**Anatomy physiology and Pathophysiology**

**Mitochondria**

The **mitochondrion** (plural **mitochondria**) is a double [membrane](https://en.wikipedia.org/wiki/Biological_membrane)-bound [organelle](https://en.wikipedia.org/wiki/Organelle) found in all [eukaryotic](https://en.wikipedia.org/wiki/Eukaryotic) organisms, although some cells in some organisms may lack them (e.g. [Red blood cells](https://en.wikipedia.org/wiki/Red_blood_cells)). A number of organisms have reduced or transformed their mitochondria into other structures.[[1]](https://en.wikipedia.org/wiki/Mitochondrion#cite_note-mitosomes-1) To date, only one eukaryote is known to have completely lost its mitochondria.[[2]](https://en.wikipedia.org/wiki/Mitochondrion#cite_note-CB1-2) The word mitochondrion comes from the [Greek](https://en.wikipedia.org/wiki/Greek_language) *μίτος*, *mitos*, i.e. "thread", and *χονδρίον*—, *chondrion*, i.e. "granule"[[3]](https://en.wikipedia.org/wiki/Mitochondrion#cite_note-OnlineEtDict-3) or "grain-like". Mitochondria have been described as "the powerhouse of the cell" because they generate most of the cell's supply of [adenosine triphosphate](https://en.wikipedia.org/wiki/Adenosine_triphosphate) (ATP), used as a source of [chemical energy](https://en.wikipedia.org/wiki/Chemical_energy).[[4]](https://en.wikipedia.org/wiki/Mitochondrion#cite_note-4)

Mitochondria are commonly between 0.75 and 3[μm](https://en.wikipedia.org/wiki/Micrometre) in diameter[[5]](https://en.wikipedia.org/wiki/Mitochondrion#cite_note-pmid26777473-5) but vary considerably in size and structure. Unless specifically stained, they are not visible. In addition to supplying cellular energy, mitochondria are involved in other tasks, such as [signaling](https://en.wikipedia.org/wiki/Cell_signaling), [cellular differentiation](https://en.wikipedia.org/wiki/Cellular_differentiation), and [cell death](https://en.wikipedia.org/wiki/Apoptosis), as well as maintaining control of the [cell cycle](https://en.wikipedia.org/wiki/Cell_cycle) and [cell growth](https://en.wikipedia.org/wiki/Cell_growth).[[6]](https://en.wikipedia.org/wiki/Mitochondrion#cite_note-6) [Mitochondrial biogenesis](https://en.wikipedia.org/wiki/Mitochondrial_biogenesis) is in turn temporally coordinated with these cellular processes.

The number of mitochondria in a cell can vary widely by [organism](https://en.wikipedia.org/wiki/Organism), [tissue](https://en.wikipedia.org/wiki/Tissue_(biology)), and cell type. For instance, [red blood cells](https://en.wikipedia.org/wiki/Erythrocyte) have no mitochondria, whereas [liver cells](https://en.wikipedia.org/wiki/Hepatocyte) can have more than 2000.[[13]](https://en.wikipedia.org/wiki/Mitochondrion#cite_note-Alberts-13)[[14]](https://en.wikipedia.org/wiki/Mitochondrion#cite_note-Voet-14) The organelle is composed of compartments that carry out specialized functions. These compartments or regions include the outer membrane, the [intermembrane space](https://en.wikipedia.org/wiki/Intermembrane_space), the [inner membrane](https://en.wikipedia.org/wiki/Inner_mitochondrial_membrane), and the [cristae](https://en.wikipedia.org/wiki/Cristae) and [matrix](https://en.wikipedia.org/wiki/Mitochondrial_matrix). Mitochondrial proteins vary depending on the tissue and the species. In humans, 615 distinct types of protein have been identified from [cardiac](https://en.wikipedia.org/wiki/Heart)mitochondria,[[15]](https://en.wikipedia.org/wiki/Mitochondrion#cite_note-15) whereas in [rats](https://en.wikipedia.org/wiki/Murinae), 940 proteins have been reported

A mitochondrion contains outer and inner membranes composed of [phospholipid bilayers](https://en.wikipedia.org/wiki/Phospholipid_bilayer) and [proteins](https://en.wikipedia.org/wiki/Protein).[[13]](https://en.wikipedia.org/wiki/Mitochondrion#cite_note-Alberts-13) The two membranes have different properties. Because of this double-membraned organization, there are five distinct parts to a mitochondrion. They are:

1. the outer mitochondrial membrane,
2. the intermembrane space (the space between the outer and inner membranes),
3. the inner mitochondrial membrane,
4. the cristae space (formed by infoldings of the inner membrane), and
5. the matrix (space within the inner membrane).

Mitochondria stripped of their outer membrane are called [mitoplasts](https://en.wikipedia.org/wiki/Mitoplast).

**Outer membrane**

The **outer mitochondrial membrane**, which encloses the entire organelle, is 60 to 75 [angstroms](https://en.wikipedia.org/wiki/Angstrom) (Å) thick. It has a protein-to-phospholipid ratio similar to that of the eukaryotic plasma membrane (about 1:1 by weight). It contains large numbers of[integral membrane proteins](https://en.wikipedia.org/wiki/Integral_membrane_protein) called [porins](https://en.wikipedia.org/wiki/Porin_(protein)). These porins form channels that allow molecules of 5000 [daltons](https://en.wikipedia.org/wiki/Atomic_mass_unit) or less in molecular weight to freely [diffuse](https://en.wikipedia.org/wiki/Diffusion) from one side of the membrane to the other.[[13]](https://en.wikipedia.org/wiki/Mitochondrion#cite_note-Alberts-13) Larger proteins can enter the mitochondrion if a signaling sequence at their [N-terminus](https://en.wikipedia.org/wiki/N-terminus) binds to a large multisubunit [protein](https://en.wikipedia.org/wiki/Mitochondrial_membrane_transport_protein) called[translocase](https://en.wikipedia.org/wiki/Translocase) of the outer membrane, which then [actively moves](https://en.wikipedia.org/wiki/Active_transport) them across the membrane.[[38]](https://en.wikipedia.org/wiki/Mitochondrion#cite_note-Neupert-38) Mitochondrial [pro-proteins](https://en.wikipedia.org/wiki/Protein_precursor) are imported through specialised translocation complexes. The outer membrane also contains [enzymes](https://en.wikipedia.org/wiki/Enzyme) involved in such diverse activities as the elongation of [fatty acids](https://en.wikipedia.org/wiki/Fatty_acid), [oxidation](https://en.wikipedia.org/wiki/Oxidation) of [epinephrine](https://en.wikipedia.org/wiki/Epinephrine), and the [degradation](https://en.wikipedia.org/wiki/Biodegradation) of [tryptophan](https://en.wikipedia.org/wiki/Tryptophan). These enzymes include [monoamine oxidase](https://en.wikipedia.org/wiki/Monoamine_oxidase), [rotenone](https://en.wikipedia.org/wiki/Rotenone)-insensitive NADH-cytochrome c-reductase, [kynurenine](https://en.wikipedia.org/wiki/Kynurenine) [hydroxylase](https://en.wikipedia.org/wiki/Hydroxylase) and fatty acid Co-A [ligase](https://en.wikipedia.org/wiki/Ligase). Disruption of the outer membrane permits proteins in the intermembrane space to leak into the cytosol, leading to certain cell death.[[39]](https://en.wikipedia.org/wiki/Mitochondrion#cite_note-Chipuk-39) The mitochondrial outer membrane can associate with the endoplasmic reticulum (ER) membrane, in a structure called MAM (mitochondria-associated ER-membrane). This is important in the ER-mitochondria calcium signaling and is involved in the transfer of lipids between the ER and mitochondria. [[40]](https://en.wikipedia.org/wiki/Mitochondrion#cite_note-40) Outside the outer membrane

**Intermembrane space**

The [intermembrane space](https://en.wikipedia.org/wiki/Intermembrane_space) is the space between the outer membrane and the inner membrane. It is also known as perimitochondrial space. Because the outer membrane is freely permeable to small molecules, the concentrations of small molecules, such as ions and sugars, in the intermembrane space is the same as in the[cytosol](https://en.wikipedia.org/wiki/Cytosol).[[13]](https://en.wikipedia.org/wiki/Mitochondrion#cite_note-Alberts-13) However, large proteins must have a specific signaling sequence to be transported across the outer membrane, so the protein composition of this space is different from the protein composition of the [cytosol](https://en.wikipedia.org/wiki/Cytosol). One protein that is localized to the intermembrane space in this way is [cytochrome c](https://en.wikipedia.org/wiki/Cytochrome_c).[[39]](https://en.wikipedia.org/wiki/Mitochondrion#cite_note-Chipuk-39)

**Inner membrane**

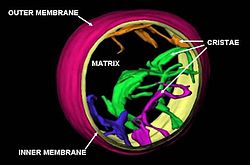
*Main article:*[*Inner mitochondrial membrane*](https://en.wikipedia.org/wiki/Inner_mitochondrial_membrane)

The inner mitochondrial membrane contains proteins with five types of functions:[[13]](https://en.wikipedia.org/wiki/Mitochondrion#cite_note-Alberts-13)

1. Those that perform the [redox](https://en.wikipedia.org/wiki/Redox) reactions of [oxidative phosphorylation](https://en.wikipedia.org/wiki/Oxidative_phosphorylation)
2. [ATP synthase](https://en.wikipedia.org/wiki/ATP_synthase), which generates [ATP](https://en.wikipedia.org/wiki/Adenosine_triphosphate) in the matrix
3. Specific [transport proteins](https://en.wikipedia.org/wiki/Membrane_transport_protein) that regulate [metabolite](https://en.wikipedia.org/wiki/Metabolite) passage into and out of the matrix
4. Protein import machinery
5. [Mitochondrial fusion](https://en.wikipedia.org/wiki/Mitochondrial_fusion) and [fission](https://en.wikipedia.org/wiki/Mitochondrial_fission) protein

It contains more than 151 different [polypeptides](https://en.wikipedia.org/wiki/Polypeptide), and has a very high protein-to-phospholipid ratio (more than 3:1 by weight, which is about 1 protein for 15 phospholipids). The inner membrane is home to around 1/5 of the total protein in a mitochondrion.[[13]](https://en.wikipedia.org/wiki/Mitochondrion#cite_note-Alberts-13) In addition, the inner membrane is rich in an unusual phospholipid, [cardiolipin](https://en.wikipedia.org/wiki/Cardiolipin). This phospholipid was originally discovered in [cow](https://en.wikipedia.org/wiki/Bos_taurus) hearts in 1942, and is usually characteristic of mitochondrial and bacterial plasma membranes.[[41]](https://en.wikipedia.org/wiki/Mitochondrion#cite_note-McMillin-41) Cardiolipin contains four fatty acids rather than two, and may help to make the inner membrane impermeable.[[13]](https://en.wikipedia.org/wiki/Mitochondrion#cite_note-Alberts-13) Unlike the outer membrane, the inner membrane doesn't contain porins, and is highly impermeable to all molecules. Almost all ions and molecules require special membrane transporters to enter or exit the matrix. Proteins are ferried into the matrix via the [translocase of the inner membrane](https://en.wikipedia.org/wiki/Translocase_of_the_inner_membrane) (TIM) complex or via Oxa1.[[38]](https://en.wikipedia.org/wiki/Mitochondrion#cite_note-Neupert-38) In addition, there is a membrane potential across the inner membrane, formed by the action of the enzymes of the [electron transport chain](https://en.wikipedia.org/wiki/Electron_transport_chain).

#### Cristae

[](https://en.wikipedia.org/wiki/File:MitochondrionCAM.jpg)

Cross-sectional image of cristae in rat liver mitochondrion to demonstrate the likely 3D structure and relationship to the inner membrane

*Main article:*[*Cristae*](https://en.wikipedia.org/wiki/Cristae)

The inner mitochondrial membrane is compartmentalized into numerous [cristae](https://en.wikipedia.org/wiki/Crista), which expand the surface area of the inner mitochondrial membrane, enhancing its ability to produce ATP. For typical liver mitochondria, the area of the inner membrane is about five times as large as the outer membrane. This ratio is variable and mitochondria from cells that have a greater demand for ATP, such as muscle cells, contain even more cristae. These folds are studded with small round bodies known as [F1 particles](https://en.wikipedia.org/wiki/F-ATPase) or oxysomes. These are not simple random folds but rather invaginations of the inner membrane, which can affect overall [chemiosmotic](https://en.wikipedia.org/wiki/Chemiosmosis) function.[[42]](https://en.wikipedia.org/wiki/Mitochondrion#cite_note-Mannella-42)

One recent mathematical modeling study has suggested that the optical properties of the cristae in filamentous mitochondria may affect the generation and propagation of light within the tissue.[[43]](https://en.wikipedia.org/wiki/Mitochondrion#cite_note-43)

### Matrix

*Main article:*[*Mitochondrial matrix*](https://en.wikipedia.org/wiki/Mitochondrial_matrix)

The matrix is the space enclosed by the inner membrane. It contains about 2/3 of the total protein in a mitochondrion.[[13]](https://en.wikipedia.org/wiki/Mitochondrion#cite_note-Alberts-13) The matrix is important in the production of ATP with the aid of the ATP synthase contained in the inner membrane. The matrix contains a highly concentrated mixture of hundreds of enzymes, special mitochondrial [ribosomes](https://en.wikipedia.org/wiki/Ribosomes), [tRNA](https://en.wikipedia.org/wiki/TRNA), and several copies of the [mitochondrial DNA](https://en.wikipedia.org/wiki/Mitochondrial_DNA) [genome](https://en.wikipedia.org/wiki/Genome). Of the enzymes, the major functions include oxidation of [pyruvate](https://en.wikipedia.org/wiki/Pyruvate) and [fatty acids](https://en.wikipedia.org/wiki/Fatty_acids), and the [citric acid cycle](https://en.wikipedia.org/wiki/Citric_acid_cycle).[[13]](https://en.wikipedia.org/wiki/Mitochondrion#cite_note-Alberts-13)

Mitochondria have their own genetic material, and the machinery to manufacture their own [RNAs](https://en.wikipedia.org/wiki/RNA) and [proteins](https://en.wikipedia.org/wiki/Protein) (*see:*[*protein biosynthesis*](https://en.wikipedia.org/wiki/Protein_biosynthesis)). A published human mitochondrial DNA sequence revealed 16,569 [base pairs](https://en.wikipedia.org/wiki/Base_pair) encoding 37 genes: 22 [tRNA](https://en.wikipedia.org/wiki/TRNA), 2 [rRNA](https://en.wikipedia.org/wiki/RRNA), and 13 [peptide](https://en.wikipedia.org/wiki/Peptide) genes.[[44]](https://en.wikipedia.org/wiki/Mitochondrion#cite_note-Anderson-44) The 13 mitochondrial [peptides](https://en.wikipedia.org/wiki/Peptides) in humans

## Function

The most prominent roles of mitochondria are to produce the energy currency of the cell, [ATP](https://en.wikipedia.org/wiki/Adenosine_triphosphate) (i.e., phosphorylation of [ADP](https://en.wikipedia.org/wiki/Adenosine_diphosphate)), through respiration, and to regulate cellular [metabolism](https://en.wikipedia.org/wiki/Metabolism).[[14]](https://en.wikipedia.org/wiki/Mitochondrion#cite_note-Voet-14) The central set of reactions involved in ATP production are collectively known as the [citric acid cycle](https://en.wikipedia.org/wiki/Citric_acid_cycle), or the [Krebs](https://en.wikipedia.org/wiki/Hans_Adolf_Krebs) cycle. However, the mitochondrion has many other functions in addition to the production of ATP.

### Energy conversion

A dominant role for the mitochondria is the production of [ATP](https://en.wikipedia.org/wiki/Adenosine_triphosphate), as reflected by the large number of proteins in the inner membrane for this task. This is done by oxidizing the major products of [glucose](https://en.wikipedia.org/wiki/Glucose): [pyruvate](https://en.wikipedia.org/wiki/Pyruvate), and [NADH](https://en.wikipedia.org/wiki/NADH), which are produced in the cytosol.[[14]](https://en.wikipedia.org/wiki/Mitochondrion#cite_note-Voet-14) This type of [cellular respiration](https://en.wikipedia.org/wiki/Cellular_respiration) known as [aerobic respiration](https://en.wikipedia.org/wiki/Aerobic_respiration), is dependent on the presence of [oxygen](https://en.wikipedia.org/wiki/Oxygen). When oxygen is limited, the glycolytic products will be metabolized by [anaerobic fermentation](https://en.wikipedia.org/wiki/Fermentation_(biochemistry)), a process that is independent of the mitochondria.[[14]](https://en.wikipedia.org/wiki/Mitochondrion#cite_note-Voet-14) The production of ATP from glucose has an approximately 13-times higher yield during aerobic respiration compared to fermentation.[[68]](https://en.wikipedia.org/wiki/Mitochondrion#cite_note-68)Recently it has been shown that plant mitochondria can produce a limited amount of ATP without oxygen by using the alternate substrate [nitrite](https://en.wikipedia.org/wiki/Nitrite).[[69]](https://en.wikipedia.org/wiki/Mitochondrion#cite_note-pmid17333252-69) ATP crosses out through the inner membrane with the help of a [specific protein](https://en.wikipedia.org/wiki/ATP%E2%80%93ADP_translocase), and across the outer membrane via porins. ADP returns via the same route.

#### Pyruvate and the citric acid cycle

*Main articles:*[*Pyruvate dehydrogenase*](https://en.wikipedia.org/wiki/Pyruvate_dehydrogenase)*,*[*Pyruvate carboxylase*](https://en.wikipedia.org/wiki/Pyruvate_carboxylase)*, and*[*Citric acid cycle*](https://en.wikipedia.org/wiki/Citric_acid_cycle)

[Pyruvate](https://en.wikipedia.org/wiki/Pyruvate) molecules produced by [glycolysis](https://en.wikipedia.org/wiki/Glycolysis) are [actively transported](https://en.wikipedia.org/wiki/Active_transport) across the inner mitochondrial membrane, and into the matrix where they can either be [oxidized](https://en.wikipedia.org/wiki/Redox)and combined with [coenzyme A](https://en.wikipedia.org/wiki/Coenzyme_A) to form CO2, [acetyl-CoA](https://en.wikipedia.org/wiki/Acetyl-CoA), and [NADH](https://en.wikipedia.org/wiki/NADH),[[14]](https://en.wikipedia.org/wiki/Mitochondrion#cite_note-Voet-14) or they can be [carboxylated](https://en.wikipedia.org/wiki/Carboxylated) (by [pyruvate carboxylase](https://en.wikipedia.org/wiki/Pyruvate_carboxylase)) to form oxaloacetate. This latter reaction ”fills up” the amount of oxaloacetate in the citric acid cycle, and is therefore an [anaplerotic reaction](https://en.wikipedia.org/wiki/Anaplerotic_reaction), increasing the cycle’s capacity to metabolize acetyl-CoA when the tissue's energy needs (e.g. in [muscle](https://en.wikipedia.org/wiki/Striated_muscle_tissue)) are suddenly increased by activity.[[70]](https://en.wikipedia.org/wiki/Mitochondrion#cite_note-stryer-70)

In the citric acid cycle, all the intermediates (e.g. citrate, iso-citrate, alpha-ketoglutarate, succinate, fumarate, malate and oxaloacetate) are regenerated during each turn of the cycle. Adding more of any of these intermediates to the mitochondrion therefore means that the additional amount is retained within the cycle, increasing all the other intermediates as one is converted into the other. Hence, the addition of any one of them to the cycle has an anaplerotic effect, and its removal has a cataplerotic effect. These anaplerotic and cataplerotic reactions will, during the course of the cycle, increase or decrease the amount of oxaloacetate available to combine with acetyl-CoA to form citric acid. This in turn increases or decreases the rate of [ATP](https://en.wikipedia.org/wiki/Adenosine_triphosphate) production by the mitochondrion, and thus the availability of ATP to the cell.[[70]](https://en.wikipedia.org/wiki/Mitochondrion#cite_note-stryer-70)

Acetyl-CoA, on the other hand, derived from pyruvate oxidation, or from the [beta-oxidation](https://en.wikipedia.org/wiki/Beta-oxidation) of [fatty acids](https://en.wikipedia.org/wiki/Fatty_acids), is the only fuel to enter the citric acid cycle. With each turn of the cycle one molecule of acetyl-CoA is consumed for every molecule of oxaloacetate present in the mitochondrial matrix, and is never regenerated. It is the oxidation of the acetate portion of acetyl-CoA that produces CO2 and water, with the energy thus released captured in the form of ATP.[[70]](https://en.wikipedia.org/wiki/Mitochondrion#cite_note-stryer-70)

In the liver, the carboxylation of [cytosolic](https://en.wikipedia.org/wiki/Cytosol) pyruvate into intra-mitochondrial oxaloacetate is an early step in the [gluconeogenic](https://en.wikipedia.org/wiki/Gluconeogenesis) pathway, which converts [lactate](https://en.wikipedia.org/wiki/Lactic_acid) and de-aminated  under the influence of high levels of [glucagon](https://en.wikipedia.org/wiki/Glucagon) and/or [epinephrine](https://en.wikipedia.org/wiki/Epinephrine) in the blood.[[70]](https://en.wikipedia.org/wiki/Mitochondrion#cite_note-stryer-70) Here, the addition of oxaloacetate to the mitochondrion does not have a net anaplerotic effect, as another citric acid cycle intermediate (malate) is immediately removed from the mitochondrion to be converted into cytosolic oxaloacetate, which is ultimately converted into glucose, in a process that is almost the reverse of [glycolysis](https://en.wikipedia.org/wiki/Glycolysis).[[70]](https://en.wikipedia.org/wiki/Mitochondrion#cite_note-stryer-70)

The enzymes of the citric acid cycle are located in the mitochondrial matrix, with the exception of [succinate dehydrogenase](https://en.wikipedia.org/wiki/Succinate_dehydrogenase), which is bound to the inner mitochondrial membrane as part of Complex II.[[71]](https://en.wikipedia.org/wiki/Mitochondrion#cite_note-71) The citric acid cycle oxidizes the acetyl-CoA to carbon dioxide, and, in the process, produces reduced cofactors (three molecules of [NADH](https://en.wikipedia.org/wiki/NADH) and one molecule of [FADH2](https://en.wikipedia.org/wiki/FADH2)) that are a source of electrons for the [*electron transport chain*](https://en.wikipedia.org/wiki/Electron_transport_chain), and a molecule of [GTP](https://en.wikipedia.org/wiki/Guanosine_triphosphate) (that is readily converted to an ATP).[[14]](https://en.wikipedia.org/wiki/Mitochondrion#cite_note-Voet-14)

#### NADH and FADH2: the electron transport chain

*Main articles:*[*Electron transport chain*](https://en.wikipedia.org/wiki/Electron_transport_chain)*and*[*Oxidative phosphorylation*](https://en.wikipedia.org/wiki/Oxidative_phosphorylation)

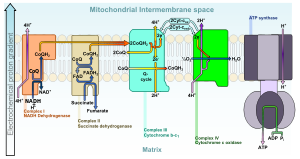
[](https://en.wikipedia.org/wiki/File:Electron_transport_chain.svg)

Diagram of the electron transport chain in the mitonchondrial intermembrane space

The redox energy from NADH and FADH2 is transferred to oxygen (O2) in several steps via the electron transport chain. These energy-rich molecules are produced within the matrix via the citric acid cycle but are also produced in the cytoplasm by [glycolysis](https://en.wikipedia.org/wiki/Glycolysis). [Reducing equivalents](https://en.wikipedia.org/wiki/Reducing_equivalent) from the cytoplasm can be imported via the [malate-aspartate shuttle](https://en.wikipedia.org/wiki/Malate-aspartate_shuttle) system of [antiporter](https://en.wikipedia.org/wiki/Antiporter) proteins or feed into the electron transport chain using a [glycerol phosphate shuttle](https://en.wikipedia.org/wiki/Glycerol_phosphate_shuttle).[[14]](https://en.wikipedia.org/wiki/Mitochondrion#cite_note-Voet-14) [Protein complexes](https://en.wikipedia.org/wiki/Electron_transport_chain#Mitochondrial_redox_carriers) in the inner membrane ([NADH dehydrogenase (ubiquinone)](https://en.wikipedia.org/wiki/NADH_dehydrogenase_(ubiquinone)),[cytochrome c reductase](https://en.wikipedia.org/wiki/Coenzyme_Q_-_cytochrome_c_reductase), and [cytochrome c oxidase](https://en.wikipedia.org/wiki/Cytochrome_c_oxidase)) perform the transfer and the incremental release of energy is used to pump [protons](https://en.wikipedia.org/wiki/Hydrogen_ion) (H+) into the intermembrane space. This process is efficient, but a small percentage of electrons may prematurely reduce oxygen, forming [reactive oxygen species](https://en.wikipedia.org/wiki/Reactive_oxygen_species) such as [superoxide](https://en.wikipedia.org/wiki/Superoxide).[[14]](https://en.wikipedia.org/wiki/Mitochondrion#cite_note-Voet-14) This can cause [oxidative stress](https://en.wikipedia.org/wiki/Oxidative_stress) in the mitochondria and may contribute to the decline in mitochondrial function associated

**Endoplasmic reticulum**

The **endoplasmic reticulum** (**ER**) is a type of [organelle](https://en.wikipedia.org/wiki/Organelle) in the [eukaryotic cells](https://en.wikipedia.org/wiki/Eukaryote) that forms an interconnected network of flattened, membrane-enclosed sacs or tube-like structures known as [cisternae](https://en.wikipedia.org/wiki/Cisterna). The membranes of the ER are continuous with the outer [nuclear membrane](https://en.wikipedia.org/wiki/Nuclear_membrane). Endoplasmic reticulum occurs in most types of eukaryotic cells, including [*Giardia*](https://en.wikipedia.org/wiki/Giardia),[[1]](https://en.wikipedia.org/wiki/Endoplasmic_reticulum#cite_note-1) but is absent from [red blood cells](https://en.wikipedia.org/wiki/Red_blood_cell) and [spermatozoa](https://en.wikipedia.org/wiki/Spermatozoa). There are two types of endoplasmic reticulum: rough and smooth. The outer ([cytosolic](https://en.wikipedia.org/wiki/Cytosol)) face of the rough endoplasmic reticulum is studded with[ribosomes](https://en.wikipedia.org/wiki/Ribosome) that are the sites of [protein synthesis](https://en.wikipedia.org/wiki/Protein_synthesis). The rough endoplasmic reticulum is especially prominent in cells such as [hepatocytes](https://en.wikipedia.org/wiki/Hepatocyte). The smooth endoplasmic reticulum lacks ribosomes and functions in [lipid](https://en.wikipedia.org/wiki/Lipid) manufacture and metabolism, the production of [steroid hormones](https://en.wikipedia.org/wiki/Steroid_hormone), and [detoxification](https://en.wikipedia.org/wiki/Detoxification).[[2]](https://en.wikipedia.org/wiki/Endoplasmic_reticulum#cite_note-bscb-2) The smooth ER is especially abundant in mammalian [liver](https://en.wikipedia.org/wiki/Liver) and [gonad](https://en.wikipedia.org/wiki/Gonad) cells. The lacy membranes of the endoplasmic reticulum were first seen in 1945 using [electron microscopy](https://en.wikipedia.org/wiki/Electron_microscopy)

The general structure of the endoplasmic reticulum is a network of membranes called [cisternae](https://en.wikipedia.org/wiki/Cisterna). These sac-like structures are held together by the [cytoskeleton](https://en.wikipedia.org/wiki/Cytoskeleton). The [phospholipid membrane](https://en.wikipedia.org/wiki/Phospholipid_membrane) encloses the cisternal space (or lumen), which is continuous with the [perinuclear space](https://en.wikipedia.org/wiki/Perinuclear_space) but separate from the [cytosol](https://en.wikipedia.org/wiki/Cytosol). The functions of the endoplasmic reticulum can be summarized as the synthesis and export of proteins and membrane lipids, but varies between ER and cell type and cell function. The quantity of both rough and smooth endoplasmic reticulum in a cell can slowly interchange from one type to the other, depending on the changing metabolic activities of the cell. Transformation can include embedding of new proteins in membrane as well as structural changes. Changes in protein content may occur without noticeable structural changes.

**Rough endoplasmic reticulum**- the Rough endoplasmic reticulum has ribosomes on their surface, therefore they are mainly involved in protein synthesis

**Smooth endoplasmic reticulum-** the smooth endoplasmic reticulum do not have ribosomes on their surface, therefore their surface are smooth.

## Functions

The endoplasmic reticulum serves many general functions, including the folding of protein molecules in sacs called[cisternae](https://en.wikipedia.org/wiki/Cisterna) and the transport of synthesized proteins in [vesicles](https://en.wikipedia.org/wiki/Golgi_apparatus#Vesicular_transport) to the [Golgi apparatus](https://en.wikipedia.org/wiki/Golgi_apparatus). Correct folding of newly made proteins is made possible by several endoplasmic reticulum [chaperone](https://en.wikipedia.org/wiki/Chaperone_(protein)) proteins, including [protein disulfide isomerase](https://en.wikipedia.org/wiki/Protein_disulfide_isomerase)(PDI), ERp29, the [Hsp70](https://en.wikipedia.org/wiki/Hsp70) family member [BiP/Grp78](https://en.wikipedia.org/wiki/Binding_immunoglobulin_protein), [calnexin](https://en.wikipedia.org/wiki/Calnexin), [calreticulin](https://en.wikipedia.org/wiki/Calreticulin), and the peptidylpropyl isomerase family. Only properly folded proteins are transported from the rough ER to the Golgi apparatus – unfolded proteins cause an [unfolded protein response](https://en.wikipedia.org/wiki/Unfolded_protein_response) as a stress response in the ER. Disturbances in [redox](https://en.wikipedia.org/wiki/Redox) regulation, calcium regulation, glucose deprivation, and viral infection[[16]](https://en.wikipedia.org/wiki/Endoplasmic_reticulum#cite_note-16) or the over-expression of proteins[[17]](https://en.wikipedia.org/wiki/Endoplasmic_reticulum#cite_note-pmid22510960-17) can lead to [endoplasmic reticulum stress response](https://en.wikipedia.org/wiki/XBP1#Endoplasmic_reticulum_stress_response) (ER stress), a state in which the folding of proteins slows, leading to an increase in [unfolded proteins](https://en.wikipedia.org/wiki/Unfolded_protein_response). This stress is emerging as a potential cause of damage in hypoxia/ischemia, insulin resistance, and other disorders.[[18]](https://en.wikipedia.org/wiki/Endoplasmic_reticulum#cite_note-18)

### Protein transport

Secretory proteins, mostly [glycoproteins](https://en.wikipedia.org/wiki/Glycoproteins), are moved across the endoplasmic reticulum membrane. Proteins that are transported by the endoplasmic reticulum throughout the cell are marked with an address tag called a [signal sequence](https://en.wikipedia.org/wiki/Signal_peptide). The N-terminus (one end) of a [polypeptide](https://en.wikipedia.org/wiki/Polypeptide) chain (i.e., a protein) contains a few [amino acids](https://en.wikipedia.org/wiki/Amino_acid) that work as an address tag, which are removed when the polypeptide reaches its destination. Nascent peptides reach the ER via the [Translocon](https://en.wikipedia.org/wiki/Translocon), a membrane-embedded multiprotein complex. Proteins that are destined for places outside the endoplasmic reticulum are packed into transport [vesicles](https://en.wikipedia.org/wiki/Vesicle_(biology)) and moved along the[cytoskeleton](https://en.wikipedia.org/wiki/Cytoskeleton) toward their destination. In human fibroblasts, the ER is always co-distributed with microtubules and the depolymerisation of the latter cause its co-aggregation with mitochondria, which are also associated with the ER

The endoplasmic reticulum is also part of a protein sorting pathway. It is, in essence, the transportation system of the eukaryotic cell. The majority of its resident proteins are retained within it through a retention [motif](https://en.wikipedia.org/wiki/Structural_motif). This motif is composed of four amino acids at the end of the protein sequence. The most common retention sequences are [KDEL](https://en.wikipedia.org/wiki/KDEL_(amino_acid_sequence)) for lumen located proteins and [KKXX](https://en.wikipedia.org/wiki/KKXX_(amino_acid_sequence)) for transmembrane protein.[[20]](https://en.wikipedia.org/wiki/Endoplasmic_reticulum#cite_note-20) However, variations of KDEL and KKXX do occur, and other sequences can also give rise to endoplasmic reticulum retention. It is not known whether such variation can lead to sub-ER localizations. There are three KDEL ([1](https://en.wikipedia.org/wiki/KDELR1), [2](https://en.wikipedia.org/wiki/KDELR2) and [3](https://en.wikipedia.org/wiki/KDELR3)) receptors in mammalian cells, and they have a very high degree of sequence identity. The functional differences between these receptors remain to be established.

**Golgi Apparatus**

The **Golgi apparatus** ([/ˈɡoʊldʒiː/](https://en.wikipedia.org/wiki/Help:IPA_for_English)), also known as the **Golgi complex**, **Golgi body**, or simply the **Golgi**, is an[organelle](https://en.wikipedia.org/wiki/Organelle) found in most [eukaryotic](https://en.wikipedia.org/wiki/Eukaryotic) [cells](https://en.wikipedia.org/wiki/Cell_(biology)).[[1]](https://en.wikipedia.org/wiki/Golgi_apparatus#cite_note-isbn3-211-76309-0-1) It was identified in 1897 by the Italian scientist [Camillo Golgi](https://en.wikipedia.org/wiki/Camillo_Golgi) and named after him in 1898.[[2]](https://en.wikipedia.org/wiki/Golgi_apparatus#cite_note-pmid9865849-2)

Part of the cellular [endomembrane system](https://en.wikipedia.org/wiki/Endomembrane_system), the Golgi apparatus packages proteins into membrane-bound [vesicles](https://en.wikipedia.org/wiki/Vesicle_(biology_and_chemistry))inside the cell before the vesicles are sent to their destination. The Golgi apparatus resides at the intersection of the secretory, lysosomal, and endocytic pathways. It is of particular importance in processing [proteins](https://en.wikipedia.org/wiki/Protein) for [secretion](https://en.wikipedia.org/wiki/Secretion), containing a set of [glycosylation](https://en.wikipedia.org/wiki/Glycosylation) [enzymes](https://en.wikipedia.org/wiki/Enzyme) that attach various sugar monomers to proteins as the proteins move through the apparatus.

**Structure-**

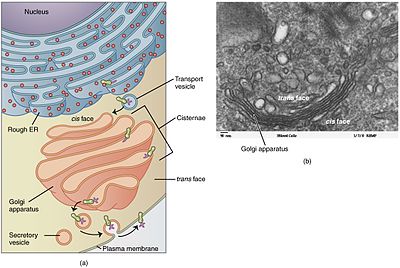
in most [eukaryotes](https://en.wikipedia.org/wiki/Eukaryote), the Golgi apparatus is made up of a series of compartments consisting of two main networks: the *cis* Golgi network (CGN) and the *trans* Golgi network (TGN). The CGN is a collection of fused, flattened membrane-enclosed disks known as [cisternae](https://en.wikipedia.org/wiki/Cisternae) (singular:*cisterna*), originating from vesicular clusters that bud off the [endoplasmic reticulum](https://en.wikipedia.org/wiki/Endoplasmic_reticulum). A mammalian cell typically contains 40 to 100 stacks.[[8]](https://en.wikipedia.org/wiki/Golgi_apparatus#cite_note-pmid18385516-8) Between four and eight cisternae are usually present in a stack; however, in some [protists](https://en.wikipedia.org/wiki/Protists) as many as sixty cisternae have been observed.[[4]](https://en.wikipedia.org/wiki/Golgi_apparatus#cite_note-url_molexpress-4) This collection of cisternae is broken down into *cis*, medial, and *trans* compartments. The TGN is the final cisternal structure, from which[proteins](https://en.wikipedia.org/wiki/Protein) are packaged into [vesicles](https://en.wikipedia.org/wiki/Vesicle_(biology_and_chemistry)) destined to [lysosomes](https://en.wikipedia.org/wiki/Lysosome), secretory vesicles, or the cell surface. The TGN is usually positioned adjacent to the stacks of the Golgi apparatus, but can also be separate from the stacks. The TGN may act as an early [endosome](https://en.wikipedia.org/wiki/Endosome) in [yeast](https://en.wikipedia.org/wiki/Yeast) and [plants](https://en.wikipedia.org/wiki/Plant).[[6]](https://en.wikipedia.org/wiki/Golgi_apparatus#cite_note-pmid20605430-6)

There are structural and organizational differences in the Golgi apparatus among eukaryotes. In some yeasts, Golgi stacking is not observed. [*Pichia pastoris*](https://en.wikipedia.org/wiki/Pichia_pastoris) does have stacked Golgi, while[*Saccharomyces cerevisiae*](https://en.wikipedia.org/wiki/Saccharomyces_cerevisiae) does not.[[6]](https://en.wikipedia.org/wiki/Golgi_apparatus#cite_note-pmid20605430-6) In plants, the individual stacks of the Golgi apparatus seem to operate independently

The Golgi apparatus tends to be larger and more numerous in cells that synthesize and secrete large amounts of substances; for example, the [antibody](https://en.wikipedia.org/wiki/Antibody)-secreting[plasma B cells](https://en.wikipedia.org/wiki/Plasma_B_cell) of the immune system have prominent Golgi complexes.

In all eukaryotes, each cisternal stack has a *cis* entry face and a *trans* exit face. These faces are characterized by unique morphology and [biochemistry](https://en.wikipedia.org/wiki/Biochemistry).[[9]](https://en.wikipedia.org/wiki/Golgi_apparatus#cite_note-pmid23881164-9) Within individual stacks are assortments of [enzymes](https://en.wikipedia.org/wiki/Enzyme) responsible for selectively modifying protein cargo. These modifications influence the fate of the protein. The compartmentalization of the Golgi apparatus is advantageous for separating enzymes, thereby maintaining consecutive and selective processing steps: enzymes catalyzing early modifications are gathered in the *cis* face cisternae, and enzymes catalyzing later modifications are found in *trans* face cisternae of the Golgi stacks

## Function

[](https://en.wikipedia.org/wiki/File:0314_Golgi_Apparatus.jpg)

The Golgi apparatus (salmon pink) in context of the secretory pathway.

The Golgi apparatus is a major collection and dispatch station of protein products received from the [endoplasmic reticulum](https://en.wikipedia.org/wiki/Endoplasmic_reticulum) (ER). Proteins synthesized in the ER are packaged into [vesicles](https://en.wikipedia.org/wiki/Vesicle_(biology_and_chemistry)), which then fuse with the Golgi apparatus. These cargo proteins are modified and destined for secretion via [exocytosis](https://en.wikipedia.org/wiki/Exocytosis) or for use in the cell. In this respect, the Golgi can be thought of as similar to a post office: it packages and labels items which it then sends to different parts of the cell or to the [extracellular space](https://en.wikipedia.org/wiki/Extracellular_space). The Golgi apparatus is also involved in [lipid](https://en.wikipedia.org/wiki/Lipid) transport and[lysosome](https://en.wikipedia.org/wiki/Lysosome) formation.[[10]](https://en.wikipedia.org/wiki/Golgi_apparatus#cite_note-Campbell-10)

The structure and function of the Golgi apparatus are intimately linked. Individual stacks have different assortments of enzymes, allowing for progressive processing of cargo proteins as they travel from the cist ernae to the trans Golgi face.[[5]](https://en.wikipedia.org/wiki/Golgi_apparatus#cite_note-Alberts-5)[[9]](https://en.wikipedia.org/wiki/Golgi_apparatus#cite_note-pmid23881164-9) Enzymatic reactions within the Golgi stacks occur exclusively near its membrane surfaces, where enzymes are anchored. This feature is in contrast to the ER, which has soluble proteins and enzymes in its [lumen](https://en.wikipedia.org/wiki/Lumen_(anatomy)). Much of the enzymatic processing is [post-translational modification](https://en.wikipedia.org/wiki/Post-translational_modification) of proteins. For example, phosphorylation of[oligosaccharides](https://en.wikipedia.org/wiki/Oligosaccharide) on lysosomal proteins occurs in the early CGN.[[5]](https://en.wikipedia.org/wiki/Golgi_apparatus#cite_note-Alberts-5) *Cis* [cisterna](https://en.wikipedia.org/wiki/Cisterna) are associated with the removal of [mannose](https://en.wikipedia.org/wiki/Mannose) residues.[[5]](https://en.wikipedia.org/wiki/Golgi_apparatus#cite_note-Alberts-5)[[9]](https://en.wikipedia.org/wiki/Golgi_apparatus#cite_note-pmid23881164-9) Removal of mannose residues and addition of [N-acetylglucosamine](https://en.wikipedia.org/wiki/N-acetylglucosamine) occur in medial cisternae.[[5]](https://en.wikipedia.org/wiki/Golgi_apparatus#cite_note-Alberts-5) Addition of [galactose](https://en.wikipedia.org/wiki/Galactose) and [sialic acid](https://en.wikipedia.org/wiki/Sialic_acid) occurs in the*trans* cisternae.[[5]](https://en.wikipedia.org/wiki/Golgi_apparatus#cite_note-Alberts-5) [Sulfation](https://en.wikipedia.org/wiki/Sulfation) of [tyrosines](https://en.wikipedia.org/wiki/Tyrosine) and [carbohydrates](https://en.wikipedia.org/wiki/Carbohydrate) occurs within the TGN.[[5]](https://en.wikipedia.org/wiki/Golgi_apparatus#cite_note-Alberts-5) Other general post-translational modifications of proteins include the addition of carbohydrates ([glycosylation](https://en.wikipedia.org/wiki/Glycosylation))[[11]](https://en.wikipedia.org/wiki/Golgi_apparatus#cite_note-Flynne2008-11) and phosphates ([phosphorylation](https://en.wikipedia.org/wiki/Phosphorylation)). Protein modifications may form a [signal sequence](https://en.wikipedia.org/wiki/Signal_peptide) that determines the final destination of the protein. For example, the Golgi apparatus adds a [mannose-6-phosphate](https://en.wikipedia.org/wiki/Mannose-6-phosphate) label to proteins destined for [lysosomes](https://en.wikipedia.org/wiki/Lysosome). Another important function of the Golgi apparatus is in the formation of [proteoglycans](https://en.wikipedia.org/wiki/Proteoglycans). Enzymes in the Golgi append proteins to [glycosaminoglycans](https://en.wikipedia.org/wiki/Glycosaminoglycan), thus creating proteoglycans.[[12]](https://en.wikipedia.org/wiki/Golgi_apparatus#cite_note-pmid10633071-12) Glycosaminoglycans are long unbranched [polysaccharide](https://en.wikipedia.org/wiki/Polysaccharide) molecules present in the [extracellular matrix](https://en.wikipedia.org/wiki/Extracellular_matrix) of animals.

|  |  |  |
| --- | --- | --- |
| **Types** | **Description** | **Example** |
| **Exocytotic vesicles*(constitutive)*** | Vesicle contains proteins destined for [extracellular](https://en.wikipedia.org/wiki/Extracellular) release. After packaging, the vesicles bud off and immediately move towards the[plasma membrane](https://en.wikipedia.org/wiki/Plasma_membrane), where they fuse and release the contents into the extracellular space in a process known as [*constitutive secretion*](https://en.wikipedia.org/wiki/Secretory_pathway). | [Antibody](https://en.wikipedia.org/wiki/Antibody) release by activated[plasma B cells](https://en.wikipedia.org/wiki/Plasma_B_cell) |
| **Secretory vesicles*(regulated)*** | Vesicles contain proteins destined for extracellular release. After packaging, the vesicles bud off and are stored in the cell until a signal is given for their release. When the appropriate signal is received they move toward the membrane and fuse to release their contents. This process is known as [*regulated secretion*](https://en.wikipedia.org/wiki/Secretory_pathway). | [Neurotransmitter](https://en.wikipedia.org/wiki/Neurotransmitter)release from[neurons](https://en.wikipedia.org/wiki/Neuron) |
| **Lysosomal vesicles** | Vesicles contain proteins and ribosomes destined for the [lysosome](https://en.wikipedia.org/wiki/Lysosome), a degradative [organelle](https://en.wikipedia.org/wiki/Organelle) containing many acid [hydrolases](https://en.wikipedia.org/wiki/Hydrolase), or to lysosome-like storage organelles. These proteins include both digestive enzymes and membrane proteins. The vesicle first fuses with the [late endosome](https://en.wikipedia.org/wiki/Endosome), and the contents are then transferred to the lysosome via unknown mechanisms. | Digestive[proteases](https://en.wikipedia.org/wiki/Protease)destined for the[lysosome](https://en.wikipedia.org/wiki/Lysosome) |

**Lysosome**-

A **lysosome** is a membrane-bounded [organelle](https://en.wikipedia.org/wiki/Organelle) found in most animal [cells](https://en.wikipedia.org/wiki/Cell_(biology)). They are spherical [vesicles](https://en.wikipedia.org/wiki/Vesicle_(biology_and_chemistry)) which contain [hydrolytic](https://en.wikipedia.org/wiki/Hydrolysis) [enzymes](https://en.wikipedia.org/wiki/Enzyme) that can break down virtually all kinds of [biomolecules](https://en.wikipedia.org/wiki/Biomolecules). Simply stated, a lysosome is a type of vesicle with specific composition, of both its [membrane proteins](https://en.wikipedia.org/wiki/Membrane_protein), and proteins of its [lumen](https://en.wikipedia.org/wiki/Lumen_(anatomy)). The lumen's pH (4.5 - 5.0)[[1]](https://en.wikipedia.org/wiki/Lysosome#cite_note-1) is optimal for the enzymes involved in hydrolysis, analogous to the activity of the [stomach](https://en.wikipedia.org/wiki/Stomach). Besides degradation of polymers, the lysosome is involved in various cell processes, including secretion, [plasma membrane](https://en.wikipedia.org/wiki/Plasma_membrane)repair, [cell signalling](https://en.wikipedia.org/wiki/Cell_signalling), and [energy metabolism](https://en.wikipedia.org/wiki/Energy_metabolism).[[2]](https://en.wikipedia.org/wiki/Lysosome#cite_note-2)

The lysosomes also act as the waste disposal system of the cell by digesting unwanted materials in the [cytoplasm](https://en.wikipedia.org/wiki/Cytoplasm), both from outside of the cell and obsolete components inside the cell. Material from the outside of the cell is taken-up through [endocytosis](https://en.wikipedia.org/wiki/Endocytosis), while material from the inside of the cell is digested through [autophagy](https://en.wikipedia.org/wiki/Autophagy). Their sizes can be very different—the biggest ones can be more than 10 times bigger than the smallest ones.[[3]](https://en.wikipedia.org/wiki/Lysosome#cite_note-3) They were discovered and named by Belgian biologist [Christian de Duve](https://en.wikipedia.org/wiki/Christian_de_Duve), who eventually received the [Nobel Prize in Physiology or Medicine](https://en.wikipedia.org/wiki/Nobel_Prize_in_Physiology_or_Medicine) in 1974.

Lysosomes are known to contain more than 50 different enzymes. Enzymes of the lysosomes are synthesised in the [rough endoplasmic reticulum](https://en.wikipedia.org/wiki/Rough_endoplasmic_reticulum). The enzymes are imported from the [Golgi apparatus](https://en.wikipedia.org/wiki/Golgi_apparatus) in small vesicles, which fuse with larger acidic vesicles. Enzymes destined for a lysosome are specifically tagged with the molecule [mannose 6-phosphate](https://en.wikipedia.org/wiki/Mannose_6-phosphate), so that they are properly sorted into acidified vesicles

**Structure and functions**- Lysosomes contain a variety of enzymes in order to be able to break down the variety of biomolecules engulfed by the cell, including [peptides](https://en.wikipedia.org/wiki/Peptides), [nucleic acids](https://en.wikipedia.org/wiki/Nucleic_acid),[carbohydrates](https://en.wikipedia.org/wiki/Carbohydrate), and [lipids](https://en.wikipedia.org/wiki/Lipid). The enzymes responsible for this hydrolysis require an acidic environment for optimal activity.

In addition to being able to break down polymers, lysosomes are capable of fusing with other organelles & digesting large structures or cellular debris; through cooperation with [phagosomes](https://en.wikipedia.org/wiki/Phagosome), they are able to conduct [autophagy](https://en.wikipedia.org/wiki/Autophagy), clearing out damaged structures. Similarly, they are able to break-down virus particles or bacteria in [phagocytosis](https://en.wikipedia.org/wiki/Phagocytosis) of [macrophages](https://en.wikipedia.org/wiki/Macrophage).

The size of lysosomes varies from 0.1–1.2 [μm](https://en.wikipedia.org/wiki/Micrometre).[[12]](https://en.wikipedia.org/wiki/Lysosome#cite_note-12) At [pH](https://en.wikipedia.org/wiki/PH) 4.5 - 5, the interior of the lysosomes is acidic compared to the slightly basic [cytosol](https://en.wikipedia.org/wiki/Cytosol) (pH 7.2). The lysosomal membrane protects the cytosol, and therefore the rest of the [cell](https://en.wikipedia.org/wiki/Cell_(biology)), from the [degradative enzymes](https://en.wikipedia.org/wiki/Degradative_enzyme) within the lysosome. The cell is additionally protected from any lysosomal acid [hydrolases](https://en.wikipedia.org/wiki/Hydrolases) that drain into the cytosol, as these enzymes are pH-sensitive and do not function well or at all in the alkaline environment of the cytosol. This ensures that cytosolic molecules and organelles are not destroyed in case there is leakage of the hydrolytic enzymes from the lysosome.

The lysosome maintains its pH differential by pumping in [protons](https://en.wikipedia.org/wiki/Proton) (H+ ions) from the cytosol across the [membrane](https://en.wikipedia.org/wiki/Cell_membrane) via [proton pumps](https://en.wikipedia.org/wiki/Proton_pump) and chloride [ion channels](https://en.wikipedia.org/wiki/Ion_channel).[Vacuolar H+-ATPases](https://en.wikipedia.org/wiki/V-ATPase) are responsible for transport of protons, while the counter transport of chloride ions is performed by [ClC-7](https://en.wikipedia.org/wiki/CLC_(gene)) Cl−/H+ antiporter. In this way a steady acidic environment is maintained.[[13]](https://en.wikipedia.org/wiki/Lysosome#cite_note-13)[[14]](https://en.wikipedia.org/wiki/Lysosome#cite_note-14)

It sources its versatile capacity for degradation by import of enzymes with specificity for different substrates; [cathepsins](https://en.wikipedia.org/wiki/Cathepsin) are the major class of hydrolytic enzymes, while lysosomal alpha-glucosidase (GAA) is responsible for carbohydrates, and [ACP2](https://en.wikipedia.org/wiki/ACP2) is necessary to release phosphate groups of phospholipid.

**Nucleus**

n [cell biology](https://en.wikipedia.org/wiki/Cell_biology), the **nucleus** (pl. *nuclei*; from [Latin](https://en.wikipedia.org/wiki/Latin) *nucleus* or *nuculeus*, meaning kernel) is a [membrane](https://en.wikipedia.org/wiki/Biological_membrane)-enclosed [organelle](https://en.wikipedia.org/wiki/Organelle) found in [eukaryotic](https://en.wikipedia.org/wiki/Eukaryote) [cells](https://en.wikipedia.org/wiki/Cell_(biology)). Eukaryotes usually have a single nucleus, but a few cell types, such as mammalian red blood cells, have [no nuclei](https://en.wikipedia.org/wiki/Cell_nucleus#Anucleated_cells), and a few others have [many](https://en.wikipedia.org/wiki/Multinucleate).

Cell nuclei contain most of the cell's [genetic material](https://en.wikipedia.org/wiki/Genetics), organized as multiple long linear [DNA](https://en.wikipedia.org/wiki/DNA) molecules in[complex](https://en.wikipedia.org/wiki/Multiprotein_complex) with a large variety of [proteins](https://en.wikipedia.org/wiki/Protein), such as [histones](https://en.wikipedia.org/wiki/Histone), to form [chromosomes](https://en.wikipedia.org/wiki/Chromosome). The [genes](https://en.wikipedia.org/wiki/Gene) within these[chromosomes](https://en.wikipedia.org/wiki/Chromosome) are the cell's [nuclear genome](https://en.wikipedia.org/wiki/Genome) and are [structured](https://en.wikipedia.org/wiki/Eukaryotic_Nuclear_Organization) in such a way to promote cell function. The nucleus maintains the integrity of genes and controls the activities of the cell by regulating [gene expression](https://en.wikipedia.org/wiki/Gene_expression)—the nucleus is, therefore, the control center of the cell. The main structures making up the nucleus are the [nuclear envelope](https://en.wikipedia.org/wiki/Nuclear_envelope), a double membrane that encloses the entire organelle and isolates its contents from the cellular [cytoplasm](https://en.wikipedia.org/wiki/Cytoplasm), and the [nuclear matrix](https://en.wikipedia.org/wiki/Nuclear_matrix) (which includes the [nuclear lamina](https://en.wikipedia.org/wiki/Nuclear_lamina)), a network within the nucleus that adds mechanical support, much like the [cytoskeleton](https://en.wikipedia.org/wiki/Cytoskeleton), which supports the cell as a whole.

Because the nuclear membrane is impermeable to large molecules, [nuclear pores](https://en.wikipedia.org/wiki/Nuclear_pore) are required that regulate [nuclear transport](https://en.wikipedia.org/wiki/Nuclear_transport) of molecules across the envelope. The pores cross both nuclear membranes, providing a [channel](https://en.wikipedia.org/wiki/Ion_channel) through which larger molecules must be actively transported by carrier proteins while allowing free movement of small molecules and [ions](https://en.wikipedia.org/wiki/Ion). Movement of large molecules such as proteins and[RNA](https://en.wikipedia.org/wiki/RNA) through the pores is required for both gene expression and the maintenance of chromosomes. Although the interior of the nucleus does not contain any membrane-bound sub compartments, its contents are not uniform, and a number of *sub-nuclear bodies* exist, made up of unique proteins, RNA molecules, and particular parts of the chromosomes. The best-known of these is the [nucleolus](https://en.wikipedia.org/wiki/Nucleolus), which is mainly involved in the assembly of[ribosomes](https://en.wikipedia.org/wiki/Ribosome). After being produced in the nucleolus, ribosomes are exported to the cytoplasm where they translate [mRNA](https://en.wikipedia.org/wiki/MRNA)..

The nucleus is the largest cellular [organelle](https://en.wikipedia.org/wiki/Organelle) in animal cells.[[5]](https://en.wikipedia.org/wiki/Cell_nucleus#cite_note-Lodish-5) In [mammalian](https://en.wikipedia.org/wiki/Mammal) cells, the average diameter of the nucleus is approximately 6 [micrometres](https://en.wikipedia.org/wiki/Micrometre) (µm), which occupies about 10% of the total cell volume.[[6]](https://en.wikipedia.org/wiki/Cell_nucleus#cite_note-MBoC-6) The viscous liquid within it is called [nucleoplasm](https://en.wikipedia.org/wiki/Nucleoplasm), and is similar in composition to the [cytosol](https://en.wikipedia.org/wiki/Cytosol) found outside the nucleus.[[7]](https://en.wikipedia.org/wiki/Cell_nucleus#cite_note-7) It appears as a dense, roughly spherical or irregular organelle.

**Nuclear envelope and pores**

*Main articles:*[*Nuclear envelope*](https://en.wikipedia.org/wiki/Nuclear_envelope)*and*[*Nuclear pores*](https://en.wikipedia.org/wiki/Nuclear_pores)

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| --- | --- |
| [https://upload.wikimedia.org/wikipedia/commons/thumb/3/38/Diagram_human_cell_nucleus.svg/280px-Diagram_human_cell_nucleus.svg.png](https://en.wikipedia.org/wiki/File:Diagram_human_cell_nucleus.svg)  The eukaryotic cell nucleus. Visible in this diagram are the [ribosome](https://en.wikipedia.org/wiki/Ribosome)-studded [double membranes](https://en.wikipedia.org/wiki/Cell_membrane) of the nuclear envelope, the [DNA](https://en.wikipedia.org/wiki/DNA)(complexed as [chromatin](https://en.wikipedia.org/wiki/Chromatin)), and the [nucleolus](https://en.wikipedia.org/wiki/Nucleolus). Within the cell nucleus is a viscous liquid called[nucleoplasm](https://en.wikipedia.org/wiki/Nucleoplasm), similar to the cytoplasm found outside the nucleus. | [https://upload.wikimedia.org/wikipedia/commons/thumb/c/c8/NuclearPore_crop.svg/250px-NuclearPore_crop.svg.png](https://en.wikipedia.org/wiki/File:NuclearPore_crop.svg)  A cross section of a [nuclear pore](https://en.wikipedia.org/wiki/Nuclear_pore) on the surface of the [nuclear envelope](https://en.wikipedia.org/wiki/Nuclear_envelope) (1). Other diagram labels show (2) the outer ring, (3) spokes, (4) basket, and (5) filaments. |

The [nuclear envelope](https://en.wikipedia.org/wiki/Nuclear_envelope), otherwise known as nuclear membrane, consists of two [cellular membranes](https://en.wikipedia.org/wiki/Cell_membrane), an inner and an outer membrane, arranged parallel to one another and separated by 10 to 50[nanometres](https://en.wikipedia.org/wiki/Nanometre) (nm). The nuclear envelope completely encloses the nucleus and separates the cell's genetic material from the surrounding cytoplasm, serving as a barrier to prevent[macromolecules](https://en.wikipedia.org/wiki/Macromolecule) from diffusing freely between the nucleoplasm and the cytoplasm.[[8]](https://en.wikipedia.org/wiki/Cell_nucleus#cite_note-Paine-8) The outer nuclear membrane is continuous with the membrane of the [rough endoplasmic reticulum](https://en.wikipedia.org/wiki/Rough_endoplasmic_reticulum) (RER), and is similarly studded with [ribosomes](https://en.wikipedia.org/wiki/Ribosomes).[[8]](https://en.wikipedia.org/wiki/Cell_nucleus#cite_note-Paine-8) The space between the membranes is called the perinuclear space and is continuous with the RER [lumen](https://en.wikipedia.org/wiki/Lumen_(anatomy)).

[Nuclear pores](https://en.wikipedia.org/wiki/Nuclear_pores), which provide aqueous channels through the envelope, are composed of multiple proteins, collectively referred to as [nucleoporins](https://en.wikipedia.org/wiki/Nucleoporin). The pores are about 125 million [daltons](https://en.wikipedia.org/wiki/Atomic_mass_unit) in [molecular weight](https://en.wikipedia.org/wiki/Molecular_weight) and consist of around 50 (in [yeast](https://en.wikipedia.org/wiki/Yeast)) to several hundred proteins (in [vertebrates](https://en.wikipedia.org/wiki/Vertebrate)).[[5]](https://en.wikipedia.org/wiki/Cell_nucleus#cite_note-Lodish-5) The pores are 100 nm in total diameter; however, the gap through which molecules freely diffuse is only about 9 nm wide, due to the presence of regulatory systems within the center of the pore. This size selectively allows the passage of small water-soluble molecules while preventing larger molecules, such as [nucleic acids](https://en.wikipedia.org/wiki/Nucleic_acid) and larger proteins, from inappropriately entering or exiting the nucleus. These large molecules must be actively transported into the nucleus instead

**Nuclear lamina**

*Main article:*[*Nuclear lamina*](https://en.wikipedia.org/wiki/Nuclear_lamina)

In animal cells, two networks of [intermediate filaments](https://en.wikipedia.org/wiki/Intermediate_filaments) provide the nucleus with mechanical support: The [nuclear lamina](https://en.wikipedia.org/wiki/Nuclear_lamina) forms an organized meshwork on the internal face of the envelope, while less organized support is provided on the cytosolic face of the envelope. Both systems provide structural support for the nuclear envelope and anchoring sites for chromosomes and nuclear pores.[[6]](https://en.wikipedia.org/wiki/Cell_nucleus#cite_note-MBoC-6)

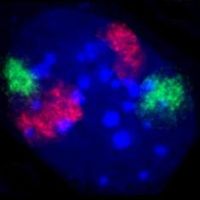
The nuclear lamina is composed mostly of [lamin](https://en.wikipedia.org/wiki/Lamin) proteins. Like all proteins, lamins are synthesized in the cytoplasm and later transported to the nucleus interior, where they are assembled before being incorporated into the existing network of nuclear lamina.[[12]](https://en.wikipedia.org/wiki/Cell_nucleus#cite_note-Sturrman-12)[[13]](https://en.wikipedia.org/wiki/Cell_nucleus#cite_note-Goldman-13) Lamins found on the cytosolic face of the membrane, such as[emerin](https://en.wikipedia.org/wiki/Emerin) and [nesprin](https://en.wikipedia.org/wiki/Nesprin), bind to the cytoskeleton to provide structural support. Lamins are also found inside the nucleoplasm where they form another regular structure, known as the *nucleoplasmic veil*,[[14]](https://en.wikipedia.org/wiki/Cell_nucleus#cite_note-RGoldman-14) that is visible using [fluorescence microscopy](https://en.wikipedia.org/wiki/Fluorescence_microscopy). The actual function of the veil is not clear, although it is excluded from the [nucleolus](https://en.wikipedia.org/wiki/Nucleolus)and is present during [interphase](https://en.wikipedia.org/wiki/Interphase).[[15]](https://en.wikipedia.org/wiki/Cell_nucleus#cite_note-Moir-15) Lamin structures that make up the veil, such as [LEM3](https://en.wikipedia.org/wiki/LEM_domain-containing_protein_3), bind [chromatin](https://en.wikipedia.org/wiki/Chromatin) and disrupting their structure inhibits transcription of protein-coding genes.[[16]](https://en.wikipedia.org/wiki/Cell_nucleus#cite_note-Spann-16)

Like the components of other [intermediate filaments](https://en.wikipedia.org/wiki/Intermediate_filament), the lamin [monomer](https://en.wikipedia.org/wiki/Monomer) contains an [alpha-helical](https://en.wikipedia.org/wiki/Alpha-helix) domain used by two monomers to coil around each other, forming a [dimer](https://en.wikipedia.org/wiki/Protein_dimer) structure called a [coiled coil](https://en.wikipedia.org/wiki/Coiled_coil). Two of these dimer structures then join side by side, in an [antiparallel](https://en.wikipedia.org/wiki/Antiparallel_(biochemistry)) arrangement, to form a [tetramer](https://en.wikipedia.org/wiki/Tetramer_protein) called a *protofilament*. Eight of these protofilaments form a lateral arrangement that is twisted to form a ropelike *filament*. These filaments can be assembled or disassembled in a dynamic manner, meaning that changes in the length of the filament depend on the competing rates of filament addition and removal.[[6]](https://en.wikipedia.org/wiki/Cell_nucleus#cite_note-MBoC-6)

Mutations in lamin genes leading to defects in filament assembly cause a group of rare genetic disorders known as [*laminopathies*](https://en.wikipedia.org/wiki/Laminopathies). The most notable laminopathy is the family of diseases known as [progeria](https://en.wikipedia.org/wiki/Progeria), which causes the appearance of premature [aging](https://en.wikipedia.org/wiki/Aging) in its sufferers. The exact mechanism by which the associated[biochemical](https://en.wikipedia.org/wiki/Biochemistry) changes give rise to the aged [phenotype](https://en.wikipedia.org/wiki/Phenotype) is not well understood.[[](https://en.wikipedia.org/wiki/Cell_nucleus#cite_note-Mounkes-17)

**Chromosomes**

*Main article:*[*Chromosome*](https://en.wikipedia.org/wiki/Chromosome)

[](https://en.wikipedia.org/wiki/File:MouseChromosomeTerritoriesBMC_Cell_Biol6-44Fig2e.jpg)

A mouse [fibroblast](https://en.wikipedia.org/wiki/Fibroblast) nucleus in which [DNA](https://en.wikipedia.org/wiki/DNA) is stained blue. The distinct chromosome territories of chromosome 2 (red) and chromosome 9 (green) are stained with [fluorescent in situ hybridization](https://en.wikipedia.org/wiki/Fluorescent_in_situ_hybridization).

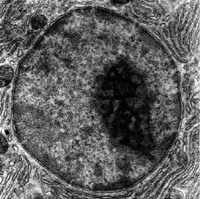
The cell nucleus contains the majority of the cell's genetic material in the form of multiple linear [DNA](https://en.wikipedia.org/wiki/DNA) molecules organized into structures called [chromosomes](https://en.wikipedia.org/wiki/Chromosome). Each human cell contains roughly two meters of DNA. During most of the [cell cycle](https://en.wikipedia.org/wiki/Cell_cycle) these are organized in a DNA-protein complex known as [chromatin](https://en.wikipedia.org/wiki/Chromatin), and during cell division the chromatin can be seen to form the well-defined [chromosomes](https://en.wikipedia.org/wiki/Chromosome) familiar from a [karyotype](https://en.wikipedia.org/wiki/Karyotype). A small fraction of the cell's genes are located instead in the [mitochondria](https://en.wikipedia.org/wiki/Mitochondria).

There are two types of chromatin. [Euchromatin](https://en.wikipedia.org/wiki/Euchromatin) is the less compact DNA form, and contains genes that are frequently [expressed](https://en.wikipedia.org/wiki/Gene_expression)by the cell.[[18]](https://en.wikipedia.org/wiki/Cell_nucleus#cite_note-Ehrenhofer-18) The other type, [heterochromatin](https://en.wikipedia.org/wiki/Heterochromatin), is the more compact form, and contains DNA that is infrequently transcribed. This structure is further categorized into [*facultative* heterochromatin](https://en.wikipedia.org/wiki/Facultative_heterochromatin#Facultative_heterochromatin), consisting of genes that are organized as heterochromatin only in certain cell types or at certain stages of development, and [*constitutive* heterochromatin](https://en.wikipedia.org/wiki/Constitutive_heterochromatin) that consists of chromosome structural components such as [telomeres](https://en.wikipedia.org/wiki/Telomere) and [centromeres](https://en.wikipedia.org/wiki/Centromere).[[19]](https://en.wikipedia.org/wiki/Cell_nucleus#cite_note-Grigoryev-19) During interphase the chromatin organizes itself into discrete individual patches,[[20]](https://en.wikipedia.org/wiki/Cell_nucleus#cite_note-Schardin-20) called *chromosome territories*.[[21]](https://en.wikipedia.org/wiki/Cell_nucleus#cite_note-Lamond-21) Active genes, which are generally found in the euchromatic region of the chromosome, tend to be located towards the chromosome's territory boundary.[[22]](https://en.wikipedia.org/wiki/Cell_nucleus#cite_note-Kurz-22)

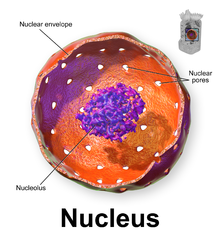
Antibodies to certain types of chromatin organization, in particular, [nucleosomes](https://en.wikipedia.org/wiki/Nucleosome), have been associated with a number of[autoimmune diseases](https://en.wikipedia.org/wiki/Autoimmune_disease), such as [systemic lupus erythematosus](https://en.wikipedia.org/wiki/Systemic_lupus_erythematosus).[[23]](https://en.wikipedia.org/wiki/Cell_nucleus#cite_note-Rothfield-23) These are known as [anti-nuclear antibodies](https://en.wikipedia.org/wiki/Anti-nuclear_antibody) (ANA) and have also been observed in concert with [multiple sclerosis](https://en.wikipedia.org/wiki/Multiple_sclerosis) as part of general immune system dysfunction.[[24]](https://en.wikipedia.org/wiki/Cell_nucleus#cite_note-Barned-24) As in the case of [progeria](https://en.wikipedia.org/wiki/Progeria), the role played by the antibodies in inducing the symptoms of autoimmune diseases is not obvious.

**Nucleolus**

*Main article:*[*Nucleolus*](https://en.wikipedia.org/wiki/Nucleolus)

[](https://en.wikipedia.org/wiki/File:Micrograph_of_a_cell_nucleus.png)

An [electron micrograph](https://en.wikipedia.org/wiki/Electron_micrograph) of a cell nucleus, showing the darkly stained[nucleolus](https://en.wikipedia.org/wiki/Nucleolus)

[](https://en.wikipedia.org/wiki/File:Blausen_0212_CellNucleus.png)

3D rendering of nucleus with location of nucleolus

The [nucleolus](https://en.wikipedia.org/wiki/Nucleolus) is a discrete densely stained structure found in the nucleus. It is not surrounded by a membrane, and is sometimes called a *suborganelle*. It forms around[tandem](https://en.wikipedia.org/wiki/Tandem) repeats of rDNA, DNA coding for [ribosomal RNA](https://en.wikipedia.org/wiki/Ribosomal_RNA) (rRNA). These regions are called [nucleolar organizer regions](https://en.wikipedia.org/wiki/Nucleolar_organizer_regions) (NOR). The main roles of the nucleolus are to synthesize rRNA and assemble ribosomes. The structural cohesion of the nucleolus depends on its activity, as ribosomal assembly in the nucleolus results in the transient association of nucleolar components, facilitating further ribosomal assembly, and hence further association. This model is supported by observations that inactivation of rDNA results in intermingling of nucleolar structures.[[25]](https://en.wikipedia.org/wiki/Cell_nucleus#cite_note-Hernandez-Verdun-25)

In the first step of ribosome assembly, a protein called [RNA polymerase I](https://en.wikipedia.org/wiki/RNA_polymerase_I) transcribes rDNA, which forms a large pre-rRNA precursor. This is cleaved into the subunits 5.8S, 18S, and 28S rRNA.[[26]](https://en.wikipedia.org/wiki/Cell_nucleus#cite_note-Lamond-Sleeman-26) The transcription, post-transcriptional processing, and assembly of rRNA occurs in the nucleolus, aided by [small nucleolar RNA](https://en.wikipedia.org/wiki/Small_nucleolar_RNA) (snoRNA) molecules, some of which are derived from spliced [introns](https://en.wikipedia.org/wiki/Intron) from [messenger RNAs](https://en.wikipedia.org/wiki/Messenger_RNA) encoding genes related to ribosomal function. The assembled ribosomal subunits are the largest structures passed through the nuclear pores.[[5]](https://en.wikipedia.org/wiki/Cell_nucleus#cite_note-Lodish-5)

**Functions-** The nucleus provides a site for genetic [transcription](https://en.wikipedia.org/wiki/Transcription_(genetics)) that is segregated from the location of [translation](https://en.wikipedia.org/wiki/Translation_(genetics)) in the cytoplasm, allowing levels of [gene regulation](https://en.wikipedia.org/wiki/Gene_regulation) that are not available to [prokaryotes](https://en.wikipedia.org/wiki/Prokaryote). The main function of the cell nucleus is to control gene expression and mediate the replication of DNA during the [cell cycle](https://en.wikipedia.org/wiki/Cell_cycle).

The nucleus is an [organelle](https://en.wikipedia.org/wiki/Organelle) found in eukaryotic cells. Inside its fully enclosed nuclear [membrane](https://en.wikipedia.org/wiki/Membrane), it contains the majority of the cell's genetic material. This material is organized as [DNA](https://en.wikipedia.org/wiki/DNA) [molecules](https://en.wikipedia.org/wiki/Molecules), along with a variety of [proteins](https://en.wikipedia.org/wiki/Proteins), to form [chromosomes](https://en.wikipedia.org/wiki/Chromosomes).

### Cell compartmentalization

The nuclear envelope allows the nucleus to control its contents, and separate them from the rest of the cytoplasm where necessary. This is important for controlling processes on either side of the nuclear membrane. In most cases where a cytoplasmic process needs to be restricted, a key participant is removed to the nucleus, where it interacts with transcription factors to downregulate the production of certain enzymes in the pathway. This regulatory mechanism occurs in the case of[glycolysis](https://en.wikipedia.org/wiki/Glycolysis), a cellular pathway for breaking down [glucose](https://en.wikipedia.org/wiki/Glucose) to produce energy. [Hexokinase](https://en.wikipedia.org/wiki/Hexokinase) is an enzyme responsible for the first the step of glycolysis, forming [glucose-6-phosphate](https://en.wikipedia.org/wiki/Glucose-6-phosphate) from glucose. At high concentrations of [fructose-6-phosphate](https://en.wikipedia.org/wiki/Fructose-6-phosphate), a molecule made later from glucose-6-phosphate, a regulator protein removes hexokinase to the nucleus,[[49]](https://en.wikipedia.org/wiki/Cell_nucleus#cite_note-Lehninger-49) where it forms a transcriptional repressor complex with nuclear proteins to reduce the expression of genes involved in glycolysis.[[50]](https://en.wikipedia.org/wiki/Cell_nucleus#cite_note-Moreno-50)

In order to control which genes are being transcribed, the cell separates some [transcription factor](https://en.wikipedia.org/wiki/Transcription_factor) proteins responsible for regulating gene expression from physical access to the DNA until they are activated by other signaling pathways. This prevents even low levels of inappropriate gene expression. For example, in the case of[NF-κB](https://en.wikipedia.org/wiki/NF-%CE%BAB)-controlled genes, which are involved in most [inflammatory](https://en.wikipedia.org/wiki/Inflammation) responses, transcription is induced in response to a [signal pathway](https://en.wikipedia.org/wiki/Cell_signaling) such as that initiated by the signaling molecule [TNF-α](https://en.wikipedia.org/wiki/TNF-%CE%B1), binds to a cell membrane receptor, resulting in the recruitment of signalling proteins, and eventually activating the transcription factor NF-κB. A [nuclear localisation signal](https://en.wikipedia.org/wiki/Nuclear_localisation_signal) on the NF-κB protein allows it to be transported through the nuclear pore and into the nucleus, where it stimulates the transcription of the target genes.[[6]](https://en.wikipedia.org/wiki/Cell_nucleus#cite_note-MBoC-6)

The compartmentalization allows the cell to prevent translation of unspliced mRNA.[[51]](https://en.wikipedia.org/wiki/Cell_nucleus#cite_note-Gorlich-51) Eukaryotic mRNA contains [introns](https://en.wikipedia.org/wiki/Intron) that must be removed before being translated to produce functional proteins. The splicing is done inside the nucleus before the mRNA can be accessed by ribosomes for translation. Without the nucleus, ribosomes would translate newly transcribed (unprocessed) mRNA, resulting in malformed and nonfunctional proteins.

**Processing of pre-mRNA**

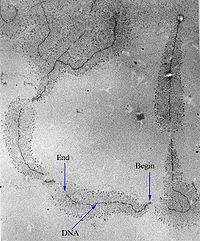
*Main article:*[*Post-transcriptional modification*](https://en.wikipedia.org/wiki/Post-transcriptional_modification)

Newly synthesized mRNA molecules are known as [primary transcripts](https://en.wikipedia.org/wiki/Primary_transcript) or pre-mRNA. They must undergo [post-transcriptional modification](https://en.wikipedia.org/wiki/Post-transcriptional_modification) in the nucleus before being exported to the cytoplasm; mRNA that appears in the cytoplasm without these modifications is degraded rather than used for protein [translation](https://en.wikipedia.org/wiki/Translation_(genetics)). The three main modifications are [5' capping](https://en.wikipedia.org/wiki/5%27_cap), 3'[polyadenylation](https://en.wikipedia.org/wiki/Polyadenylation), and [RNA splicing](https://en.wikipedia.org/wiki/RNA_splicing). While in the nucleus, pre-mRNA is associated with a variety of proteins in complexes known as [heterogeneous ribonucleoprotein particles](https://en.wikipedia.org/wiki/Heterogeneous_ribonucleoprotein_particle) (hnRNPs). Addition of the 5' cap occurs co-transcriptionally and is the first step in post-transcriptional modification. The 3' poly-[adenine](https://en.wikipedia.org/wiki/Adenine) tail is only added after transcription is complete.

RNA splicing, carried out by a complex called the [spliceosome](https://en.wikipedia.org/wiki/Spliceosome), is the process by which [introns](https://en.wikipedia.org/wiki/Intron), or regions of DNA that do not code for protein, are removed from the pre-mRNA and the remaining [exons](https://en.wikipedia.org/wiki/Exon) connected to re-form a single continuous molecule. This process normally occurs after 5' capping and 3' polyadenylation but can begin before synthesis is complete in transcripts with many exons.[[5]](https://en.wikipedia.org/wiki/Cell_nucleus#cite_note-Lodish-5) Many pre-mRNAs, including those encoding [antibodies](https://en.wikipedia.org/wiki/Antibody), can be spliced in multiple ways to produce different mature mRNAs that encode different[protein sequences](https://en.wikipedia.org/wiki/Primary_structure). This process is known as [alternative splicing](https://en.wikipedia.org/wiki/Alternative_splicing), and allows production of a large variety of proteins from a limited amount of DNA.

**Gene expression**

*Main article:*[*Gene expression*](https://en.wikipedia.org/wiki/Gene_expression)

[](https://en.wikipedia.org/wiki/File:Transcription_label_en.jpg)

A micrograph of ongoing [gene transcription](https://en.wikipedia.org/wiki/Gene_transcription) of [ribosomal RNA](https://en.wikipedia.org/wiki/Ribosomal_RNA)illustrating the growing [primary transcripts](https://en.wikipedia.org/wiki/Primary_transcript). "Begin" indicates the [5' end](https://en.wikipedia.org/wiki/5%27_end) of the DNA, where new RNA synthesis begins; "end" indicates the [3' end](https://en.wikipedia.org/wiki/3%27_end), where the primary transcripts are almost complete.

Gene expression first involves [transcription](https://en.wikipedia.org/wiki/Transcription_(genetics)), in which DNA is used as a template to produce RNA. In the case of genes encoding proteins, that RNA produced from this process is [messenger RNA](https://en.wikipedia.org/wiki/Messenger_RNA) (mRNA), which then needs to be [translated](https://en.wikipedia.org/wiki/Translation_(genetics)) by [ribosomes](https://en.wikipedia.org/wiki/Ribosomes) to form a protein. As ribosomes are located outside the nucleus, mRNA produced needs to be exported.[[52]](https://en.wikipedia.org/wiki/Cell_nucleus#cite_note-52)

Since the nucleus is the site of transcription, it also contains a variety of proteins that either directly mediate transcription or are involved in regulating the process. These proteins include [helicases](https://en.wikipedia.org/wiki/Helicase), which unwind the double-stranded DNA molecule to facilitate access to it, [RNA polymerases](https://en.wikipedia.org/wiki/RNA_polymerase), which synthesize the growing RNA molecule, [topoisomerases](https://en.wikipedia.org/wiki/Topoisomerase), which change the amount of [supercoiling](https://en.wikipedia.org/wiki/Supercoil) in DNA, helping it wind and unwind, as well as a large variety of [transcription factors](https://en.wikipedia.org/wiki/Transcription_factor) that regulate expression.