4. Lysosomes, Smooth Endoplasmic Reticulum, Mitochondria, and Inclusions
**Objective**

Lysosomal ultrastructure and function/dysfunction along with continued discussion on protein sorting and protein targeting.

Smooth endoplasmic reticulum ultrastructure and function in typical cells and those specialized to secrete steroids.

Mitochondrial ultrastructure, function, origin, and incorporation of cytoplasmic proteins.

Inclusions.
Ribosomes translate mRNA in the production of protein.
Reactions

- Scaler reactions
  \[ a + b = c \]

- Vectorial reactions
  \[ a + b = c \]

Cytosolic proteins

membranes

RER proteins
• **Cytosol** is the part of the cytoplasm that is not held by any of the organelles in the cell. On the other hand, cytoplasm is the part of the cell which is contained within the entire cell membrane.

• **Cytoplasm** is cytosol plus organelles = every thing between the cell membrane and the nuclear envelope
Free ribosomes in cytosol

Cytosolic proteins

Membrane-bound ribosomes

RER proteins

Scalor reactions

Vectorial reactions
Lysosome

Enzymes present - phosphatases, proteases, nucleases, lipid degrading enzymes
Lysosome

Method of detection - localization of enzymes as primary lysosomes look like secretory granules

Histochemical reaction using the local enzyme plus substrate to produce black precipitate
Localization of lysosomal enzymes
Lysosome

Negative charges on inner leaflet of lysosomal membrane - protect from enzymes degradation

ACID HYDROLASES
nucleases
proteases
glycosidases
lipases
phosphatases
sulfatases
phospholipases

pH-7.2

H^+

pH-5

CYTOSOL

ATP

ADP + P
Cisternal and postcisternal phases of secretion

Induced secretion
Mannose-6-Phosphate = signal for sorting enzyme to lysosome via receptors
Function / actions of lysosomes

Programmed cell death

- Remodeling as in an embryo or tadpole (frog)
Function / actions of lysosomes

Housekeeping function
- Remove worn organelles (autophagy)
Function / actions of lysosomes

Unprogrammed cell death

Damage/death to cardiac cells in ischemia associated with myocardial infarctions
FUNCTION / ACTIONS OF LYSOSOMES

PRE-STENT

POST-STENT
In summary: Membranes allow cells a high degree of chemical heterogeneity

Surfaces and interfaces - sites important for physiological processes
Enzymes - catalyze chemical transformations
**Internal partition of cytoplasm** - enzymes, substrates, products
Efficiency of complex chemical reaction amplified area

Gradients - by permeability and rate of active transport
Regulate cell’s activity
Hold reserve a large repertoire of unexpressed biochemical reactions
Heterophagy
Ingest and digest things outside the cell

Function / actions of lysosomes
LYSOSOME

LATENCY CHARACTERISTIC
LEAD TO DISCOVERY OF LYSOSOMES
RESULTS FROM ENZYME BEING LOCATED WITHIN MEMBRANES

RESIDUAL BODY
REMAIN AFTER DIGESTION HAS STOPPED = LIPOFUSCIN
Lysosome storage disease (I-cell disease or inclusion disease)

- No mannose-6-phosphate (no signal for sorting enzyme to lysosome)
- No enzymes in lysosomes I-cell individuals
Lysosomes (summary)

- Single membrane
- Rich hydrolytic enzymes (50 enzymes)
- Enzymes safely contained by membrane
- Pathological conditions
- Primary lysosomes produced by RER and Golgi
- Mannose-6-phosphate on protein **signals** for transport to lysosome
Functions (summary)

- Cell digestion - embryonic development
- Defense against microbial invasion
- Intracellular digestion of cellular material
  - Residual bodies, exocytosis
    - Autophagic vacuole
    - Primary lysosome
    - Secondary lysosome *(enzymes of primary + substrate)*
Smooth endoplasmic reticulum

- Smooth membrane

lipid
Smooth endoplasmic reticulum

• Origin of SER and its enzymes is RER
Membrane and receptors

**Figure 6-6** Different types of movement possible for phospholipid molecules in a lipid bilayer.

RER, Golgi, and secretion
Smooth endoplasmic reticulum

- Function:
  - Synthesis & transport of lipids in the intestines
Smooth endoplasmic reticulum

- **Function:**
  - Detoxification in liver
Toxicology

What is **toxicology**? The study of the effects of poisons.

**Poisonous substances** are produced by plants, animals, or bacteria.

**Phytotoxins**

**Zootoxins**

**Bacteriotoxins**

**Toxicant** - the specific poisonous chemical.

**Xenobiotic** - man-made substance and/or produced by but not normally found in the body.
*Recall: Foreign chemicals that are synthesized within the body are termed xenobiotics (Gr. *Xenos* meaning “strange”)*

- Xenobiotics may be naturally occurring chemicals synthesized by plants, microorganisms, or animals (including humans).
- Xenobiotics may also be synthetic chemicals synthesized by humans.

*Poisons are xenobiotics, but not all xenobiotics are poisonous.*
Xenobiotics at Work

TOXICOKINETICS

Storage in Tissues (fat, bone, plasma proteins)

Xenobiotic

Plasma

Dose

Exposure

Excretion

Site of Action

Mechanism of Action

Metabolism
General Scheme of Xenobiotic Metabolism

Metabolism

Lipophilic (parent compound)

1) Decrease biological activity
2) Increase excretability

Phase I (oxidative)
Bioactivation Detoxification

Metabolites
polarity functionality

Phase II (synthetic)
Detoxification

Metabolites
size ionization water solubility
Increase excretability

Hydrophilic (metabolite)
Smooth endoplasmic reticulum

- **Function:**
  - Steroid synthesis
Smooth endoplasmic reticulum

- **Function:**
  - Ca$^{++}$

Regulation in muscle cells
Smooth endoplasmic reticulum

The sarcoplasmic reticulum is smooth endoplasmic reticulum
SER - structure and function (summary)

No ribosomes (smooth surface)
  – No ribophorins to bind them

Synthesis of triglycerides, cholesterol, and steroids

Has enzymes for conjugation, oxidation, and methylation

Metabolizes and detoxifies drugs

Sequester and release Ca^{++}
  – Muscle contraction (sarcoplasmic reticulum)
Mitochondria – convert **sun energy** stored in **food** (plant and animal) into a usable source (**ATP high-energy bond**) for biosynthesis & movement
Mitochondria - energy for biosynthesis & movement

- Size = 0.3 um X 4 um
- Double membrane
  - Smooth contoured outer membrane
  - Inner membrane forms cristae (number related to energy requirement)
Mitochondria - energy for biosynthesis & movement

Two compartments
Larger intercristal space
Intracristal space
  • Inner membrane - cytochrome oxidase and other enzymes
  • Subunits projecting into space – enzymes for oxidative phosphorylation of ADP and hydrolysis of ATP
Mitochondria - energy for biosynthesis & movement

Mitochondria are found where energy is needed in cells
Mitochondria - energy for biosynthesis & movement

Mitochondria are found where energy is needed as in these intestinal absorptive cells.
Mitochondria - energy for biosynthesis & movement

Mitochondria are found where energy is needed as in these cardiac cells
Functions of mitochondria

Make ATP, Kreb’s cycle enzymes
Cellular respiration is the process by which organic compounds (preferably glucose) are broken apart, releasing energy that is used to produce ATP molecules. Cells need to have ATP because it’s the gasoline that powers all living things. ATP is a high energy nucleotide which acts as an instant source of energy within the cell.

Since ATP is found in all living things, it’s sometimes called the energy currency of cells, which is the product of aerobic respiration in mitochondria.

Here is the overall simplified reaction for aerobic respiration:

\[
\text{C}_6\text{H}_{12}\text{O}_6 + 6\text{O}_2 \xrightarrow{\text{enzymes \\ coenzymes}} 6\text{CO}_2 + 6\text{H}_2\text{O} + \text{Release of Energy} \leq 38 \text{ ATP} + \text{Heat}
\]

In order to make ATP, you need food (sugar) and oxygen. If you don’t have food, you can’t make ATP and you’re going to die. Even if I brought in all the food in the world and then I diabolically suck all the oxygen out of this room, you’re still going to die. You need oxygen to unlock the energy that’s in the food. Cellular respiration also explains why we are breathing oxygen in, why we exhale carbon dioxide out as well as why we are warm blooded.
Transport in/within mitochondria
Transport in/within mitochondria

How about transport of O2, CO2, and water?

Transport in/within mitochondria. Mitochondria - double membrane

How about transport of enzymes?

Cytoplasmic proteins incorporation
Mitochondria - double membrane

Cytoplasmic proteins incorporation
Proteins in inner membrane of mitochondria

- Transport
- Respiration – electron transport chain
- ATP synthesis
- Krebs cycle - generate proton (pH) gradient
Functions of mitochondria

Store Ca^{++}

Figure 9–23  Calcium is actively moved into mitochondria by a transport process that is driven by the membrane potential. Because most of the calcium inside the mitochondrion is thought to be precipitated as calcium phosphate, it seems likely that only a relatively small amount of work is necessary to accumulate Ca^{++}.
Mitochondria – Double membrane

Varied shapes of crista
Mitochondria - double membrane

- Ultrastructure - outer membrane, cristae, matrix
Functions of mitochondria

Cholesterol - side chain cleavage in steroid synthesis
Mitochondria - double membrane

Origin
Mitochondria - double membrane

- Origin from the mother
  - Division
Mitochondria - double membrane

• Origin
  – Use nuclear and mitochondria DNA and mitochondrial ribosomes for biogenesis
Mitochondria - double membrane

Use nuclear and mitochondria DNA and mitochondrial ribosomes for biogenesis
Inclusions - expendables inside cells

Nutrients
- Glycogen
- Lipid
Inclusions - expendables inside cells

Secretory granules
– Zymogen granules
Inclusions - expendables inside cells

Pigments
- Melanin granules
Inclusions - expendables inside cells

Pigments
- Lipofuscin
Inclusions - expendables inside cells

Pigments
- Lipofuscin

Lysosome

Lysosome storage disease
( I-cell disease or inclusion disease)
= No mannose-6-phosphate (no signal for sorting enzyme to lysosome)
  • No enzymes in lysosomes I-cell individuals

Enzymes are constitutively released
• https://www.youtube.com/watch?v=FzcTgrxMzZk
• https://www.youtube.com/watch?v=B_zD3NxSsD8
Next time

TRANSPORT, ENDOCYTOSIS, and PHAGOCYTOSIS