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## The Cell Cycle and Mitosis Tutorial

This exercise is designed to introduce you to the events that occur in the cell cycle and the process of mitosis that divides the duplicated genetic material creating two identical daughter cells.

### DNA

The nucleus is a membrane bound organelle that contains the genetic information in the form of chromatin, highly folded ribbon-like complexes of deoxyribonucleic acid (DNA) and a class of proteins called histones. When a cell divides, chromatin fibers are very highly folded, and become visible in the light microscope as chromosomes. During interphase (between divisions), chromatin is more extended, a form used for expression genetic information. The DNA of chromatin is wrapped around a complex of histones making what can appear in the electron microscope as "beads on a string" or nucleosomes. Changes in folding between chromatin and the mitotic chromosomes is controlled by the packing of the nucleosome complexes. DNA or **d**eoxyribonucleic **a**cid is a large molecule structured from chains of repeating units of the sugar deoxyribose and phosphate linked to four different bases abbreviated A, T, G, and C. We will later show how the simple structure of DNA contains the information for specifying the proteins that allow life. The process of mitosis is designed to insure that exact copies of the DNA in chromosomes are passed on to daughter cells.

### Stages of the Cell Cycle

The cell cycle is an ordered set of events, culminating in cell growth and division into two daughter cells. Non-dividing cells not considered to be in the cell cycle. The stages, pictured above, are G1-S-G2-M. The G1 stage stands for "GAP 1". The S stage stands for "Synthesis". This is the stage when DNA replication occurs. The G2 stage stands for "GAP 2". The M stage stands for "mitosis", and is when nuclear (chromosomes separate) and cytoplasmic (cytokinesis) division occur. Mitosis is further divided into 4 phases, which you will read about on the next page.

### Cdk

Cdk (cyclin dependent kinase, adds phosphate to a protein), along with cyclins, are major control switches for the cell cycle, causing the cell to move from G1 to S or G2 to M.

### Mpf

MPF (Maturation Promoting Factor) includes the CdK and cyclins that triggers progression through the cell cycle.



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### p53

p53 is a protein that functions to block the cell cycle if the DNA is damaged. If the damage is severe this protein can cause apoptosis (cell death).

- p53 levels are increased in damaged cells. This allows time to repair DNA by blocking the cell cycle.
- A p53 mutation is the most frequent mutation leading to cancer. An extreme case of this is Li Fraumeni syndrome, where a genetic defect in p53 leads to a high frequency of cancer in affected individuals.

### p27

p27 is a protein that binds to cyclin and cdk blocking entry into S phase. Recent research (Nature Medicine 3, 152 (1997)) suggests that breast cancer prognosis is determined by p27 levels. Reduced levels of p27 predict a poor outcome for breast cancer patients.

## Mitosis

### Definition

What is (and is not) mitosis? Mitosis is nuclear division plus cytokinesis, and produces two identical daughter cells during prophase, prometaphase, metaphase, anaphase, and telophase. Interphase is often included in discussions of mitosis, but interphase is technically not part of mitosis, but rather encompasses stages G1, S, and G2 of the cell cycle.

### Pre-Mitosis: Interphase

The cell is engaged in metabolic activity and performing its prepare for mitosis (the next four phases that lead up to and include nuclear division). Chromosomes are not clearly discerned in the nucleus, although a dark spot called the nucleolus may be visible. The cell may contain a pair of centrioles (or microtubule organizing centers in plants) both of which are organizational sites for microtubules.

### Stage I: Prophase

Chromatin in the nucleus begins to condense and becomes visible in the light microscope as chromosomes. The nucleolus disappears. Centrioles begin moving to opposite ends of the cell and fibers extend from the centromeres. Some fibers cross the cell to form the mitotic spindle.

### Stage II: Prometaphase

The nuclear membrane dissolves, marking the beginning of prometaphase. Proteins attach to the centromeres creating the kinetochores. Microtubules attach at the kinetochores and the chromosomes begin moving.



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### **Stage III: Metaphase**

Spindle fibers align the chromosomes along the middle of the cell nucleus. This line is referred to as the metaphase plate. This organization helps to ensure that in the next phase, when the chromosomes are separated, each new nucleus will receive one copy of each chromosome.

### **Stage IV: Anaphase**

The paired chromosomes separate at the kinetochores and move to opposite sides of the cell. Motion results from a combination of kinetochore movement along the spindle microtubules and through the physical interaction of polar microtubules.

### **Stage V: Telophase**

Chromatids arrive at opposite poles of cell, and new membranes form around the daughter nuclei. The chromosomes disperse and are no longer visible under the light microscope. The spindle fibers disperse, and cytokinesis or the partitioning of the cell may also begin during this stage.

### **Post-Mitosis: Cytokinesis**

In animal cells, cytokinesis results when a fiber ring composed of a protein called actin around the center of the cell contracts pinching the cell into two daughter cells, each with one nucleus. In plant cells, the rigid wall requires that a cell plate be synthesized between the two daughter cells.