Nuclear envelope, nuclear pores, nucleocytoplasmic transport

- Know the organization of the nuclear envelope and associated proteins.
- Understand the organization of the nuclear pore complex.
- Understand the role of different types of nucleoporins.
- Be able to describe the nuclear import and nuclear export of proteins, and know the required components.
- Know different mechanisms by which nuclear import can be regulated.
- Know the basic principles of RNA nuclear export.
Nuclear envelope, nuclear pores, nucleocytoplasmic transport

Figure 4-9. Molecular Biology of the Cell, 4th Edition.
Nuclear lamina (animal cell)
SEVERAL MAJOR INTEGRAL MEMBRANE PROTEINS OF THE INNER NUCLEAR MEMBRANE INTERACT WITH BOTH THE NUCLEAR LAMINA AND CHROMATIN.

• The lamin B receptor (LBR), lamina-associated protein 2 (LAP2), Man-1, and emerin all bind lamin B.

• LBR associates with chromatin via HP1.

• The other three associate with chromatin via BAF.

• Emerin and LAP1 also bind to lamin A.
HUMAN DISEASES ASSOCIATED WITH NUCLEAR ENVELOPE ABNORMALITIES.
Nuclear pores (NP) in nuclear envelope (NE)

Freeze fracture viewed with electron microscope
Electron micrograph of a thin section showing face-on views of negatively stained nuclear pores.
Nuclear pores as viewed by SEM, from the nuclear side of the nuclear envelope. This type of image clearly shows the nuclear basket. Xenopus oocytes nuclei have a very night density of nuclear pores, and are often used for these studies.
Figure 12-9(A)
The molecular architecture of the nuclear pore complex.


The Outer Ring Complex Nups Form “Solenoid-Beta Propeller” Structures

Outer Ring Nups are Similar to Vesicle Coat Proteins

![Diagram of Clathrin/AP-2 Complex with variants of CCVs, COPI, COPII, and NPC]

<table>
<thead>
<tr>
<th></th>
<th>CCVs</th>
<th>COPI</th>
<th>COPII</th>
<th>NPC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clathrin-N</td>
<td>α-subunit-N</td>
<td>Sec13</td>
<td>Sec13-N</td>
<td>Sec13-N</td>
</tr>
<tr>
<td>β-subunit-N</td>
<td>(Seh1)</td>
<td>Sec31-N</td>
<td>Seh1</td>
<td>Nup133-N</td>
</tr>
<tr>
<td>Sec31-N</td>
<td></td>
<td>Sec13</td>
<td>Nup120-N</td>
<td></td>
</tr>
<tr>
<td>α/γδε-subunit</td>
<td>β-subunit-C</td>
<td>Sec31-C</td>
<td></td>
<td>Nup133-C</td>
</tr>
<tr>
<td>β-subunits</td>
<td>β-subunit</td>
<td></td>
<td></td>
<td>Nup120-C</td>
</tr>
<tr>
<td>γ-subunit</td>
<td></td>
<td></td>
<td></td>
<td>Nup85</td>
</tr>
</tbody>
</table>

Model of nuclear pore evolution

Nuclear pores are similar across kingdoms

Yeast

Higher Plants

Vertebrates

Cytoplasm

Nucleoplasm
Nuclear pores act as a diffusion barrier

Molecules larger than ~50kDa cannot freely enter the nucleus

Figure 12-10
A nuclear localization signal is necessary and sufficient for transport into the nucleus.

**Figure 12-11**

(A) LOCALIZATION OF T-ANTIGEN CONTAINING WILD-TYPE NUCLEAR IMPORT SIGNAL

(B) LOCALIZATION OF T-ANTIGEN CONTAINING A MUTATED NUCLEAR IMPORT SIGNAL
Nuclear Localization Signals Bind to an Import Receptor (or “Importin”)
Binding to Importins is Regulated by Ran

- Ran-GTP
- Binding site for cargo protein
- Import receptor
Binding to Importins is Regulated by Ran

Figure 12-15
The Ran Cycle

Impβ (or CAS)

Ran-GAP

P_i

Ran-GDP

GDP

NTF2

Impβ (or CAS)

GTP

Ran-GTP

GTP

NTF2

CYTOSOL

NUCLEUS

chromatin

Figure 12-14
It is, of course, more complicated...
Nuclear Export Uses the Same Principles as Import

“Exportins” are related to Importin β

Figure 12-15 Molecular Biology of the Cell 5/e (© Garland Science 2008)
Nuclear export of proteins
Regulation of nuclear transport

Import may be regulated by:
- protein modification
- protein conformation
- protein interaction
- cytosolic retention

Export may be regulated by:
- protein modification
- protein conformation
- protein interaction
- nuclear retention
Regulated nuclear import is a step in signal transduction!

Calcineurin (protein phosphatase) and NF-AT are involved in the process. In activated T cells, high [Ca^{2+}] leads to nuclear import, activating gene transcription. In resting T cells, low [Ca^{2+}] results in nuclear export and dephosphorylation.
Regulated nuclear import in plants

Different RNAs exported from nucleus
Overview of the different RNA export pathways and the export factors
Transcription-coupled or splicing-coupled mRNA export
Nuclear envelope, nuclear pores, nucleocytoplasmic transport

• Know the organization of the nuclear envelope and associated proteins.
• Understand the organization of the nuclear pore complex.
• Understand the role of different types of nucleoporins.
• Be able to describe the nuclear import and nuclear export of proteins, and know the required components.
• Know different mechanisms by which nuclear import can be regulated.
• Know the basic principles of RNA nuclear export.