TOPIC: MITOCHONDRIA

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Ultra structure of Mitochondria:-

The electron microscope shows the mitochondrion as the vesicles bounded by an envelope of two unit membranes and filled with a fluid matrix.

Membranes- Both the inner and the outer mitochondrial membranes resemble the plasma membrane in molecular structure. Each of them is 60-70Å, trilamellar and composed of two layers of phospholipid molecules sandwiched between two layers of protein molecules. However, the two membranes differ in the kinds of protein and lipids they have and also in their properties. Both the outer and the inner membranes contain specific pumps or channels, for the transport of molecules through them. The membranes may be connected at adhesion sites through which proteins are transferred from the outer to the inner membrane. The outer and the inner membrane are separated from each other by a narrow space called the inter-membrane space or outer chamber or peri-mitochondrial space. It is about 80Å wide. It contains a clear homogeneous fluid.

Outer Membrane- The outer membrane is smooth permeable to most small molecules, having trans-membrane channels formed by the protein '**porin**'. It consists of about 50% lipid, including a large amount of cholesterol. It contains some enzymes but is poor in protein.

Inner Membrane- The inner membrane is selectively permeable and regulates the movement of materials into and out of the

mitochondrion. It is rich in enzymes and carrier proteins **permease**. It has a very high protein/lipid ratio (about 4:1 by weight). It lacks cholesterol. Cardiolipin is closely associated with certain integral proteins and is apparently required for their activity.

Matrix- The space between the cristae called the inner chamber is filled with a gel like material termed the mitochondrial matrix. It contains proteins, lipids, some ribosomes, RNA, one or two DNA molecules and certain fibrils, crystals and dense granules.

Cristae- The inner mitochondrial membrane bears plate like infoldings called the cristae. They extend inwards to varying degrees, and may fuse with those from the opposite side, dividing the mitochondrion into compartments. They are arranged in a characteristic manner in different cells. Normally they run at right angles to the long axis of the rod shaped mitochondria. In cells of the proximal parts of the kidney tubules, the cristae are longitudinal folds parallel to the long axis of mitochondrion. In many protozoans, in insect flight muscles cells and in adrenal endocrine cells the cristae are tubular. Cristae are lamellar in hepatocytes. In heart muscle cells cristae are zig-zag.

They also vary in number. The active cells may have numerous cristae whereas the inactive cells may have only a few. The cristae have in them a narrow intra-crista space. It is continuous with the inter-membrane space. The cristae greatly increase the inner surface of the mitochondrion to provide enough space for housing enzyme assemblies. The cristae also allow for expansion or swelling of mitochondria under different metabolic and environmental conditions.

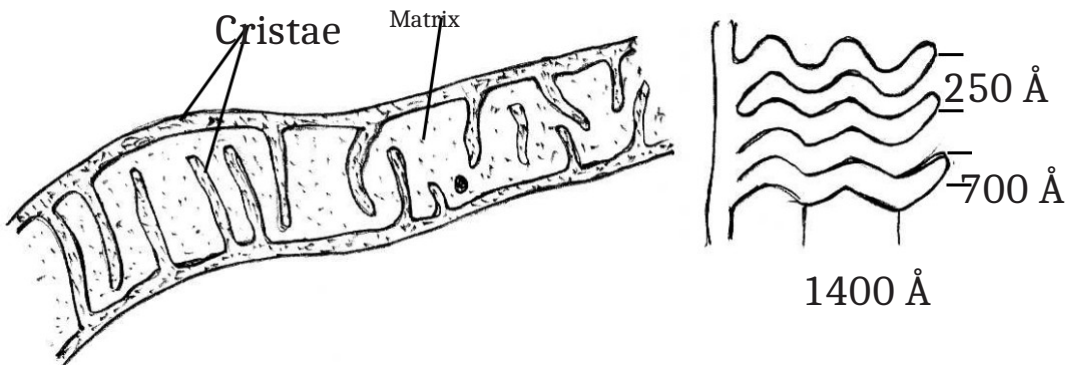


Fig. 3.2: Cristae in a mitochondrion of an endothelial cell of human being

Oxysomes- The inner mitochondrial membrane bears minute regularly spaced

particles known as the inner membrane subunits or **elementary particles (EP) or oxysomes**. An oxysome consists of three parts- a rounded **head piece or F_1 subunit** joined by a short stalk to a **base piece or F_0 subunit** located in the inner membrane. There may be 100,000 to 1000,000 oxysomes in a single mitochondrion.

Matrix in Inner Matrix or M

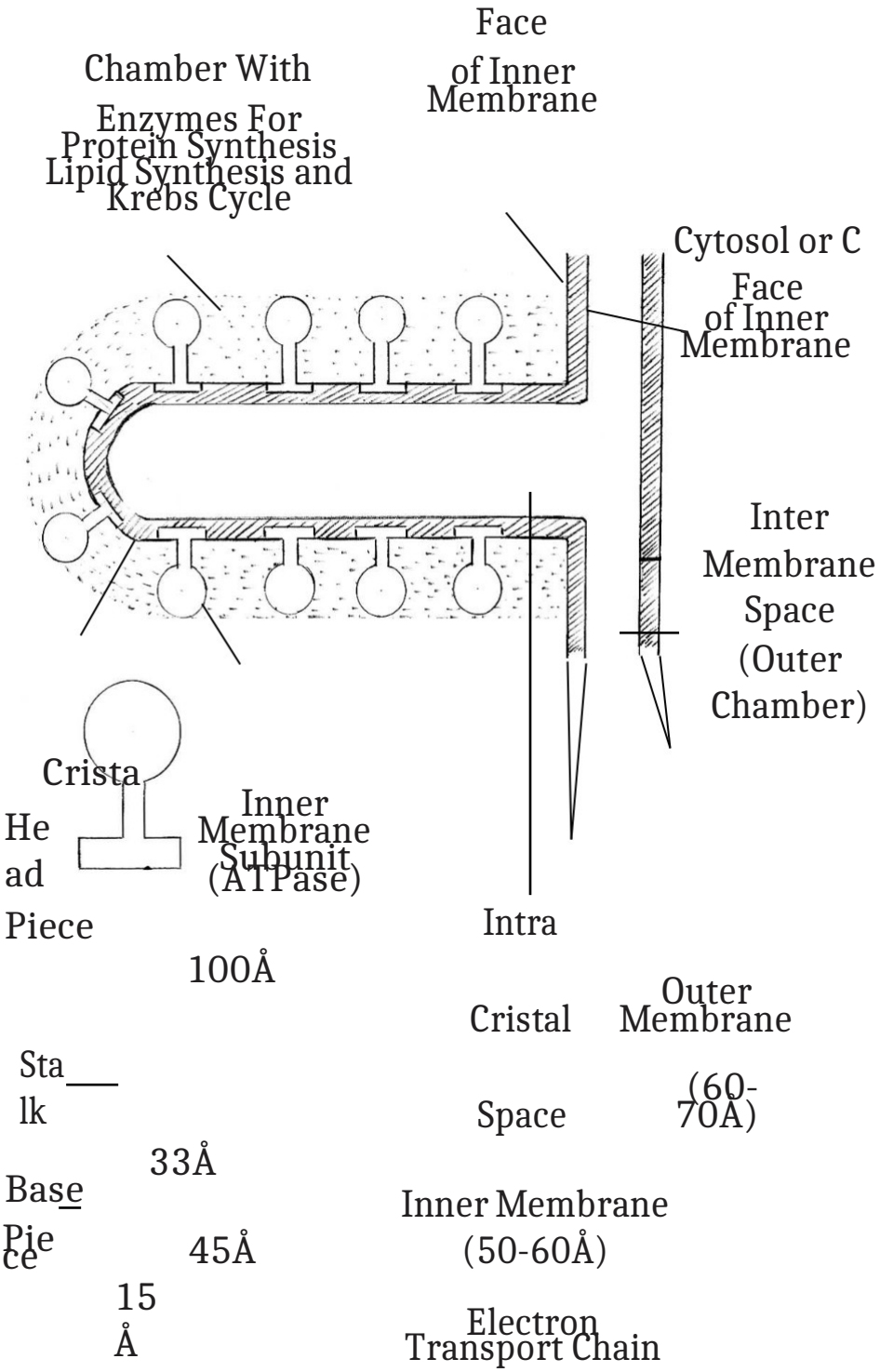


Fig. 3.3: Detailed structure of a crista and an oxysome

Biogenesis of Mitochondria:-

The formation of new mitochondria has been explained with the following hypothesis.

De Novo Synthesis- According to this hypothesis mitochondria arises de novo from precursors in the cytoplasm.

Origin from membrane- This hypothesis proposes that the mitochondria arises from the invaginations of plasma membrane, endoplasmic reticulum, Golgi apparatus or nuclear envelop. The membrane invaginates and extends into the cytoplasm as a tubular structure. It gradually becomes curved and folded and forms a double walled structure, the mitochondrion.

Develop from Micro bodies- It is held that they mitochondria are developed by the accumulation of micro bodies in the cytoplasm. A micro body consists of a single outer membrane and a dense matrix with a few cristae which eventually develops into fully formed mitochondria.

Prokaryotic Origin- It is believed that mitochondria are originated from bacteria. It is supported by many evidences.

First is the localization of enzymes of respiratory chain, which in case of bacteria, are localized in plasma membrane which can be compared with the inner membrane of the mitochondrion.

In some bacteria, plasma membrane forms membranous projections (called mesosomes) like cristae of mitochondria. These mesosomes possess respiratory chain enzymes.

The mitochondrial DNA is circular as it is in bacteria. Replication process of mitochondria is similar to bacteria.

Ribosomes in mitochondria are smaller and similar in size to that of bacterial ribosomes.

Chloramphenicol inhibits the synthesis of protein in mitochondria as well as in bacteria. Furthermore, in the process of protein synthesis, mitochondria depend partially on mitochondrial matrix and DNA and partially on nucleus and cytoplasm of the eukaryotic cells. It exhibits the symbiotic nature of mitochondria. These evidences support the prokaryotic origin of mitochondria.

Replication- It is held that mitochondria are self-replicating organelles. New mitochondria arise by some type of splitting process from pre-existing mitochondria.

The last hypothesis seems probable. Since the mitochondria have their own DNA and ribosomes, they can replicate new mitochondria. However, there is a nuclear control over the process as the mitochondria synthesize some of their proteins themselves and get others from the cytoplasm of the cell formed under the direction of the nuclear DNA.

Functions of Mitochondria:-

Mitochondria perform the following functions:-

Cell respiration takes place in mitochondria and so they are known as the '**power house' of the cell.** They bring about stepwise oxidation of food stuffs or "low-grade" fuel of the cell and transfer the energy so released to the energy carrier ATP, the "high-grade" fuel of the cell. ATP is used to bring about the energy-requiring activities in the cells, namely, biosynthesis, active transport, transmission of nerve impulse, muscle contraction, cell growth and division and bioluminescence.

Mitochondria provide **intermediates** for the **synthesis of important biomolecules** such as chlorophyll, cytochromes, steroids etc.

Some **amino acids** are also formed in the mitochondria.

Mitochondria actively **accumulate calcium ions** as calcium phosphate precipitate.

They regulate the calcium ions concentration in the cytoplasm by storing and releasing Ca^{+}. The calcium ions regulate numerous biochemical activities in the cell.

Respiratory Chain Complex or Electron Transport System:-

Respiratory chain complex or electron transport system consists of a series of complex proteins, which take part in the respiratory chain. There are **five complexes formed of lipoproteins and two mobile electron carriers** — coenzyme Q (CoQ) or ubiquinone (UQ) and cytochrome C.

Complexes:-

Complexes are the sites where hydrogen ions released during Krebs's cycle are oxidized and their energy is trapped in ATP.

Complex I (NADH-CoQ reductase). It consists of the following components.

NADH dehydrogenase- It consists of flavoprotein with FMN as prosthetic group. The protein is a single polypeptide chain with molecular weight 70,000.

Non-heme iron (NH_I)- Protein with iron-sulphur centers (Fe-S).There are six Fe-S centers, i.e., Fe-SN1a, Fe-SN1b, Fe-SN2, Fe-SN3, Fe-SN4 and Fe-SN5. It is the largest complex with molecular weight 8, 50,000 and includes a flavoprotein containing FMN. This is the first step in the electron transport chain. Electrons are taken into this complex by NAD+ which is located at the matrix side of the membrane.

Complex II (Succinate-CoQ reductase). It has the following components.

Succinic dehydrogenase with the molecular weight 70,000 it has covalently bound FAD as prosthetic group and two Fe-S centers, i.e., Fe-SS1 and Fe-SS2.

Fe-SS 3 protein of molecular weight 27, 000 and

Cytochrome b with absorbance 557.5 nm

Coenzyme Q (CoQ) or Ubiquinone (UQ) - It is mobile carrier between complex I and III, and II and III. Complex II precedes the electron transport chain and is coupled to succinate by way of FAD (flavinadenine dinucleotide).

Complex III (CoQH2-Cyt.C-reductase). This complex contains:

Cytochrome b of molecular weight 30,000

Cytochrome e of molecular weight 50,000

Cytochrome c_1 having two polypeptides of molecular weight 29,000 and 15,000.

NH_1 protein with Fe-S centre and molecular weight 26,000

Core proteins

Antimycin-binding protein.

Cytochrome c- It is mobile carrier between complexes III and IV with molecular weight 13,000.

Complex IV (Cytochrome C-Oxidase). It contain cytochrome a (Cyt. a) not

inhibited by CO, cytochrome a3 (Cyt. a3) inhibited by CO and two atoms of copper (Cu and Cu). The final oxidation of hydrogen occurs in it, resulting in water (H_2O) formation.

Complex V (ATPase complex). It contains head piece, stalk and base piece. Head piece (F1) consists **of 5 subunits** and inhibitor of molecular weight 3, 60,000.

α — Subunits 2 or 3 with molecular weight 53,000

— Subunits 2 or 3 with molecular weight 50,000

— Subunits 1 or 2 with molecular weight 33,000

— Subunits 1 or 2 with molecular

weight 7,500 E — Subunits 1 or 2

with molecular weight 7,000 F1

inhibitor protein I with molecular

weight 10,000

Stalk has F_5 or oligomycin sensitivity conferring protein (OSCP) of molecular weight 18,000 and F_6 (Fe_2) of molecular weight 8,000.

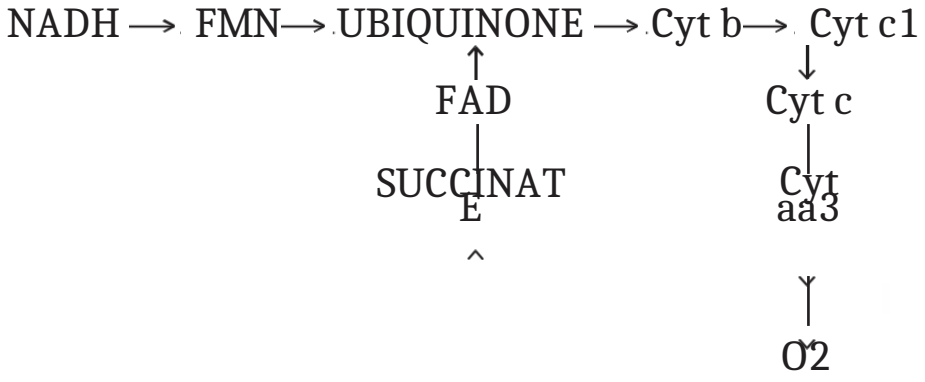
Base piece (F_0) is made of proteolipids — a hydrophobic protein complex forming proton channel. There are four proteins of molecular weight 29,000, 22,000, 12,000 and 7,800.

All these complexes and the phosphorylation system are organized within the inner mitochondrial membrane in an asymmetrical manner. The electron transport system is only accessible to NADH and succinate from matrix side of the membrane, while cytochrome c is reached from cytoplasm side of the membrane. This molecular organization is consistent with the transfer of proton (H+) across the membrane from matrix side to cytoplasm side of the membrane.

The respiratory chain is coupled at three points with the system in which phosphorylation of ADP to ATP takes place. The six protons that originated in the respiratory chain are translocated across the inner mitochondrial membrane from matrix side to cytoplasm side, and these six protons will give rise to three molecules of ATP through the use of mitochondrial ATPase.

Electron Transport Mechanism:-

In the electron transport chain electrons are transferred from a donor molecule to an acceptor molecule, thus, it consists of a several electron receptors. Molecular oxygen is the final hydrogen acceptor. The respiratory chain is located in the inner mitochondrial membrane. In the respiratory chain, the electron transfer is done in stepwise fashion in which the electron pairs are passed from one acceptor to another, thus, delivering energy more gradually. Flow of electrons in mitochondria occurs as follows:



Summary:-

The term Mitochondria was coined by Benda (1897-98). Mitochondria are the 'power house' which by oxidation, release the energy contained in the fuel molecules or nutrients and make other forms of chemical energy. Mitochondria are lacking in bacterial cells, where oxidation of organic material is carried out in plasma membrane. They may move freely in the cytoplasm in some cells or they are fixed permanently in others depending upon the requirement of ATP energy in that particular part of the organ.

Ultra structure of mitochondria reveals that it is a double membrane bounded organelle. The outer membrane is smooth contoured and is freely permeable while, the inner membrane is selectively permeable. It regulates the movement of materials into or out of the mitochondria. The salient feature of the inner

membrane is that it is thrown into a series of infoldings in the cavity of mitochondrion. These infoldings are known as cristae. Between the outer and the inner membrane is a space called peri-mitochondrial space or intracristal space. It contains a homogeneous fluid of low density. The cavity of mitochondria is filled with dense fluid known as mitochondrial matrix. In the matrix are present proteins, lipids few ribosomes, one or two DNA molecules, RNA and certain other granules. A larger chunk of the mitochondrial proteins represent enzymes.

A number of functions are performed by mitochondria; these include oxidation, dehydrogenation, oxidative phosphorylation and respiratory activity. A large number of enzymes and numerous cofactors and metals essential to mitochondrial functions, work together in an orderly fashion. Besides, oxygen the only fuel that a mitochondrial needs is phosphate and adenosine diphosphate (ADP). The principal final products are ATP plus CO_2 and H_2O.

The respiratory chain takes in succinic acid (succinate) and NADH from Krebs's cycle enzymes. These together with oxygen, respiratory chain produce many molecules of ATP and finally CO_2 and water. As the electrons carried by NADH and succinic acid travel down the chain they give up their energy, which is used up for the conversion of ADP to ATP. During respiratory chain a series of pigments, chemicals and enzymes are involved. In the major pathway chief line of oxidation-reduction reactions of the cell is the removal of hydrogen from substrate by dehydrogenases. Hydrogen is usually picked up by the coenzyme part of dehydrogenase from substrate and carried to flavoprotein, which act as a hydrogen carrier (i.e. FAD-flavin adenine dinucleotide). From FAD, each hydrogen is discharged as ion in the cell fluid and electrons are passed on to the pigments — cytochromes which are a, b, c, c_1 and c_3 types mainly. From cytochromes, electrons are given to the enzymes cytochrome

oxidase, which finally discharges electrons to oxygen. This oxygen unites with hydrogen ions to form water.

Glossary:-

Plasma membrane: The membrane forming the surface of cytoplasm and consisting of a bimolecular phospholipids layer between an inner and outer layer of protein molecules.

Neuron: The nerve cell with its outgrowths, structural unit of nervous system.

Adenosine Triphosphate (ATP): a molecule containing high energy bonds that provides energy for many biochemical cellular processes by undergoing enzymatic hydrolysis.

Diaphragm: a muscular or ligamentous partition that separates the thorax from the abdomen in mammals.

I-band: In a sarcomere, I-band is the zone of thin filaments that is not superimposed by thick filaments.

Myofibril: Myofibrils are the rod like units of muscle cells. They are composed of repeating sections of sarcomere, which appear under the as dark and light bands.

Oocytes: Oocyte is a female gametocyte or an immature ovum involved in reproduction. It is produced in the ovary during female gametogenesis and it undergoes meiotic division to form an ovum.

Vesicles: A vesicle is a small structure within a cell, consisting of fluid enclosed by a lipid bilayer membrane.

Porin: The beta barrel proteins that acts as transport protein which cross a cellular membrane and act as a pore through which molecules can diffuse. Porins are large enough to act as channels that are specific to different types of molecules.

Permease: The permease is membrane transport proteins that facilitate the diffusion of a specific molecule in or out of the cell by passive transport.

Cardiolipin: Cardiolipin is an important component of the inner mitochondrial membrane where it constitutes about 20% of the total lipid composition. It is essential for the optimal function of numerous enzymes that are involved in mitochondrial energy metabolism.

Cristae: A cristae is a fold in the inner membrane of the mitochondrion. It provides a large amount of surface area for the chemical reactions to occur on.

Oxysomes: It is a structural unit of cellular cristae.

***De novo*:** *De novo* is a Latin expression meaning "from the beginning," "afresh," "anew,"
"beginning again."

Microbody: A microbody is a type of organelle that is found in the cells of plants, protozoa and animals and microbody include peroxisome, glyoxysome and glycosome.

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