The Cell

Cell Theory

Robert Hooke invented the first microscope and noticed the microstructures of a cork.
Leeuwenhoek viewed a living cell

1. All things are composed of cells
2. The cell is the basic functional unit of life
3. Cells arise only from preexisting cells

These were a part of the original form of cell theory

4. Cells carry genetic information in the form of deoxyribonucleic acid (DNA). This info is passed on from parent to daughter cell.

- Viruses are not considered living organisms since they violate tenet 3 & 4.

Eukaryotic Cells

The most general distinction made between living organisms is if the organism is composed of eukaryotic or prokaryotic cells

- **Eukaryotic Cells** contain a true nucleus enclosed in a membrane, while **Prokaryotic Cells** do not contain a nucleus.

Membrane Bound Organelles

Every cell has a cell membrane enclosing a semifluid cytosol in which the **organelles** are suspended. For eukaryotic cells, the organelles are protected by a membrane, which typically consist of a phospholipid bilayer.

- Phospholipid Bilayers have a hydrophilic (like water) surface, and a hydrophobic (repel water) inner wall.
- The Cytosol allows for the diffusion of molecules throughout the cell
- The Nucleus encodes genetic material into DNA which is organized into chromosomes.
- Eukaryotic cells are reproduced by mitosis.

The Nucleus

The control center of the cell, and contains all the genetic information needed for replication.

- The nucleus is surrounded by the Nuclear Membrane (Envelope): A double membrane that maintains a nuclear environment separate and distinct form the cytoplasm.
    - Nuclear Pores allow for the selective two-way exchange of material
- DNA contains Genes which are genetic coding regions. The initially linear DNA is wound around organizing proteins known as Histones.
- The histones are further wound into chromosomes
    - This setup permits the compartmentalization of DNA transcription and RNA translation.
- The Nucleolus is where the ribosomal RNA (rRNA) is created. Takes up 25% of the nucleus volume and is identified by a dark spot.

Mitochondria

Are considered the power plant of the cell and contain a dual layer membrane

- Outer Layer of membrane is a barrier between the cytosol and the inner environment

- Inner Layer of membrane has numerous folds known as cristae. This membrane contains the molecules and enzymes necessary for the electron transport chain.
    - Intermembrane Space: the space between inner and outer membrane
- Matrix: The space inside the inner membrane.
- Mitochondria are semi-autonomous. Contain their own genes and replicate independently of the nucleus through binary fission.
    - Main example of Cytoplasmic or Extranuclear inheritance: means that transmission of genetic material is independent of the nucleus.
- Is also capable of killing the cell by releasing enzymes which starts apoptosis.

Lysosomes

Are membrane-bound that contain enzymes which break down many substrates

- Function in conjunction with endosomes. Endosomes transport material to the trans-Golgi, to the membrane or to the lysosomal pathway for degradation.
- The membrane is used to ensure that encased enzymes do not cause damage to the cell
    - Autolysis: is when the enzymes are released into the cell which results in apoptosis. The enzymes directly kill the cell (different from mitochondria)

Endoplasmic Reticulum

Series of interconnected membranes that continue from the nuclear envelope.

- Double membrane is folded to create complex structures, but there is a central lumen.
- Rough ER is studded with ribosomes that permit the translation of proteins.
- Smooth ER is for lipid synthesis and for the detoxification of certain drugs/poisons.
    - The SER transports proteins from the RER to the Golgi Apparatus

Golgi apparatus

Consists of stacked membrane-bound sacs. The material is transferred from the ER in vesicles

- The cellular products are sometimes modified once in the G.A.
    - Various groups such as carbohydrates, phosphates and sulfates can be added.
    - May also use signal sequences that direct the delivery of the product to a specific cellular location.
- Once the cellular products are modified and sorted in the G.A, they are repackaged in vesicles and transferred to the appropriate cell location
    - If the product is for **secretion** then the vesicle merges with the membrane, and the contents are released via **exocytosis**

Peroxisomes

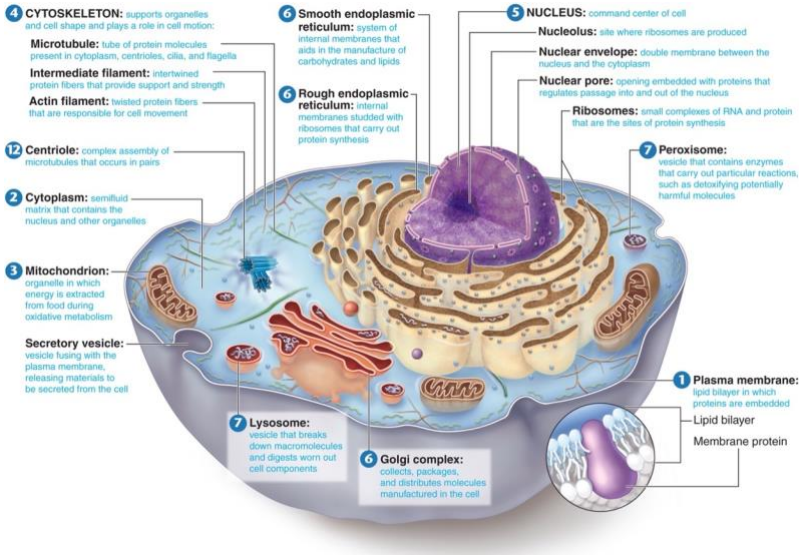
These contain hydrogen peroxide and are meant to breakdown very long chain fatty acids via oxidation. They also participate in the synthesis of phospholipids.

Cytoskeleton

Provides structure to the cell and helps it maintain its shape. Also a conduit for transport of material around the cell.

- Microfilaments: Made up of solid rods of **actin**. These filaments can resist both compression and fracture. **Provide protection for the cell.**
    - If Actin interacts with Myosin and uses ATP, force will be generated to move cell.

    - Play a role in Cytokinesis. The **cleavage furrow** is formed from microfilaments organized as a ring at the site of division. As actin filaments contract, the ring gets smaller and the connection is eventually pinched off.
- Microtubules: hollow polymers of **tubulin** proteins.
    - Are found throughout the cell and form the pathways for motor proteins (kinesin and dynein) to carry vesicles
    - Cilia & flagella are composed of microtubules
        - Cilia are projections from the cell primarily used for in movement of materials along the cell
        - Flagella are involved in the movement of the cell itself (like sperm).
            - Both structures have a characteristic **9+2 Structure**. (9 pairs on outside and two microtubules on center).
    - Centrioles**:** found in the **centrosome** and are the organizing center of microtubules. Have a structure of nine triplets with a hollow center.
        - Are involved in mitosis. Organize mitotic spindle, use **kinetochores** to attach to chromosomes and exert force to pull them apart.
- Intermediate Filaments: filamentous proteins including keratin, desmin, vimentin and lamins.
    - Involved in cell-cell adhesion or maintain overall integrity of cytoskeleton.
    - Are able to withstand tension and make the cell structure more rigid
    - Anchor other organelles.



Tissue formation

- Epithelial tissue: covers the body and line the cavities. Provide protection from pathogen invasion and desiccation. Can also be involved in absp, secr, and sensation.
    - Basement Membrane: cells tightly joined to each other on this layer of connective tissue. Maintain cohesiveness.
    - In most organs, tissue constitutes **the parenchyma** (the functional parts of the organ).

    - Are often Polarized: one side faces a lumen (hollow inside or the outside world), while other side interacts with underlying blood vessels and cells.
    - Classifications based on:
        - Number of Layers: **Simple Epithelia** have one layer of cells, **Stratified epithelia** have multiple layers, and **Pseudostratified epithelia** have a difference in cell height of one layer causes the illusion of multiple layers.
        - Shape: **Cuboidal** are cube shaped, **Columnar** are long and thin; and **Squamous** cells are flat and scale like.
- Connective Tissue: supports the body and provides framework for epethilial cells to carry out functions.
    - Are main contributors to the **Stroma** (support structures).
    - Bone, cartilage, tendons, ligaments, adipose tissue, and blood
    - Most cells produce and secrete materials such as collagen and elastin to form the **extracellular matrix**

Classification and Structure of Prokaryotic Cell

Simplest of all organisms and include all bacteria. Do not contain any membrane bound organelles.

- DNA is a single circular molecule concentrated in the **nucleoid region**

Prokaryotic Domains

Three overarching domains of life: Archaea, Bacteria, and Eukarya. Archaea and Bacteria are prokaryotic and were initially classified together.

- Archaea: Single celled organisms that are visually similar to bacteria.
    - Contain genes and several metabolic pathways similar to eukaryotic cell
    - Extremophiles: originally classified as cells which were only found in harsh environments of high temperature, high salt and no light.
        - Have now been found in human body
    - Have the ability to use alternative sources of energy. Use photosynthesis or chemosynthesis (able to generate energy from non-organic compounds)
    - Similarities to Eukaryotes: start translation with methionine, contain similar RNA polymerase, and associate DNA with histones
        - Differences: contain single circular chromosome. Use binary fission for division and share an overall structure similar to bacteria.
- Bacteria: contain cell membrane and cytoplasm and some have flagella or fimbriae (like cilia). As such they have similar structures to eukaryotes, which makes it difficult to develop medicine that specifically treats bacteria.
    - However, some structures are different enough to allow for targeting. E.g – bacterial flagella are different or bacterial ribosome (smaller).
    - Bacteria outnumber human cells in the body by 10:1. Some are **Mutualistic symbiotes:** both human and bacteria benefit (Vit K in human gut). Other bacteria are **pathogens** or **parasites** in that they provide no benefit to the host human body.

Classification of Bacteria by Shape

- Cocci: Spherical shaped bacteria. E.G – common pathogens
- Bacilli: Rod-Shaped. E.G – E.Coli
- Spirilli: Spiral shaped bacteria. E.g – syphilis bacteria. Very few are shaped this way

Aerobes and Anaerobes

Bacteria that require oxygen for survival are termed **obligate aerobes.** Bacteria that use fermentation or other forms of cellular metabolism without oxygen are termed **anaerobes.**

- Obligate Anaerobes: cannot survive in an environment containing oxygen. Causes production of radicals which result in cell death
- Facultative Anaerobes: can toggle between oxygen-dependent metabolic processes and anaerobic metabolism.
- Aerotolerant anaerobes: Are not able to use Oxygen but are not harmed by its presence.

Prokaryotic Cell Structure

Do not have a nucleus or membrane bound organelles and are single-celled organisms. Means that each cell must be able to perform all necessary life functions on its own.

- Cell Wall: forms outer barrier of the cell. **Cell membrane** is composed of phospholipids is the next layer. These two structures are known as the **envelope.** Responsible for the protection.
    - Provides structure and controls the movement of solutes into and out of the bacterium.
    - Gram-Positive Cell Wall: If envelope appears dark purple after crystal violet stain
        - Thick layer of **peptidoglycan** (made up of sugars and amino acids). Provides structural barrier functions. May also aid a pathogen by providing protection from a host organisms immune system.
        - Contain **lipteichoic acid:** function unknown but may be used in immune.
    - Gram-Negative Cell Wall: much thinner than positive and contain small amount of peptidoglycan.
        - Peptidoglycan cells beside cell membrane and separated by **Periplasmic Space.**
        - **Outer Membrane**: contains phospholipids and **lipopolysaccharides**. These saccharides are what triggers an immune response in humans
- Flagella: Long, whiplike structures that are used for propulsion.
    - Chemotaxis: ability of cell to detect chemical stimuli and move towards or away.
    - Filament: hollow, helical structure composed of **flagellin**
    - Basal Body: anchors flagellum to the cytoplasmic membrane and is also the motor of the flagellum.
    - Hook: connects filament and basal body so that when the basal body rotates, it exerts a tourque on the filament.
    - Slight differences in flagella between different cell wall types. Also present in Archae but not commonly tested due to complexity.
- Other Organelles: concentrate DNA in nucleoid region (do not contain nuclear envelope. DNA is carried on single circular protein which is coiled around histone-like proteins. However, only archaea contain true histones.

    - Plasmids carry DNA that is not necessary for survival of the prokaryote.
        - DNA from external sources, not apart of genome of bacterium.
    - Lack mitochondria, complex cytoskeleton (have a primitive one).
        - Contain ribosomes but are different size as compared to eukaryotes (30S/50S and 40S/60S respectively)

Genetics and Growth of Prokaryotic Cells

Binary Fission

Simple form of asexual reproduction. Circular chromosome attaches to cell wall and replicates while the cell continues to grow in size. Plasma membrane and cell wall begin to grow inwards along middle (invagination). Two identical daughter cells are produced. This proceeds more rapidly than mitosis.

Genetic Recombination

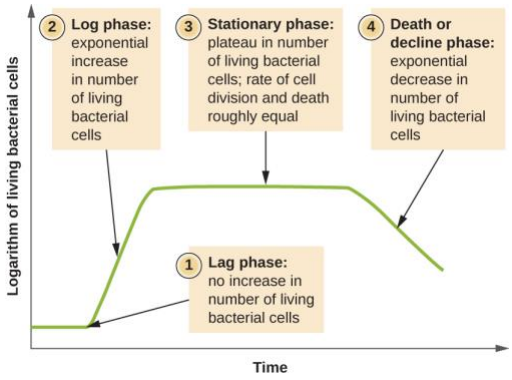
Involves the replication and integration of the extrachromosomal material on the plasmids. These genes often impart benefits to the bacterium. Plasmids can also carry **virulence factors** that increase how pathogenic a bacterium is. Subset of plasmids are called **episomes** and are capable of integrating into the genome of the bacterium. This helps increase diversity and permits the evolution of the species over time.

- Transformation: integration of foreign genetic material into the host genome. Material most often comes from other bacteria that spill their contents after lysing.
- Conjugation: bacterial form of mating.
    - Conjugation Bridge: facilitates transfer of genetic material between two cells. Transfer is unidirectional from **donor male (+)** to **recipient female (-)**.
        - Sex Pili: Bridge is made out of these appendages that come from male.
            - Sex Factors: Plasmids which are needed to for Pili. Bet studied sex factor is **F (Fertility) Factor** in *E. coli.*
    - This process allows for rapid acquisition of antibiotic resistance or virulence factors.
    - If the donor cell attempts to transfer entire copy of genome to recipient. The recipient cells are referred to as **Hfr** (high frequency of recombination).
- Transduction: requires a **Vector** which is a virus that carries genetic material
    - Viruses are obligate intracellular pathogens which means that they cannot reproduce outside of a host cell.
    - **Bacteriophages** (viruses that infect bacteria) can accidently trap a segment of host DNA. When this bacteriophage infects another bacterium, it releases the trapped DNA into the new host cell, which could sub-sequentially allow for the integration of the transferred DNA into the genome.
- Transposons: genetic elements capable of inserting or removing themselves from the genome. Not limited to prokaryotes.

Growth

As bacteria first adapt to new conditions, they go through a **lag phase**. As adaptation occurs, more rapid binary fission takes place and the **exponential/log phase** occurs. The resources are often reduced during this period and rate of reproduction is slowed in the **stationary phase**.

After the bacteria have exceeded the ability of the environment to support the number of bacteria, a **death phase** occurs.



Viruses and Subviral Particles

Viral Structure

Composed of genetic material, a protein coat and sometimes an envelope containing lipids. Genetic info may be circular or linear, single- or double-stranded, and composed of either DNA or RNA.

- Protein coat is known as a **capsid.** Envelope surrounds the capsid and is composed of phospholipids and virus-specific proteins.
    - Envelope is sensitive to heat, detergents and dessication. Thus are easier to kill.
- Obligate intracellular parasites: must express and replicate genetic info within a host cell since they lack ribosomes to carry out protein synthesis.
- Virions: cell replicates and produces this viral progeny (replication). Virion can be released to infect other cells
- Bacteriophages: Don't enter bacteria, instead inject their genetic material inside the cell.
    - Contain a tail sheath and tail fibers in addition to capsid
        - Tail Sheath: acts like a syringe, injects genetic material
        - Tail fibers: help recognize and connect to the host cell

Viral Genomes

- Single stranded RNA viruses may be positive sense or negative sense
    - **Positive Sense** implies that the genome may be directly translated to functional proteins by the ribosomes of the host cell like mRNA.
    - **Negative Sense** require synthesis of an RNA strand complementary, which can then be used as a template for protein synthesis.
        - These must carry an **RNA replicase** in the virion to ensure that the complementary strand Is synthesized.
- Retroviruses: Enveloped, single-stranded RNA viruses. Virion contains two identical RNA molecules.
    - Carry an enzyme known as **reverse transcriptase** that synthesizes DNA from a single stranded RNA. DNA enters host cell genome, where it is replicated and transcribed as if it the host cells own DNA.
        - Allows cell to be infected indefinitely (think HIV) until cell is killed.

Viral Life cycle

- Infection: viruses can only infect specific cells. The cell must have specific receptors for the virus to bind to. Otherwise the cell is basically invisible to the virus.
    - Once the virus binds to the correct receptor, the virus and cell are brought into close proximity.
    - Enveloped viruses fuse with the plasma membrane of the cell
    - Sometimes a cell may misinterpret a virus and will bring it using endocytosis.
    - Bacteriophages inject their viral genome into the cell after anchoring
- Translation and Progeny Assembly: translation must occur after infection in order for the virus to reproduce. This means that the material needs to be translocated to the correct location in the cell. A single cirus can create up to many thousands of new virions within single host cell.
    - Most DNA viruses must be taken to the nucleus in order to be transcribed to mRNA. The mRNA then goes to the cytoplasm where it is translated to proteins
        - For positive-sense RNA viruses, the genetic material stays in the cytoplasm where it can be directly translated to protein by ribosomes
        - Negative-sense RNA viruses require synthesis of a complementary RNA strand (using RNA replicase) which is then translated to form proteins.
        - Retroviruses use reverse transcription, which needs to travel to the nucleus where it is integrated into the host genome.
    - Using the ribosomes, tRNA, amino acids, and enzymes from the host cell, the viral RNA is translated into protein. Many proteins form capsid which allow for the creation of new virions in the host cell's cytoplasm.
    - Once the viral genome has been replicated, it can be packaged with capsid.
- Progeny Release:
    1. Viral invasion may initiate cell death. Viral progeny is spilled
    2. Host Cell may lyse (destruction of cell membrane by excessive volume of virions): causes progeny to be spilled out, Disadvantage since virus can no longer use host cell.
    3. Extrusion: virus leaves cell by fusing with plasma membrane. Known as the **productive cycle** since host cell does not die.
- Lytic and Lysogenic Cycles: the growth cycle determines if a bacteriophage will a lytic or lysogenic cycle.
    - Lytic cycle: maximal use of cell's machinery. Cell becomes swollen with new virions, cell lyses and other bacteria can be infected. Bacteria in this phase are termed **virulent.**
    - Lysogenic Cycle: if bacterium is not lysed, the virus may integrate into the host genome as a **provirus** or **prophage.** May be integrated indefinitely, however, environmental factors (radiation, light, chemicals) will eventually cause the provirus to enter the Lytic cycle.
        - May be some advantages for bacterium: allows for transduction of genes from one bacterium to another when provirus leaves the genome; if infected by one strain, it makes the bacterium less susceptible to

superinfection; proviruses are relatively harmless so it could be seen as beneficial.

Prions and Viroids

- Prions are infectious proteins are non-living things. Cause disease by triggering the misfolding of other proteins. This drastically reduces the solubility of the protein. Eventually more of these disfigured proteins are formed and the cell functionality is reduced.
- Viroids: small pathogens consisting of very short single-stranded RNA that infect pants. Can bind to large number of RNA sequences and will silence genes in that genome. Consequentially, this prevents synthesis of necessary proteins and can cause metabolic and structural derangements in the plant cell.
    - Can be found in humans (Hep D)