INVESTIGATION 7

CELL DIVISION: MITOSIS AND MEIOSIS

How do eukaryotic cells divide to produce genetically identical cells or to produce gametes with half the normal DNA?

BACKGROUND

One of the characteristics of living things is the ability to replicate and pass on genetic information to the next generation. Cell division in individual bacteria and archaea usually occurs by binary fission. Mitochondria and chloroplasts also replicate by binary fission, which is evidence of the evolutionary relationship between these organelles and prokaryotes.

Cell division in eukaryotes is more complex. It requires the cell to manage a complicated process of duplicating the nucleus, other organelles, and multiple chromosomes. This process, called the cell cycle, is divided into three parts: interphase, mitosis, and cytokinesis (Figure 1). Interphase is separated into three functionally distinct stages. In the first growth phase (G_1), the cell grows and prepares to duplicate its DNA. In synthesis (S), the chromosomes are replicated; this stage is between G_1 and the second growth phase (G_2). In G_2, the cell prepares to divide. In mitosis, the duplicated chromosomes are separated into two nuclei. In most cases, mitosis is followed by cytokinesis, when the cytoplasm divides and organelles separate into daughter cells. This type of cell division is asexual and important for growth, renewal, and repair of multicellular organisms.

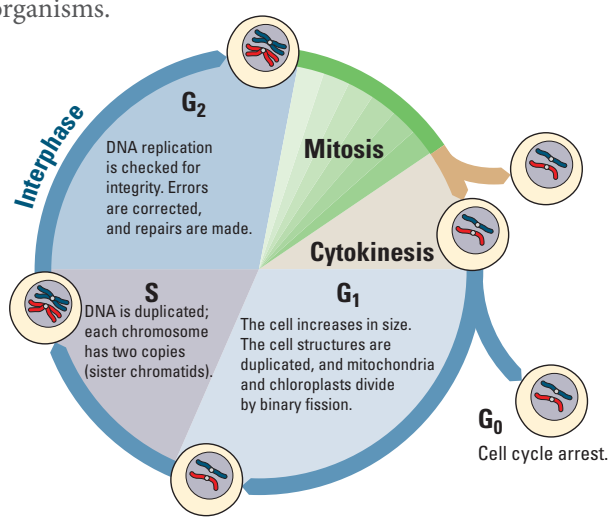

Figure 1. The Cell Cycle Showing G_1, S, and G_2 Phases, Mitosis, and Cytokinesis

Cell division is tightly controlled by complexes made of several specific proteins. These complexes contain enzymes called cyclin-dependent kinases (CDKs), which turn on or off the various processes that take place in cell division. CDK partners with a family of proteins called cyclins. One such complex is mitosis-promoting factor (MPF), sometimes called maturation-promoting factor, which contains cyclin A or B and cyclin-dependent kinase (CDK). (See Figure 2a.) CDK is activated when it is bound to cyclin, interacting with various other proteins that, in this case, allow the cell to proceed from G_2 into mitosis. The levels of cyclin change during the cell cycle (Figure 2b). In most cases, cytokinesis follows mitosis.

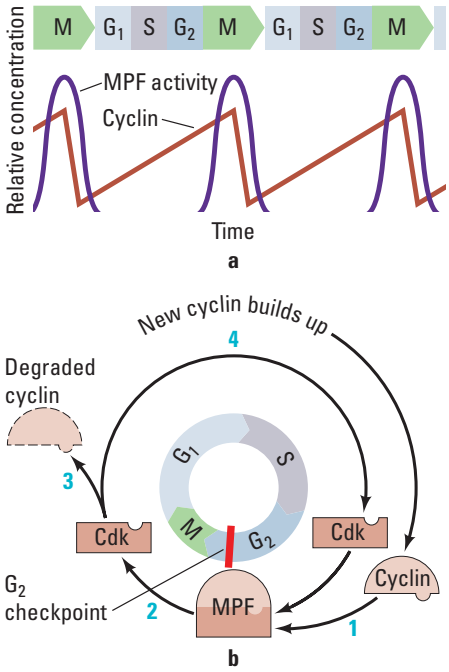

Figure 2. MPF Production During the Cell Cycle

As shown in Figure 3, different CDKs are produced during the phases. The cyclins determine which processes in cell division are turned on or off and in what order by CDK. As each cyclin is turned on or off, CDK causes the cell to move through the stages in the cell cycle.

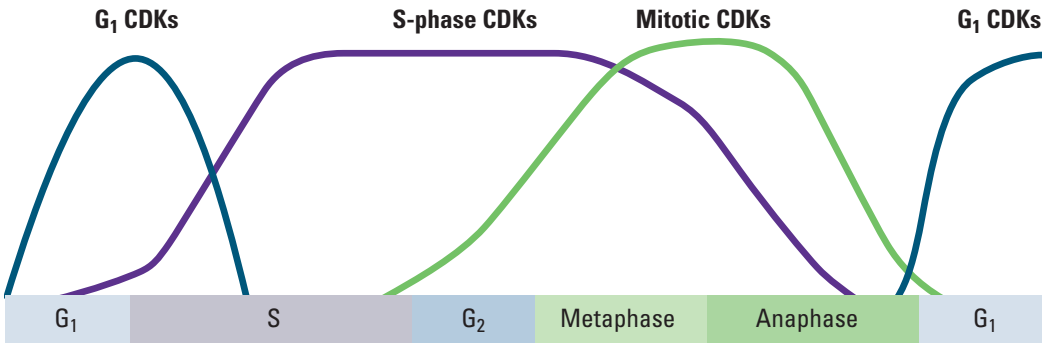

Figure 3. Levels of CDKs During the Cell Cycle

Cyclins and CDKs do not allow the cell to progress through its cycle automatically. There are three checkpoints a cell must pass through: the G_1 checkpoint, G_2 checkpoint, and the M-spindle checkpoint (Figure 4). At each of the checkpoints, the cell checks that it has completed all of the tasks needed and is ready to proceed to the next step in its cycle. Cells pass the G_1 checkpoint when they are stimulated by appropriate external growth factors; for example, platelet-derived growth factor (PDGF) stimulates cells near a wound to divide so that they can repair the injury. The G_2 checkpoint checks for damage after DNA is replicated, and if there is damage, it prevents the cell from going into mitosis. The M-spindle (metaphase) checkpoint assures that the mitotic spindles or microtubules are properly attached to the kinetochores (anchor sites on the chromosomes). If the spindles are not anchored properly, the cell does not continue on through mitosis. The cell cycle is regulated very precisely. Mutations in cell cycle genes that interfere with proper cell cycle control are found very often in cancer cells.

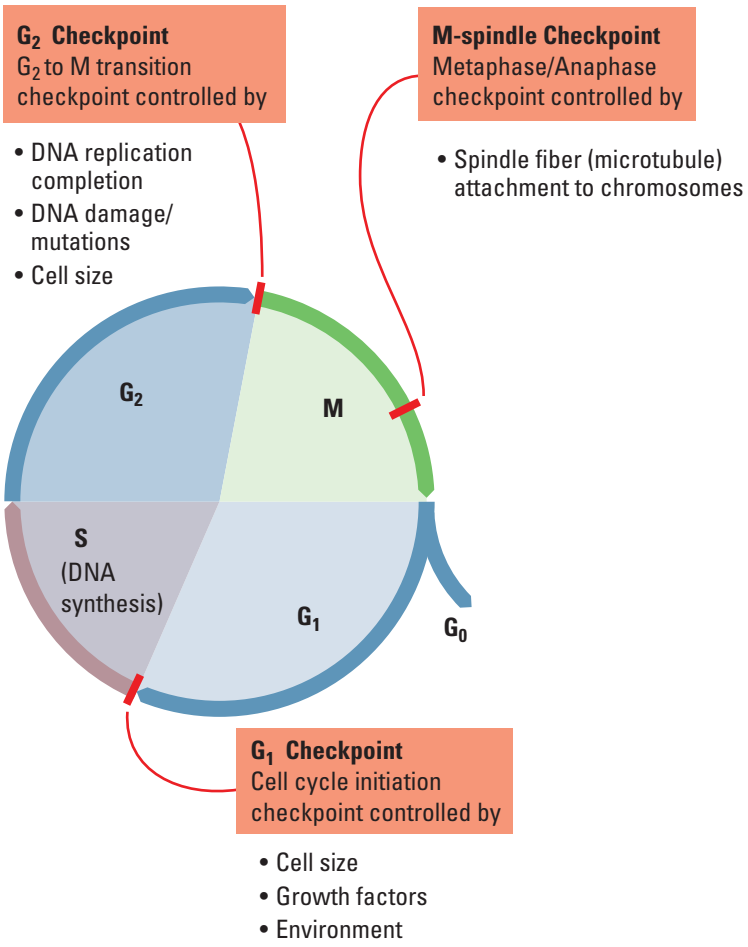

Figure 4. Diagram of the Cell Cycle Indicating the Checkpoints

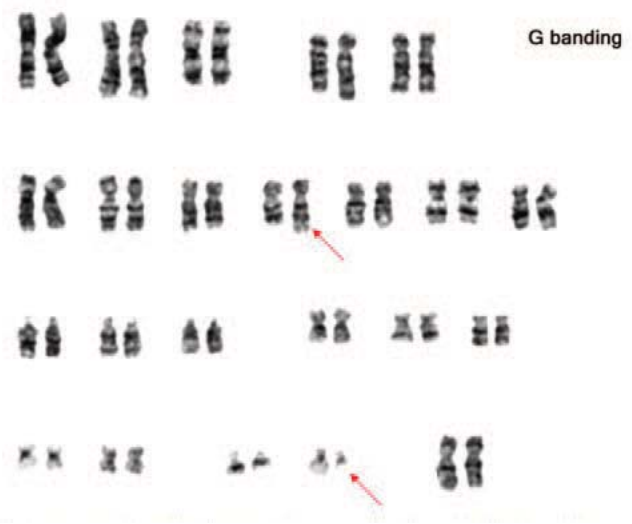

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Figure 5. Karyotype of a Patient with Chronic Myelogenous Leukemia Indicating Chromosomal Deformity

Part 4: Modeling Meiosis

Meiosis resembles mitosis but serves a very different purpose. Meiosis is a cell division resulting in the halving, or reduction, of chromosome number in each cell. A diploid organism has two sets of chromosomes (2n), while a haploid cell or organism has one set (1n). Meiosis produces gametes (ova and sperm) in animals and spores in fungi, plants, and protists. Three other important characteristics of meiosis are the exchange of genetic material ("crossing over") between homologous chromosomes, the independent assortment of the chromosomes, and the separation of alleles of the same gene (Figure 6). These characteristics, along with random fertilization, increase the genetic variability in the offspring. These mechanisms are essential to our understanding of genetics and evolution in sexually reproducing organisms.

The hallmark of sexual reproduction is the great diversity seen in the gametes and in the resulting offspring produced by fertilization. Meiosis is integral to this process because this type of cell division produces the sex cells, gametes. Before you begin the modeling exercise, your teacher will ask you to discuss these questions.

- How do sexually reproducing organisms produce gametes from diploid progenitors?
- How does the process increase gamete diversity?
- What are the outcomes from independent assortment and crossing over?
- How does the distance between two genes or a gene and a centromere affect crossover frequencies?

Use the model chromosomes from Part 1 to explain meiosis and crossing-over events. During your investigation, answer the following questions:

- When is the DNA replicated during meiosis?
- Are homologous pairs of chromosomes exact copies of each other?
- What is crossing over?
- What physical constraints control crossover frequencies?
- What is meant by independent assortment?
- How can you calculate the possible number of different kinds of gametes?
- What happens if a homologous pair of chromosomes fails to separate, and how might this contribute to genetic disorders such as Down syndrome and cri du chat syndrome?
- How are mitosis and meiosis fundamentally different?

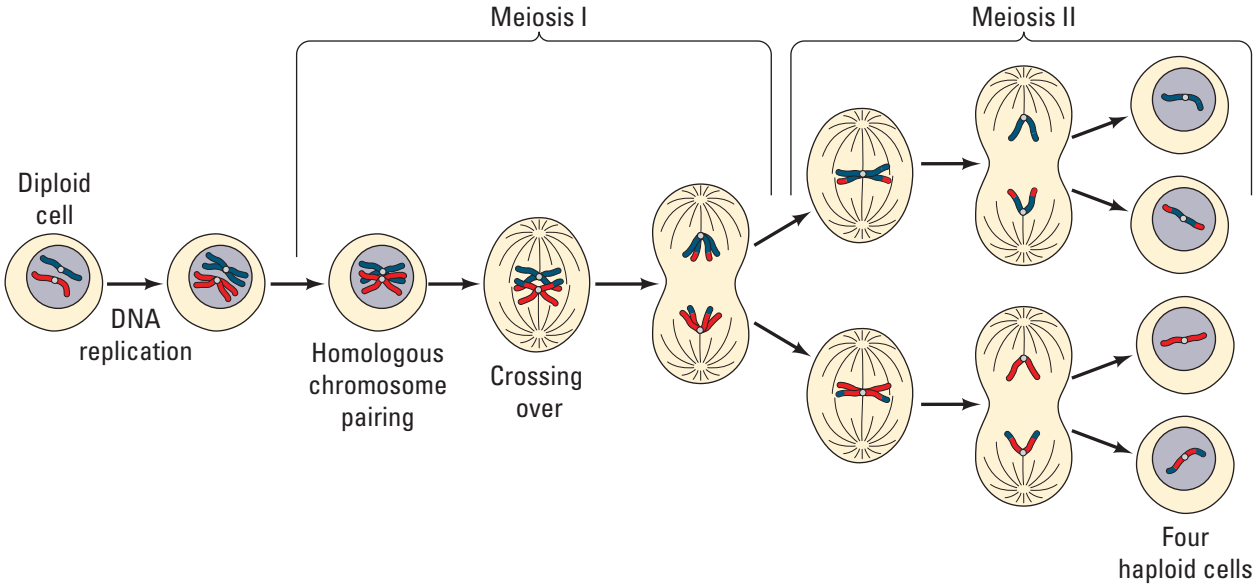

Figure 6. Meiotic Cell Division Emphasizing Chromosome Movement

Part 5: Meiosis and Crossing Over in *Sordaria*

The fungus *Sordaria fimicola* exchanges genetic material when two mycelia meet and fuse. The resulting zygote undergoes meiosis to produce asci; each ascus contains eight haploid spores. A single gene determines the spore color.

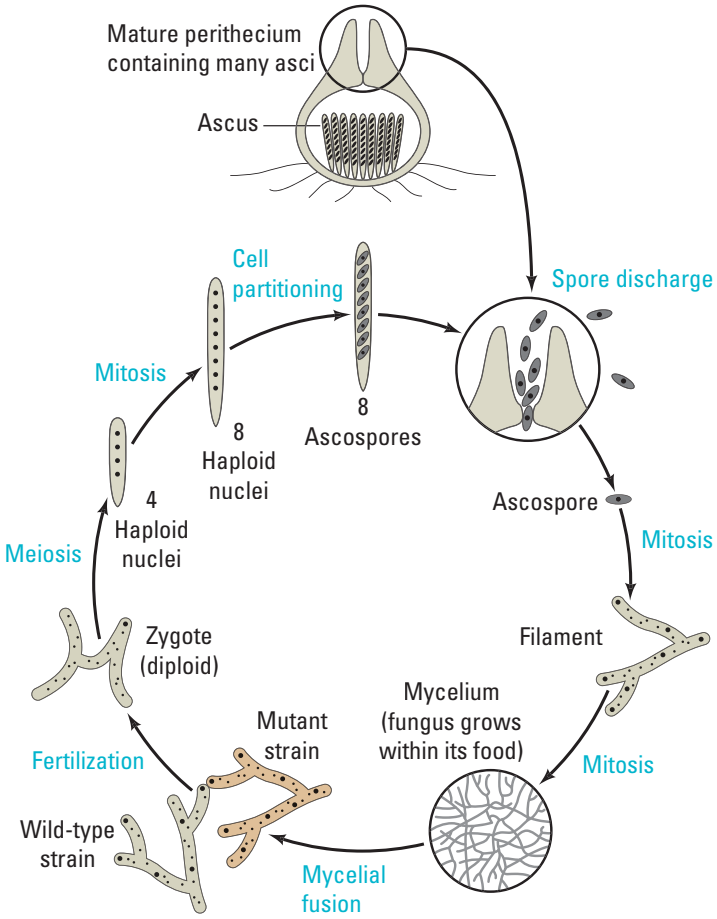

Figure 7. *Sordaria* Life Cycle

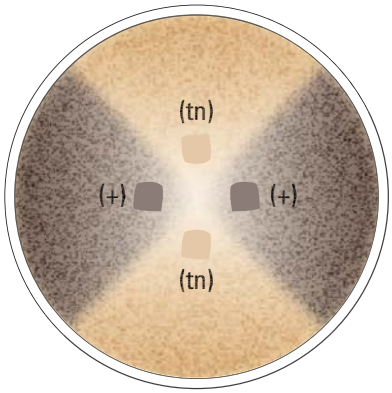

Figure 8: *Sordaria* Cross Plate

A cross was made between wild type (+; black) and tan (tn) strains. The resulting zygote produces either parental type asci, which have four black and four tan spores in a row (4:4 pattern), or recombinant asci, which do not have this pattern.

- How do you explain the differences between the recombinant asci and the parental types?
- What meiotic event can account for this difference?
- Using the model chromosomes from Part 4, predict the possible meiotic outcomes.

1. Place a drop of water onto the microscope slide.
2. Gently scrape some perithecia from the agar plate near where the two strains meet.
3. Place a cover slip over the perithecia and put a scientific cleaning wipe over the cover slip.
4. Gently press down on the cover slip using the eraser end of a pencil.
5. Count at least 50 asci, and score them as either parental or recombinant (crossing over).
6. Enter the data in Table 3 and make the calculations. One map unit equals one recombinant per 100 total events. The percentage of asci showing crossover divided by 2 equals the map units in this activity. This is done because each spore produced by meiosis undergoes a mitotic division.

Table 3. Analysis of Results

Number of Asci Showing 4:4 Pattern	Number of Asci Showing Crossover	Total # of Asci	% Asci Showing Crossover Divided by 2	Gene to Centromere Distance (Map Units)