Lecture 14

Protein targeting to peroxisomes

The sequence Ser- Lys-Leu (SKL in one-letter code) or a related sequence at the C-terminus is necessary for peroxisomal targeting

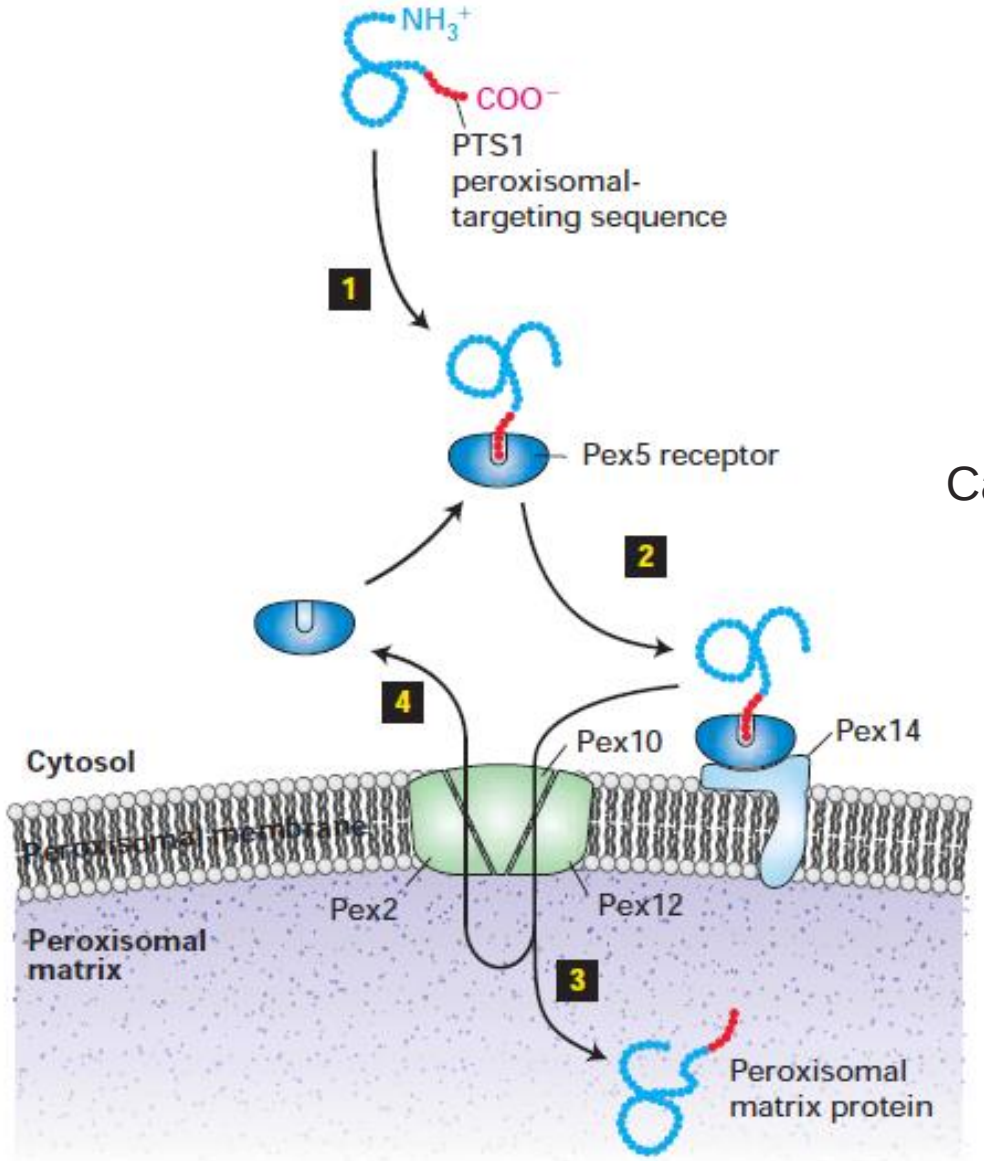
The PTS1 binds to a **soluble receptor protein** in the cytosol (Pex5), which in turn binds to a **receptor** in the peroxisome membrane (Pex14).

The soluble and membrane-associated peroxisomal import receptors appear to have a function analogous to that of the SRP and SRP receptor in targeting proteins to the ER lumen

The imported protein then moves through a multimeric translocation channel,

Pex5 dissociates from the peroxisomal matrix protein and is recycled back to the cytoplasm

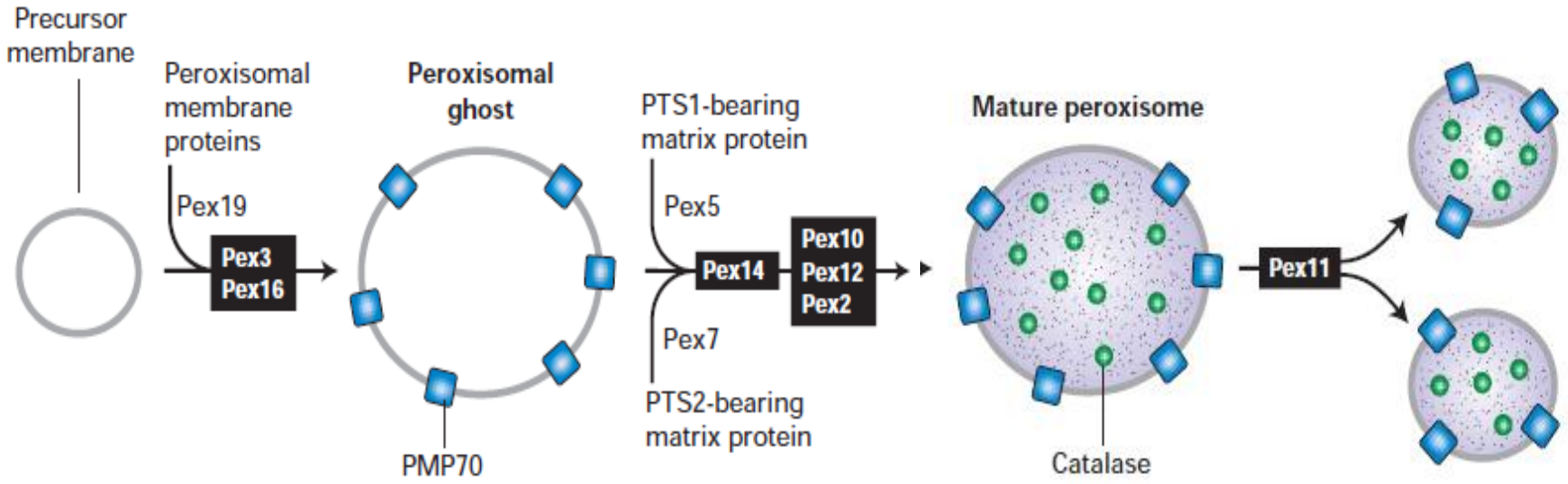
The PTS1 sequence is **not cleaved from proteins** after their entry into a peroxisome



Can translocate folded proteins across the membrane

Different pathways are used for importing peroxisomal matrix proteins versus inserting proteins into the peroxisomal membrane.

Although most peroxisomes are generated by division of preexisting organelles, these organelles also can arise de novo by the two-stage process



In contrast with the oxidation of fatty acids in mitochondria, which produces CO_2 and is coupled to the generation of ATP, **peroxisomal oxidation of fatty acids yields acetyl groups and is not linked to ATP formation.**

The energy released during peroxisomal oxidation is converted into heat, and the acetyl groups are transported into the cytosol, where they are used in the synthesis of cholesterol and other metabolites.

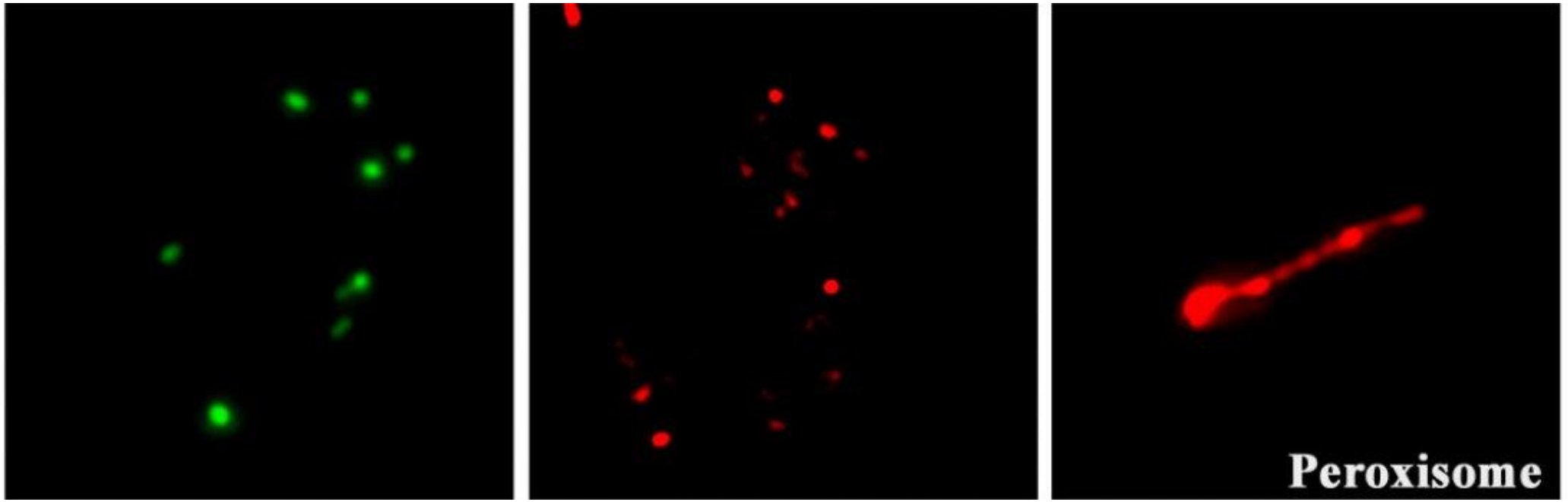
In most eukaryotic cells, the peroxisome is the principal organelle in which fatty acids are oxidized, thereby generating precursors for important biosynthetic pathways.

Particularly in liver and kidney cells, various toxic molecules that enter the bloodstream also are degraded in peroxisomes, producing harmless products

Very long chain fatty acids containing more than about 20 CH_2 groups are degraded only in peroxisomes;

In mammalian cells, mid-length fatty acids containing 10–20 CH_2 groups can be degraded in both peroxisomes and mitochondria.

In contrast to mitochondrial oxidation of fatty acids, which is coupled to generation of ATP, peroxisomal oxidation of fatty acids is not linked to ATP formation, and the released energy is converted to heat.


Peroxisome

NUCLEIC ACIDS: STRUCTURE AND PROPERTIES

Central Dogma

Friedrich Miescher

Nuclein

Altmann

Kossel

Chargaff

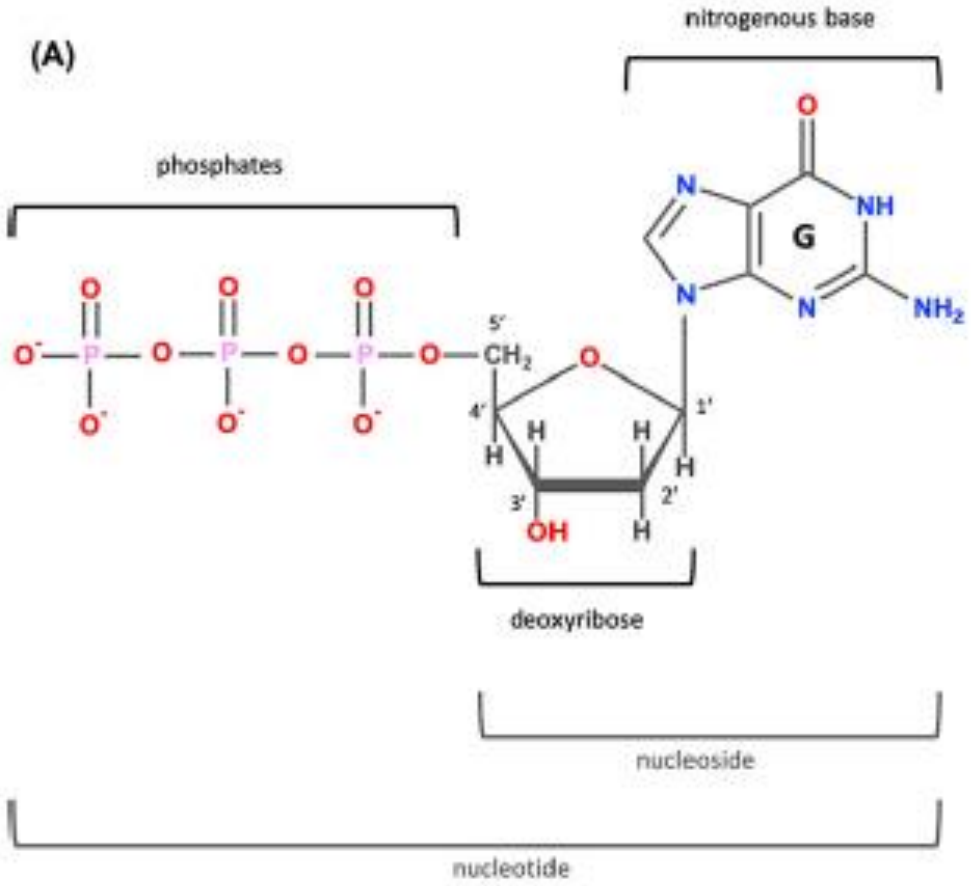
Fredrick Griffith, Oswald Avery, Colin MacLeod and Maclyn McCarty

Alfred Hershey and Martha Chase

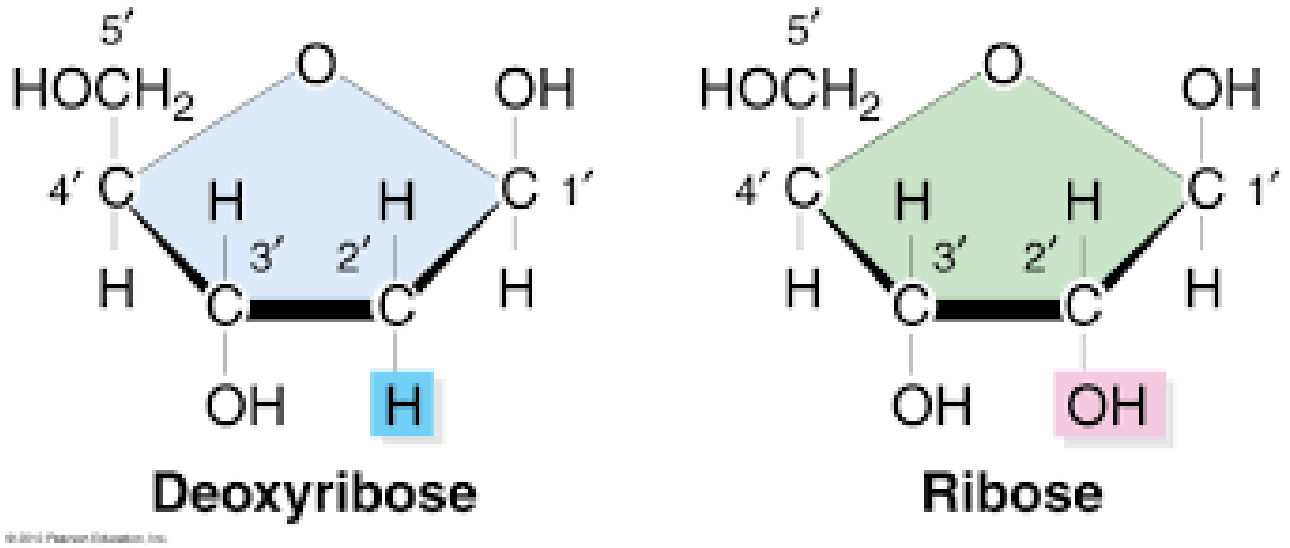
Nucleotides: Nitrogenous base+sugar+phosphate (phosphate as diesters)
Nucleoside: Nucleotide - phosphate

Nitrogenous base:
PURINES AND PYRIMIDINES

- Sugar-phosphate back bone (both in DNA and RNA)
- However, Ribose sugar and deoxy-ribose sugar
- Difference in the nitrogenous base

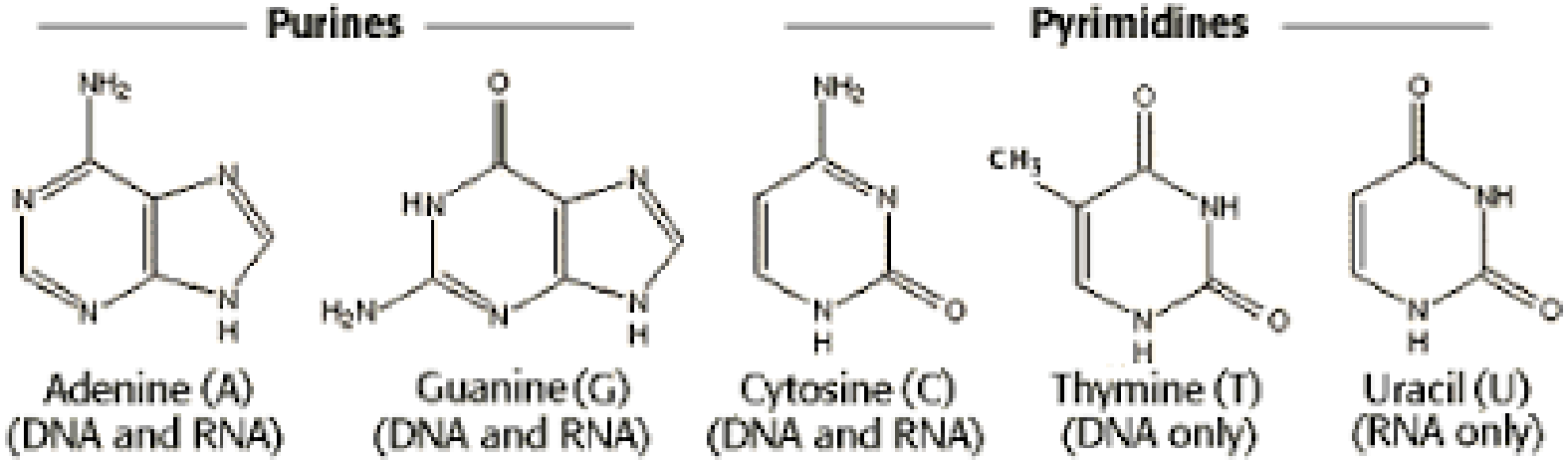


Ribose sugar and deoxy-ribose sugar

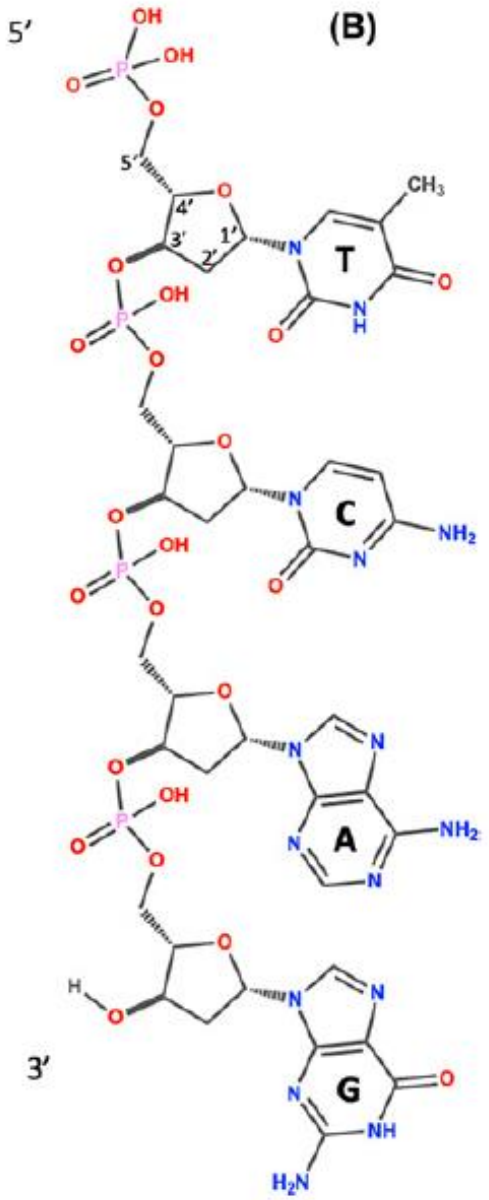


4 types of nucleotides
RNA –A,C,G,U
DNA – A,C,G,T

Purines – A,G (5 and 6 member, hetero carbon-nitrogen rings)
Pyramidines – T,C,U (6 member, hetero carbon-nitrogen rings)



Nucleic acid -?



The phosphate group is acidic, hence the name nucleic acid.

Chargaff's rules

The four nucleotide bases of DNA occur in different ratios in the DNAs of different organisms and the amounts of certain bases are closely related.

Data collected from DNAs of a great many different species, led Chargaff to the following conclusions:

1. The base composition of DNA generally varies from one species to another.
2. DNA specimens isolated from different tissues of the same species have the same base composition.
3. The base composition of DNA in a given species does not change with an organism's age, nutritional state, or changing environment.
4. In all cellular DNAs, regardless of the species, the number of adenosine residues is equal to the number of thymidine residues (that is, A T), and the number of guanosine residues is equal to the number of cytidine residues (G C).

From these relationships it follows that the sum of the purine residues equals the sum of the pyrimidine residues

This was a key to establishing the three dimensional structure of DNA and yielded clues to how genetic information is encoded in DNA and passed from one generation to the next.