

Cytology lecture 8 summary

The Cytoskeleton and Cell movement :

Microtubules

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وَتَوَكَّلْ عَلَى الْحَيِّ الَّذِي لَا يَمُوتُ وَسَبِّحْ بِحَمْدِهِ
وَكَفَىٰ بِهِ بَدُنُوبٍ عِبَادَةٍ خَيْرًا

In order to organize ideas + further check :

- slides: 3,16,17 --> page 1
- slide: 4 --> page 2
- slides: 5,6,7,8,9--> page 3
- slides: 10,11,12,13 --> page 4
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All are from the modified slides

Microtubules

Microtubules : rigid + hollow rods

- They are dynamic structure , **why?**

Because they undergo polymerization and depolymerization
(like actin filaments)

Functions :

1) cell shape

2) route for intracellular organelles to transport --> **such as:**
lysosomes, endosomes, vesicles

3) separation of chromosomes during mitosis

4) Cell movements (for some cells)

Recall : Cell movement depends on actin filaments

Other functions of microtubules:

1) positions membrane-enclosed organelles(hold and stabilize them) , Ex: *ER, mitochondria ...*

2) sperm motility (through dynamic instability) , to link :
mutations in the microtubules' motor protein--> Infertility

3) transportation of mRNA molecules in cells (by Kinesin and dynein)

Microtubules structure :

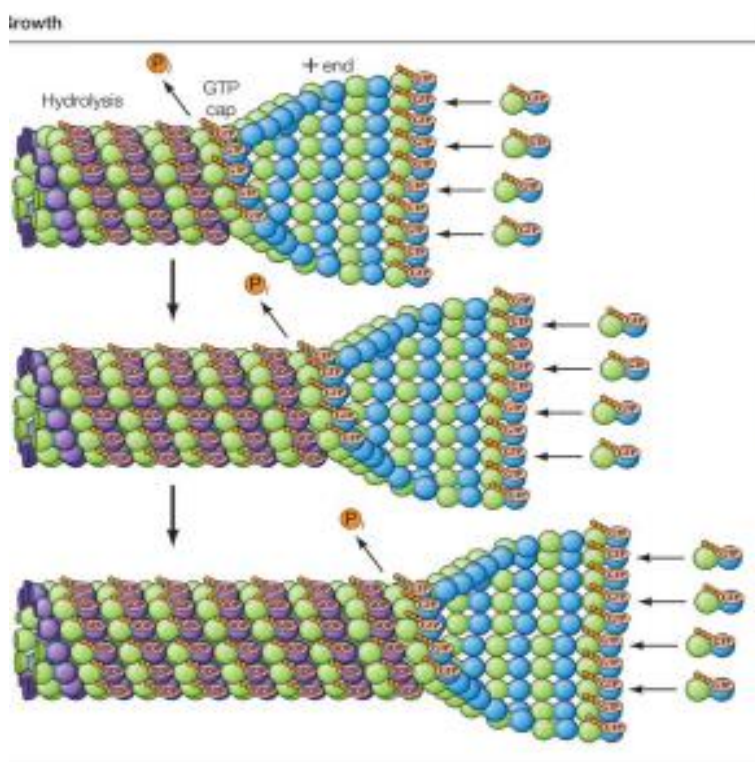
Microtubules structure :

Dimers of : α -tubulin and β -tubulin

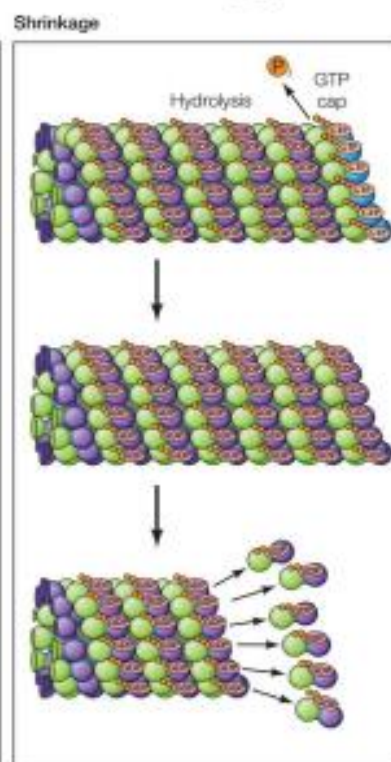
dimers of (α and β tubulins) --> polymerize --> protofilaments

Globular protein	α -tubulin	β -tubulin	γ -tubulin
Function :	Binds to GTP (remains bind)	Binds to GTP (can be hydrolyzed to GDP) \rightarrow that's why GTP+ β -tubulin is the one responsible for function .	Present at the centrosome , initiates (starts) the microtubules assembly for chromosomal separation
Involved in the microtubules structure	Yes	Yes	No

Growth



Shrinkage



Treadmilling and dynamic instability concept :

plus end : polymerization (assembly)

minus end : depolymerization (disassembly)

same as treadmill idea

Dynamic instability: The alternation of microtubules between cycles of growth (rescue)(more polymerization) and shrinkage (catastrophe)(more depolymerization)

- stable GTP- β tubulin --> growth (rescue)
- hydrolysis of GTP- β tubulin \rightarrow becomes GDP- β tubulin \rightarrow unstable (reduces binding affinity for neighboring molecules)
 \rightarrow dissociates \rightarrow shrinkage (too much shrinkage= catastrophe)

if the rate of polymerization (adding of GTP- β tubulin) is faster than the rate of depolymerization (hydrolysis of GTP- β tubulin)

\rightarrow the microtubule will grow

Drugs:

Drug:	Colchicine and colcemid	Vinblastine and vincristine	Taxol
Function:	Bind to tubulins \rightarrow inhibit polymerization block \rightarrow mitosis	bind to tubulin \rightarrow inhibit polymerization block \rightarrow mitosis	Stabilizes(stuck) microtubules \rightarrow blocks cell division
Extra info :	colchicine is used for immune diseases such as rheumatoid arthritis	used in cancer, have huge side effects	

Regulatory proteins:

- For sure we need to regulate the microtubules dynamic behavior, (بدنا نتحكم بسرعة البناء والتحطيم حسب وضع الخلية) and the **Microtubule-associated proteins (MAPs)** are the one who performs this role , **How ?**

- 1) **Regulating** (by activation or inhibition of enzymes)
 - polymerization by **polymerases**
 - depolymerization by **depolymerases**

- 2) **Rescue** the microtubule from the catastrophe (by **CLASP proteins**) The hero :)

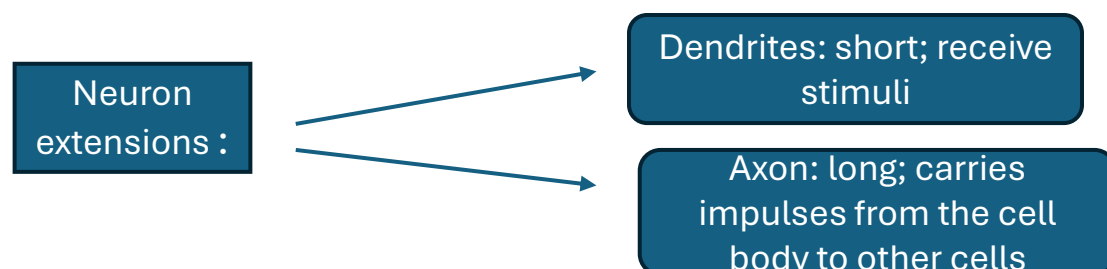
Organization of microtubules within cells:

In neurons, microtubules are organized for efficient transport and function (عشان تلائم وظيفتها) :

- **Dendrites** have microtubules oriented in **both directions**
- **Axons** have microtubules with their plus (+) ends pointing **outward** → allowing movement toward the axon tip.

Tau Protein(MAPs protein) : stabilizes microtubules in axons but can aggregate in Alzheimer's disease, causing cell death and dementia.

Note : molecules moves from (-) end to (+) end --> والله منطق



Microtubules-motor proteins:

are proteins that use ATP to move along microtubules

- 1) **Kinesin**: moves toward the plus end, carries molecule/vesicle from cell body → axonal end
- 2) **dynein**: moves toward the minus end, carries molecule/vesicle from dendritic end → cell body

How do they move ?

Similar to how our legs moves, through the binding and hydrolysis of ATP

Kinesins and diseases

Kinesins uses 2 mechanisms to transport NT (neurotransmitters)

- 1) directly binding to microtubules
- 2) using vesicles that attach to microtubules.

Mutations in kinesin proteins can lead to :

- 1) **Amyotrophic Lateral Sclerosis (ALS)**: loss of muscle control
- 2) **Alzheimer's Disease**: associated with dementia
- 3) peripheral neuropathies, such as **Charcot-Marie-Tooth disease** (recall Lamin a mutations)

Coordination between actin filaments and microtubules :

Before we start , **myosin** carries organelles over actin filaments but for short distances

Suppose we have a vesicle, and we want it to fuse with the plasma membrane , **how can that work?**

vesicle binds to kinesins via microtubules → transport near the end (near the plasma membrane) → vesicle jumps from the microtubule to the actin filaments and interact with the myosin

→ Finally , it fuses with the plasma membrane (**this step is regulated by Ca^{+2}**)

Centrosome :

Definition : The centrosome is a microtubule-organizing center that initiates microtubule assembly , anchoring their minus (-) ends inside allowing them to grow outward toward the cell periphery (plus + end)

- **In interphase**, the centrosome is located near the nucleus, with microtubules extending outward.
- **During mitosis**, centrosomes duplicate and move to opposite ends of the cell, reorganizing microtubules to form the mitotic spindle.

What is the function of this interaction (chromosomes + microtubules) ? Shrinkage of microtubules (depolymerization) leads to pulling the chromosomes toward opposite ends of the cell during cell division

#ارحموا الافريج