# LOCATION AND ENVIRONMENTAL CONTROL

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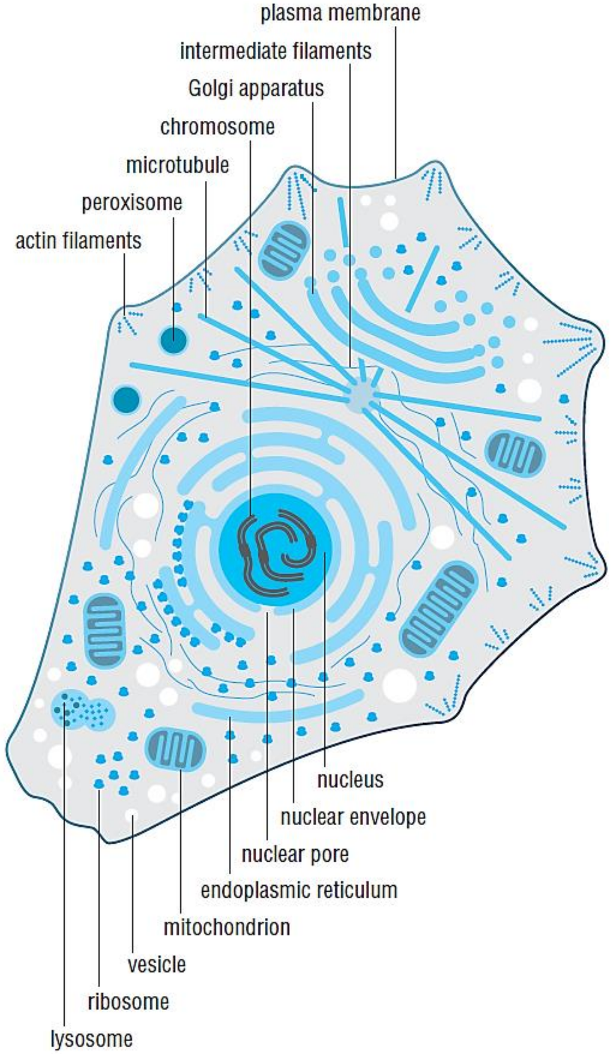
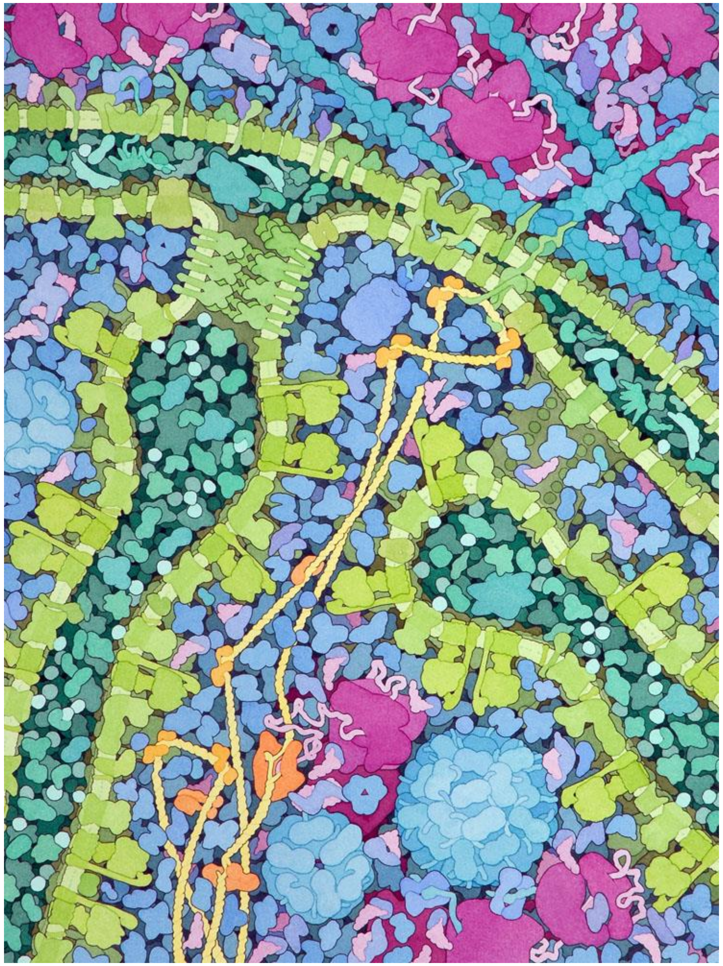
SUSTC

# The internal structure of cells

# Protein function in cell is context-dependent

- Temporal control
  - Gene expression
  - Protein turnover
- Spatial control
  - Every protein location is constrained



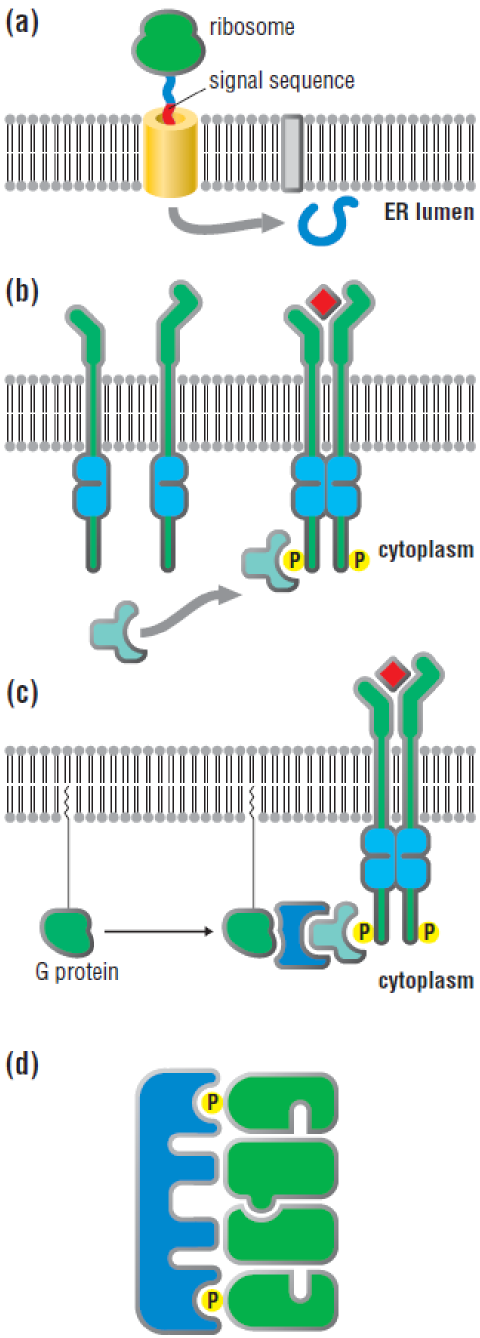
Cross-section of mitochondria
Drew by Goodsell

# Precise localization of proteins is a central feature of both spatial and temporal organization

- Activities of protein kinases are highly depended on their locations
- The number of protein kinase genes in the human genome is ~500
- The number of identified human protein phosphorylation site is more than 100,000
- Thus, kinases must have less than absolute specificity
- How are kinases prevented from phosphorylating “wrong” protein at an inappropriate time and place?
- One answer is to target the kinase to the same location as its “correct” substrate, a location different from that for any other potential substrate
  - Specificity can be altered if required by relocation of kinase and/or substrate

# Protein targeting

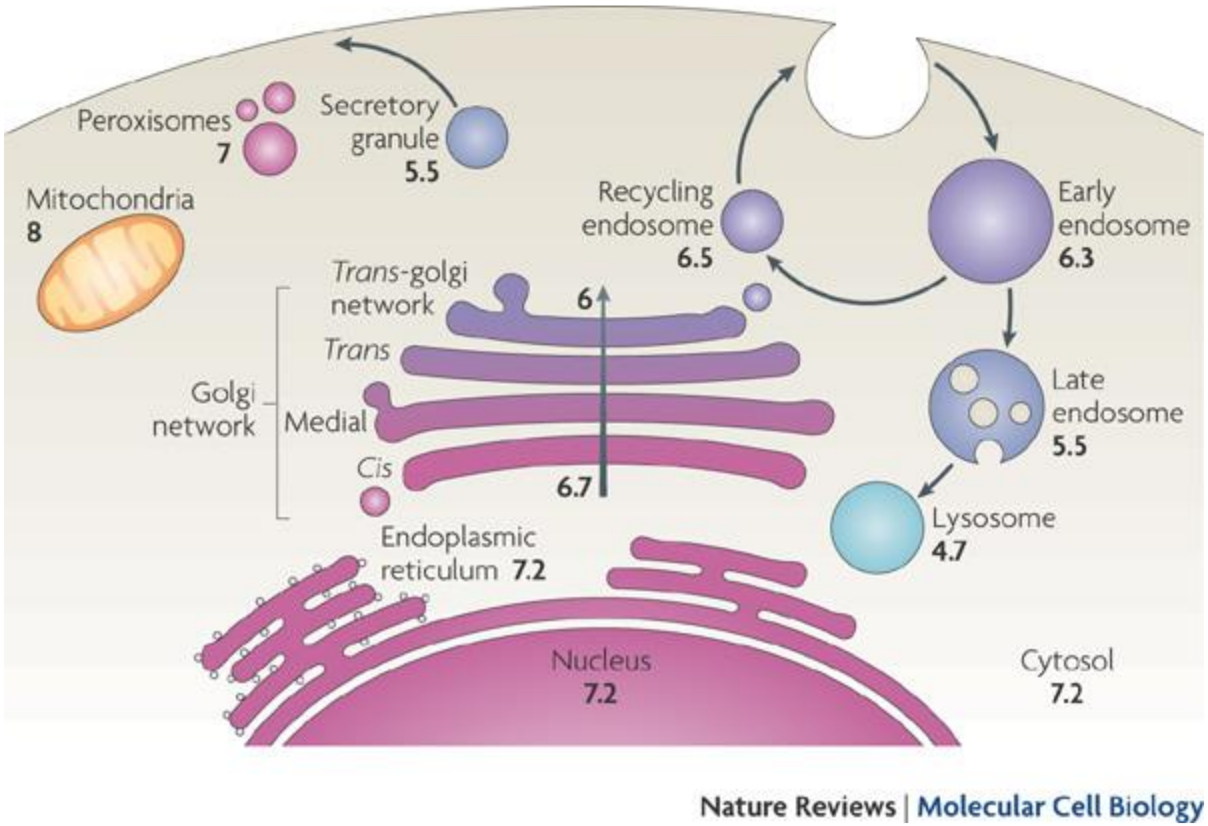
- How can proteins be targeted to their destinations
- Signal sequence/motif
  - ER: “KDEL”
  - Nucleus: “KRKR”
- Post-translational targeting mechanism
  - Signaling complex: phosphorylation
  - Plasma membrane: lipid anchor
- Protein-protein interaction
  - Scaffold proteins



# Environmental conditions for proteins


- Proteins are diverse while their working environment is similar
- pH
  - ~7 in cell
- Redox potential
  - Reducing environment in the interiors of cells
  - Disulfide bonds are difficult to form in cytosol

# pH changes in specialized compartments




Endosomal vesicles with acidic pH regulated by ATP-dependent proton pump

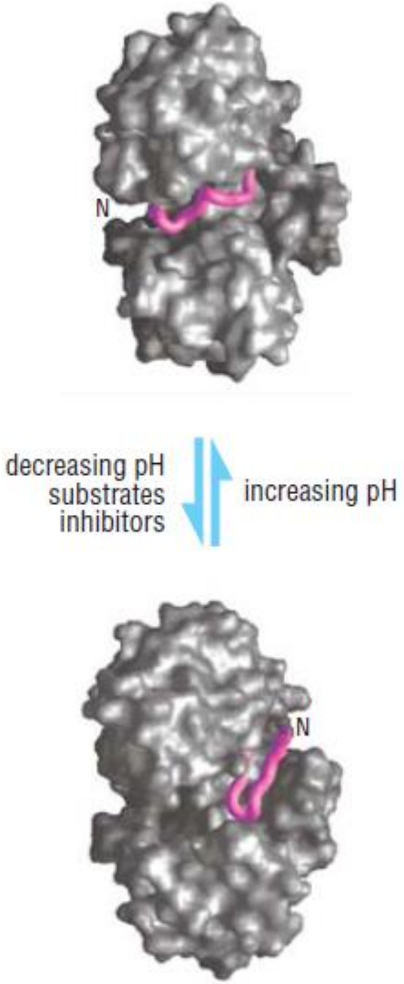
Nature Reviews Molecular Cell Biology, 2010

# Control by pH

- Changes in pH can drastically alter protein structure and function
- pH changes leads to
  - Surface charge distribution
  - Changes of electrostatic interactions inside a protein or between proteins

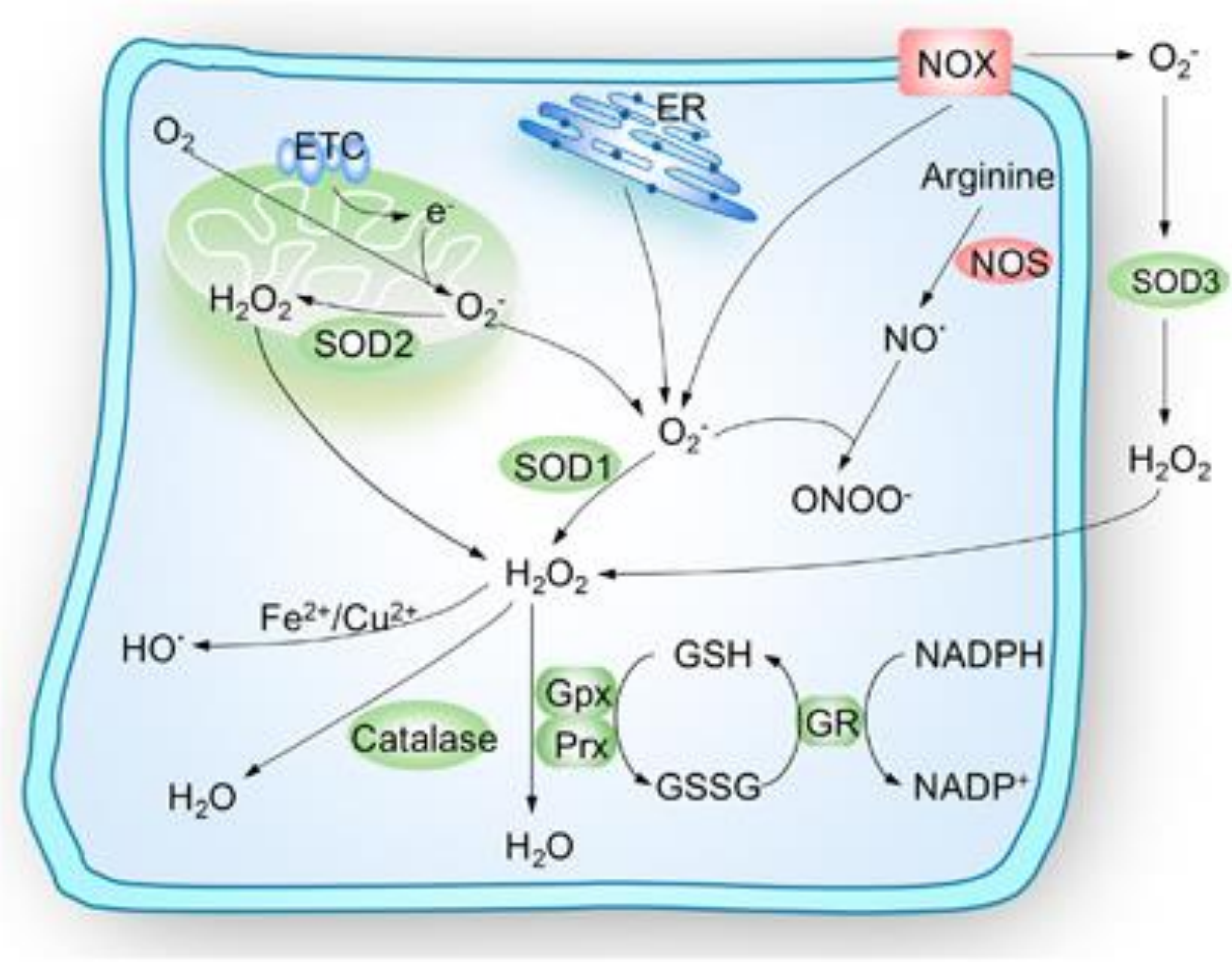
**Cathepsin D**
A aspartyl protease

Inactive in neutral pH (cytosol)



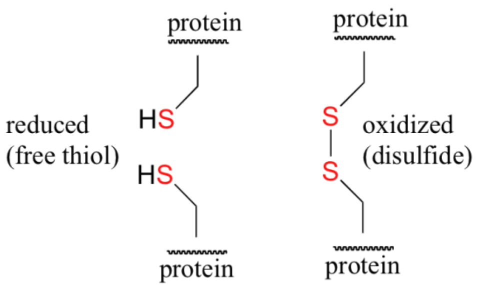

Active in low pH (endosome)

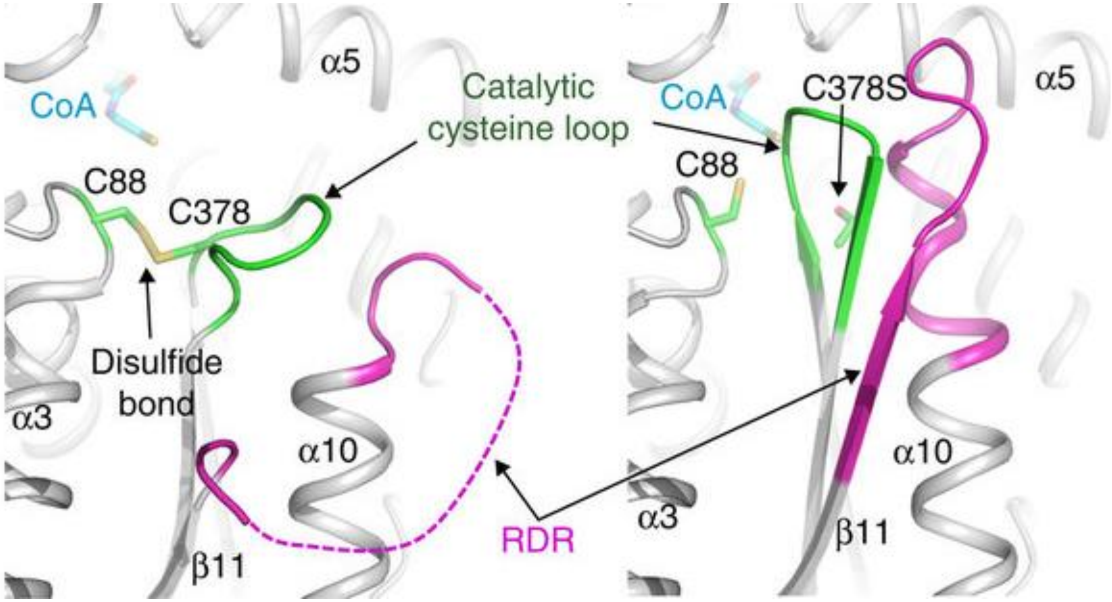
# Redox potential regulators in cell




Cell Death and Disease, 2013

# Control by redox environment




The redox switch of thiolase

Nature Communication, 2015

# Diphtheria toxin