Cytology lecture 6 summary
The Nucleus

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DOPAMINE
SCIENTIFIC TEAM

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

The following include :
1) Structure of nucleus and the function of each part
2) How are the nucleus releated to the ECM

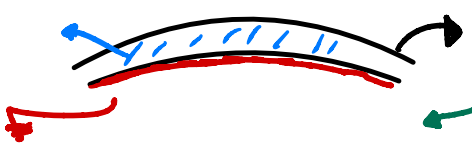
The nucleus : storage of genetic information

The nuclear envelope(membrane)

it's connected to the to the nuclear lamina from the inner membrane side .

perinuclear space

similar to ER lumen



outer membrane

continuous with the ER and is functionally similar to it , but it has different protein composition

inner membrane

proteins that bind the lamina

connected to each other by pore complex

So , what is the nuclear lamina? ***--> network of intermediate filament protiens (lamins)*** → Lamin A / Lamin B → Depending on cell type.

Lamin polypeptides --> dimers --> tetramers --> filaments

Function? ***--> support***
How is it connected to the inner membrane ?-->
1) prenylation
2) protiens (LBR)

How is it connected to the cytoskeleton ? ***--> LINK complex (note that the cytoskeleton is connected to the ECM , so any effect on it will procceed futher to the nuclear lamina***

How is it connected to the chromatin ?--> the lamins interact with it leading to localization of the heterochromatin

The following include : nuclear lamina diseases and the genes causing them

Emery-Dreifuss muscular dystrophy , caused by either :
- The emerin gene (X-linked disease)
- The lamin A gene (autosomal dominant disease)

Muscle wasting *(Marie-Charcot-Tooth disease)*
Premature aging *(Hutchinson-Gilford progeria)*.
Fat distribution problems *(Dunnigan-type lipodystrophy)*.

How Does One Gene Cause So Much Trouble?

Mechanical Stress Theory:

Imagine the nucleus as a house. The **Lamin A mutation** weakens the walls, making the structure vulnerable to any external pressure

Gene Expression Theory:

The **Lamin A mutation** messes with the “gene switches” in the nucleus

The following include : nuclear pore complex and functions releated to it

What is the nuclear pore complex made of? --> nucleoporins -NUP- (allows nucleocytoplasmic transport)

*__**small molecules**__ pass through passive diffusion
__*** large molecules**__ pass through specific signals
Nuclear Localization Sequence (NLS):
Specific sequence of Bipartite basic amino acids that allows large molecules to pass inside the nucleus

What if there is a deficiency in nucleocytoplasmic transport ? --> neuro degenerative diseases will occur

importin binds to the NLS of a protein --> this complex transport through the pore into the nucleus by the help of **Ran/GTP** --> then **Ran/GTP** plays 2 roles here :

1) Diassociates the importin from the protein
2) Deliver the importins back to the cytosol
after these 2 roles , it is hydrolyzed from GTP to GDP in order to release the importin --> finally it returns back to the nucleus in order to perform its role again

GDP--> GTP catalyzed by **GEF** enzyme inside the nucleus
GTP--> GDP catalyzed by **GAP** enzyme at the cytosol

exportins binds to the NLS of a protein (export signals) --> this complex transport through the pore out of the nucleus by the help of **Ran/GTP** --> Ran/GTP plays 2 roles here :

1) Diassociates exportin from the protein
2) Deliver it back to the nucleus , it is hydrolyzed from GTP to GDP in order to release the exportin ,

Importin and exportin proteins that can transport nuclear molecules are known as **Karyopherins**.

The following include : nuclear transport

rRNA= ribosomal RNA
How are rRNA transported outside the nucleus ?--> as complexes **associated with ribosomal proteins**(found at nucleolus) by the help of **exportin protein** (based on nuclear export signals)

How does the mRNA transported outside the nucleus ?
mRNAs export:
• does not involve karyopherins
• is independent of Ran,
• are transported through the nuclear pore complex by an exporter complex
• Are released by a helicase in the cytoplasm

Note : nucleolus is a structure found in the cell's nucleus whose primary function is to **produce ribosomes** and it's the **site where ribosomal RNA genes are transcribed**

The following include : organization of chromosomes and types of it

Chromosomes(chromatin) : complex of DNA + histone

we have 2 types based on the activity of it (ability to transcribe)

1) Heterochromatin (condensed DNA containing transcriptionally inactive genes)-s localized in the **exterior** of the nucleus as lamin-associated domains (LADs) or surrounding the nucleolus-

2) Euchromatins (loose DNA containing transcriptionally active genes)-localized to the **interior** of the nucleus-

Note: Euchromatic and heterochromatic DNA regions are well-organized within the nucleus, leading to the formation of distinct areas. One key area is the nucleolus, where rRNA and ribosomal proteins are synthesized

The following includes: nuclear factories

DNA replication (synthesis) --> occurs within discrete clustered regions called **replication factories**

Transcription (RNA synthesis) --> occurs at clustered sites **(transcription factories)**

Coregulated genes--> gather in the same area (factory) in the nucleus to be processed or **transcribed at the same time**

Nuclear bodies : non-membranous, discrete regions with specific functions
Ex:
nucleolus :
Number -->1-4
Function --> rRNA transcription, processing and ribosome assembly