Colposcopy of VIN and Vulvar Cancer

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Learning Objectives

- **To understand colposcopy of vulvar abnormalities**
- **To understant the neoplastic potential of VIN**
- **To recognize vulvar intraepithelial neoplasia and vulvar cancer**
- **To list the gross and colposcopic findings of VIN and vulvar cancer**

Other Means of Magnification
Spalding Magnifiers Part 81-33-05 Toll free 1-888-855-8666
Local 713-466-3113
Houston, Texas.

Colposcopic Techniques

- 5% acetic Acid
- Soak initially for 3-5 minutes
- Use copious amounts
- Reapply often
- A void using in presence of breaks in epithelium or inflammation.

? Other Solutions

- Lugol's
    - Not useful (little glycogen present outside Hart's line)

- Toluidine blue (1%)
    - Historic- stains normal tissue

Clinical Pitfalls of vulvar Colposcopy

- Acetowhitenings is nonspecific
- Normal anatomic variants- like vestibular micropapillae- often confused with HPV colposcopically and histologically
- Marked acetowhite changes in up to 65% of normal women.

Vulvar Biopsy Techniques

- Anesthesia
  - 1 % xylocaine with or without epinephrine
  - 27-30 gauge needle to inject 1-3 cc's of anesthetic agent
  - Inject subepidermally
- Punch Biopsy
  - Tischler cervical biopsy
  - Keyes punch

  + 3-5 mm diameter dermatologic instruments (usually 4 mm)
- Fine suture (3.0 or 4.0 Vicryl Rapide) vs. Monsel's/ Silver nitrate

Condyloma

- Over 100 types of VPH
  - 30 are found on the genital area
- May cause itching, bleeding and occasionally pain

Intraepithelial Neoplastic Disorders of the Vulvar Skin and Mucosa

A. Squamous
1. Vulvar intraepithelial neoplasia type 1 (VIN I)
   - mild dysplasia
2. VIN II – moderate dysplasia
3. VIN III – Severe dysplasia

B. Other
1. Paget's disease (intraepithelial)
2. Melanoma in situ (level I)

*Classification system developed by the International Society for the Study of Vulvovaginal Diseases.

ISSSUD 2003 new terminology

1986	*2002 -2003*
VIN 1	*HPV effect*
VIN 2	*VIN*
VIN 3	*VIN*
VIN 3	*Diferentiated VIN*
Diff Type	*- Unclassified VIN (NOS)*

Incidence of Vulvar Intraepithelial Neoplasia (VIN)

- Incidence increasing
- Over the past 20 years, incidence has doubled, especially in women less than 40 years of age (50% of all cases)
- Progression to carcinoma appears to be uncommon in this age group, in the non-immunosuppressed patient.

Low grade VIN High grade VIN → Risk of cancer

History of VIN III

- Before 1970, VIN was found most often in women in the fifth or sixth decade of life
    - Older women with VIN more often have solitary lesions with a higher risk for progression to cancer

Increasing Incidence of VIN

- Heightened awareness of neoplasia
- Increased tendency to perform biopsies
- Commonly associated with other lower genital tract neoplasia (anus, vagina, cervix) and/or carcinomas

Human Papillomavirus and VIN

- HPV 16 and 33 are the most common subtypes detected in VIN (90% of VIN lesions associated with these two types)
- 1/3 of patients with HPV are at risk for recurrence of disease after treatment

Risk Factors for VIN

History of HPV (vulva, Vagina, cervix)
Early age of onset of Sexual intercourse

Multiple lifetime sexual Partners

Cigarette smoking

Immunosuppression
*** Pregnancy**
*** HIV**
*** Autoimmune connective tissue disorders**

*** Diabetes**

*** Transplant recipient**
*** Cronic hepatitis**
*** Chemotherapy**

Relationship of VIN to Various Factors

	Group I	Group II
Age (y)	**35-65**	**55-85**
Condyloma history	**Common**	**Uncommon**
STD history	**Common**	**Uncommon**
Prior vulvar lesion	**VIN**	**LS, SCH**
Histology	**Basaloid**	**Keratinizing**
Cervical neoplasia	**High Presence**	**Low presence**
Smoking	**High Presence**	**Low Presence**
HPV DNA	**Common**	**Seldom**

Vulvar Intraepithelial Neoplasia Squamous Type

- VIN I
  -< 1/3 mild dysplasia (formerly mild atypia) 40% of VIN (ICD9=624.8)
- VIN II
  - 1/3 to 2/3 moderate dysplasia (formerly moderate atypia) 14% of VIN (ICD9=624.8)
- VIN III
  - > 2/3 severe dysplasia (formerly severe atypia), (carcinoma in situ) 46% of VIN (ICD9=233.3)

Es mas alta la frecuencia de VPH en vulva que no es diagnósticada por ser infección subclínica.

VIN of low Grade: A Challenging Diagnosis

- Micheletti L. Barbero M, Preti M, et al
- Eur J Gynaecol Obstet 1994 ;15 ;70-4

VIN III

- **VIN III** (Squamous cell CIS, Bowen's disease, Erythroplasia of Queyrat, CLS simplex)

Symptoms and Signs

- **Most – completely asymptomatic**
- **Itching or burning**
- **Irritation**
- **Dyspareunia**
- **Labial erythema**
- **Patient notes a lesion**

VIN

- **Distribution**
  - **Most commonly found on the non-hairbearing areas**
  - **Posterior vulva and periclitorial area**
  - **May extend to involve the anus, vagina, clitoris, or urethra**

VIN Lesions

- Unifocal or multifocal
  - White
  - Gray-brown
  - Red

Colposcopic Features of VIN

- Similar to but not as prominent as with CIN
  - Leukoplakia
  - Acetowhitening (70%)
  - Punctation
  - Atypical vessels

VIN Thiickness

		Depth (mm)		
	No.	**Deep**	**Shallow**	**Mean**
Hairy skin				
Labial majora	**2085**	**1.04**	**0.08**	**0.37**
Non-hairy skin				
Labial minora	**945**	**0.86**	**0.11**	**0.38**
Posterior fourchette	**70**	**0.69**	**0.15**	**0.38**
Perineum	**195**	**0.85**	**0.11**	**0.47**

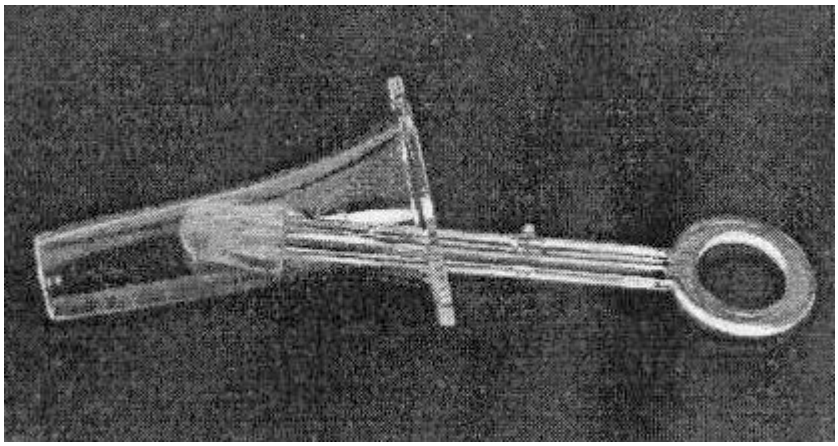
Shatz P. Bergeron C. Wilkinson EJ. Arseneau J. Ferenczy A. Vulvar intraepithelial neoplasia and skin appendage involvement.
Obstetrict & Gynecology. 74(5): 769-74,1989 Nov.

Anoscopy

- Perianal involvement is noted in 33% of patients

INSTRUMENTS

- Hinkel-James Anoscope
- Fansler Operative Anoscope



POSITIONS

- Exaggerated Lithotomy Position
- Left Lateral or Sim´s Position
- Knee-Shoulder Position

Non- squamous Types

- Paget's disease
- Melanoma in situ

Paget's Disease

- Multifocal, Eczematoid red weeping area Brick red Scales, Eczematoid plaque Sharply demarcated border

Lesiones acetoblancas nítidas sobre mucosa eccematosa (enrojecida y humeda)

- Occurs most commonly on the nipple and areola, where its presence signifies an underlying adenocarcinoma of the breast
- Apocrine gland origin
- Red velvety area with white islands of hyperkeratosis and at times may be pinkish, and eczematoid

Paget's Disease
Association with Adenocarcinoma

- Genital
  - Vaginal, Cervical, Uterine
- Urologic
  - Urethre, Bladder
- Gastrointestinal
  - Anorectal,Rectal
- Breast

Paget's Disease
workup

- History and PE
  - Symptoms include itching, burning
  - Signs include velvety appearance and bleeding
- Papanicolaou smear
- Mammogram
- Cystoscopy
- Colonoscopy

Differentiating Paget's From Other Conditions

- Positive mucin as well as immunoperoxidase CEA staining can be used to differentiate

Paget's disease from melanoma

- Paget's (mucin and CEA positive)
- Melanoma (mucin and CEA negative)

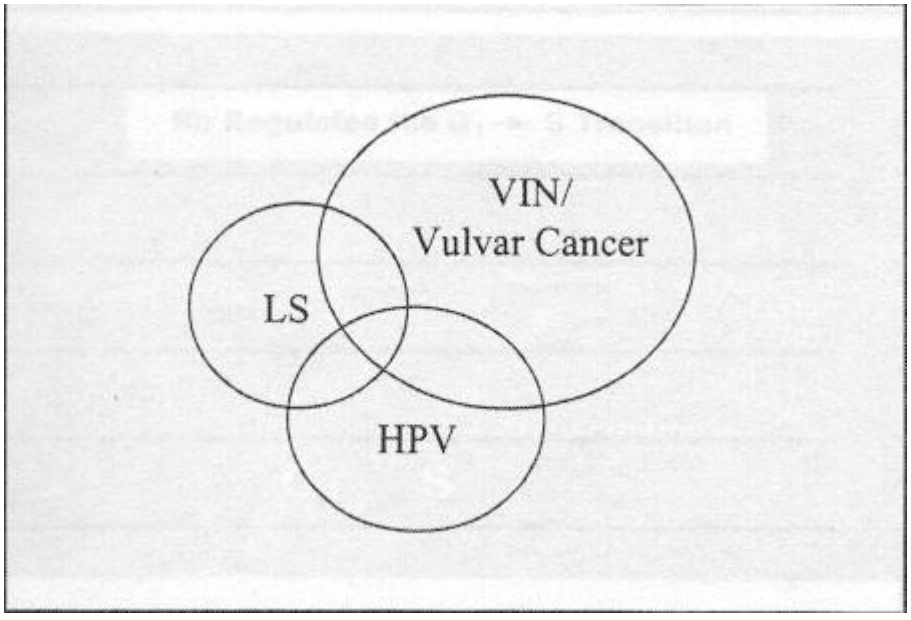
Paget's Disease

- Paget's Disease
  - Wide local excisión (how far?)
  - Margins
    + Extends beyond the visibly demarcated margin
    + Adequate surgical margins difficult to obtain
    + Local recurrence
      - 31 % -radical vulvectomy
      - 43% wide local excision

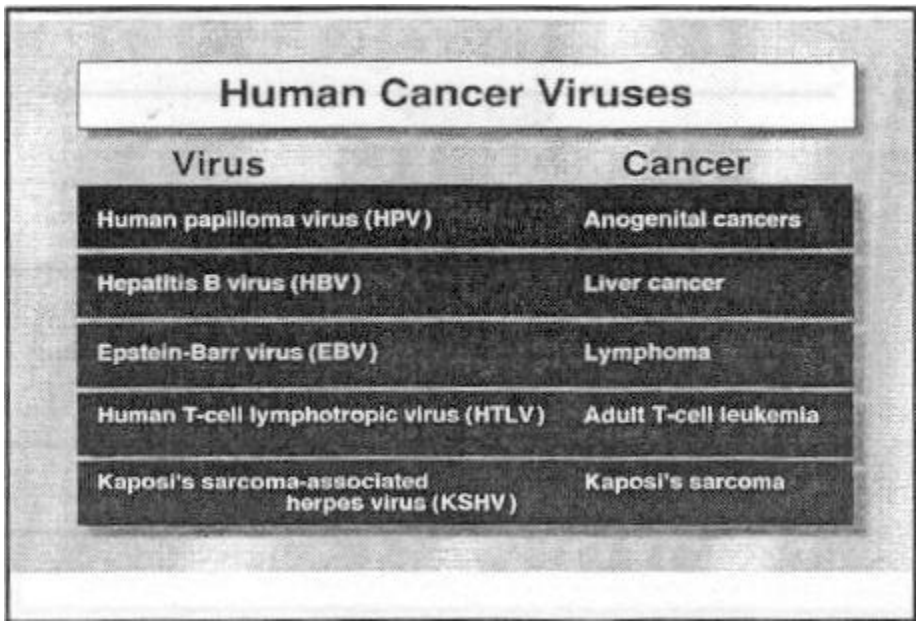
Adenocarcinoma association as high as 26%

Melanoma in Situ

Melanoma in situ is a lesion of uncertain natural history, but it can be treated effectively with conservative surgery



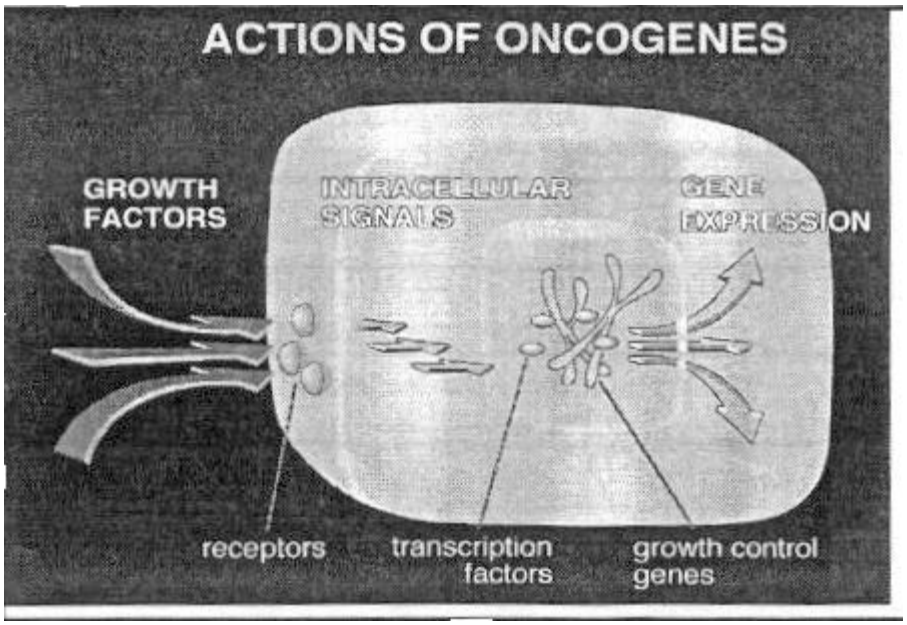
LS
VIN/ Vulvar Cancer
HPV

- 

Human Cancer Viruses

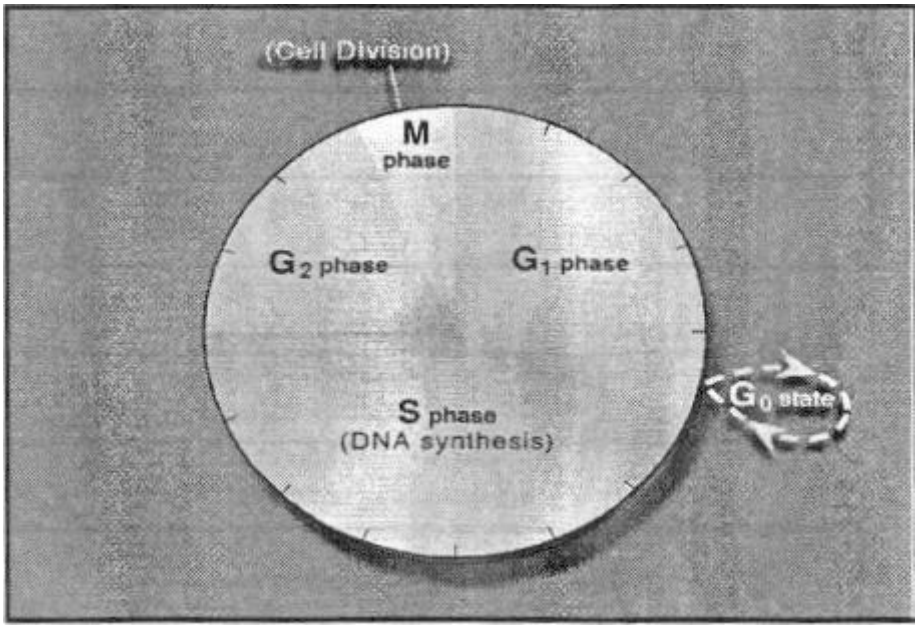
Virus Human papilloma virus (HPV)
Hepatitis B virus (HBV)
Epstein-Barr virus (EBV)
Human T-cell lymphotopic virus (HTLV)
Kaposi´s sarcoma-associated herpes virus (KSHV)

Cancer
Anogenital cancers
Liver ancer
Lymphoma
Adult T-cell leukemia
Kaposi´s sarcoma



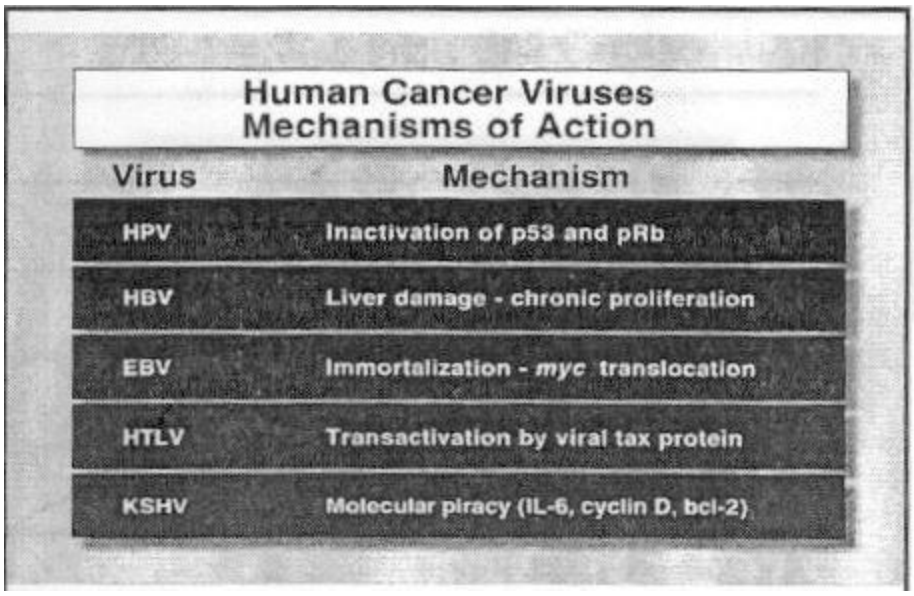
Actions of Oncogenes

Growth factors
Intrecellular signals
Gene expression
Receptors
Transcription factors
Growth control genes

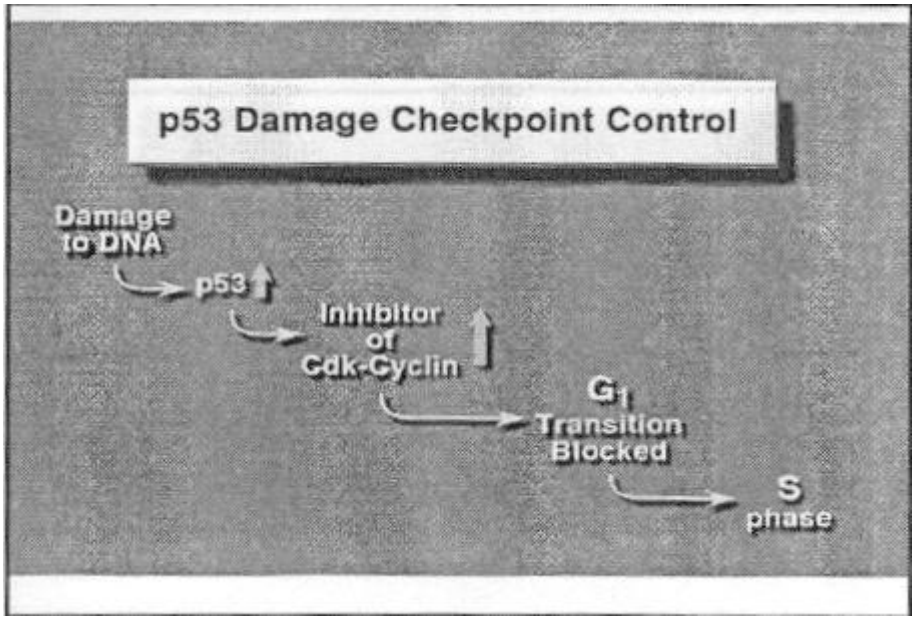


(cell division)
M phase

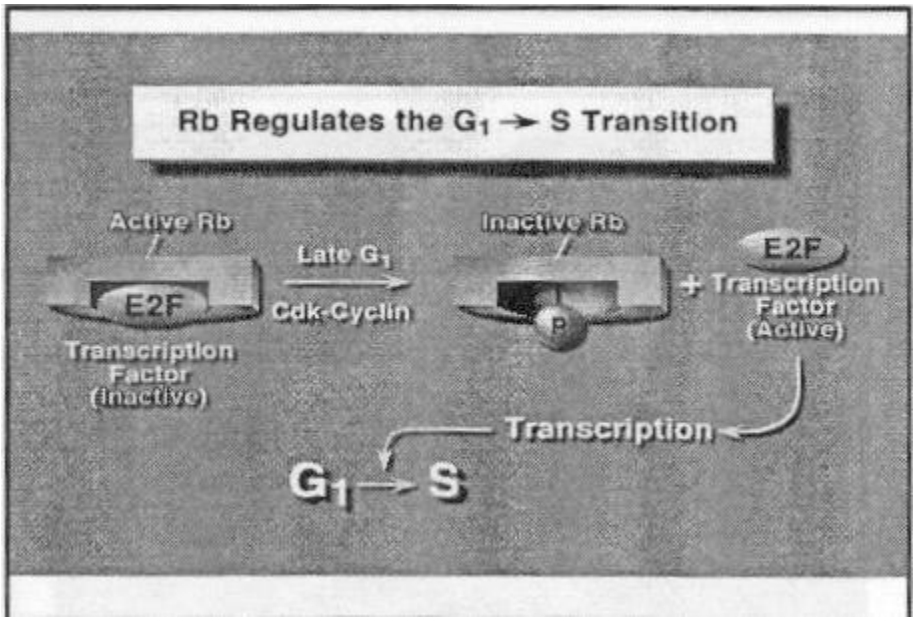
G2 phase
G1 Phase
S phase
(DNA synthesis)

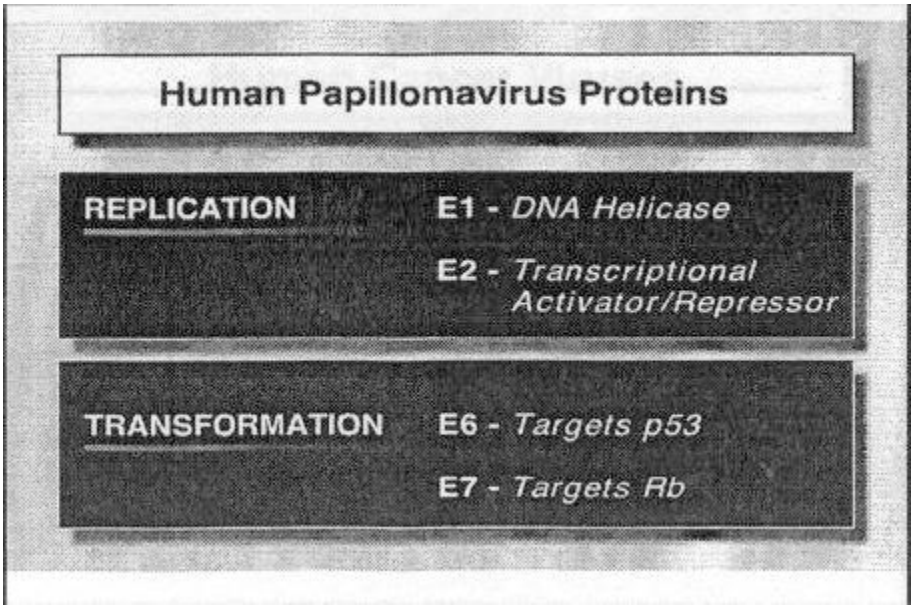


Human cancer viruses mechanisms of action
Virus mechanism
HPV Inactivation of P53 and pRb
HBV Liver damage – chronic proliferation
EBV Immortalization- myc translocation
HTLV Transactivation by viral tax protein
KSHV Molecular piracy (IL-6, cyclin D, bcI-2)



P53 Damage Checkpoint Control
Damage to DNA- p53- Inhibitor of Cdk-Cyclin –G1 Transition Blocked- S phase





Human Papillomavirus Proteins

REPLICATION E1- DNA Helicase
E2- Transcriptional Activator/Repressor
TRANSFORMATION E6- Targets p53
E7- Targets Rb

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