MITOCHONDRI

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INTRODUCTION

- **Mitochondrion** (**mitochondria**) is a membrane-enclosed structure found in eukaryotic cells. Mitochondrion word has Greek origin , *mitos*, “thread”, and *chondrion*, "granule”. Its size ranges from 0.5 to 1.0 μm ϕ.
- This organelle is a "cellular power plant" because it generates the cellular energy (ATP), used as a source of chemical energy.
- In addition they are involved in signalling, cellular differentiation, cell death, control of the cell cycle and cell growth.
- Human diseases related to mitochondria includes mitochondrial disorders, cardiac dysfunction and aging process.

- Mitochondria are found in nearly all eukaryotes. They vary in number and location according to cell type.
- A single mitochondrion is often found in unicellular organisms. Conversely, numerous mitochondria are found in human liver cells, with about 1000–2000 mitochondria per cell.
- Mitochondrion consists of following regions that carry out specialized functions: outer membrane, intermembrane space, the inner membrane, cristae and matrix.
- Mitochondrial proteins vary depending on the tissue and the species. In humans, 615 distinct types of proteins have been identified from cardiac mitochondria whereas 940 in rats.
- The mitochondrial proteome is thought to be dynamically regulated. Although most of a cell's DNA is contained in the cell nucleus, the mitochondrion has its own independent genome. Further, its DNA shows substantial similarity to bacterial genomes.

HISTORY

- Mitochondria were discovered first time in cell in 1840s.
- Richard Altmann (1894), described them as cell organelles and called "bioblasts".
- The term "mitochondria" was coined by Carl Benda in 1898.
- Leonor Michaelis (1900) discovered Janus green as a vital stain for mitochondria.
- Friedrich Meves (1904) made the first observation of mitochondria in plants (*Nymphaea alba*).
- Claudius Regaud (1908), suggested that they contain proteins and lipids.
- Benjamin Kingsbury (1912), first related them with cell respiration exclusively based on morphological observations.
- Warburg and Otto Heinrich Warburg (1913) stated that extracted particles from guinea-pig liver were linked to respiration called "grana".

STRUCTURE

- A mitochondrion contains outer and inner membranes composed of phospholipid bilayers and proteins. The two membranes have different properties. There are five distinct regions of a mitochondrion:
- the outer mitochondrial membrane,
- the intermembrane space (the space between the outer and inner membrane),
- the inner mitochondrial membrane,
- the cristae space (formed by infoldings of the inner membrane)
- the matrix (space within the inner membrane).
- Mitochondria stripped of their outer membrane and then called mitoplasts.

Outer membrane

Outer membrane encloses the entire organelle. It has a protein-to-phospholipid ratio(1:1 by weight).

It contains large numbers of integral proteins called *porins* which form channels that allow molecules of 5000 Da or less in Mw to freely diffuse through the membrane.

Larger proteins can enter the mitochondrion if a signaling sequence at their N-terminus binds to a large transport protein called translocase of the outer membrane, which then actively transport them across the membrane.

Disruption of the outer membrane permits proteins of the intermembrane space to leak into the cytosol, leading to certain cell death.

The mitochondrial outer membrane may associate with the endoplasmic reticulum (ER) membrane, in a structure called MAM (mitochondria-associated ER-membrane). MAM is important in the ER-mitochondria calcium signaling and involved in the transfer of lipids between the ER and mitochondria.

- **Intermembrane space**

  The intermembrane space is the space between the outer membrane and the inner membrane. It is also known as perimitochondrial space. The outer membrane is freely permeable to small molecules.

  Therefore, the concentrations of small molecules such as ions and sugars in the intermembrane space is same as of the cytosol.

  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.

  One of the proteins, Cytochrome-c is localized in intermembrane space.

Inner membrane

The inner membrane contains more than 151 different polypeptides, and has a very high protein-to-phospholipid ratio (3:1 by weight). The inner membrane is rich in a phospholipid, cardiolipin. Cardiolipin contains four fatty acids rather than two, and may help to make the inner membrane impermeable.

The inner membrane is highly impermeable to all molecules. Almost all ions and molecules require special membrane transporters (translocase) to enter or exit the matrix.

In addition, there is a membrane potential across the inner membrane, formed by the action of the enzymes of the electron transport chain.

The inner mitochondrial membrane contains proteins with five types of functions:

(i) Perform the redox reactions of the oxidative phosphorylation

(ii) ATP synthase, which generates ATP in the matrix

(iii) Specific transport proteins that regulate metabolite passage into and out of the matrix

(iv) Protein import machinery.

(v) Mitochondria fusion and fission protein.

- The cristae of inner membrane expand the surface area of the inner membrane, enhancing its ability to produce ATP.
- For typical liver mitochondria, the area of the inner membrane is five times larger as compared to the outer membrane. This ratio is variable depending on the demand of ATP by the cell. Such as muscle cells contain more cristae.
- The cristae are studded with small round bodies known as F_1 particles or oxysomes.
- 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.

Matrix

The matrix is the space enclosed by the inner membrane. It contains about 2/3 of the total protein in a mitochondrion.

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, ribosomes, tRNA and several copies of the mitochondrial DNA genome.

The major functions of enzymes include oxidation of pyruvate and fatty acids, and the citric acid cycle

Mitochondria have their own genetic material, and the machinery to manufacture their own RNAs and proteins.

Human mitochondrial DNA sequence revealed 16,569 base pairs encoding 37 total genes: 22 tRNA, 2 rRNA, and 13 peptide genes.

- **Mitochondria-associated ER membrane (MAM)**

- MAM is recognized for its critical role in cellular physiology and homeostasis.
- By cell fractionation techniques it was found that ER vesicle contaminants that appeared in the mitochondrial fraction have been identified as membranous structures derived from the MAM.
- By EM physical connection between ER and mitochondrion was observed and recently confirmed with fluorescence microscopy.
- Purified MAM has shown to be enriched in enzymes involved in phospholipid exchange and Ca^{2+} signaling channels.
- MAM provided the basis of mechanism of apoptosis.
- MAM intimate physical and functional coupling of the endomembrane system and symbiosis.

Function

- **Energy production/conversion**

  The most prominent roles of mitochondria are to produce the energy ATP through respiration (Citric acid cycle or Krebs Cycle), and to regulate cellular metabolism.

  The production of ATP takes place by large number of proteins (ATPase) in the inner membrane by oxidizing the major products of glucose, pyruvate, and NADH, which are produced in the cytosol. Mitochondria play a role in the aerobic and anaerobic respiration.

Additional functions

- Mitochondria play a central role in many other metabolic tasks, such as:
- Signaling through mitochondrial reactive oxygen species
- Regulation of the membrane potential
- Apoptosis-programmed cell death[
- Calcium signaling.
- Regulation of cellular metabolism
- Certain heme synthesis reactions
- Steroid synthesis.
- Some mitochondrial functions are performed only in specific types of cells. For example, mitochondria in liver cells contain enzymes that allow them to detoxify ammonia, a waste product of protein metabolism. A mutation in the genes regulating any of these functions can result in mitochondrial diseases.

Mitochondrial DNA

- A mitochondrion contains DNA, as circular chromosome. This mitochondrial chromosome contains genes. The mitochondrial genome codes for some RNAs of ribosomes, and the twenty-two tRNAs necessary for the translation of messenger RNAs into protein. The circular DNA is also found in prokaryotes. However, the exact relationship of the ancestor of mitochondria to the prokaryotes remains controversial.
- The ribosomes of mitochondria similar to those from bacteria in size and structure 70S ribosome.
- Mitochondria descended from bacteria survived endocytosis by another cell, and became incorporated into the cytoplasm about 1.7 to 2 billion years ago.

The end

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