The Nucleus

- Definition
- Structure
- Ultrastructure
- Molecular organization of nuclear components

Definition

- The largest organelle
- Membrane-bounded (nuclear envelope)
- Contains *most* of the cell's DNA
- Role: protection of genetic information, assuring its transmission, and further on its use

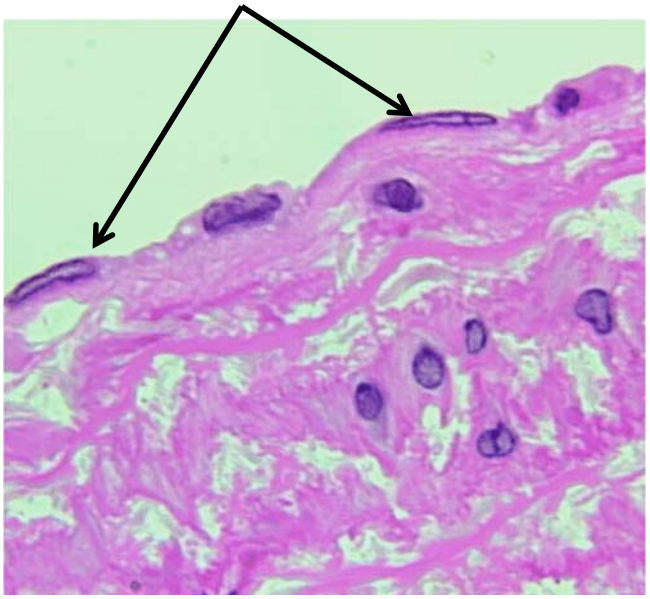
- ALL SOMATIC CELLS OF ONE ORGANISM HAVE THE SAME GENES

Nucleus structure

LM – staining characteristics

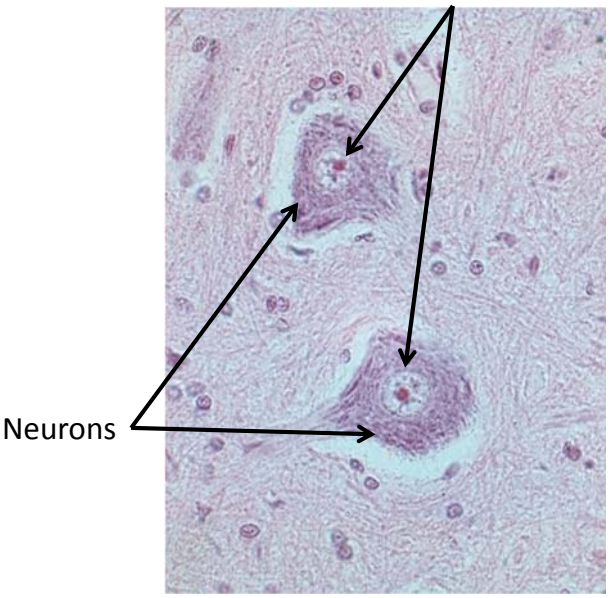
Heterochromatic nuclei

Endothelial nuclei



Euchromatic nuclei

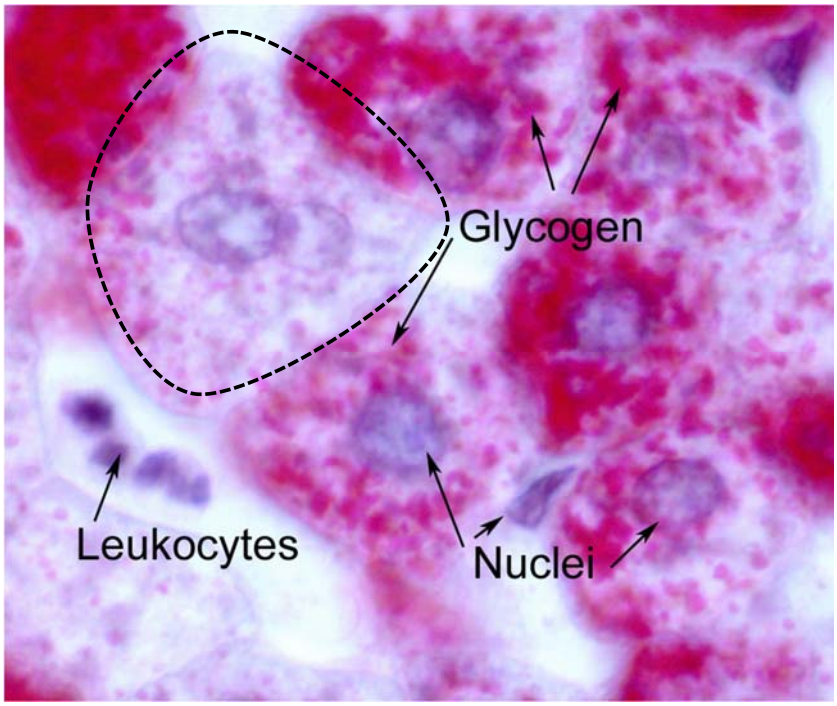
Nuclei with obvious nucleoli



Nucleus structure

LM - Number

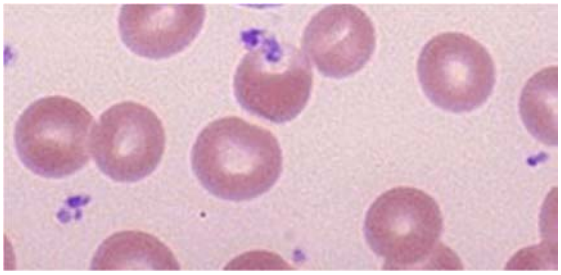
The rule: one cell – one nucleus



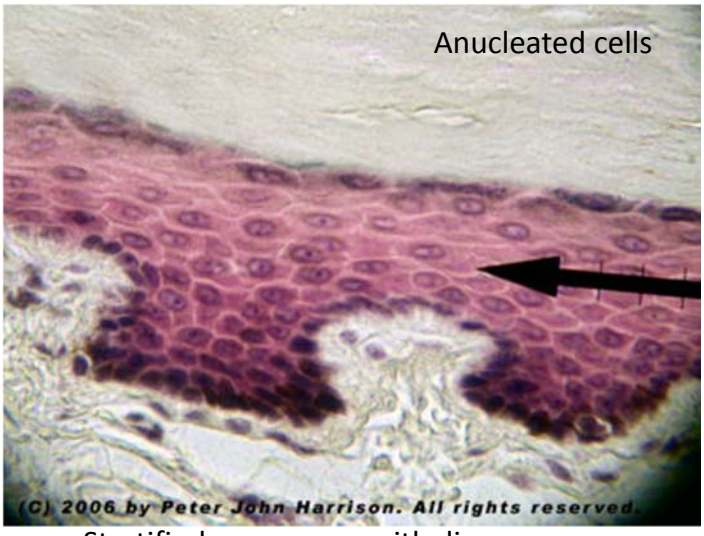
Liver – Best Staining 80x

Transitional epithelium
in urinary bladder – HE 40x

Nucleus structure
LM - Number

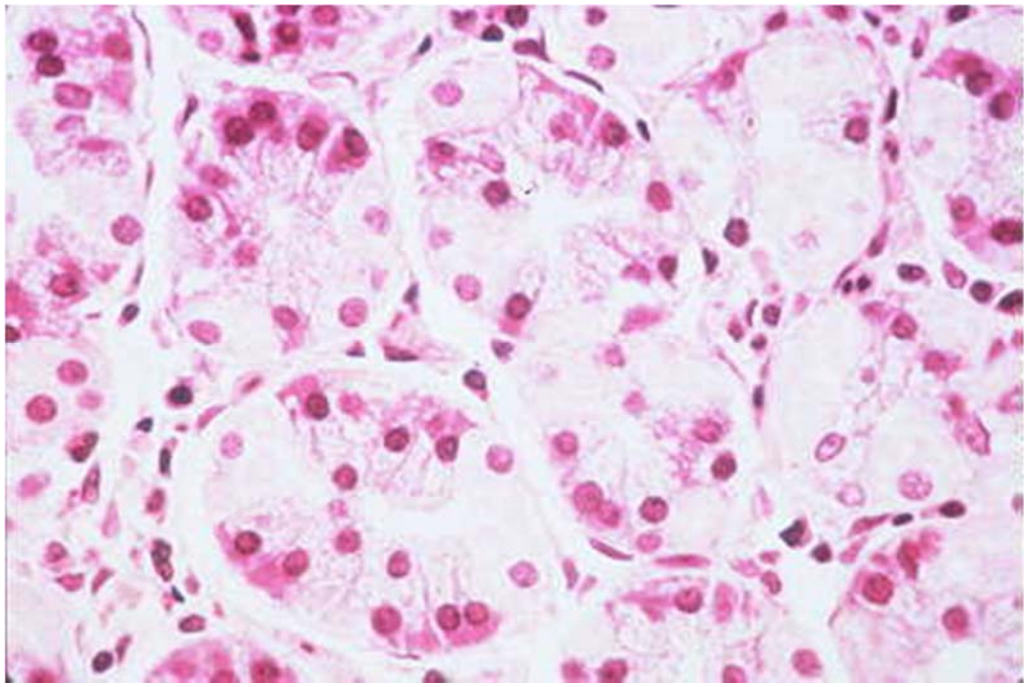


Erythrocytes



Stratified squamous epithelium

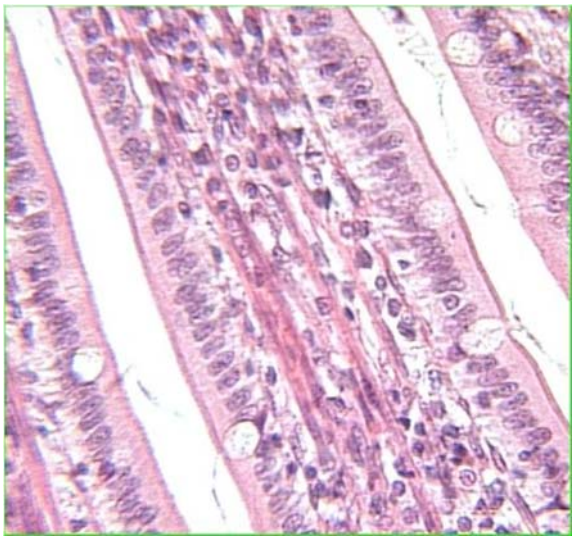
Nucleus structure
LM – morphology (shape)



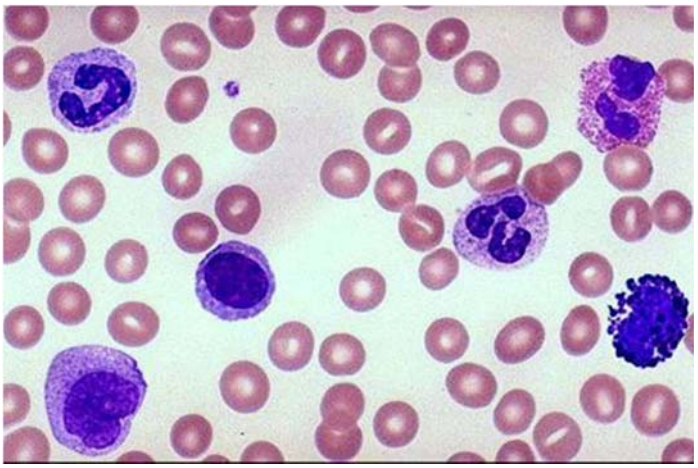
Gastric glands – cross section HE 40x

Nucleus structure

LM – morphology (shape)



Intestinal villus HE-60x



http://www.pathologystudent.com/wp-content/uploads/2009/04/leukocytes.jpg

Nucleus ultrastructure

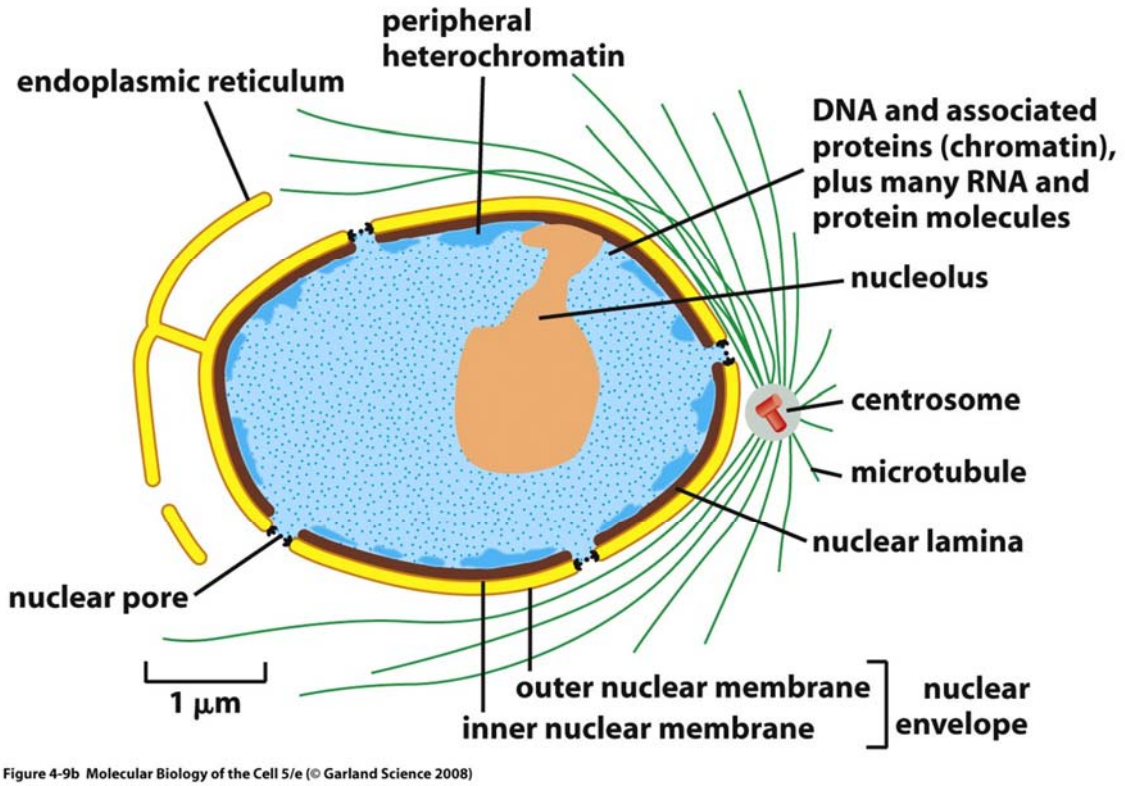
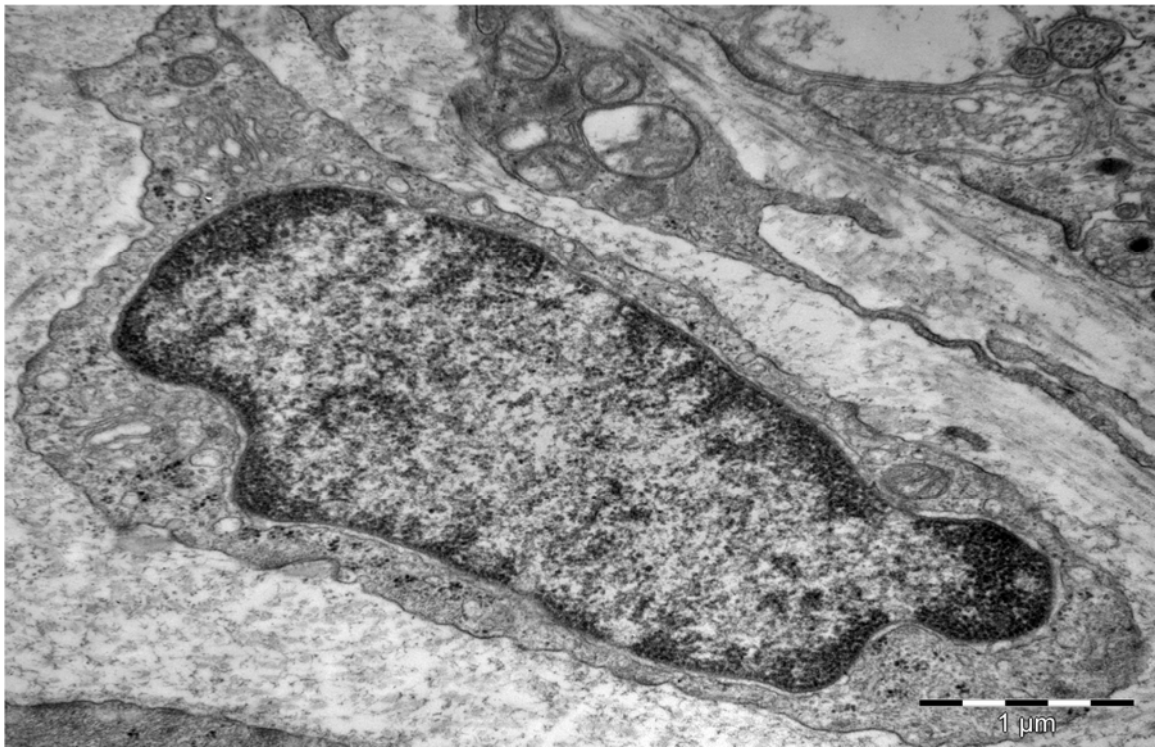


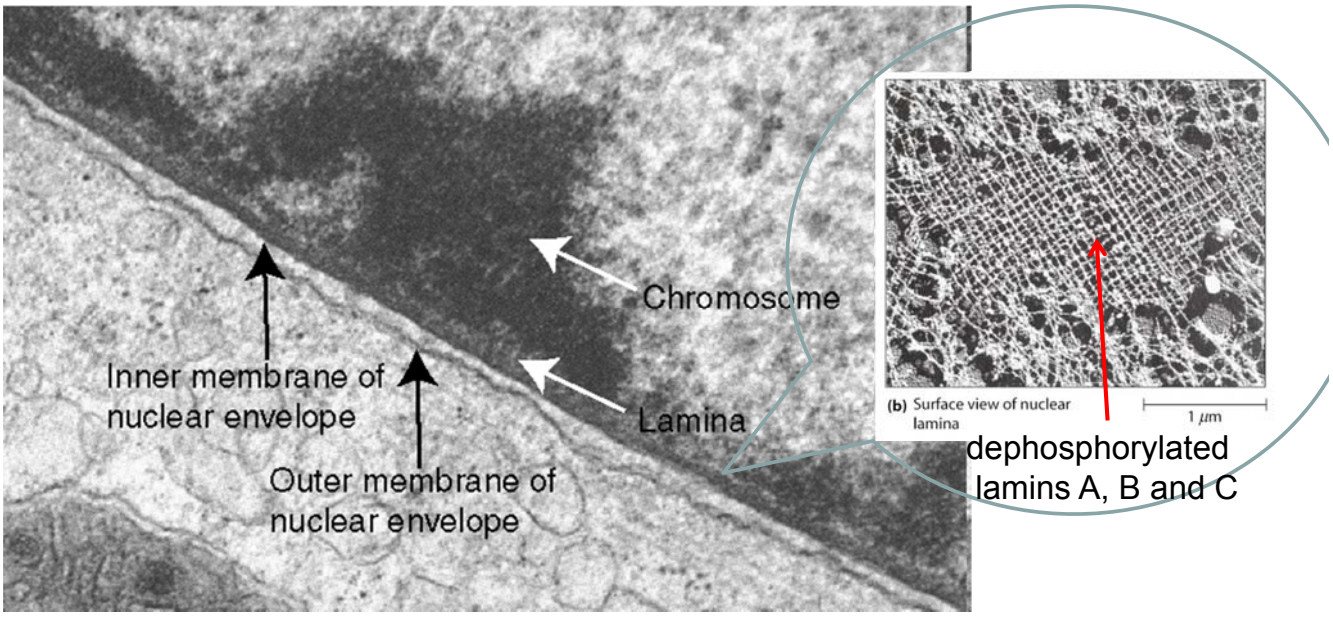
Figure 4-9b Molecular Biology of the Cell 5/e (© Garland Science 2008)

Nucleus ultrastructure

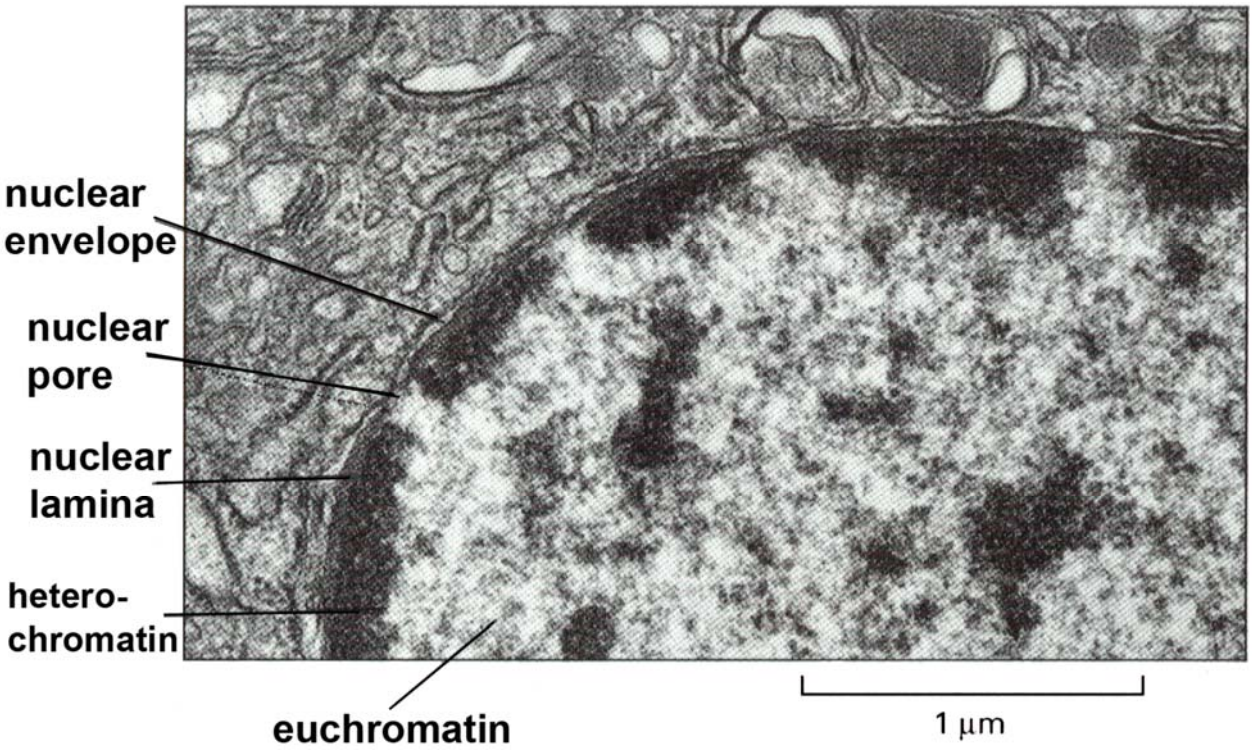


Nucleus ultrastructure

Nuclear envelope



Nucleus ultrastructure



Nucleus organization

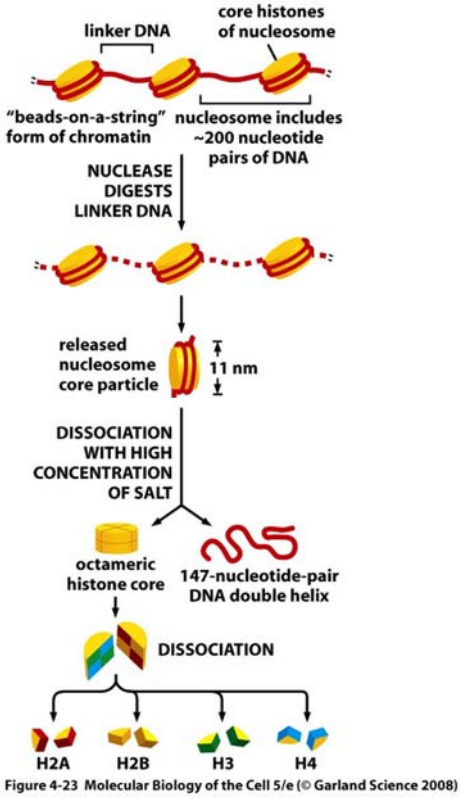
- Chromatin organization
- Transcription
- Nucleolus
- Nuclear envelope

Chromatin organization

- 24 DNA molecules ($50x10^6$ – $250x10^6$ bp)
- 24 chromosomes (22 autosome, 2 sex)
- $2x3x10^9$ bp in human DNA ➔ 1,7 – 8,5 cm/molecule
- Chromatin – a complex of DNA with histones and non-histonic chromosomal proteins
- Histones – highly positive proteins (lysine and arginine):
  - Nucleosomal histones (H2A, H2B, H3, H4) – 102-135 aa
  - Histone H1 (6 subtypes) – 220 aa (linker histone)

Nucleosome

the structural unit of chromatin



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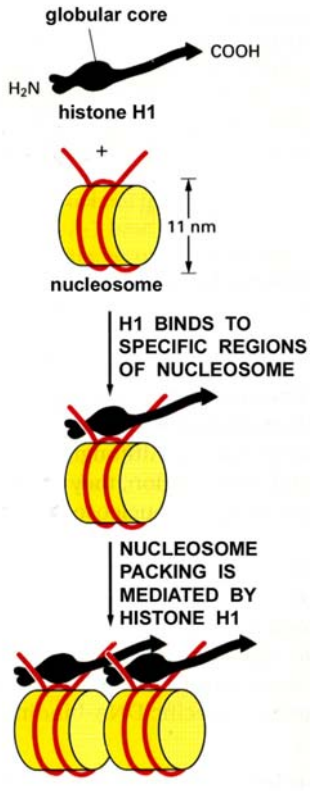
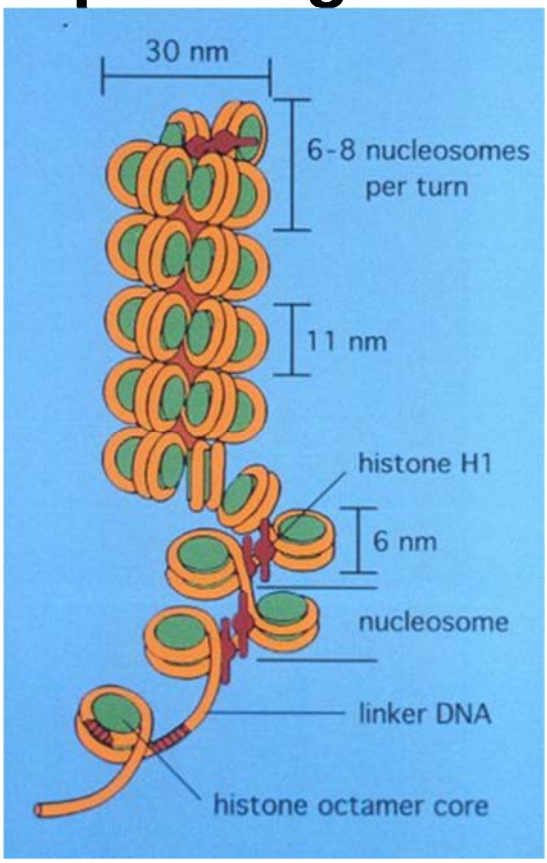
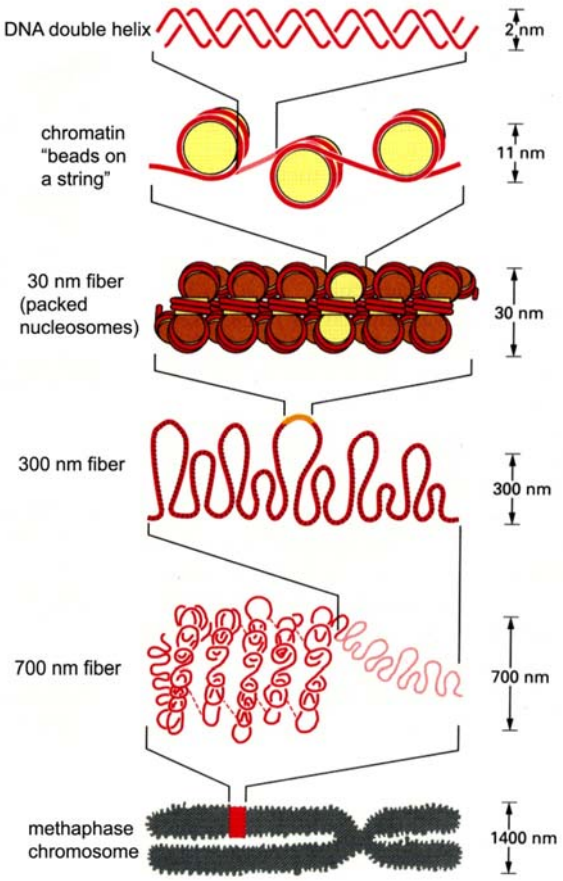
Nucleosome packing

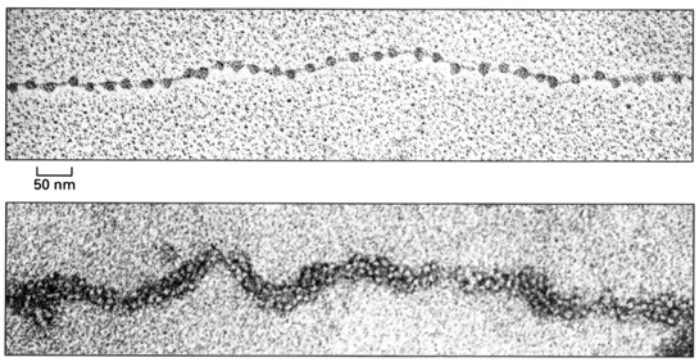




http://bricker.tcnj.edu/Amb/amble9.html

Chromatin folding levels





Chromosome – sequences

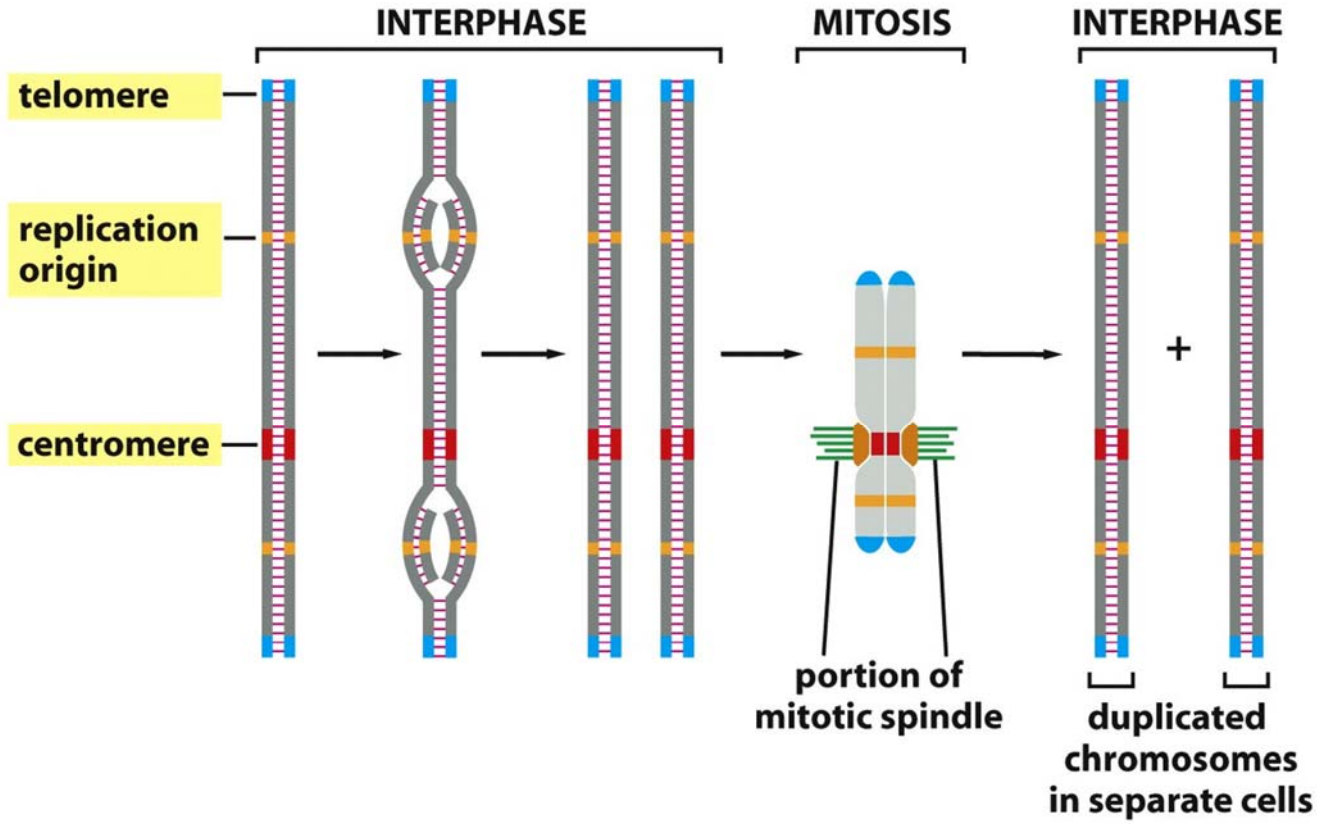


Figure 4-21 Molecular Biology of the Cell 5/e (© Garland Science 2008)

Human chromosomes

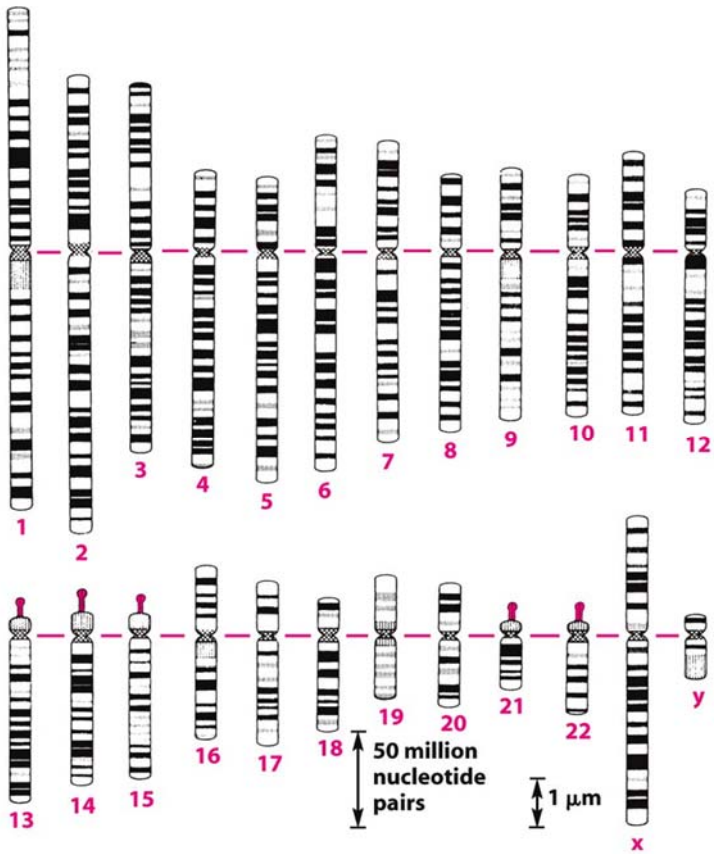
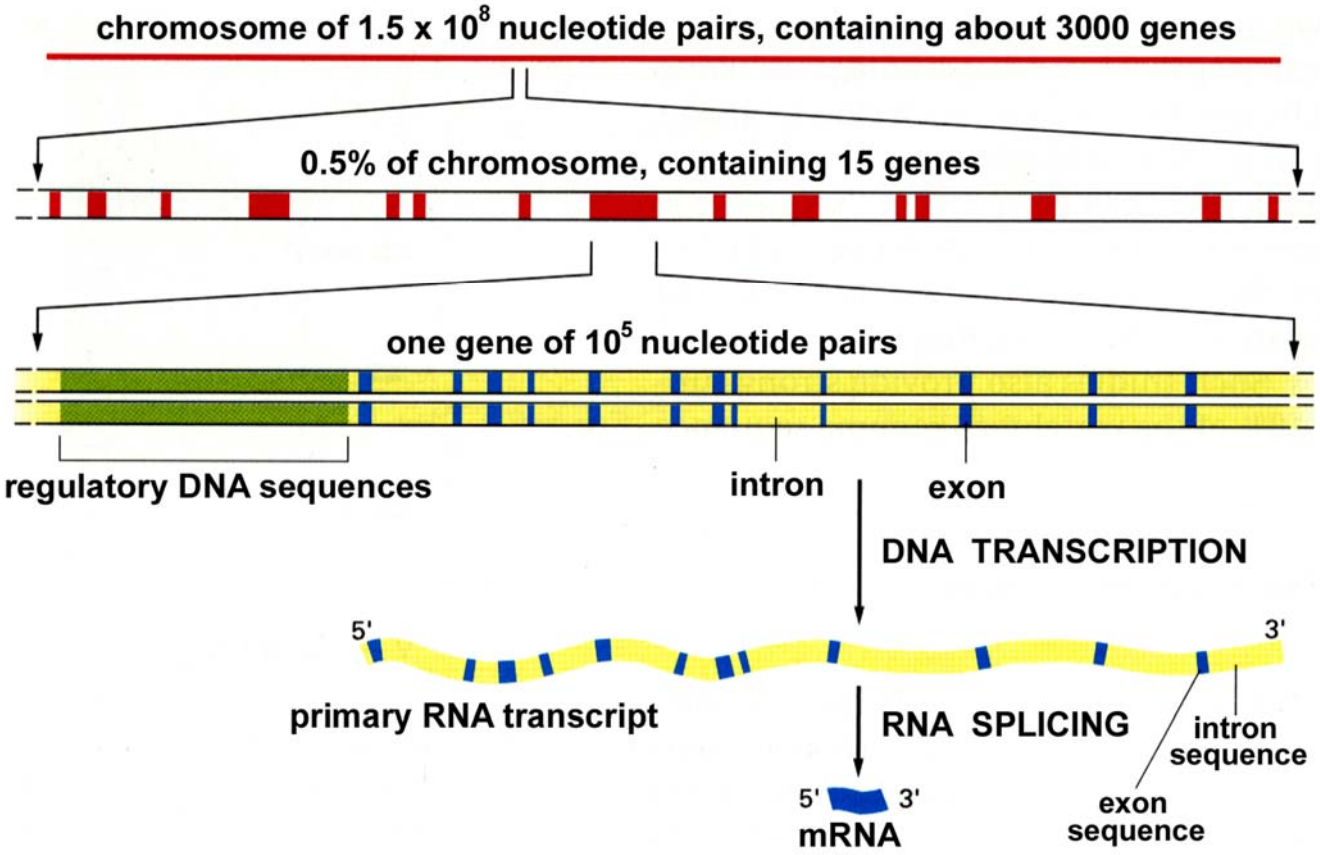


Figure 4-11 Molecular Biology of the Cell 5/e (© Garland Science 2008)

Transcription (Gene Expression)

- RNA biosynthesis
  - 3 types of RNA polymerases (I, II, III)
- mRNA biosynthesis
  - RNA polymerase II
- rRNA biosynthesis
  - RNA polymerase I (28S, 18S, 5,8S)
  - RNA polymerase III (5S)
- tRNA biosynthesis
  - RNA polymerase III

RNA biosynthesis



Gene Expression Control/Regulation

- Cell signaling (external regulation)
  - Signaling by lipophilic ligands
  - JAK/STAT signaling pathway
- Epigenetics (internal mechanisms to control gene accessing and expression)
  - DNA methylation
  - Histone acetylation
  - Histone methylation
  - Histone (mono)ubiquitination

Nucleolus – ultrastructure

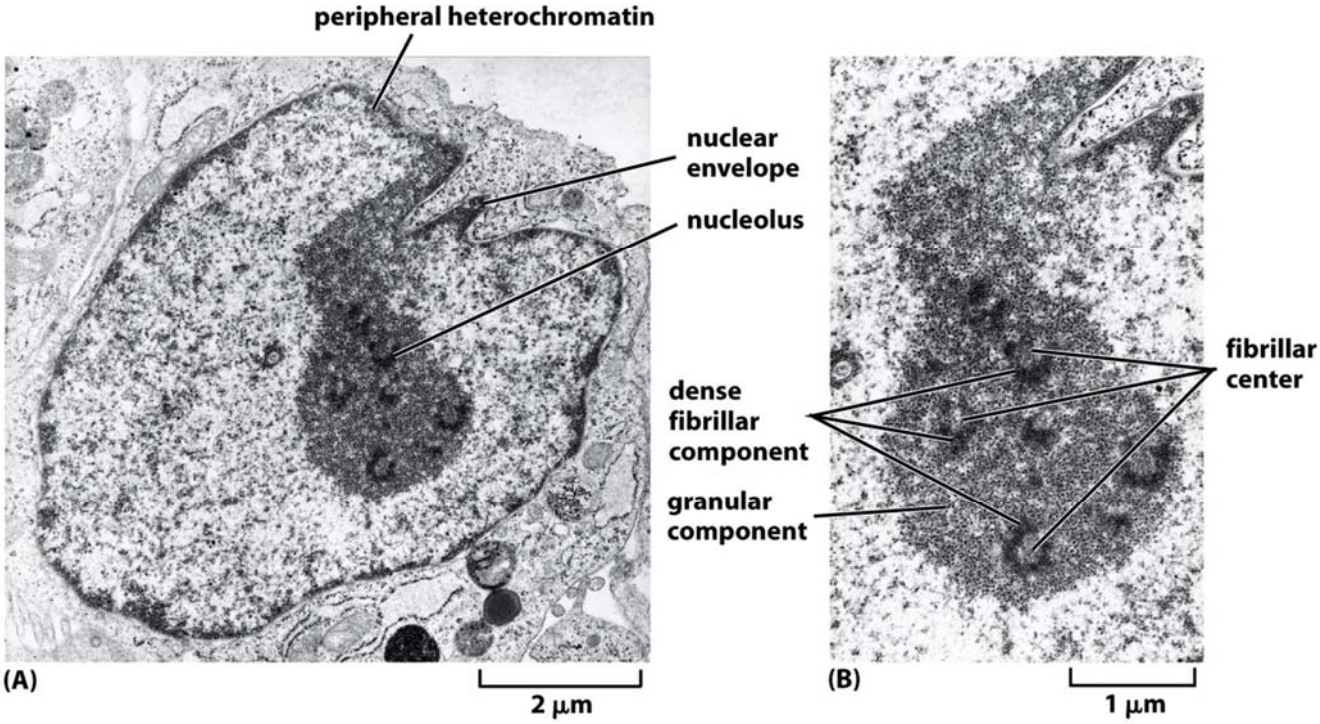


Figure 6-44 Molecular Biology of the Cell 5/e (© Garland Science 2008)

Nucleolus function

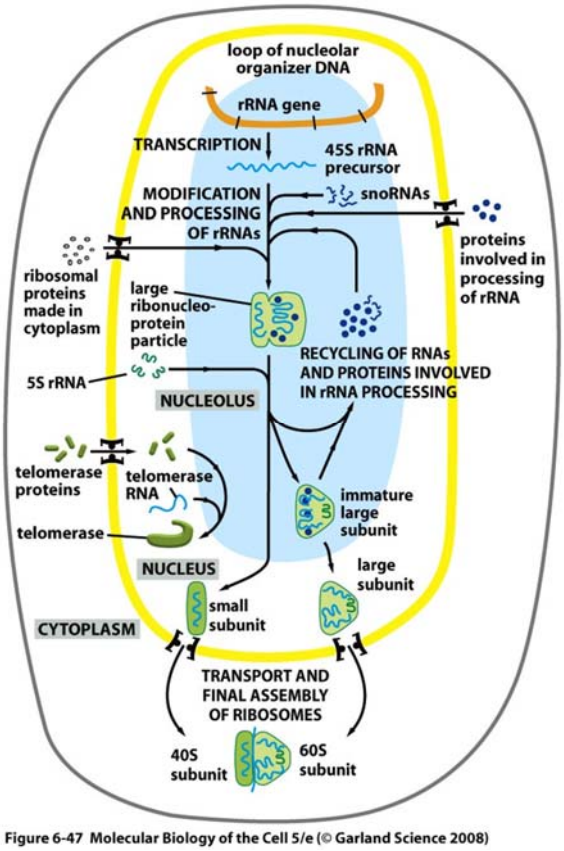


Figure 6-47 Molecular Biology of the Cell 5/e (© Garland Science 2008)

The nuclear envelope

- Endomembrane bounded structure
- External membrane; attached polyribosomes
- Internal membrane; attached nuclear lamina
- Lumen; anastomosed with ER lumen
- Nuclear pores
- Role:
  - DNA hostage, protection and usage (chromatin)
  - Control of nucleus - cytosol transport events

Nuclear lamina

- A fibrillar network organized by proteins belonging to intermediate filament category – lamins (60-80kDa)
- Three classes of lamins: A, B and C
- Attached to internal face of the inner membrane of the nuclear envelope

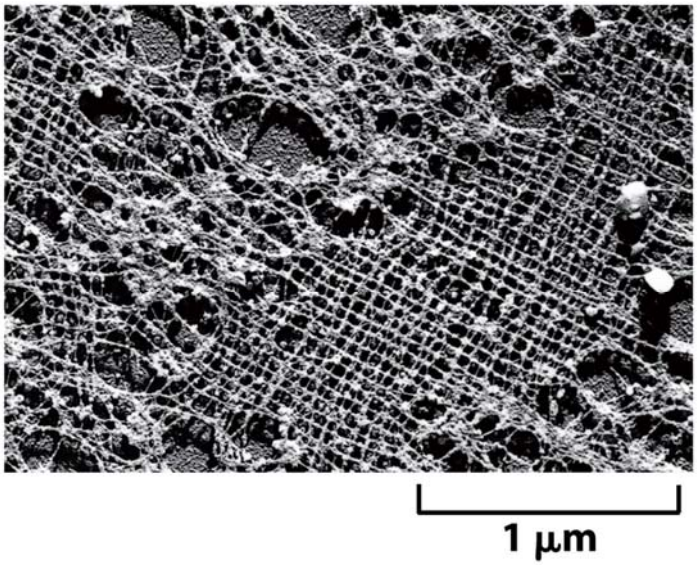


Figure 12-19 Molecular Biology of the Cell 5/e (© Garland Science 2008)

Functions of the nuclear lamina:
- chromatin organization and DNA replication
- nuclear envelope organization control (interphase *versus* mitosis):
  - lamins' phosphorylation = disorganization
  - lamins' dephosphorylation = reorganization
- defects in nuclear lamina organization → diseases = laminopathies (genetic disorders):
  - Emery-Dreifuss muscular dystrophy – a muscle wasting disease
  - Progeria – premature aging
  - Restrictive dermopathy – a disease inducing extremely tight skin and other severe neonatal abnormalities

Nucleus to cytoplasm transport

Nuclear pore complex – nucleoporins (Nup)
~ 30 types of Nup

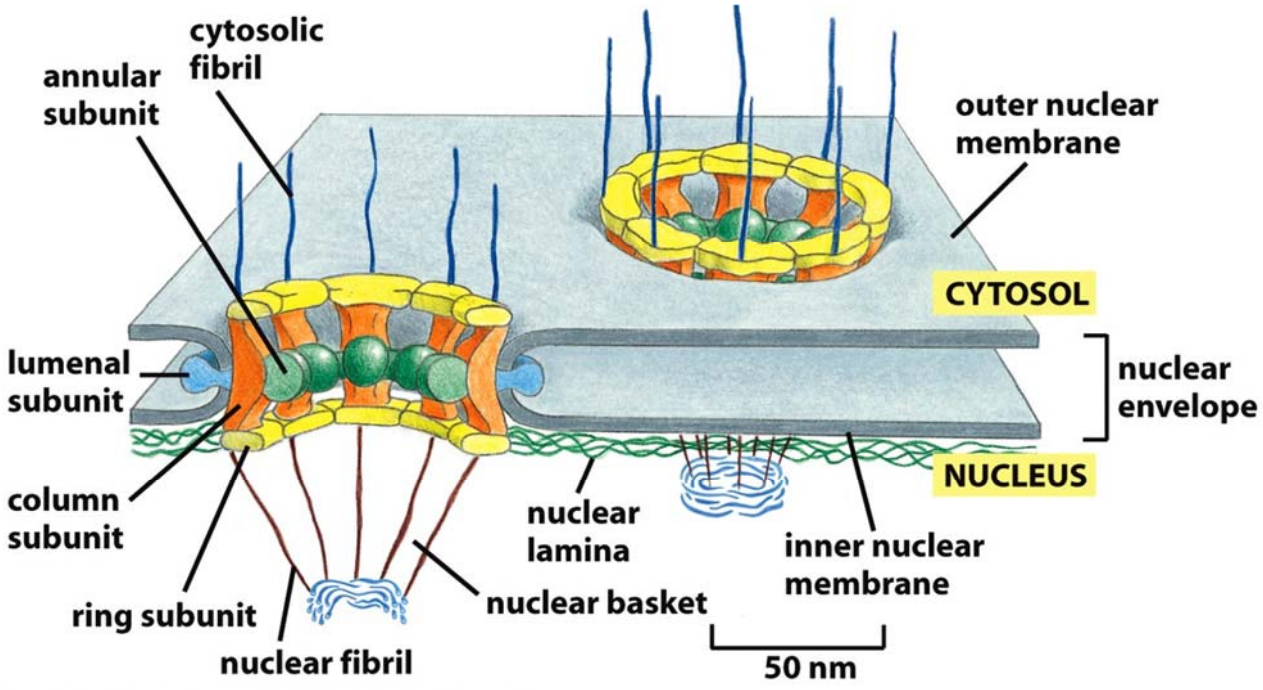


Figure 12-9a Molecular Biology of the Cell 5/e (© Garland Science 2008)

The nuclear pore complex

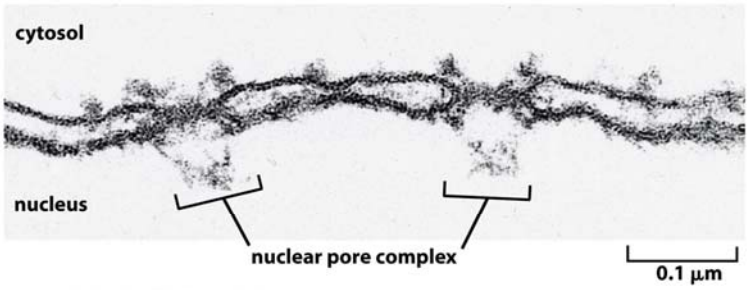


Figure 12-9c Molecular Biology of the Cell 5/e (© Garland Science 2008)

- octagonal "symmetry"
- >450 protein molecules
- several structural subunits
- Mr >120 millions of Da
- central channel – ~9nm
- total diameter – ~120nm

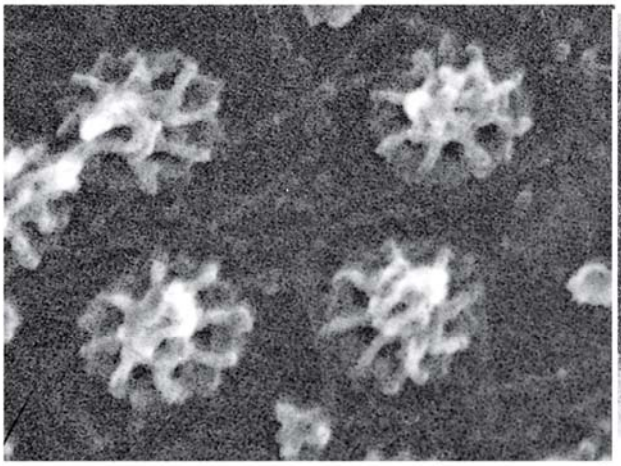


Figure 12-9b Molecular Biology of the Cell 5/e (© Garland Science 2008)

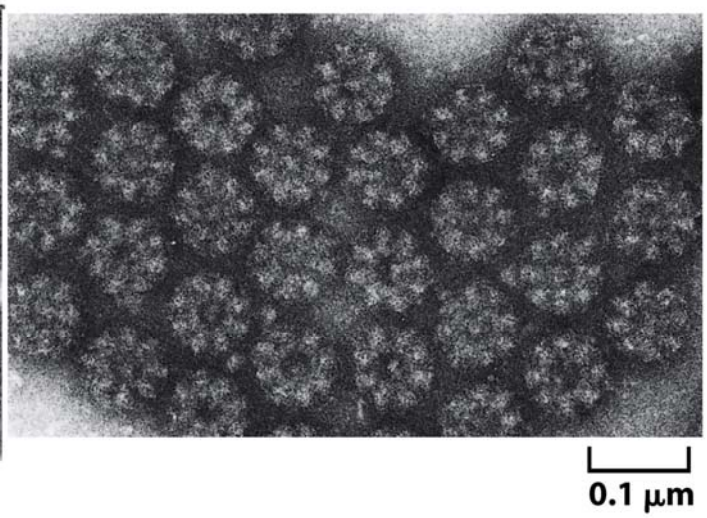


Figure 12-9d Molecular Biology of the Cell 5/e (© Garland Science 2008)

Protein import into nucleus

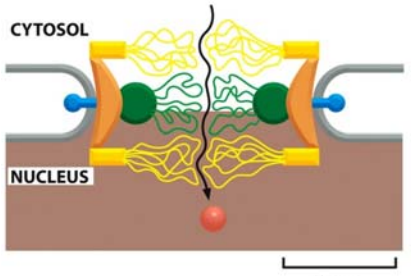


Figure 12-10 Molecular Biology of the Cell 5/e (© Garland Science 2008)

size of molecules that enter nucleus by free diffusion

Mr below 40kDa

size of macromolecules that enter nucleus by active transport

Mr higher than 40kDa

Signal peptide

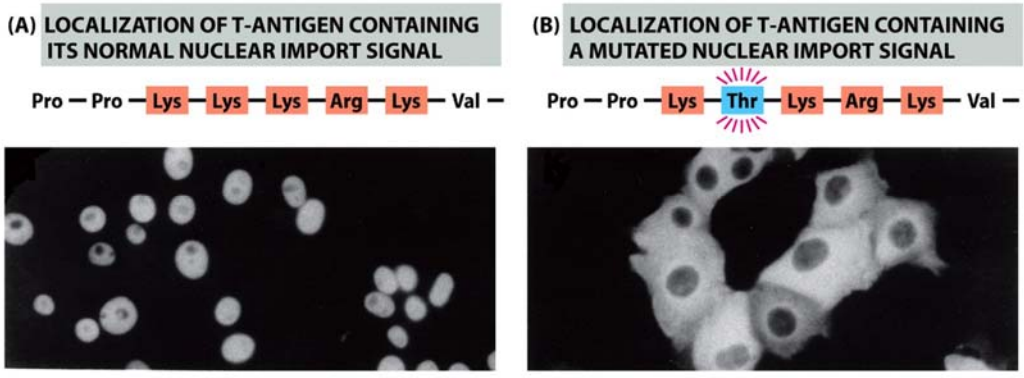
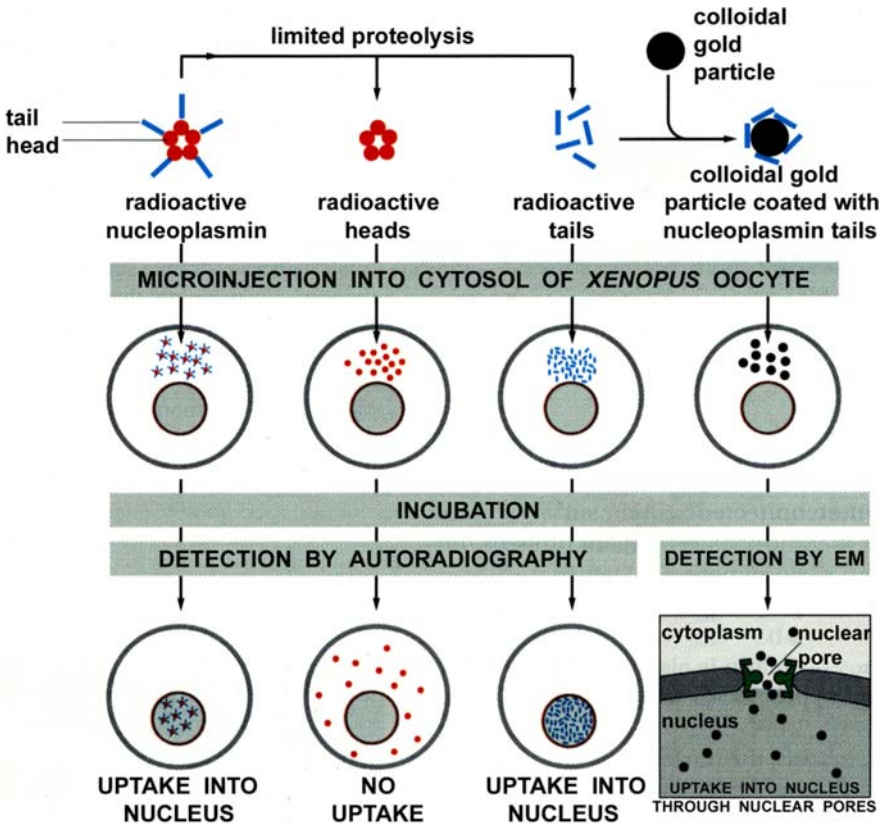


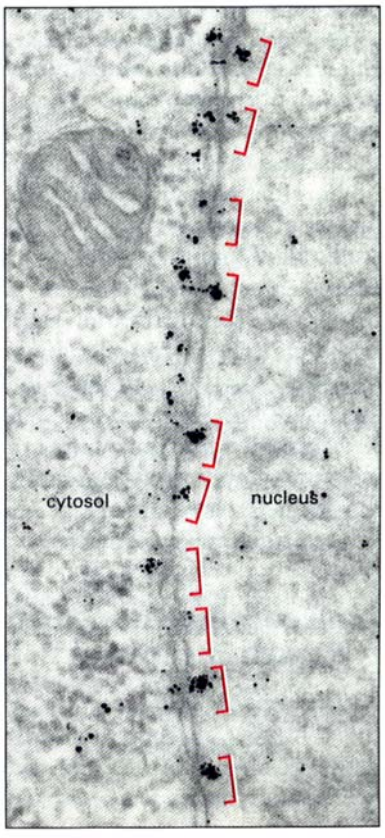
Figure 12-11 Molecular Biology of the Cell 5/e (© Garland Science 2008)

Factors assuring/controlling transport through nuclear pores

- Signal peptide – nuclear localization signals (NLS) or nuclear export signals (NES)
- Karyopherins – importins or exportins
- Small GTP-ases (Ran GTP-ases; Ran from **Ra**s-related **n**uclear protein)
- Pathological implications:
  - several malignancies (myeloid leukemia, other cancers)
  - viral infections (i.e. DNA viruses)
  - some autoimune diseases (systemic lupus erythematosus, rheumatoid arthritis and primary biliary cirrhosis)

Cytoplasm to nucleus transport – active transport





Summary on nucleus

- Is the compartment for genetic information protection, usage, conserving and transmission
- Contains all necessary enzymes for replication and transcription of genetic information
- Prepares essential components for genetic information translation (ribosomal subunits, mRNA)
- Nucleus function needs a permanent exchange of substance and information with the cytoplasm
- These exchanges are assured by the specific structure of nuclear envelope, allowing under a rigorous control a transport from nucleus to the cytosol (in both directions), through the nuclear pores
- There are pathologies related to the right organization and function of the nuclear elements (e.g. laminopathies)