CYTOSIS - THE SCIENCE BEHIND THE GAME

I. A Summary of the Human Cell

The Science: Cells are the building blocks of all living creatures, from microscopic bacteria to complex multi-cellular organisms, like humans. In order to grow, develop, and function properly, the human body requires all of its different cell types to work together, a complex undertaking considering there are approximately 200 distinct types comprising trillions of cells! Cells provide structure for the body and its organs, and they perform important functions within the body, such as fighting off viruses, digesting food, and producing hormones and enzymes.

Despite their differences, all eukaryotic cells (fungi, plant, and animal cells) are enclosed within a protective barrier consisting of two layers of lipids. This lipid bi-layer is commonly referred to as a plasma membrane. Cells are filled with a watery fluid called cytoplasm and contain a number of specialized structures called organelles. Most organelles are separated from the cytoplasm by their own lipid membrane, but their shapes can vary from simple spherical shapes (as in the nucleus) to complicated, folded networks of membrane (as in the Golgi apparatus). Cells rely on these organelles to produce and use energy, carry and organize genetic information, and perform the functions that the cell must carry out to fulfil its role in the body.

The Game: When playing Cytosis, you perform some of the key cellular processes that keep each cell functioning properly within the body. Hence, you (you'll take actions in the game by placing flasks) will produce energy, remove harmful toxins that enter the cell, and assemble essential macromolecules, and build receptors and hormones that mediate communication between cells, and enzymes that facilitate important cellular reactions. As you perform these functions you will gain health points in a race against other players.

II. The Nucleus - Transcription and messenger RNA

The Science: The nucleus is an extremely important organelle and is one of the features that defines a eukaryotic cell (including OUR cells!). In fact, the name eukaryotic means "kernel" in Latin and the nucleus is the organelle behind the name. The nucleus is important because it contains and protects the cell's genetic material, which is like the instruction manual for the cell. This genetic material is called deoxyribonucleic acid (DNA), which is an extremely long molecule in the shape of a double helix (this shape resembles a twisted ladder). DNA molecules are made up of complementary strands of nucleotides, the building blocks of DNA. Each DNA molecule is organized into individual chromosomes, which contain thousands of smaller sections that we call genes. These genes contain instructions for assembling specific proteins. Proteins are large, complex molecules that provide many of a cell's essential structures and functions.

While DNA provides the cell's instructions, it is most often proteins that actually do the work of building the cell and maintaining its function. Complex interactions between DNA, proteins, and the cells' environment control the development, structure, and behavior of every cell, and thus how the entire organism appears and functions.

Inside the nucleus, the instructions encoded in specific genes within the DNA are copied into a new molecule called messenger Ribonucleic Acid (mRNA) in a process called DNA transcription. This mRNA is then transported across the membrane of the nucleus (the nuclear membrane) into the cell's cytoplasm where it will be translated into a protein by ribosomes.

The Game: In Cytosis, when you place a flask in the Nucleus space, you activate the process of DNA Transcription in which the cell makes an mRNA copy of a gene, represented by the black mRNA resources that you collect.

III. The Free Ribosomes - Translation of mRNA to Proteins and Enzyme Synthesis

The Science: Ribosomes are one of the most unique and possibly most ancient of the organelles; they are the only organelle to be found in all cells across all biological domains. Ribosomes act like an assembly line, making specific proteins using the instructions encoded in an mRNA molecule. This process is called translation. Ribosomes translate this code into a chain of amino acids (also known as a polypeptide chain), the building blocks of proteins. These amino acid chains then fold very precisely to form functional proteins.

Some of the cell's ribosomes are free-floating in the cytoplasm. Free ribosomes are responsible for making proteins that will be used within the cell itself. These proteins include enzymes that catalyze, or speed up, cellular reactions by finding appropriate proteins and wrestling them into shape.

The Game: In Cytosis, placing a flask on the Free Ribosome spot triggers mRNA translation, allowing you to exchange one or more mRNA (black resources) for one or more proteins (red resources).

IV. The Smooth ER - Lipids, Steroid Hormone Synthesis, and Alcohol Detoxification

The Science: The Endoplasmic Reticulum (ER) is an extensive network of tubular membranes connected to the plasma membrane of the nucleus. The ER functions as a factory: it manufactures, packages, and transports products throughout the cell. It also comes in two varieties: smooth and rough. The Smooth ER (SER) has a smooth appearance under a microscope due to the lack of ribosomes on its surface.

One of the main functions of the SER is manufacturing lipids (fats), which are important components of cell membranes. In some cells, the SER is responsible for manufacturing steroid hormones (e.g., cortisol, testosterone, estrogen, progesterone). In liver cells, the SER is responsible for detoxifying metabolic products, drugs, and alcohol into safe, water-soluble by-products. Everything produced by the SER is packaged and transported to the Golgi apparatus within transport vesicles, which are small parcels of cytoplasm surrounded by plasma membrane.

The Game: In Cytosis, when you place a flask on a SER Lipid Synthesis spot, you produce Lipids (yellow resources), adding these to your personal resource stock. If you place a flask on the SER Steroid Hormone Synthesis spot, one of two processes is activated: ATP can be spent to detoxify alcohol (Alcohol Detoxification Card), or you may begin building a steroid hormone by placing Lipids from your personal resource stock onto one of your Transport Vesicle Disks, readying it to be transported to the Golgi Apparatus.

V. The Rough ER - Synthesis of Protein Hormones and Receptors

The Science: The Rough ER (RER) is an extension of the smooth ER that appears 'rough' under a microscope because it is covered with ribosomes. These ribosomes produce amino acid chains that are then folded into precise protein structures and transported either within or out of the cell, depending on the protein's function. Some proteins (like insulin) function as a type of signaling molecule that allows distant cells in the body to communicate, called a hormone.

To aid in communication, other proteins called cell-surface receptors are embedded in the plasma membrane to receive messages from specific extracellular signaling molecules, such as hormones. When a protein hormone docks with a receptor (imagine a sort of handshake), it triggers a signal inside the cell, causing a specific response.

The Game: In Cytosis, when you place a flask on the Rough ER, you trigger the process of translation, turning mRNA resources into protein resources. You must place a transport vesicle on an available RER location and then exchange mRNA (black resources) for protein(s) (red resources). Protein(s) from this process are required to complete any of the Protein Hormone cards, Protein Hormone Receptor cards, and Steroid Hormone Receptor cards.

VI. The Golgi Apparatus - Modifying Hormones and Receptors

The Science: The Golgi apparatus (GA) receives newly formed proteins from the RER via transport vesicles and sends completed proteins to their intended destination, essentially functioning as a "post office". The GA is generally situated near the RER and receives the bulk of proteins produced by the RER, including enzymes, hormones, receptors and neurotransmitters.

The GA checks each protein for accuracy; if a protein is incorrectly folded it will be degraded later on by the cell. Correctly folded proteins are sorted into new vesicles and processed according to their "mailing" labels. At this stage, some proteins undergo modifications and/or further labelling through the addition of carbohydrates and lipids, also known as post-translational modifications. These modifications can change a protein's chemical structure or activate a hormone, thus making it ready for use by the cell.

The Game: By placing a flask at the GA, you can move your Transport Vesicle Disk from either the SER or the RER and then add a carbohydrate (green resource) or lipid (yellow resource) as indicated on the Hormone or Receptor Cell Component Card you are working to complete.

VII. The Plasma Membrane - Exocytosis of Hormones and Receptors

The Science: The plasma membrane is a flexible barrier that encloses all cells and many organelles, protecting them

from their surroundings. The plasma membrane is a lipid bilayer embedded with proteins. These proteins perform many critical functions, such as transporters to ferry molecules across the membrane or receptors to relay messages into the cell. The plasma membrane is also where cells release molecules, such as hormones, through a process called exocytosis. Hormones are packaged into transport vesicles inside the cell and transferred to the plasma membrane where the vesicle will fuse with the membrane and release its contents into the outside environment. Once outside the cell, hormones can bind to receptors on the surface of other cells. Likewise, receptors are delivered to the plasma membrane in transport vesicles that fuse with the plasma membrane, but the receptors remain embedded in the membrane ready to detect and relay signals from outside the cell.

The Game: In Cytosis, once you have added all the necessary macromolecule resources to your Transport Vesicle Disk (according to the Cell Component Card you're trying to complete), you then place a flask on an available Plasma Membrane Exocytosis space and move your loaded Transport Vesicle Disk from the Golgi apparatus to the outside of the cell, mimicking the process of exocytosis. This completes the process of synthesizing and delivering a receptor or hormone (according to your Cell Component Card) and allowing you to score health points.

VIII. The Plasma Membrane - Import of Carbohydrates through the Glucose Transporter

The Science: Transporters are proteins embedded in a cell's plasma membrane and are responsible for actively ferrying molecules across the membrane. There are many different types of transporters and each is highly specialized to transport specific molecules or classes of molecules.

For example, Glucose is an essential molecule in our bodies and in our cells. Glucose is either absorbed from food by the small intestine or it is made in the liver, then released into the bloodstream for distribution to cells all over the body. A type of transporter called a glucose transporter brings glucose and other carbohydrates into cells. These transporters are crucial for a cell's survival because glucose is the primary fuel for making ATP, the cell's key energy transfer molecule. However, transporters do not work for free, and a cell must spend ATP to actively move molecules into the cell. The amount of glucose the transporters bring into a cell is controlled by many factors, including the hormone insulin and the concentration of glucose already in the cell.

The Game: In Cytosis, you can import carbohydrates (green resources) into the cell by placing a flask on a Glucose Transporter spot on the Plasma Membrane. For every ATP spent, you will gain the same amount of carbohydrates.

IX. The Mitochondria - ATP Production

The Science: Mitochondria are known as the "powerhouses of the cell" and are responsible for producing energy in a form the cell can use. We get our energy from the food we eat, but for our cells to actually use the energy stored in food, especially carbohydrates, it must be converted into an energy carrying molecule called adenosine triphosphate, or ATP. Almost everything that your body does is a result of a chemical reaction, and ATP is the molecule that fuels those reactions. This makes ATP an essential molecule for all of life.

Mitochondria are able to produce ATP through a series of chemical reactions (i.e., cellular respiration) that convert the energy stored in molecules such as proteins, carbohydrates, and lipids into ATP. The number of mitochondria in a cell depends on the cell type; for example, muscle cells require more energy to function and will often have up to 2000 mitochondria in a single cell!

The Game: In Cytosis, you make ATP by placing a flask on the Mitochondria space. You can either gain 2 or 3 ATP tokens without using any carbohydrates (green resource), or you can gain up to 6 ATP by spending one carbohydrate. Fun fact: in a real cell, one molecule of glucose would actually produce about 32 molecules of ATP!

X. The Laureates in Biology, Grey Flasks, and the Cell Component Card Area

The Science: The Nobel Prize is given to recipients to recognize significant contributions in many fields, e.g., Chemistry, Literature, Peace, etc. Nobel Prizes in Physiology or Medicine have been awarded since 1901 by the Karolinska Institute in Sweden to scientists who develop an important new technique or explain a specific aspect of biology. Each recipient earns the title "Laureate".

Some important Laureates in the field of biology include: Beadle and Tatum (1958) for discovering how genes are related to protein activity; Ochoa and Kornberg (1959) for understanding how DNA and RNA are made; Crick, Watson and Wilkins (1962) for determining the structure of DNA; Holley, Khorana, and Nirenberg (1968) for decoding the language of RNA and detailing how it is converted into proteins; Delbrück, Hershey, and Luria (1969) for determining how viruses replicate and are organized; Sutherland (1971) for work on hormone function; Claude, de Duve, and Palade (1974) for discoveries about cell organization; and Blobel (1999), Rothman, Schekman, and Südhof (2013) for work on protein movement within a cell.

The Game: In Cytosis, when you place a flask on the Laureates in Biology spot, you gain the First Player Marker. You may also either take one ATP Token or place a Goal Marker on a Goal Card. This goal action is a salute to the Nobel Laureates who set themselves remarkable career goals and achieved results through dedication and hard work!

By using the Grey Flasks spot, you can pay 4 ATP Tokens to recruit extra help from a Nobel Laureate. As your Nobel Laureate (Grey Flask) is an expert in cell biology, you can even place them next to placement spots that are already occupied by other players and obtain the full benefits!

XI. Viruses - A Summary of what a Virus is and how it functions

The Science: Viruses are entities many times smaller than cells and consist of bundles of genetic material, either DNA or RNA, enclosed in a protective protein shell. Most viruses contain only the information needed to make more copies of themselves, however they can't do it alone. They must hijack the machinery and resources within a cell (referred to as a host cell) in order to reproduce.

Viruses have special proteins on their shell that let them attach to proteins on a host cell's plasma membrane, causing the host cell to bring the virus (or just its genetic material) into the cell. Once the genetic material is in the host cell, the virus uses the cell's transcription and translation machinery to make many copies of itself. Once new viruses are assembled, they exit the cell, often causing damage to, or destruction of, the host cell.

The Game: In the Virus Expansion for Cytosis, three different strains of virus cards are added to the game - Ebola virus, Influenza, and Rhinovirus. When any of these cards become active, it initiates a "virus attack" and may cause players to lose resources and health, just as we do when we get sick.

XII. Antibodies and Viruses - How our bodies defend themselves

The Science: Viruses, Bacteria, and other foreign organisms that cause disease are referred to as pathogens. When pathogens invade our body, our immune system responds to specific proteins, called antigens, from these pathogens. Our immune system is made up of many types of specialized cells that identify, contain, and neutralize an invading pathogen.

For example, B cells are a class of white blood cell that have receptors capable of recognizing antigens. When B cells identify an antigen, they create antibodies that specifically target that antigen.

An antibody (or immunoglobulin) is a Y-shaped molecule that can bind to a target antigen, thereby marking the pathogen (e.g., a virus) for destruction by other immune cells. Even after a pathogen is eliminated, the immune system retains a memory of the antigen and can quickly respond to the same virus if it's encountered again.

FUN FACT: This antigen memory is how immunizations work! We inject our body with a non-pathogenic antigen (or an antigen that is inactive) so our bodies can produce specific antibodies and be better prepared for future infections.

The Game: After viral attacks are resolved in Cytosis, you have the option to spend energy (ATP) to produce antibodies specific to the strain of the infecting virus. These antibody markers prepare the cell for defense against future attack by the same virus, thus mimicking the way our bodies produce antibodies against invading pathogens to fight off an infection.