Human papillomavirus infections

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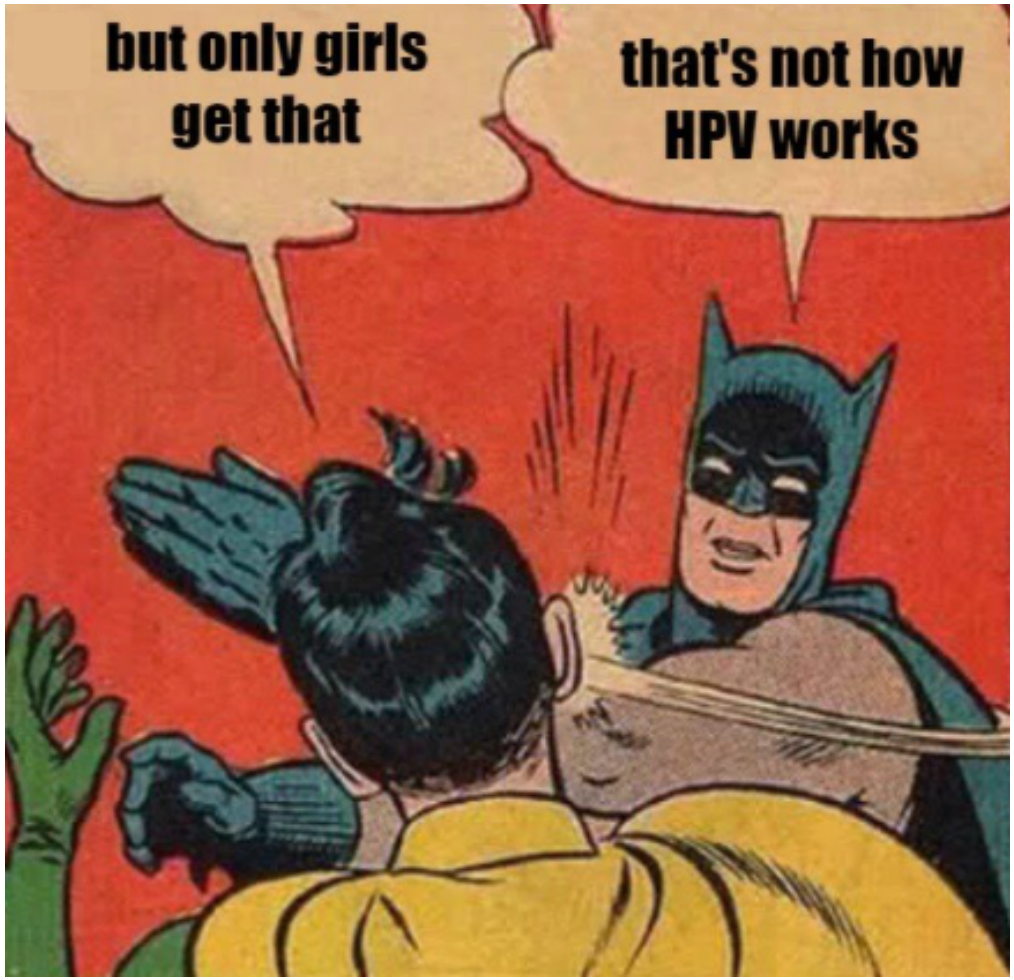


Papilloma viruses make up a group of more than 300 viruses

About 200 different papillomavirus types infect humans. Infection is either:

- Asymptomatic (the vast majority of HPVs)
- Causes genital or skin warts.
- Carry a risk of becoming cancerous

Human papillomaviruses (HPVs) are the most common sexually transmitted infection in the US.

HPVs infection is commonly spread during vaginal or anal sex.

>80% of men and women will be infected with at least one type of HPVs in their lives

Most people infected with HPVs are asymptomatic and will clear the infection on their own, usually within two years

However, sometimes the virus persists and results could lead to complications, including genital warts and cancer. In fact HPV causes virtually all cases of cervical cancer, 95 percent of anal cancer and about 70 percent of throat cancers.

Low and high risk papilloma

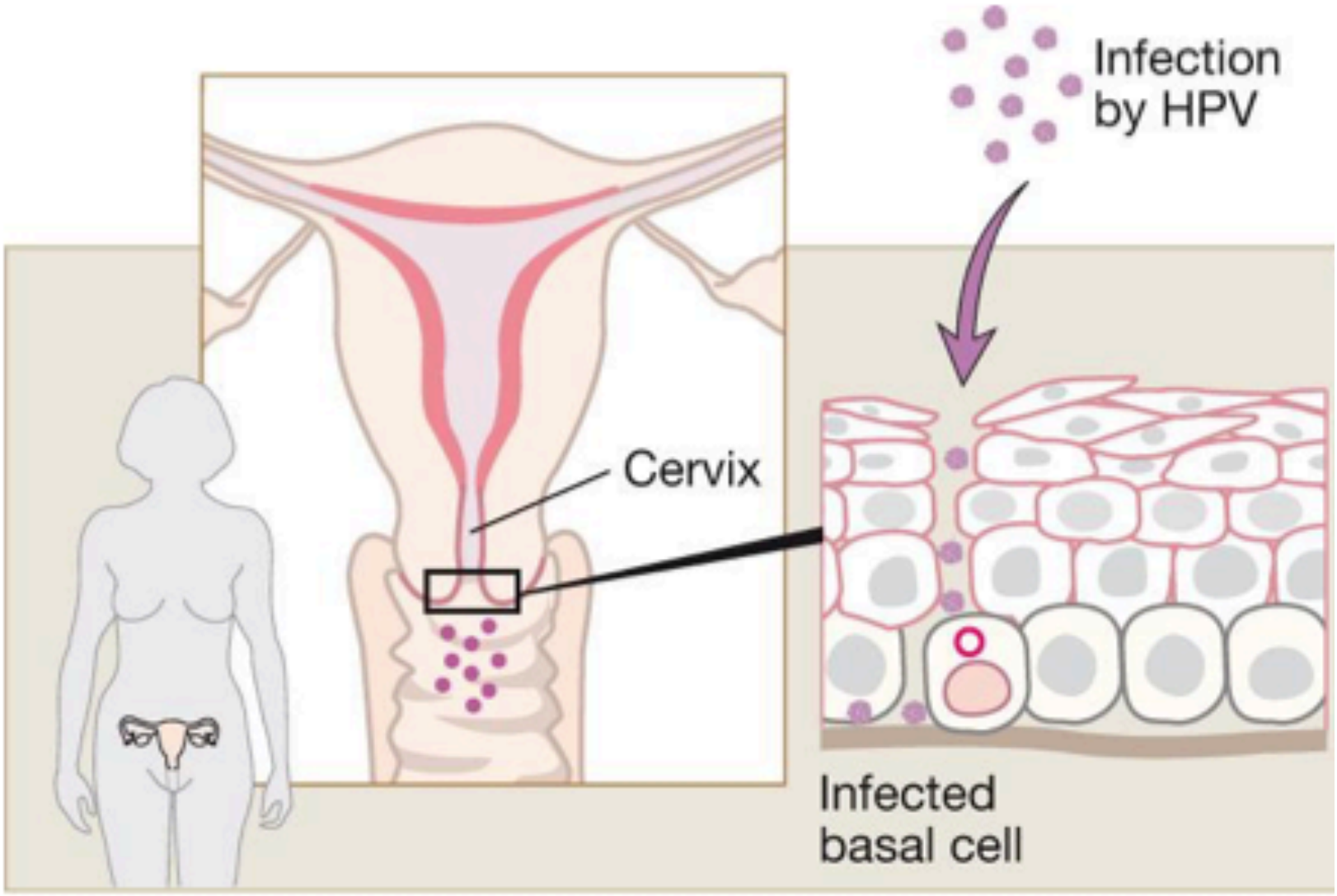
Low-Risk Human Papillomavirus

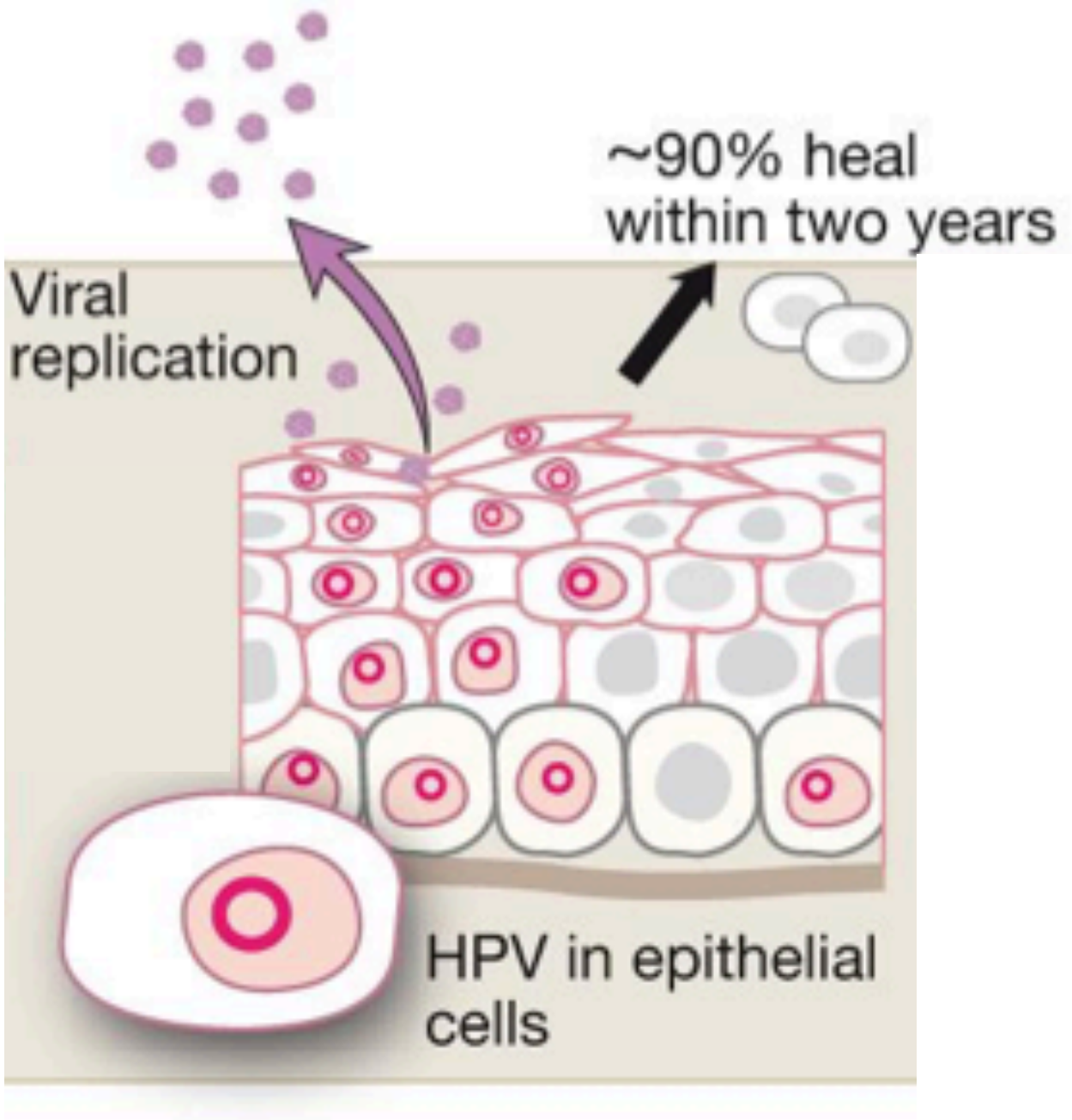
Infection with most low-risk genital HPV strains doesn't cause symptoms. These strains have no association with cancer but can lead to genital warts. HPV6 and HPV 11 are the main example

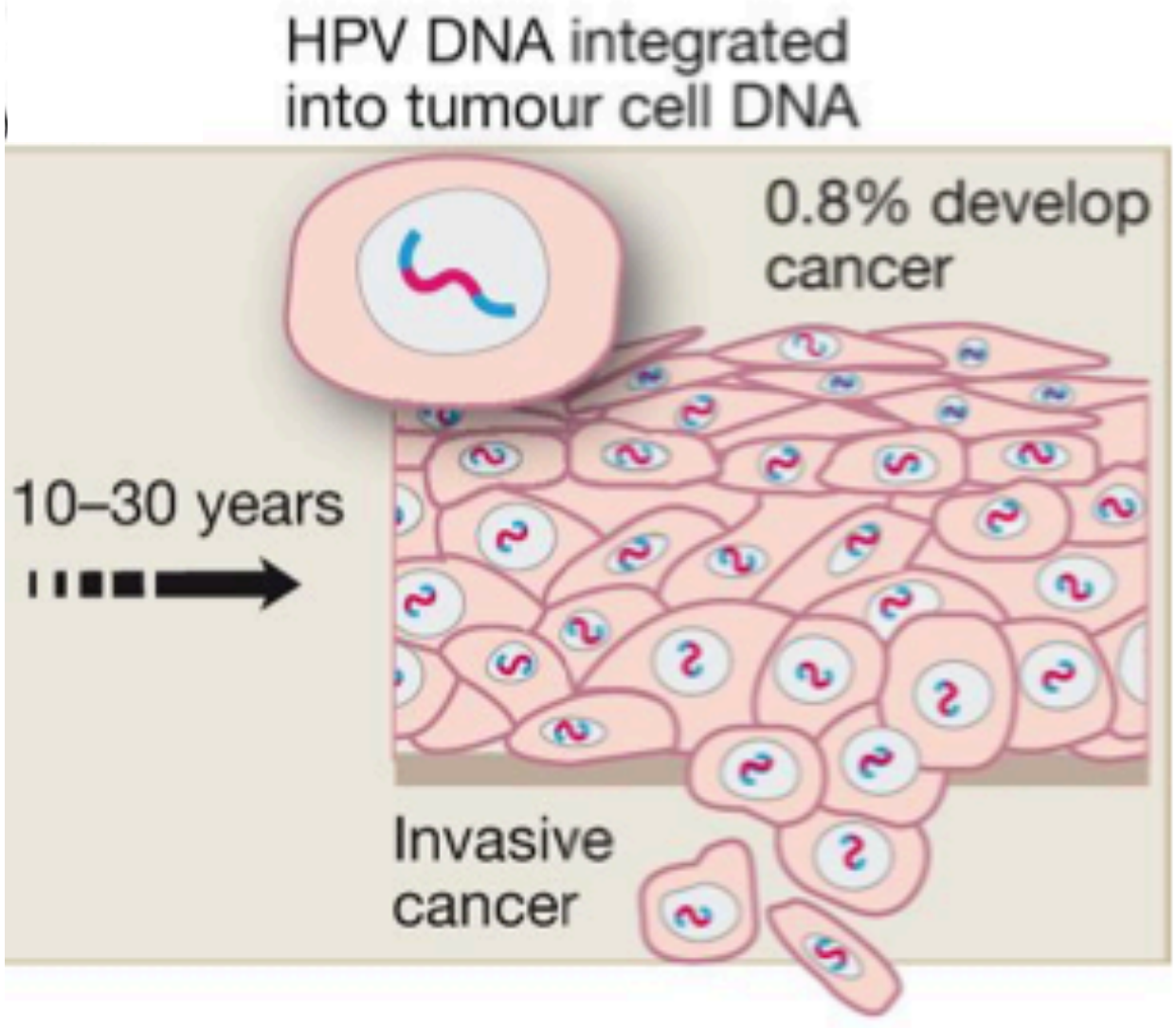
High-Risk Human Papillomavirus

Infection with high-risk HPV can lead to extensive cervical dysplasia and certain types of cancer. There are several high-risk strains of HPV, but only two—types 16 and 18—cause the majority of HPV-related cancers (70%).

Initial infection



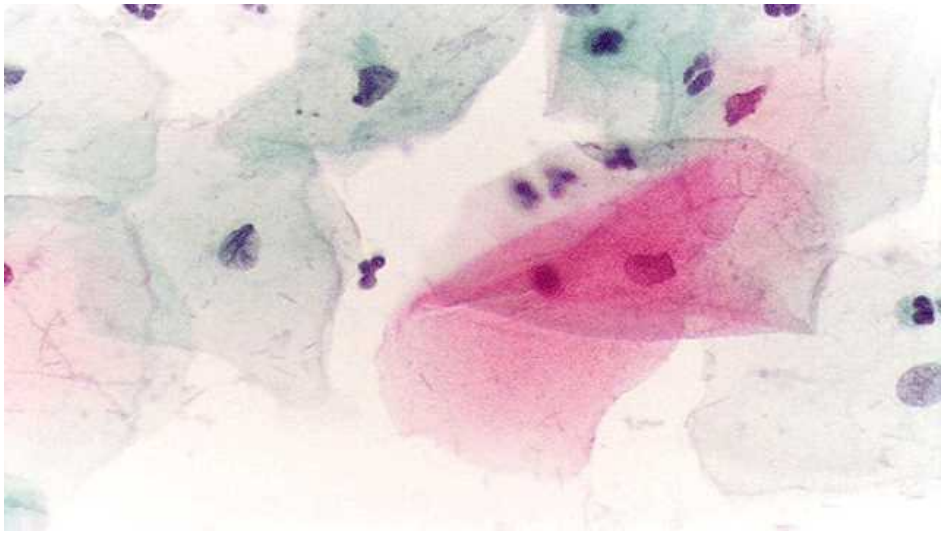

~90% heal
within two years
Viral
replication
HPV in epithelial
cells


HPV DNA integrated
into tumour cell DNA
0.8% develop
cancer
10–30 years
Invasive
cancer

Prevention

Safe sex practices
—> Not 100% effective

Pap test and HPV test
—> to detect abnormal cell proliferation in the cervix and to determine the HPV type involved



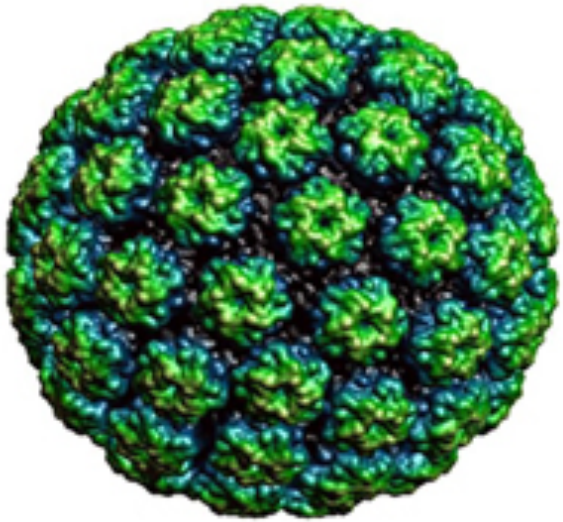
Normal squamous epithelial cells. Staining epithelial cells collected during a pap smear shows whether there are any abnormal cells that may be cancerous.

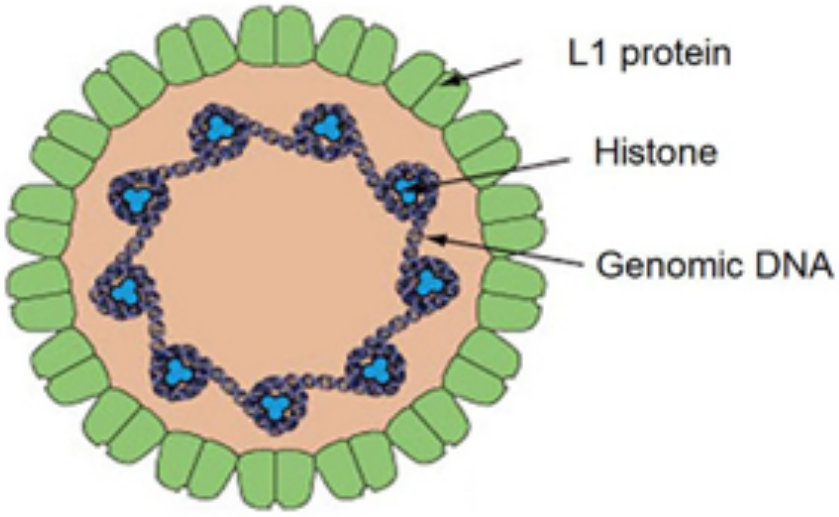
The virion

Small viruses (50 nm)

Their capsid is made of the protein L1

The genome is DNA





HPV vaccines

The HPV vaccine is made of the L1 protein. This protein naturally assembles to form virus like capsids (empty virions)

The first generation vaccines (approved in 2006-2007)
Cervarix: protects against HPV 16 and 18.
Gardasil: protects against HPV 16, 18, 6 and 11

A second generation vaccine (approved in 2019)
Gardasil 9: protects against HPV 16, 18, 31, 33, 45, 52, 58, 6 and 11

HPVs 16 and 18 cause 70% of the cervical cancers

HPVs 31, 33, 45, 52 and 58 cause 20% of the cervical cancers

Types of genes linked to cancer

Many of the genes that contribute to cancer development fall into broad categories:

- **Proto-oncogenes:** proteins that normally contribute positively to cell proliferation.

- **Tumor suppressor genes:** proteins that prevent the unwanted proliferation of mutant cells.

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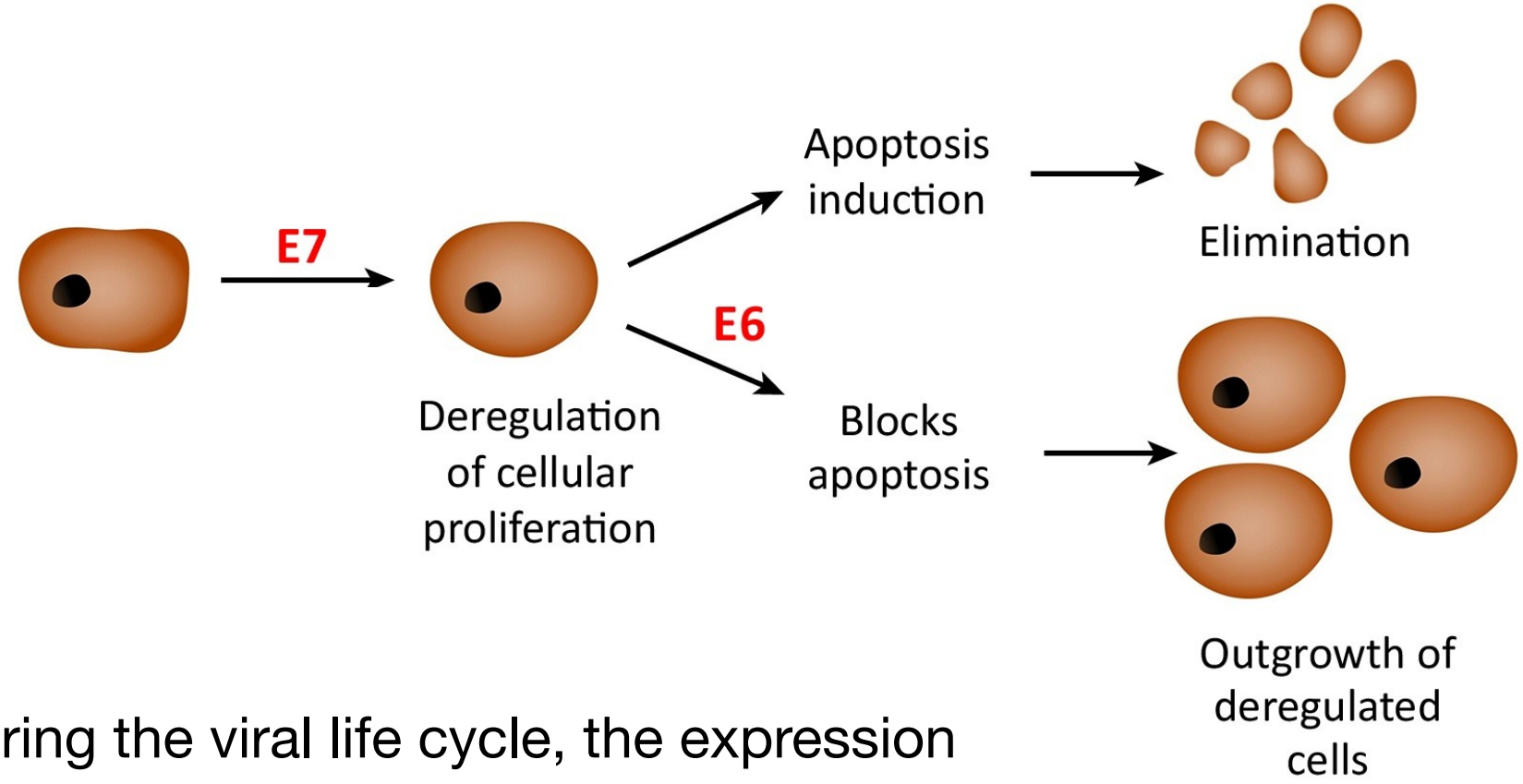
Many of the genes that contribute to cancer development fall into broad categories:

- **Proto-oncogenes:** proteins that normally contribute positively to cell proliferation.
  - Mutations might alter the regulation of these proto-oncogenes, preventing them to be turned off. These “constantly activated” proto-oncogens are called **oncogenes**

- **Tumor suppressor genes:** proteins that prevent the unwanted proliferation of mutant cells.
  - Mutations might render these tumor suppressor genes ineffective

The HPV E6/E7 Oncogenes



During the viral life cycle, the expression of the viral oncogenes E6 and E7 is transient and regulated

Trends in Microbiology

HPV infection leads to cervical cancer (as well as others *)

Although most HPV infections clear up on their own and most pre-cancerous lesions resolve spontaneously, there is a risk for all women that HPV infection may become chronic and pre-cancerous lesions progress to invasive cervical cancer.

It takes 15 to 20 years for cervical cancer to develop in women with normal immune systems.

It can take only 5 to 10 years in women with weakened immune systems, such as those with untreated HIV infection.

* Oral cancers (mouth, tongue, oropharynx), anal cancers, vulvar and vaginal cancers, penile cancers

E6 and E7 is expressed in tumor cells

HPVs are found integrated in most cancer cells.

Integration is a genetic accident (this is not part of the viral life cycle). In fact, integration is a dead end for the virus, as it is no longer able to form a small, circular genome that can be packaged and transmitted to a new host.

Integration results in dysregulation of expression of the viral E6 and E7 oncogenes. This gives cells a selective growth advantage and promotes oncogenic progression. In these cells, E6 and E7 is not shut down

Summary

Viruses can encode oncogenes and tumor suppressor inhibitors. This is to force the infected cells into entering a phase of the cell cycle compatible with viral replication

Viruses cause cancer by accident, this is not part of their life cycle.

Viruses are necessary but not sufficient for cancer. Additional genetic mutations are also probably required

E6 and E7 are two HPV-encoded oncogenes. They are always expressed in cervical cancers


THANK YOU