Categories of malignant tumour

There are two categories of malignant tumour

1. Solid tumours are initially confined to a specific tissue or organ. As the growth of the primary solid tumour progresses, cells detach from the original tumour mass, invade the surrounding tissue, and enter the blood and lymph system to spread to distant sites.

2. Liquid (Hematologic) tumours involve cells normally found within the blood and lymph, thereby making them disseminated diseases from the beginning, E.g. **leukemia** and **lymphomas.**

Cancer in situ

Cancer in situ (Locally malignant tumours): is a group of malignant tumour that spread only locally (invasive) with no distant spread (metastasis).

Depending on its location, cancer in situ usually can be removed surgically or treated so that the chances of recurrence are small.

For example:

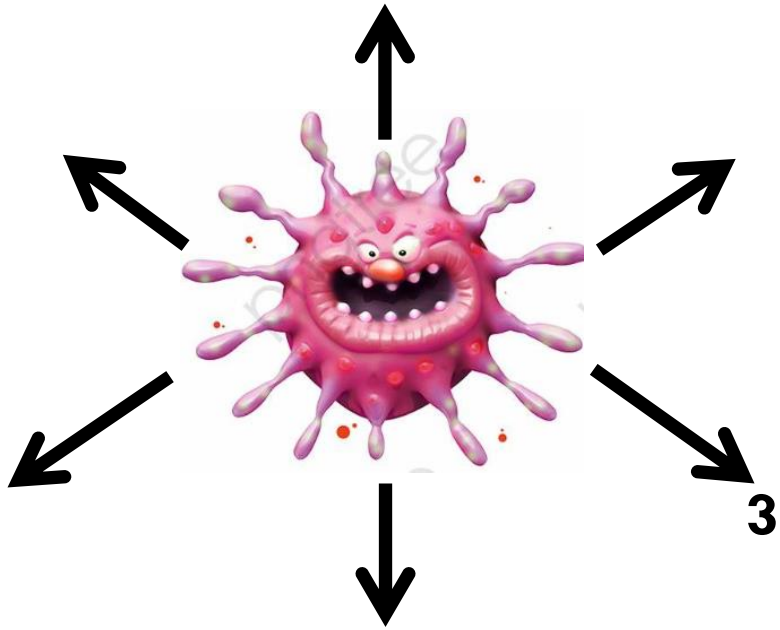
In breast **Ductal Carcinoma In Situ (DCIS)** the cells have not crossed the basement membrane.

Cancer in situ of the cervix is essentially 100% curable.

Hallmarks of cancer cells

1. Uncontrolled cell proliferation

6. Inducing angiogenesis



2. Resisting Apoptosis

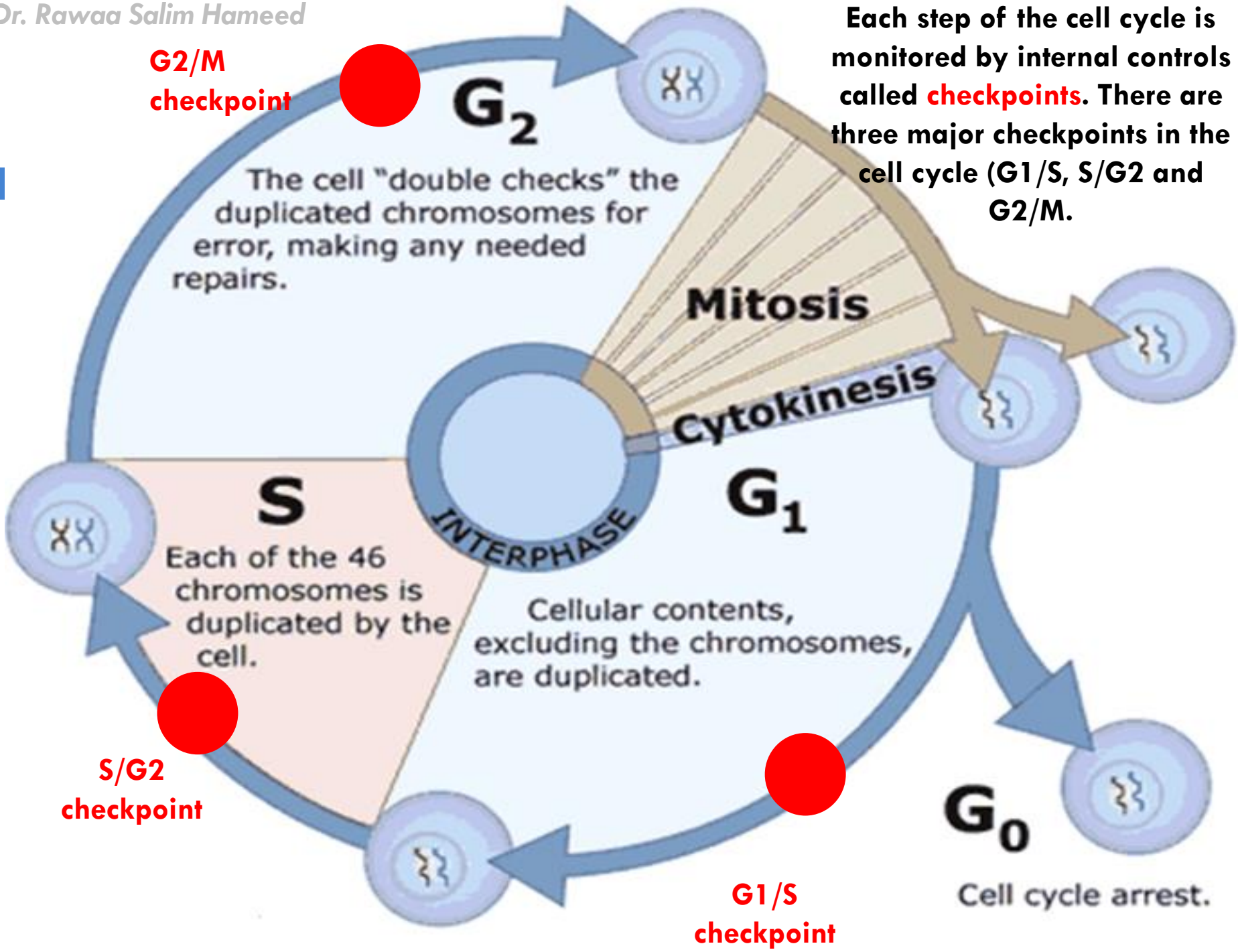
5. Evading the immune system

3. Enabling replicative immortality

(cancer cells are able to replicate unlimitedly)

4. Invasion and metastasis

Each step of the cell cycle is monitored by internal controls called checkpoints. There are three major checkpoints in the cell cycle (G1/S, S/G2 and G2/M.



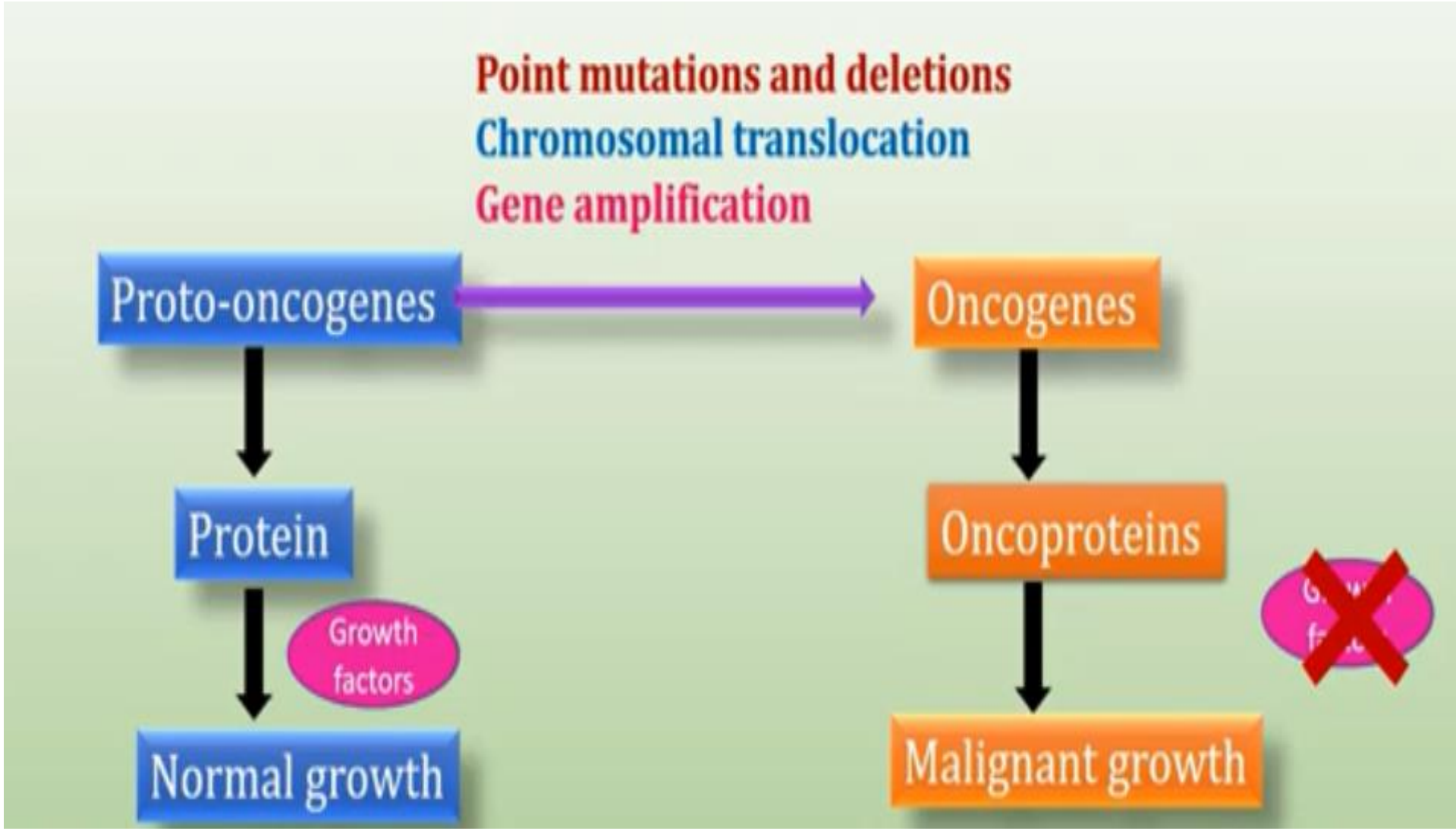
Cancer-Associated Genes

Most cancer-associated genes can be classified into **two main categories**:

1. The proto-oncogenes: are a class of normal genes that produce proteins to **enhance cell division and prevent cell death.** These genes become cancer-causing **oncogenes** if mutated.

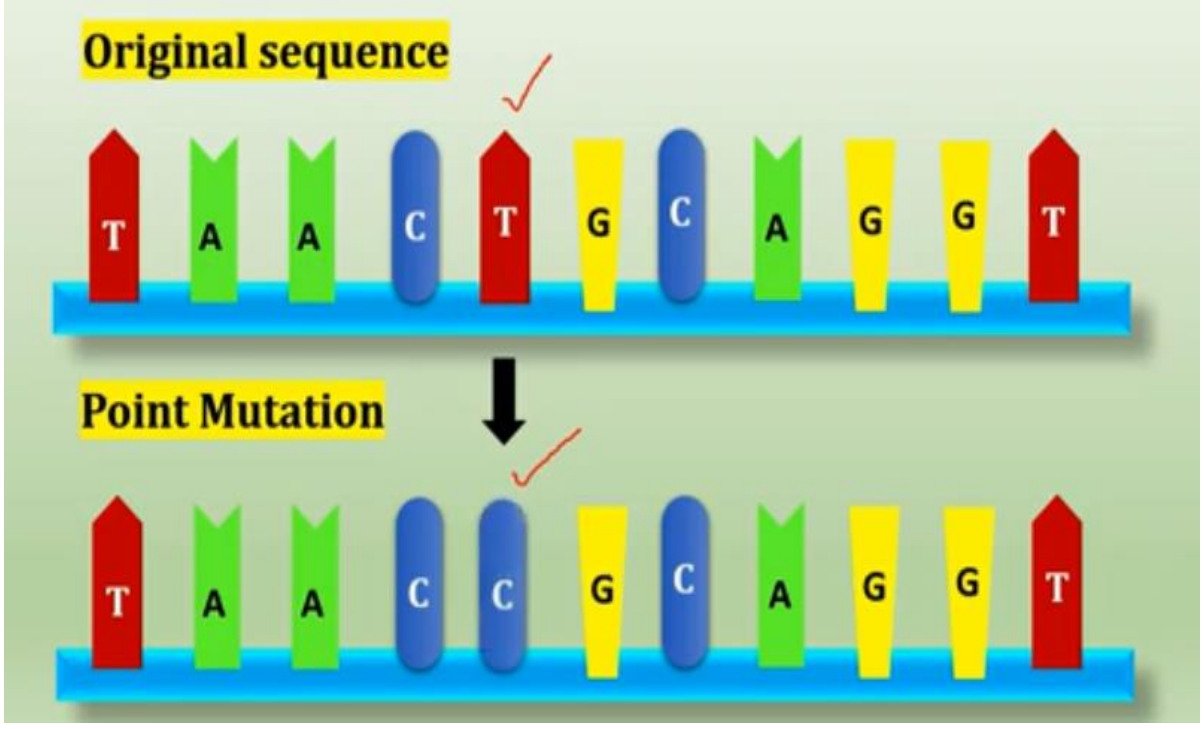
E.g. The most important example is ***RAS*** oncogene carried in many human tumours such as **bladder and pancreatic cancers.**

Genetic Events Leading to Oncogene Formation or Activation



Point Mutation

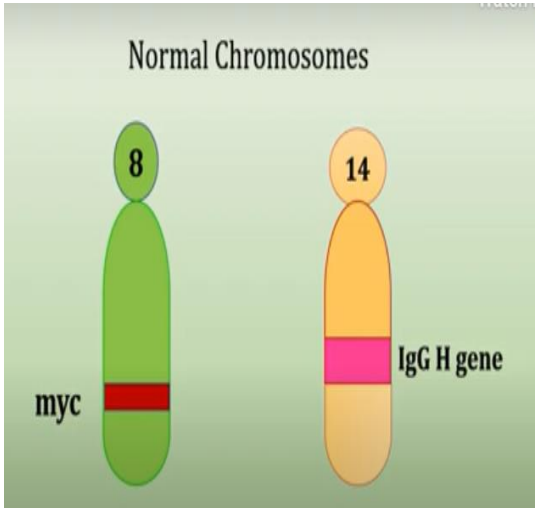
1. A point mutation in which there is a single nucleotide base change due to an insertion, deletion, or substitution.

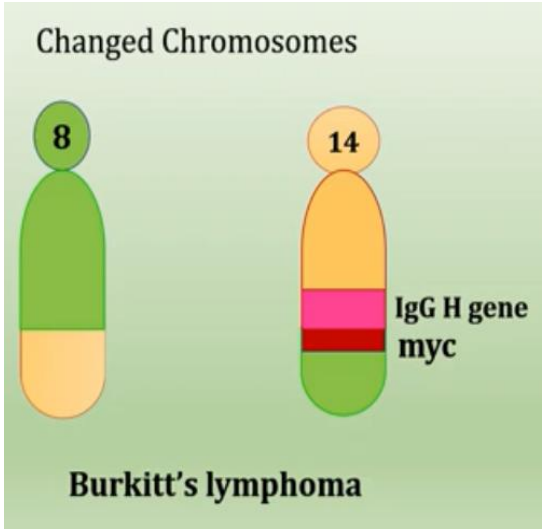


Chromosomal translocation

2. Chromosomal translocations have traditionally been associated with cancers such as **Burkitt lymphoma** in which the **C-myc gene**, which encodes a growth signal protein, is translocated from its normal position on **chromosome 8 to chromosome 14**, placing it at the site of an **immunoglobulin gene**.

The formation of an abnormal fusion protein promotes cell proliferation.

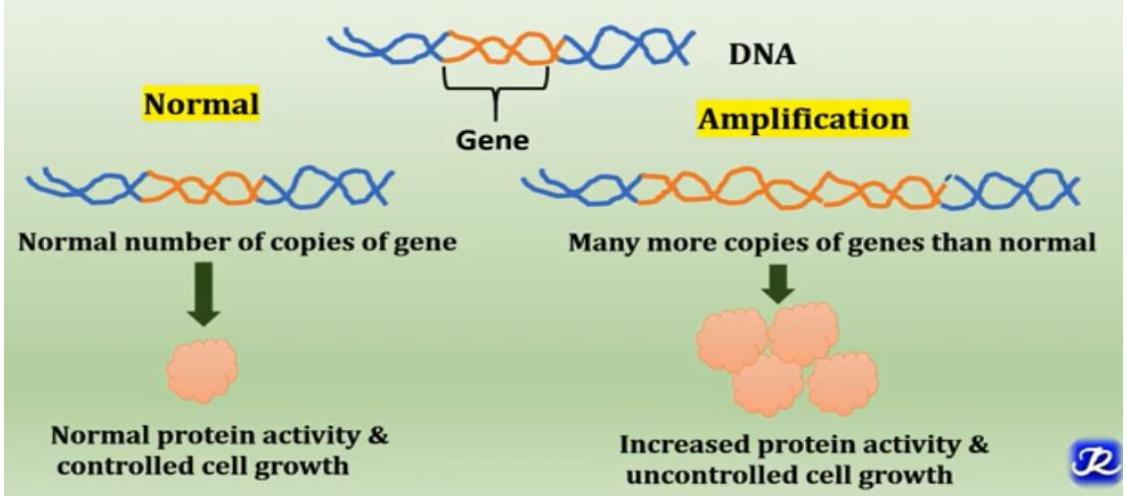




Gene amplification

3. Gene amplification is multiple copies of certain genes that may cause overexpression with higher than normal levels of proteins that increase cell proliferation. For example, the **human epidermal growth factor receptor-2 (HER-2) gene** is amplified in up to 30% of **breast cancers** and indicates a tumour that is aggressive with a poor prognosis.

One of the agents used in the treatment of HER-2 overexpressing breast cancers is **Herceptin** which selectively binds to HER-2, thereby inhibiting the proliferation of tumour cells that overexpress HER-2.



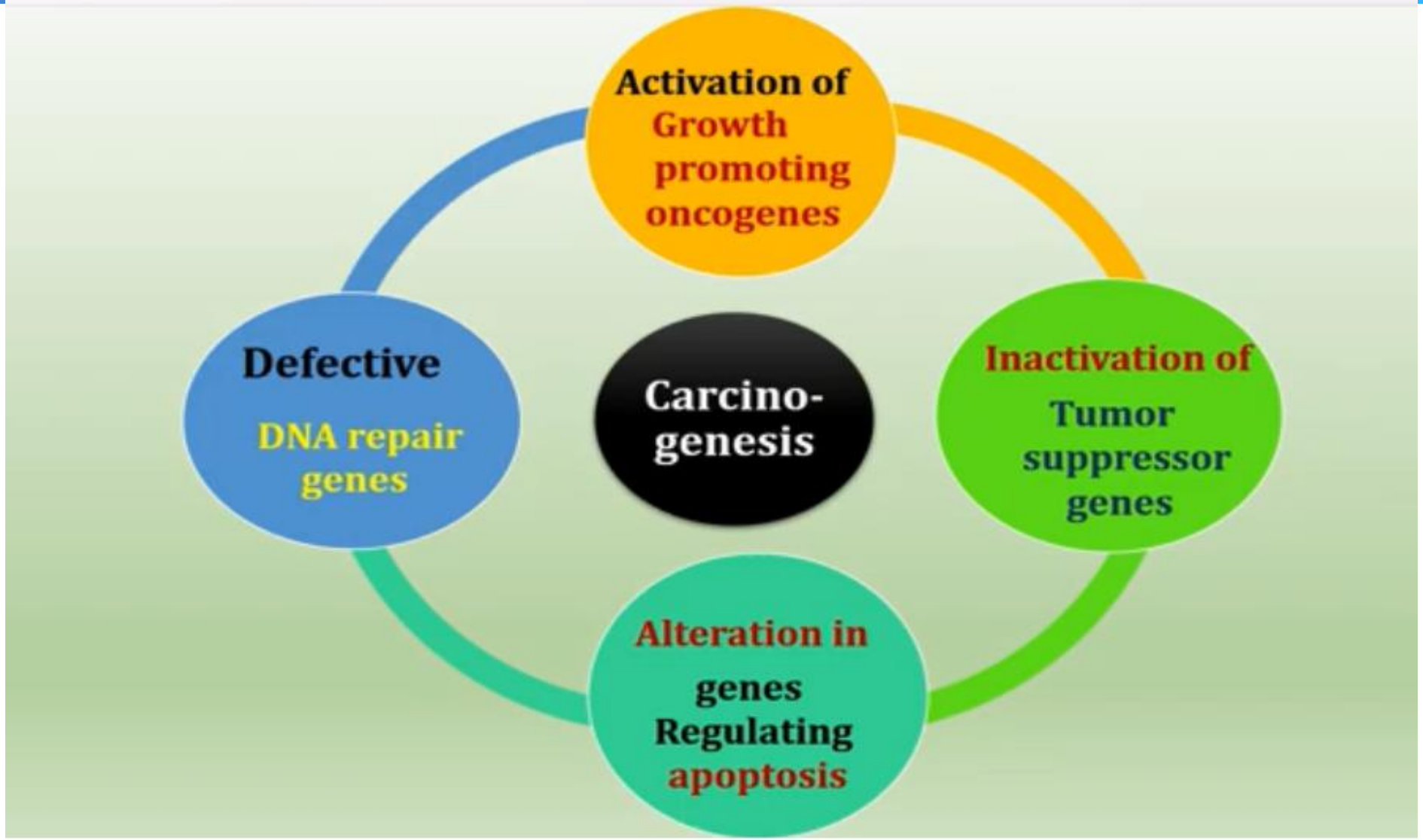
Cancer-Associated Genes

2. Tumour-suppressor genes: are a class of genes that produce proteins to **inhibit cell division, repair DNA mistakes, and control the cell death.**

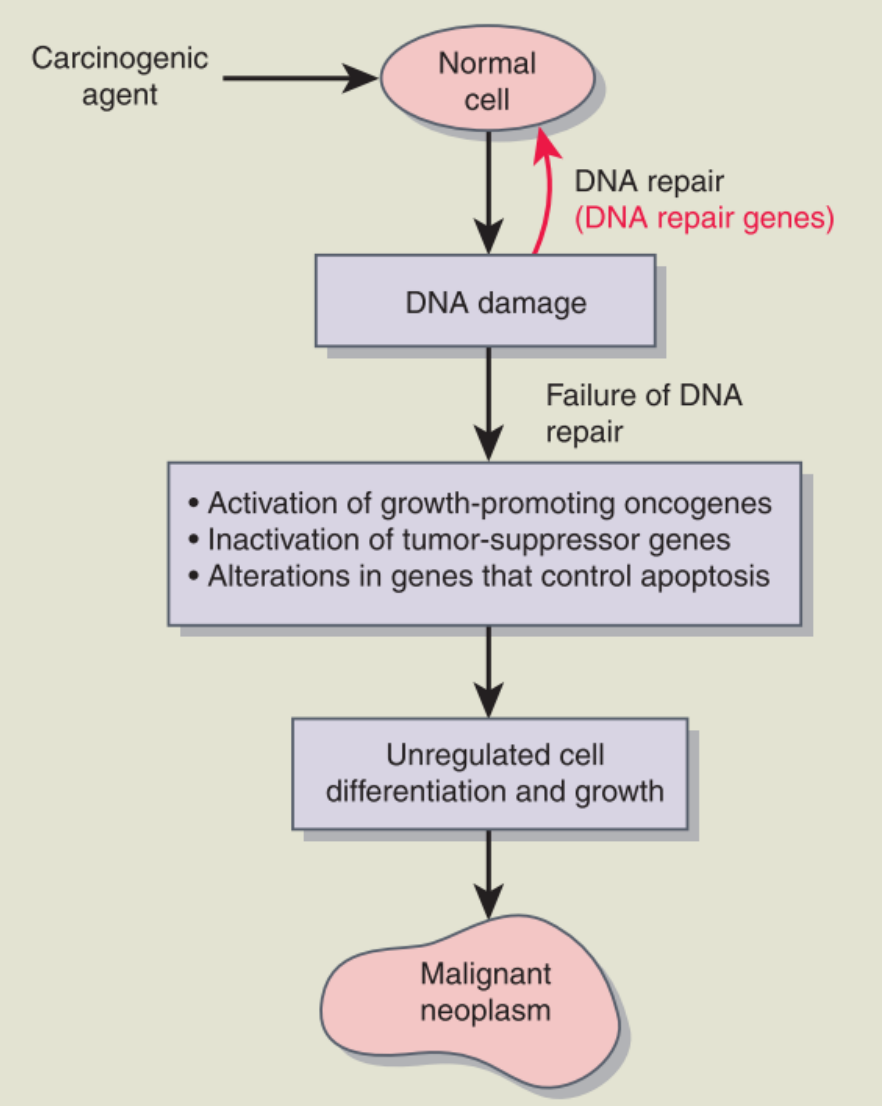
E.g. 1. *P53* (guardian of the genome): senses DNA damage and assists in DNA repair or **initiating apoptosis** in a cell that cannot be repaired. Mutations in the p53 gene can occur in virtually every type of cancer including **lung, breast, and colon cancers.**

2. *BRCA-1* (breast carcinoma 1) and ***BRCA-2*** (breast carcinoma 2) their mutations are associated with an increased risk for several cancer types including **breast and ovarian cancers.**

Cancer-Associated Genes

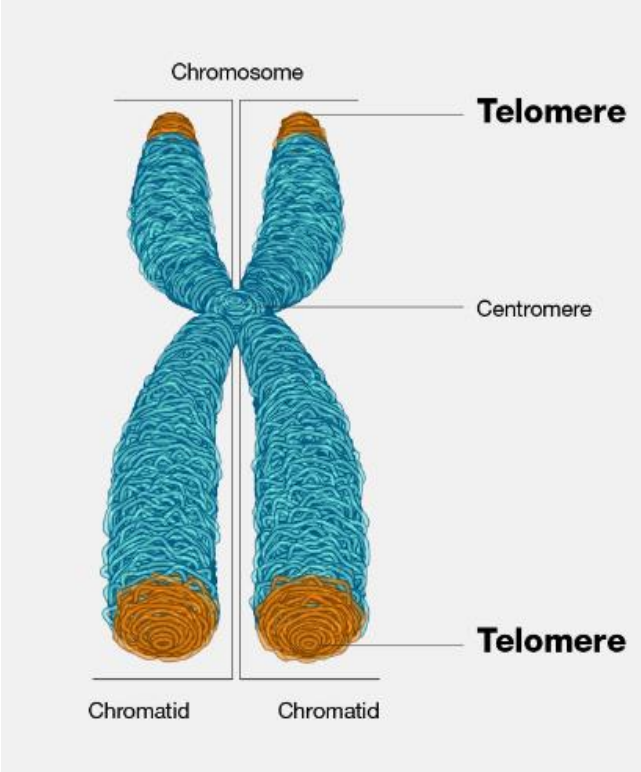


The stages of a malignant neoplasm development



Role of Telomeres in cell division

A telomere is repetitive DNA sequences at the end of a chromosome.



Functions of Telomeres

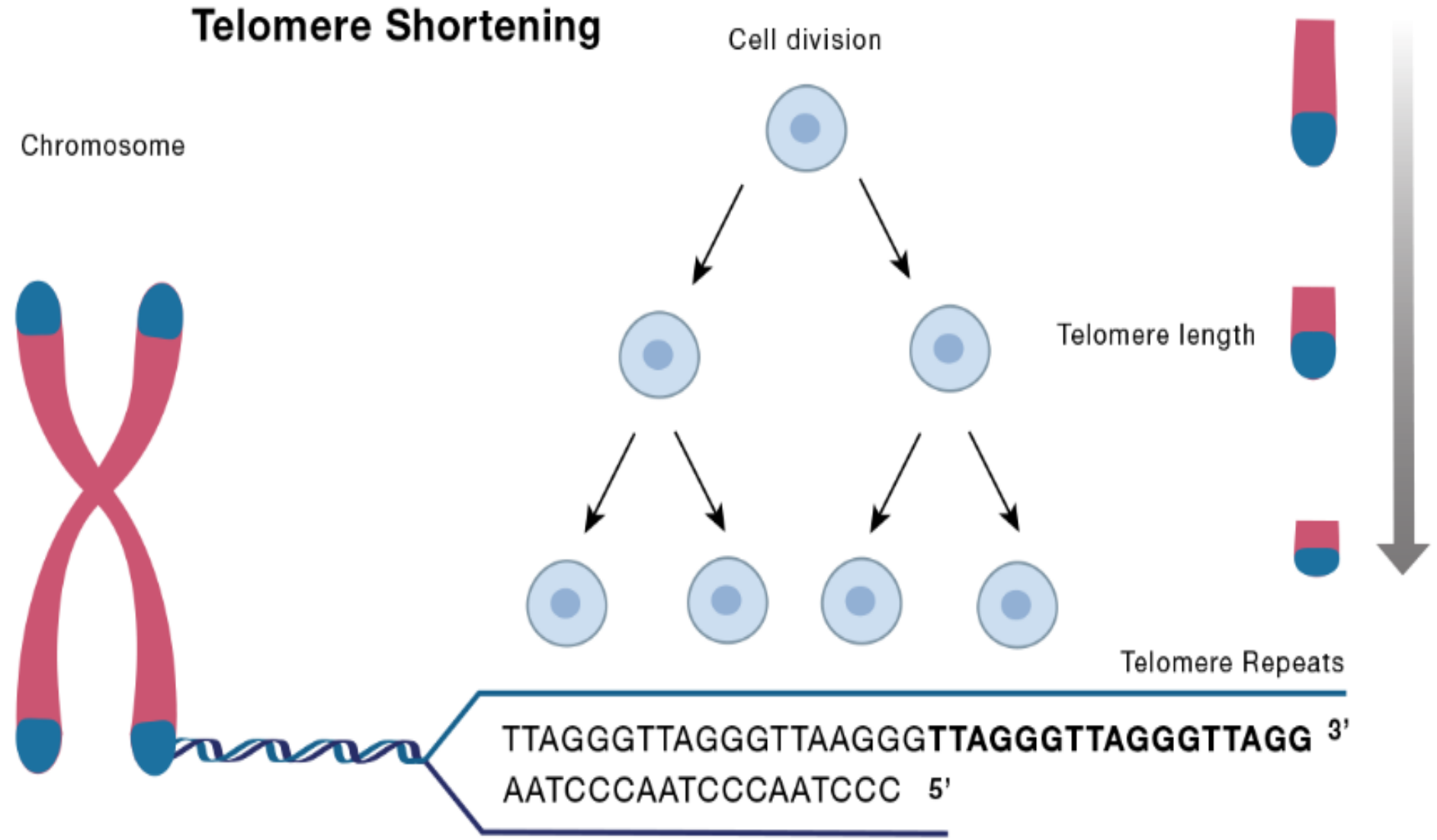
1. Telomeres protect the ends of chromosomes from degradation.
2. Telomeres have **a role in cell division**: Each time a cell divides, the telomeres become slightly shorter.

As most somatic cells age, their telomeres become shorter and they exit the cell cycle, resulting in an inability to generate new cells to replace damaged ones.

Telomere length is maintained by nucleotide addition mediated by an enzyme called **telomerase**.

In cancer cells, telomerase is usually reactivated and telomere length is stabilized, allowing the cells to proliferate indefinitely.

Role of Telomeres in cell division



Invasion and metastasis

1. Direct invasion and extension: There is a reduced tendency of cancer cells to stick together due to a loss of cell surface **adhesion molecules**. Most cancers synthesize and secrete enzymes that break down proteins and contribute to the infiltration, invasion, and penetration of the surrounding tissues.

2. Seeding of cancer cells in body cavities: It occurs during the surgical removal of cancers, where it is possible to accidentally introduce free cancer cells into a body cavity such as the **peritoneal pleural, pericardial cavities**.

3. Metastatic spread: The term metastasis **(meta=change, stasis= position)** is used to describe the development of a secondary tumour in a location distant from the primary tumour.

All malignant tumours can metastasize, except **gliomas** a malignant neoplasm of the glial cells in the central nervous system and **basal cell carcinomas** of the skin.

In general, the likelihood of metastasis of a solid tumour correlates with other features of malignancy including **lack of differentiation, aggressive local invasion, rapid growth, and large size.**

The pathogenesis of metastasis

To metastasize, a cancer cell must be able to:

1. break loose from the primary tumour.
2. secrete enzymes that break down the surrounding extracellular matrix to move through the degraded matrix and gain access to a blood vessel.
3. gain protection from the antitumor host cells by aggregating and adhering to circulating blood components, particularly platelets, to form tumour emboli **(Evading the immune system).**
4. exit from the circulation by adhesion to the vascular endothelium followed by movement through the capillary wall into the site of secondary tumour formation.

The pathogenesis of metastasis