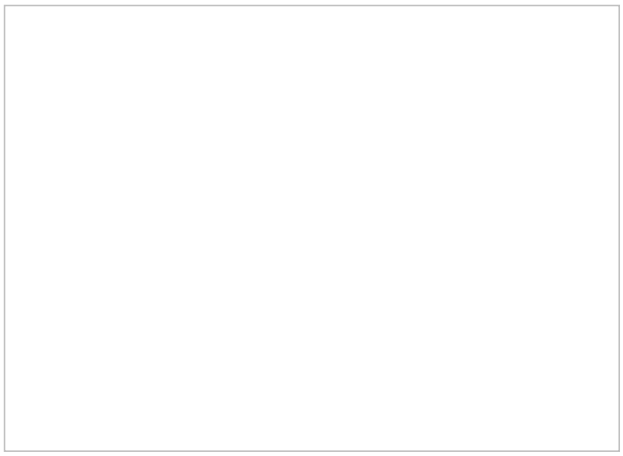
Cell Division

Printed from https://www.cancerquest.org/cancer-biology/cell-division on 11/22/2026



During a lifetime, many of the cells that make up the body age and die. These cells must be replaced so that the body can continue functioning optimally. Reasons that cells are lost and must be replaced include the following:

- Sloughing off of epithelial cells such as those lining the skin and intestines. The old, worn out cells on the surface of the tissues are constantly replaced. A special case of this is the monthly replacement of the cells lining the uterus in pre-menopausal women.
- Wound healing requires that cells in the area of the damage multiply to replace those lost. Viral diseases such as hepatitis may also cause damage to organs that then need to replace lost cells.
- Replacement of the cells that make up blood. Red blood cells carry oxygen to tissues. White blood cells such as B and T lymphocytes are part of the body's immune system and help to ward off infections. Most of these cells have very short lifespans and must be constantly replaced. The precursors of these cells are located in bone marrow. These precursors, or stem cells, must reproduce at a very high rate to maintain adequate amounts of the blood cells.

The process by which a cell reproduces to create two identical copies of itself is known as mitosis. The goal of mitosis is the formation of two identical cells from a single parent cell. The cells formed are known as daughter cells. In order for this to happen, the following must occur:

- The genetic material, the DNA in chromosomes, must be faithfully copied. This occurs via a process known as replication.
- The organelles, such as mitochondria, must be distributed so that each daughter cell receives an adequate amount to function.
- The cytoplasm of the cell must be physically separated into two different cells.

As we will see, many of the features of cancer cells are due to defects in the genes that control cell division. The cell division process occurs as an orderly progression through four different stages. These four stages are collectively known as the cell cycle. Further information on the topics on this page can also be found in most introductory Biology textbooks, we recommend Campbell Biology, 11th edition.[1] The following pages describe the cell cycle in detail.

Sections included on this page:

- Normal Cell Division
- Cancer Cell Division
- Cell Division Summary

Normal Cell Division

There are several safeguards built into the cell division process to assure that cells do not divide unless they have completed the replication process correctly and that the environmental conditions in which the cells exist are favorable for cell division. Among others, there are systems to determine the following:

- Is the DNA fully replicated?
- Is the DNA damaged?
- Are there enough nutrients to support cell growth?

If these checks fail, normal cells will stop dividing until conditions are corrected. Cancer cells do not obey these rules and will continue to grow and divide.

Now that we have discussed the cell cycle, we will briefly address the ways in which cells are signaled to divide.

Most cells in the body are not actively dividing. They are performing their functions, such as the production of enzymes to digest food or helping to move the arms or legs. Only a small percentage of cells are actually going through the process just described.

Cartoon of normal cell division showing need for constant external signals.

Normal cell division requires constant signals (man standing on switch). When the signals are removed, the cells stop dividing.

Cells divide in response to external signals that 'tell' them to enter the cell cycle. These signals may take the form of estrogen or proteins such as platelet derived growth factor (PDGF). These signaling molecules, depicted as an X-shaped molecule in the animation below, bind to their target cells and send signals into the nucleus. The result is that the genes responsible for cell division are turned on and the cell divides. For example, a cut in the skin leads certain blood cells, platelets, to produce a growth factor (that causes the skin cells to reproduce and fill the wound. Cell division is a normal process that allows the replacement of dead cells.

Normal Cell Division II

What are the signals that make cells **stop** dividing?

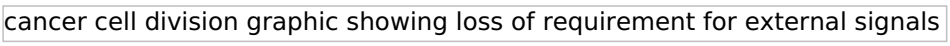
A lack of positive external signals causes cells to stop dividing.

Contact inhibition
Cells are also able to sense their surroundings and respond to changes. For instance, if a cell senses that it is surrounded on all sides by other cells, it will stop dividing. In this way, cells will grow when needed but stop when their goal has been met. To revisit our wound example, the cells fill in the gap left by the wound but then they stop dividing when the gap has been sealed. Cancer cells do not exhibit contact inhibition. They grow even when they are surrounded by other cells causing a mass to form. The behavior of normal (top animation) and cancer cells (bottom animation) with regard to contact inhibition is depicted below.

The round containers in which the cells are depicted in the animations are called petri dishes. In the laboratory, cells are often grown in these, covered with a nutrient-rich liquid.

Cellular Senescence
Most cells also seem to have a pre-programmed limit to the number of times that they can divide. Interestingly, the limit seems to be based, in part, on the cell's ability to maintain the integrity of its DNA. An enzyme, telomerase, is responsible for upkeep of the ends of the chromosomes. In adults, most of our cells don't utilize telomerase so they eventually die. In cancer cells, telomerase is often active and allows the cells to continue to divide indefinitely. For more information on telomerase, see the Cancer Genes section

Cancer Cell Division



Cancer cell division. Cancer cells divide even when the cells are not being 'told' to (no man standing on the switch).

When it comes to cell division, cancer cells break just about all the rules!

- **Cancer cells can divide without appropriate external signals**.This is analogous to a car moving without having pressure applied to the gas pedal. An example would be the growth of a breast cancer cell without the need for estrogen, a normal growth factor. Some breast cancer cells actually lose the ability to respond to estrogen by turning off expression of the receptor for estrogen within the cell. These cells can still reproduce by bypassing the need for the external growth signal.
- **Cancer cells do not exhibit contact inhibition**.While most cells can tell if they are being 'crowded' by nearby cells, cancer cells no longer respond to this stop signal. As shown above, the continued growth leads to the piling up of the cells and the formation of a tumor mass.
- **Cancer cells can divide without receiving the 'all clear' signal**.While normal cells will stop division in the presence of genetic (DNA) damage, cancer cells will continue to divide. The results of this are 'daughter' cells that contain abnormal DNA or even abnormal numbers of chromosomes. These mutant cells are even more abnormal than the 'parent' cell. In this manner, cancer cells can evolve to become progressively more abnormal.

Continued cell division leads to the formation of tumors. The genetic instability that results from aberrant division contributes to the drug resistance seen in many cancers. Mutations in specific genes can alter the behavior of cells in a manner that leads to increased tumor growth or development.

More information on this topic may be found in Chapter 8 of The Biology of Cancer by Robert A. Weinberg.

Cell Division Summary

Cell Division Control

- Cell division is a normal process.
- Mechanisms exist to ensure DNA replication occurs correctly and the environmental conditions are favorable for cell division. Replication errors may also be corrected after they occur.
- Normal cells stop dividing when there is genetic damage or conditions are not favorable. Cancer cells continue to divide even when conditions are not appropriate.

Cell Division Signaling

- Most cells in the body are not actively dividing, but are carrying out their normal functions.
- Cells divide in response to external signals in the form of protein or steroid growth factors.

- Cells stop dividing for several reasons, including:
    1. A lack of positive external signals
    2. The cell senses that it is surrounded on all sides by other cells-contact dependent (density dependent) inhibition
    3. Most cells seem to have a pre-programmed limit of the number of times they can divide

Cell Division in Cancer Cells

- Cancer cells can divide without appropriate external signals.
- Cancer cells do no exhibit contact inhibition.
- Cancer cells continue dividing in the presence of genetic damage.
- The uninhibited, continued division of genetically damaged cells can lead to tumor formation.

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1 Urry, L. A., Cain, M. L., Wasserman, S. A., Minorsky, P. V., & Reece, J. B. (2017). Campbell Biology (11th ed.). Pearson.