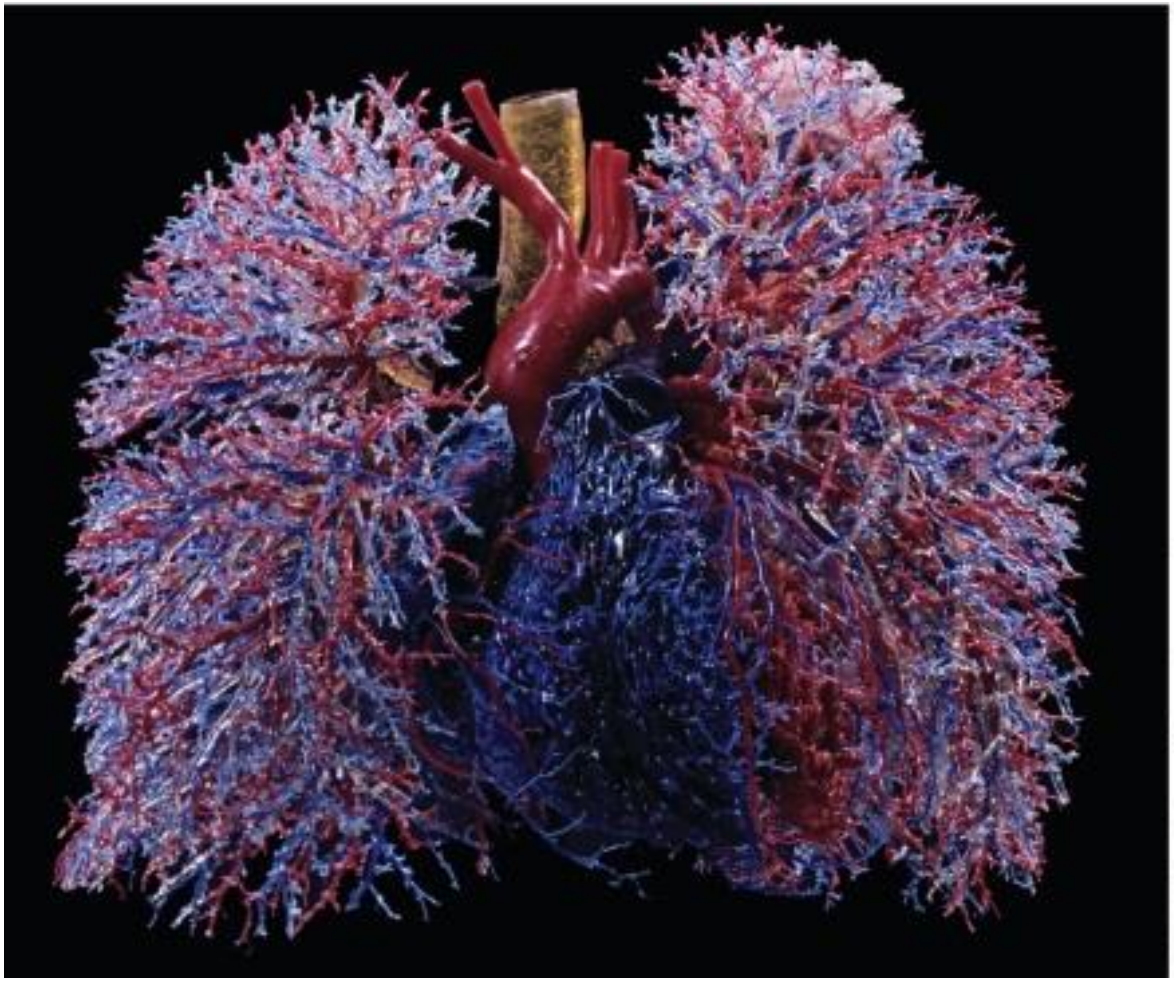
CHAPTER 9

Mitochondrion and Aerobic Respiration



Ralph Hutchings / Getty Images, Inc.

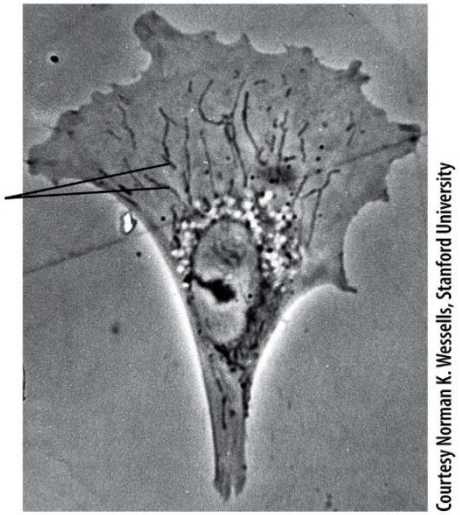
9.0 | Why We Need to Breathe

To satisfy cellular oxygen demand, our blood runs red with hemoglobin.

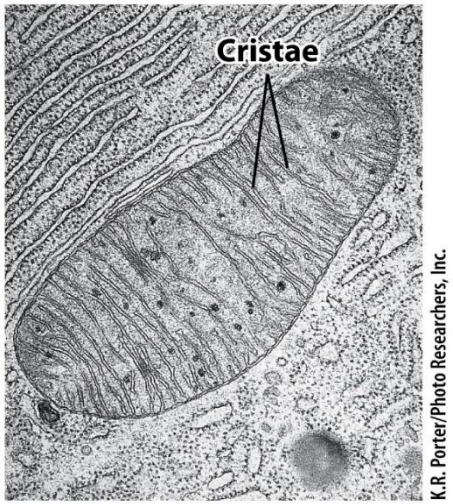
Much of human anatomy and physiology is devoted to ensuring an adequate oxygen supply.

Oxygen is used to power cellular metabolism by providing energy through the biochemical pathway of respiration, much of which takes place within mitochondria.

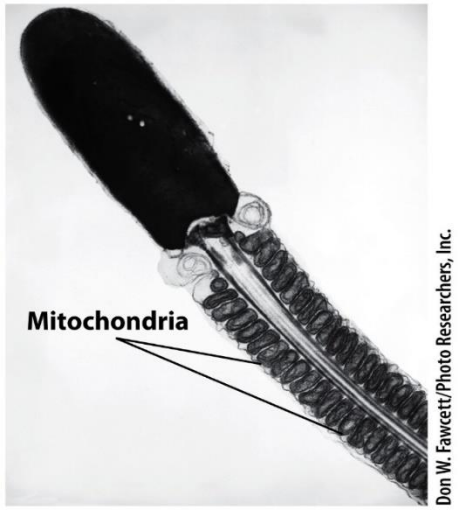
9.1 | Mitochondrial Structure and Function



Elongated mitochondria of fibroblast



Transmission electron micrograph



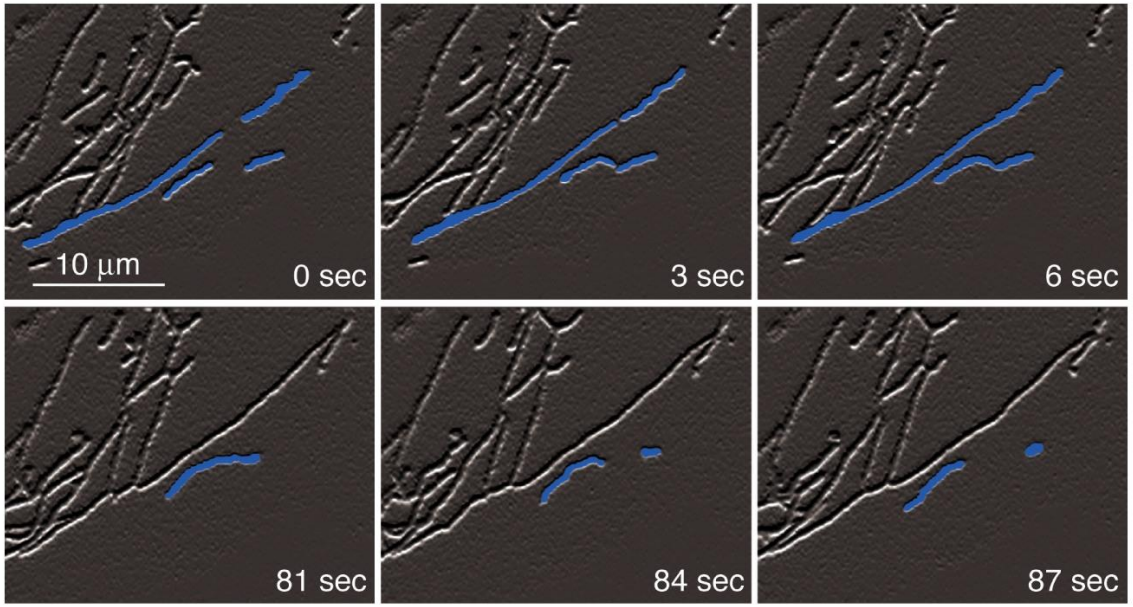
Mitochondria in the sperm mid-piece

Depending on the cell type, mitochondria can have a very different overall structure.

Typical mitochondria are bean-shaped organelles but may be round or threadlike.

Size and number of mitochondria reflect the energy requirements of the cell.

9.1 | Mitochondrial Structure and Function



From David C. Chan, Cell 125:1242, © 2006, with permission of Elsevier.

Dynamic nature of mitochondria revealed in mouse fibroblasts with a fluorescent tagged mitochondrial protein.

Mitochondria can fuse with one another, or split in two.

The balance between fusion and fission is likely a major determinant of mitochondrial number, length, and degree of interconnection.

9.1 | Mitochondrial Structure and Function

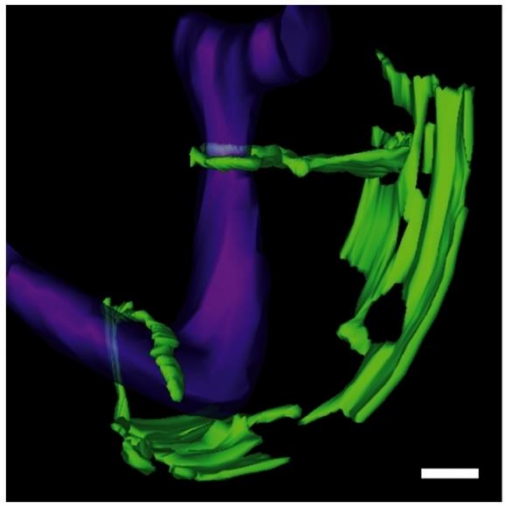
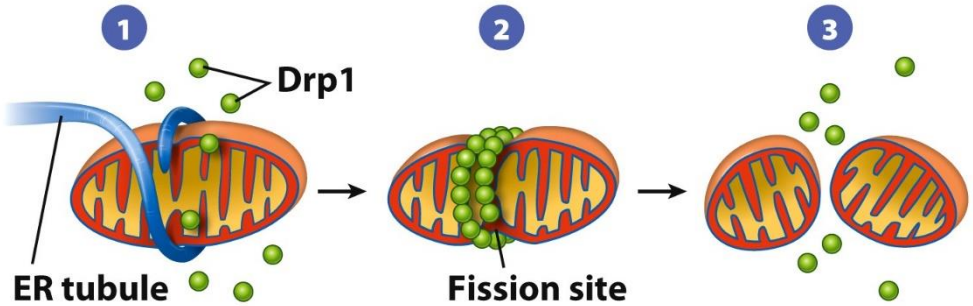


Image by M. West from Friedman et al., Science 334: 359, 2011, reprinted with permission from AAAS.

3D model of contacts between ER and mitochondria



Model for mitochondrial fission: ER tubules and Drp1 mediate mitochondrial constriction.

Mitochondrial fission is apparently induced by contact with thin tubules from the ER, which can encircle the mitochondrion like a noose.

These ER tubules appear to initiate constriction, which is then completed through the action of soluble proteins that are recruited to the outer surface of the mitochondrion from the cytosol.

9.1 | Mitochondrial Structure and Function

Mitochondria occupy 15 to 20 percent of the volume of an average mammalian liver cell and contain more than a thousand different proteins.

To generate ATP, mitochondria are often associated with fatty acid-containing oil droplets from which they derive raw materials to be oxidized.

While energy metabolism has been the focus of interest in the study of mitochondria, these organelles are also involved in other activities.

Mitochondria are the sites of synthesis of numerous substances, including certain amino acids and the heme groups.

Mitochondria also play a vital role in the uptake and release of calcium ions, which are essential triggers for cellular activities

Cell death, which plays an enormous role in the life of all multicellular animals, is also regulated by events that occur within mitochondria.

9.1 | Mitochondrial Structure and Function

Mitochondrial Membranes

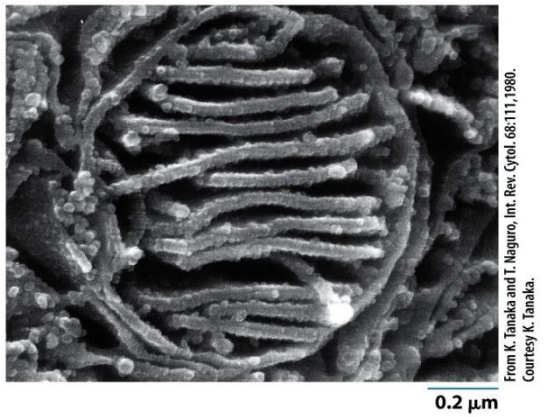
The outer boundary of a mitochondrion contains two membranes: the outer mitochondrial membrane and the inner mitochondrial membrane.

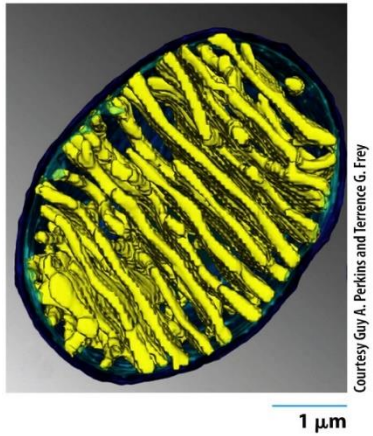
The outer mitochondrial membrane serves as its outer boundary and the inner mitochondrial membrane is divided into two major domains that carry out distinct functions.

The *inner boundary membrane domain* is rich in the proteins responsible for the import of mitochondrial proteins.

The other domain lies in the interior of the organelle as a series of invaginated membranous sheets, called **cristae**.

Scanning electron micrograph of a macerated mitochondrion





3D reconstruction of a mitochondrion based on a micrographs taken with a high-voltage electron microscope

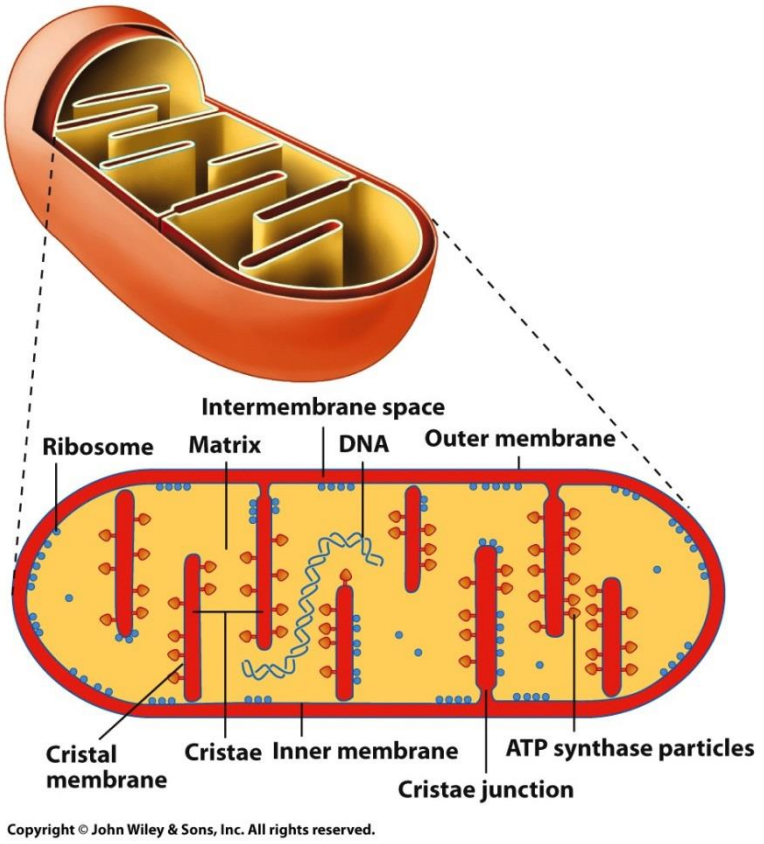
9.1 | Mitochondrial Structure and Function

Mitochondrial Membranes

The cristae houses the machinery needed for aerobic respiration and ATP formation.

The inner boundary membrane and internal cristal membranes are joined to one another by narrow tubular connections, or cristae junctions.

The membranes of the mitochondrion divide the organelle into two aqueous compartments, one within the interior of the mitochondrion, called the matrix, and a second between the outer and inner membrane, called the intermembrane space.



Schematic diagrams showing the 3D internal structure and a thin section of a mitochondrion from bovine heart tissue

9.1 | Mitochondrial Structure and Function

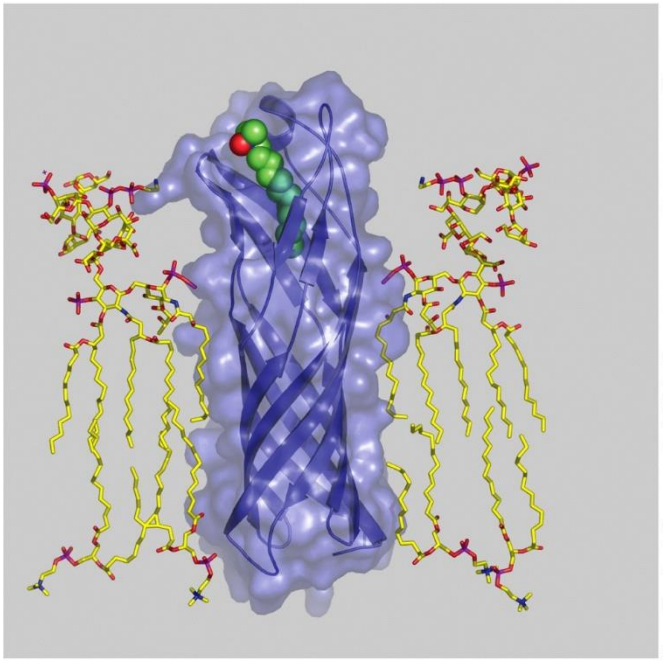
Mitochondrial Membranes

The outer membrane is about 50%; the inner membrane is more than 75% protein.

The inner membrane contains cardiolipin but not cholesterol, both are true of bacterial membranes.

The outer membrane contains a large pore-forming protein called *porin*.

The inner membrane is impermeable to even small molecules, virtually all molecules and ions require special membrane transporters to gain entrance to the matrix.



From Heedeok Hong, et al., J. Biol. Chem. 281, cover of #11, © 2006, The American Society for Biochemistry and Molecular Biology; image courtesy of Bert van den Berg.

Porin motif: a β-sheet barrel that forms an opening for passage of moderate-sized molecules

9.1 | Mitochondrial Structure and Function

Mitochondrial Matrix

The mitochondrial matrix contains ribosomes and several molecules of circular DNA to manufacture their own RNAs and proteins.

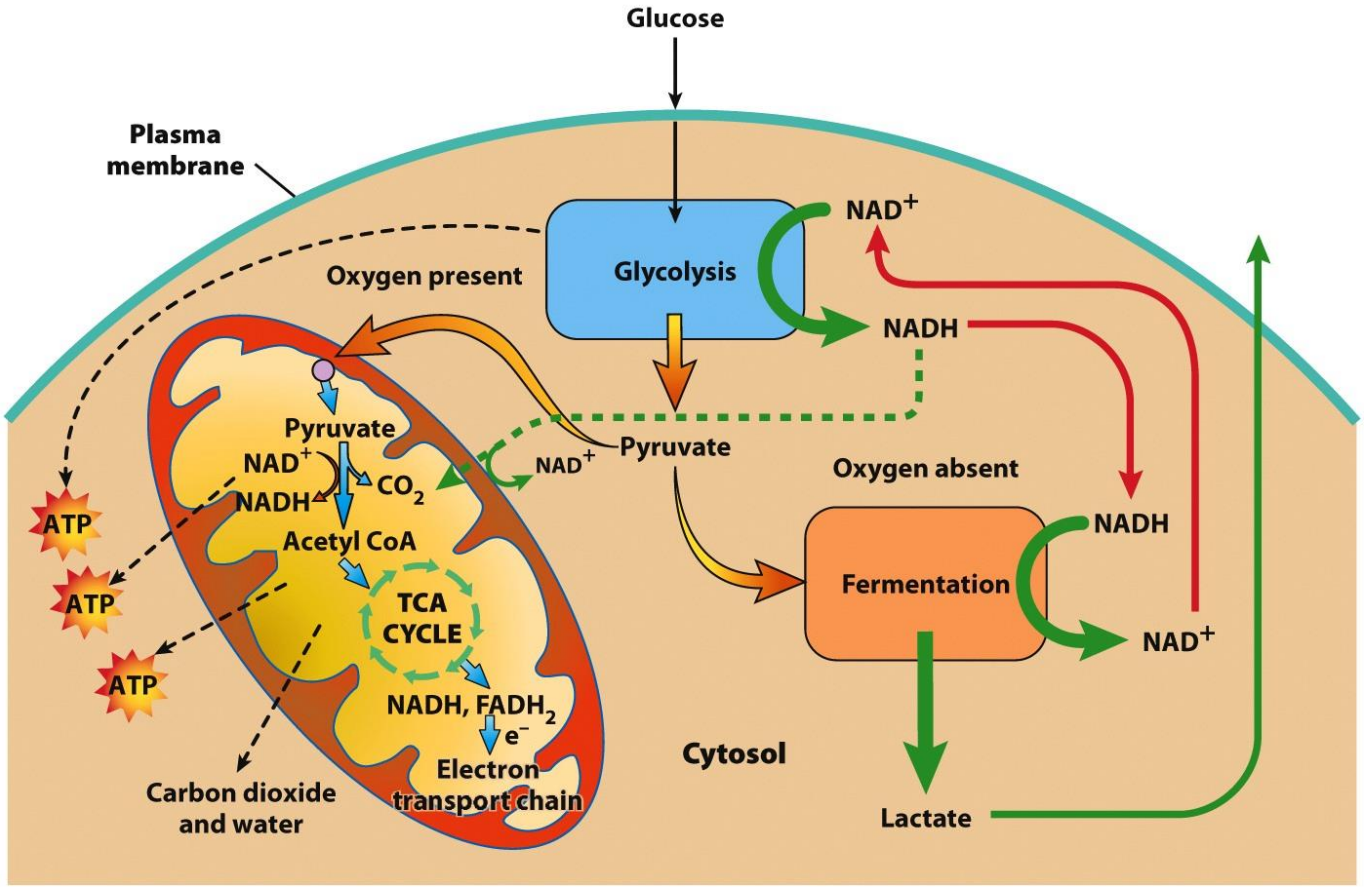
The DNA encodes a small number of mitochondrial polypeptides (13 in humans) that are tightly integrated into the inner mitochondrial membrane along with polypeptides encoded by genes residing within the nucleus.

Mitochondrial DNA (mtDNA) is a relic thought to be the legacy from a single aerobic bacterium that took up residence in the cytoplasm of a primitive cell that ultimately became an ancestor of all eukaryotic cells.

For a number of reasons, mtDNA is well suited for use in the study of human migration and evolution.

9.1 | Mitochondrial Structure and Function

Mitochondrial Matrix



Coupling cytosolic glycolysis and pyruvate production to the mitochondrial TCA cycle and ATP formation

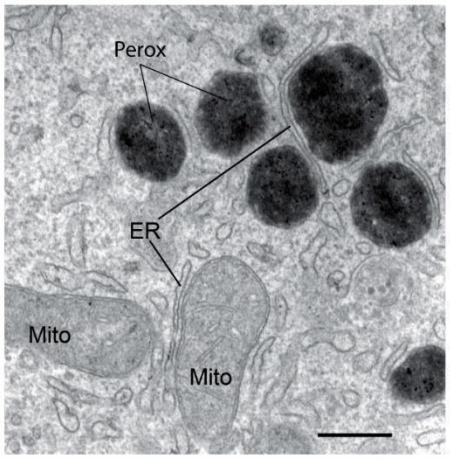
9.9 | Peroxisomes

Peroxisomes are membrane-bound vesicles that contain oxidative enzymes.

They oxidize very-long-chain fatty acids, and synthesize plasmalogens (a class of phospholipids).

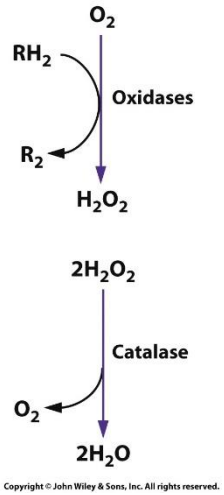
They form by splitting from pre-existing organelles, import preformed proteins, and engage in oxidative metabolism.

Hydrogen peroxide (H_2O_2), a reactive and toxic compound, is formed in peroxisomes and is broken down by the enzyme catalase.



From Michael Schrader and Yisang Yoon, Bioess. 29:1106, 2007. © 2007, John Wiley & Sons.

Electron micrograph of a rat liver cell section stained for catalase



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Peroxisomes contain enzymes to carry out the two-step reduction of molecular oxygen to water

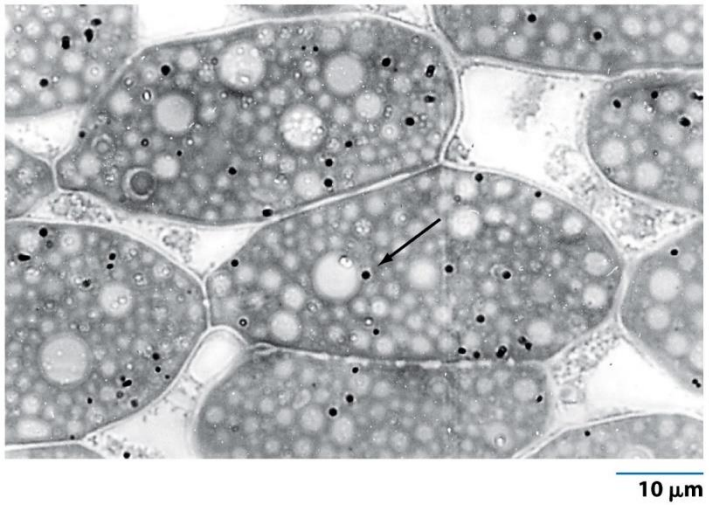
9.9 | Peroxisomes

Peroxisomes are also present in plants; plant seedlings contain a specialized type of peroxisome, called a glyoxysome.

Plant seedlings rely on stored fatty acids to provide the energy and material to form a new plant.

One of the primary metabolic activities in these germinating seedlings is the conversion of stored fatty acids to carbohydrate.

Citrate is converted into glucose by a series of enzymes of the glyoxylate cycle localized in the glyoxysome.



From Richard N. Trelease and Kend D. Chapman, J. Cell Biol. 115:998, 1991, Fig. 1. © 1991 Rockefeller University Press

Glyoxysome localization within plant seedlings. Light micrograph of a section through cotyledons from imbibed cotton seeds. Glyoxysomes (arrow) have been made visible by a stain for catalase.

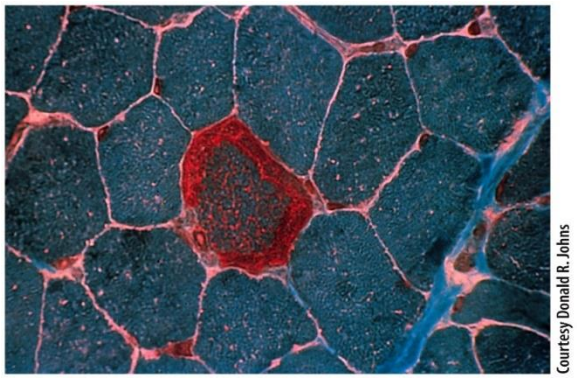
The Human Perspective

II. Diseases that Result from Abnormal Mitochondrial or Peroxisomal Function

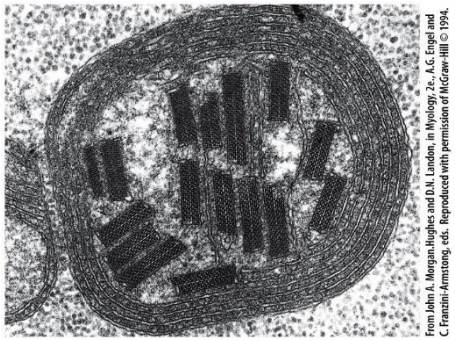
A variety of disorders result from abnormalities in mitochondria structure and function; most are characterized by degeneration of muscle or brain tissue, both use large amounts of ATP.

Conditions range from diseases that lead to death during infancy; to disorders that produce seizures, blindness, deafness, and/or stroke-like episodes; to mild conditions like intolerance to exercise or non-motile sperm.

The majority of mutations linked to mitochondrial diseases are traced to mutations in mtDNA and are inherited maternally.



Degenerating muscle shows red-staining “blotches” due to abnormal proliferation of mitochondria



Electron micrograph showing crystalline structures within the mitochondrial matrix

The Human Perspective

II. Diseases that Result from Abnormal Mitochondrial or Peroxisomal Function

Courtesy Jeff Miller, University of Wisconsin, Madison. Image provided by G.C. Kujoth.

A premature-aging phenotype caused by increased mutations in mtDNA. The defective nuclear gene encodes for the DNA polymerase responsible for mtDNA replication

Accumulations of mutations in mtDNA is considered a major cause of aging.

Mice homozygous for a mutant gene (called *Polg*) that encodes the enzyme that replicates mtDNA accumulate more mutations than normal littermates.

These “mutator” mice appear normal for the first 6 to 9 months of age, but then rapidly develop signs of premature aging, such as hearing loss, graying hair, and osteoporosis; their lifespan is reduced in half.

Additional findings suggest that mutations in mtDNA may cause premature aging but are not sufficient for the *normal* aging process.

The Human Perspective

II. Diseases that Result from Abnormal Mitochondrial or Peroxisomal Function

Zellweger syndrome (ZS) is a rare inherited disease characterized by a variety of neurologic, visual, and liver abnormalities leading to death during early infancy.

Patients with Zellweger syndrome lack peroxisomal enzymes due to defects in translocation of proteins from the cytoplasm into the peroxisome.

ZS can arise from mutations in at least 12 different genes, all encoding proteins involved in the uptake of peroxisomal enzymes from the cytosol.

Adrenoleukodydstrophy (X-ALD) is caused by lack of a peroxisomal enzyme, leading to fatty acid accumulation in the brain and destruction of the myelin sheath of nerve cells.