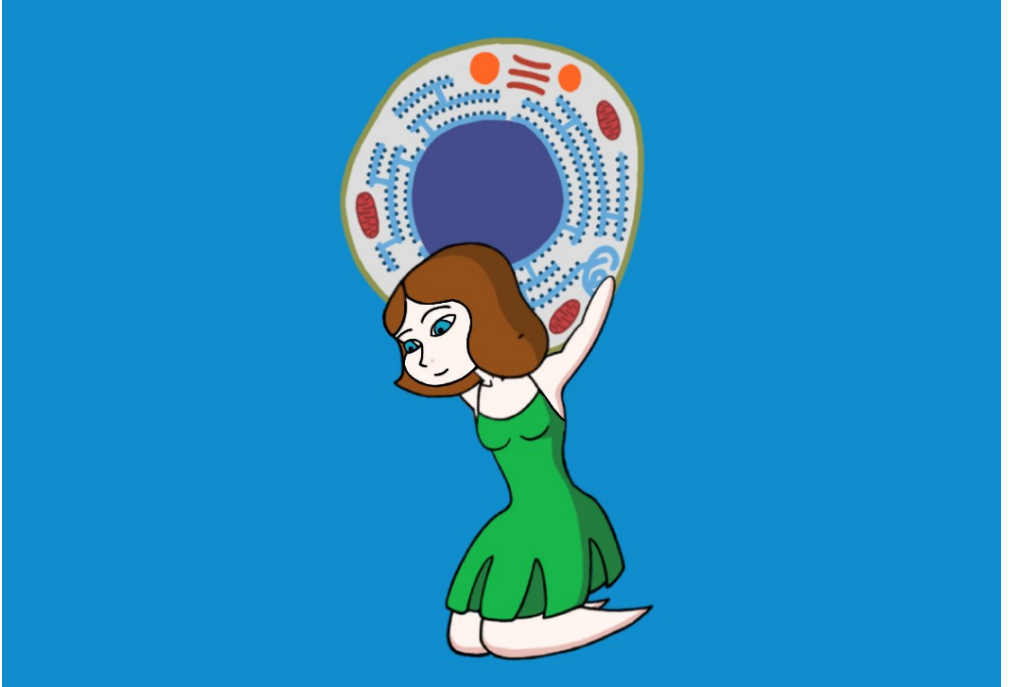


Fabrienne explains cell biology



Cells not working the way they should
can become quite a burden

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Fabrienne explains cell biology

Part 1: What is a cell?

Cell biology is a heavy subject, so we'll start with something basic: what is a cell?

A cell is the smallest unit of life; the smallest organisms that live do in fact consist of single cells. As such, cells have everything that is necessary for life. Three important functions are:

1. Reproduction. Cells can make copies of themselves.
2. Cell repair. If a part gets damaged, cells can make replacement parts.
3. Energy production. Many of a cell's processes require energy, and cells have ways of providing that energy.

In a multicellular organism like humans, many cells are highly specialized for specific functions, and not all cells are capable of all three functions.

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Part 1: What is a cell?

Now, how do cells do all of that? Essentially, a cell is a water balloon with a chemical plant inside. For their different functions, cells have their own little organs called organelles. I'll introduce these different organelles at a later time, and explain the different roles they play for the functions I mentioned above.

The human body consists of tens of trillions of cells of many different cell types. Most cells are so small that they are only visible under a microscope. That's why I made a drawing of a white blood cell, which you can find on the last page of this document.

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Part 2: Cell membrane and cytosol



That's the cell membrane, and that too,
and that too ...

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Part 2: Cell membrane and cytosol

In the last chapter, I described a cell as a water balloon. In cell biology, that balloon is called the cell membrane and the water is called cytosol. The cell membrane has two layers consisting mainly of different fatty substances (lipid bilayer). The membrane also contains proteins that are important for its different functions. In addition to keeping the inside in and the outside out, the cell membrane has the following functions:

1. Letting the right substances in
2. Letting the right substances out
3. Communication with other cells

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Part 2: Cell membrane and cytosol

In the human body, many cells are highly specialized, and thus highly dependant on other cells. For example, insulin is needed by many cells of the body, but only produced in the pancreas. That's why cells need to be able to absorb nutrients and signalling molecules produced by other cells, and to transport cellular waste and its own signalling molecules out.

Cytosol is the liquid that surrounds the organelles within a cell. Cytosol plus organelles is called cytoplasm. Cytosol is more than just water; many substances are dissolved in it, like different types of salt and proteins. But when you hear that most of the human body consists of water, most of that water is cytosol.

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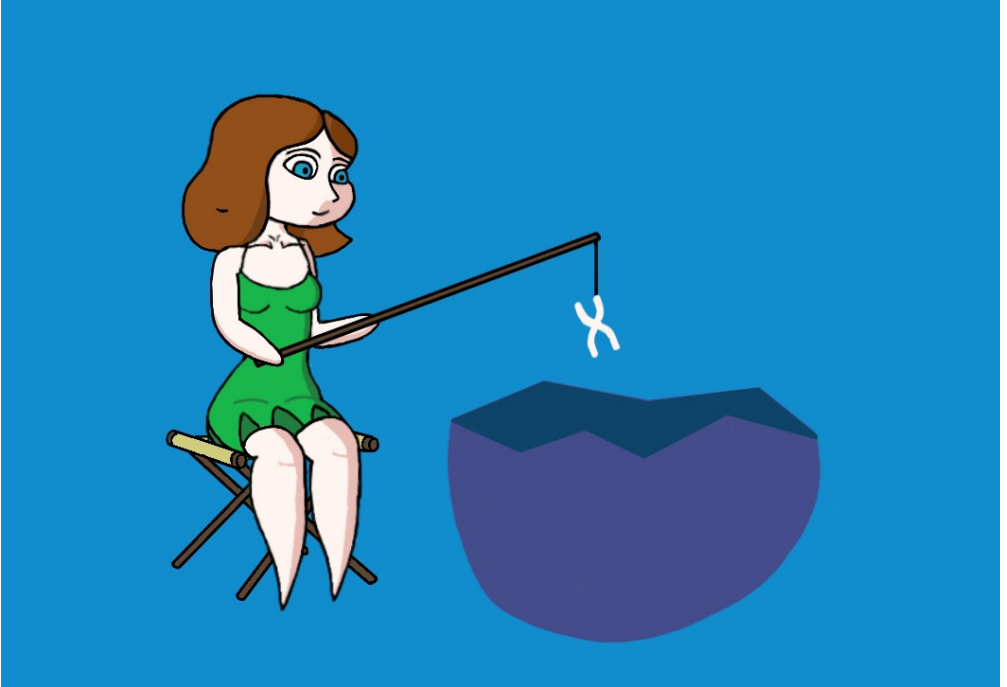
Part 2: Cell membrane and cytosol

Organelles don't just float inside the cytosol, but are anchored by a cytoskeleton made of protein strands. Did you ever feel your muscles contract? That's your muscle cells' cytoskeleton at work.

Although much of the chemistry inside a cell takes place inside of organelles, a lot of chemistry happens in the cytosol, too. Apart from that, it has an important function for the transport of substances between organelles, the membrane and the nucleus, our next topic.

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Part 3: Nucleus and ribosomes



I caught a chromosome

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Part 3: Nucleus and ribosomes

In some ways, the nucleus is a bit like a cell in a cell. Like a cell, the nucleus has a membrane. But unlike the cell membrane, a nucleus has a double membrane consisting of two lipid bilayers. Similar to the membrane proteins of a cell membrane, the nuclear membrane contains nuclear pores for the transport of molecules through the membrane. Like a cell, the nucleus is filled with a liquid, the nucleosol, and a network of protein strands called lamina provides mechanical support. The nucleus contains a small number of organelle-like structures called nuclear bodies.

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Part 3: Nucleus and ribosomes

One of these nuclear bodies is called nucleolus, and it plays an important role in the production of ribosomes. For the production of ribosomes, specific proteins are imported from the cytosol through the nuclear pores into the nucleus, and then assembled into ribosomes inside the nucleolus. After assembly, the ribosomes are transported back in two parts through the nuclear pores into the cytosol. Ribosomes play an important role in the production of proteins. Proteins consist of 20 different amino acids that are linked together into chains of varying length. The order in which those amino acids occur determines the shape of a protein, and its shape determines its function. In every cell, countless ribosomes constantly link amino acids together into proteins (red blood cells, having no nuclei, are an exception).

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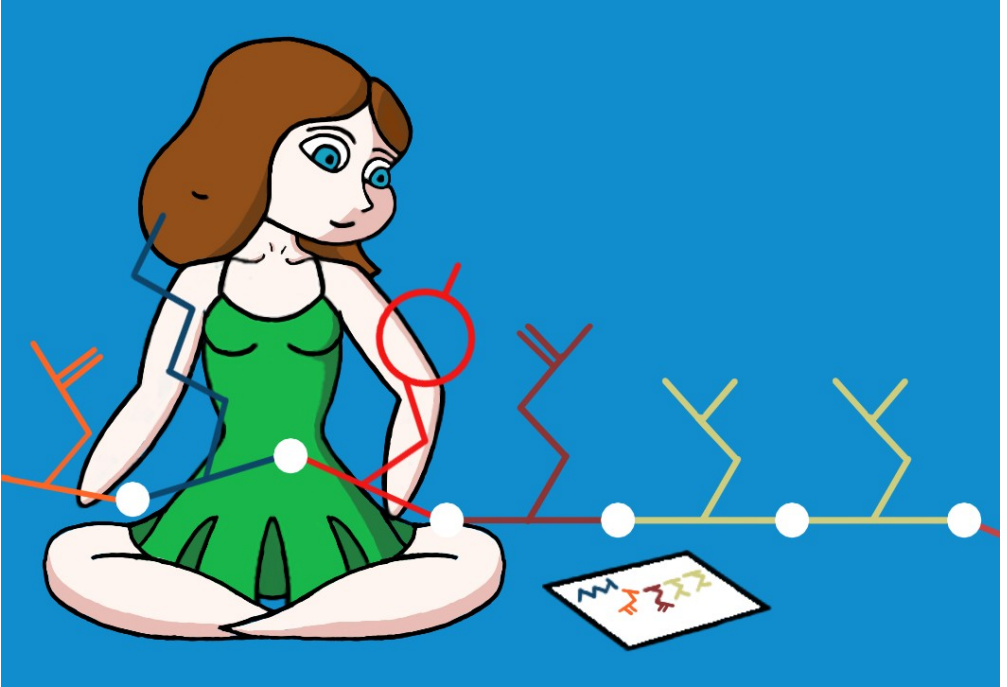
Part 3: Nucleus and ribosomes

How do ribosomes know the correct order of amino acids? That's what your genetic material, your DNA is for. For every different protein, DNA contains a long list detailing the correct order of amino acids for each protein (unless you have a genetic mutation, like I do).

In addition to building ribosomes, storing DNA is the other important function of the nucleus. DNA is divided up into 46 chromosomes (for humans, with some exceptions). It's very interesting how DNA is stored and read and translated into proteins, but also very difficult. That's why I'll leave that for another series on genetics.

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Part 4: Endoplasmic reticulum



Protein folding is hard -
especially with a mutation

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Part 4: Endoplasmic reticulum

In the last chapter, I explained how ribosomes chain together amino acids into long chains in an order that is determined by a person's DNA. Short chains of several dozens of amino acids are called peptides, whereas proteins have hundreds or up to thousands of amino acids. Proteins and peptides have many functions like transport of molecules, communication in and between cells, structural support, and facilitating chemical reactions. Those latter proteins are called enzymes.

A certain group of proteins takes a special route through the cell. Those are proteins that are either destined for the lysosomes, for the cell membrane or for locations outside of the cell. The first step of those proteins' journey takes place inside the endoplasmic reticulum.

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Part 4: Endoplasmic reticulum

The endoplasmic reticulum (abbreviated ER) is a large labyrinth-like cell organelle that is wrapped around the nucleus. A large part of the endoplasmic reticulum is studded with ribosomes that feed proteins into the ER as they are being produced. These ribosomes give this part of the ER the name „rough ER“, and the other part is called „smooth ER“. Once they enter the ER, proteins start to fold into a shape that allows them to perform their function. Mutations like mine disrupt this folding process. The resulting ER stress is a major topic of my videos.

Although not all proteins are folded inside the ER, and the ER has other functions besides folding proteins, protein folding is one of the major functions of the ER.

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Part 4: Endoplasmic reticulum

The smooth endoplasmic reticulum is the location where certain fatty substances are produced, like cholesterol and ceramide. Ceramide is the basic sphingolipid, one of several groups of fatty substances that form part of the cell membrane. Both the enzymes needed to produce these fatty substances and the chaperones that assist in the folding of proteins are proteins.

After production, proteins travel to the Golgi apparatus for further modification. The Golgi apparatus is also involved in the transformation of ceramide into complex sphingolipids. And this Golgi apparatus will be our next topic.

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Part 5: Golgi apparatus



This protein has finished folding
but it still needs a sugar tree

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Part 5: Golgi apparatus

Proteins that are folded inside the endoplasmic reticulum aren't finished. And many of the fatty substances that are produced in the smooth endoplasmic reticulum also need further modification. Many of these modifications are initiated inside the endoplasmic reticulum and completed inside the Golgi apparatus.

The Golgi apparatus is a cell organelle that is made up of a number (in humans: usually four to eight) of disc-like structures, that are connected through protein filaments. The first one is called the *cis*-Golgi, the last one the *trans*-Golgi, and in between are medial compartments. This structure allows the different modifications to be performed in the correct order.

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Part 5: Golgi apparatus

An example for such a modification is *N*-linked glycosylation. The *N* in this case is an abbreviation for the amino acid asparagin, and the word „glycosylation“ has the same origin as the word glucose; it means the addition of sugars, not necessarily glucose, though. In the endoplasmic reticulum, this process starts with the addition of a few sugar molecules, and in the Golgi apparatus, this is turned into a complex branching chain consisting of many sugars with a tree-like structure. These sugar chains are used for sorting proteins inside the Golgi apparatus according to their destinations.

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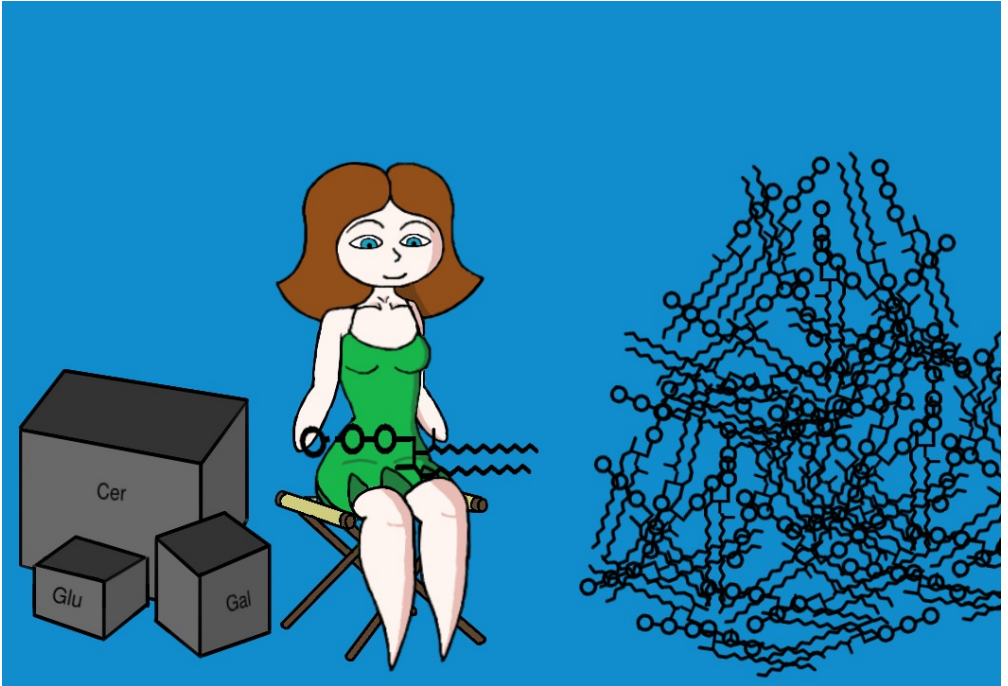
Part 5: Golgi apparatus

Not all substances travel from the *cis*-Golgi through the medial compartments to the *trans*-Golgi. Ceramide, one of the fatty substances that is produced inside the smooth endoplasmic reticulum, may be delivered directly to the *trans*-Golgi, where it is then turned into sphingomyelin. If ceramide takes another route through the Golgi apparatus, other complex sphingolipids are created.

The Golgi apparatus also plays a role in the creation of lysosomes. Proteins with sugar chains that are rich in mannose-6-phosphate gather in the *trans*-Golgi and are packed inside transport containers called vesicles. And what happens to those proteins after that will be our next topic.

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Part 6: Lysosomes



Everything I don't manage to disassemble
ends up in lysosomal storage

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Part 6: Lysosomes

Two times already I have mentioned lysosomes. Now it's time to explain what they are. However, that's not so easy, because lysosomes are not just cell organelles, but a group of closely related but still different cell organelles. What they have in common is their function: breakdown of cell material.

Breakdown of cell material is more than just recycling. Cells constantly adapt to new situations, and in doing so, their needs change as well. For example, muscle cells might need different proteins during exercise than at rest. And to produce those new proteins, amino acids are needed. And those amino acids can in part be provided by breaking down old proteins. One function of lysosomes is thus redistribution of resources according to a cell's current needs.

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Part 6: Lysosomes

Lysosomes can degrade many different types of substances. Those can be parts of a lysosome's own cell, from simple proteins to entire cell organelles like mitochondria (our next subject). A cell's nutrient uptake often involves the creation of transport containers called vesicles from the cell membrane containing those nutrients, which then fuse with a lysosome to digest those nutrients to substances the cell can use. Some white blood cells can enclose entire bacteria in a membrane (phagosome), which can also fuse with a lysosome for digestion. If extracellular material needs to be degraded, like old bone material, lysosomes can fuse with the cell membrane to spill their contents outside the cell.

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Part 6: Lysosomes

For the breakdown of so many different types of substances, lysosomes need dozens of different enzymes. All of these enzymes are folded inside the endoplasmic reticulum and transported through the Golgi apparatus. And lysosomes need more than just enzymes; some enzymes also need additional proteins like saposin to function.

Failure to digest specific substances leads to their accumulation inside the lysosomes. Such failure is often caused by gene defects affecting enzymes, but mutations in genes for associated proteins can cause similar problems. Because there are dozens of lysosomal enzymes, there are also dozens of such lysosomal storage diseases, like Gaucher's disease and Fabry disease.

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Part 7: Mitochondria



I didn't manage to capture a bacterium
to help me produce energy

Fabienne explains cell biology

Part 7: Mitochondria

The last cell organell we'll discuss is the mitochondrion. The history of mitochondria began when an archaeon (archaea are unicellular organisms that are similar to bacteria) managed to capture a bacterium to help it produce energy. As descendants from independent bacteria, mitochondria have their own DNA. Mitochondrial DNA consists of a single circular chromosome, as is typical for bacteria. Usually, there are several copies of this chromosome. Most mitochondrial proteins are encoded by nuclear DNA, but mitochondria make some proteins by themselves (13 out of ~1500 proteins). For this, they have their own ribosomes, built from proteins that are encoded by nuclear DNA. In turn, protein production from nuclear DNA is dependent on the energy that is provided by mitochondria.

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Part 7: Mitochondria

Like the nucleus, mitochondria have two membranes. The inner membrane of mitochondria, however, is not aligned with the outer membrane, but forms a number of folds projecting inwards. Between the outer and inner membrane, there's the intermembrane space, and the fluid filling the inner membrane is called the matrix.

Energy production begins in the cytosol with the breakdown of sugar or fat. The breakdown products react with oxygen inside the mitochondria, and the energy that is generated is used to pump protons from the matrix to the intermembrane space. On their way back through the inner membrane, the energy is stored as ATP, which is provided to the whole cell. The folds of the inner membrane increase its surface to enhance this process.

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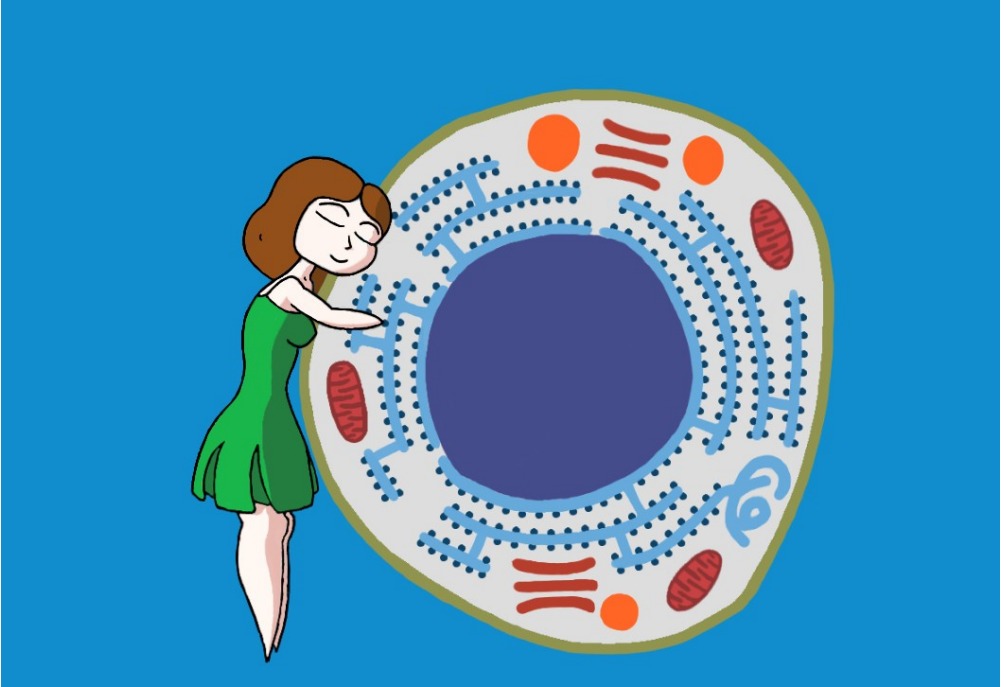
Part 7: Mitochondria

Many of a cell's chemical reactions, most of which are supported by enzymes, require an additional source of energy. This energy is usually provided in the form of adenosine triphosphate (ATP), the cell's basic unit of energy. When releasing energy, the ATP molecules lose a phosphate, thus turning into adenosine diphosphate (ADP). So, ATP is like a charged battery, and ADP is the discharged variant. ADP can be recharged to ATP by adding a phosphate, which for the most part happens inside the mitochondria.

Besides energy production, mitochondria have many additional functions for the metabolism of the entire cell.

Fabrienne explains cell biology

Part 8: Final remarks



Even if my cells sometimes do stupid things,
I couldn't live without them

Fabrienne explains cell biology

Part 8: Final remarks

The body doesn't consist exclusively of cells. A large part of the body consists of extracellular matrix (ECM). ECM is an important part of connective tissue. Examples of connective tissue are bones, with an ECM containing mineral substances, blood, with a liquid ECM, and tendons, with an ECM consisting for a large part of proteins like collagen. All different types of ECM are maintained by cells, and problems affecting the ECM are thus problems of the associated cells. So even if you have problems with your collagen, that collagen consists of proteins that are produced by cells, and those cells cause the problems. And that's why understanding cell biology is so important.

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Part 8: Final remarks

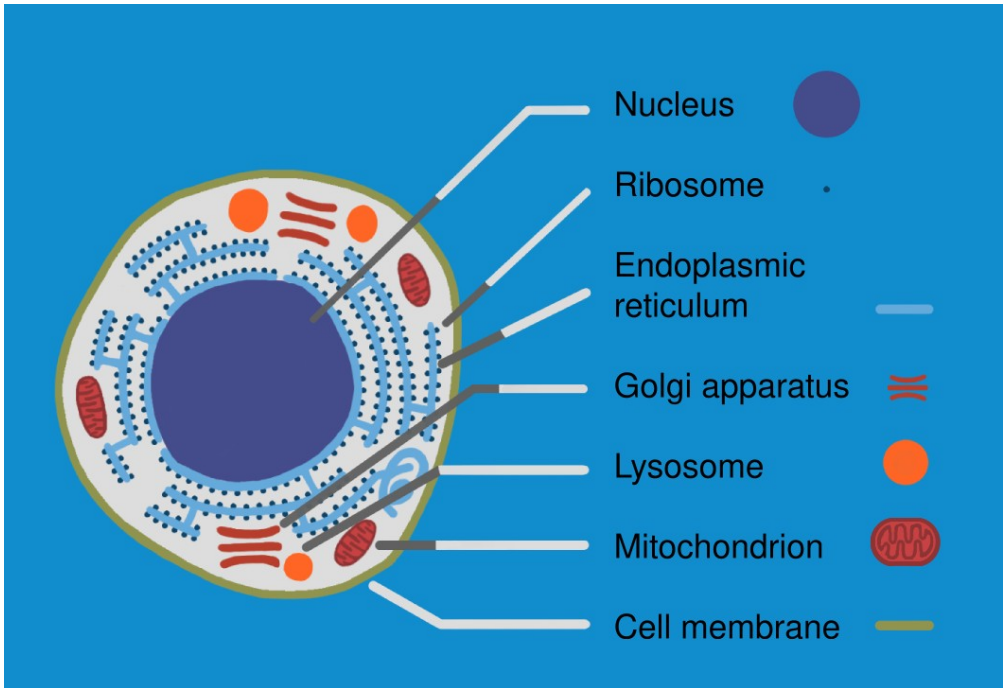
The genetic information that is stored in DNA contains most of the necessary information for a cell's metabolism, growth and replication. However, DNA by itself is not sufficient for the creation of new cells. New cells only arise through the process of cell division. Before this process begins, a full copy of the nuclear DNA is made. During cell division, both daughter cells can thus inherit a full set of genetic material. Because some organelles, like mitochondria, also multiply by division (which can occur independently from cell division), both daughter cells also receive a set of organelles. In this way – through countless cycles of cell divisions – all cells currently alive derive from the very first single-celled organisms.

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Part 8: Final remarks

We now have discussed a number of cell organelles and their importance for the overall functioning of a cell. Of course, it's possible to write entire volumes about each organelle (in fact, people have), but this series is just about mentioning the names and some functions of the cell organelles you are most likely to encounter in discussions regarding chronic diseases. So, we have seen that ribosomes produce proteins, that many proteins are folded inside the endoplasmic reticulum (ER) and that lysosomes do more than just waste disposal. I sure learned a lot.

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