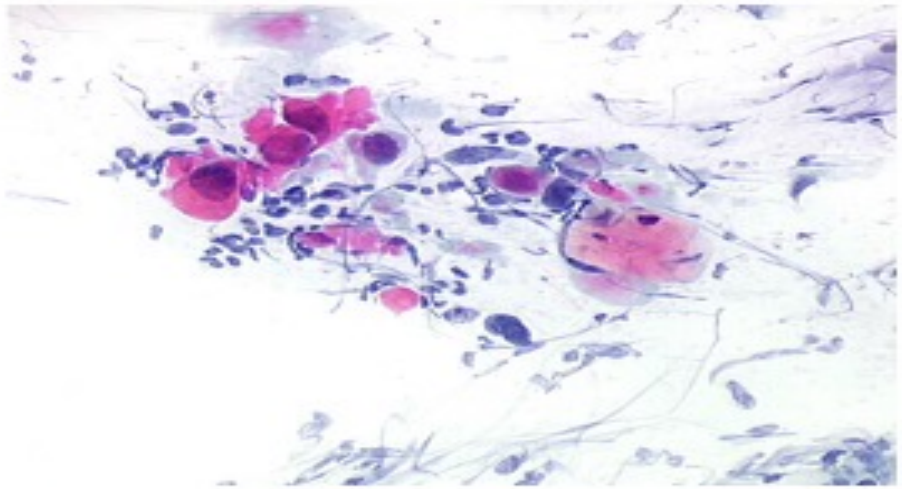


Estrategias de DETECCIÓN temprana

Pruebas de tamización

- No diagnostica enfermedad
- Identifica individuos con mayor probabilidad de tener una enfermedad o un precursor de la enfermedad

Tamización

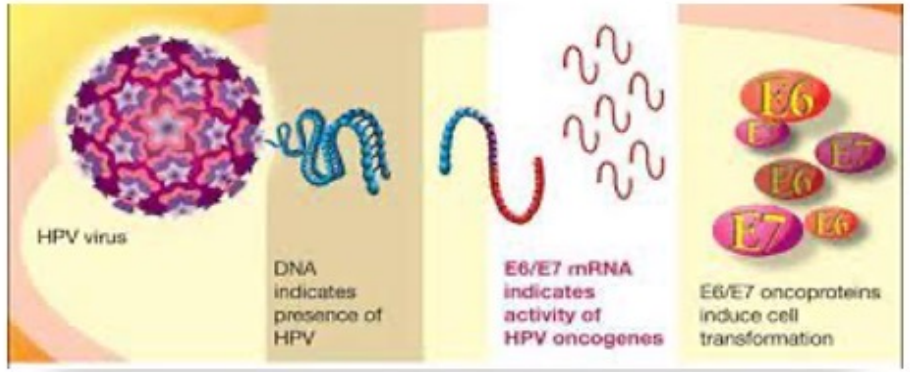


PRUEBA	SENSIBILIDAD	ESPECIFICIDAD
Citología ***Enfermedad***	30-87%	98.6%
Prueba VPH ***Infección***	87-98%	86-95%

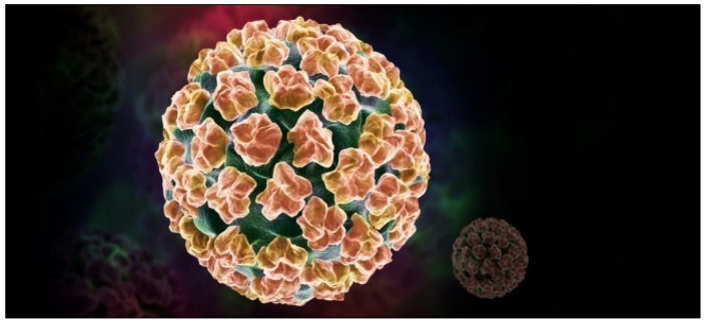
Fuente: Hechos & Acciones INC-ESE Vol 4 No 1-Enero 2012


Detección del VPH
Cervical Sampler
Transport Medium

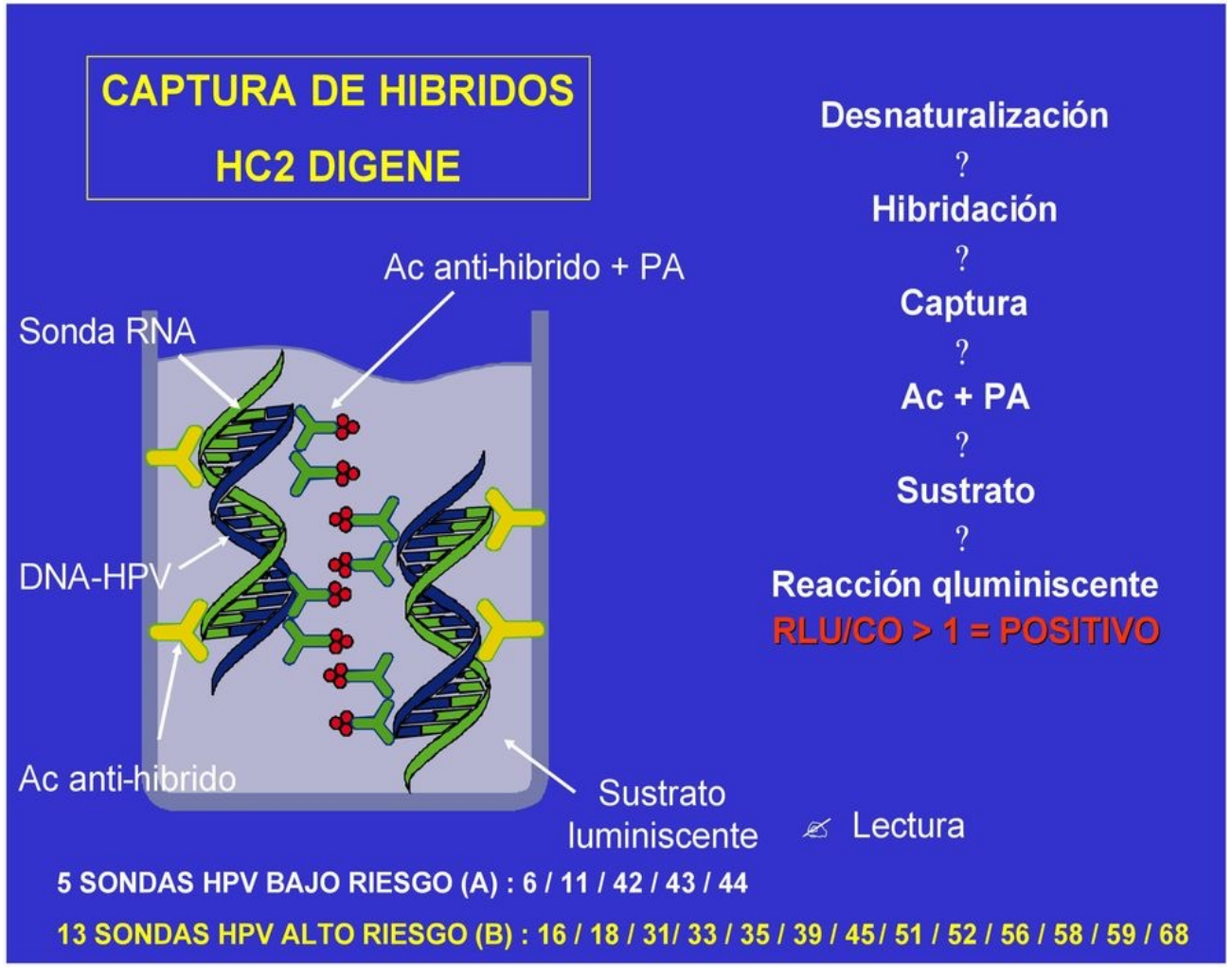
Pruebas moleculares



Interpretación



- Para seleccionar la prueba se deben considerar los resultados de los ensayos clínicos, la validación clínica de la prueba y otros aspectos operacionales logísticos



Pruebas directas

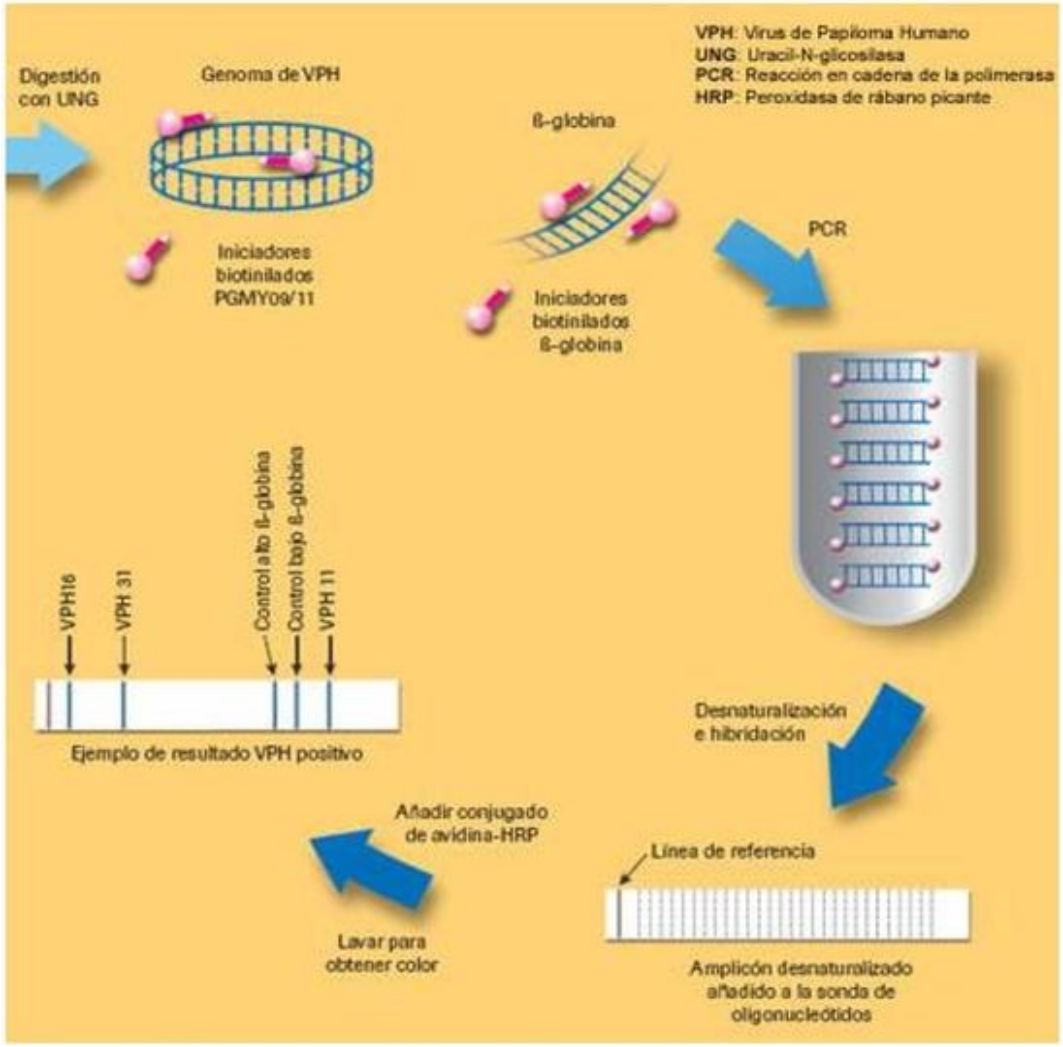
DESDE EL 2000
APROBADA POR LA FDA

ALTA SENSIBILIDAD Y
ALTO VALOR
PREDICTIVO NEGATIVO

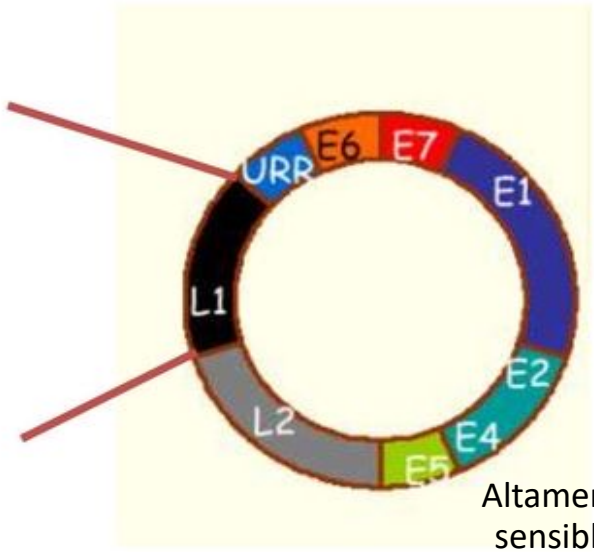
ESPECIFICIDAD
LIMITADA

REACCIONES CRUZADAS
CON SONDAS DE BAJO
RIESGO

Detección de HPV mediante PCR



https://es.slideshare.net/



PRUEBAS DE AMPLIFICACIÓN DE ADN

Permite obtener millones de copias a partir de un fragmento de ADN particular

Se han diseñado diferentes conjuntos de primers o cebos, la mayoría van dirigidos a la región L1

Altamente sensible, susceptible a contaminación

- PCR Genéricas: Tipo específicas y reportan algunos tipos virales
- PCR Múltiples: Identifican varios fragmentos del genoma

Tipos de pruebas utilizadas para tamizaje del VPH

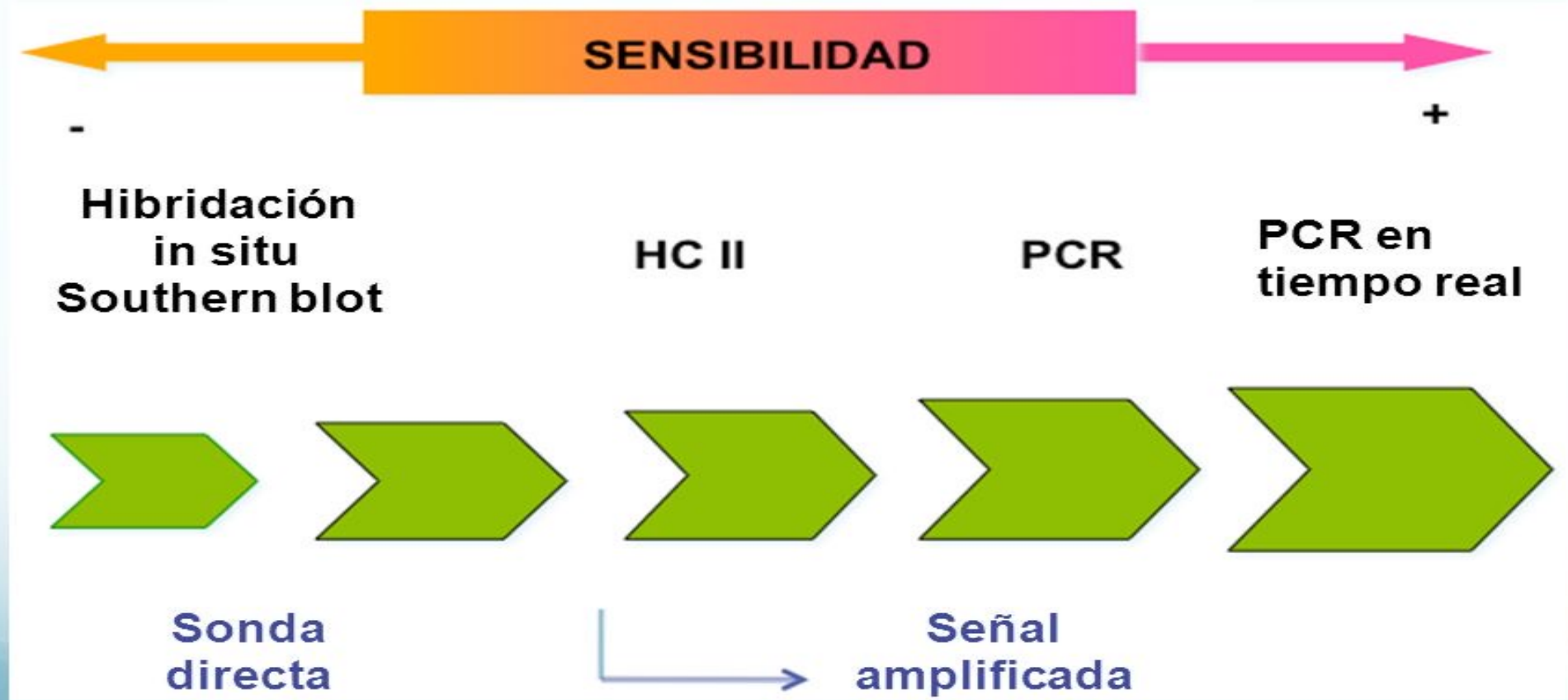
PRUEBAS	TIPO DE TECNICA	NOMBRE
ADN	Directas-Detección del genoma	Hybrid Capture 2
		CareHPV test
	Amplificación	GP5+/GP6+bio PCR-EIA
		Cervista HPV HR (14)
	Amplificación y genotipificación del VPH-16 /18 (16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66 y 68)	Cervista HPV 16/18
		Cobas HPV test (14): 16/18
		Xpert HPV
		Real Time High-Risk HPV (14): 16/18
		PapilloCheck
ARN	Amplificación de proteínas E6/E7	Optima HPV (14)
		PreTect HPV-Proofer HV
	Anticuerpos monoclonales	Avantage HPV E6 Test

Rendimiento de las pruebas de VPH utilizadas para tamizaje primario

PRUEBA	SENSIBILIDAD	ESPECIFICIDAD
Captura de Híbridos 2	97.5	84.3
Care HPV	90.0	84.2
Cervista HPV 16/18	100	
Cobas 4800 HPV	97.3	84.5
RealTime	95.0	87.2
Aptima HPV	97.6	90.2
Xpert HPV	100	81.5

Fuente: Cuzick J et al.2003

Sensibilidad de distintas técnicas de detección de VPH



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journal homepage: www.elsevier.com/locate/jviromet

HPV Direct Flow CHIP: A new human papillomavirus genotyping method based on direct PCR from crude-cell extracts☆

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HPV Genotyping
Hybrid Capture 2
Linear Array
CLART HPV2
HPV Direct Flow CHIP

ABSTRACT

HPV Direct Flow CHIP is a newly developed test for identifying 18 high-risk and 18 low-risk human papillomavirus (HPV) genotypes. It is based on direct PCR from crude-cell extracts, automatic flow-through hybridization, and colorimetric detection. The aim of this study was to evaluate the performance of HPV Direct Flow CHIP in the analysis of 947 samples from routine cervical screening or the follow-up of abnormal Pap smears. The specimens were dry swab samples, liquid-based cytology samples, or formalin-fixed paraffin-embedded tissues. The genotype distribution was in agreement with known epidemiological data for the Spanish population. Three different subgroups of the samples were also tested by Linear Array (LA) HPV Genotyping Test (n = 108), CLART HPV2 (n = 82), or Digene Hybrid Capture 2 (HC2) HPV DNA Test (n = 101). HPV positivity was 73.6% by HPV Direct Flow CHIP versus 67% by LA, 65.9% by HPV Direct Flow CHIP versus 59.8% by CLART, and 62.4% by HPV Direct Flow CHIP versus 42.6% by HC2. HPV Direct Flow CHIP showed a positive agreement of 88.6% with LA ($k = 0.798$), 87.3% with CLART ($k = 0.818$), and 68.2% with HC2 ($k = 0.518$). In conclusion, HPV Direct Flow CHIP results were comparable with those of the other methods tested. Although further investigation is needed to compare the performance of this new test with a gold-standard reference method, these preliminary findings evidence the potential value of HPV Direct Flow CHIP in HPV vaccinology and epidemiology studies.

1. Introduction

Cervical cancer is the third most common cancer among women and the second female cancer-related cause of death worldwide (Jemal et al., 2011). It has been extensively proven that persistent human papillomavirus (HPV) infection is necessary for the development of cervical intraepithelial lesions and invasive carcinoma (Bosch et al., 2002; Walboomers et al., 1999). Although most HPV infections resolve spontaneously, persistence of the so-called high-risk genotypes (Munoz et al., 2003) is directly linked to the malignant progression of the lesions (Kjaer et al., 2002; Remmink et al., 1995; Wallin et al., 1999), with HPV 16 and 18 accounting for approximately 70% of all cervical cancers (IARC, 2005; Munoz et al., 2006).

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0166-0934/$ – see front matter © 2013 The Authors. Published by Elsevier B.V. All rights reserved.
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Otras muestras

- Detección y genotipado de 36 tipos de HPV de manera simultanea
- No requiere la extracción /purificación de DNA
- Compatible con citología líquida, torundas citológicas y muestras de tejido parafinado

Cervico Vaginal Self Collection KIT

healthcare

MDPI

Article

Comparison of Different Self-Sampling Devices for Molecular Detection of Human Papillomavirus (HPV) and Other Sexually Transmitted Infections (STIs): A Pilot Study

Illari Sechi [1], Clementina Elvezia Cocuzza [2,*], Marianna Martinelli [2], Narcisa Muresu [1], Santina Castriciano [3], Giovanni Sotgiu [4] and Andrea Piana [1]

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Abstract: Background: Cervical cancer is the fourth most common cancer in women, and it is well known that high-risk human papillomavirus (hrHPV) infections are the necessary carcinogenic factors for the development of cervical tumors. Moreover, the interaction between HPV and other sexually transmitted infections (STIs) may increase the risk of cancer progression. Self-sampling has been demonstrated to represent a valid and well-accepted alternative, favoring women's participation in screening programs. This study aimed to investigate the use of FLOQSwabs® (FS) as compared to two other vaginal self-collection devices for the detection of hrHPV and other sexually transmitted infections. Methods: Cervical and vaginal self-samples were collected, using two different combinations of vaginal self-sampling devices, from 40 women referred to colposcopy for a documented abnormal Pap smear. All samples were tested for hrHPV and seven STI pathogens using two commercial molecular assays. Results: Data on hrHPV detection from the first group of women showed an almost perfect agreement (kappa: 0.89) between cervical vs. FS vaginal self-samples, and a substantial agreement (kappa: 0.79) between cervical and HerSwab™ (HS) samples. In the second group of women, an almost perfect agreement (kappa: 0.90) was demonstrated in the detection of hrHPV between cervical samples vs. FS, and a moderate agreement (kappa: 0.60) for cervical vs. Evalyn®Brush (EB) self-collected samples. STI detections showed a very good agreement (kappa: 0.89 and kappa: 1.00) both among FS vs. HS and FS vs. EB, respectively. There was no statistically significant difference between the different devices used. The most frequently detected hrHPV genotypes in the studied population were HPV 16, 31, 35, 51, and 56; whilst the most frequently identified STI pathogens were *Ureaplasma parvum* and *Mycoplasma hominis*. Overall, investigated women did not report any discomfort in using the different vaginal self-collection devices. Conclusion: Evaluation of the three different vaginal self-collection devices confirmed their overall good acceptability by the studied population, as well as a similar agreement for hrHPV detection as compared to cervical samples. Our study indicated that the use of self-collected samples offers an alternative strategy to improve women's participation in cervical cancer screening programs, but also underlined the importance of evaluating the concordance in hrHPV detection of collection devices in combination with the molecular hrHPV assay.

Keywords: HPV (human papillomavirus); high-risk human papillomavirus (hrHPV); sexually transmitted infections (STIs); vaginal self-sampling devices; self-collected samples; clinical accuracy; acceptability

check for updates

Citation: Sechi, I.; Cocuzza, C.E.; Martinelli, M.; Muresu, N.; Castriciano, S.; Sotgiu, G.; Piana, A. Comparison of Different Self-Sampling Devices for Molecular Detection of Human Papillomavirus (HPV) and Other Sexually Transmitted Infections (STIs): A Pilot Study. *Healthcare* **2022**, *10*, 459. https://doi.org/10.3390/healthcare10030459

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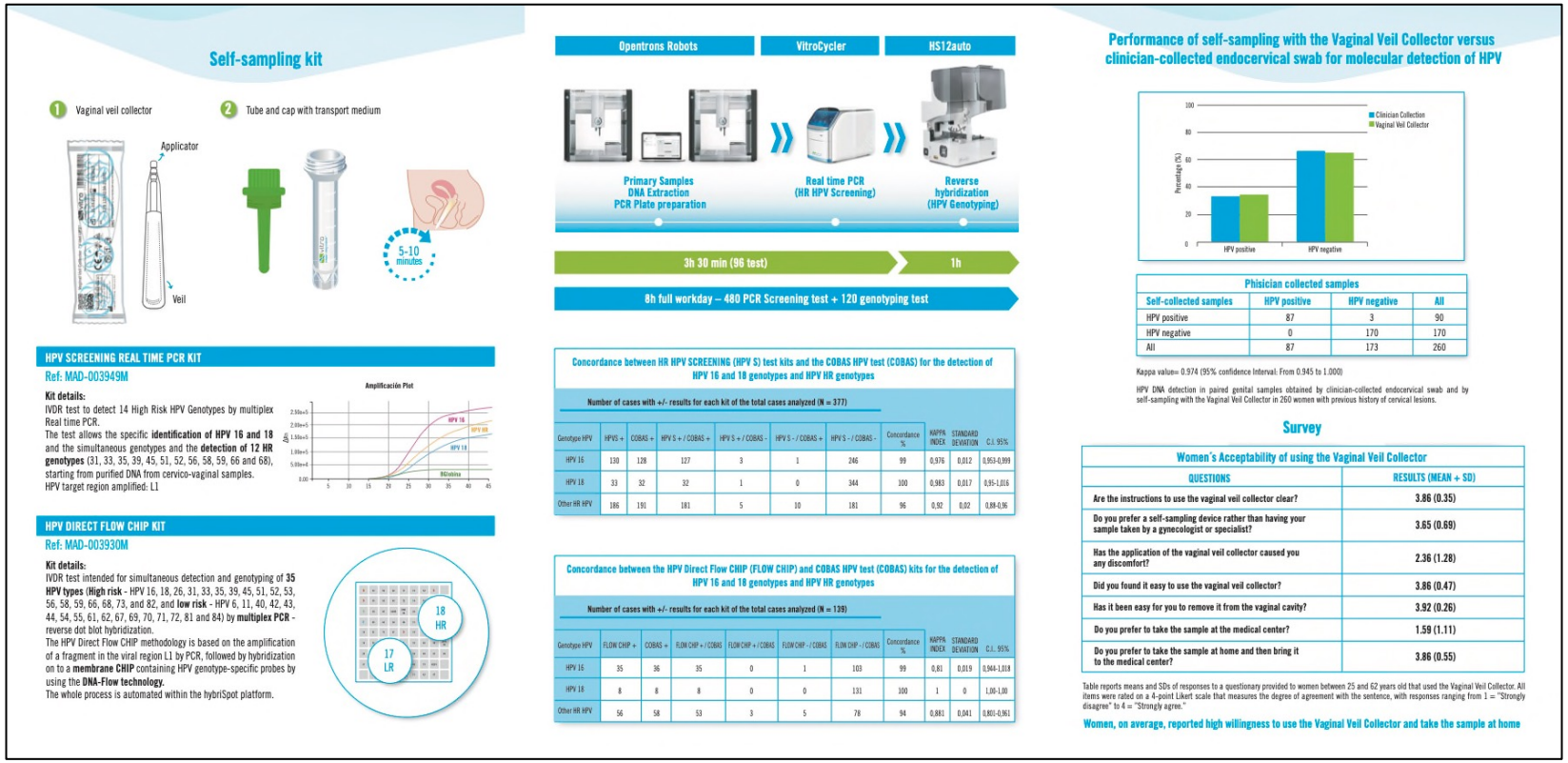

Triptico vitro master diagnostica

- Puede realizarse con una muestra vaginal tomada por la propia mujer
- Es ampliamente aceptada en diversas poblaciones
- Varios estudios demuestran una alta sensibilidad y especificidad comparada con la muestra tomada por un médico o enfermera

International Journal of
Environmental Research and Public Health

MDPI

Review

Diagnostic Test Accuracy of First-Void Urine Human Papillomaviruses for Presence Cervical HPV in Women: Systematic Review and Meta-Analysis

Peter Bober [1,*], Peter Firment [2] and Ján Sabo [1]

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Abstract: First-void urine usually contains exfoliated cells of the debris and mucus from the female genital organs and cervix, i.e., high concentration of human papillomavirus deoxyribonucleic acid (HPV DNA). We conducted a meta-analysis of published data and determined an accuracy of HPV detection in first-void urine compared to the women's cervix. According to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, we carried out a comprehensive literature search. Eligible articles published from 2011 until 2021 were gathered by searching Embase, PubMed and Cochrane Library Central databases. The patient selection, index test, standard test, and patient flow were the factors involved in quality evaluation. A meta-analysis of 15 studies (3412 women) based on 5054 potential records was conducted. Pooled sensitivity for high-risk HPV detection in urine of 78% (70–84%) and specificity of 89% (81–94%) were calculated. Any HPV detection in urine of 87% (74–94%) and 91% (83–96%) were pooled sensitivity and specificity, respectively. HPV 16 and 18 had a pooled sensitivity of 77% (76–77%) and specificity of 98% (98–98%). Meta-analysis indicated variations between the pooled specificities and sensitivities. In meta-regression analysis, a heterogeneity in accuracy by using covariates (bias in patient selection, purpose, sample timing, storage temperature and HPV detection method) were not detected. Our meta-analysis demonstrates the accuracy of detection of HPV in urine for the presence of cervical HPV. Although progress is continuously made in urinary HPV detection, further studies are needed to evaluate and to improve the accuracy of the first-void urine test in order to be comparable with other screening methods.

Keywords: human papillomavirus; HPV DNA; cervical cancer; CIN; first-void urine

check for updates

Citation: Bober, P.; Firment, P.; Sabo, J. Diagnostic Test Accuracy of First-Void Urine Human Papillomaviruses for Presence Cervical HPV in Women: Systematic Review and Meta-Analysis. *Int. J. Environ. Res. Public Health* **2021**, *18*, 13314. https://doi.org/10.3390/ijerph182413314

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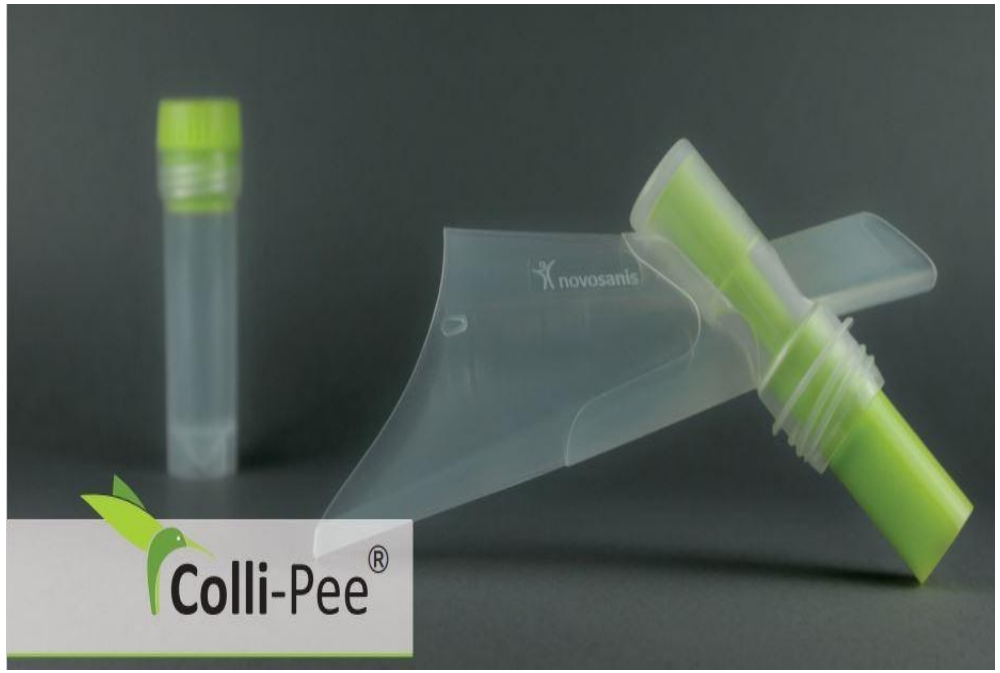
1. Introduction

Is widely known that HPV is the primary cause of cervical cancer [1]. Cervical cancer presents the fourth-most cause of cancer deaths in women worldwide [2]. HPV is detected in almost all cervical cancer biopsies with more than 90% presence in high-grade squamous intraepithelial lesions (HSIL) [3]. More than 200 genotypes of HPV have been identified to date [4]. Of them, HPV16 and HPV18 represent the high-risk oncogenic genotypes, as they cause approximately 70% of nearly all cervical cancer [5–7].

A major impediment to controlling cervical cancer is lack of attendance for screening, i.e., in those countries without well-developed screening programs, from 50% to more than 80% of women are not screened [8]. In addition, in countries with well-organised screening programmes, half of all potentially detectable carcinomas are found in women who have not attended screening programmes [9].

There has been a drastic decline in the incidence, as well as the mortality, of cervical cancer worldwide since the introduction of the Pap test [10,11]. However, screening



- Metaanálisis de 15 estudios /3412 mujeres)
- Sensibilidad del 78% y especificidad del 89%
- VPH 16 y 18 sensibilidad combinada del 77% y especificidad del 98%
- Precisión para la detección de VPH
- Se necesitan más estudios para evaluar y mejorar la precisión de la prueba de orina de la primer evacuación

Biomarcadores en sangre

Original Article

Blood-Based Biomarkers of Human Papillomavirus–Associated Cancers: A Systematic Review and Meta-Analysis

Sanjana Balachandra, BSA; Samuel B. Kusin, BA; Rebecca Lee, MD[1]; James-Michael Blackwell, MPH[2]; Jasmin A. Tiro, PhD[2,3]; Lindsay G. Cowell, PhD[2,4]; Cheng-Ming Chiang, PhD[3,5,6]; Shwu-Yuan Wu, PhD[3,5]; Sanskriti Varma, MD[7]; Erika L. Rivera, MD[8]; Helen G. Mayo, MLS[9]; Lianghao Ding, PhD[10]; Baran D. Sumer, MD[1]; Jayanthi S. Lea, MD[11]; Aditya Bagrodia, MD [12]; Linda M. Farkas, MD[13]; Richard Wang, MD [14]; Carole Fakhry, MD, MPH [15]; Kristina R. Dahlstrom, PhD [16]; Erich M. Sturgis, MD, MPH [16]; and Andrew T. Day, MD, MPH[1,3]

BACKGROUND: Despite the significant societal burden of human papillomavirus (HPV)–associated cancers, clinical screening interventions for HPV-associated noncervical cancers are not available. Blood-based biomarkers may help close this gap in care. **METHODS:** Five databases were searched, 5687 articles were identified, and 3631 unique candidate titles and abstracts were independently reviewed by 2 authors; 702 articles underwent a full-text review. Eligibility criteria included the assessment of a blood-based biomarker within a cohort or case-control study. **RESULTS:** One hundred thirty-seven studies were included. Among all biomarkers assessed, HPV-16 E seropositivity and circulating HPV DNA were most significantly correlated with HPV-associated cancers in comparison with cancer-free controls. In most scenarios, HPV-16 E6 seropositivity varied nonsignificantly according to tumor type, specimen collection timing, and anatomic site (crude odds ratio [cOR] for p16+ or HPV+ oropharyngeal cancer [OPC], 133.10; 95% confidence interval [CI], 59.40-298.21; cOR for HPV-unspecified OPC, 25.41; 95% CI, 8.71-74.06; cOR for prediagnostic HPV-unspecified OPC, 59.00; 95% CI, 15.39-226.25; cOR for HPV-unspecified cervical cancer, 12.05; 95% CI, 3.23-44.97; cOR for HPV-unspecified anal cancer, 73.60; 95% CI, 19.68-275.33; cOR for HPV-unspecified penile cancer, 16.25; 95% CI, 2.83-93.48). Circulating HPV-16 DNA was a valid biomarker for cervical cancer (cOR, 15.72; 95% CI, 3.41-72.57). In 3 cervical cancer case-control studies, cases exhibited unique microRNA expression profiles in comparison with controls. Other assessed biomarker candidates were not valid. **CONCLUSIONS:** HPV-16 E6 antibodies and circulating HPV-16 DNA are the most robustly analyzed and most promising blood-based biomarkers for HPV-associated cancers to date. Comparative validity analyses are warranted. Variations in tumor type–specific, high-risk HPV DNA prevalence according to anatomic site and world region highlight the need for biomarkers targeting more high-risk HPV types. Further investigation of blood-based microRNA expression profiling appears indicated. ***Cancer* 2020;0:1-15**. © *2020 American Cancer Society*.

KEYWORDS: anal cancer, biomarker, blood biomarker, cancer prevention, cancer surveillance, cervical cancer, human papillomavirus (HPV), oropharyngeal cancer, penile cancer, screening.

INTRODUCTION

Human papillomavirus (HPV)–associated cancers impose a substantial burden on society. HPV causes more than 30,000 oropharyngeal, cervical, and other anogenital cancers in the United States each year.[1] HPV-associated oropharyngeal cancer (OPC) has risen rapidly in incidence and has recently overtaken cervical cancer, and its incidence is expected to continue to increase over the next few decades.[2,3] The treatment of HPV-associated cancers is associated with substantial morbidity, and more than 8000 patients die of the disease annually.[4] These cancers are also expensive: the cost of cancer care totals approximately $1 billion, and population-level cancer prevention costs an estimated $8 billion annually.[5]

Ongoing primary and secondary preventive interventions targeting HPV-associated cancers effectively protect particular populations[6] but fail to address all individuals vulnerable to HPV-related cancers. For example, prophylactic HPV vaccination is recommended only for females and males aged 9 to 26 years and is optional for adults aged 27 to 45 years.

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MISS KRISTINA KVIST JENSEN (Orcid ID : 0000-0001-6001-8569)

Article type : Original Manuscript

Circulating human papillomavirus DNA as a surveillance tool in head and neck squamous cell carcinoma: a systematic review and meta-analysis

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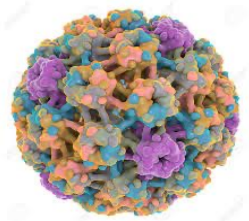
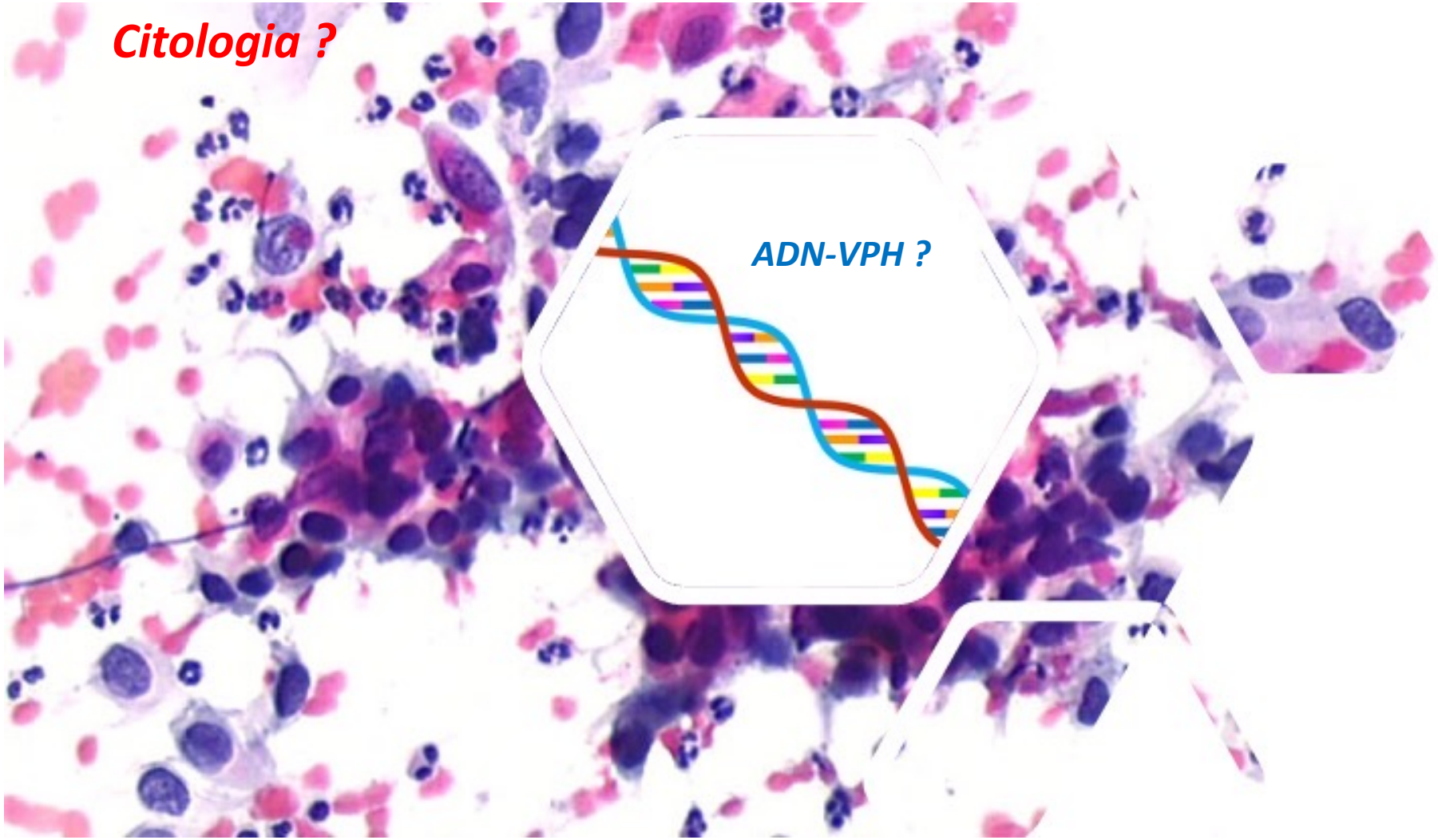


Representan una modalidad potencial ideal para la detección temprana o la vigilancia de los cánceres asociados con el VPH en todos los sitios.

Consideraciones para selección de la prueba de VPH

- Antes de seleccionar una prueba de VPH entre la amplia variedad disponible en el mercado, se debe analizar un análisis de costo-beneficio y considerar la factibilidad de implementar la prueba en el contexto de un programa de tamizaje
- Se deben elegir solo pruebas de VPH que tienen una validación clínica
- Las pruebas autorizadas por agencias reguladoras , tal como la FDA, son opciones seguras
- Introducir una prueba en un programa y luego cambiarla por otra es difícil y tendrá implicaciones de costos
- Las pruebas tienen fecha límite , por ejemplo 9 meses o 12 meses, y hay que tomar en cuenta los aspectos de la gestión de la cadena de abastecimiento al elegir la prueba


Citologia ?
ADN-VPH ?

Por que el co-testing ?

WILEY CANCER CYTOPATHOLOGY

Comparison of Cervical Cancer Screening Results Among 256,648 Women in Multiple Clinical Practices

ABSTRACT

BACKGROUND

METHODS

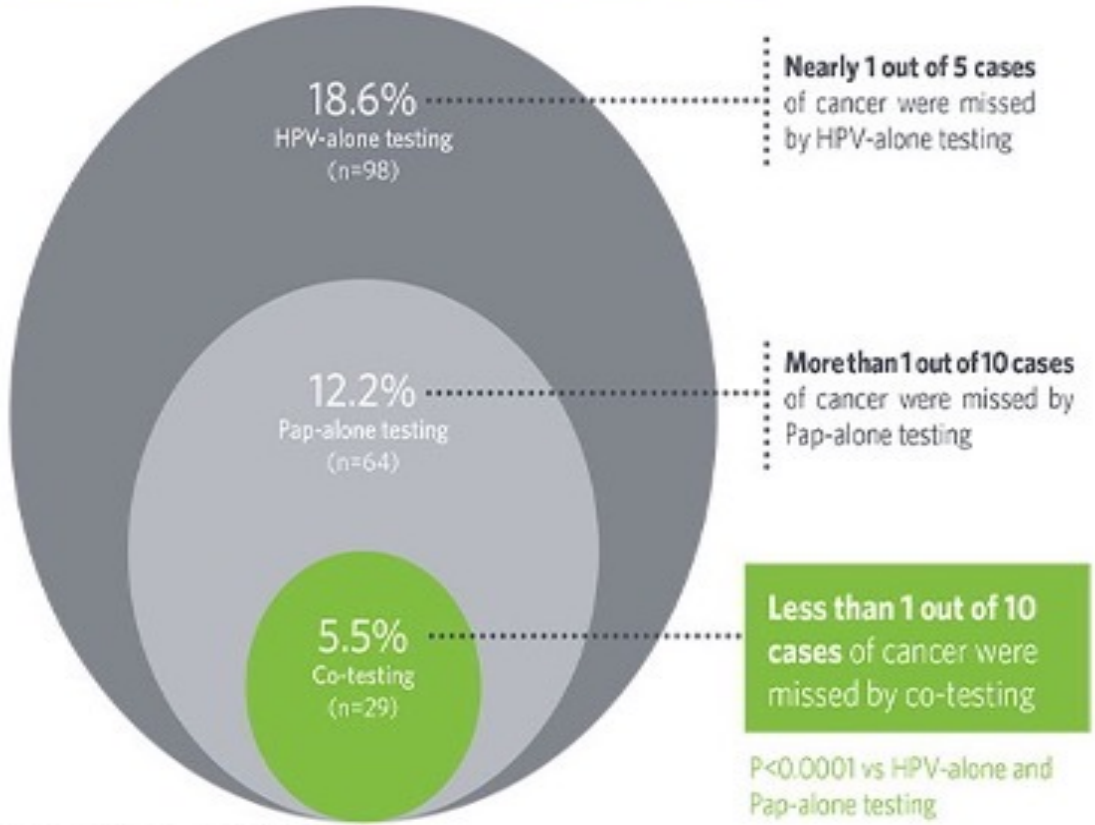
RESULTS

CONCLUSIONS

INTRODUCTION

CO-TESTING HAD THE FEWEST MISSED CASES OF CERVICAL CANCERS THAN HPV OR PAP TESTING ALONE

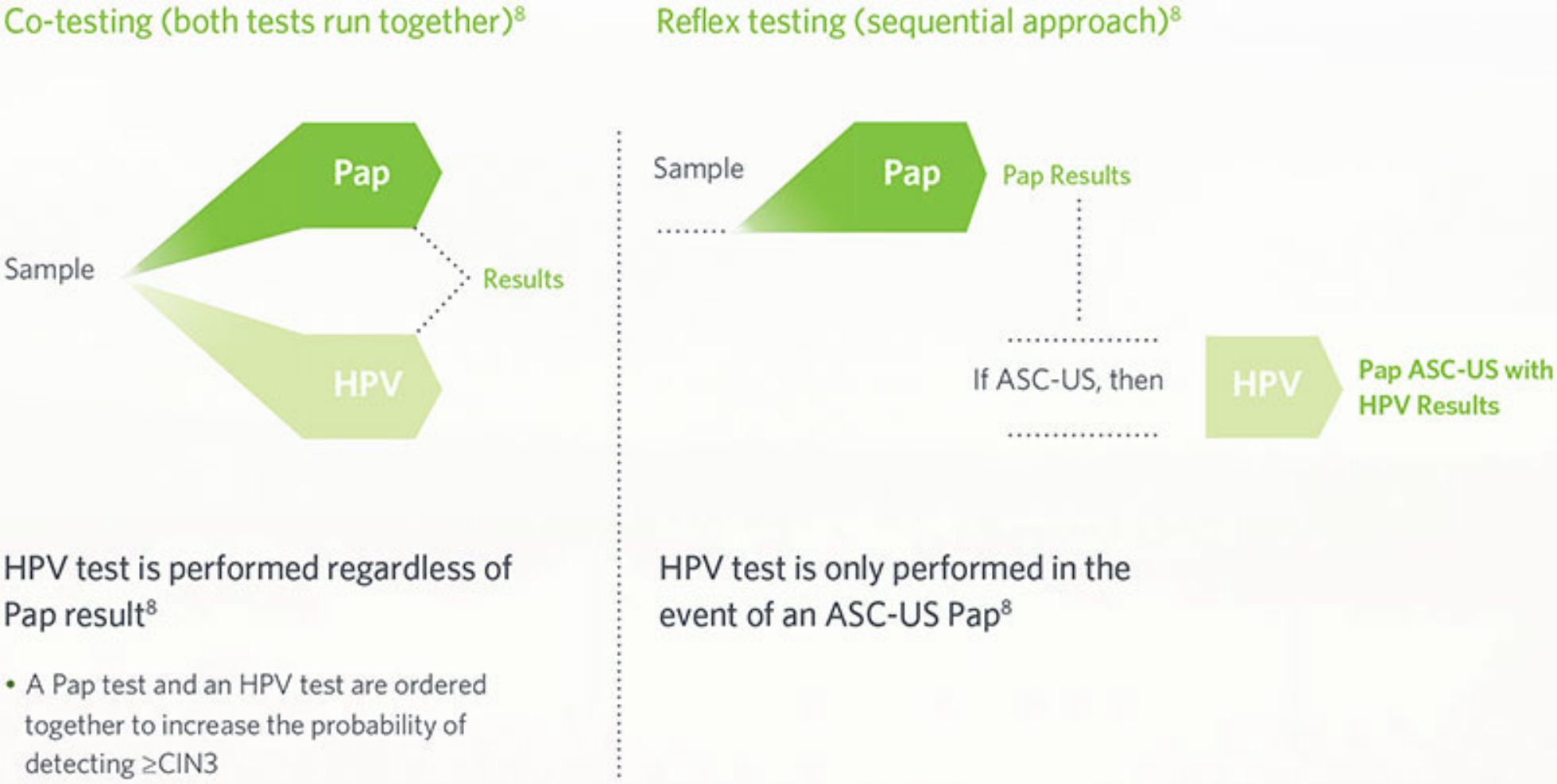
Percentage of missed cases of cervical cancer (n=526) by screening method



† Co-testing is preferred, but Pap testing every 3 years is also acceptable.

1.Blatt AJ, Kennedy R, Luff RD, et al. Comparison of cervical cancer screening results among 256,648 women in multiple clinical practices. Cancer Cytopathol. 2015;123(5):282-288.

Recomendaciones



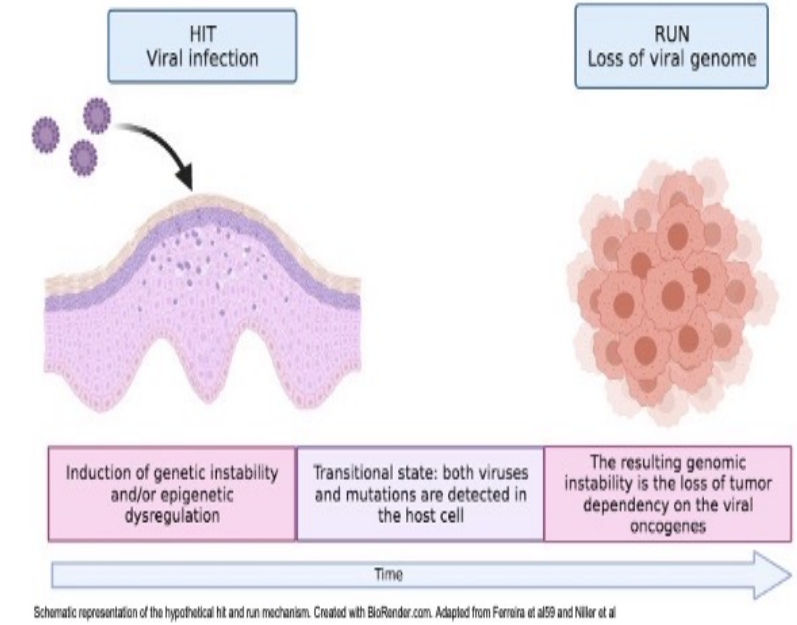
1.Blatt AJ, Kennedy R, Luff RD, et al. Comparison of cervical cancer screening results among 256,648 women in multiple clinical practices. Cancer Cytopathol. 2015;123(5):282-288.

Cáncer de cérvix/PCR DNA Negativo

- ***Cotesting:*** Identifica mayor número de mujeres en biopsias con CIN3 que solo la prueba molecular
- Solo prueba molecular: 19% de falsos negativos en LEI-AG

Problemas asociados:

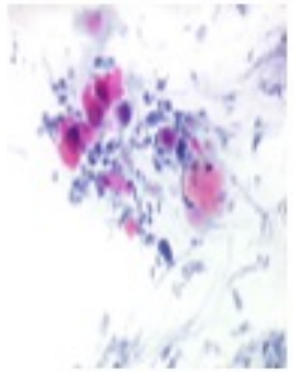
- Inhibición de la PCR, muestra hemorrágica , muestra mucoide
- Decremento de la concentración de DNA por estadio de la enfermedad
- Recolección de la muestra, conservación del virus en el medio de transporte. Relevancia del control interno endógeno
- Deficiencia de la fase de extracción de DNA prueba PCR
- Niveles de DNA-VPH disminuye en infecciones de alto grado,



Schematic representation of the hypothetical hit and run mechanism. Created with BioRender.com. Adapted from Ferreira et al59 and Niller et al

Human papillomavirus-independent cervical cancer

Fernandes A, et al. Int J Gynecol Cancer 2021;0:1–7. doi:10.1136/ijgc-2021-003014



CO-TESTING IS THE BEST CERVICAL CANCER SCREENING FOR WOMEN AGES 30 TO 65

- Published data show that co-testing offers the best protection versus HPV-only, Pap-only, and reflex testing
- Current cervical cancer screening guidelines all recommend co-testing as the preferred screening method for women ages 30 to 65

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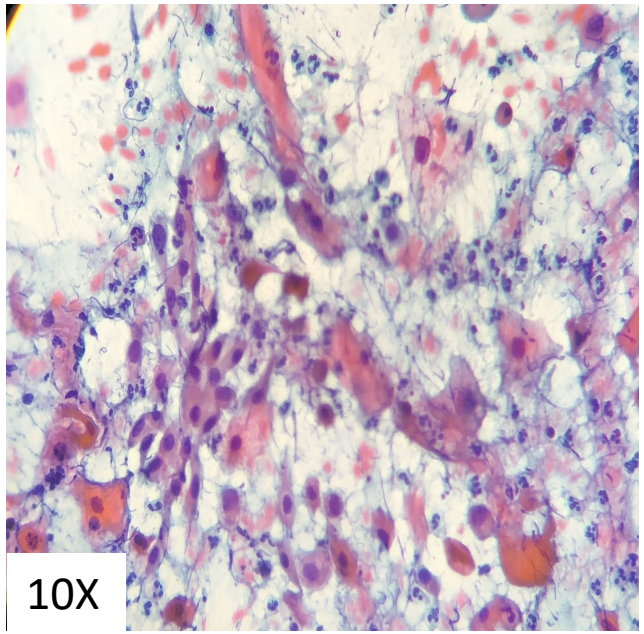
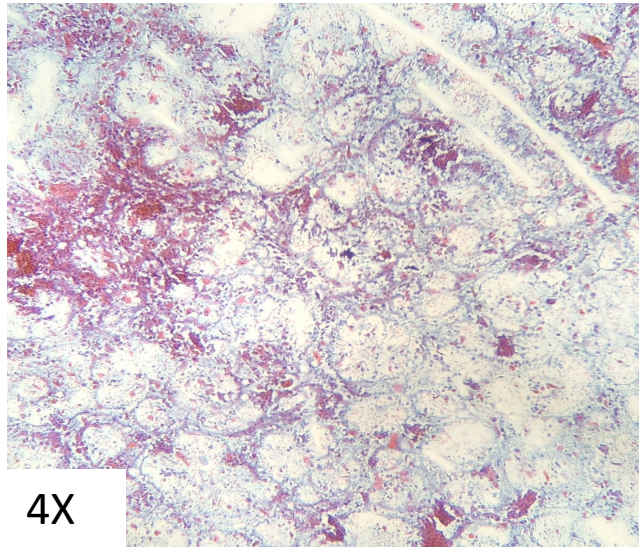
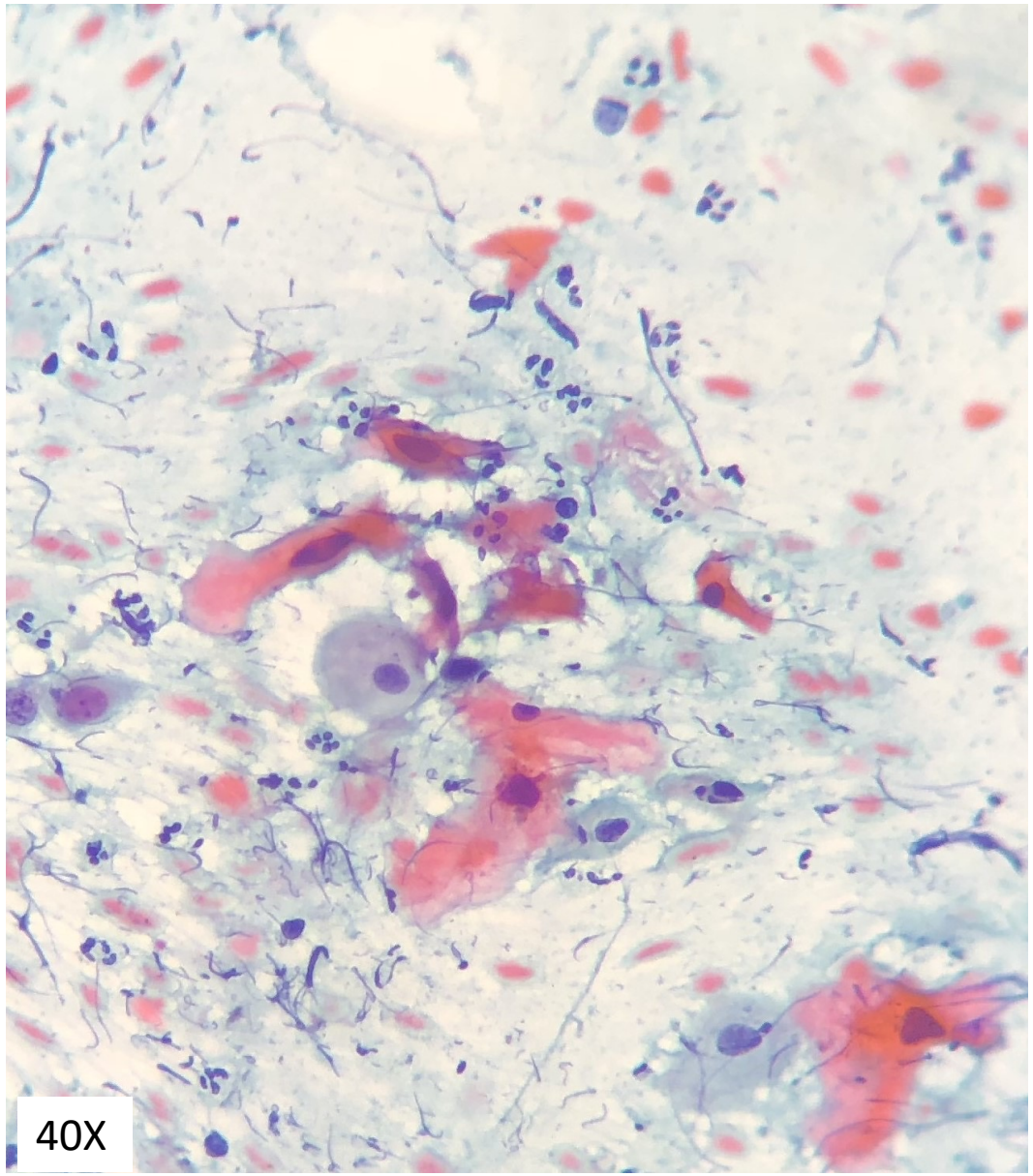
Casos clínicos







53 años

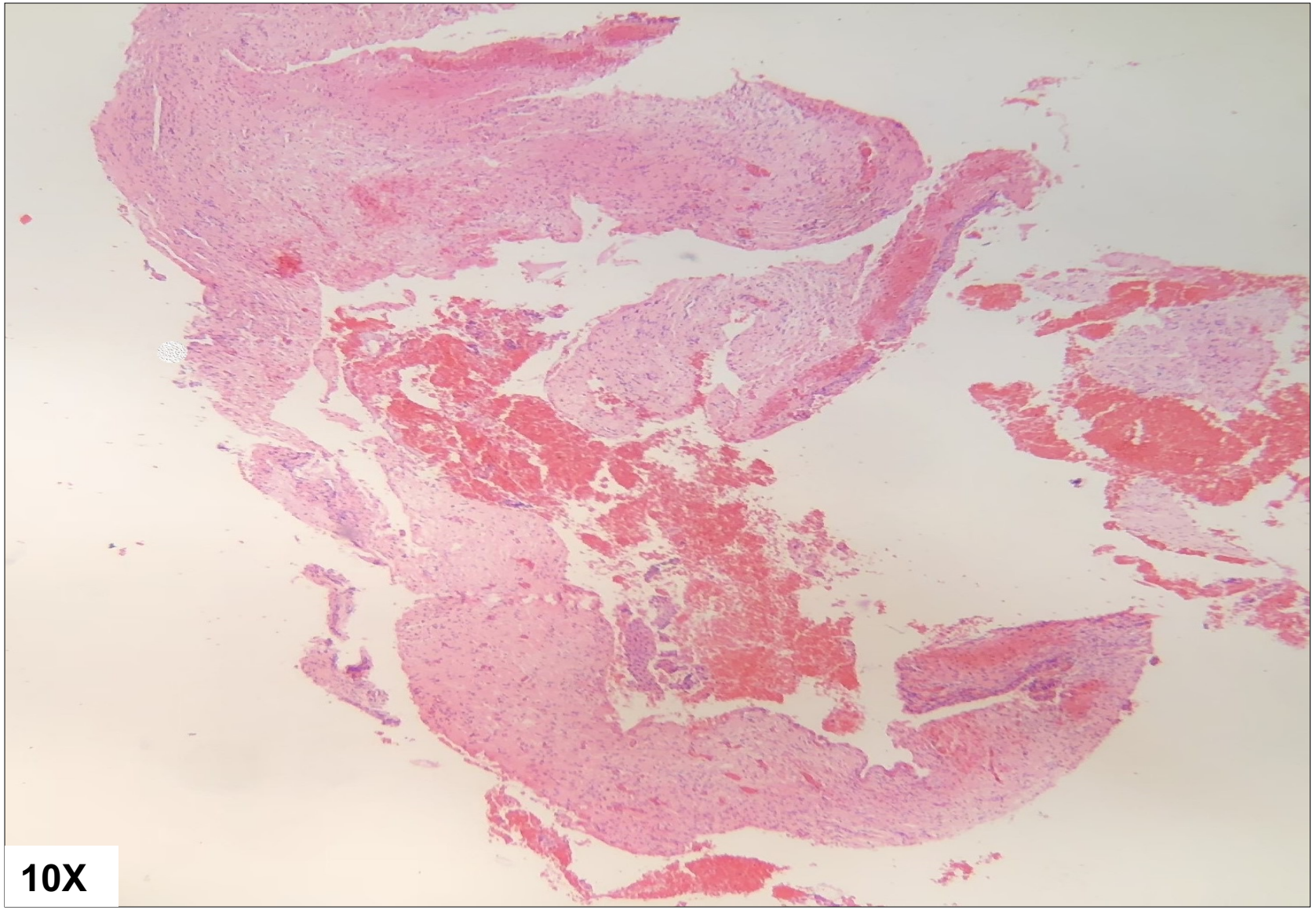
G3 P3 A0 C0

Isabel Cristina Almonacid U

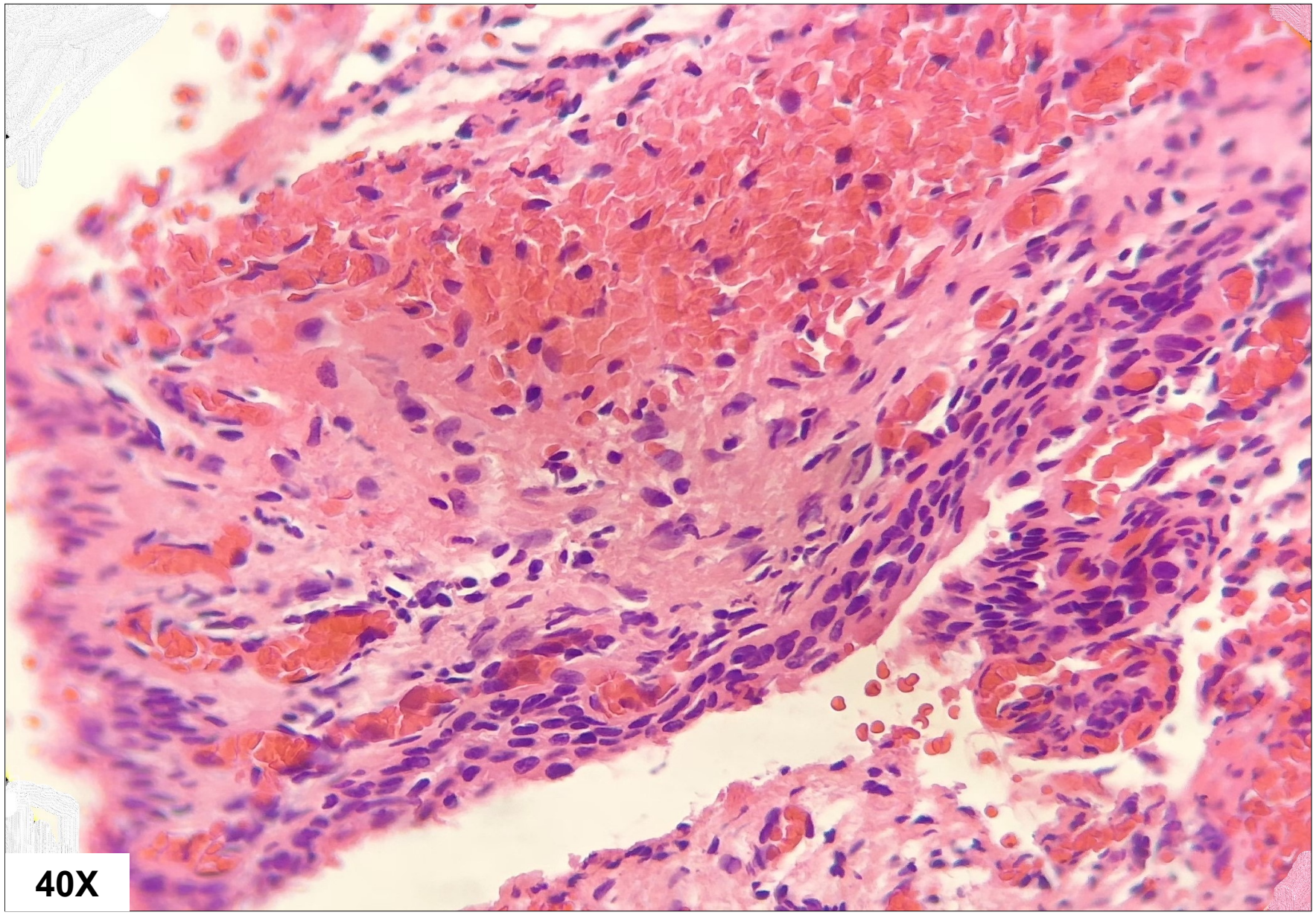
https://sp.depositphotos.com/stock-photos/colposcopia.htm

- Colposcopia:
- Cuello corto, atrófico, cupulizado
- Completa inadecuada con metaplasia a las 11 y 3

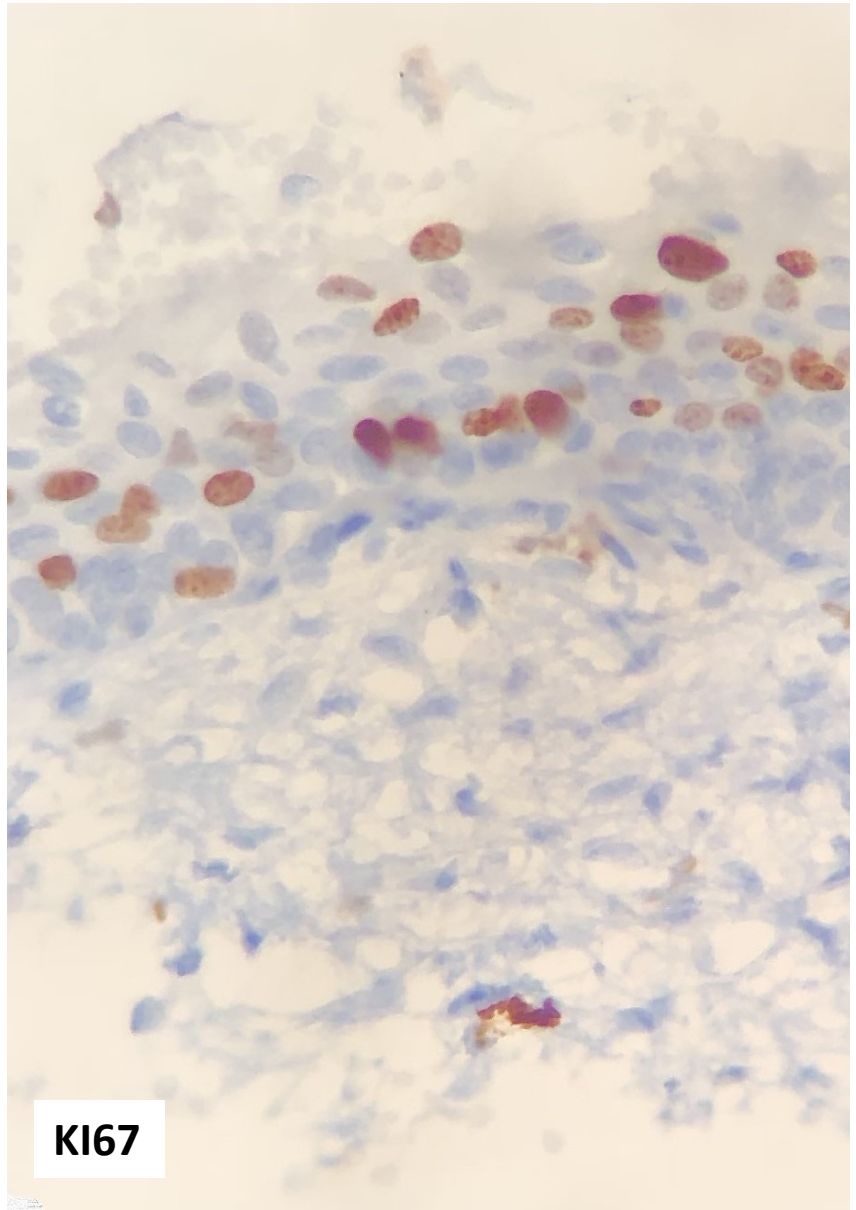
- Genotipificación: Negativo para VPH- AR

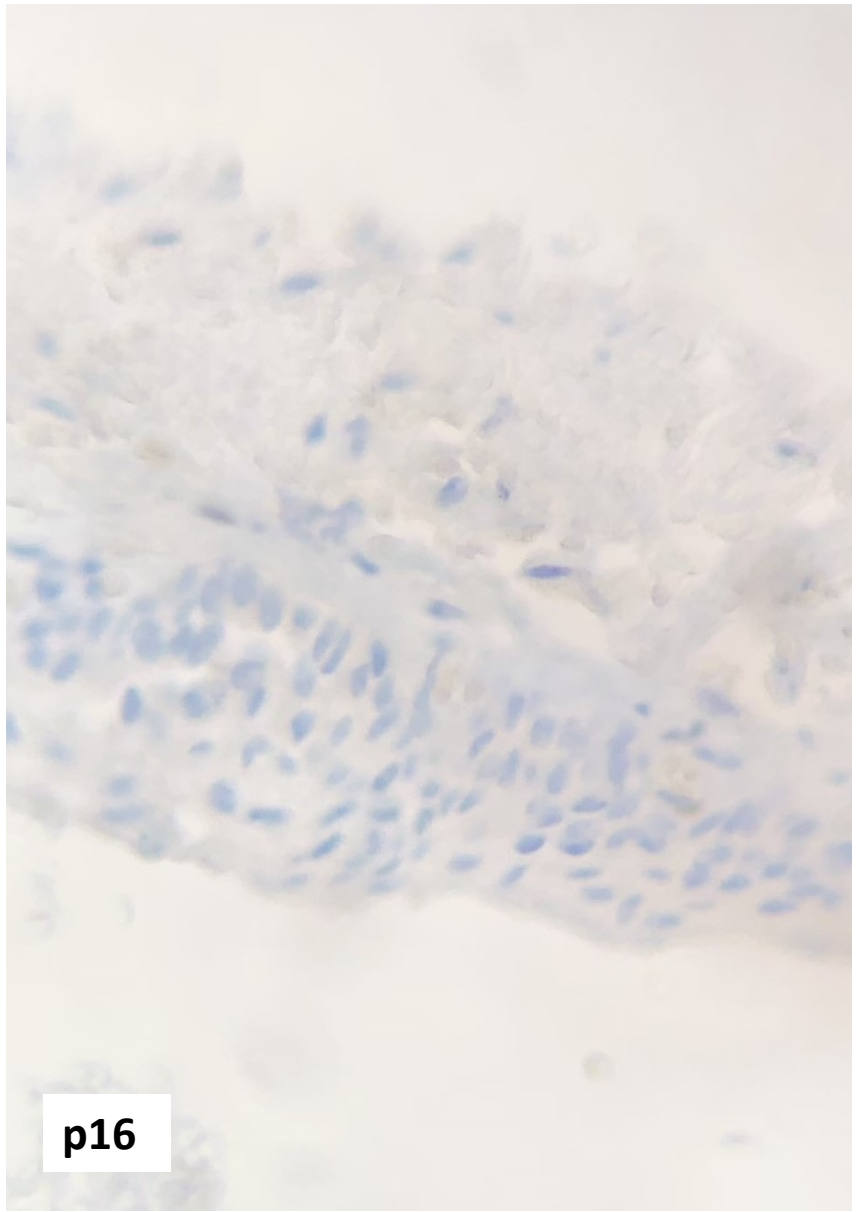


Isabel Cristina Almonacid



Isabel Cristina Almonacid





Isabel Cristina Almonacid

Diagnóstico

Mujer de 56 años de edad con citología positiva para anormalidades en células epiteliales escamosas.

Cuello corto , atrófico, cupulizado. Colposcopia inadecuada

Prueba molecular negativa para VPH-AR

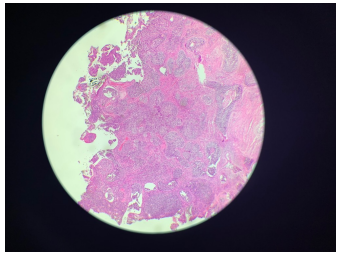
Biopsia con atipia citológica, p16 no expresado. Ki-67 expresado en la basal

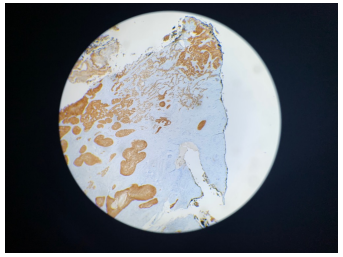
Lesión alta

Conización diagnóstica

Biopsias de cervix

EDAD	DIAGNOSTICO Citologia/Biopsia	GENOTIPICACION	Cuantificación de ácido nucleico ng/uL Metodología: Espectofotometría	Resultados (INNO-LIA)
68	Carcinoma escamocelular		1.95	NEGATIVO
43	Lesión intraepitelial escamosa de alto grado	Negativa	2.18	VPH-56
35	Lesión intraepitelial escamosa de alto grado	VPH Otros	2.15	VPH 56-68





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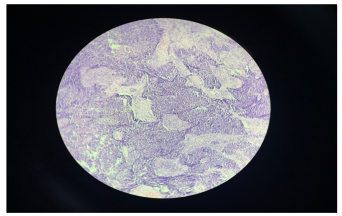

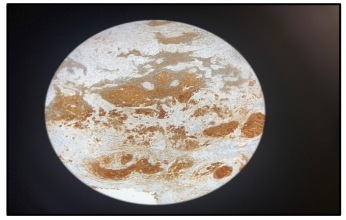

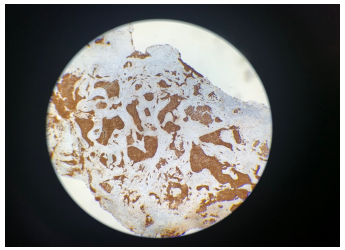

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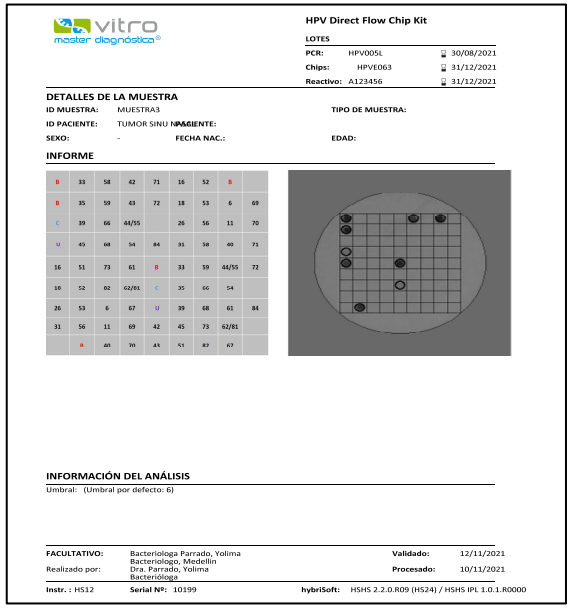
Otras biopsias

28	Carcinoma sinunasal	VPH-16
17	Carcinoma escamocelular de lengua	VPH-16
53	Carcinoma nasal	VPH-16



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HPV Direct Flow Chip Kit

LOTES

PCR:	HPV005L	30/08/2021
Chips:	HPVE063	31/12/2021
Reactivo:	A123456	31/12/2021

DETALLES DE LA MUESTRA

ID MUESTRA: MUESTRA3 **TIPO DE MUESTRA:**

ID PACIENTE: TUMOR SINU NASAL **PACIENTE:**

SEXO: - **FECHA NAC.:** **EDAD:**

INFORME

B	33	58	42	71	16	52	B	
B	35	59	43	72	18	53	6	69
C	39	66	44/55		26	56	11	70
U	45	68	54	84	31	58	40	71
16	51	73	61	B	33	59	44/55	72
18	52	82	62/81	C	35	66	54	
26	53	6	67	U	39	68	61	84
31	56	11	69	42	45	73	62/81	
	B	40	70	44	51	82	67	

INFORMACIÓN DEL ANÁLISIS

Umbral: (Umbral por defecto: 6)

FACULTATIVO:	Bacterióloga Parrado, Yolima Bacteriologo, Medellin	**Validado:**	12/11/2021
Realizado por:	Dra. Parrado, Yolima Bacterióloga	**Procesado:**	10/11/2021
Instr. : HS12	**Serial Nº:** 10199	**hybriSoft:**	HSHS 2.2.0.R09 (HS24) / HSHS IPL 1.0.1.R0000

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SEXO: - **FECHA NAC.:** **EDAD:**

INFORME

HPV POSITIVO

Muestra positiva para:

Alto Riesgo:

16

Nota: Material insuficiente.

Muestra negativa para el resto de genotipos incluidos en el test HPV direct flow chip.

PROTOCOLO

Detección y genotipado del virus HPV mediante PCR y reverse dot blot, genotipos:
- Alto riesgo: 16, 18, 26, 31, 33, 35, 39, 45, 51, 52, 53, 56, 58, 59, 66, 68, 73, 82.
- Bajo riesgo: 6, 11, 40, 42, 43, 44/55, 54, 61, 62/81, 67, 69, 70, 71, 72, 84.

Preparación de la muestra/extracción del ADN
- Usar la suspensión celular/DNA para amplificar por PCR.
- Protocolo PCR (estándar) HPV Direct Flow Chip: 1x 25°C 10 min, 1x 94°C 3min; 15x94-42-72°C (30"-30"-30"), 35x 94-60-72°C (30"-30"-30"), 1x 72°C 5 min.
- Protocolo PCR (liofilizado) HPV Direct Flow Chip: 1x 25°C 10 min, 1x 94°C 3min; 15x94-47-72°C (30"-30"-30"), 35x 94-65-72°C (30"-30"-30"), 1x 72°C 5 min.

Protocolo REVERSE-DOT BLOT:
- Hibridación del producto de PCR biotinilado con HPV CHIP
- Lavados post-hibridación
- Incubación con enzima Estreptavidina-Fosfatasa
- Revelado con NBT-BCIP

Análisis automático de resultados

NOTAS

FACULTATIVO:	Bacterióloga Parrado, Yolima Bacteriologo, Medellin	**Validado:**	12/11/2021
Realizado por:	Dra. Parrado, Yolima Bacterióloga	**Procesado:**	10/11/2021
Instr. : HS12	**Serial Nº:** 10199	**hybriSoft:**	HSHS 2.2.0.R09 (HS24) / HSHS IPL 1.0.1.R0000

OPEN

2019 ASCCP Risk-Based Management Consensus Guidelines for Abnormal Cervical Cancer Screening Tests and Cancer Precursors

Rebecca B. Perkins, MD, MSc,[1] Richard S. Guido, MD,[2] Philip E. Castle, PhD,[3] David Chelmow, MD,[4] Mark H. Einstein, MD, MS,[5] Francisco Garcia, MD, MPH,[6] Warner K. Huh, MD,[7] Jane J. Kim, PhD, MSc,[8] Anna-Barbara Moscicki, MD,[9] Ritu Nayar, MD,[10] Mona Saraiya, MD, MPH,[11] George F. Sawaya, MD,[12] Nicolas Wentzensen, MD, PhD, MS,[13] and Mark Schiffman, MD, MPH[14] for the 2019 ASCCP Risk-Based Management Consensus Guidelines Committee

Key Words: cervical cytology, HPV testing, management of abnormal cervical cancer screening tests, guidelines

(*J Low Genit Tract Dis* 2020;24: 102–131)

Table of Contents

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R.B.P. and R. S. G. contributed equally to the development of this manuscript and are co-first authors.

The guidelines effort received support from the National Cancer Institute and ASCCP. Participating organizations supported travel for their participating representatives. All participating consensus organizations, including the primary funders, had equal and balanced roles in the consensus process including data analysis and interpretation, writing of manuscript, and decision to submit for publication. No industry funds were used in the development of these guidelines. The corresponding authors had final responsibility for the submission decision.

The National Cancer Institute (including M.S. and N.W.) receives cervical screening results at reduced or no cost from commercial research partners (Qiagen, Roche, BD, MobileODT, Arbor Vita) for independent evaluations of screening methods and strategies. A.-B.M. is an advisory board member of Merck and GSK. R.S.G. is an ASCCP consultant of Inovio Pharmaceuticals DSMB. W.K.H. is connected with Inovio Pharmaceuticals DSMB. P.E.C. has received HPV tests and assays at a reduced or no cost from Roche, Becton Dickinson, Arbor Vita Corporation, and Cepheid for research. M.H.E. has advised companies and participated in educational activities but does not receive any honoraria or payments for these activities. In some cases, his employer, Rutgers, receives payment for his time for these activities from Papivax, Cytvec, Merck, Hologic, and PDS Biotechnologies. He has been the overall PI or local PI for clinical trials from Johnson&Johnson, Pfizer, Iovance, and Inovio. Funding for these activities is for the research related costs of the trials. The other authors have declared they have no conflicts of interest.

Disclaimer: The conclusions, findings, and opinions expressed by authors contributing to this journal do not necessarily reflect the official position of the US Department of Health and Human Services, the Public Health Service, the Centers for Disease Control and Prevention, or the National Cancer Institute.

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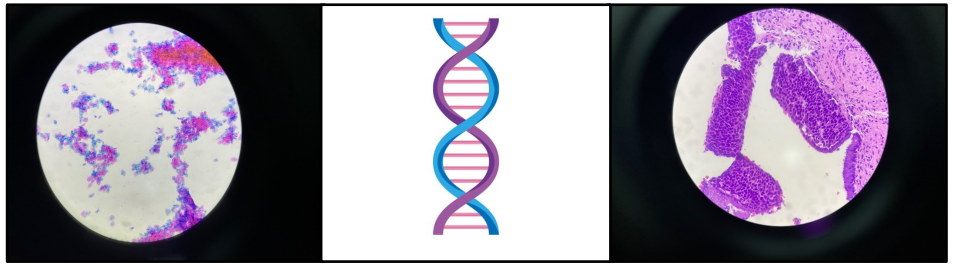
Recomendaciones basadas en el riesgo no en resultados



Utilidad de las pruebas de alta especificidad para detectar anomalías de alto grado

Utilidad de las nuevas tecnologías para mejorar el diagnóstico y manejo

Seguimiento longitudinal para distinguir infecciones por VPH nueva de las persistentes

Reducción de pruebas innecesarias y procedimientos invasivos en pacientes de bajo riesgo

Identificación de pacientes de alto riego que se beneficiaran de una vigilancia más intensa

Maximizar los beneficios de la prevención del cáncer y minimizar los daños de las pruebas y tratamiento excesivo

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INVESTIGACIÓN SOBRE VIRUS DEL PAPILOMA HUMANO (VPH)

DURMIENDO CON EL ENEMIGO

Isabel Cristina Almonacid

CONCLUSIONES

El VPH es un virus oncogénico, agente causal de diferentes tumores epiteliales

Pruebas de tamización identifica individuos con mayor probabilidad de tener una enfermedad o un precursor de la enfermedad

Pruebas moleculares alta sensibilidad, citologia alta especificidad

Prueba conjunta incrementa probabilidad de detectar LEI-AG y cáncer

Manejo basado en el riesgo no en resultados

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Gracias