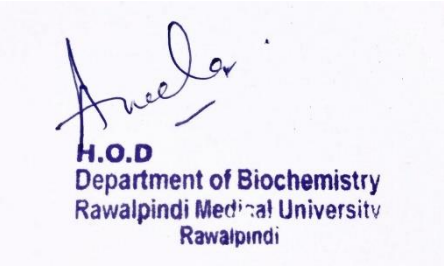

بسم الله الرحمن الرحيم

Foundation Module

1st Year MBBS(LGIS)

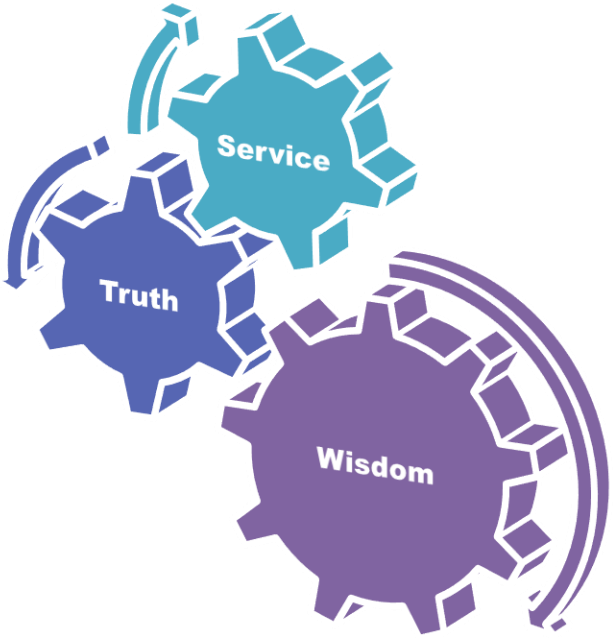
Cell Organelles-1



Presenter: Dr Nayab Ramzan
Deptt of Biochemistry
RMU

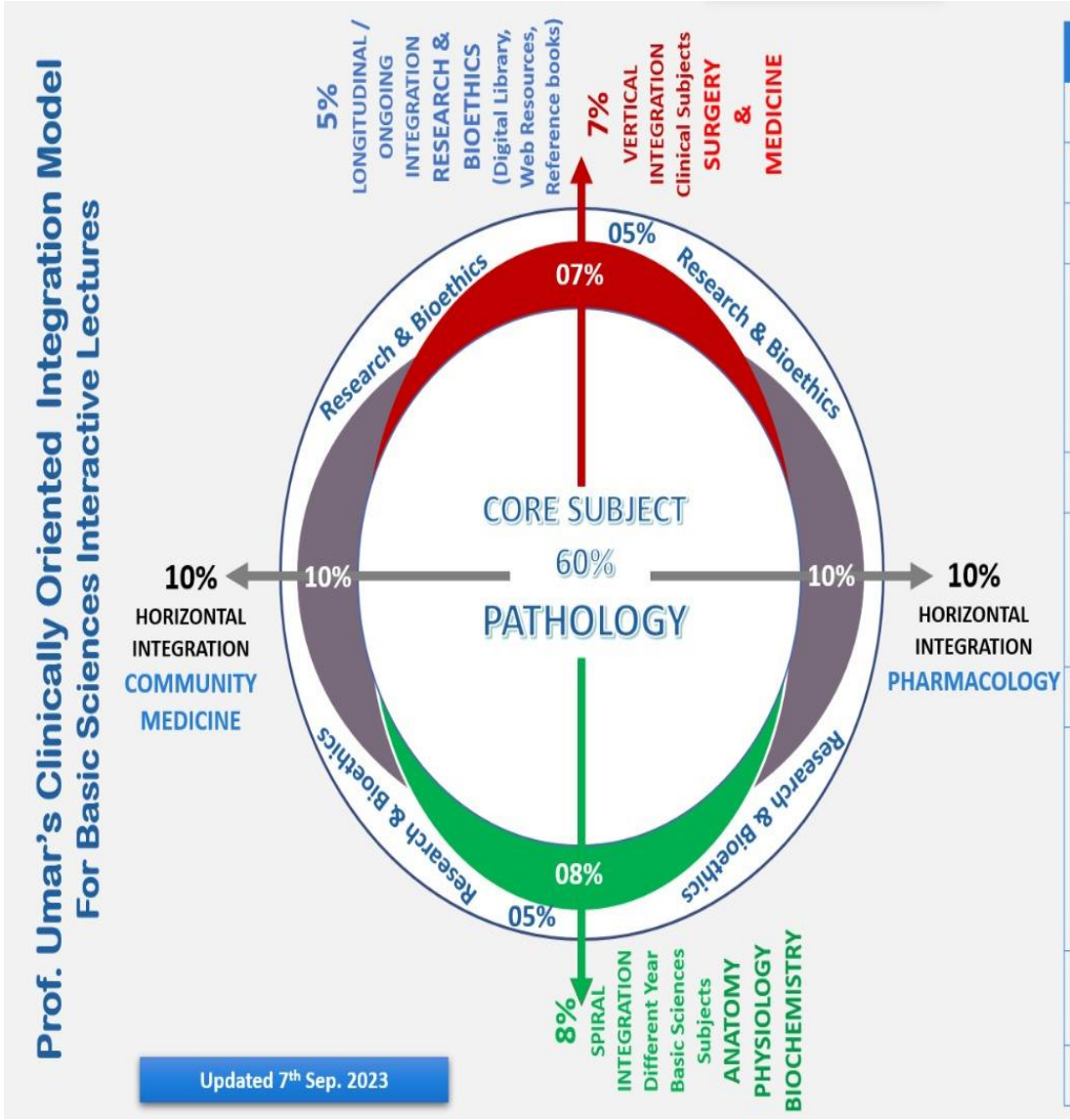
Date: 06-02-25

Motto, Vision, Dream



- To impart evidence based research oriented medical education
- To provide best possible patient care
- To inculcate the values of mutual respect and ethical practice of medicine

Professor Umar Model of Integrated Lecture



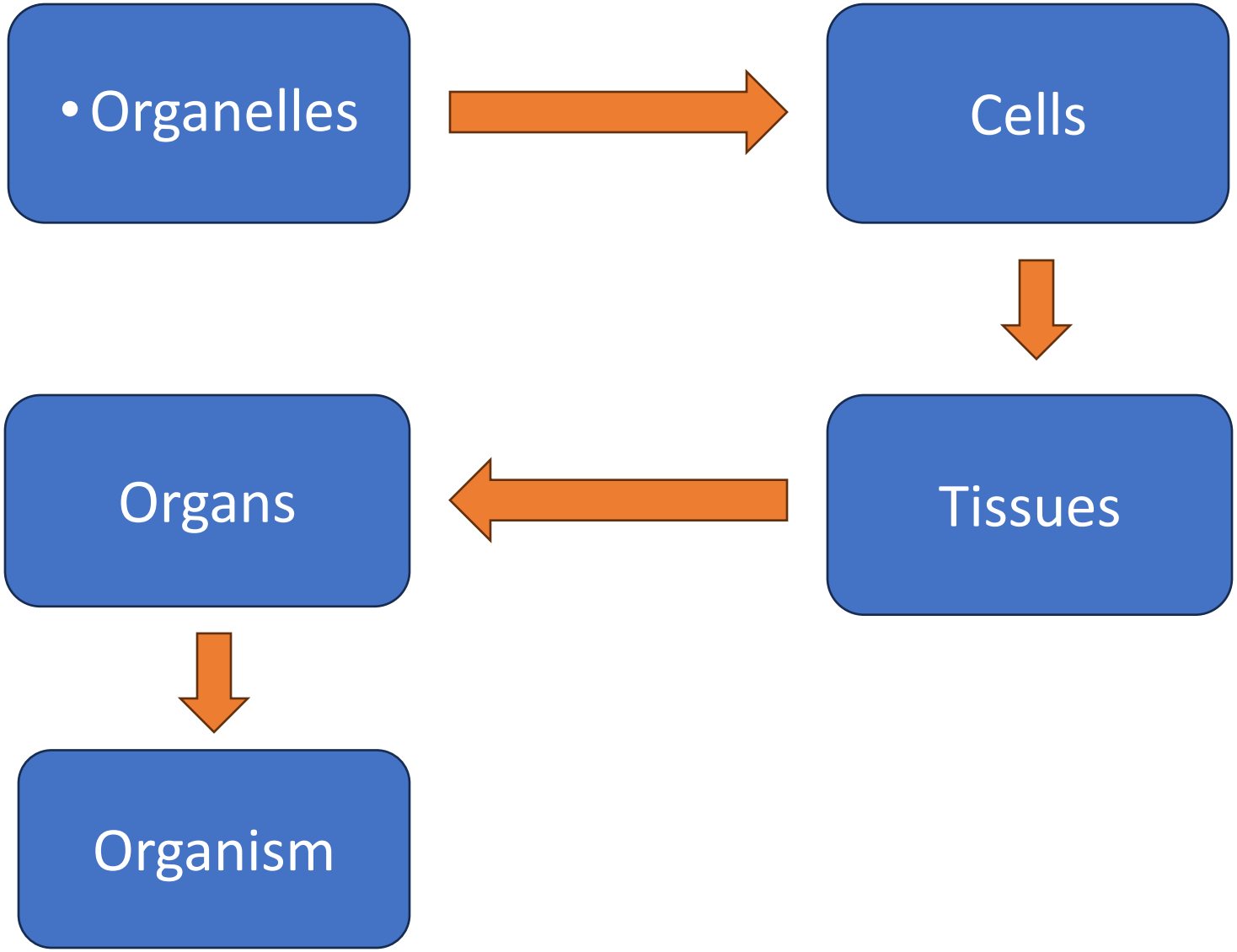
Model 3rd Year Pathology LGIS (≈30 slides)	
Core Subject – 60% (≈ 18-20 slides)	
Pathology (≈ 18-20 slides)	
Horizontal Integration – 20% (≈ 5-6 slides)	
Same Year Subjects	• Pharmacology (10%) (≈ 2-3 slides) • Community Medicine (10%) (≈ 2-3 slides)
Vertical Integration – 07% (≈ 2-3 slides)	
Clinical Subjects	• Medicine (3-5%) (≈ 1-2 slides) • Surgery (3-5%) (≈ 1-2 slides)
Spiral Integration – 08% (≈ 2-3 slides)	
Different Year Basic Sciences Subjects	• Anatomy (1-3%) (≈ 1-2 slides) • Physiology (1-3%) (≈ 1-2 slides) • Biochemistry (1-3%) (≈ 1-2 slides)
Longitudinal / Ongoing Integration – 05% (≈ 1-2 slides)	
Research & Bioethics (≈ 1-2 slides)	

Learning Objectives

At the end of this session students should be able to:

- Explain composition of normal cell & methods to separate different organelles of cell.
- Describe structure, functions and marker enzymes of mitochondria and nucleus.
- Correlate with the clinical conditions
- Practice the principles of bioethics in the related scenario
- Apply strategic use of A.I in the given scenario
- Read relevant research articles related to the Core Knowledge.

Cell & Cell Organelles



Fundamental Statements About Cell

- Cell is basic structural and functional **unit**.
- Cells arise from **Existing Cells.**
- The **Genetic Information** for **maintenance of existing** and **production of new cells** passes through cell.
- **Metabolism** takes place inside cells.

Methods for Studying Cell Structure and Isolation of Cell Organelles

Homogenization

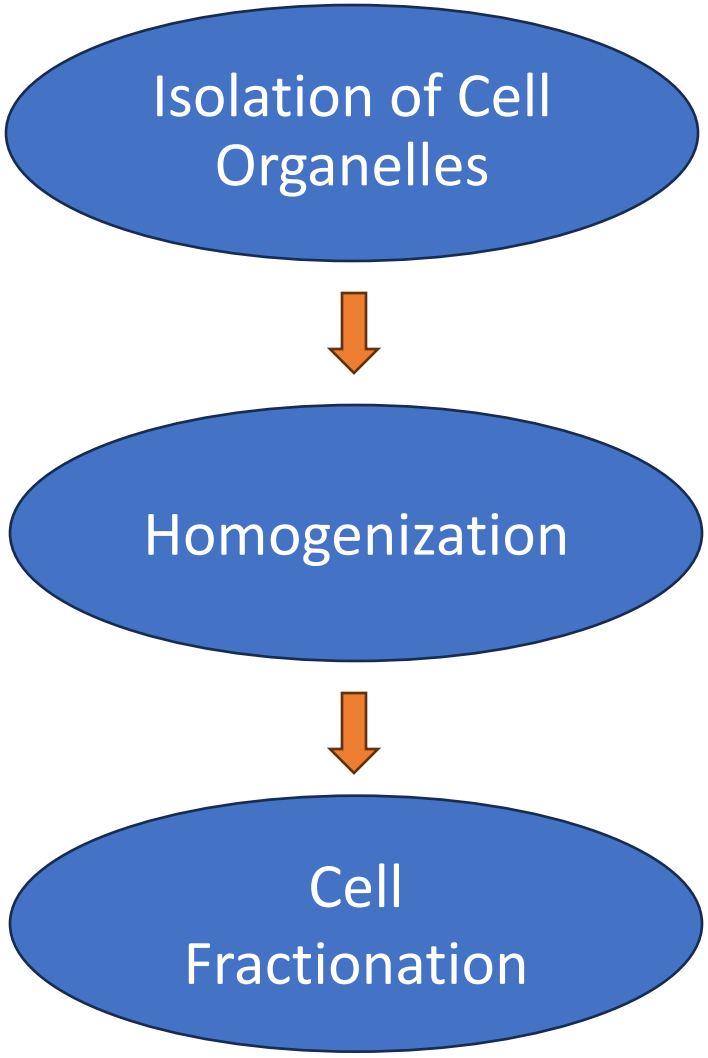
- Isolation starts with **Disruption** of the tissue being examined- **gently broken**

Differential Centrifugation

- Subsequent to Homogenization, cells are **separated** into different components by Differential Centrifugation **at various forces of gravity (g)**

Density Gradient Method - Ultracentrifugation

To isolate **Individual** cell organelles



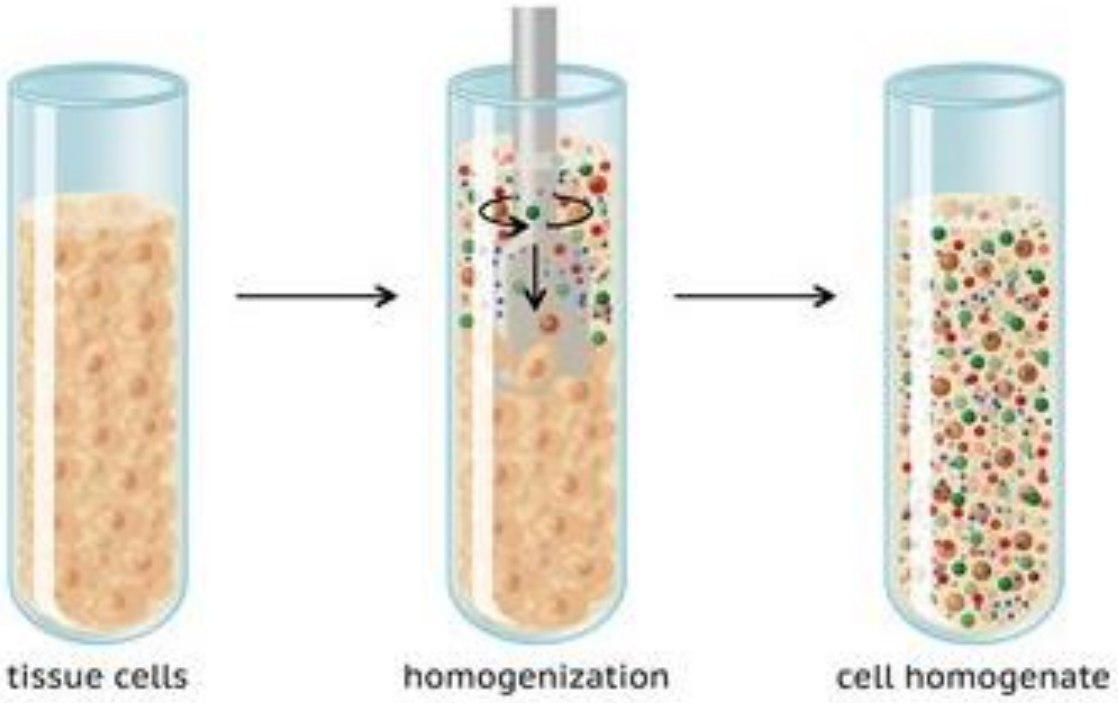
Core Knowledge

Cell Homogenization

- Breaking of the cell membrane
- Mixing up of the cellular contents

Methods:

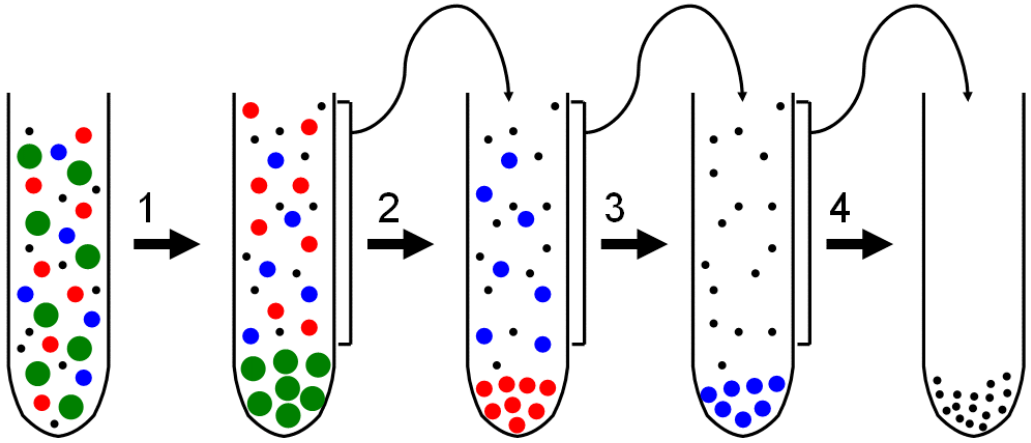
- **Using potter** - Suitable for animal tissues. A gentle method used to isolate fragile structures and molecules
- **Enzymatic lysis**
- Placing cells in **Hypotonic solutions**, fat solvents or detergent solutions
- Repeated **Freezing** and **Thawing**



Cell Fractionation

The **Goal** of **Cell Fractionation** is to **separate** the major organelles - **Individual cell function study**

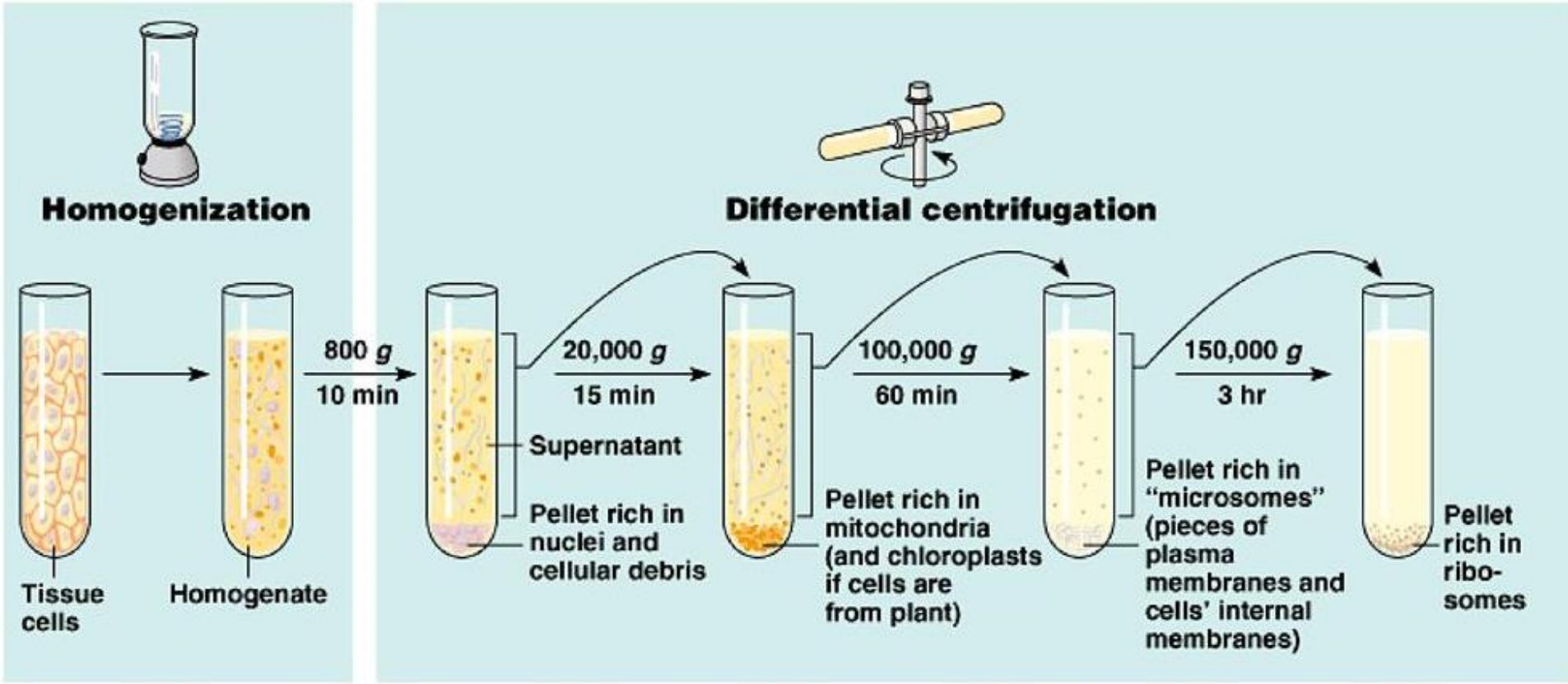
- Coarse filtration through gauze
- Differential Centrifugation
- Successive Sedimentation
- Supernatant from the last centrifugation contains cytosol with cell's soluble components.



Core Knowledge

Isolation of Various Cell Organelles

The **Goal** of **Cell Fractionation** is to **separate** the major organelles of the cells so that their individual functions can be studied.



Core Knowledge

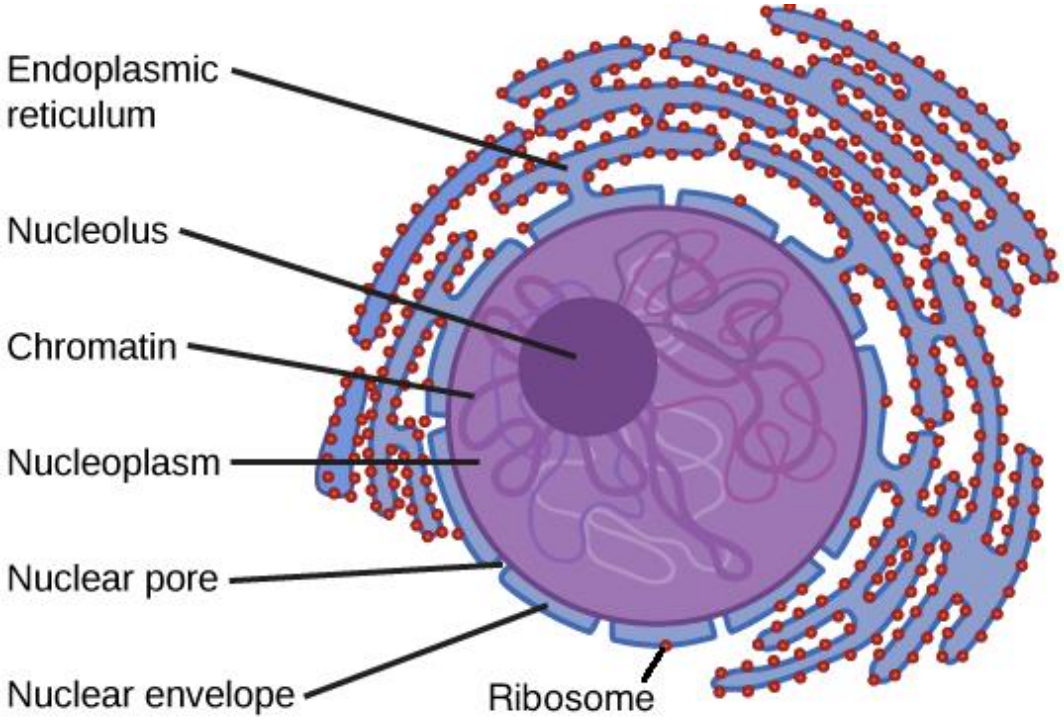
Nucleus

- Surrounded by **Double Membrane Nuclear Envelope** separating it from rest of cell (the cytoplasm)

Largest cellular organelle in Eukaryotic cells

- **Outer membrane** of envelope is **continuous** with the **membrane of RER**

- **Pores** in both membranes allow communication b/w nuclear content and cytoplasm - **to control traffic of molecules**



Core Knowledge

Nucleus

Nuclear Lamina

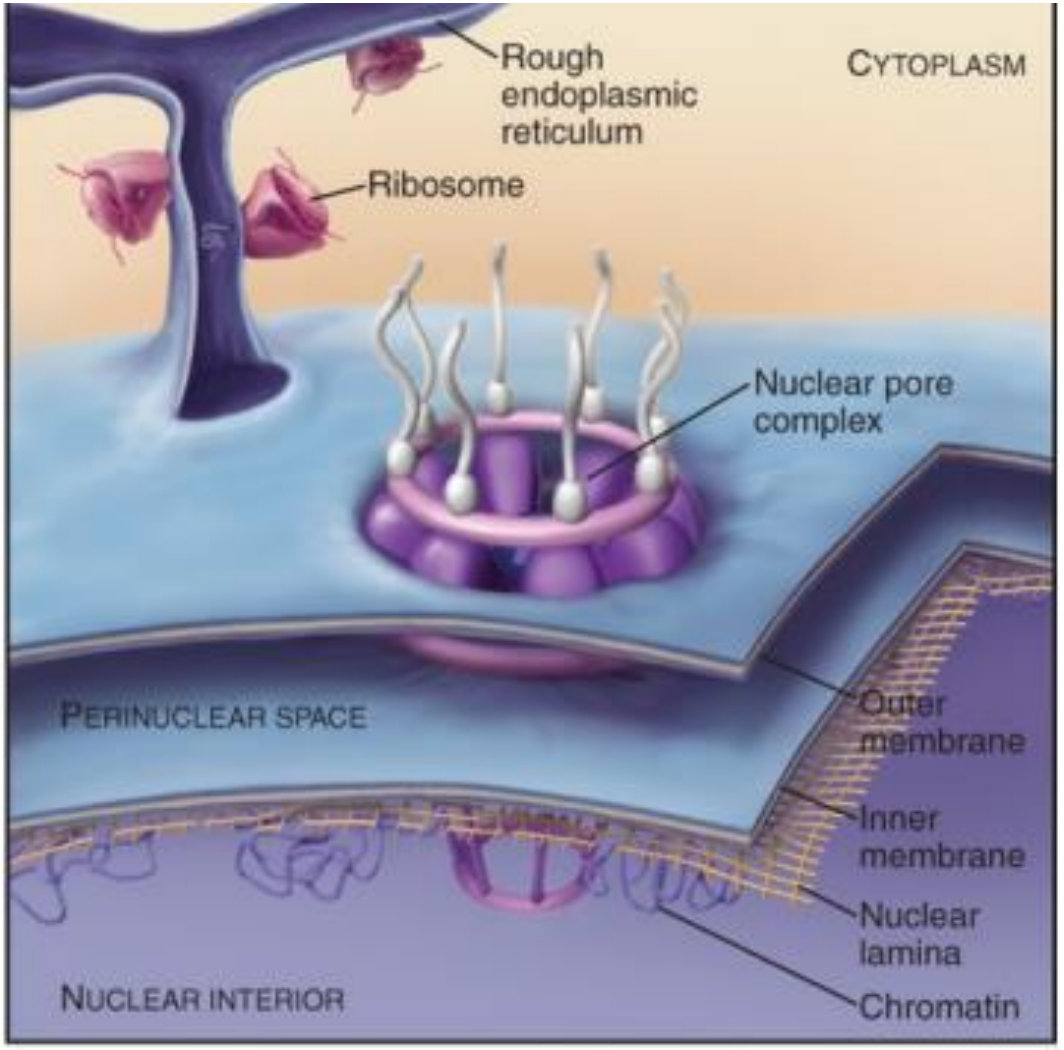
- A layer of **proteins** inside the nuclear membrane responsible for **stabilizing** it

Nucleolus

- Is closely associated with **Inner Nuclear Membrane**.
- It is rich in **RNA** especially rRNA (ribosomal RNA)
- It provides a site for **synthesis of ribosomes**

Nucleoplasm

- Ground material of nucleus which is rich in Enzymes



Core Knowledge

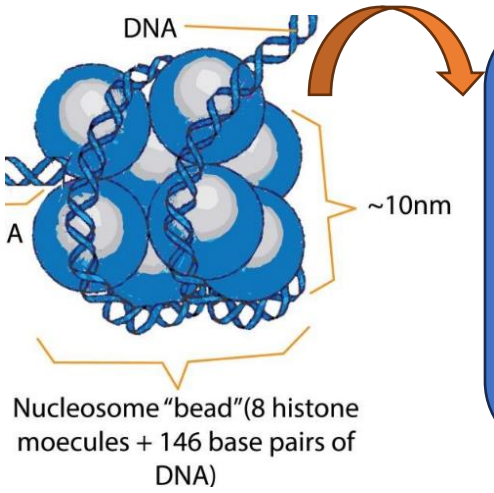
Nucleus

Genetic material is located inside **Chromosomes** (**46-23Pairs)** which are composed of numerous **Chromatin Fibers**

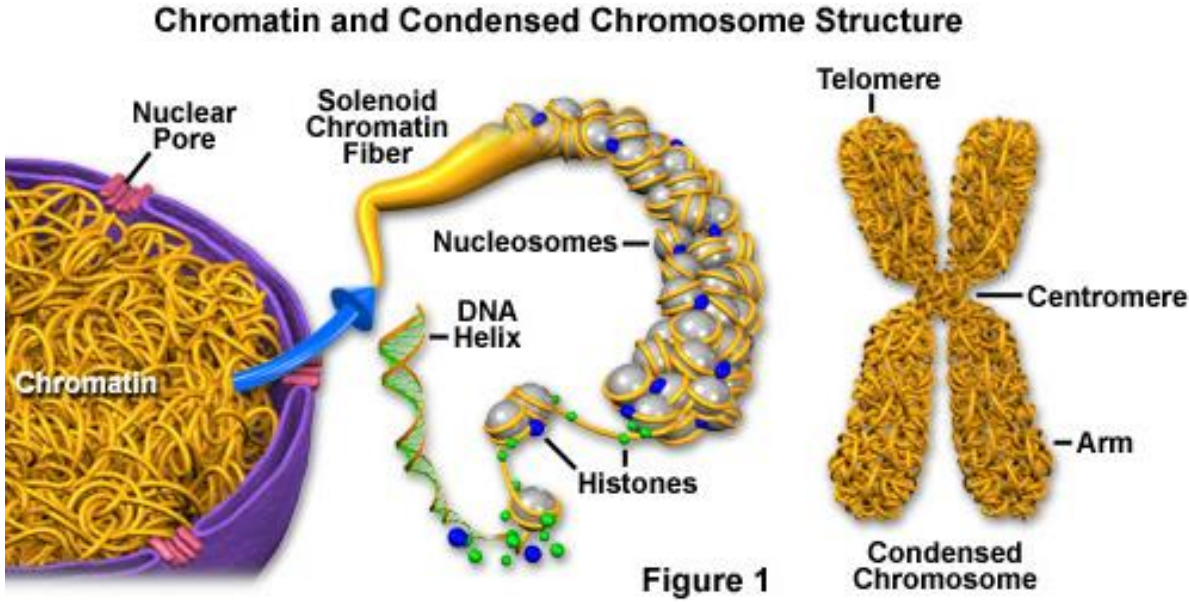
Chromatin fibers of chromosomes are composed of assembly
of **nucleosomes**

Nucleosome formed by **DNA** & **Basic Proteins** (Histones) in 1:1 ratio

A Single chromosome is composed of about a million nucleosomes.



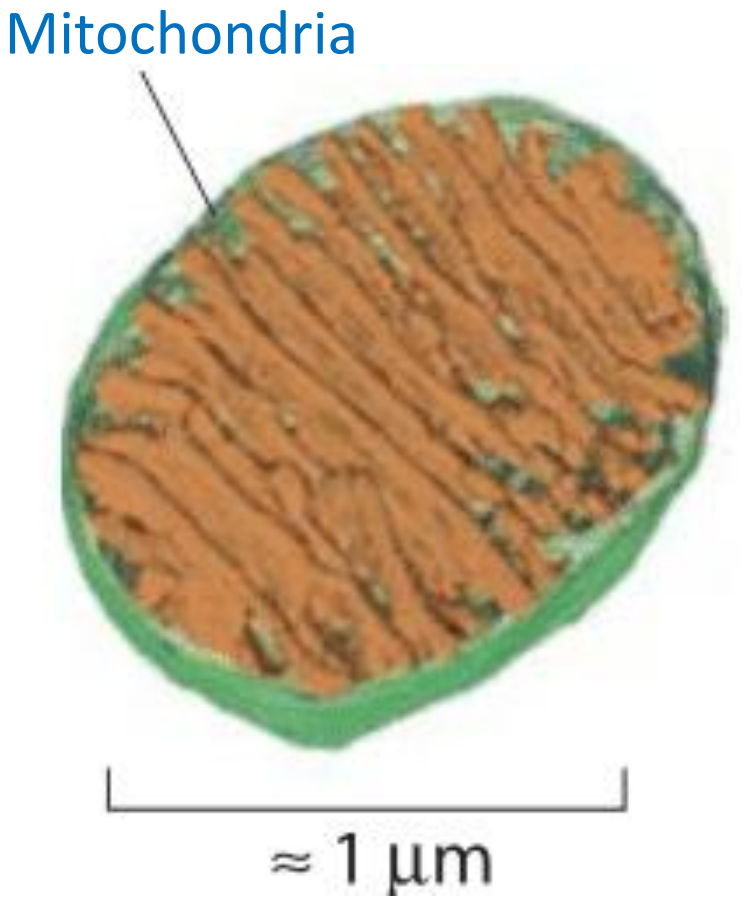
A Nucleosome is the basic structural unit of chromatin. It is made up of a coil of DNA wound around a histone core.



Core Knowledge

Mitochondria

- Produce most of chemical energy required by cell
- Regarded as **Power House** of cell
- Centre for **Cellular Respiration** and **Energy Metabolism**
- **Shape:** Rod like or filamentous bodies but shape is not static
- **Size**: variable range-0.2-0.8µ in diameter, 0.5-1.0µm length
- **Number:** About 2,000 mitochondria occupy 1/5th of cell volume



Core Knowledge

Structure of Mitochondria

Surrounding Envelope - composed of:

- Outer membrane
- Inner membrane

Outer membrane

- **Smooth** and envelops the organelle
- Consists of **Phospholipids** & contains a considerable amount of cholesterol
- Also contains copies of Integral Protein called **Porins**

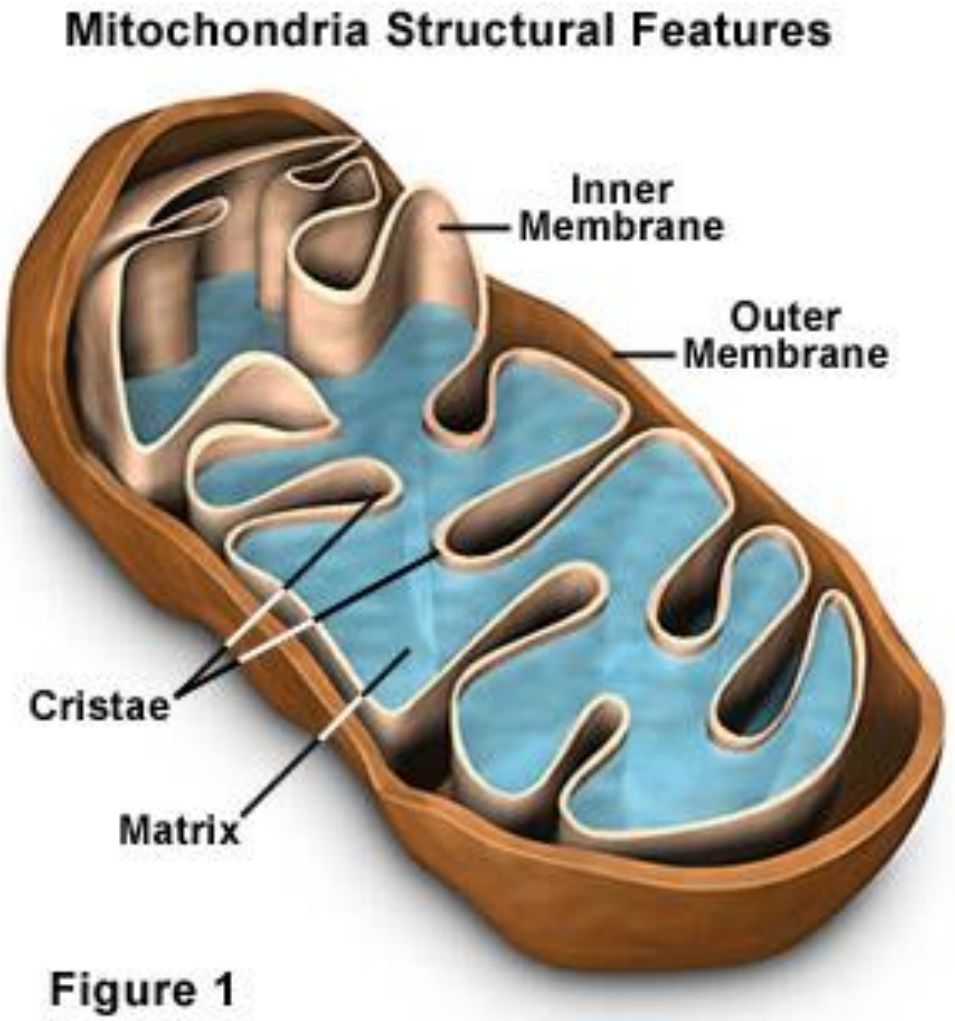


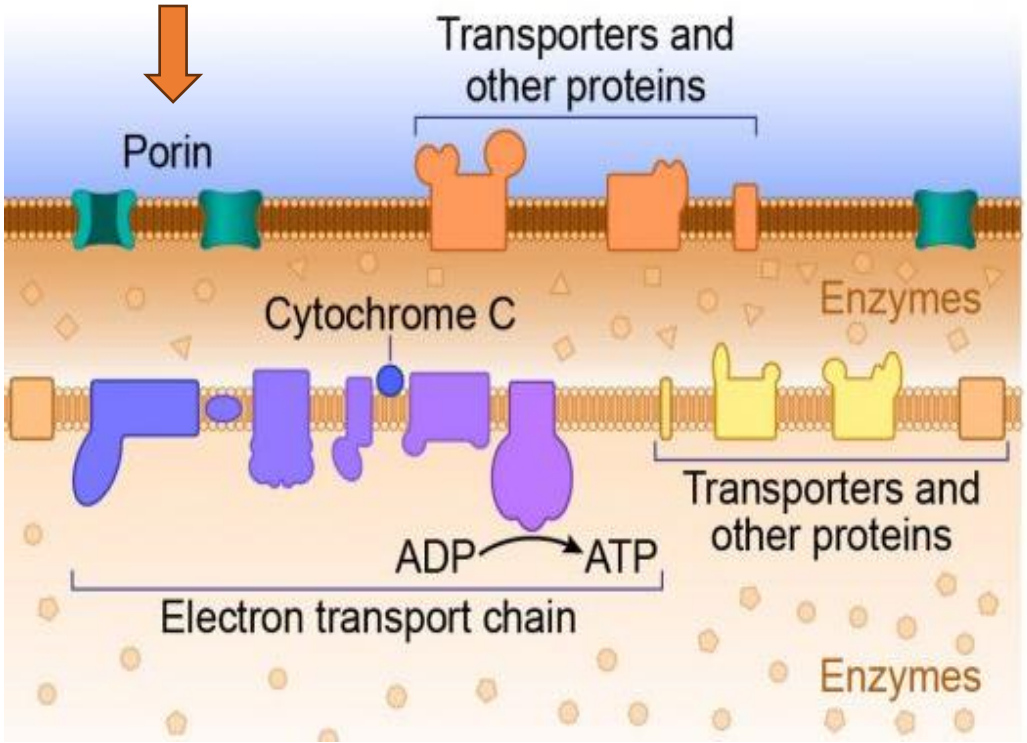
Figure 1

Core Knowledge

Inner Mitochondrial Membrane

Inner Membrane

- Folded to form **Cristae** which occupy large surface area
- Rich in **Protein** and very small lipid content
- **Impermeable** to polar and ionic substances
- These substances enter the mitochondrial matrix through **Specific**/**Transport Protein**
- Contains components/Enzymes of **Electron Transport Chain & Oxidative Phosphorylation**

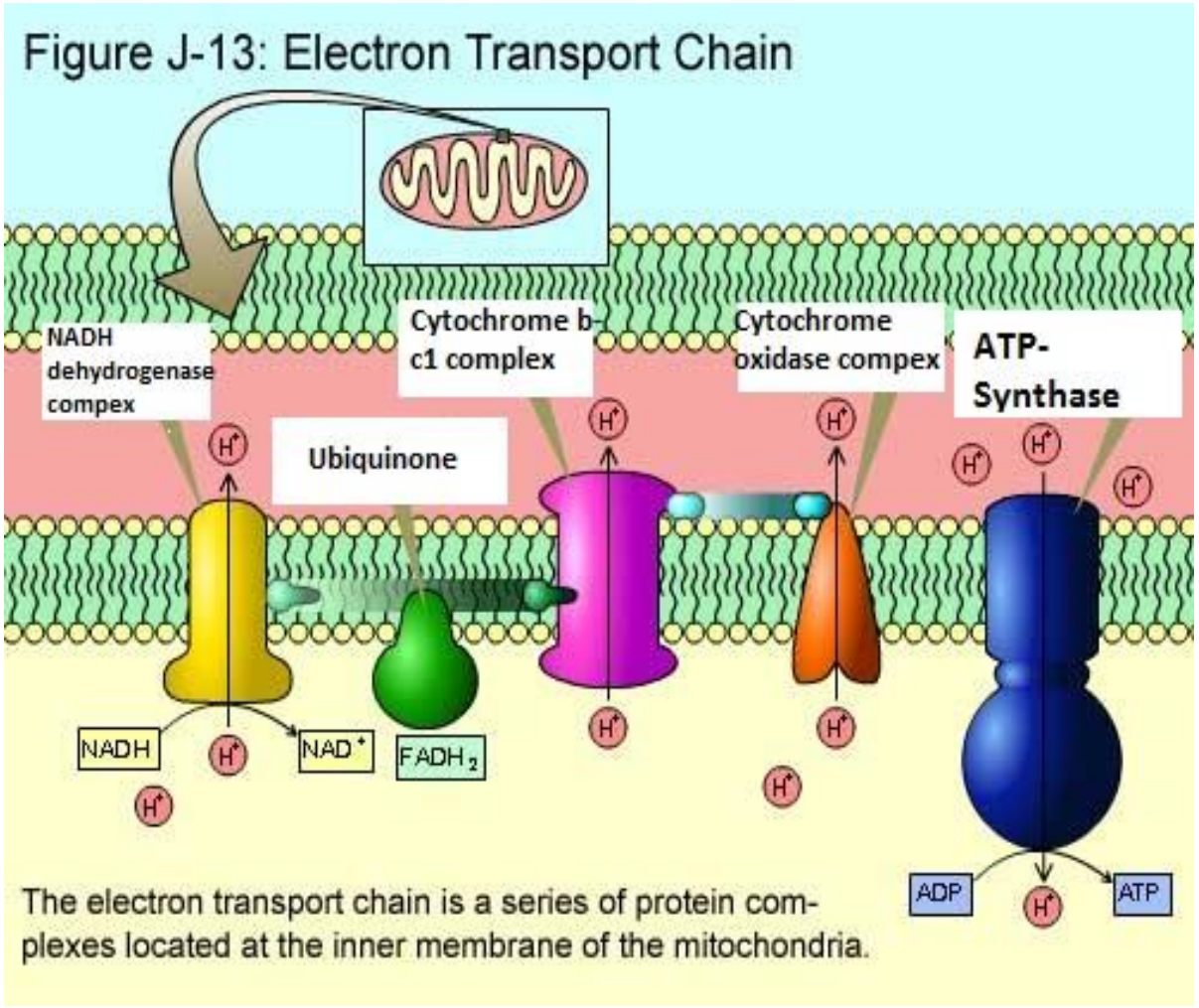


Core Knowledge

Inner Mitochondrial Membrane

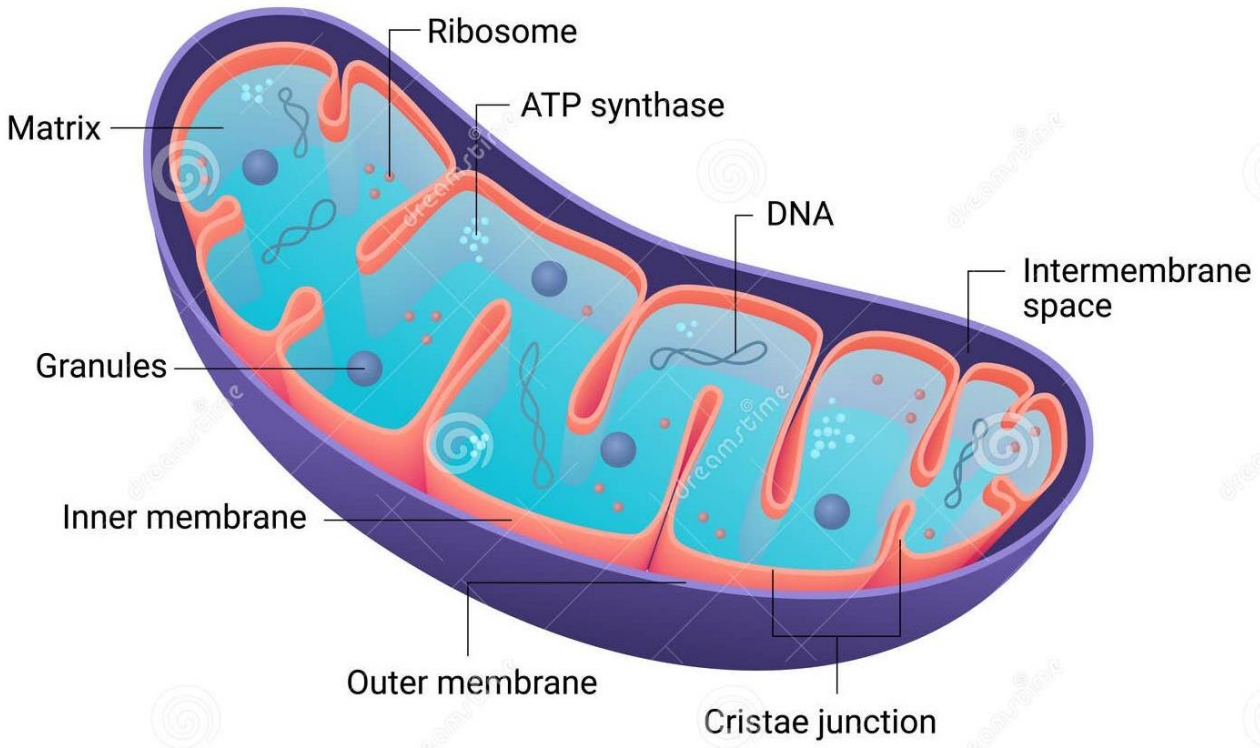
- Inner membrane particles which project into mitochondrial matrix, represent **ATP Synthase**

- **Charged State** - Its side facing mitochondrial matrix is **negatively** charged, that facing intermembrane space is **positively** charged



Intermembrane Space

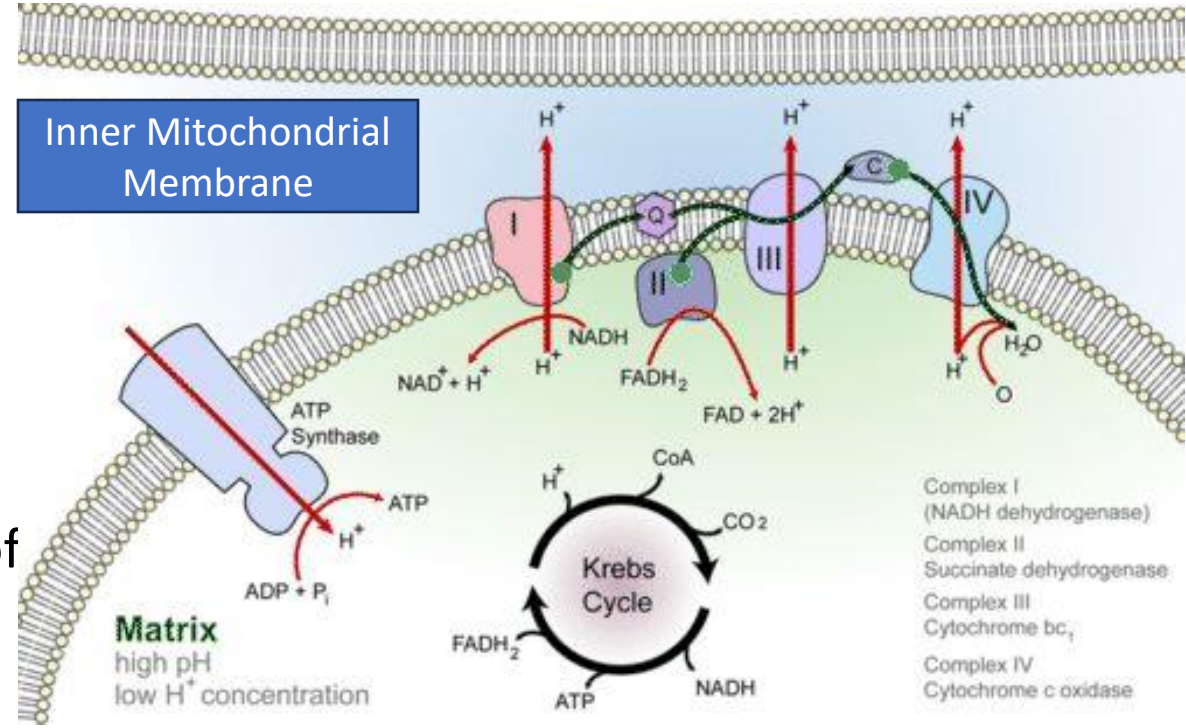
- Space **Between Inner and Outer Membranes**
- Outer membrane is freely permeable to small molecules, **Intermembrane Space has same Ionic Composition as the Cytosol**



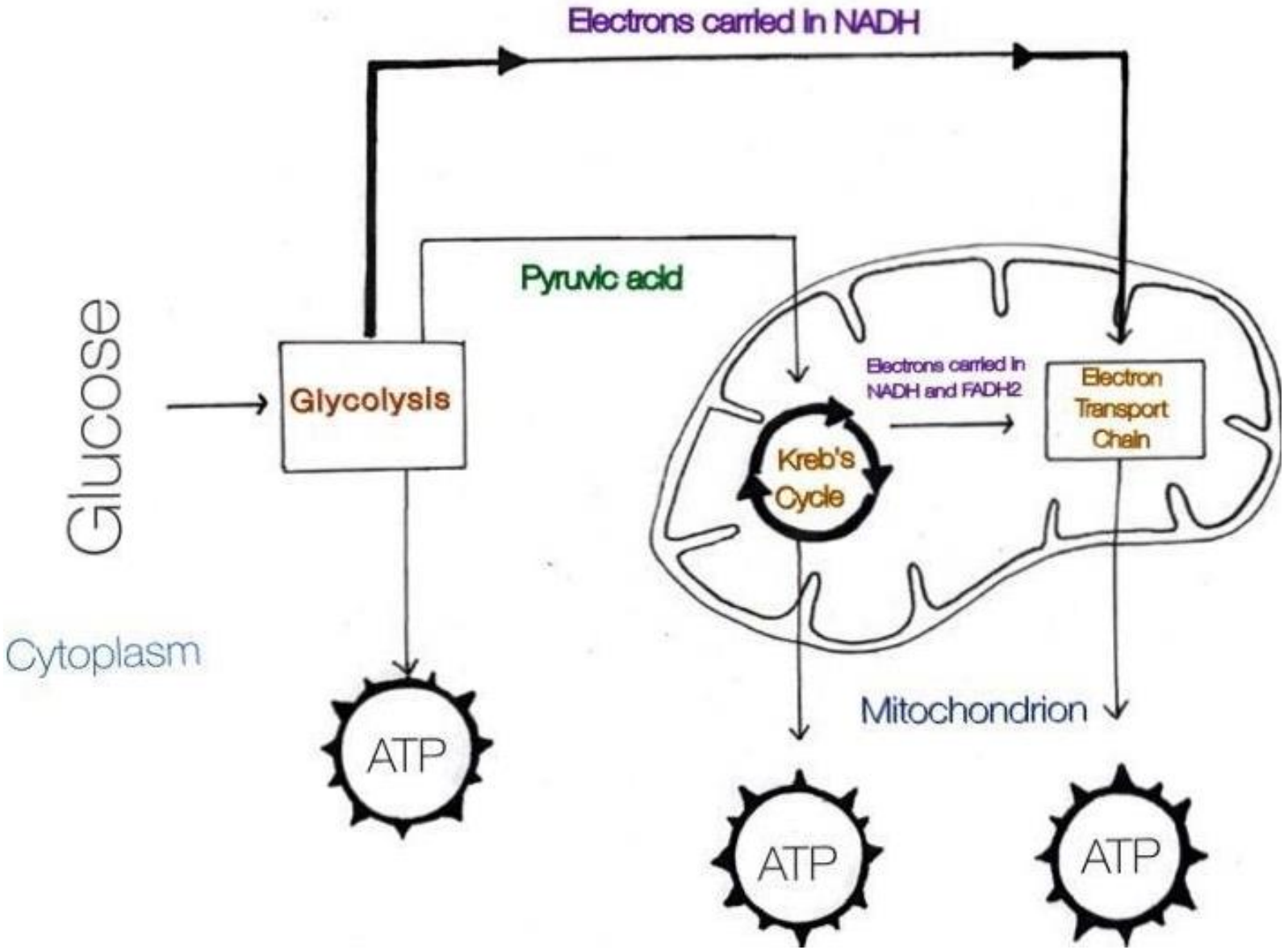
Core Knowledge

Mitochondrial Matrix

- Region enclosed by inner membrane called mitochondrial matrix or **Mitosol**
- Contains several **Enzymes** concerned with **Energy Metabolism** of Carbohydrates, Lipids & Amino Acids.
- The matrix enzymes also participate in the synthesis of **Heme** & **Urea**
- Matrix contains a circular double stranded **DNA**, **RNA** and **Ribosomes -** Independent Protein Synthesizing Machinery

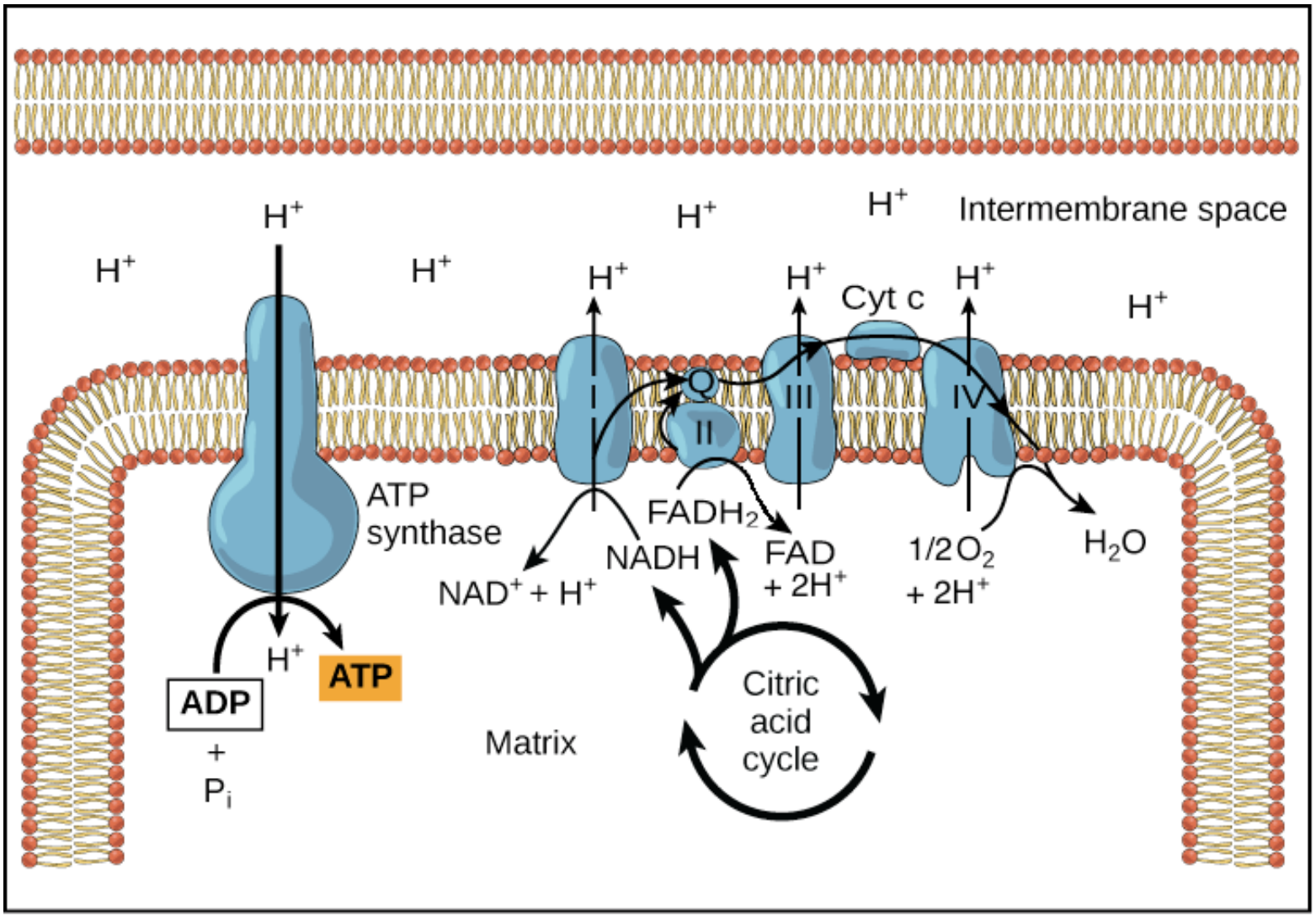


Mitochondrial Matrix

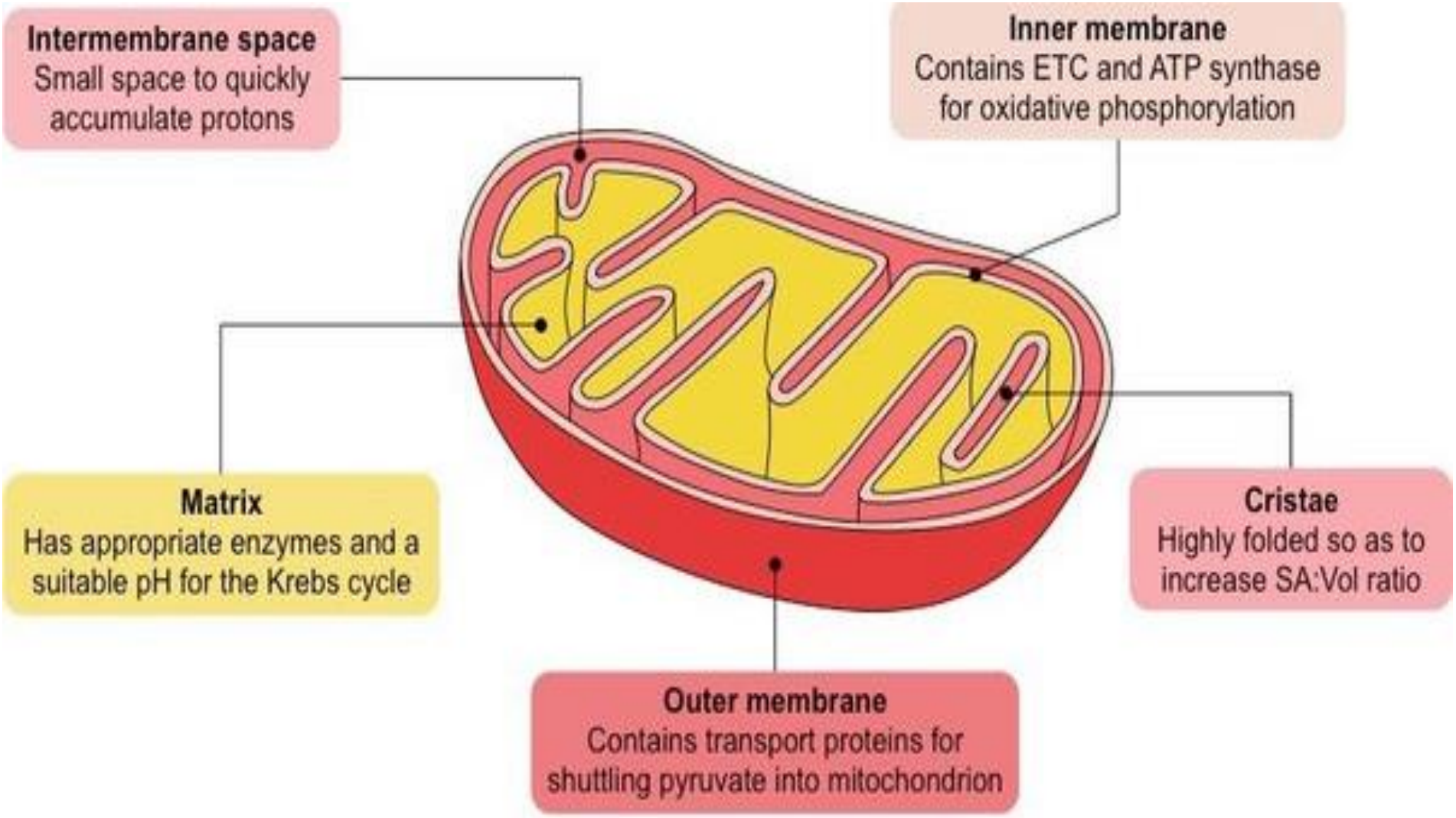


Mitochondrial Matrix

Mitochondrion specialized for rapid oxidation of **NADH** and **$FADH_2$**, traps and stores energy as **ATP**

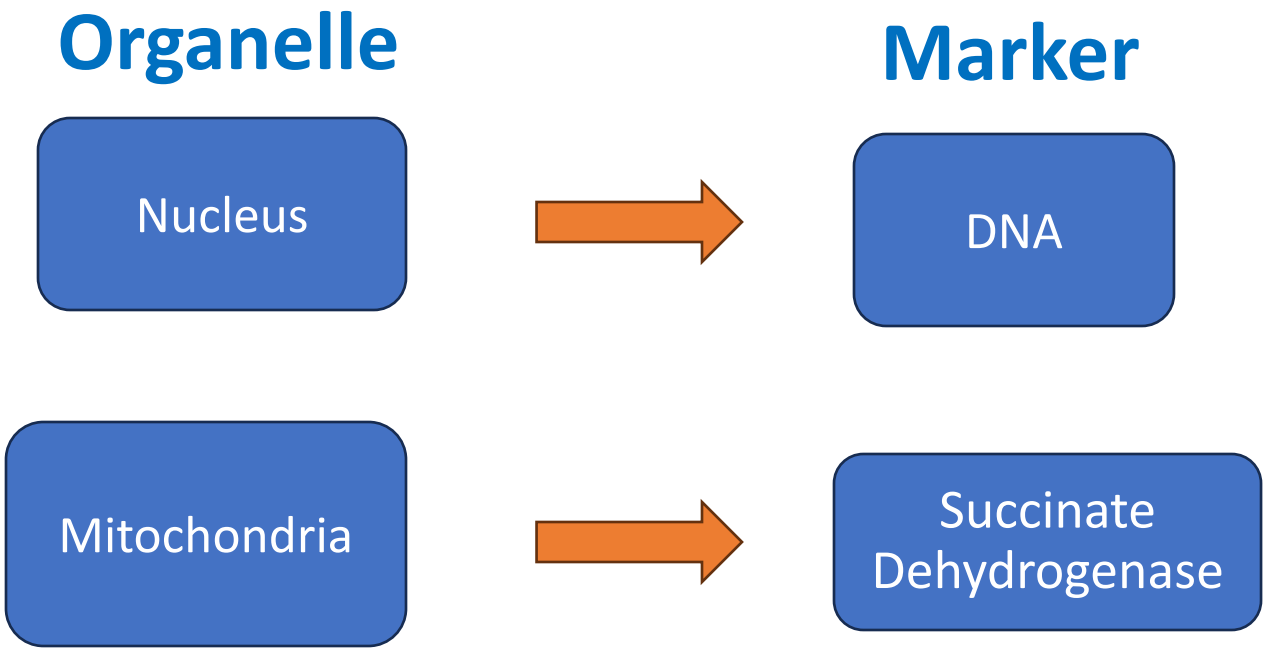


Functions of Mitochondria



Major Intracellular Markers

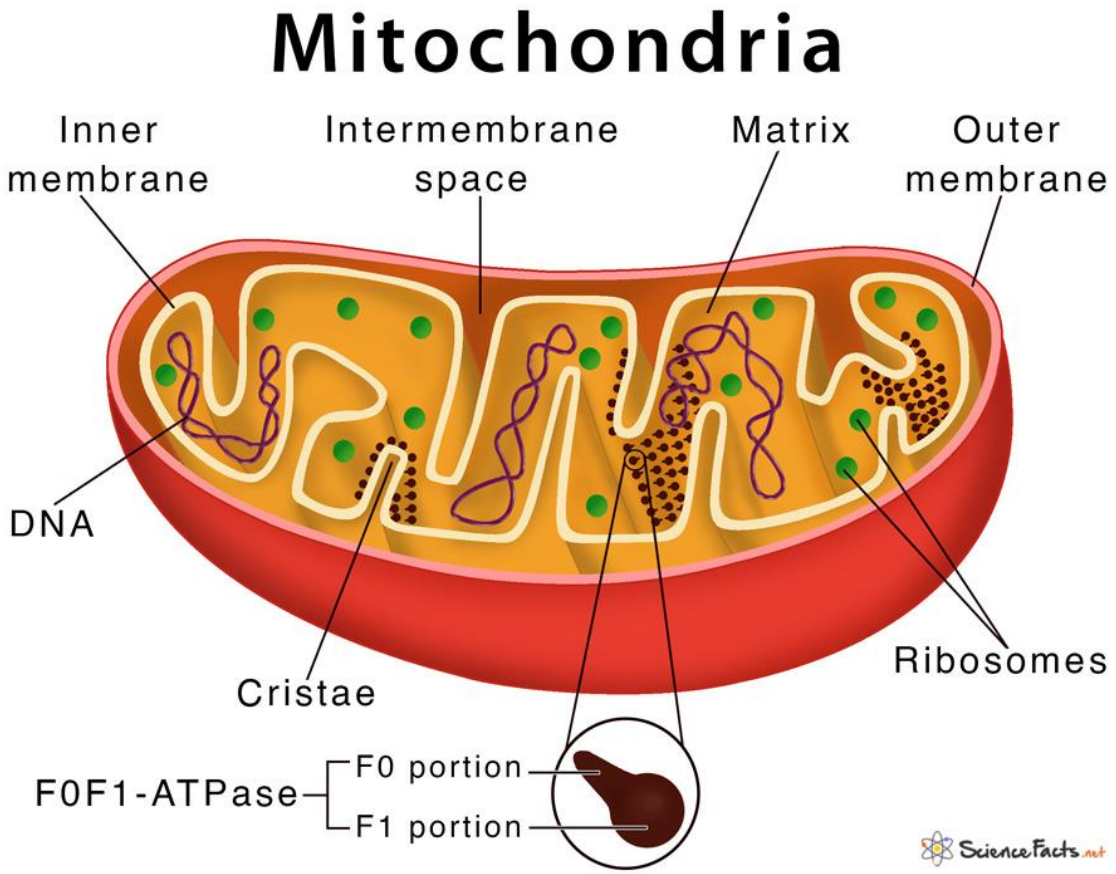
- All Cells express characteristic markers - used to **Distinguish** them from other cell types, such as proteins Lipids & Glycosylation.
- **Cell Markers** can be expressed **Extracellularly** on the surface or inside the cell as an **Intracellular** molecule



Physiology of Mitochondria

- **Functions of Mitochondria**

- Production of **ATP** (energy)
- Regulation of **Immunity**
- **Calcium** balance
- Cell death and renewal
- (**Autophagy**)
- Stem cell regulation



Clinical Correlates

Mitochondrial Diseases

- Many conditions can lead to secondary mitochondrial dysfunction including:
- Alzheimer's disease
- Muscular dystrophy
- Lou Gehrig's disease
- Diabetes
- Cancer

Clinical Correlates

Nucleus Abnormalities

- Certain **Diseases** can lead to abnormalities in the nuclei, analysis of shape and structure of nuclei in cells can lead to diagnoses.

- **Gene Mutations** or other **Abnormal Activation** of cellular genes – esp **Proto-Oncogenes** are causes of most Cancers

- **Proto-Oncogenes** - **Code** for proteins controlling normal cell function – when mutated or excessively activated become abnormally functioning **Oncogenes –** capable of causing cancer

- Oncogenes, Tumor Suppressor Genes, and DNA Repair Genes - **Balance**

- **Acute Myeloid Leukaemia** causes **Nuclei** to become **Cup-Shaped**

Clinical Correlates

Nucleus Abnormalities

- Abnormalities in the nucleoli can lead to some forms of rare **Hereditary** disease, as well as **Degenerative** diseases such as **Huntington's** and **Alzheimer's**.

- Several diseases can also result from changes in the **Nuclear Envelope**. These include **Cardiomyopathy** and **Muscular Dystrophy**

Management of Mitochondrial Diseases

Symptom Management:

- Address specific symptoms like muscle weakness, seizures, and hearing loss with appropriate therapies (e.g., anticonvulsants for seizures, hearing aids for hearing loss).

Nutritional Support:

- Ensure proper nutrition and vitamin supplementation, particularly coenzyme Q10, B vitamins, and L-carnitine, which may help support mitochondrial function.

Physical Therapy:

- Implement exercise programs and physical therapy to improve muscle strength, mobility, and function while avoiding excessive fatigue.

Pharmacological Therapy:

- Use medications like antioxidants (e.g., idebenone) and other mitochondrial-targeted drugs when available, aiming to reduce oxidative stress.

Genetic Counseling and Support:

- Provide genetic counseling for affected families. Preconception counseling and prenatal testing.

Psychological Support:

- Offer psychological counseling and support for patients and families coping with chronic illness and progressive disability.

Ethical Considerations

- From an ethical standpoint, the scenario raises considerations regarding **patient autonomy**, **informed consent**, and **confidentiality**
- The physician must ensure that patient fully understands her diagnosis, treatment options, and potential implications
- Discuss the necessity of a healthy lifestyle & treatment plan. This requires clear communication and understanding of risks and benefits.
- Additionally, the physician must respect patient's privacy and confidentiality throughout the diagnostic and treatment process

Role of AI in Management of Mitochondrial Diseases

- AI can potentially aid in **enhancing diagnostic accuracy and efficiency.**
- AI-powered decision support systems can also help clinicians in **selecting appropriate treatment modalities**
- AI-driven predictive models may help **anticipate the risk of complications of the Disease** in susceptible populations

The fountain of youth of mitochondrial research

Link:
https://www.researchgate.net/publication/374280893_The_fountain_of_youth_of_mitochondrial_research_Research_is_targeting_mitochondrial_dysfunction_to_tackle_aging_and_much_more_but_hype_is_an_increasing_concern

Journal Name: EMBO Reports, Sept 2023

Title: The fountain of youth of mitochondrial research: Research is targeting mitochondrial dysfunction to tackle aging and much more, but hype is an increasing concern

Author Name: Andrea C Rinaldi

Abstract: Mitochondria in our cells take components from the food we eat and turn them into energy. This essential role in energy metabolism is fundamental to the way cells work and the existence of complex life. Mitochondria are not only essential cellular energy factories; they also have critical functions that extend to cell signaling and are essential for everything from muscle and neuronal function to responses to viral infections. However, as they play such a pivotal role in health, defects in mitochondrial functions can also be responsible for a wide range of diseases. One group includes primary mitochondrial diseases, a range of genetic disorders that can result in heart failure, blindness, muscle weakness, and death. Another is secondary mitochondrial diseases: neurodegenerative disorders, cancer, diabetes, and obesity that have a component of mitochondrial dysfunction. Critically, defects in mitochondria, as well as primary and secondary mitochondrial diseases, have also been linked with aging associated processes.

How To Access Digital Library

Steps to Access HEC Digital Library

a) Go to the website of HEC National Digital Library
b) On Home Page, click on the INSTITUTES
c) A page will appear showing the universities from Public and Private Sector and other Institutes which have access to HEC National Digital Library HNDL
d) Select your desired Institute
e) A page will appear showing the resources of the institution
f) Journals and Researches will appear
g) You can find a Journal by clicking on JOURNALS AND DATABASE and enter a keyword to search for your desired journal

Learning Resources

- Textbook of Biochemistry, Lippincott 8th edition, chapter no 6 & 30. , page no. 81-82 & 461
- Guyton and Hall Textbook of Medical Physiology 13th Edition, Chapter-2, pages- 11, 16, 17 & 18
- Essentials of Medical Biochemistry, Mushtaq Ahmad, Volume-1, 9th Edition, Chapters 1 & 8, Pages 2, 3-5 & 181-183
- Harper's Illustrated Biochemistry 32nd Edition
- Google Scholar
- Google Images

THANK YOU