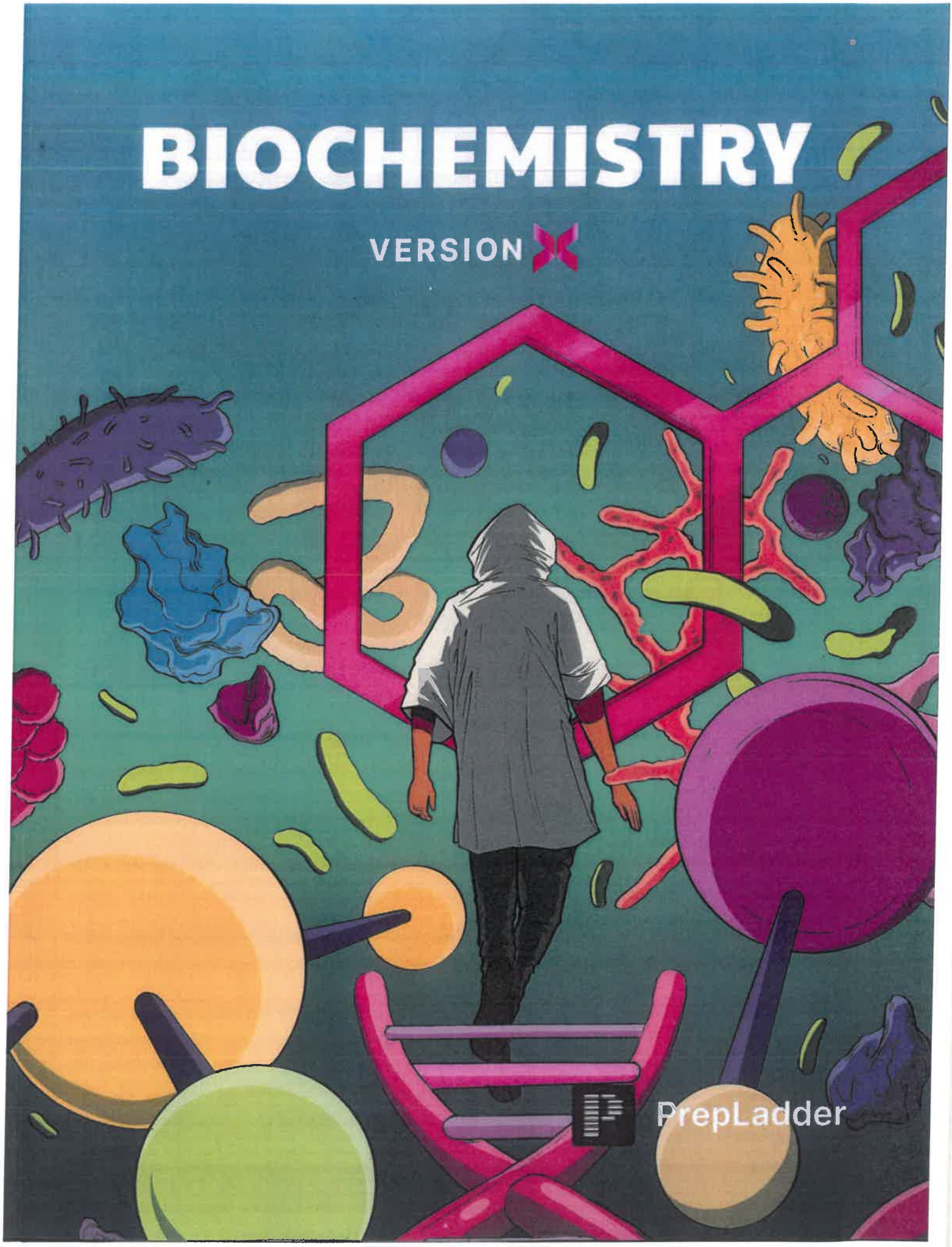
BIOCHEMISTRY

VERSION X



Structured Notes According to

BIOCHEMISTRY

Revision friendly Fully Colored Book/Structured Notes

For Best results, watch the video lectures along with reading notes

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(Author)

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Biochemisty

LIPID METABOLISM

AMINO ACIDS AND PROTEINS CHEMISTRY

AMINO ACIDS METABOLISM

GENETICS

HEME METABOLISM

VITAMINS

MINERALS

1. CELL AND SUBORGANELLES

PATHWAYS AND SUBORGANELLES

00:00:58

PATHWAY	SUBORGANELLES
Glycolysis	Cytoplasm
PDH	Mitochondria
TCA cycle	Mitochondria
Glycogen metabolism	Cytoplasm
Gluconeogenesis	Mitochondria, Cytoplasm, Endoplasmic reticulum
HMP shunt	Cytoplasm
Fatty acid synthesis	Cytoplasm
Fatty acid oxidation	Mitochondria Very Long Chain FA – Peroxisomes
Ketone body synthesis	Mitochondria
Cholesterol synthesis : Steroid	Cytoplasm, Smooth endoplasmic reticulum
Bile acid synthesis : Steroid	Smooth endoplasmic reticulum
Urea cycle	Cytoplasm, Mitochondria
Heme synthesis	Cytoplasm, Mitochondria

GLYCOLYSIS

00:01:12

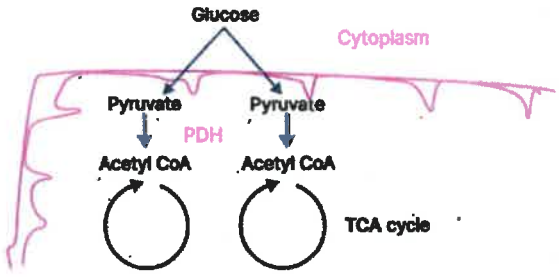
PRODUCTS

Aerobic : 2 Pyruvate, 7 ATPs

Anaerobic : 2 Lactate, 2 ATPs

- Glycolysis : Only pathway generating ATP in absence of O_2

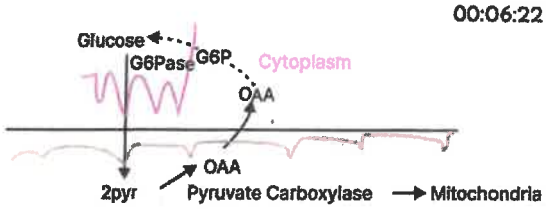
GLYCOLYSIS, PDH, AND TCA CYCLE



GLYCOLYSIS AND GLUCONEOGENESIS

00:06:22

- Gluconeogenesis : Reversal of glycolysis
- [redacted]
  - Present in mitochondria
- Last step : G-6-P formation
- Glucose-6-phosphate dehydrogenase : Enzyme of HMP shunt
- Glucose -6-phosphatase : Last enzyme
  - Marker enzyme of endoplasmic reticulum



FUNCTIONS OF PEROXISOMES

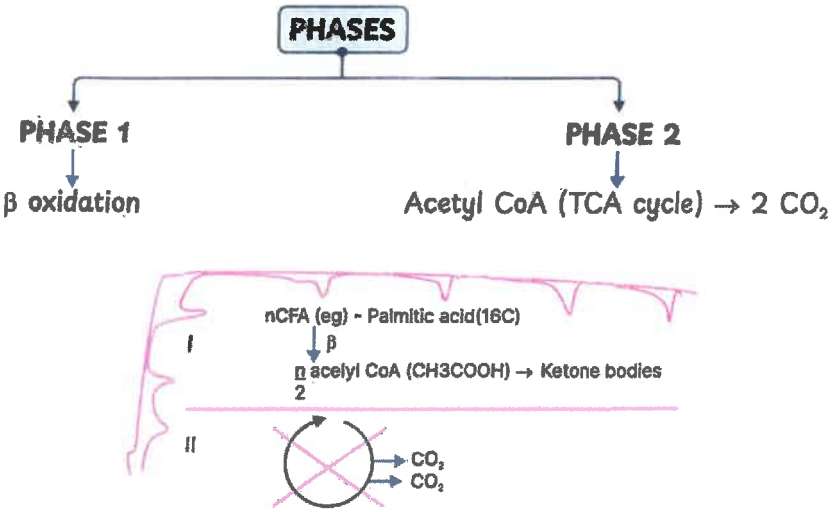
00:10:25

- VLCFA oxidation
- Branched-chain FA oxidation (Defect - Refsum's Disease), Ether lipid synthesis
- Glycine and Taurine conjugation of bile acids

Cholesterol (modification)
↓
Bile acids
↓
Conjugation with Glycine, Taurine
↓
Bile salt
↓
Lipid digestion and absorption

FATTY ACID OXIDATION

00:13:03



- When Acetyl CoA does not enter TCA cycle
  - Acetyl CoA → [redacted]

Important Information

- Smooth endoplasmic reticulum : Steroid synthesis
- Rough endoplasmic reticulum : Protein synthesis

UREA CYCLE

- Detoxification of ammonia
- Major source of ammonia : Amino acid catabolism
- [redacted]

SUB ORGANELLES AND MARKER ENZYMES

00:21:01

ORGANELLE	MARKER ENZYME
Nucleus	• Replication-DNA polymerase • Transcription- RNA polymerase
Endoplasmic Reticulum	• Glucose-6-Phosphatase
Golgi Complex (Glycoprotein synthesis)	• Glucosyl/ Galactosyl transferase
Mitochondria	• Outer membrane o Monoamine oxidase (MAO) • Inner membrane (ETC complex) o Complex V/ATP synthase o Complex II/Succinate dehydrogenase
Lysosome	Cathepsin (Proteases)
Cytoplasm (glycolysis)	Lactate dehydrogenase
Peroxisome (H_2O_2)	Catalase

- Chromosome : Long ds DNA condensed with help of proteins

PROTEIN SYNTHESIS AND SORTING

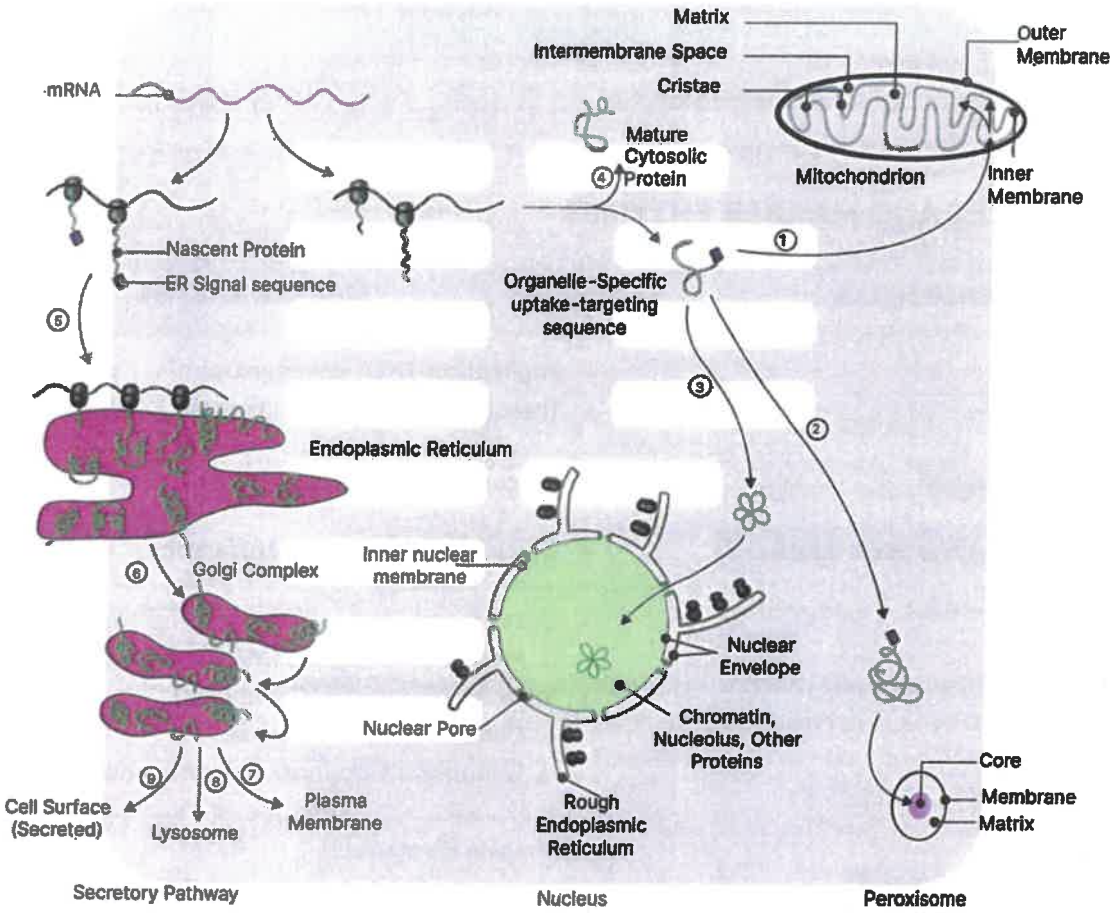
00:28:48

PROTEINS SYNTHESIS

- Initially : Free ribosomes

Read mRNA 5'-3' (read codons 1 by 1)
↓
Recruit complementary anti-codon-containing tRNA molecules (drags AA)
↓
Translation
↓
Polypeptide chain : Amino-terminal (1st AA) end → Carboxyl terminal end (last AA)

- Proteins synthesized
  - o Mitochondrial/Nuclear/Cytoplasmic proteins



OTHER TYPES OF PROTEINS

- *Lysosomal proteins : Mannose-6-phosphate*
- *Membrane proteins : Lipid side chain*
- *Secretory proteins*

- *Requires specific targeting sequences → ER and Golgi complex*
- *Initiated by free ribosomes and involves Rough ER*
- *Amino-terminal end : Signal recognition peptide sequence*

↓

Guides ribosome (attach to ER) → Rough ER

- *Ribosome : Translate mRNA and growing polypeptide chain*
- *On RER formation → Remove signal recognition peptide sequence*

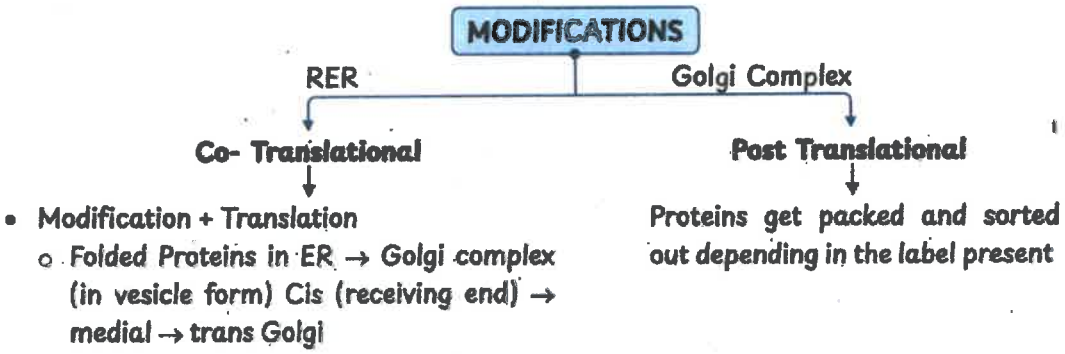
Preproproteins

↓

Proproteins

↓

Proteins



LABEL	TARGET
Mannose-6-residue	Lysosome
Lipid side chain	Membrane
No lipid or mannose	Secretory protein

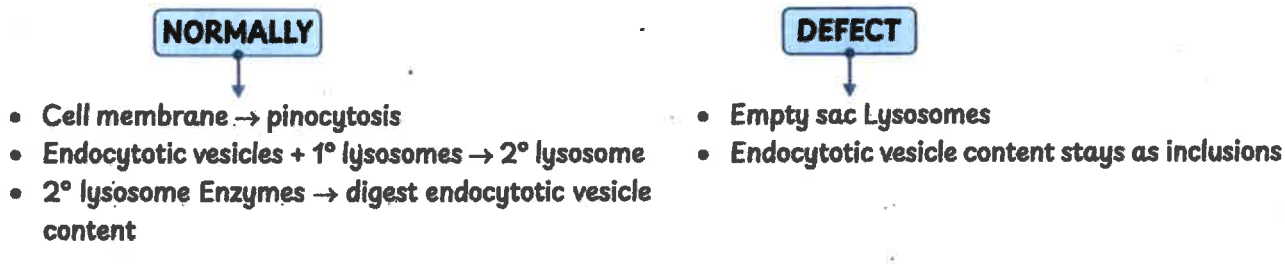
- Nuclear protein, Cytoplasmic protein, Mitochondrial protein : Free ribosome
- Lysosomal, Membrane, Secretory Proteins : Free ribosome (initial) → ER

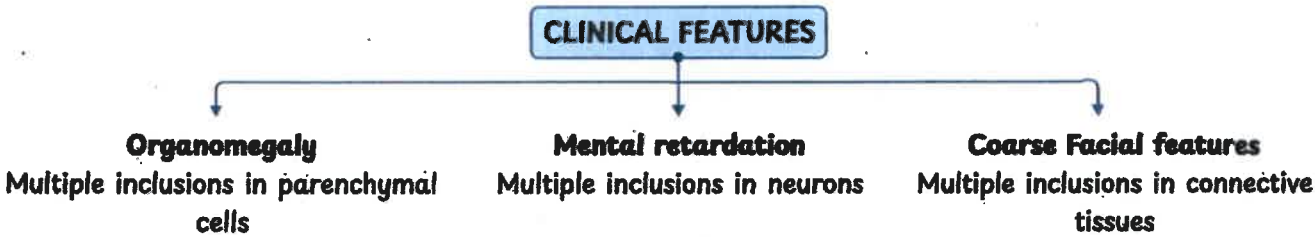
PROTEIN TARGETING DEFECTS

00:45:44

I CELL DISEASE/ INCLUSION CELL DISEASE

- Lysosomal storage Disorder
- [redacted]
  - N-Acetylglucosamine Phosphotransferase : Form Mannose-6-P → Target lysosomal proteins to lysosomes
- No Mannose-6-P, Empty bag lysosome





- [redacted]
- ↓Tissue lysosomal enzyme

HYPEROXALURIA

00:52:49

- Recurrent renal stones

CAUSES

Secondary Hyperoxaluria

↑Oxalate-rich food diet → Chocolates, Tea, beetroots, Green leafy vegetables

Enteric hyperoxaluria → Fat malabsorption

Primary Hyperoxaluria

Type 1
- Protein targeting defect
- Glyoxylate Alanine aminotransferase : misplaced in mitochondria instead of peroxisome
- No Reversible reaction
- Excess Glyoxalate → Oxalic acid

Type 2
- Defective Glyoxalate reductase
- Excess Glyoxalate → Oxalic acid

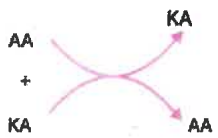
SECONDARY HYPEROXALURIA

Normally
- 5-10% of dietary oxalate absorbed in intestine
- Remaining Combines with calcium → Calcium oxalate (insoluble) → excreted in feces

Fat Malabsorption
- FA accumulation + calcium → Soap
- No calcium oxalate formation
- [redacted]

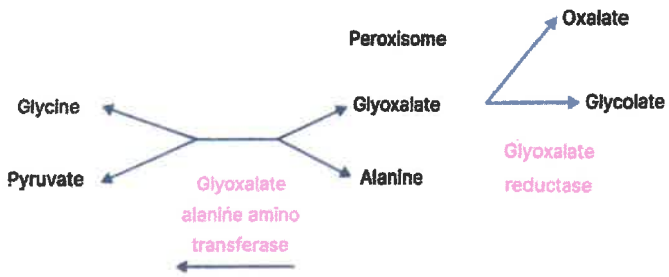
PRIMARY HYPEROXALURIA

- Glycine metabolism



Transamination reaction

  - Glycine (AA) + Pyruvate (KA) → Glyoxylate (KA) + Alanine (AA)
  - Site : Peroxisome
- Reaction : Reversible
- Enzyme : [redacted]
- No glyoxalate reductase action
  - Glyoxalate → Oxalic acid

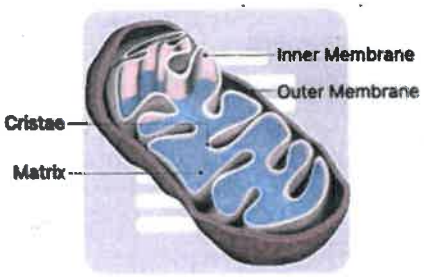


MCQ's

IMAGE-BASED MCQ'S

01:02:52

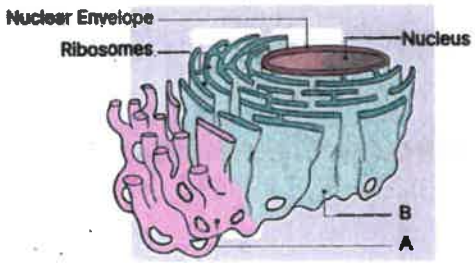
Q. Identify the sub-organelle, mention its function and the marker enzyme



Ans:

- Sub-organelle : Mitochondria
- Function
  - ETC complexes present
  - Oxidative phosphorylation
  - Citric acid cycle
  - Fatty acid oxidation
  - Heme synthesis and urea cycle
- Marker enzyme
  - For outer membrane- Monoamine oxidase
  - For inner membrane
    - → Complex V/ATP synthase
    - → Complex II/Succinate dehydrogenase

Q. Identify the sub-organelle marked as A and B, mention their function and the marker enzyme

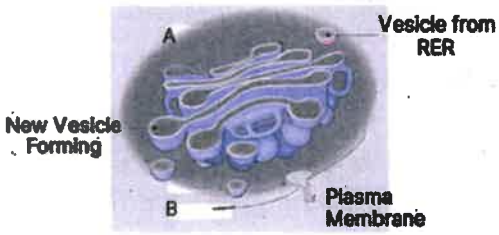


Ans:

- A : Smooth endoplasmic reticulum
- B : Rough endoplasmic reticulum
- Functions
  - Smooth endoplasmic reticulum – steroid synthesis
  - Rough endoplasmic reticulum – protein synthesis

- Marker enzymes : Glucose-6-phosphatase

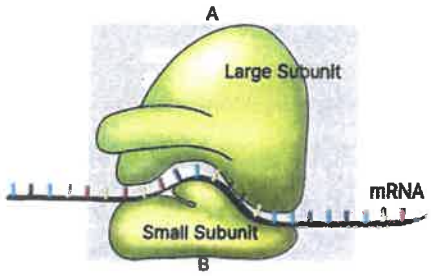
Q. Identify the sub-organelle marked as A and B, mention their function and the marker enzyme



Ans:

- A : Cis Golgi – receiving side of Golgi apparatus
- B : Trans Golgi- shipping side of Golgi apparatus
- Function
  - Protein modifications and sorting
  - Post-translational modifications
- Marker enzyme : Glucosyl/ Galactosyl transferase

Q. Identify the sub-organelle marked as A and B in Eukaryotes and mention their function.



Ans:

- A : 60s – large subunit of ribosome
- B : 40s - small subunit of ribosome
- Function : Protein synthesis and translation

MCQs

Q. Which of the following pathways only takes place in a cell's cytoplasm? (FMGE JAN 2023)

a. Glycolysis
b. Beta oxidation
c. TCA
d. Urea cycle

Ans (a)

Q. The marker enzyme of microsomes is?

a. Galactosyl Transferase
b. Cathepsin
c. Lactate Dehydrogenase
d. Glucose-6-Phosphatase

Ans (d)

Q. Cytoplasmic proteins are synthesized in?

a. Ribosomes
b. Nucleus
c. Smooth Endoplasmic Reticulum
d. Rough Endoplasmic Reticulum

Ans (a)

Q. Secretory proteins are synthesized in:

a. Ribosomes
b. Smooth Endoplasmic Reticulum
c. Rough Endoplasmic Reticulum
d. First in the Ribosomes and then in the Endoplasmic Reticulum

Ans (d)

Q. A child is present with coarse features, HSM, and mental retardation. The clinician suspects LSD and asks the IEM lab to perform a few lysosomal enzyme activities, including Hexosaminidase A. All lysosomal enzyme activities were high. What is probably the diagnosis?

a. Tay Sachs Disease
b. Mucopolysaccharidosis I
c. Mucopolysaccharidosis II
d. I Cell Disease

Ans (d)

Q. A 39-year-old man came to the emergency department because of severe back pain. An ultrasound was taken, and renal stones were found. Following lithotripsy, a sample of the stone was sent for biochemical analysis. Results revealed the presence of oxalate and glyoxylate. He was diagnosed with primary hyperoxaluria Type I. It is caused by?
a. Protein Folding defect
b. Silent Mutation
c. Protein Targeting Defect
d. Acceptable Mutation

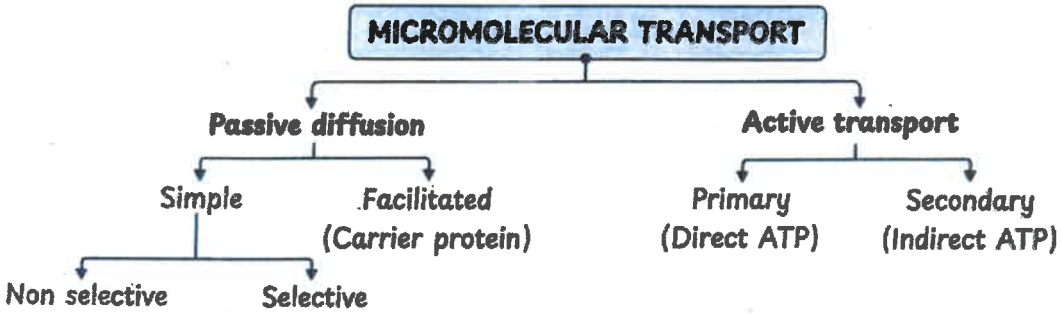
Ans (c)

2. TRANSPORT AND RECEPTORS

TRANSPORT

00:01:23

- Types of transport mechanism
  - Micromolecular transport mechanism
  - Macromolecular transport mechanism

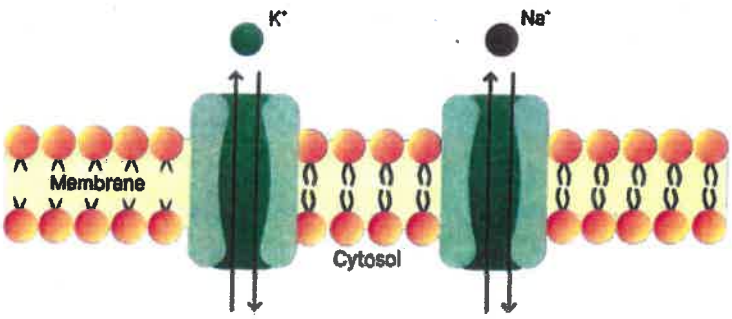


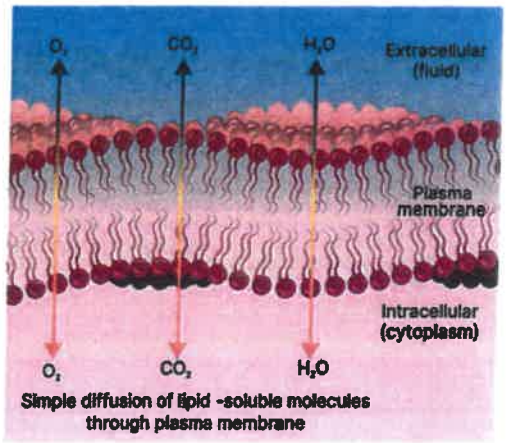
PASSIVE DIFFUSION

- Passive diffusion : [redacted]

SIMPLE PASSIVE DIFFUSION

- Nonselective simple passive diffusion : CO_2 and urea diffusion
- Selective simple passive diffusion : ION channels
- Rate of diffusion = concentration gradient



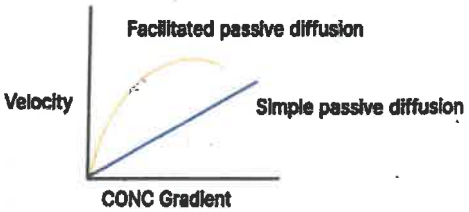


FACILITATED PASSIVE DIFFUSION

- GLUT transporters : carrier proteins
- Epithelial sodium channels : [redacted]
- Aquaporin 2 channels : Vasopressin acting on V2 receptors

KINETICS

- ↑ concentration gradient
  - Passive simple diffusion
    - → Rate of transport ↑ linearly
    - → Follow linear kinetics



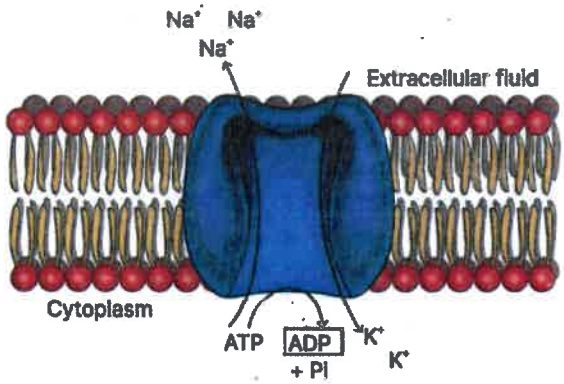
- Facilitated passive diffusion
  → Initially linearly → Reaches plateau
  → [redacted]
- Every transport mechanism follows saturation kinetics except passive simple diffusion

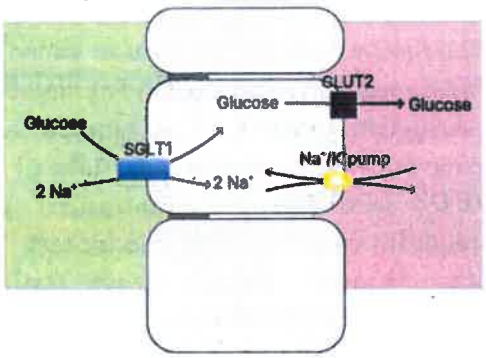
ACTIVE TRANSPORT

00:13:14

- Transport substances against concentration gradient (low → high)
- Energy required

PRIMARY ACTIVE TRANSPORT	SECONDARY ACTIVE TRANSPORT
• Na^+/k^+ ATPase pump • Calcium ATPase • H^+/k^+ ATPase	• Na^+ amino acid cotransporters • Na^+ glucosecotransporters • Na^+ bicarbonate cotransporters • Na^+/H^+ antiporter





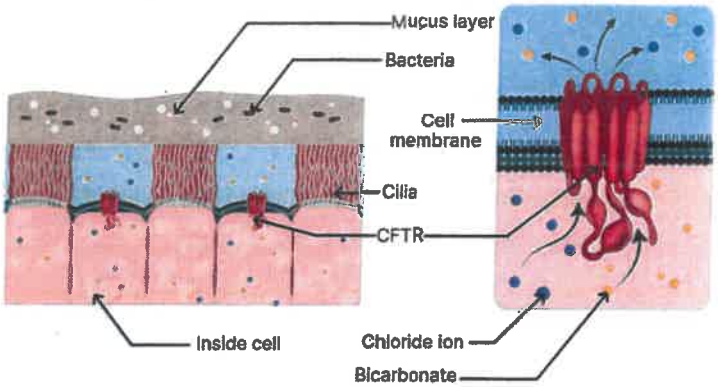
NA^+/K^+ ATPASE PUMP	CALCIUM ATPASE	H^+/K^+ ATPASE
• ICF to ECF : 3 Na^+ out 2 K^+ in against concentration gradient • Carrier protein uses ATP directly	• Pumps calcium → sarcoplasmic reticulum against concentration gradient • Hydrolyse ATP directly	• Gastric parietal cells : to secrete H^+ into gastric lumen • Pumps K^+ into ICF • Against concentration gradient • Hydrolyse ATP directly

TYPE OF TRANSPORT	EXAMPLE
Nonselective simple passive diffusion	CO_2 and urea diffusion
Selective simple passive diffusion	Ion channels
Facilitated passive diffusion	GLUT transporter, ENAC, Aquaporin 2 channels
Primary active transport	Na^+/K^+ ATPase , calcium ATPase , H^+/K^+ ATP
Secondary active transport	• Na^+ amino acid cotransporters • SGLT1, SGLT2 • Na^+ bicarbonate cotransporters • Na^+/H^+ antiporter

CYSTIC FIBROSIS

00:23:54

- Autosomal recessive
- CFTR (cystic fibrosis transmembrane conductance regulator) protein defect
- Function of CFTR protein in airways
  - ATP binds to ion channel → ions moved from epithelial cells to duct: Cl^-, $HCO3^-$ (high to low concentration)
  - Duct secretion : Rich in Cl^- and $HCO3^-$ → Retain na+ → Osmotically active → Retain water → Thin and aqueous secretions



CFTR protein in airways

- Mutation of CFTR protein : No Cl^- and $HCO3^-$ in secretions → no Na+ and water retention → Thick and mucous secretion
  - Recurrent respiratory tract infection → M/c cause of morbidity
  - Obstructive jaundice, neonates → Neonatal jaundice
  - Obstructed pancreatic duct → Fat malabsorption, steatorrhea and vit k deficiency
  - Obstruction in male & female reproductive organs ducts → sexual maturation defects
- Function of CFTR in sweat glands : Take Cl^- and HCO_3^- into epithelial cells
  - Defect : sweat chloride concentration↑ → pilocarpine iontophoresis
  - Diagnostic criteria : sweat chloride test
  - Other diagnostic methods : Genetic testing
- M/c mutation in cystic fibrosis : CFTR gene mutation - δ f508 mutation (δ - deletion, f- phenyl alanine)
- Mutation
  - Normal CFTR gene : 507, 508 codons: ATC (isoleucine) - TTT (phenylalanine)
  - δ f508 mutation : [redacted]
  - Resultant codon : ATT (isoleucine)
  - Deleted phenylalanine : protein folding affected
- Phenylalanine deletion → no protein folding → degradation of most proteins

MCQ's

00:33:19

Q. Voltage gated sodium channels are examples of
a. Simple passive diffusion
b. Facilitated passive diffusion
c. Primary active transport
d. Secondary active transport

Ans (a)

Q. GLUT transporters are examples of:
a. Simple passive diffusion
b. Facilitated passive diffusion
c. Primary active transport
d. Secondary active transport

Ans (b)

Q. The transport mechanism which follows linear kinetics is:
a. Simple passive diffusion
b. Facilitated passive diffusion
c. Primary active transport
d. Secondary active transport

Ans (a)

Q. Neutral amino acid transporter is an example of:
a. Simple passive diffusion
b. Facilitated diffusion
c. Primary active transport
d. Secondary active transport

Ans (d)

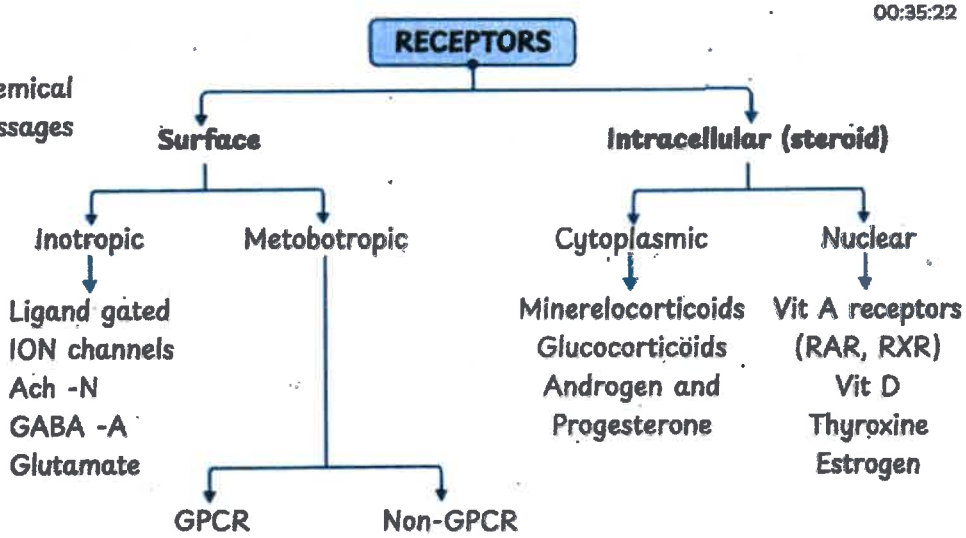
Q. Which of the following disorders follows autosomal recessive inheritance pattern? (NEET 2022)
a. Huntington's disease
b. Treacher collins syndrome
c. Cystic fibrosis
d. Achondroplasia

Ans (c)

RECEPTORS

00:35:22

- Depending upon location
- Chemical messengers : Chemical substance transmitting messages to cells through receptors



G PROTEIN RECEPTOR

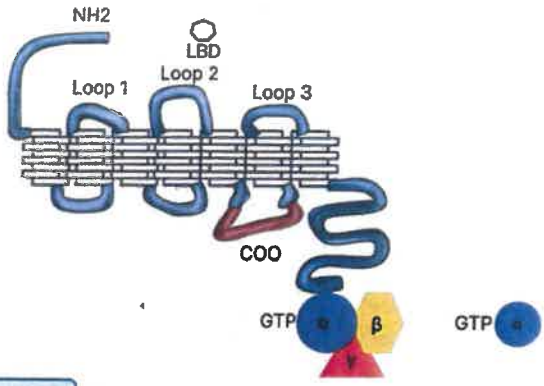
G PROTEIN

00:40:36

- Proteins which get activated on binding to GTP
- 2 types
  - Small G protein
  - Heterotrimeric G protein : 3 subunits → α, β, γ
- G protein coupled receptors only couples with heterotrimeric G protein

RECEPTOR

- 7 Transmembrane domains (serpentine receptors)
- Heterotrimeric G protein attach with carboxy terminal end
- Ligand binding domain – 3rd transmembrane domain
- No ligand/chemical messenger on ligand binding domain: α subunit attach to GDP
- Chemical messenger binding to ligand binding domain: GDP replaced by GTP
- α bound to GTP dissociate from β, γ → mediate intracellular enzyme activities



TYPES OF GPCR

- **G_s** – Stimulates Adenylyl cyclase (cAMP, PKA) → Glucagon, β Receptors, All Dopaminergic receptors except D2, PTH, ACTH, CRH, FSH, LH, hCG, V2 receptor
- **G_i** – Inhibits Adenylyl cyclase → α2, M2, D2
- **G_q** – Stimulates PLC (IP3, DAG) → α1, M1, M3, V1A, GnRH, Oxytocin, Angiotensin II
- **G_t** – Stimulates PDE (↓ cGMP) → Rods and Cones

G_s	G_i	G_q	G_t
• Stimulates adenylyl cyclase o Convert ATP into cAMP (second messenger) o Activates protein kinase a o Phosphorylates intracellular protein	• Inhibits adenylyl cyclase o ↓ cAMP level o Inhibited intracellular activities	• α -Subunit attached to GTP - stimulates PLC • Acts on PIP_2 (phosphatidyl inositol diphosphate) • Converts into IP_3 and DAG • IP_3 – cause Ca^{2+} release • DAG : activates protein kinase c. • Actions of vasopressin o Vasoconstriction (v1a) o Water reabsorption (by v2 receptors acting on basolateral side of intercalated cells of late DCT and collecting duct cells)	• Stimulates PDE (cGMP) • Convert cGMP – 5' GMP • ↓ cGMP

- Action initiated :
- Action termination : α subunits → intrinsic GTPase activity → Acts on GTP → GDP → α subunit attach to GDP and reassociate with β, γ

ACTION OF CHOLERA TOXIN

- Acts on [redacted]
- G_s type G coupled receptor protein
- Effect: α subunit lose intrinsic GTPase activity
  - Continuous binding to GTP
  - Continuous stimulation of adenylyl cyclase and generate continuous cAMP
  - cAMP opens chloride channels in the enterocytes → chloride oozing
  - ↑↑ chloride in intestinal lumen → attracts Na^+ and water → osmotic diarrhoea

NON GPCR RECEPTORS

00:57:04

- Intrinsic enzymatic activity
- 2 types of activity
  - **Guanylyl cyclase activity**
    → e.g., ANP (Atrial natriuretic peptide), NO
  - **Tyrosine kinase activity**
    → Intrinsic: insulin, cytokines - EGF (epidermal growth factor), PDGF (platelet-derived growth factor)
    → JAK-STAT pathway : growth hormone, prolactin, cytokines

TYPE OF RECEPTOR	EXAMPLES
Intranuclear	RAR, RXR, VIT D, Thyroxine, Estrogen
Intracytoplasmic	Mineralocorticoid, Glucocorticoid, Androgen,Progesterone
Inotropic	Ach - n, GABA - A, Glutamate - kainate, AMPA, NMDA
Gs	Glucagon, β Adrenergic receptors, All dopaminergic receptors except d2, PTH, vasopressin v2, ACTH, CRH, FSH, LH, HCG
Gi	α2, m2, d2
Gq	α1, m1, m3, v1a, GNRH, oxytocin, angiotensin ii (goa)
Gt	Rods and Cones
Intrinsic tyrosine kinase	Insulin, EGF, PDGF
JAK STAT	GH, prolactin, all other cytokines
Guanylyl cyclase	ANP, NO