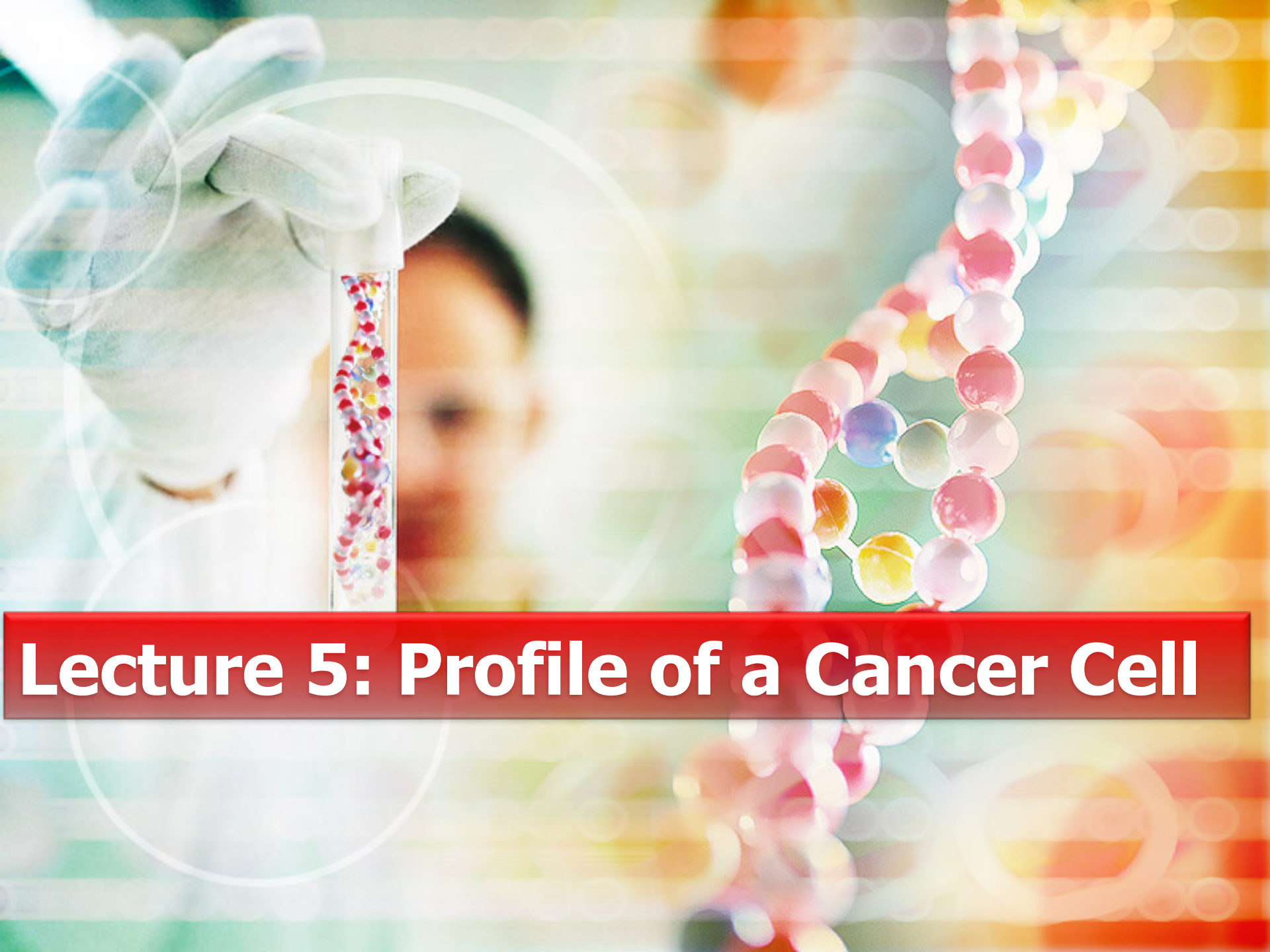


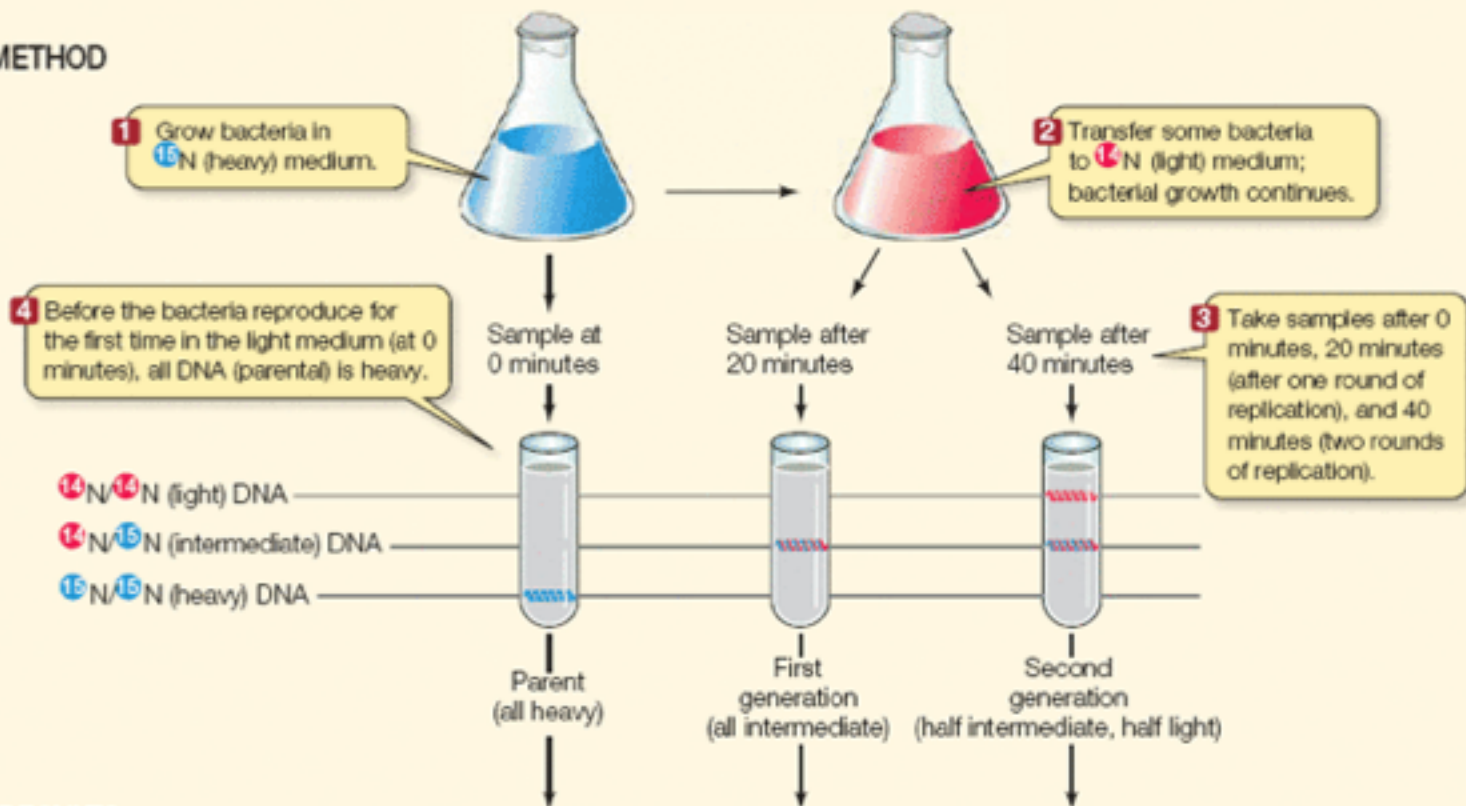


Lecture 5: Profile of a Cancer Cell

EXPERIMENT

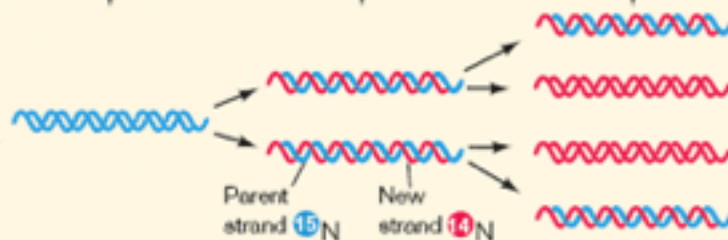
HYPOTHESIS: DNA replicates semiconservatively.

METHOD



RESULTS

After 2 generations, half the DNA was intermediate and half was light only; there was no heavy-only DNA.



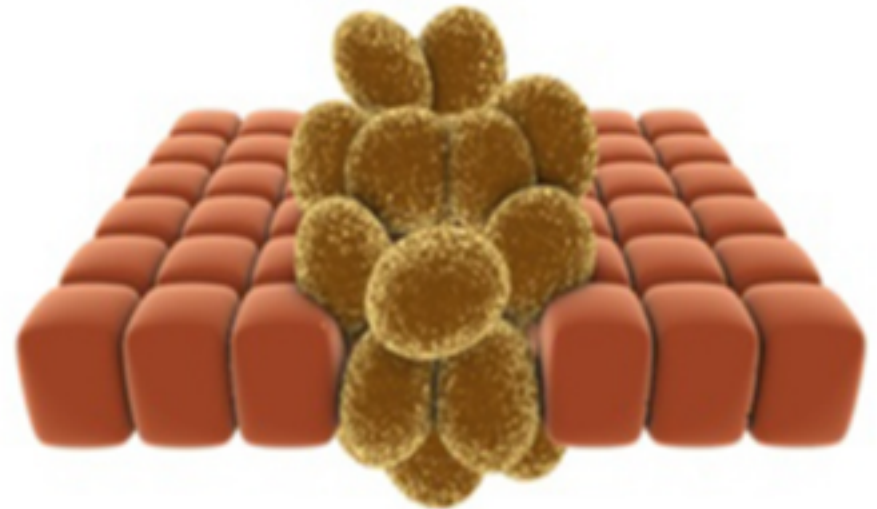
CONCLUSION: This pattern could only have been observed if each DNA molecule contains a template strand from the parental DNA; thus DNA replication is semiconservative.

Characteristics of a Normal cell

- ❑ Reproduce themselves exactly
- ❑ Stop reproducing at the right time
- ❑ Stick together in the right place
- ❑ Self destruct if they are damaged
- ❑ Become specialized or mature

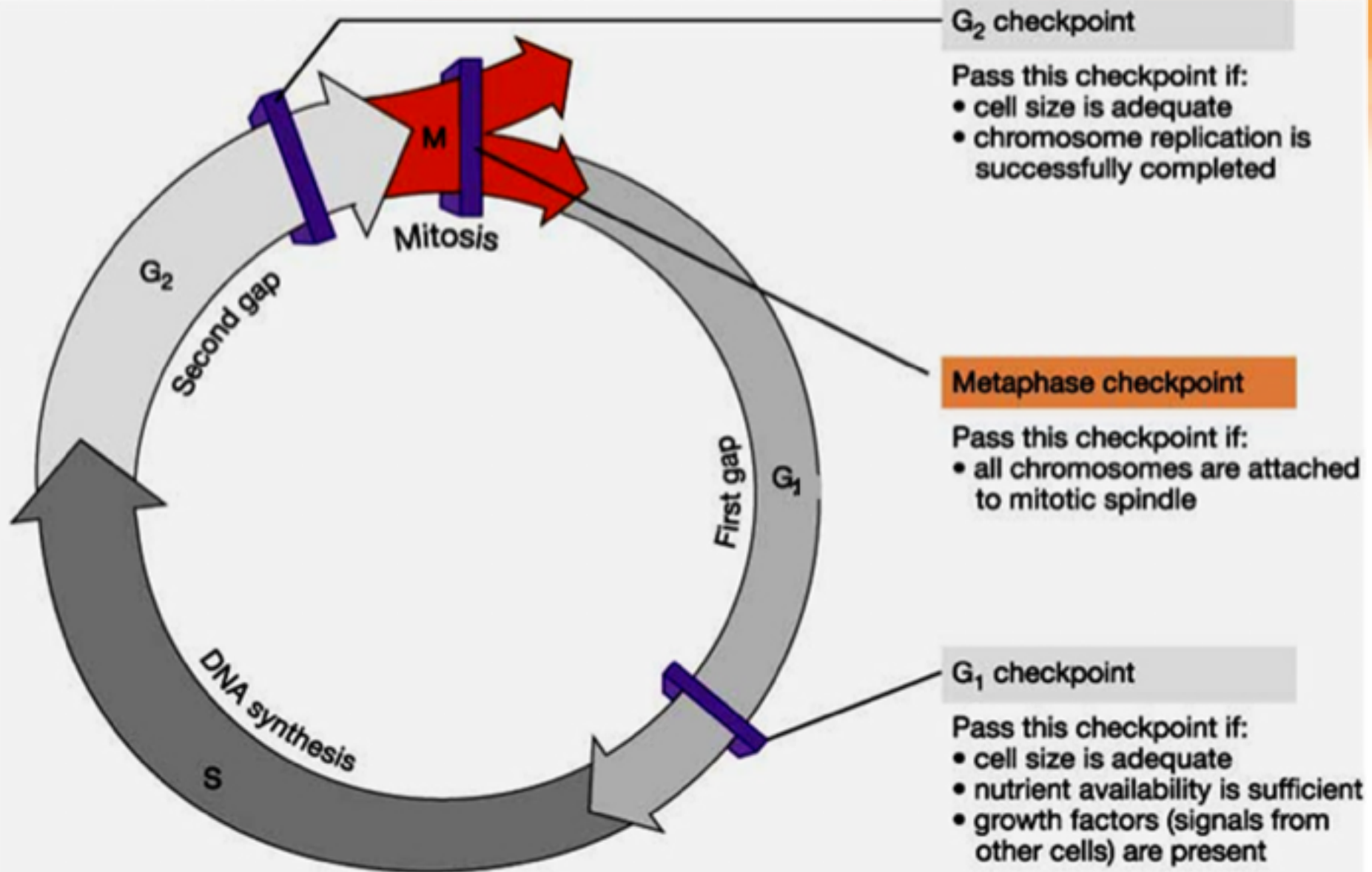


Normal: regulated cell growth



Cancer: uncontrolled cell growth

The Cell Cycle and Checkpoints



Cancer Begins with DNA Damage

POSSIBLE CAUSES OF CANCER

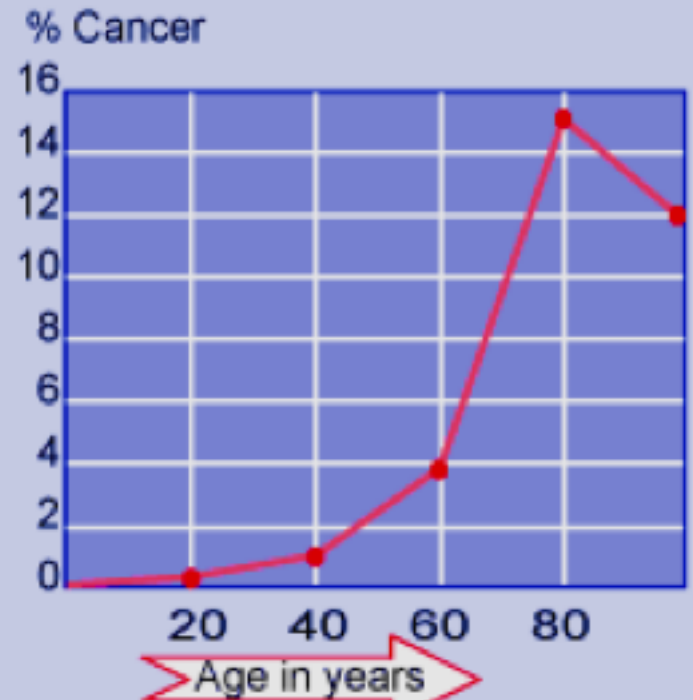


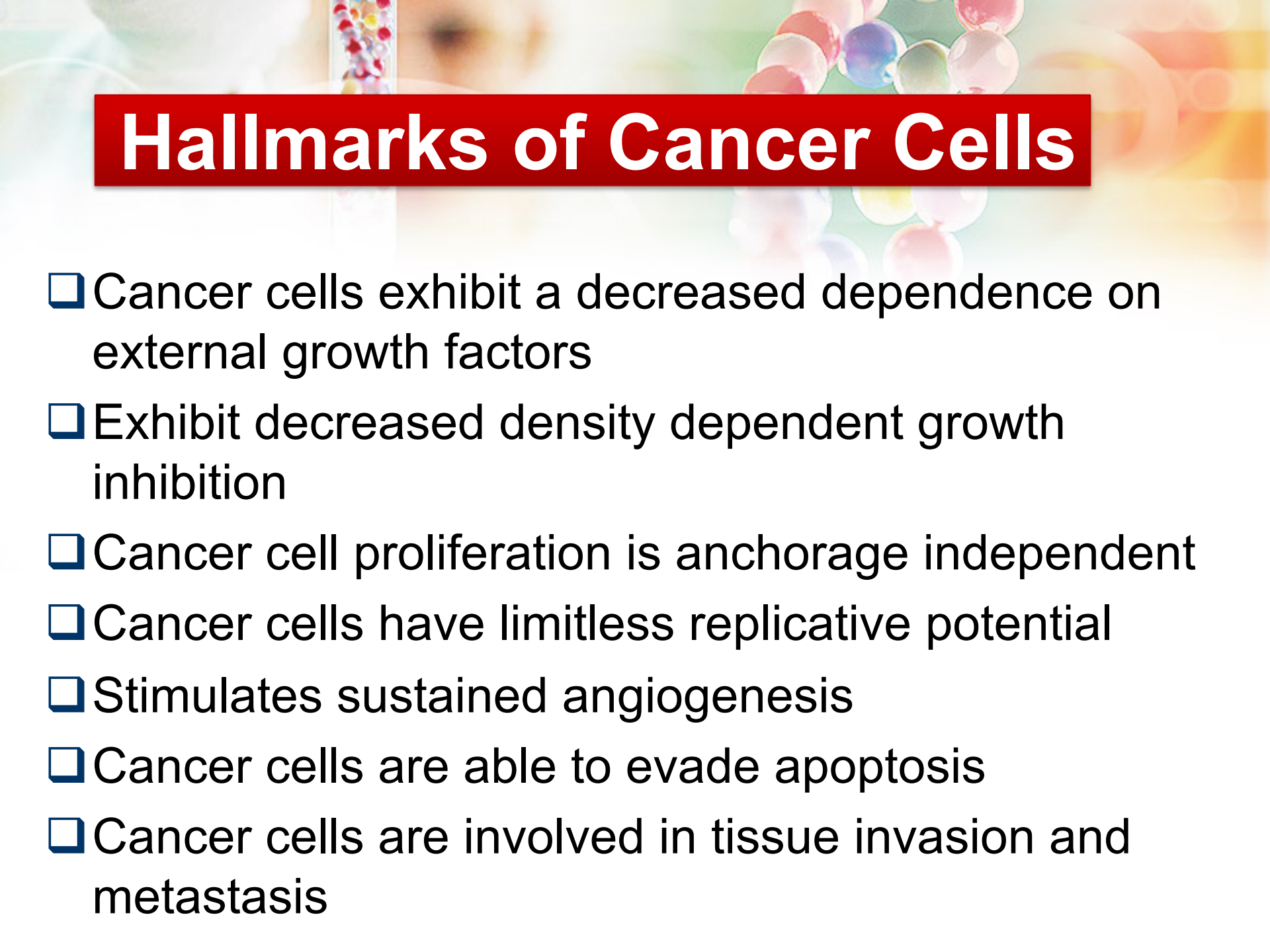
DNA DAMAGE OR MUTATION

AS A RESULT OF:

- Exposure to Radiation
- Exposure to Toxins
- Hormonal Abnormalities
- Inherited Abnormalities
- Nutrition and Diet
- Tobacco Use
- Viral Infection

Cancer incidence increases with age

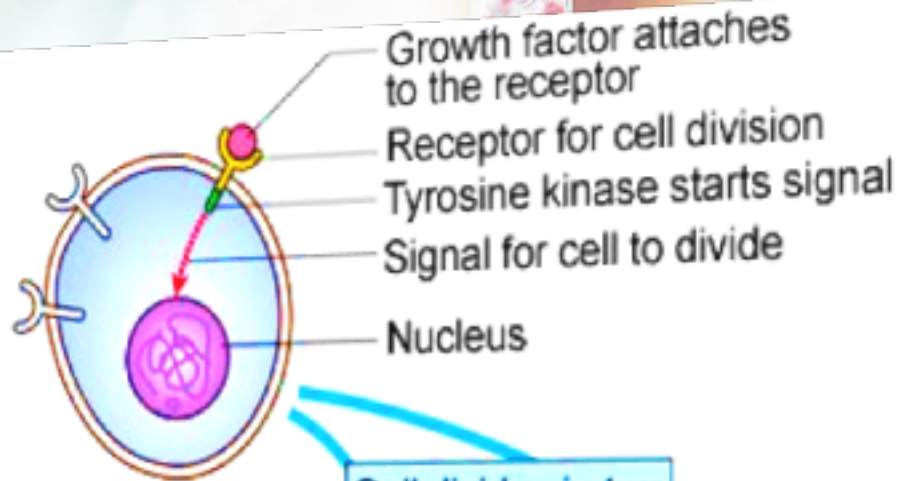




Hallmarks of Cancer Cells

- ❑ Cancer cells exhibit a decreased dependence on external growth factors
- ❑ Exhibit decreased density dependent growth inhibition
- ❑ Cancer cell proliferation is anchorage independent
- ❑ Cancer cells have limitless replicative potential
- ❑ Stimulates sustained angiogenesis
- ❑ Cancer cells are able to evade apoptosis
- ❑ Cancer cells are involved in tissue invasion and metastasis

How Growth Factors Work



Cell divides in two

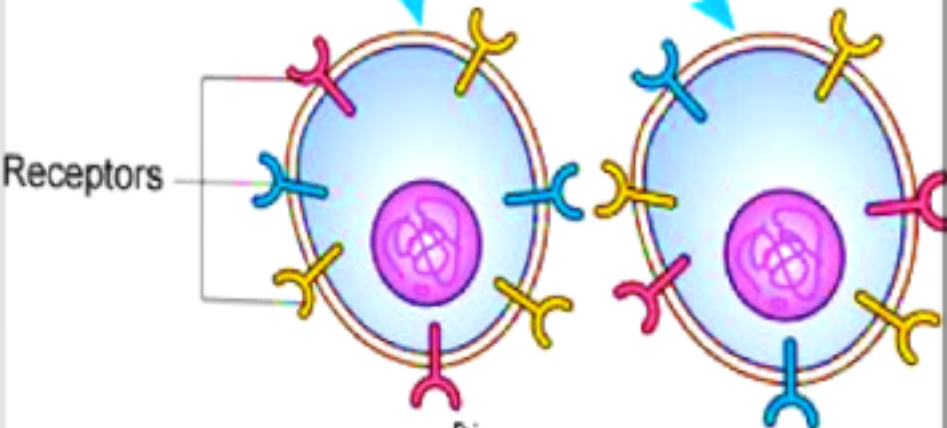
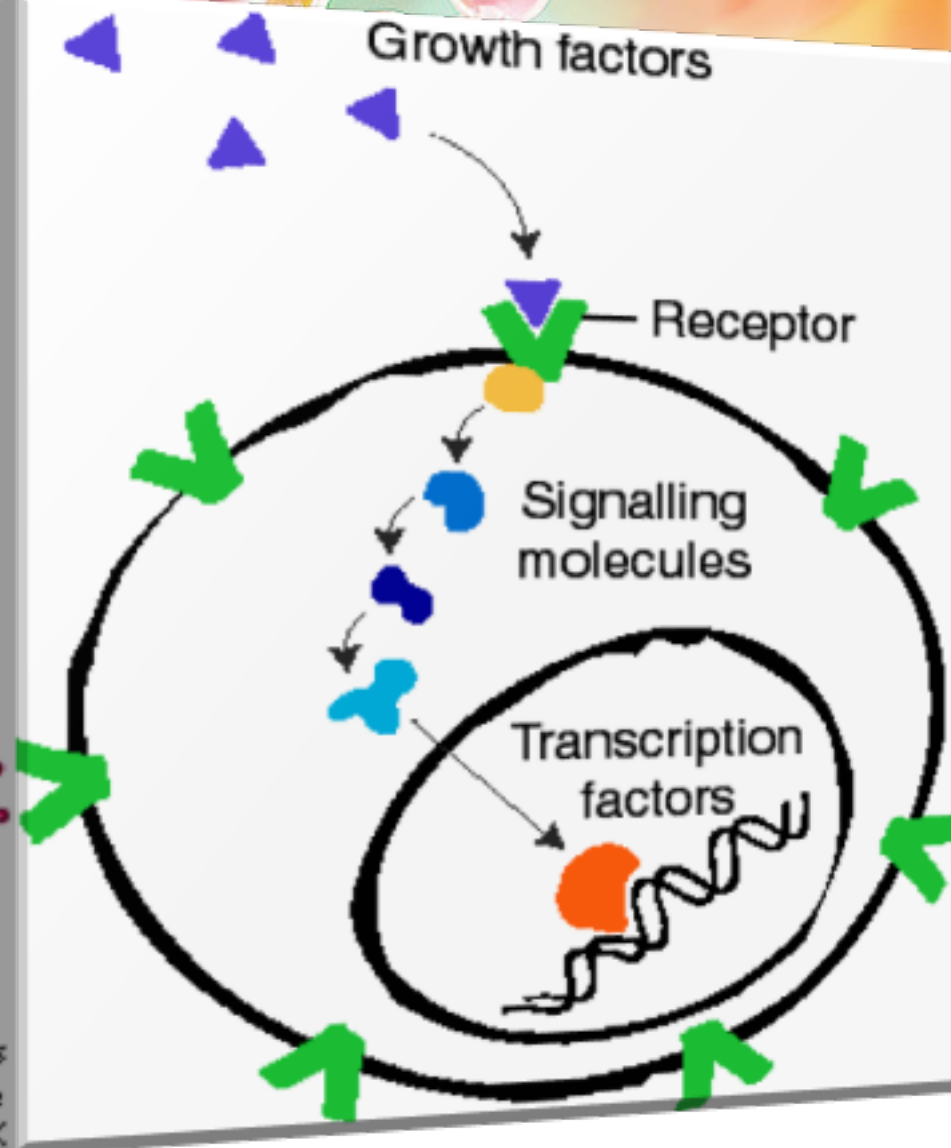
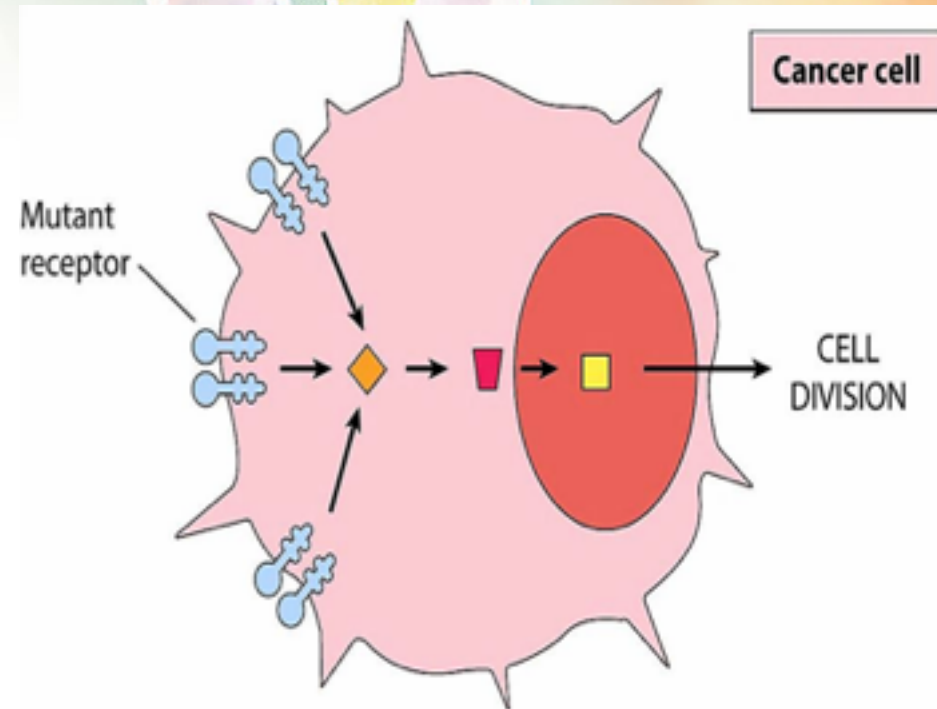
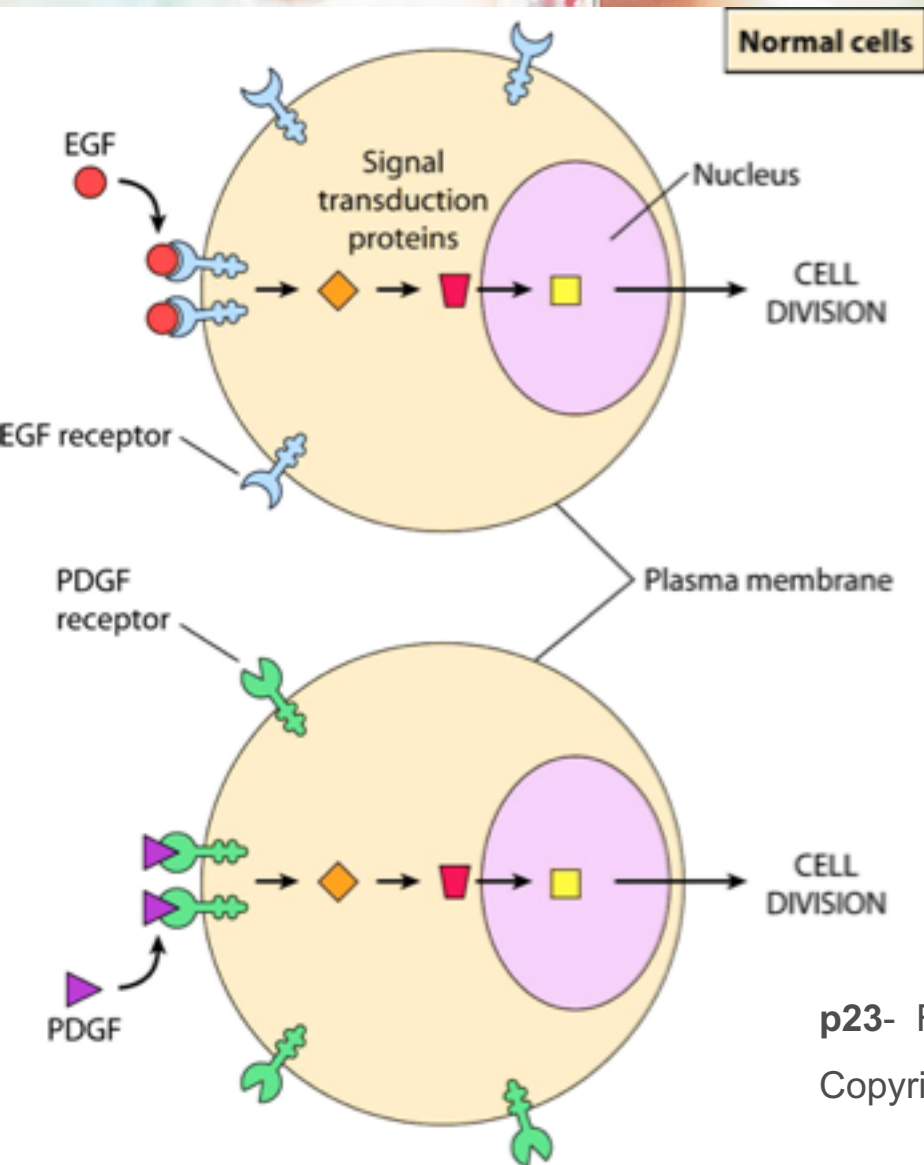


Diagram showing how growth factors
signal to the cell to grow and divide
Copyright © CancerHelp UK



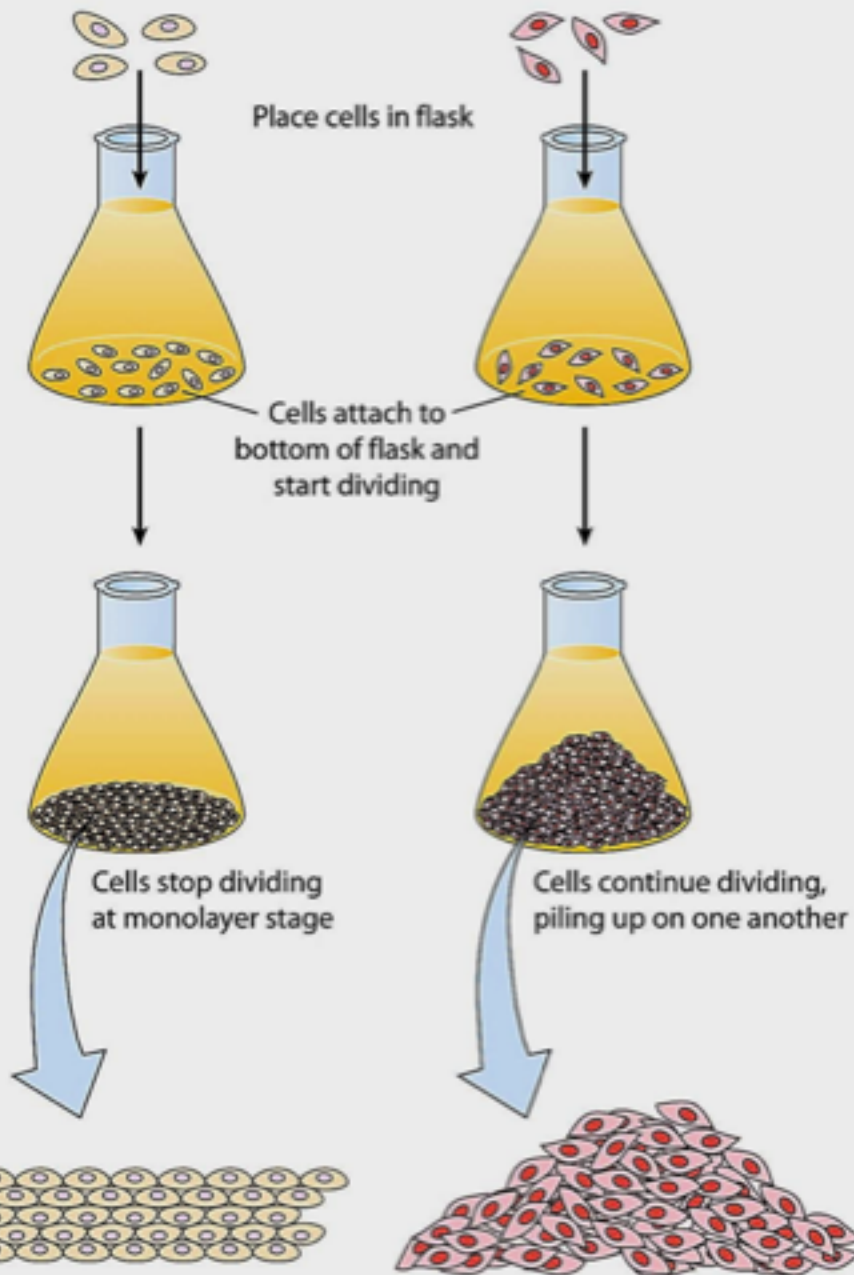
Decreased Dependence on External Growth Factors



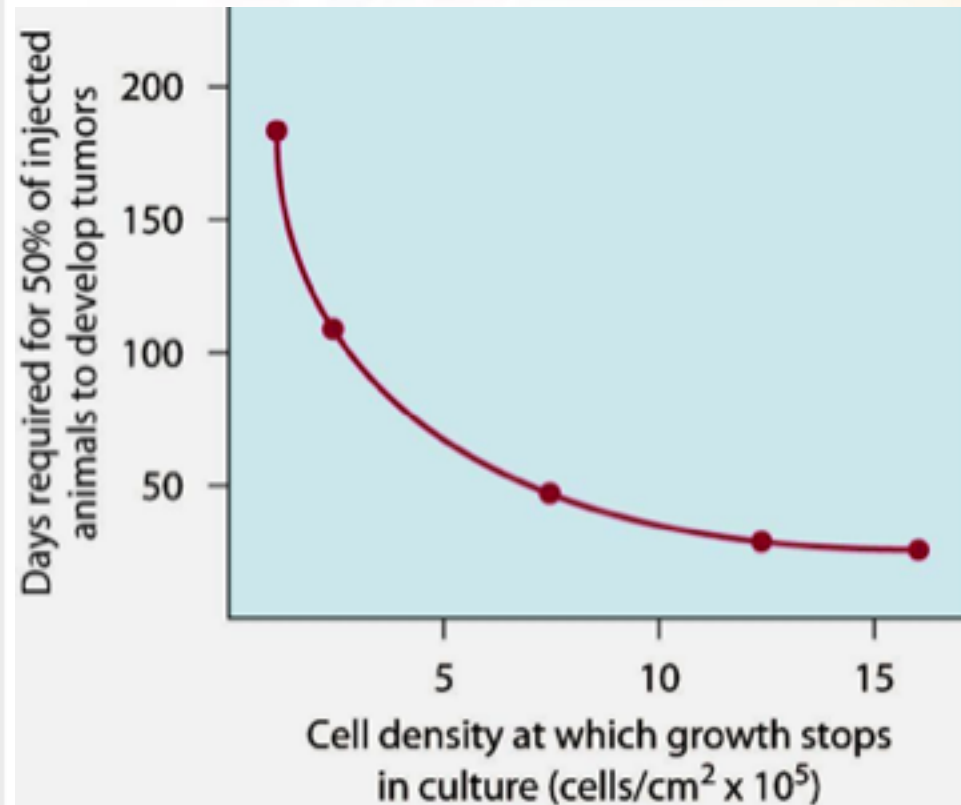
p23- From L. J. Kleinsmith, *Principles of Cancer Biology*.
Copyright (c) 2006 Pearson Benjamin Cummings.

Normal cells

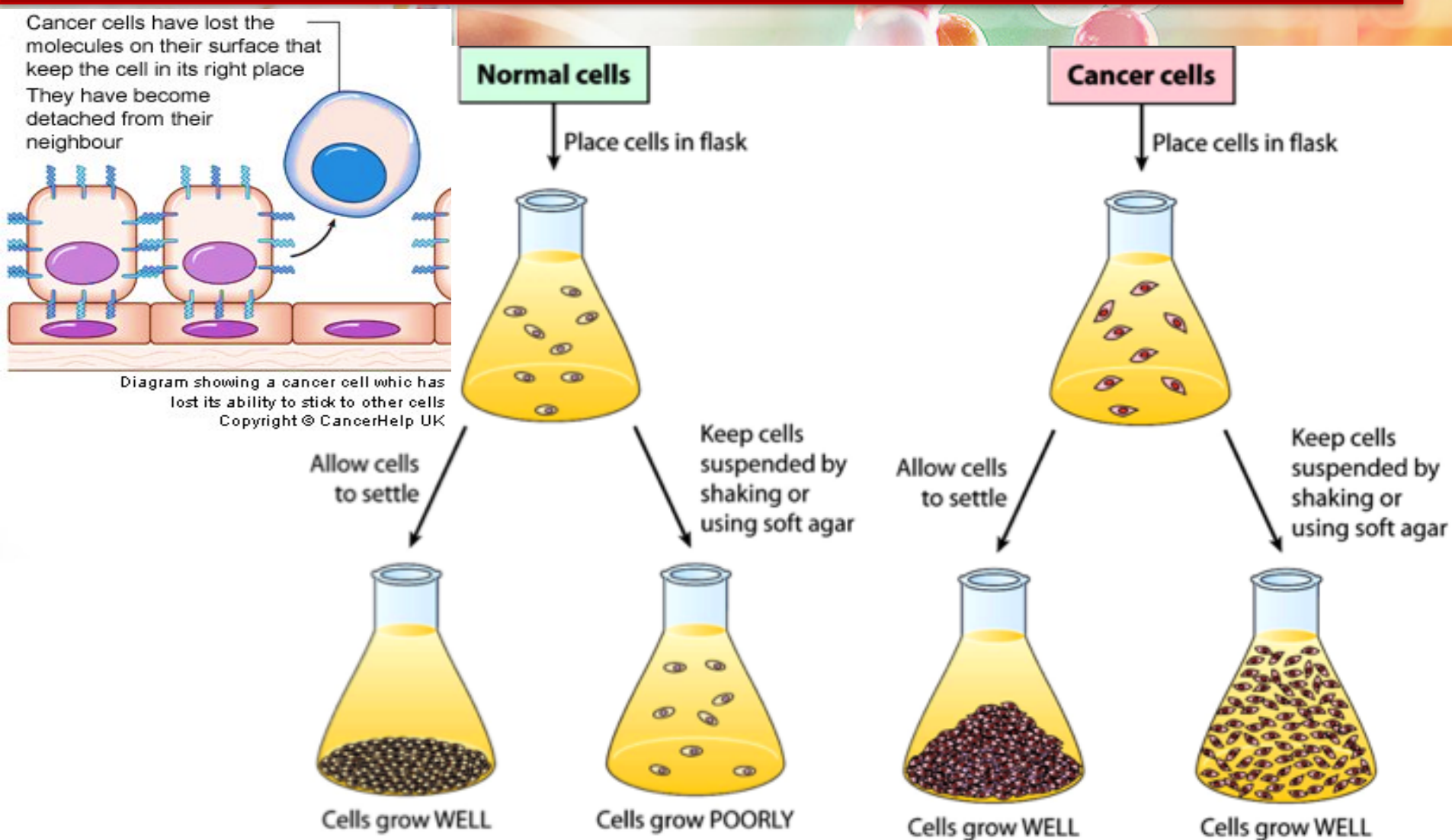
Cancer cells



Density-dependent Inhibition of Growth by Cancer Cells



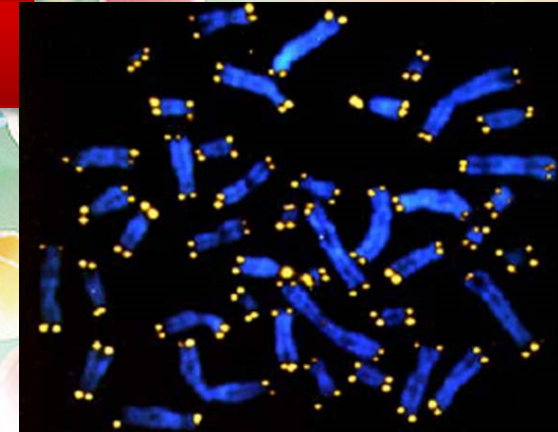
Anchorage Independent Growth



Anoikis - homelessness

p20 - - From L. J. Kleinsmith, *Principles of Cancer Biology*. Copyright (c) 2006 Pearson Benjamin Cummings.

Telomeres: DNA Unlaced

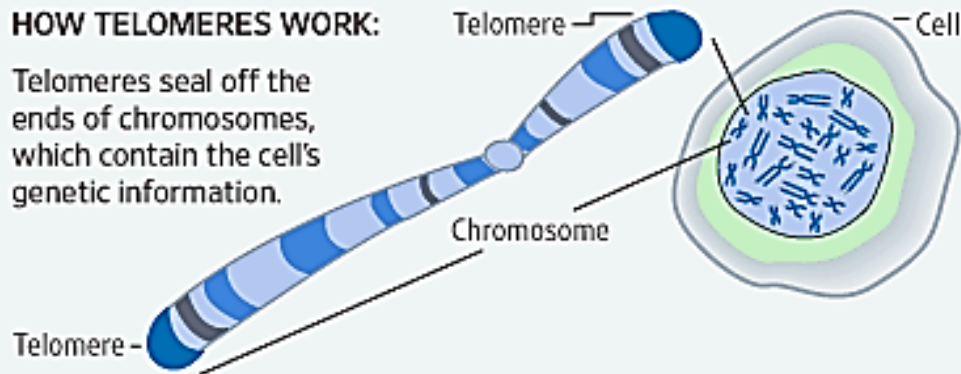


Unraveling a Cellular Mystery

The Nobel Prize went to scientists who described the workings of the telomere, which helps protect cells from age-related damage.

HOW TELOMERES WORK:

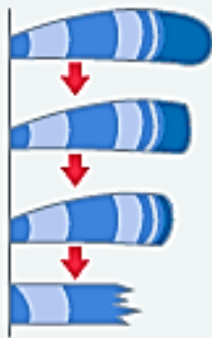
Telomeres seal off the ends of chromosomes, which contain the cell's genetic information.



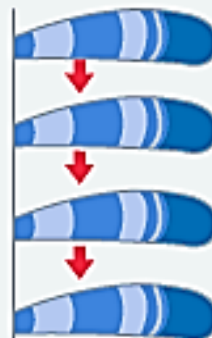
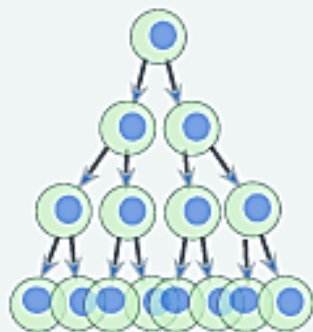
As cells replicate, telomeres can fray, allowing chromosomes to become damaged. This becomes increasingly common with age.

Scientists discovered a protein called telomerase, which maintains the telomeres, keeping chromosomes intact longer.

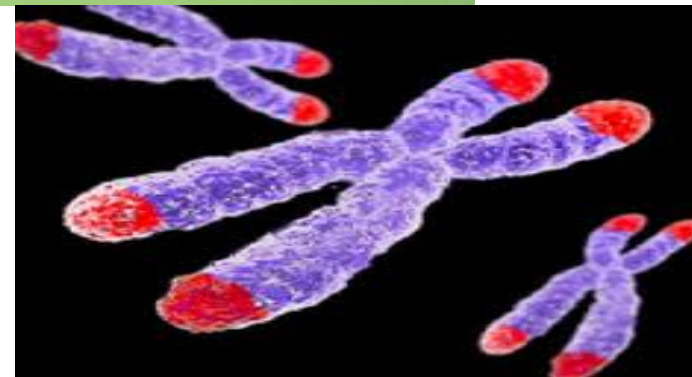
CELL DIVISION



Chromosome tips without telomerase



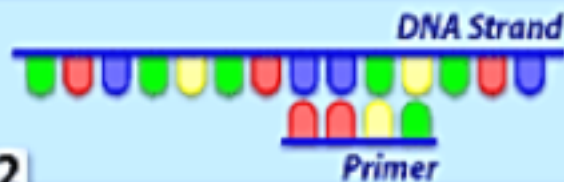
Chromosome tips with telomerase



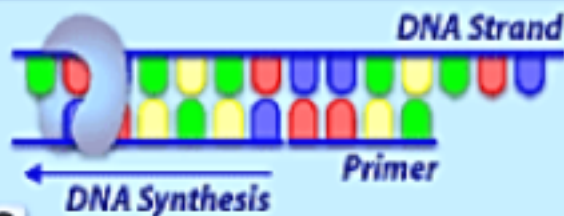
Telomerase Make Cancer Cells Immortal

The Long and short on Telomeres

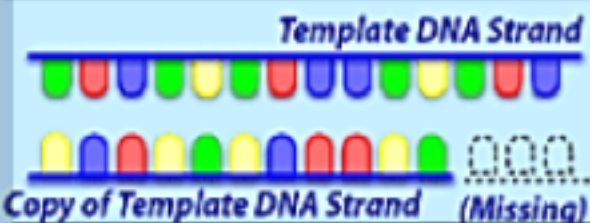
1
When DNA replicates during cell division, a short piece of RNA called a "primer" helps it to get started.



2
Once a primer attaches, cellular machinery can copy the DNA strand.



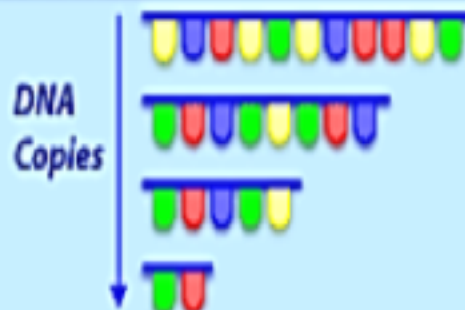
3
Since the primer does not attach to the very end of the DNA strand, the copy is missing a section of DNA.



4
The next time the cell divides, the copied DNA loses more of the end section.



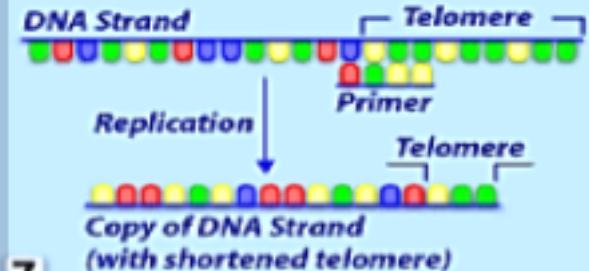
5
As cell division continues, the end section of each new DNA strand gets shorter and shorter. In humans, about 50 - 250 base pairs are lost per cell division.



How do our cells have any DNA left?

TELOMERASE!

6
Telomeres are repeated sequences on the ends of DNA strands. They help protect the DNA strand from getting shorter during cell division.



7
In germline cells (egg and sperm), an enzyme called telomerase is responsible for adding more repeat sequences to the end of the DNA, thus making them "immortal".



8
In somatic cells, the telomerase enzyme functions at much lower levels, making these cells "mortal".

DNA from old somatic cell (no telomere left)

9
When the telomeres in a somatic cell shorten to a critical level, that cell no longer divides. This phenomenon contributes to some of the changes we see in aging.

Telomeres



SOME FACTORS IN AGING

Telomere Shortening

chromosomes lose telomeres over time



Chronological Age

risk factors increase over time



Oxidative Stress

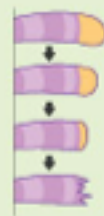
oxidants damage DNA, proteins and lipids



Glycation

glucose sugar binds to and inhibits DNA, proteins and lipids





Low telomerase activity

Without telomerase the chromosomes are shortened each time the cell divides.

Mutations in genes encoding telomerase or telomere-binding proteins are found in a group of rare inherited diseases with manifestations in bone marrow, lung and skin.

These diseases are linked to the presence of short telomeres and to defects in stem cell maintenance. In the bone marrow insufficient cell divisions in the stem cell compartment lead to severe anemia.



High telomerase activity in cancer cells

Cancer cells can divide infinitely and therefore must preserve their telomeres. Telomerase activity is increased in 80-90% of cancers.

Hope is raised that new cancer therapies can be developed by targeting telomerase. Clinical trials are underway including studies evaluating vaccines directed against cells with elevated telomerase.

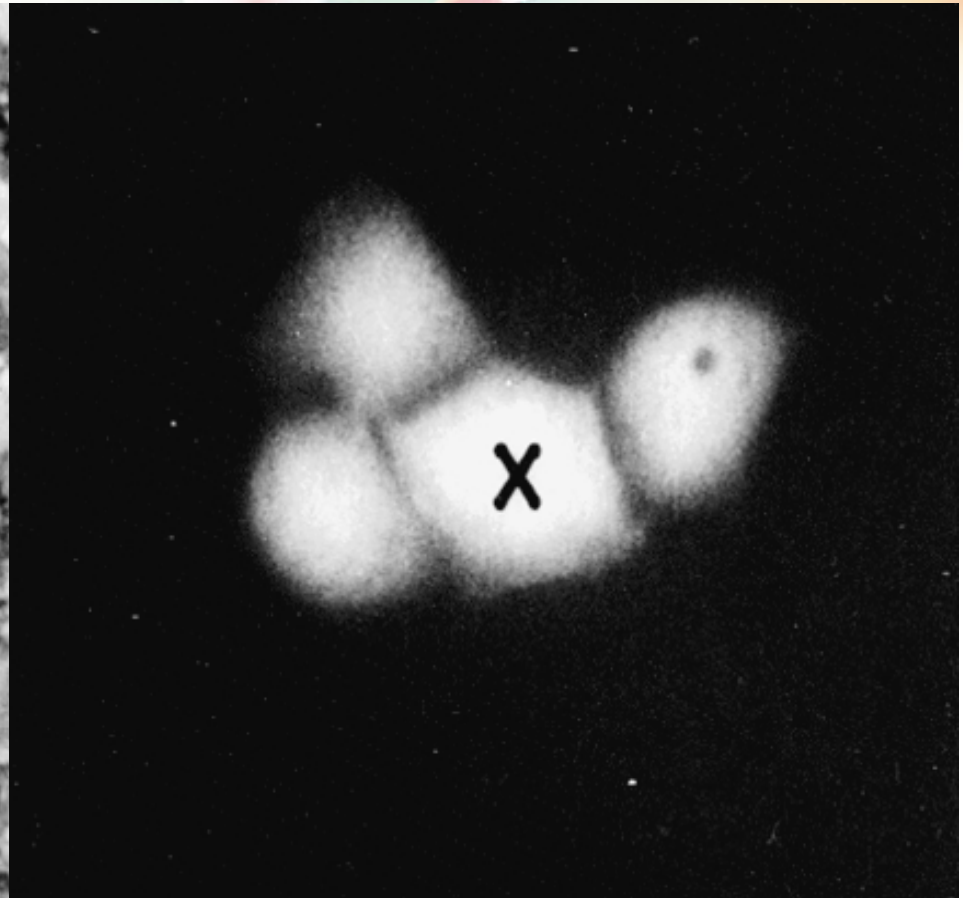


Malignant melanoma

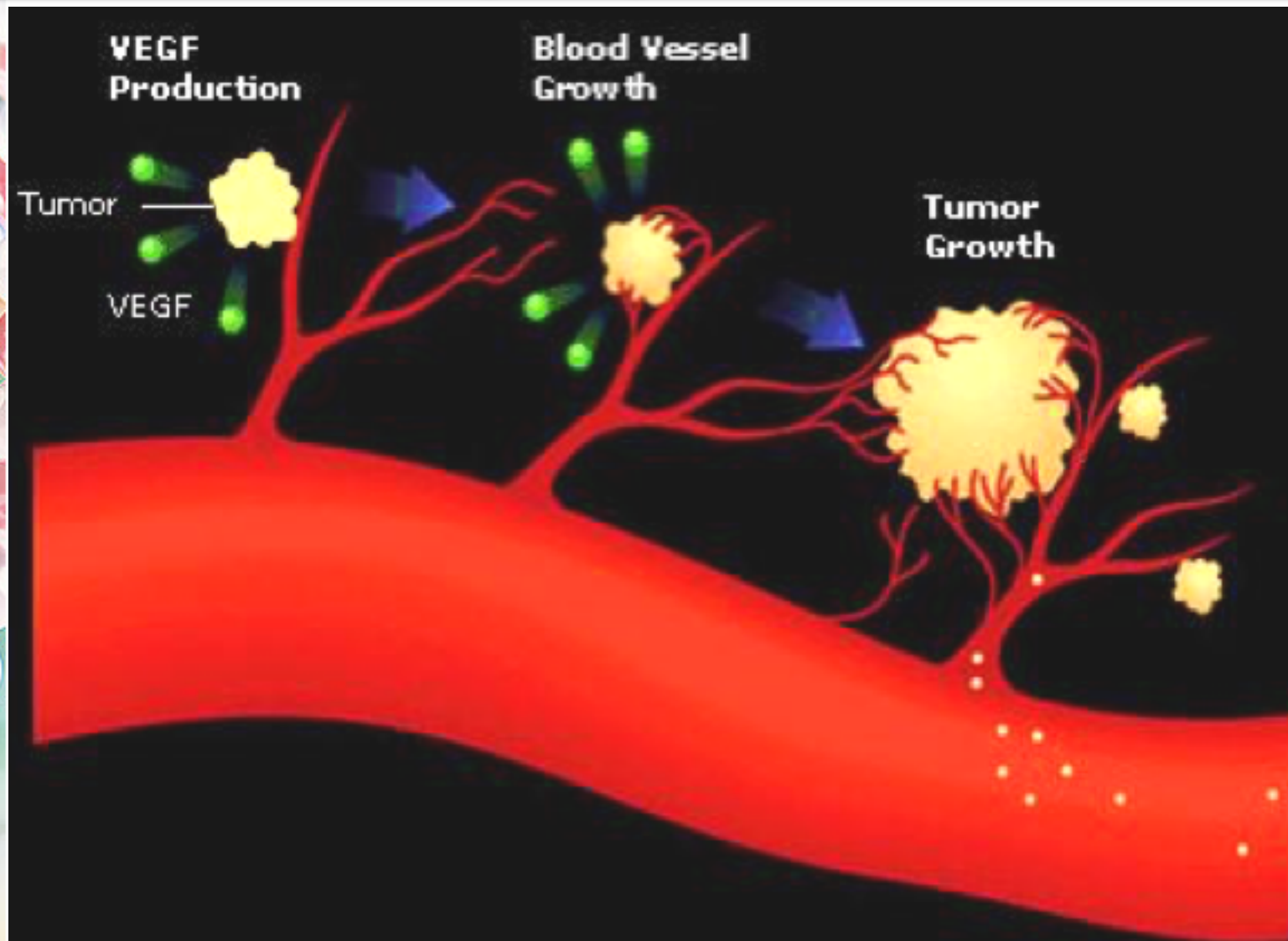


Telomerase: expressed in embryo (setting the clock)
then mostly off except for cancers

Evidence of Decreased Cell-Cell Communication in Cancer Cells



Angiogenesis



Vascular Endothelial Growth Factor (VEGF)
Epidermal growth Factor (EGF)

Profile of a Cancer Cell Summary

