Cytology lecture 7 summary
The cytoskeleton and cell movement

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وَتَوَكَّلْ عَلَى الْحَيِّ الَّذِي لاَ يَمُوتُ وَسَبِّحْ بِحَمْدِهِ ۚ وَكَفَىٰ بِهِ بِذُنُوبِ عِبَادِهِ خَبِيرًا

Cytoskeleton

Definition

Dynamic *network of protein filaments extending throughout the cytoplasm*

Types

- actin microfilaments
- intermediate filaments
- microtubules

Functions

1) Structural **support** (framework)

2) **Determines** the -->
   1) organization of the cytoplasm
   2) cell shape and movement
   3) overall positions of organelles inside the cell

3) **Route** for the organelles to move
Ex: Secretory vesicles, Endocytic vesicles, mRNA transfer

How can we identify it under the microscope ?

By using fluorescence stain -->specific molecule binds to actin --> emits green/ red

Actin	Intermediate filaments	Microtubules
Highly concentrated around the cell membrane + extends throughout the cell	Thick structure around the nucleus and membrane +extends throughout the cell	Come out from around the nucleus (centrosome)+ extending outwards

actin fillaments

actin filaments (actine microfilament) :

(thin + flexible) fibers that forms --> **bundles** (thick and straight structure)

—>**network** (such as semisolid gels)

Note: Different types of cross-linking proteins connects the filaments together

How are they regulated ?

by various actin binding proteins (microtubles are also regulated by this way)

Where are they most abundant ?

beneth the plasma membrane --> forming a network (Ex: actin cortex (3D)

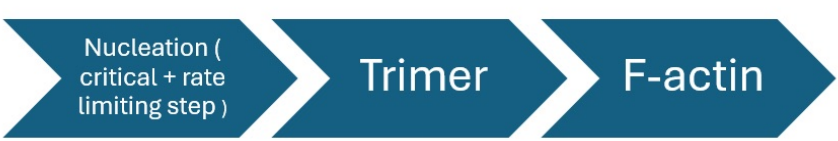
• Mammalian cells have at least 6 distinct actin genes -->

—>4 in different types of muscle cells (specific)

—> 2 in non muscle cell

note : actin proteins are conserved among species.(90% similarity between yeast and human) --> (الخالق واحد, سبحانه وتعالى)

The actin polymerization :



Formation of a trimer of G-actin

Grow to F-actin by adding monomers to the 2 polar ends

It's a dynamic structure : not fixed(adding and removing of G-actin on both ends

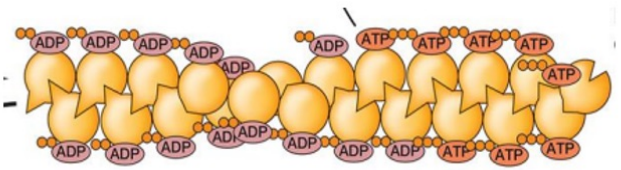
G-actin= Globular actin (monomer)

F-actin= Filamentous actin (polymer)

Minus end:

1) Mainly dissociation
2) G-actin bound to ADP (less stable)

Why ADP? → because after some time the ATP at the plus end is hydrolyzed to ADP



Plus end :

1) Mainly **association**
2) G-actin bound to **ATP**

Note : ATP is **not** required for the nucleation ,

1) It is **hydrolyzed** into ADP following assembly,
2) It **speeds** up polymerization,
3) It **stabilizes** binding

Note : both ends can polymerize and depolymerize

Note: Polymerization of G-actin leads to the formation 3D structure

Actin-binding proteins

Cellular role	Protein
Filament initiation and polymerization	Arp2/3 , formin note : ARP 2/3 initiates branching & controls it
Filament stabilization	Tropomyosin
Filament cross linking	-
Filament depolymerization (severing)	Cofilin
Actin Filament linkage to other proteins	Dystrophin, spectrin
Monomer binding	Profilin

Tropomyosin (filament stabilizing) --> by binding capping proteins to both ends

cofilin (filament severing) --> breaks up the actin filament

RBC and muscle cells

(**RBC** must be flexible to fit its role) = **Spectrin** is the major actin-binding protein that provides the structural basis of RBCs

Spectrin--> links actin filaments to transmembrane proteins **of RBC** via --> 1) ankyrin 2) protein 4.1

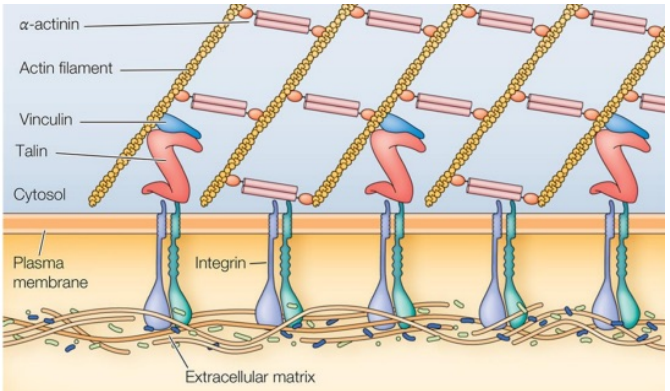
Dystrophin : links the actin filaments to transmembrane proteins **of muscle cells** --> maintaining cell stability during muscle contraction

Defective dystrophin (muscular dystrophy) :

Duchenne muscular dystrophy --> **absent** protein; **severe** disease (diagnosed in early childhood + it's progressive)

Becker muscular dystrophy --> **Defective** protein, **less severe** (dystrophin is shorter than normal)

Note :most cell surfaces have extensions (to perform a function) --> actin makes these extensions (either it's permanent or quickly rearranging)



Specialized regions: focal adhesions

Importance: stabilize the cell & allow motility.

ECM proteins (secreted by fibroblasts) ---------->integrins<---------- stress fibers

think of it as integrin is holding both with different hands

Note : Mesenchymal cells(Ex: fibroblast) are **elongated** + **motile** cells that move faster than epithelial cells.

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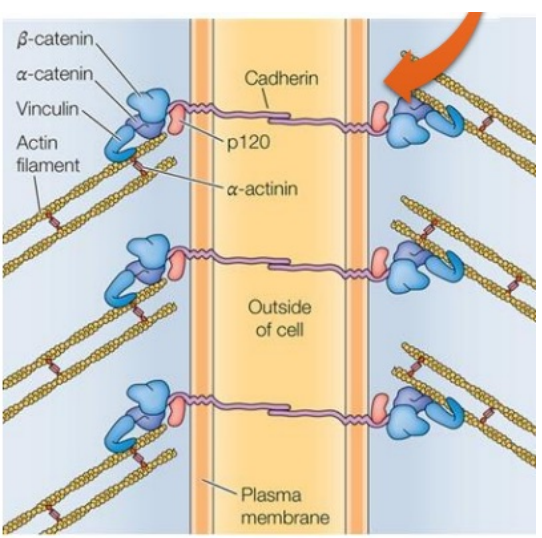

Specialized structure: Adherins junctions

Importance: cell-cell communication & signal transmission

adherens junctions : site of interaction between 2 cells (connect epithelial cells together)

made by : **cadherins**

Cadherins attach to actin filaments via **catenins**

Note : Epithelial cells lose cadherins when they become cancerous becoming fibroblast-like

Specialized regions:
Transient surface protrusions

Pseudopodia	Lamellipodia	Filopodia
network of actin filament Ex: phagocytosis	network of actin filament found at the leading edge of moving fibroblasts.	Very thin projections that extend from lamellipodia for sensory purposes

these extentions forms by the assembly and disassembly of actin filaments.

Cell migration :

1) **Attachment**: The cell anchors to a surface using focal adhesions and stress fibers

2) **Initiation**: It senses external signals and establishes direction (polarity).

3) **Protrusion**: The leading edge extends with structures like lamellipodia and filopodia.

4) **Actin Extension**: Actin filaments grow, creating new adhesions.

5) **Movement**: The rear detaches, and the cell moves forward.

This process is used by cells like fibroblasts, cancer cells, and immune cells.

Rho family proteins:

Rho: Forms stress fibers (helps with contraction).

Rac: forms lamellipodia (broad cell edges for movement).

Cdc42: Forms filopodia (cell direction).

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