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Function: ① intracellular vesicular transport
② movement of cilia and flagella
③ cell division (مهم في فصل الكروموسومات وتكميل الانقسام mitotic spindle)
④ cell movement
⑤ cell shape and orientation حيث إنه يعطي الـ PM شكل
وبالتالي يحتاج support ويتم من خلال الـ cytoskeleton وأحد عناصره MT

HISTOLOGY LECTURE "4" سلام خالد الهباش

→ non-membranous organelles → cytoskeleton (the cell is a fragile structure → mechanical stress مقاومة لـ + support) تحتاج

① microtubules ② microfilaments (actin filament) ③ intermediate filament

• قطرها diameter ← 24 n.m

• تتكون من polymerized proteins/units (α and β tubulin)

→ microtubule والـ dimers تكون

يتكون من وحدات متسلسلة من هذه الـ dimers

التي بترتبط مع بعض عن طريق الـ polymerization

• تتميز بالـ assembly and ← إضافة وحدات / بناء

disassembly ← dissociation of these units or dimers

• found in cytoplasm

originate from MTOC في مركز الخلية ويتكون بشكل أساسي من centriole وحوله amorphous proteinous material ملوش شكل

→ 2 tubular structures (right angle بيلتقوا)

MTOC → تنشأ منه الـ microtubules من مركز الخلية وتتم تتجه للـ peripheral part لعند حدود الخلية (plasmamembrane)

Near the nucleus and extend peripherally

contains centrioles and amorphous pericentriolar matrix of more than 200 proteins organized in ring-shaped structures including γ-tubulin

→ في microtubules تتجه للـ peripheral part وبتعطي للخلية strength and support

ويوجد أيضاً للخلية extensions لها وظائف محددة زي cilia موجودة في respiratory system ← في كل سطح الخلية / apical surface → air عكس اتجاه دخول cilia تتحرك

حتى تطرد الـ particles اللي قدرت تصل رغم وسائل الحماية الموجودة بالـ respiratory system

→ تحتوي على core of microtubules اسمه axoneme يتكون من

9 doublets + 2 in center

	cilia	flagellum
structure	short, numerous membrane extensions supported by microtubules, which occur on exposed membrane surfaces of some cells	Long, singular membrane extension supported by microtubules; present on sperm cells (spermatozoon)
function	move substances (e.g, mucus and dissolved materials) over the cell surface	propels sperm

* ال cilia و flagella تنشأ من structure بيتكون بالميكروتيوب é
اسمه ال basal body
9 triplets + 0 in center
basal body و centriole ← نفس ال structure
ال core اللي بينشأ منها ال cilia
← centrioles من أهم وظائفها تكوين mitotic spindle + Axons ⊳
neuron ال extension اللي بينقل الإشارة للخلية التالية
• microtubule يكون ال skeleton لل cilia عشان يعمل الحركة نتيجتها
• microtubule تتجه لل peripheral part of the cell من وظائفها:
① mechanical support
② intracellular vesicular transport (similar to railroad) ← ال motor proteins بتمسك ال vesicle وتتحرك ال microtubules

at rest ⊳ MTOC ⊳ microtubules تنشأ من المركز وتتجه للأطراف وفجأة يتحللها diassemble ← chameleon tongue
← حيث يسير detection لسان الحرباء وتوضح من الـ monitoring لمختلف الأمور التي تحدث داخل الخلية.
داخل الخلية

* The MTOC can be compared to a feeding chameleon, which fires its long, projectile tongue to make contact with potential food. The chameleon then retracts its tongue back into its mouth and repeats this process until it's successful in

obtaining food. The same strategy of "firing" dynamic microtubules from the MTOC toward cell periphery and subsequently retracting them enables microtubules to search the cytoplasm. When the fired microtubule encounters stabilizing factors (such as MAPs), it's captured and changes its dynamic behavior. This selective stabilization process allows the cell to establish an organized system of microtubules linking peripheral structures and organelles with the MTOC.

→ Functions of microtubules:

1. intracellular vesicular transport
2. movement of cilia and flagella
3. cell division (mitotic spindle)
4. cell movement → الخلية fragile و الـ microtubules بتصل للـ plasma membrane فلما بنتحرك الخلية باتجاه معين بيهزا الاتجاه بتستمر الـ assembly فتضغط على الـ plasma membrane وبتخليه يمتد في الاتجاه هذا والـ microtubules اللي في الاتجاه المعاكس بيصير لها disassembly (elongation)
5. cell shape and orientation → Lining epithelium الموجودة في GIT وظيفتها اتجاهها معاكس (من الـ lumen للـ blood vessels لتنتقل لباقي أنحاء الجسم) فبتكون لها apical and basal surface → اللي بحدد هذا الـ orientation يكون لها علاقة مباشرة بالـ microtubular system داخل الخلية

يكون بسبب الـ cytoskeleton وأهم شيء microtubules (part)

1. → movement of secretory vesicles, endosomes and lysosomes. Microtubules create a system of connections within the cell, frequently compared with railroad tracks originating from the grand central station, along which vesicular movement occurs.
3. → attachement of chromosomes to the mitotic spindle and their movement during mitosis and meiosis.
5. → maintenance of cell shape, particularly its asymmetry.

* microtubules' wall consists of 13 circularly arrayed globular dimeric tubulin molecules. the tubulin dimer is formed from α-tubulin

and β-tubulin molecules. The dimers polymerize in an end-to-end fashion, head to tail, with the α molecule of one dimer bound to the β molecule of the next dimer in a repeating pattern.

α- and β- tubulin dimer

* each microtubule possesses a nongrowing (-) end that corresponds to α-tubulin; in the cell, it's usually embeded in the MTOC and often stabilized by actin-capping proteins. The growing (+) end of microtubules corresponds to β-tubulin and extends the cell periphery. نهاية ال + end يكون β

← lateral bonds حيث أن tubulin dimers ترتبط مع بعضها من الجنب

* Longitudinal contacts between dimers link them into a linear structure called a ~~protofilament~~.

← ال - end يبدأ من γ-tubulin (gamma) يشكل ال template التي يبدأ تراكم وحدات dimers عليها و ال capping protein ← stabilizing the structure (كله منشأه MTOC)

* +end يرتبط بـ MTOC ، -end تكون assembly و disassembly

* microtubules' wall (Dimer thickness) = 5n.m thick

~~نظريتين عن كيف تتم عملية ال assembly لل microtubules~~

microtubule ① تتصاف dimers وحدة ورا وحدة وتتكون ال

② أول شي تتكون sheet ثم يحصل لها folding فتتكون tubule ال

← العملية تحتاج لطاقة فال α- and β-tubulin يكون dimer

مرتبط بـ GTP واللي يعتبر من مصادر الطاقة

⇒ polymerization needs GTP and mg++.

* ~~microtubules grow from γ-tubulin rings within the MTOC~~ that serves as ~~nucleation sites for each microtubule.~~

Microtubules formation can be traced to hundreds of γ-tubulin rings that form an integral part of MTOC and function as templates for the correct assembly of microtubules. The α- and β-tubulin dimers are added to a γ-tubulin ring in an end-to-end fashion. ① The most simplistic model used in the past described microtubule assembly as a process of adding tubulin dimers one by one onto the growing end of a fully formed microtubule. However, ② a number of experimental studies using cryoelectron microscopy reported the initial assembly occurs from a curved sheet made of tubulin dimers, which in turn closes into a tube at the growing end of the microtubule.

* polymerization of the tubulin dimers requires the presence of guanosine triphosphate (GTP) and Mg^{2+}. Each tubulin molecule binds GTP before it's incorporated into the forming microtubule. The tubulin dimers containing GTP have a conformation that favors stronger lateral interactions between dimers resulting in polymerization. At some point, GTP is hydrolyzed to guanosine diphosphate (GDP). As a result of this polymerization pattern, microtubules are polar structures (end +, −) because all of the dimers in each protofilament have the same orientation.

- microtubules يحصلها assembly and disassembly
وبيكون في توازن بين العمليتين فلما يحصل disassembly بيكون
فيه tubulin dimers free in the cytoplasm ولما نحتاجها بترجع بترتبط
بالـ GTP وبتتم عملية الـ assembly
- low T (حرارة) and high P (ضغط) تقود للـ disassembly

- في الوضع المعتاد الـ microtubules تكون instable
"dynamic instability"
أنها باستمرار في assembly and disassembly حسب ما ظهر
في الميكروسكوبات المتطورة.

* Tubulin dimers dissociate from microtubules in the steady state, which adds a pool of free tubulin dimers to the cytoplasm. This pool is in equilibrium with the polymerized tubulin in microtubules; therefore, polymerization and depolymerization are in equilibrium.

* The equilibrium can be shifted in the direction of depolymerization by exposing the cell or isolated microtubules to low T or high p. Repeated exposure to alternating low and high T is the basis of purification technique for tubulin and microtubules.

* The speed of polymerization and depolymerization can be modified ~~by interaction with specific microtubule associated proteins (MAPs)~~. These proteins, such as MAP-1, -2, -3 and -4, MAP-τ, and TOGp, ① regulate microtubule assembly and ② anchor the microtubules to specific organelles. MAPs are also ③ responsible for the existence of stable populations of nondepolymerizing microtubules in the cell, such as those found in cilia and flagella.

* The length of microtubules changes dynamically as tubulin dimers are added or removed in a process of dynamic instability.

↓

constant remodeling process linked to a pattern of GTP hydrolysis during the microtubule assembly and disassembly process.

* The tubulin dimers bound to GTP at the growing end (+) of the microtubule ~~protect it from disassembly~~. In contrast, tubulin dimers bound to GDP are ~~prone to depolymerization~~ that leads to a rapid microtubule disassembly and shrinking. During disassembly, the tubulin dimers bound to GDP lose lateral interaction with each other and protofilaments of the tubulin dimers curl away from the end of the microtubule, producing "split ends" The process of switching from a growing to a shrinking microtubules is often called a microtubule catastrophe.

* MAPs block the dynamic instability in cilia and flagella.

* **molecular motor proteins:** → فيزيولوجيين مفهوم

① Dyneins
- move toward the - end
- e.g. the axonemal dynein in cilia and flagella

* cytoplasmic dyneins are capable of transporting organelles from cell periphery toward the MTOC. → axonemal dynein in cilia and flagella is responsible for the sliding of one microtubule against an adjacent microtubule of the axoneme that affects their movement.
* Kinesins → moving organelles from cell center toward the cell periphery.
* dyneins move chromosomes along the microtubules of the mitotic spindle.
- kinesins → movement of polar microtubules

(2) kinesin
- toward the + end

→ Both dyneins and kinesi ... sis.

(2) actin filament = m...

globular G-actin (protein) ... s

* actin molecules assemble b... lical array to form filaments 6 t... shorter and more flexible th...

* Free actin molecules in the cytoplasm are referred to as G-act... actin), in contrast to the polymerized actin of the filament, whic... called F-actin (filamentous actin)

* An actin filament or microfilament is a polarized structure; its fast growing end is refferred to as the plus (barbed) end, and its slow-growing end is referred to as the minus (pointed) end.

* The dynamic process of actin polymerization that occurs mainly on the plus end of the actin filament requires the presence of K^+, Mg^{2+} and ATP. After each G-actin is incorporated into the filament, ATP is hydrolyzed to ADP.

* The control and regulation of the polymerization process depends (1) on the local concentration of G-actin and (2) the interaction of actin-binding proteins (ABPs), which can (1) prevent or enhance polymerization (2) also responsible for filaments' organization

← actin microfilament يتراكم بشكل مكثف تحت ال plasmamembrane
في منطقة اسمها "terminal web" غنية بعناصر cytoskeleton ← 3

← لما يكون G-actin مرتبط مع ATP و يصير له hydrolysis بيتفكك
ATP → ADP + phosphate مش طول بتنفصل حيث بيكون في transitional فترة
وبعد فترة بتنفصل ال phosphate وبيضل ال ADP

However, the phosphate group release from ATP hydrolysis is not immediate, and the transient form of actin bound bound to ADP and the free phosphate group persist in filaments.

→ actin filaments are often grouped in bundles close to the plasma membrane.

② kinesin
- toward the + end

→ Both dyneins and kinesins are involved in mitosis and meiosis.

② actinfilament = microfilament

globular G-actin (protein) → كما ترتبط هذه الوحدات مع بعض بشكل F-actin

- actin molecules assemble by polymerization into a linear helical array to form filaments 6 to 8 n.m in diameter. They're thinner, shorter and more flexible than microtubules
- Free actin molecules in the cytoplasm are referred to as G-actin (globular actin), in contrast to the polymerized actin of the filament, which is called F-actin (filamentous actin)
- An actin filament or microfilament is a polarized structure; its fast growing end is referred to as the plus (barbed) end, and its slow-growing end is referred to as the minus (pointed) end.
- The dynamic process of actin polymerization that occurs mainly on the plus end of the actin filament requires the presence of K^+, Mg^{2+} and ATP. After each G-actin is incorporated into the filament, ATP is hydrolyzed to ADP.
- The control and regulation of the polymerization process depends ① on the local concentration of G-actin and ② the interaction of actin-binding proteins (ABPs), ① which can prevent or enhance polymerization. ② also responsible for filaments' organization

plasma membrane الـ actin microfilament يتراكم بشكل مكثف تحت
3- cytoskeleton في منطقة اسمها "terminal web" تنتشر بشكل شبكة
كما يكون G-actin مرتبط مع ATP ويسير الـ hydrolysis بشكل
transitional فترة ADP+phosphate ATP مش بطول بتفصل حيث يتكون
وبعد فترة بتفصل الـ phosphate ويبقى الـ ADP

However, the phosphate group release from ATP hydrolysis is not immediate, and the transient form of actin bound bound to ADP and the free phosphate group persist in filaments.

→ actin filaments are often grouped in bundles close to the plasma membrane.

(3) intermediate filaments:

- diameter 8-10 n.m
- significant divesity and tissue specifity من أهم ميزاتها

← كل نوع من الخلايا بيكون ليها intermediate filament
مختلف في تركيبه وتكوينه عن الخلايا الأخرى
وهذا الاشي مفيد في ال immunohistochemistry أنه نعرف ال cancer
من وين منشأه حيث أن أحيانا شكل ال cancercell بيتغير
فبنقدرش نعرف الأصل اللي نشأت منه من خلال الشكل
فنلجأ لل immunohistochemistry عشان نعرف إذا في بروتين معين أي IF معين
فنعرف منشأه (أو على الأقل لو ما قدرنا نجزم بمنشأه بهذه الطريقة
فنكون على الأقل قللنا الاحتمالات وبوسائل أخرى نستطيع
أن نجزم من أين منشأ ال cancer

- non polar filaments with no enzymetic activity

← بناء وهدم غير موجودين زي actin filaments + microtubules
فوظيفته بشكل أساسي ← structural role
↳ يؤمن mechanical support للخلايا
زي keratin (الطبقة الأخيرة الموجودة على سطح الجلد)
تتكون داخل squameous epithelium وبشكل الطبقة اللي بتعمل
حماية من العالم الخارجي

- No growing nor reforming
- primarly structural role

Histology A Text and Atlas ← P. 78 ← Fig 2.49

الخلايا التي تبطن ال small intestine وتقوم بعملية الامتصاص
تكون شكلها columnar ولها بسطحها microvilia
لتزود مساحة السطح وتقوم بعملية الامتصاص بكفاءة أكبر
كل microvili له core من actin filaments، وشبكة معقدة من IF
بالإضافة لل microtubules ← بيعطوا ال apical part ال
mechanical strength

* IF are assembled from a pair of helical monomers (protein) that twist around each other to form coiled-coil dimers. Then, 2 coiled-coil dimers twist around each other in antiparallel fashion (parallel but pointing in opposite directions)

to generate a staggered tetramer of 2 coiled-coil dimers, thus forming the nonpolarized unit of the IF. → (heterogeneous group of cytoskeletal elements found in various cell types)

6 major classes of IF:

→ they're organized on the basis of gene structure, protein composition, and cellular distribution.

① class 1 and 2

- most diverse groups of IF and are called keratins (cytokeratins)
  يعني ال epithelial tissue حتى انك ربما حاد ال tissue موجودة فيكون → الاقل ادنا موجود نوع من ال keratins
- these classes contain more than 50 different isoforms and account for most of the IF (about 54 genes of the total 70 human IF genes are linked to keratin molecules)
- keratins only assemble as heteropolymers: an acid cytokeratin (class 1) and a basic cytokeratin (class 2) molecule form a heterodimer.

② class 3

→ أشهر عناصره vimentin وهاد موجود في الخلايا اللي مصدرها Mesnchymal tissue
ال embryo بيتكون من 3 طبقات رئيسية →

كل layer بينشأ منها شغلات {
① endoderm (inner layer) → GIT طبقات تبطين
② ectoderm (outer layer) → skin, CNS
③ mesoderm (middle layer) → عظم، عضلات، fat
}

→ mysnchymal tissue تنشأ منها
فيه → IF (vimentin)

→ desmin → IF → (موجود في ال muscles كلها) خاص بالعضلات
→ GFAP (glial fibrillar acidic protein)
CNS → neuron
فيه خلايا أساسية ونيورونات
glial cells مجموعة مساعدة
→ neurons وظيفتها: تعطي ال mechanical support +

✱ vimentin is the most common class 3 IF protein and is found in most cells derived from embryonic mesenchyme. Important vimentin-like proteins include desmin found in almost all muscle cells and GFAP found especially in astrocytes, supporting cells of central nervous system tissue.

→ contain IF proteins that are expressed mostly in axons of nerve cells.

3. class 4

neurons الـ axons ⇐ neurofilament NF ← IF

3 types of different molecular weights

1. NF-L (a low-weight protein)
2. NF-M (a medium-weight protein)
3. NF-H (a high-weight protein)

4. class 5

- network associated with the nuclear envelope
- almost in all differentiated cells
- Lamins, specifically nuclear lamins, form a network-like structure that's associated with the nuclear envelope. Lamins are represented by 2 types of proteins, Lamin A and B.

→ in contrast to other types of IF found in the cytoplasm, lamins are located within the nucleoplasm of almost all differentiated cells in the body.

5. class 6

- lens specific → خاص بعدسة العين IF
- phakinin and filensin

→ This is a lens-specific group of IF, or "beaded filaments" containing 2 proteins, phakinin and filensin. The periodic bead-like surface appearance of these filaments is attributed to the globular structure of the carboxy-terminus of the filensin molecule, which projects out from the assembled filament core.

→ IF:

1. highly variable central rod shaped domain
   - differ in a a sequence
   - some variation in molecular weight
   - share a homologous region
2. with strictly conserved globular domains at either end.

④ centrioles and MTOC:

→ centrioles حصا

- paired, short, rod like cytoplasmic cylinders
- Built from 9 microtubule triplets (peripheral part)
- Right angle to the other
- close to the nucleus, partially surrounded by the golgi apparatus

• starting point for MT

→ centrioles + amorphous proteinous material = centrosome / MTOC

paired strctures متقاطعين

200 protein حوالي ← peri centriolar material

ومن ضمنهم الـ γ - tubulin واللي هما الحلقات الموجودة على السطح الخارجي ومنهم تنشأ الـ MT بالإضافة لل capping proteins وبروتينات أخرى

• where most MT are formed
• Basal body formation for cilia and Flagella
• mitotic spindle formation

→ basal body تركيبها مشابه لل centriole لكن موجودين في القاعدة التي تنشأ منها الـ cilia

→ centriole لها دور مهم في نشأة الـ mitotic spindle أثناء عملية الانقسام

Histology A Text and Atlas ← p.81 ← Fig 2.52

لونهم أخضر ومتبطين centrioles وحولهم amorphous protein وحلقات حولهم γ-tubulin تنشأ منها الـ MT في الاتجاهات المختلفة وعلاقة وضعة بال nucleus وال golgi apparatus

✱ microvilli → small intestine في

للامتصاص ومش متحركة وتزود مساحة

cilia → respiratory system متحركة وتبطن الـ

نفس المرجع ← p.81 ← Fig 2.53

في cilia ← 9 doublets + 2 in center

(تنشأ منه الـ cilia) basal body ← 9 triplets

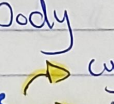
basal bodies: تنشأ منه الـ axoneme أو الـ MT الخاص cilia →

- a requirement for cilia
- Derived from centrioles
- serves as "organizing centers" for the assembly of cilium MT
- axoneme 9 doublets + 2 في المنتصف (the doublets are continous with A and B MT of the basal bodies from which they develop)

* one of the important functions of centricle is to provide basal bodies, which are necessary for the assembly of cilia and flagella. Basal bodies are formed either de novo formation without contact with the preexisting centrioles (the acentriolar pathway) or by duplication of existing centrioles (the centriolar pathway).

* Developement of cilia on the cell surface requires the presence of basal bodies, structures derived from centrioles.

→ Each cilium requires a basal body. The generation of centricles, which occurs during the process of ciliogenesis, is responsible for the production of basal bodies. The newly formed centrioles migrate to the apical surface of the cell and serves as organizing centers for the assembly of the MT of the cilium. The core structure (axoneme) of a motile cilium is composed of a complex set of MT consisting of 2 central MTs surrounded by 9 MT doublets (9+2 configuration). The organizing role of the basal body differs from that of the MTOC. The axonemal MT doublets are continous with the A and B MTs of the basal bodies from which they develop by addition of α- and β-tubulin dimers at the growing (+) end.



→ doublets

A و B ← يتم بناء MT عليهم

triplets / basal body ←

← في بروتينات أخرى تؤمن انزلاق tubules لـ بعضها البعض

8 → basal body

أول حلقة بتحتوي 13 والباقي 10 (كل حلقة 10)

⑤ inclusions
→ cytoplasmic or nuclear
→ metabolic products

← منتجات تنتج أثناء العمليات الحيوية منها Lipid, pigmented materials,

← ممكن يتواجد في كل الخلايا ← fat cells ← وظيفتها تصنيع وتخزين الـ Fat

ممكن يتواجد الـ lipid فيها بشكل دائم

→ glycogen (liver cells) → metabolism of glycogen

يتم في الـ liver

- lipofuscin → غالبا lysosome الهضمي = تعمل residual body بسبب تراكم

التي لم تهضم تتراكم (أخيرا) residual body بشكل (في) مقياس لـ aging (بزيادة عمر الخلية) neuron

→ + indicator of cellular stress (تعب/ يتجدد) ← حاجات واجهتها الخلية خلال حياتها

- **hemosiderin** عمرها أيام RBC الـ ⇐ hemoglobin الحديد موجود في الـ
تتكون باستمرار في تراكم للحديد نتيجة الـ degradation
~~لتخزين الحديد الذي ينشأ من الأماكن المختلفة وخاصة complex~~
~~الـ RBC~~

- **glycogen** ⇐ ممكن يتراكم في بعض الخلايا
- **lipid** ⇐ قد يكون موجود بشكل مؤقت أو دائم
adipocyte morphology ⇐ الـ fatty tissue
} ⇐ Lipid storage diseases.

- **crystalline inclusions**: contained in certain cells are recognized in the Light microscop. Such inclusions are found in the ~~sertoli (sustentacular)~~ and ~~leydig (interstitial) cells of the testis.~~
~~testrone~~ ← ~~بتكون~~   ~~supportive cells~~ ← ~~حول الخلايا اللي بينشأ منها الـ sperm أو spermatozoa~~

- with the TEM, crystalline inclusions have been found in many cells types and in virtually all parts of the cell, including the nucleus and most cytoplasmic organelles.
- some of these inclusions contain viral proteins, storage material, or cellular metabolites

***lipofuscin:** is a brownish-gold pigment visible in routine H &E preparation. It's easily seen in non-dividing cells such as neurons and skeletal and cardiac muscle cells.
- ⇒ accumlates during the years as a result of cellular senescene (aging); thus, it's often called the "wear and tear pigement".
- ⇒ قد نجد lipofuscin أيضاً في phagocytotic cells

***hemosiderin:** an iron storage complex found within the cytoplasm of many cells. It's most likely formed by the indigestible residues of hemoglobin, and its presence is related to phagocytosis of RBC.
- ⇒ easily demonstrated in the spleen, where aged erthrocytes are phagotysed, but it can also be found in alveolar macrophages in the lung tissue, especially after pulmonary infection accompanied by small hemorrhage into the alveoli.
- ⇒ visible in light microscopy as a deep brown granule.

* glycogen : highly branched polymer used as a storage material for glucose. It's not stained in the routine H&E preparation. but, it may be seen in the light microscope with special fixation and staining procedures (such as toluidine blue or PAS).
→ liver and striated contain large amounts of glycogen

* lipid inclusions (fat droplets) : usually nutritive inclusions that provide energy for cellular metabolism.
→ they may appear for a breif time (in intestinal absorptive cells) or may reside for a long period (adipocytes)
→ In individuals with genetic defects of enzymes involved in lipid metabolism, lipid droplets may accumlate in abnormal locations or in abnormal amounts → lipid storage diseases

: يعني

inclusions are cytoplasmic or nuclear structures with charactrestic staining properties that are formed from the metabolic products of the cell. They're considered nonmoving and nonliving components of the cell. Some of them, such as pigment granules, are surrounded by a plasma membrane; others (lipid droplets or glycogen) instead reside within the cytoplasmic or nuclear matrix.

⑥ cytoplasmic matrix

- concentrated aqueous gel consisting of molecules of various sizes and shapes
  electrolytes, metabolites, RNA and proteins (بتتحرك)
- The largest compartement in the cell
- The site of physiologic processes:
  - protein synthesis and degradation (الريبوسومات الحرة في الخلية)
  - Break down of nutrients (تتواجد فيه)
- studies ~~with~~ revealed a complex 3D structural network of thin microtrabecular strands and cross-linkers. This network provides a structural substratum on which ① cytoplasmic reactions occur, such as those involving free ribosomes, and along which ② regulated and directed cytoplasmic transport and movement of organelles occur. ③

elongated (muscle cells) — rounded, oval

عادة تكون كروية لكن حسب شكل ووظائف الخلية ممكن يتغير ديبر حتى تكون بروبيادهم

Overview of the nucleus:

① the genome and machinery of replication, transcription and processing

حتى تتم عملية الانقسام

ال packaging لل DNA مُعقد حيث أنه عبارة عن سلسلة طويلة double strand

له ومش عشوائي حيث أن الجزء الذي نحتاجه يكون accessible

وقابل للنسخ لـ RNA لتتكون منه البروتين

→ بروتينات histones لها دور أساسي في ال packaging لل DNA وفيما

بعد تبين أن لها دور أيضاً في التحكم في ال DNA يعني نسخ بروتين او [illegible] الانقسام

→ في الوضع العادي يكون DNA ← chromatin لكن أثناء الانقسام

يبدأ العزيز من coiling وبيتشكل ال chromosomes

→ 50% من وزن ال chromatin عبارة عن histones

chromatin:
- euchromatin ← جزء نشط بيحصله نسخ — light, pale areas
- heterochromatin ← غير فعال — condensed, coiled

DNA (rRNA genes) — site of rRNA synthesis ↩

→ nucleolus بيتكون من جزء من ال DNA اللي له علاقة بتكوين او نسخ rRNA

→ ويوجد أيضاً أنواع أخرى RNA + regulatory cell cycle proteins

* the nucleus contains genetic information, together with the machinery for DNA Replication and RNA transcription and processing. The nucleus of nondividing (interphase) cell has the following:
chromatin, nucleolus, nuclear envelope, nucleoplasm (nuclear content

لها (chromatin + nucleolus

- ~~double membrane system that surrounds the nucleus and it consists of an inner and outer membrane separated by perinuclear cisternal space and perforated by nuclear pores.~~
- ~~The outer membrane is continous with rER and studded with ribosomes~~

nucleus (interphase cell) = nuclear envelope + nucleosome (other contents)

له الوحدة اللي بيتكون منها نظام ال packaging لل DNA

chromatin:
- 6 billion (10^9) bits of information
- 1,8 m total length
- 100,000 times longer than the nuclear diameter
- highly folded and tightly packed nucleoprotein complex ← chromatin + nucleic acid مع بروتينات أخرى يشكلوا nucleoprotein
- further folding ... chromosomes
- packaging is important for effective transcription.

nucleotides يتكون من ← helical ← double ← nucleic acid
N. base ——→ كل base بترتبطوا stranded
phosphate group → base pair
sugar
• sequencing human genome was successfully completed in 2003
• 2,85 billion basepair → مش كلها بيتكون منها بروتينات
noncoding ← DNA الأغلبية العظمى من , جزء منها بتستعمل coding
23,000 protein coding genes
dark matter بتسمى الـ non coding الجزء الـ
له دور في التحكم بالعمليات داخل الخلية

• The human genome contains a 2,85 billion base pair consensus sequence of nucleotides, which are arranged in about 23,000 protein-coding genes.

heterochromatin → peripheral غالبا بتكون في part أطراف النواة
- constitutive heterochromatin
• Inactive condensed DNA
• highly repetitive → نفس التتابع ← chromatids
• Near the centromeres and telomeres
- Facultative heterochromatin ← ممكن يحصل فيه transcription
• Not repetitive ← أوقات → أحيانا تكون وحدات متكررة من
• Inconsistent localization نيوكليوتيدات
• May undergo active transcription in certain cells

heterchromatin is disposed in 3 locations:
1. marginal chromatin: is found at the periphery of the nucleus (the structure light microscopists formerly referred to as the nuclear membrane actually consists largely of marginal chromatin)
2. karyosomes: discrete bodies of chromatin irregular in size and shape that are found throughout the nucleus.
3. Nucleolar associated chromatin: is chromatin found in association with the nucleoslus.

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