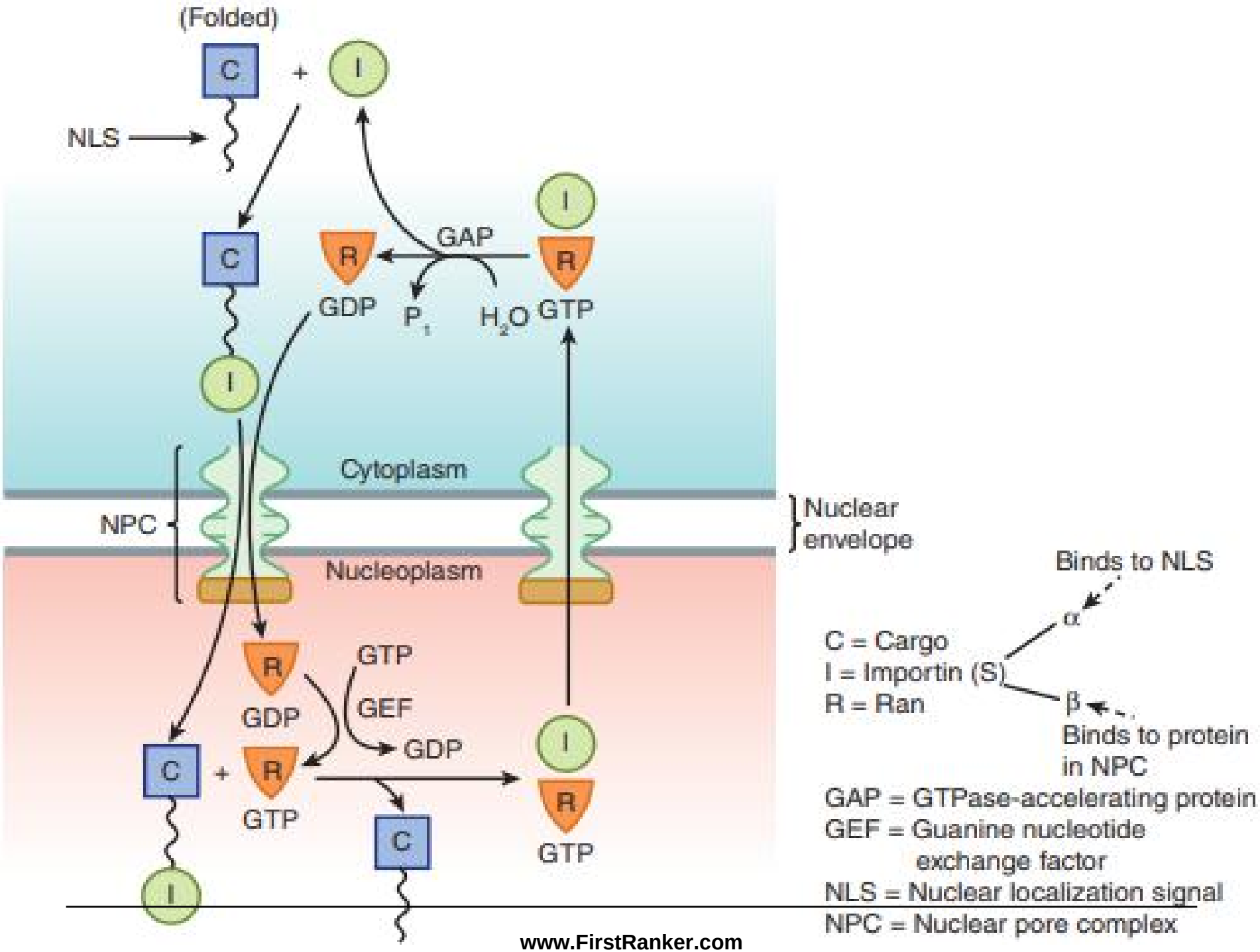
Transport into the nucleus

- All proteins found in the nucleus are synthesized in the cytoplasm
- Examples:
  - Histones
  - Ribosomal proteins
  - DNA and RNA polymerases
  - Transcription factors

- Transport requires nuclear localization sequences (NLS)
- Transport occurs through the nuclear pores
  - Nuclear import receptor (Importin α and β)
  - Energy from GTP
  - GTPase Ran
- Fully folded proteins are transported

- Importin α and β bind to the protein to be transported
  - Nuclear localization signal binds to importin α
- The complex is translocated through the nuclear membrane
- Activated Ran (GTP) causes the complex to dissociate
- Ran transports importin β back to cytosol
- Importin α becomes a part of export receptor



- Proteins similar to importins, referred to as exportins, are involved in the export of many macromolecules (various proteins, tRNA molecules, ribosomal subunits and certain mRNA molecules) from the nucleus
- Cargo molecules for export carry nuclear export signals (NESs).
- Ran proteins are involved in this process also
- The family of importins and exportins are referred to as karyopherins
- Another system is involved in the translocation of the majority of mRNA molecules.
- These are exported from the nucleus to the cytoplasm as ribonucleoprotein (RNP) complexes attached to a protein named mRNP exporter

Peroxisomes

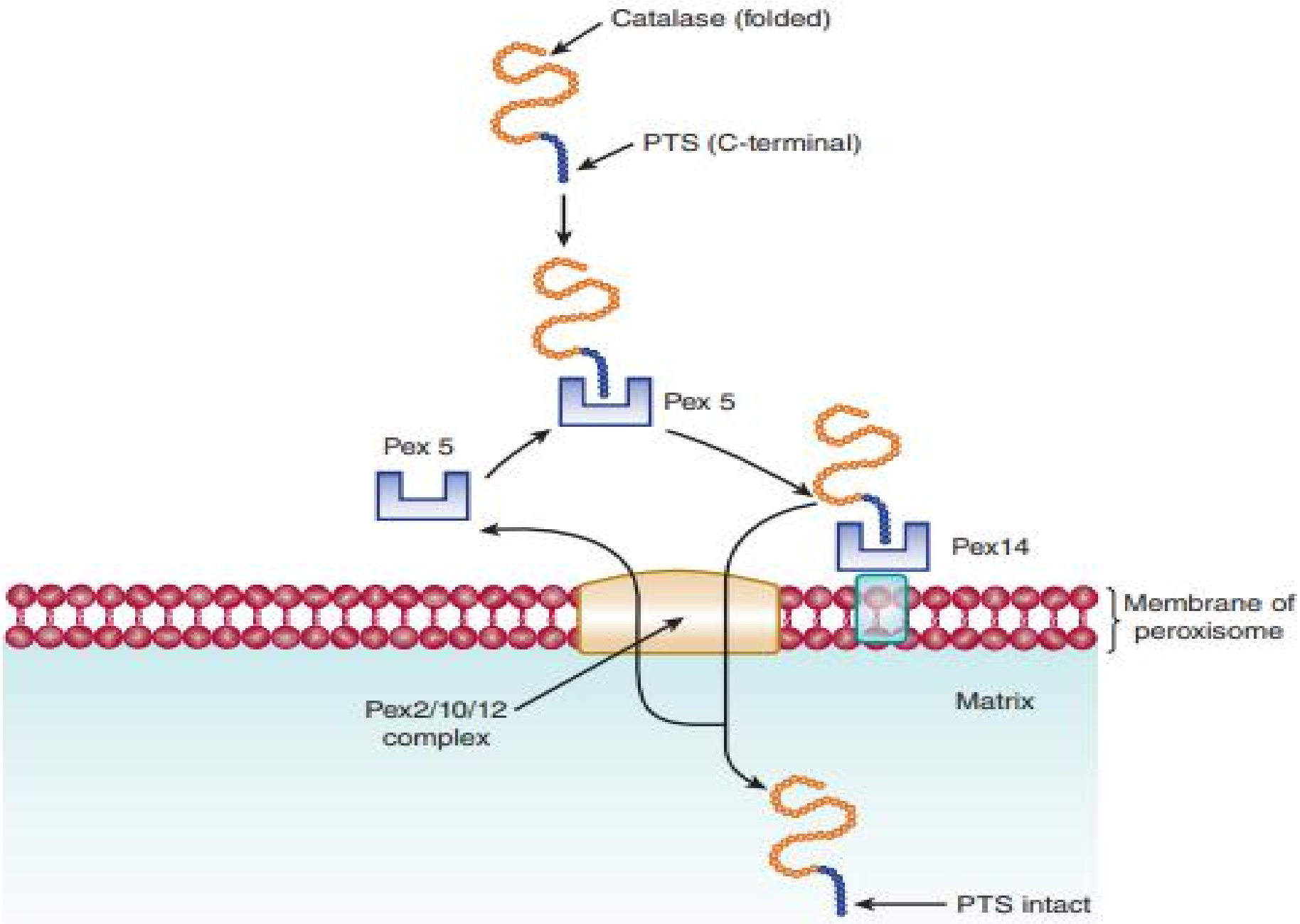
- Single membrane organelle
- Matrix contains oxidative enzymes
  - Lipid oxidation without ATP production
- Proteins encoded by nuclear DNA (all have to be imported).

Transport into peroxisomes

- Proteins are synthesized and fully folded in cytosol
- Fully functional, fully folded protein is transported!
- Import requires ATP hydrolysis
- Peroxisome targeting sequences
  - PTS1 on C-terminus, very conserved
  - PTS2 on N-terminus, just few proteins

Transport into peroxisomes

- Peroxins - peroxisome transport receptors
- Bind to proteins with PTS1 and dock to the translocation channel
- The complex is transported through the membrane
- Protein is released
- Peroxin is recycled



Zellweger syndrome

- Usually caused by mutations in genes encoding certain proteins—the PEX family of genes, also called peroxins—involved in various steps of peroxisome biogenesis
- Number of peroxisomes can vary from being almost normal to being virtually absent in some patients
- Apparent at birth and is characterized by profound neurologic impairment, victims often dying within a year
- Biochemical findings include an accumulation of very-long-chain fatty acids, abnormalities of the synthesis of bile acids, and a marked reduction of plasmalogens
- Two closely related conditions are neonatal adrenoleukodystrophy and infantile Refsum disease.