The Cell

Cytoplasmic compartments and organelles

Prof. Dr. Özgür Çınar

1

Histology

- Histo- (tissue) + -ology (logos, branch of science)
- Marcello Malpighi (10 March 1628 – 29 November 1694) was an Italian biologist and physician, who is referred to as the "Father of microscopical anatomy, histology, physiology and embryology". (wikipedia)

2

Histology

- Histology, also microanatomy, is the branch of biology which studies the tissues of animals and plants using microscopy.
- It is commonly studied using a light microscope or electron microscope, the specimen having been sectioned, stained, and mounted on a microscope slide.

3

Recommended references

- Histology: A Text and Atlas, Ross and Pawlina
- Histology and Cell Biology: An Introduction to Pathology, Kierszenbaum A.L
- Color Atlas and Text of Histology, Gartner LP
- Junqueira's Basic Histology: Text and Atlas, Mescher A
- Molecular Biology of the Cell, Alberts B
- The Cell: A Molecular Approach, Cooper GM
- *Anatomy & Physiology: The Unity of Form and Function, Saladin KS*

4

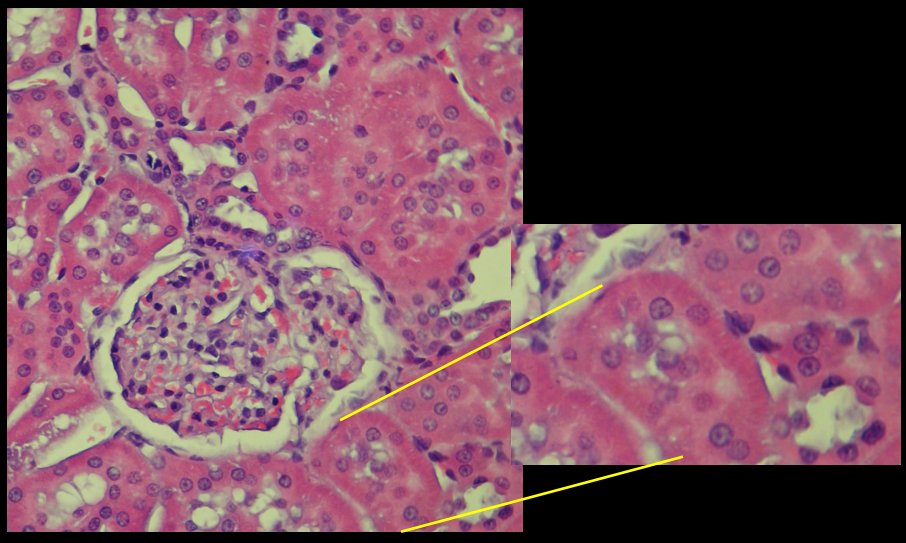
Cytoplasm, Protoplasm, Cytoplasmic matrix

- The liquid plasm of the cell
- Contains water, ions, proteins etc.

- Protoplasm = Cytoplasm + Nucleoplasm
- Cytosol = Ground substance = water of the cell

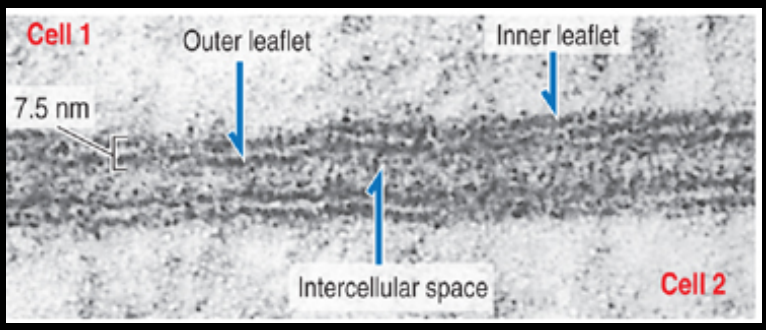
5

Can cell membrane be seen by a light microscope?



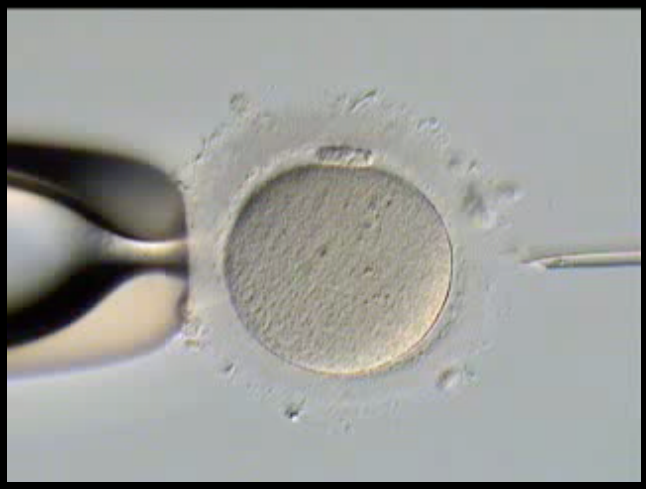
6

Electron microscope



Kaynak: Histology and Cell Biology: An Introduction to Pathology, Kierszenbaum A.L

7



8

Membranous Organelles

- Nucleus
- Rough endoplasmic reticulum
- Smooth endoplasmic reticulum
- Golgi apparatus
- Mitochondrion
- Peroxisomes
- Lysosomes
- Endosomes
- Secretory vesicles

9

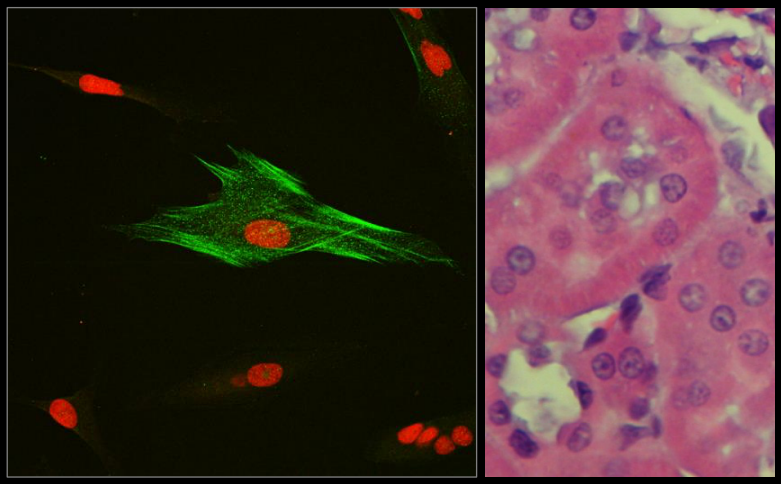
Nonmembranous Organelles

- Proteasome
- Ribosome
- Centrosome
- Inclusions
- Cytoskeleton components

10

Nucleus (karyon)

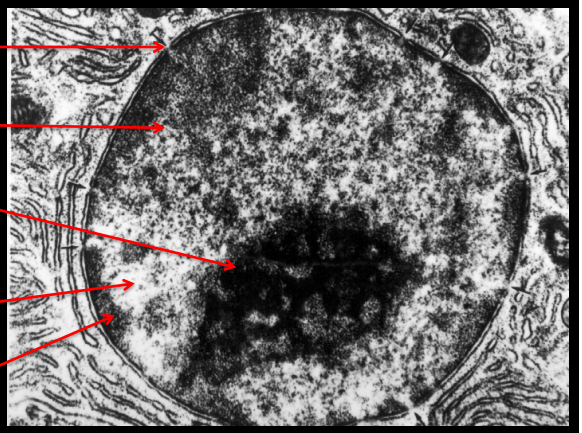
The nucleus is a membrane-limited compartment that contains the genome in eukaryotic cells.



11

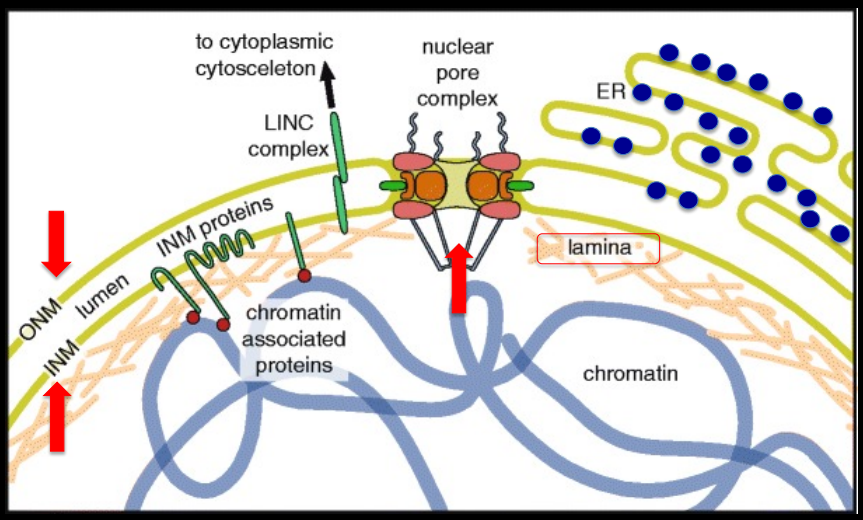
Nucleus

- Nuclear envelope
- Nucleoplasm
- Nucleolus
- Chromatin
  - Euchromatin
  - Heterochromatin



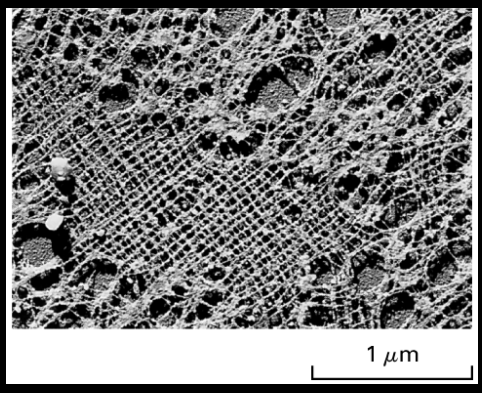
12

Nuclear envelope



13

- The nuclear lamina, a thin, electron-dense intermediate filament network like layer, resides underneath the nuclear membrane.
- If the membranous component of the nuclear envelope is disrupted by exposure to detergent, the nuclear lamina remains, and the nucleus retains its shape.



14

Nuclear lamina

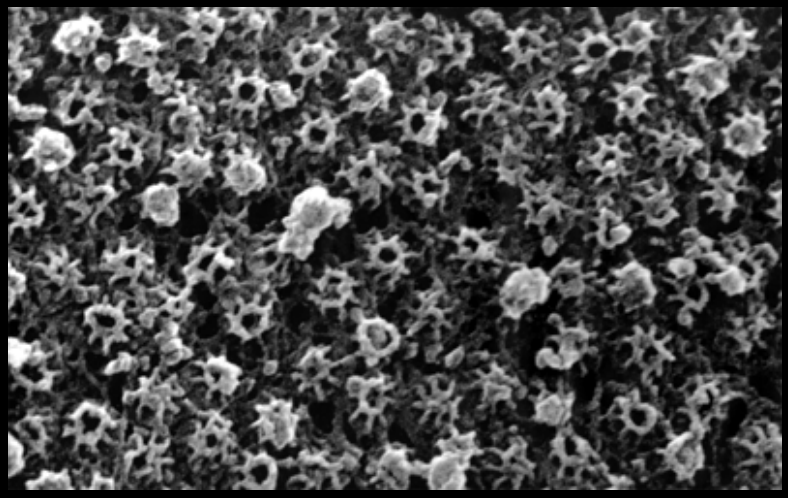
- Composed of "Lamin" proteins.
- Lamin a and c are structural, lamin b is binding proteins.
- Lamin receptors
  - Emerin: binds both lamin A and lamin B
  - Nurim: binds lamin A
  - Lamin B receptor (LBR)
- Impairment in nuclear lamina architecture or function is associated with certain genetic diseases (laminopathies) and apoptosis.

15

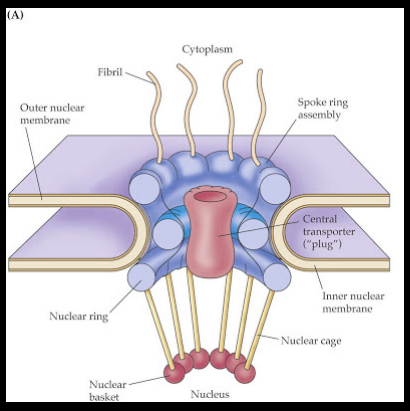
Nuclear Pore Complex

16

Nuclear Pore Complexes



17



18

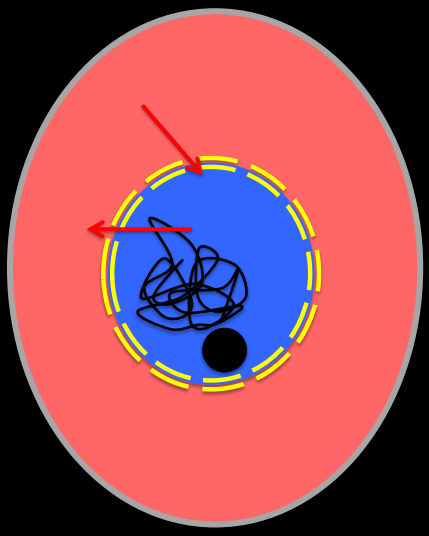
Structure and function

- Formed by 50 type of nucleoporin (Nup) proteins
- < 40 kDa (9 nm) passes through
- How about the bigger ones!

19

Karyopherin family members proteins

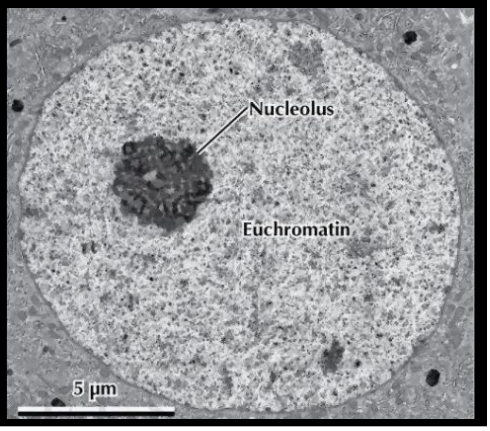
importin x exportin



20

Nucleolus

- Nonmembranous part of the nucleus
- The site of rRNA synthesis and initial ribosomal assembly.
- Can be more than one



21

The nucleolus has three morphologically distinct regions

- Fibrillar Center
  - rRNA genes (chromosomes– 13, 14, 15, 21, 22)
  - RNA polymerase I
  - Transcription factors
- Fibrillar Material (Pars fibrosa)
  - Synthesized rRNA
- Granular Material (Pars granulosa)
  - initial ribosomal assembly
  - preribosomal particles.

} nucleolonema

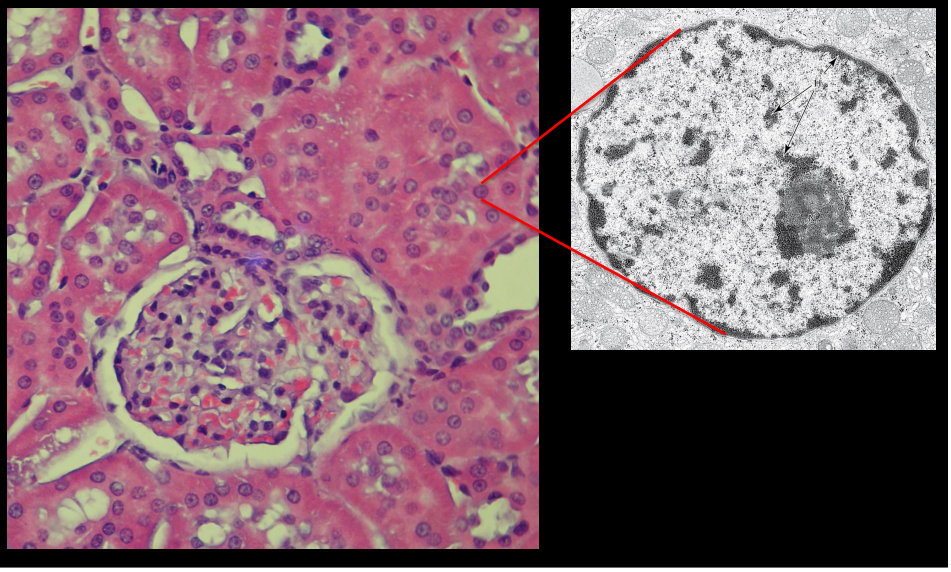
22

The nucleolus is involved in regulation of the cell cycle.

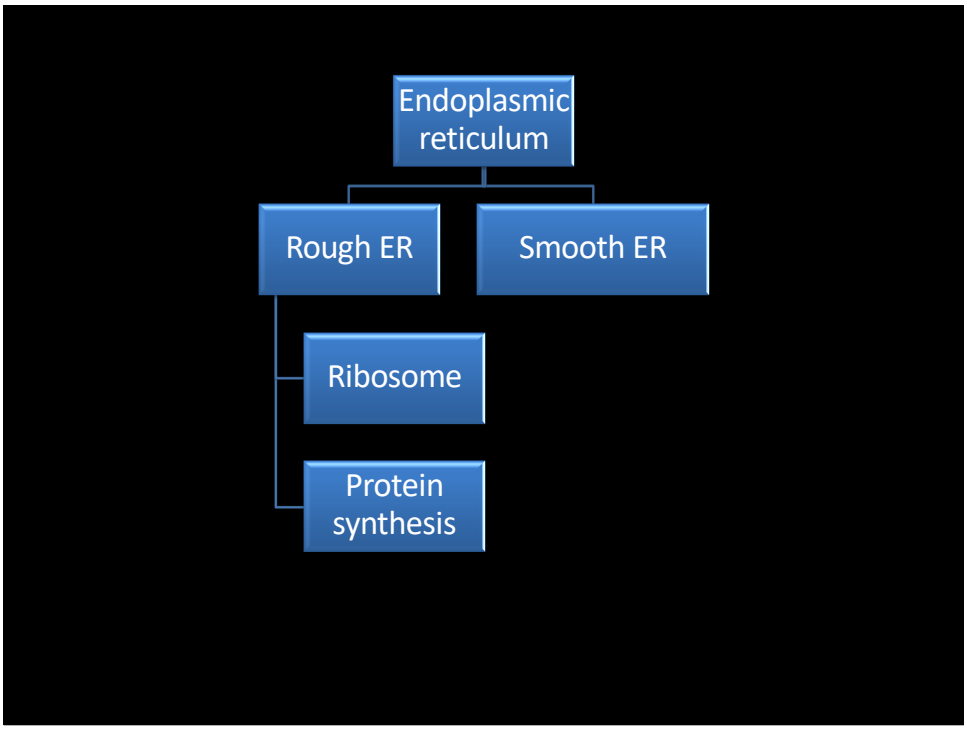
- Nucleostemin
  - p53-binding protein and regulates cell cycle
  - high in malignant cells
  - low in differentiated cells
- The nucleolus stains intensely with hematoxylin and basic dyes and metachromatically with thionine dyes.

23

Euchromatin - Heterochromatin



24



25

Rough endoplasmic reticulum

With the TEM, the rER appears as a series of interconnected, membrane-limited, flattened sacs called cisternae, with particles located at the exterior surface of the membrane.

26

Rough endoplasmic reticulum

- Basophilic staining (ergastoplasm)
- Nissl bodies

27

Smooth endoplasmic reticulum

The sER consists of short anastomosing tubules that are not associated with ribosomes.

28

Smooth endoplasmic reticulum involved in:

- lipid and steroid metabolism,
- glycogen metabolism and gluconeogenesis
- membrane formation and recycling
- detoxification
- lipoprotein synthesis
- storage of calcium – sarcoplasmic reticulum
- division of mitochondrion
- removing of nonfunctional organelles

29

Golgi Complex (Apparatus, Body)

- Camillo Golgi
  - osmium-impregnation around nucleus of a nerve cell
- Golgi complexes are NOT stained with H&E
- Heavy metal impregnation (like. silver, osmium)

30

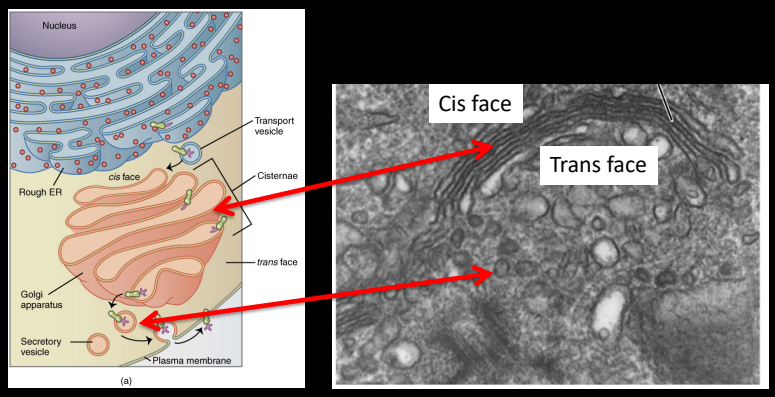
Golgi Complex (Apparatus, Body)

- In the light microscope, secretory cells that have a large Golgi apparatus typically exhibit a clear area partially surrounded by ergastoplasm.
- In EM, it appears as a series of stacked, flattened, membrane-limited sacs or cisternae and tubular extensions embedded in a network of microtubules near the microtubule organizing centers.

31

Golgi Complex (Apparatus, Body)

- It exhibits polarization as cis and trans face.



32

Golgi Complex (Apparatus, Body)

- Post-translational modification,
- Sorting and packaging of proteins
- M-6-P is added to lysosomal proteins.
- Synthesis of sphingomyelin and glycosphingolipid

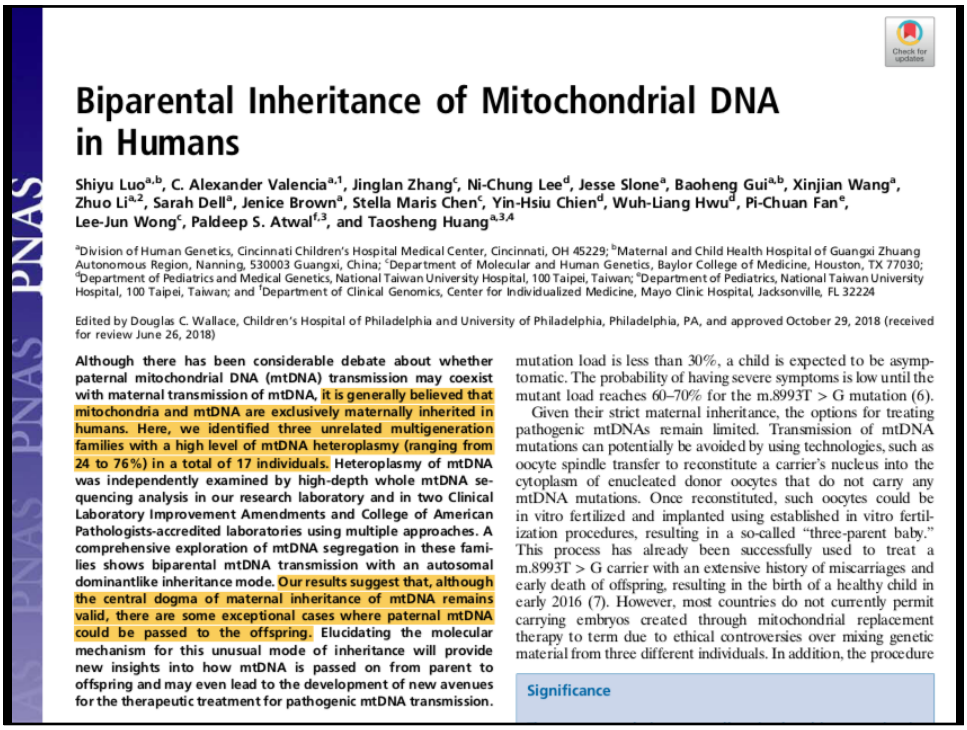
33

Mitochondrion (mitos + chondros)

- 1840, Richard Altman, Bioblast
- 1898, Carl Benda, thread (fibre) + granules
- 0,4 – 0,8 x 4 – 8 um
- Circular DNA,
- Ability of self-division and protein synthesis
- Double membrane

Mitochondria are believed to have evolved from an aerobic prokaryote (Eubacterium) that lived symbiotically within primitive eukaryotic cells.

34



Biparental Inheritance of Mitochondrial DNA in Humans

Shiyu Luo[a,b], C. Alexander Valencia[a,1], Jinglan Zhang[c], Ni-Chung Lee[d], Jesse Slone[a], Baoheng Gui[a,b], Xinjian Wang[a], Zhuo Li[a,2], Sarah Dell[a], Jenice Brown[a], Stella Maris Chen[c], Yin-Hsiu Chien[d], Wuh-Liang Hwu[d], Pi-Chuan Fan[e], Lee-Jun Wong[c], Paldeep S. Atwal[f,3], and Taosheng Huang[a,3,4]

[a]Division of Human Genetics, Cincinnati Children's Hospital Medical Center, Cincinnati, OH 45229; [b]Maternal and Child Health Hospital of Guangxi Zhuang Autonomous Region, Nanning, 530003 Guangxi, China; [c]Department of Molecular and Human Genetics, Baylor College of Medicine, Houston, TX 77030; [d]Department of Pediatrics and Medical Genetics, National Taiwan University Hospital, 100 Taipei, Taiwan; [e]Department of Pediatrics, National Taiwan University Hospital, 100 Taipei, Taiwan; and [f]Department of Clinical Genomics, Center for Individualized Medicine, Mayo Clinic Hospital, Jacksonville, FL 32224

Edited by Douglas C. Wallace, Children's Hospital of Philadelphia and University of Philadelphia, Philadelphia, PA, and approved October 29, 2018 (received for review June 26, 2018)

Although there has been considerable debate about whether paternal mitochondrial DNA (mtDNA) transmission may coexist with maternal transmission of mtDNA, it is generally believed that mitochondria and mtDNA are exclusively maternally inherited in humans. Here, we identified three unrelated multigeneration families with a high level of mtDNA heteroplasmy (ranging from 24 to 76%) in a total of 17 individuals. Heteroplasmy of mtDNA was independently examined by high-depth whole mtDNA sequencing analysis in our research laboratory and in two Clinical Laboratory Improvement Amendments and College of American Pathologists-accredited laboratories using multiple approaches. A comprehensive exploration of mtDNA segregation in these families shows biparental mtDNA transmission with an autosomal dominantlike inheritance mode. Our results suggest that, although the central dogma of maternal inheritance of mtDNA remains valid, there are some exceptional cases where paternal mtDNA could be passed to the offspring. Elucidating the molecular mechanism for this unusual mode of inheritance will provide new insights into how mtDNA is passed on from parent to offspring and may even lead to the development of new avenues for the therapeutic treatment for pathogenic mtDNA transmission.

mutation load is less than 30%, a child is expected to be asymptomatic. The probability of having severe symptoms is low until the mutant load reaches 60–70% for the m.8993T > G mutation (6).

Given their strict maternal inheritance, the options for treating pathogenic mtDNAs remain limited. Transmission of mtDNA mutations can potentially be avoided by using technologies, such as oocyte spindle transfer to reconstitute a carrier's nucleus into the cytoplasm of enucleated donor oocytes that do not carry any mtDNA mutations. Once reconstituted, such oocytes could be in vitro fertilized and implanted using established in vitro fertilization procedures, resulting in a so-called "three-parent baby." This process has already been successfully used to treat a m.8993T > G carrier with an extensive history of miscarriages and early death of offspring, resulting in the birth of a healthy child in early 2016 (7). However, most countries do not currently permit carrying embryos created through mitochondrial replacement therapy to term due to ethical controversies over mixing genetic material from three different individuals. In addition, the procedure

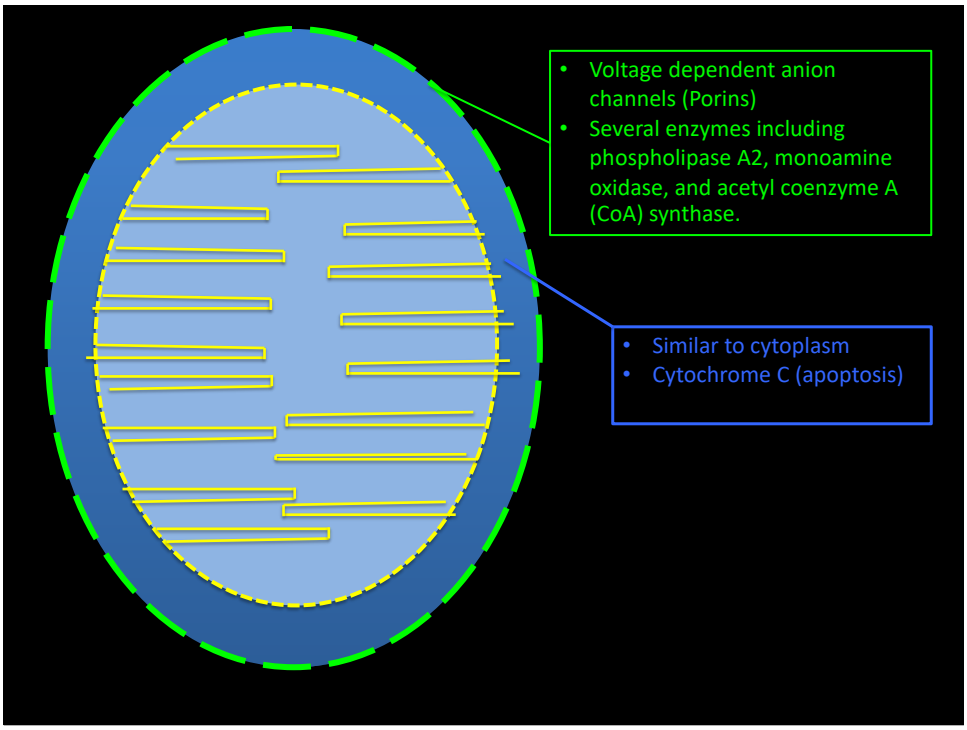
Significance

35

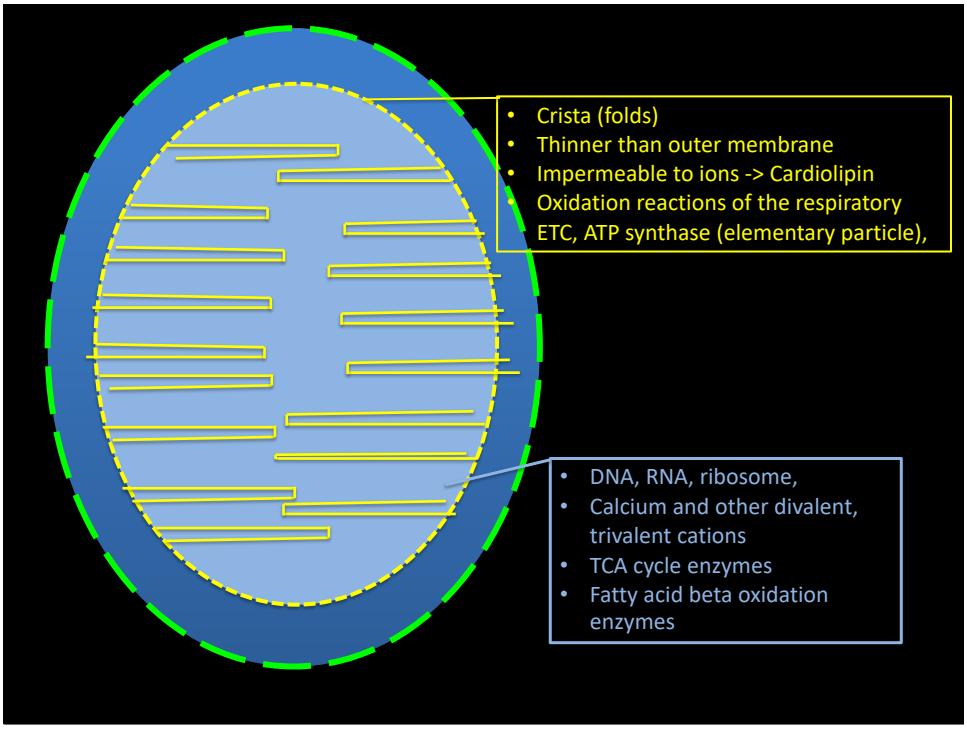
Mitochondria

- Present in all cells except red blood cells and terminal keratinocytes.
- Abundant in cells that generate and expend large amounts of energy.
- Fixed by potassium bichromate or osmium tetroxide
- Staining:
  - Vital: Janus green B
  - Iron hematoxylin
  - Acidophilic staining

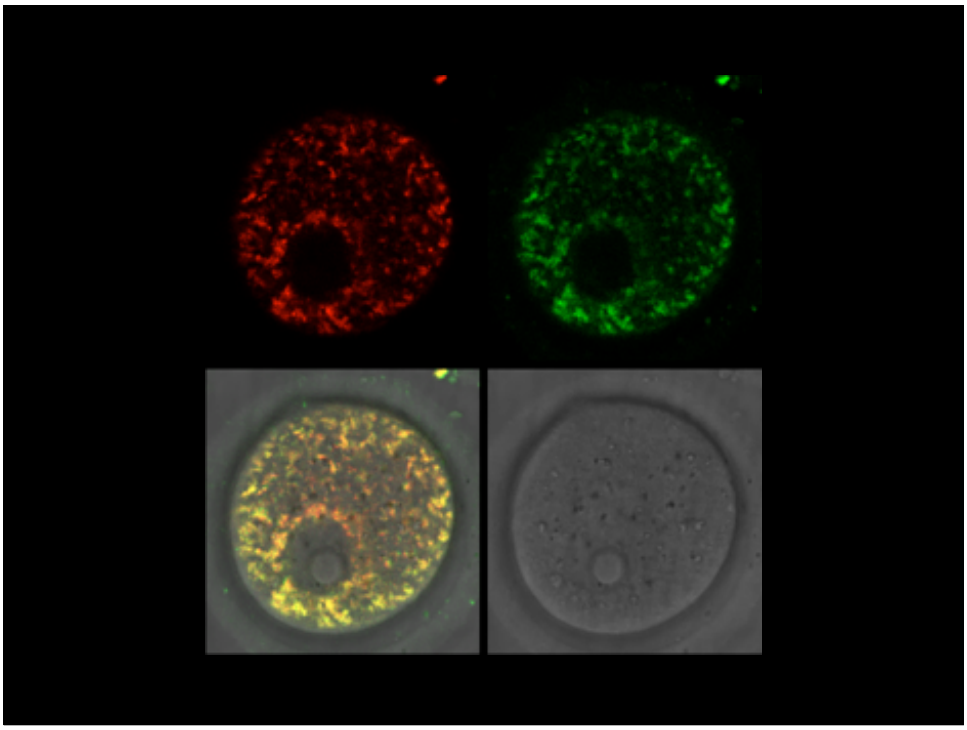
36


Voltage dependent anion channels (Porins)
Several enzymes including phospholipase A2, monoamine oxidase, and acetyl coenzyme A (CoA) synthase.
Similar to cytoplasm
Cytochrome C (apoptosis)

37


Crista (folds)
Thinner than outer membrane
Impermeable to ions -> Cardiolipin
Oxidation reactions of the respiratory ETC, ATP synthase (elementary particle),
DNA, RNA, ribosome,
Calcium and other divalent, trivalent cations
TCA cycle enzymes
Fatty acid beta oxidation enzymes

38



39

Peroxisomes (Microbodies)

- Single membrane-bounded organelles containing oxidative enzymes like catalase and other peroxidases.

$$2\ H_2O_2 \xrightarrow[\text{Catalase}]{} 2\ H_2O + O_2$$

  - Almost all oxidative enzymes produce hydrogen peroxide as a product of the oxidation reaction.
- Beta oxidation of fatty acids.

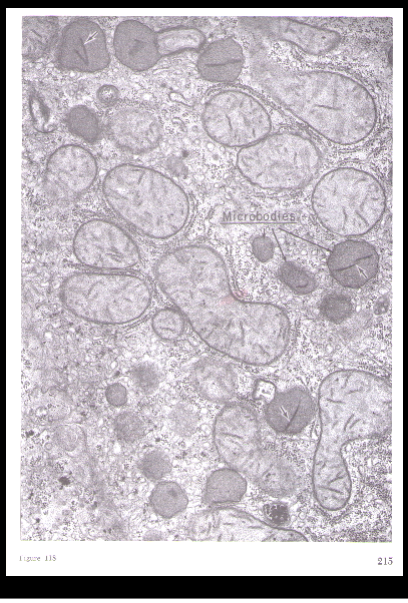
40

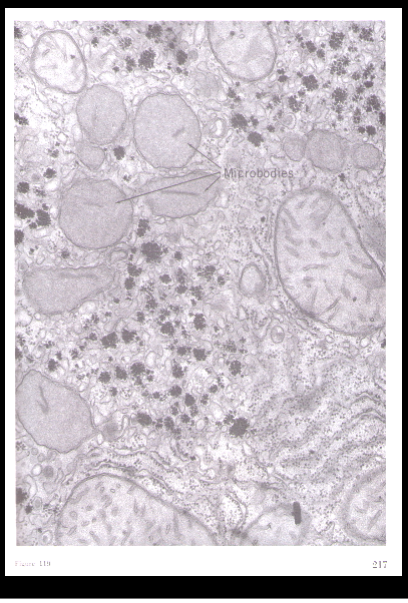
Peroxisomes (Microbodies)

- Detoxify alcohol to acetaldehyde in hepatocyte.
- Catalyze the first reactions in the formation of plasmalogens, which are the most abundant class of phospholipids in myelin.

41

Peroxisomes (Microbodies)





42

- Zellweger syndrome
- Adrenoleukodystrophy

43

Proteasome

- is large cytoplasmic or nuclear protein complexes.
- destroys abnormal proteins (proteolysis)
  - nonfunctional
  - misfolded, denaturated, or contain abnormal amino acids

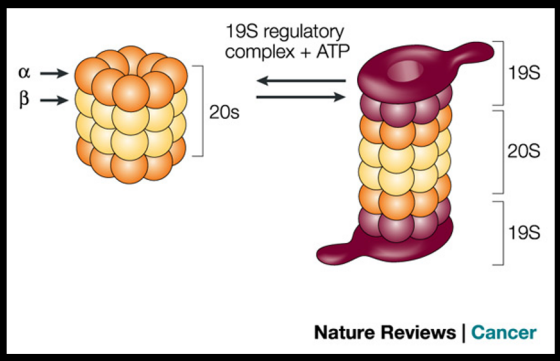
44

Proteolysis

Ubiquitin

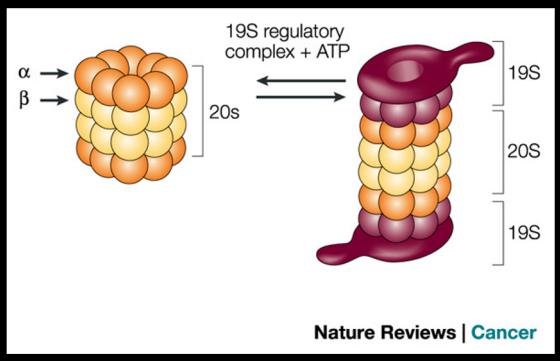
Activation (E1)
Conjugation (E2)
Ligation (E3)

ATP AMP



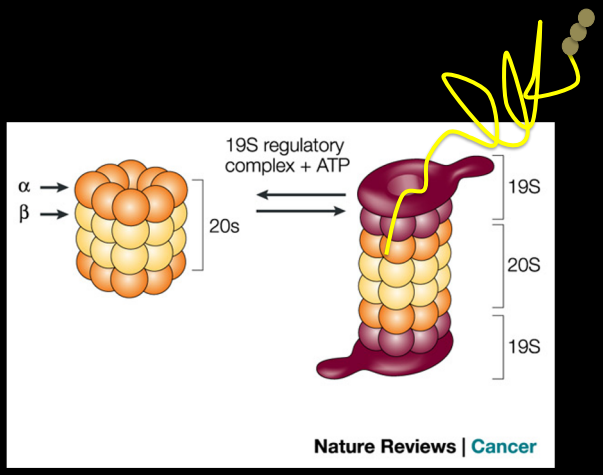
45

Proteolysis



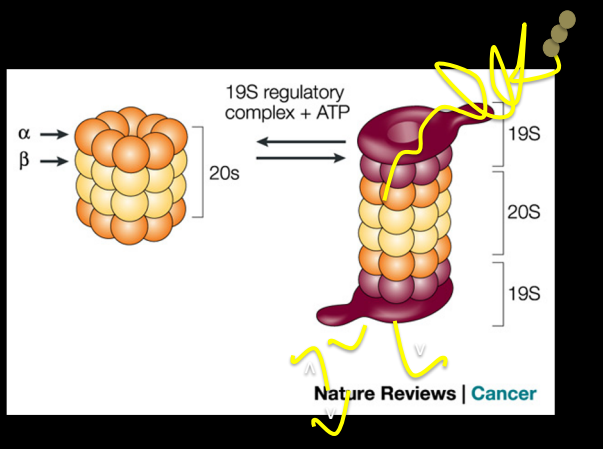
46

Proteolysis



47

Proteolysis



48

Inclusions

- Endogenous
  - Melanin
  - Lipid
  - Glycogen
  - Hemoglobin
  - Lipofuscin
- Exogenous
  - Carbon
  - Carotene
  - Tattoo
  - Gun powder

49

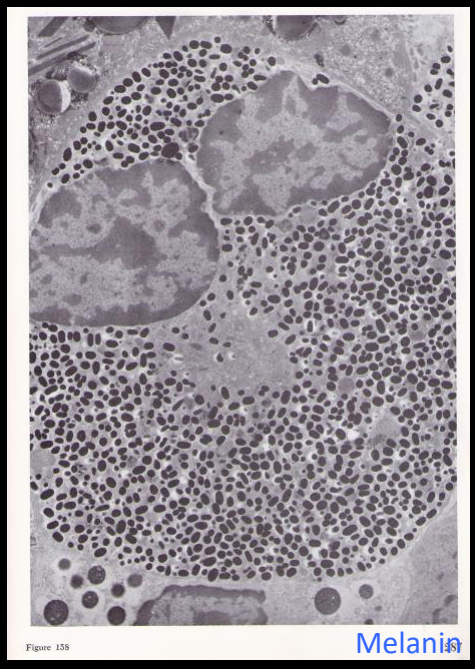
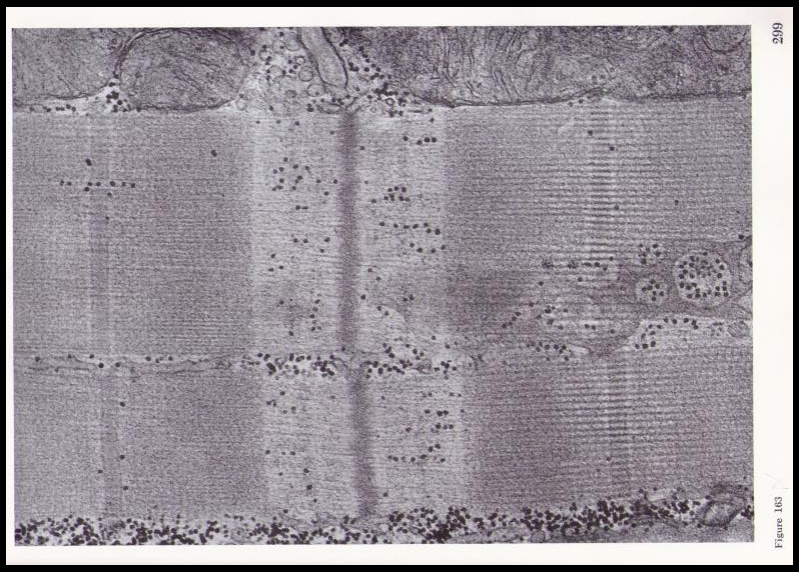


Figure 158

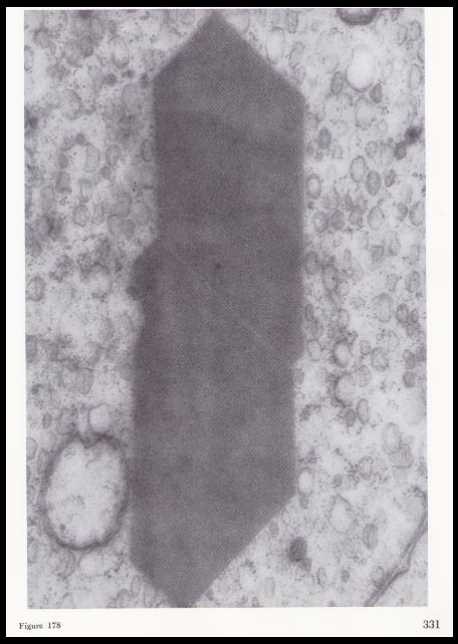
Melanin

50



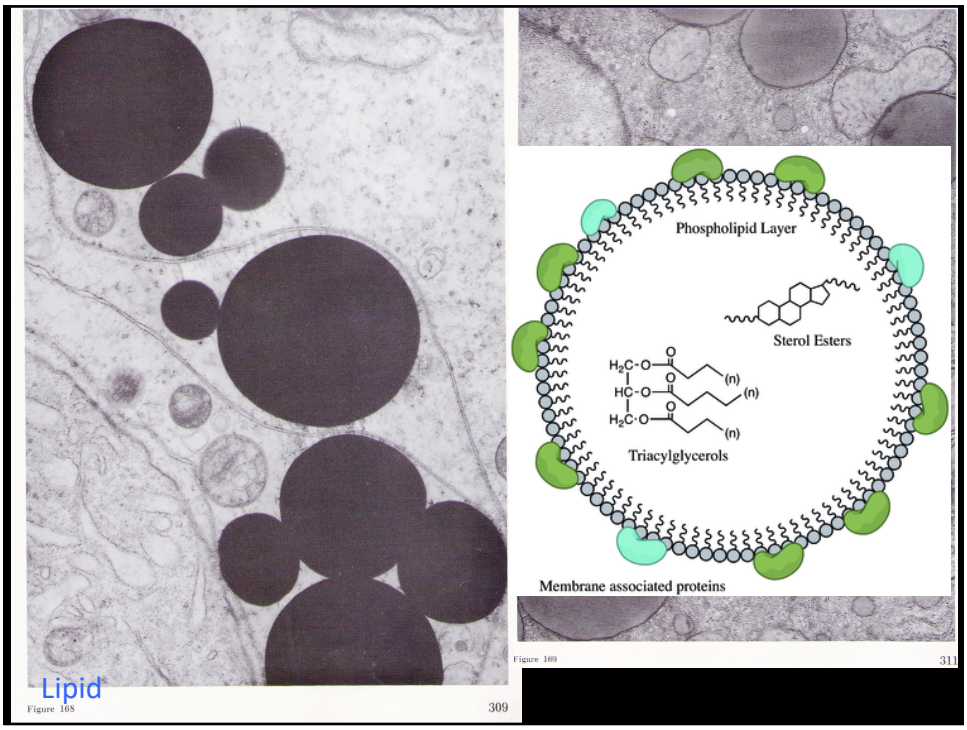
Glycogen

51



Reinke crystal, Leydig cell

52


Phospholipid Layer
Sterol Esters
Triacylglycerols
Membrane associated proteins
Figure 168
309
Figure 169
311

Lipid

53