MITOSIS, CYTOKINESIS, MEIOSIS AND APOPTOSIS

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Summary

The eukaryotic cell cycle comprises clear stages. Two major stages are the synthesis phase, where the cell replicates its genetic information, and the mitotic phase, where the cell divides into two daughter cells. They are separated by gap phases 1 and 2. These

stages prepare the cell for the following step in the cell cycle. Mitosis is characterized by distinctive steps: prophase, metaphase, anaphase, telophase and cytokinesis. Meiosis is another form of cell division that results in the formation of haploid daughter cells containing a single copy of the chromosome set. This process is important in the formation of gametes.

The cell cycle is controlled by an extremely complex pathway of interacting protein signals. They are called protein kinases and are regulated by small proteins called cyclins. Different cyclin-protein kinase combinations trigger different stages in the cell cycle. The cell cycle can be halted, if necessary, by protein kinase inhibitors binding to the enzyme. Growth regulators trigger cellular replication by initiating the cell cycle. The cell is also able to kill itself by initiating a process of programmed cell death or apoptosis. This process allows the cell to compartmentalize its components and target itself for degradation. Cancer can result from mutations in certain growth regulatory proteins. They may either be nonfunctional growth inhibitors or tumor repressors, or over stimulated growth signals. This would allow the cells to grow without any regulation or control.

1. The eukaryote cell cycle

When a eukaryotic cell divides, it makes a copy of its complete set of chromosomes which have to be evenly distributed between the two daughter cells. The process is more complicated and time-consuming than that for prokaryotes and entails several different stages. The cell cycle is the complete period of taking the cell from one division to the following cell division.

1.1. Phases

DNA synthesis occurs during the interphase which itself can be divided into three stages:

1. The first gap phase (G1) where the cell prepares itself for DNA synthesis.
2. The synthesis or S phase where the DNA is duplicated
3. The second gap phase (G2) where the cell prepares itself for mitosis.

The cell usually spends most of its life in the G1 phase or the G0 phase, a resting form of G1. Mitosis occurs after the interphase and takes up a very small period in a normal adult cell life cycle. A cell replicating in a day would spend 42% of the time in G1 phase, 38% in S phase, 16% in G2 phase and finally, 4% in the mitotic phase. The periodicity of cell division depends on the cell type and signals received from the surrounding tissues. For example, a gut cell replicates twice a day whereas a liver cell normally multiplies once every one to two years.

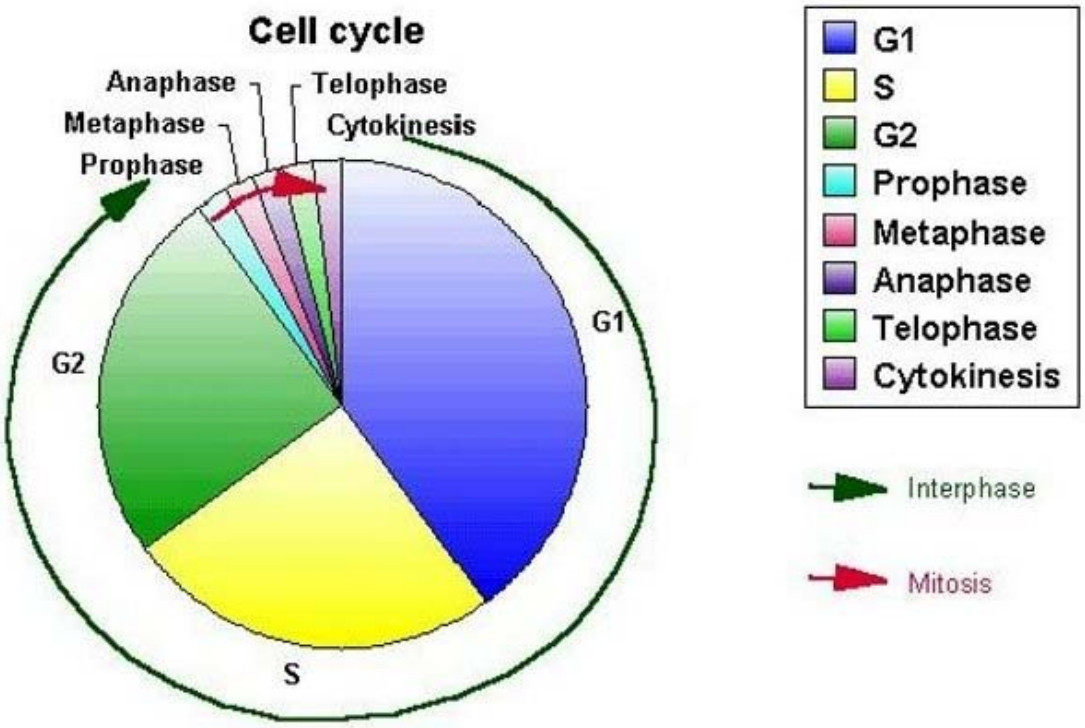

Figure 1. Diagram illustrating the cell cycle.

During G1 phase the cell contains the normal complement of chromosomes—or is said to be diploid (2N) in that it contains two copies of each chromosome, one from each parent. The G1 phase allows the cell to synthesize all the necessary proteins in order to replicate the host DNA. Synthesis of enough histones to accommodate the newly synthesized DNA is essential. Some cells progress to a suspended state within the cell cycle called G0 (Gzero). This entails dismantling many of the signaling molecules required for the cell cycle to progress past G1. Most animal cells require signals from neighboring cells in order to initiate proliferation of cells. If signals are lacking, the cell arrests in G1 and progresses to G0.

The cell progresses to the S phase once all the machinery and accessories have been synthesized, and replication of the DNA proceeds. By the end of the S phase the cell contains four copies of each chromosome. and is said to be 4N. The new histones have associated with the newly generated DNA strands to form chromosome structures.

The cell now progresses to the G2 phase where the cell prepares itself for cell division or cytokinesis. This entails synthesis of all the necessary proteins and enough cell material to generate two daughter cells with a full complement of organelles and structures. The cell now still contains four copies of each chromosome (4N) or carries two complete diploid sets of chromosomes.

Mitosis entails several stages, namely prophase, metaphase, anaphase and telophase. At the start of the prophase, the cell contains a duplicate number of chromosomes in the nucleolus, During the middle prophase, the chromosomes become visible and spread

throughout the nucleus. They are clearly composed of two chromatids bound by a centromere. The centrosomes move from the center of the cell toward opposite poles inside the cytoplasm. A spindle starts forming and, by the end of the prophase, is complete. The nucleolus disappears by the end of the prophase. During the metaphase, the chromosomes align themselves along the equator of the cell. The nuclear envelope has disappeared and the centromeres can attach to the spindle microtubules. During the early anaphase the centromeres become uncoupled, allowing single chromosomes to move to opposite ends of the cell. Towards the end of the anaphase stage, the single sets of chromosomes are nearing the poles and cytokinesis is initiated. The nuclear membrane is regenerated during the telophase stage and the cell divides into two. The chromosomes become thinner and less distinct and arrange themselves into a nucleolus once again.

Some cells do not replicate at all and withdraw into a non-cycling state resembling G1, but where the cell is unable to proceed directly to the S phase. Certain cells can be triggered to return to the G1 phase from G0 by inducing synthesis of the necessary cell cycle enzymes. The cell can then progress to the S phase normally.

2. Mitosis

Prior to mitosis, the complete DNA complement of the nucleus has been replicated to generate two copies of the host chromosome. The two copies are held together at the centromere sequence and its associated proteins.

2.1 Prophase

The interphase cell carries a single centromere from which the microtubules radiate throughout the cell. As the cell nears mitosis, the centromere duplicates itself. Each centromere then migrates to opposite end of the cell about to undergo mitosis. This signals the beginning of the prophase. Energy in the form of ATP is used to allow the centrosomes to move along the microfilaments to the opposite poles of the cell. Two independent sets of microtubules are generated, one from each centrosome, creating the mitotic spindle. The two sets of microtubules are undergoing constant polymerization and depolymerization to generate dynamic structures that interact with each other at the equator of the cell. A more permanent mitotic spindle is formed when two opposing microfilaments bind along the equatorial plane. Their interaction allows for the separation of the chromosomes. Each chromosome develops a kinetochore on each side of the centromere which joins the sister chromatids together.

2.2 Metaphase

The metaphase can be divided into the prometaphase stage, followed by the metaphase proper. The prometaphase is initiated when the nuclear envelope rapidly breaks down into small vesicles. The nuclear lamina is also disassembled. The microtubules now can attach the released chromosomes at the kinetochore. The human kinetochore can bind an average of 30 microtubules, whereas a yeast chromosome binds just a single microtubule. The chromosomes are arranged on the equator by the mitotic spindle, thereby initiating the metaphase proper.

2.3 Anaphase

The chromatids are separated and pulled to the opposite poles of the cell by the mitotic spindle. The centromeres are cleaved by proteolosis and the centromere region of DNA is replicated to completion. The sister chromatids are then segregated with a full complement of chromosomes moving to each pole. The separation of the chromosomes is facilitated by microfilament depolymerization and shortening of tubulin subunits at the kinetochore, known as anaphase A. In addition to this segregation process a second means of moving apart is operating known as the anaphase B process. This second system allows the centrosome poles actually move away from each other and is thought to occur via lengthening of the polar microfilaments that stretch round the central region containing the chromosomes.

2.4 Telophase

Vesicles of nuclear membrane material start to associate with the chromosomes at each pole of the cell. The vesicles fuse together to generate two nuclear membranes, one round each set of daughter chromosomes at opposite end of the parental cell. The process of assembly includes the formation of the new nuclear membrane, nuclear lamina and nuclear pores. The nucleus enlarges in size and allows the chromatids to relax and transcription to occur.

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Biographical Sketch

Michelle Gehringer is a visiting scientist at the School of Biotechnology and Biomolecular Sciences of the University of New South Wales in Sydney, Australia. She is continuing her work on the toxic effects of the cyanobacterial toxins, microcystin and cylindrospermopsin, on humans and animals that accidently ingest them from contaminated drinking water sources. This research has provided insight into the way the body deals with the toxin as well as potential means of offering dietary protection to potential victims.

Dr Gehringer has several years of lecturing experience form the University of Port Elizabeth, South Africa, where she was actively involved in introducing the topics of Biochemistry and Microbiology to the general public and school goers. Her MSc was obtained at the University of Cape Town, South Africa where she worked on means to control Cucumber Mosaic Virus infections of crop plants.