

Exam 3 Study Guide

Intercellular Compartments and Protein Sorting

All Eukaryotic Cells Have the Same Basic Set of Membrane Enclosed Organelles

- Cytosol comprises the majority of the cell (54% of a Hepatocyte)
- Internal membranes have a large surface area—ER membranes have 12-15 times the surface area of the plasma membrane in liver and pancreatic cells
- Pancreatic cells have majority cell membrane in Rough ER, where Liver cells have much more contributing to mitochondria

Complex organelle structures develop through specialization of membranes

- Chloroplasts develop thylakoid vesicles in a *proplastid* before becoming thylakoid membranes in a *chloroplast*
- Complex organelles evolved from prokaryotes and membrane specializations
 - Nucleus
 - Endoplasmic reticulum (originally membrane-bound ribosomes)
- Invagination and pinching off of membranes is important in all of these evolutionary and developmental mechanisms that create organelles
 - Mitochondria membranes derived from a eukaryotic cell, allowing it to then become aerobic

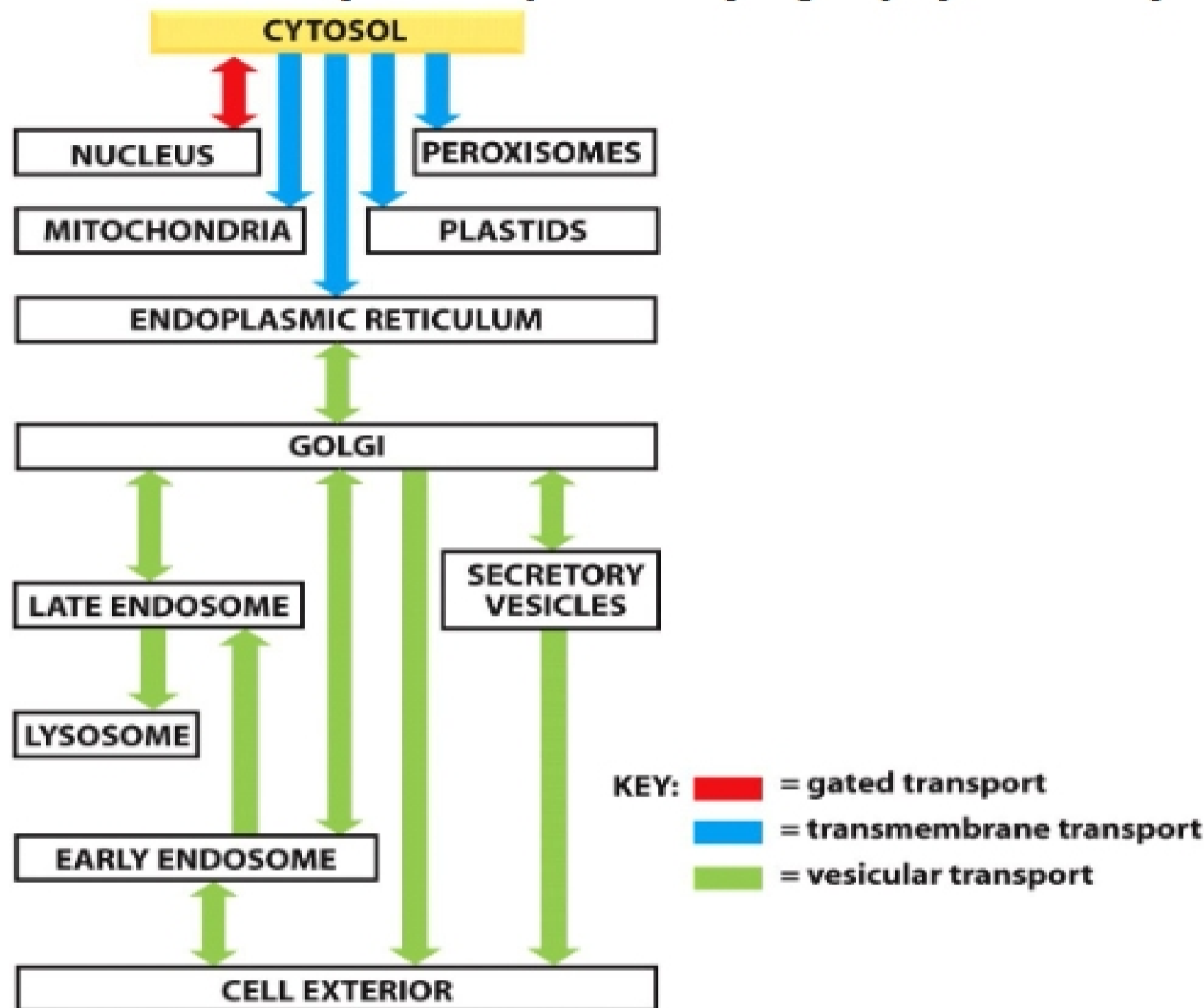
Constant endocytotic, fusion, and budding events between membrane structures create TOPOLOGICALLY EQUIVALENT compartments

- Between which molecules can travel without crossing a membrane
 - Endoplasmic reticulum
 - Lysosomes
 - Endosomes
 - Golgi Apparatus

Movement of proteins between cellular compartments (Three fundamental mechanisms)

- In Gated Transport, the protein traffic between the cytosol and nucleus Nuclear Pore Complexes which function as selective gates that actively transport specific macromolecules and macromolecular assemblies, although they also allow free diffusion of smaller molecules
 - It is important to note that the Nucleus and Cytosolic Compartments are topologically identical
- In Transmembrane transport, membrane-bound protein translocators directly transport specific proteins across a membrane from the cytosol into a space that is Topologically Distinct.
 - The transported protein molecules usually must unfold to snake through the translocator.
 - The initial transport of selected proteins from the cytosol into the ER lumen or from the cytosol into mitochondria, for example, occurs this way.
- In Vesicular Transport, membrane-enclosed transport intermediates—which may be small, spherical transport vesicles or larger, irregularly shaped organelle fragments—ferry proteins from one compartment to another

- o The transfer of soluble proteins from the ER to the Golgi apparatus, for example, occurs in this way.
- o Because the transported proteins do not cross a membrane, vesicular transport can move proteins only between topologically equivalent compartments



Signal Sequences

- Signal sequences are amino acid sequences at the N-terminals of proteins that are recognized by the transport proteins that move proteins across compartments
- Signal peptides “target” a newly made protein to a specific compartment
- They are cleaved off the protein after use by enzymes “signal peptidases” trapping the protein in its target compartment

Transport between nucleus and cytosol

- The nuclear envelope of all eukaryotes is perforated by large, elaborate structures known as nuclear pore complexes
 - o Each complex has an estimated molecular mass of about 125 million and is thought to be composed of more than 50 different proteins, called Nucleoporins, that are arranged with a striking octagonal symmetry
- Nuclear Pores: The more active the nucleus is in transcription, the greater the number of pore complexes its envelope contains
 - o The nuclear envelope in a typical mammalian cell contains 3000-4000 pore complexes
 - o If the cell is synthesizing DNA, it needs to import about 10^6 histone proteins from the cytosol every 3 minutes to package the newly made DNA into Chromatin.

- On average, each pore complex needs to transport about 100 histone molecules per minute
- If the cell is growing rapidly, each complex also needs to transport 6 newly assembled ribosomal subunits per minute FROM the nucleus, where they are produced, TO the cytosol, where they are used.
 - That is only a very small part of pore complex traffic
- Each pore contains one or more open *Aqueous* channels through which SMALL water-soluble molecules can passively diffuse (5000 daltons or less)
- Specific nuclear signal sequences (NLSs) are present only in nuclear proteins

Nuclear Transport

- The mechanism of macromolecular transport across nuclear pore complexes is fundamentally different from the transport mechanisms involved in protein transfer across the membranes of other organelles
- It occurs through a large aqueous pore rather than through a protein transporter spanning one or more lipid bilayers
- For this reason, nuclear proteins can be transported through a pore complex while they are in a fully folded conformation

Nerve Cells- Release of neurotransmitter in the spinal cord

- To initiate nuclear import, nuclear localization signals must be recognized by nuclear import receptors, which are encoded by a family of related genes
- The nuclear export of large molecules, such as new ribosomal subunits and RNA molecules, also occurs through nuclear pore complexes and depends on a selective transport system
- The transport system relies on nuclear export signals on the macromolecules to be exported, as well as on complementary nuclear export receptors
 - These receptors bind both the export signal and nucleoporins to guide their cargo through the pore complex to the cytosol
- The import of nuclear proteins through the pore complex concentrates specific proteins in the nucleus, thereby increasing order in the cell- a process which must consume energy
 - The energy is thought to be provided by the hydrolysis of GTP by the monomeric GTPase Ran.
 - Ran is found both in the cytosol and the nucleus, and it is required for both the nuclear import and export systems
 - Ran like other GTP-binding proteins exists in two states
 - One with GTP attached
 - One with GDP attached
 - A nuclear protein, RAN-GEF catalyzes the binding of GTP to RAN inside the nucleus
 - Another enzyme, RAN-GAP in the cytosol hydrolyzes GTP attached to RAN.
 - This creates a gradients of RAN-GTP across the nuclear pore- with more RAN GTP inside the nucleus than outside
 - RAN-GTP binds to nuclear import receptors after they diffuse through the nuclear pore and into the nucleus and causes them to release their cargo proteins, which therefore accumulate inside the nucleus.