Cell Cycle

Chapter 8
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Cell Division

- Unicellular organisms divide to produce new organism
- Multicellular organisms reproduce to increase cell surface area, produce specialized tissue cells, and replace worn-out/ dead cells.
- Eukaryotes follow similar Cell Cycle

Cell Cycle

- Cell Cycle
  - Interphase
    - G1 (Gap 1)- prereplication, cell growth, makes RNA, proteins, performs specific tissue's function.
    - S (DNA synthesis)- DNA of each chromosomes is replicated, doubling each gene in the nucleus.
    - G2 (Gap 2)- cell prepares for mitosis by making specific type of RNA and proteins.
  - Mitosis- nuclear division to provide each daughter cell with full set of chromosomes.
    - Prophase
    - Metaphase
    - Anaphase
    - Telophase
  - Cytokinesis- splits cells apart.

Cell Cycle

- G0- stopping point in G1, performing normal cell functions, not actively dividing, most mature cells.
- Restriction point- cell in G0 or G1 receives signals to passes this point and begins cell division. "point of no return"

DNA Replication

- Before cell division the DNA of a cell must be copied.
- Replication begins at several regions on chromosomes called replication origins.
- All the enzymes and proteins at the replication origin is called the replisome.
- Here, the enzyme helicase unwinds and separates the strands of DNA by breaking the hydrogen bonds between base pairs.
- Single-strand binding (SSB) proteins hold the DNA strands apart.
- DNA Polymerase III can only add DNA nucleotides to an existing strand in the 5'-3' direction.

DNA Replication

- Primase adds a 5-15 nucleotide long RNA primer.
- DNA polymerase III adds complimentary nucleotides to the RNA primer in the 5'-3' direction.
- The leading strand (the 3'-5' parent strand) will be made continuously towards the replication fork.
- The lagging strand (the 5'-3' parental strand) will be made discontinuously away from the replication fork in short Okazaki fragments.
- DNA polymerase I will replace the RNA primers with DNA.
- DNA ligase will connect the Okazaki fragments.

DNA Replication

- After DNA Replication the genetic material is copied, but the number of chromosomes remains the same.
- DNA Replication is "semi-conservative". After DNA replication each molecule of DNA will contain a new strand and an original (parental) strand of DNA.

Mistakes during DNA Replication

- DNA polymerase is accurate in adding complimentary nucleotides. (1 mistake for every 10,000 bases)
- DNA polymerase can check for mistakes and can pause and replace any mismatched nucleotides. Increases efficiency to only 1 mistake in 10,000,000 bases.

Mistakes during Interphase

- Mutations- mistakes in the genetic code, can be caused by mutagenic chemicals or radiation.
- Mutations during interphase can be fixed by Excision Repair.
- A repair enzyme identifies the mismatched bases, binds to the DNA, and can break the sugar-phosphate backbone of the damaged or mutated section of DNA.
- DNA polymerase will add the correct complimentary nucleotides.
- DNA ligase will replace the sugar-phosphate bonds of the segment.

Mitosis

- After DNA replication each gene has an extra copy resulting in a duplicated chromosome- two sister chromatids held together by the centromere.

Prophase

- Chromatin condense into chromosomes.
- Nuclear membrane disappears.
- Mitotic spindle, made of microtubules, forms around nucleus.
- Centrioles move to the poles, are surrounded and anchored by spindle pores.
- Microtubules attach to the centrioles.
- Microtubules attach to proteins around the centromeres of the chromosomes called kinetochore.

Metaphase

- Chromosomes line up at cell's equator.
- Sister chromatids are pushed to the equator by attached spindle fibers.
- The metaphase plate (lineup of chromosomes) is perpendicular to spindle.
- Metaphase plate ensures that each daughter cell will get one copy of each chromosome.

Anaphase

- Sister chromatids separate.
- Motor proteins of kinetochores pull the chromatids along the spindle microtubules to opposite spindle poles.

Telophase

- Chromosomes begin to uncoil into chromatin.
- Nuclear envelope forms two identical nuclei.
- Mitotic spindle breaks down.
- Cytokinesis separates cytoplasm, forms a cleavage furrow to divide cell membrane.
- Results in two identical daughter cells.

Control of Cell Cycle

- Cell fusion experiments- when S phase cells were fused to G1 DNA in the G1 cell began to replicate.
- When G2 cells were fused to S-phase cells the DNA in the G2 cell did not replicate.
- Something in S-phase can cause G1 cells to replicate.
- When cells leave G0, cyclins- proteins that regulate progression through the cell cycle, form and disappear during the cell cycle.

Control of Cell Cycle

- Cyclins bind to various Cdk's (cyclin dependent kinases)-enzymes that transfer phosphate groups from ATP to other enzymes to activate them.
- Amount of kinases remain the same, but amount of cyclins fluctuate during cell cycle.
- G1 cyclins- accumulate in late G1 and peak in S.
  - activates replication, cauuse cells to leave G0

Control of Cell Cycle

- Mitotic (M) cyclins- accumulate in S and G2 and peak during Metaphase of Mitosis.
- Mitotic Cyclins bind with kinases to activate pathways that
  - lead to breakdown of nuclear envelope, condensation of chromosomes.
  - leads to formation of mitotic spindle to regulate steps of Mitosis
  - breakdown proteins that hold sister chromatids together
  - breakdown mitotic cyclins (to ensure the cell will leave Mitosis)

Cell Cycle Checkpoints

- Checkpoints- protein that detect mistakes and damage can cause Cell Cycle Arrest- stopping the cell cycle so repairs can be made.
- G1 checkpoint- checks for damaged DNA.
- S checkpoint- checks for unreplicated DNA.
- G2 checkpoint- checks for damaged DNA.
- M checkpoint- checks for defective spindle.

G1 checkpoints

- Retinoblastoma (Rb) binds to E2F to prevent this factor from initiating mitosis.
- G1 Checkpoint is passed when G1 cyclin-cdk interact with Rb to release E2F. E2F will initiate Mitosis.
- P16 will bind to cyclin/kinases complexes to prevent the release of Rb.
- If protein p53 finds mismatched DNA, it will activate cell cycle inhibitors (p21) that prevent G1 cyclins from activating kinases, preventing cell from entering S-phase.
- When DNA is repaired p53 becomes inactive- S-phase begins.

Genes that regulate Cell Cycle

- There are two types of genes that regulate cells leaving G0
- Proto-oncogenes- promote cell division.
  - codes for signal recievers, transcription regulators, etc.
- Tumor Supressor genes- inhibit cell division.
  - codes for proteins to stop cell division by preventing cyclins and Cdk's from binding.

Cancer

- When both proto-oncogenes and tumor suppressor genes are mutated, cells repeatedly divide causing cancer.
- Constant division leads to tumors which can interfere with normal functions of tissue.
- Cancer cells reproduce as quickly as possible with no regulation of cell cycle.
- Metastasis- when cancer cells move through the blood stream into other tissues.