BIOLOGIA CELULAR B

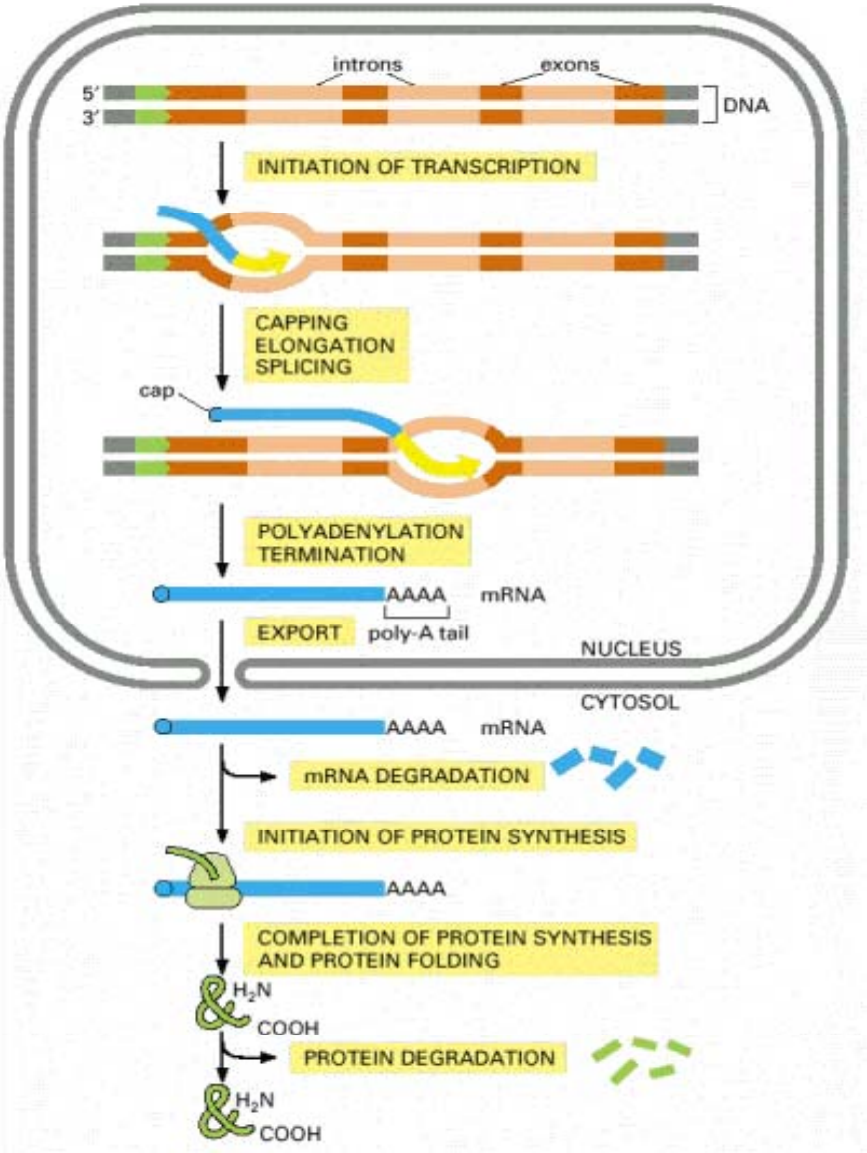
Vias de controlo de qualidade

Modificações pós-tradução

Moléculas chaperons

Degradação pelo proteossoma

Production of a protein by a eucaryotic cell



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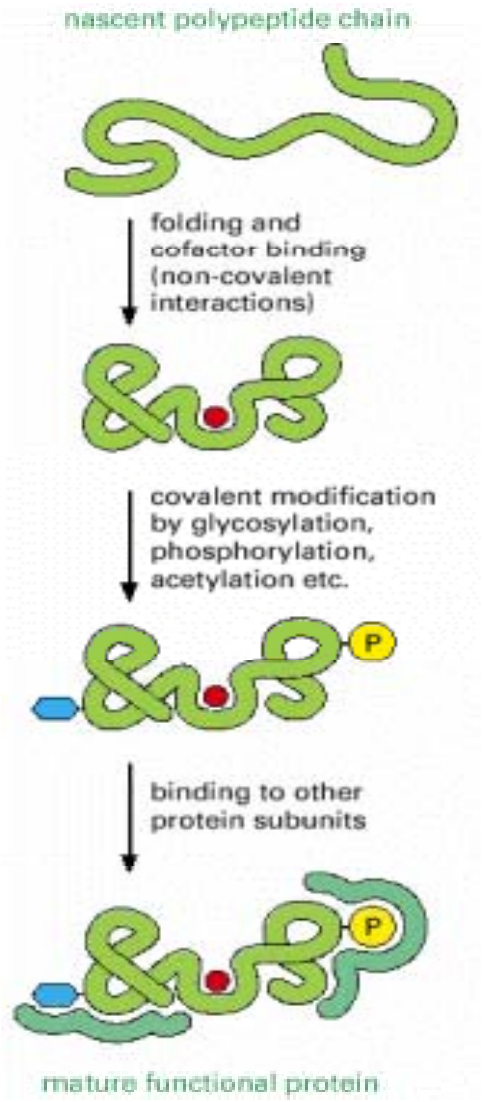

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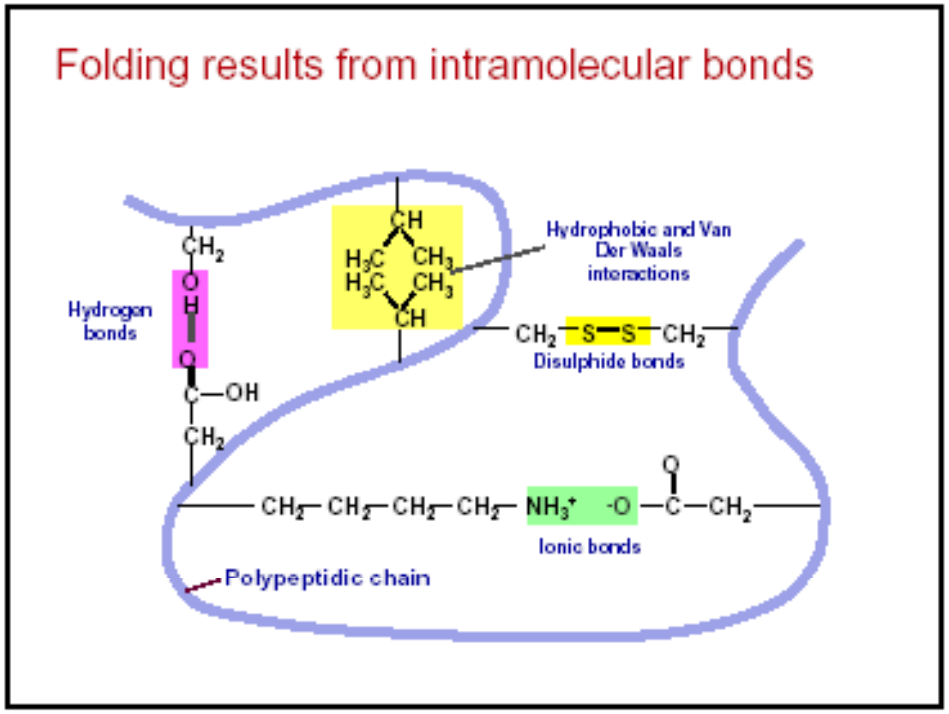
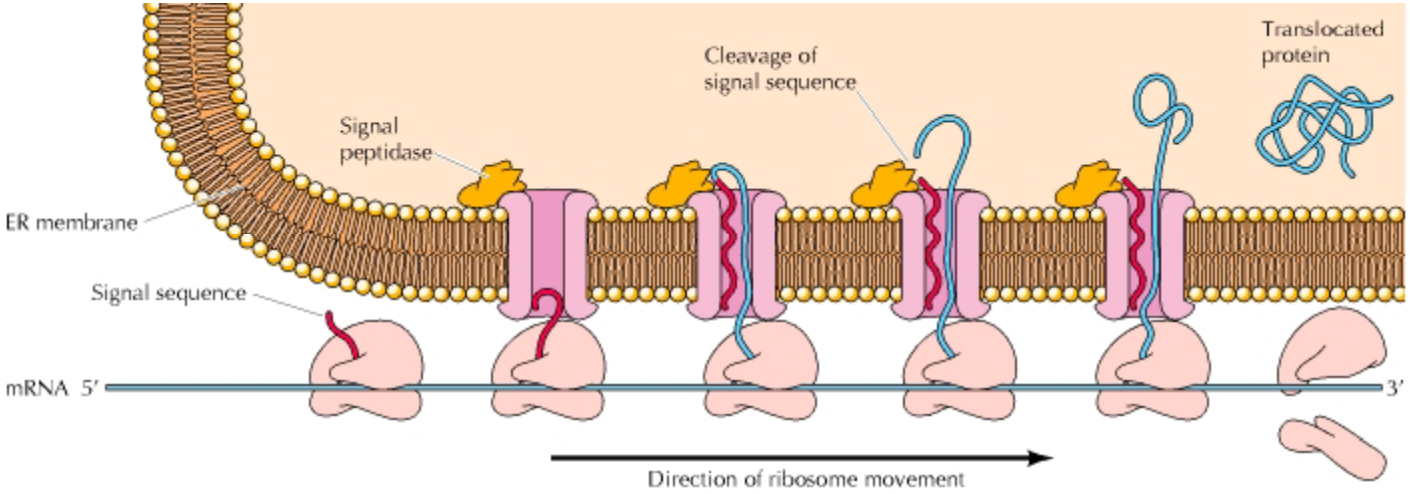
Protein Folding and Processing

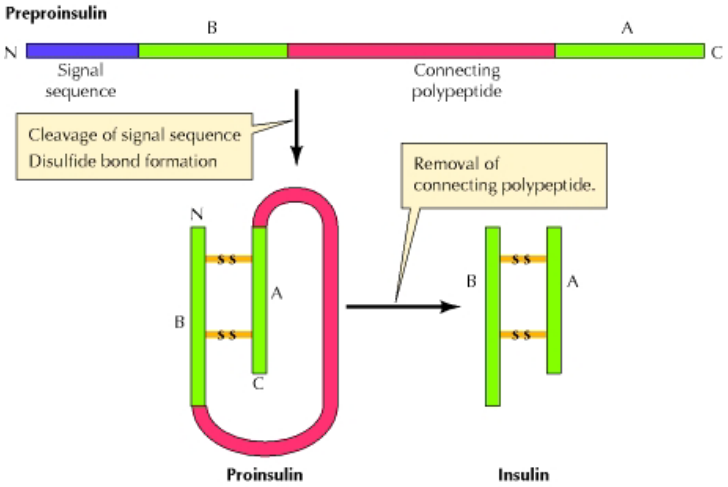


The polypeptide chain must :
- fold correctly into its three-dimensional conformation
-bind any cofactors required
-covalent modifications
-assemble with its partner protein chains (if any).

Proteolytic processing



signal sequence is cleaved by the action of signal peptidase



Insulin is synthesized as a precursor polypeptide (preproinsulin) The removal of aminoterminal signal sequence yields a second precursor (proinsulin), which is converted to insulin removing the internal connecting polypeptide

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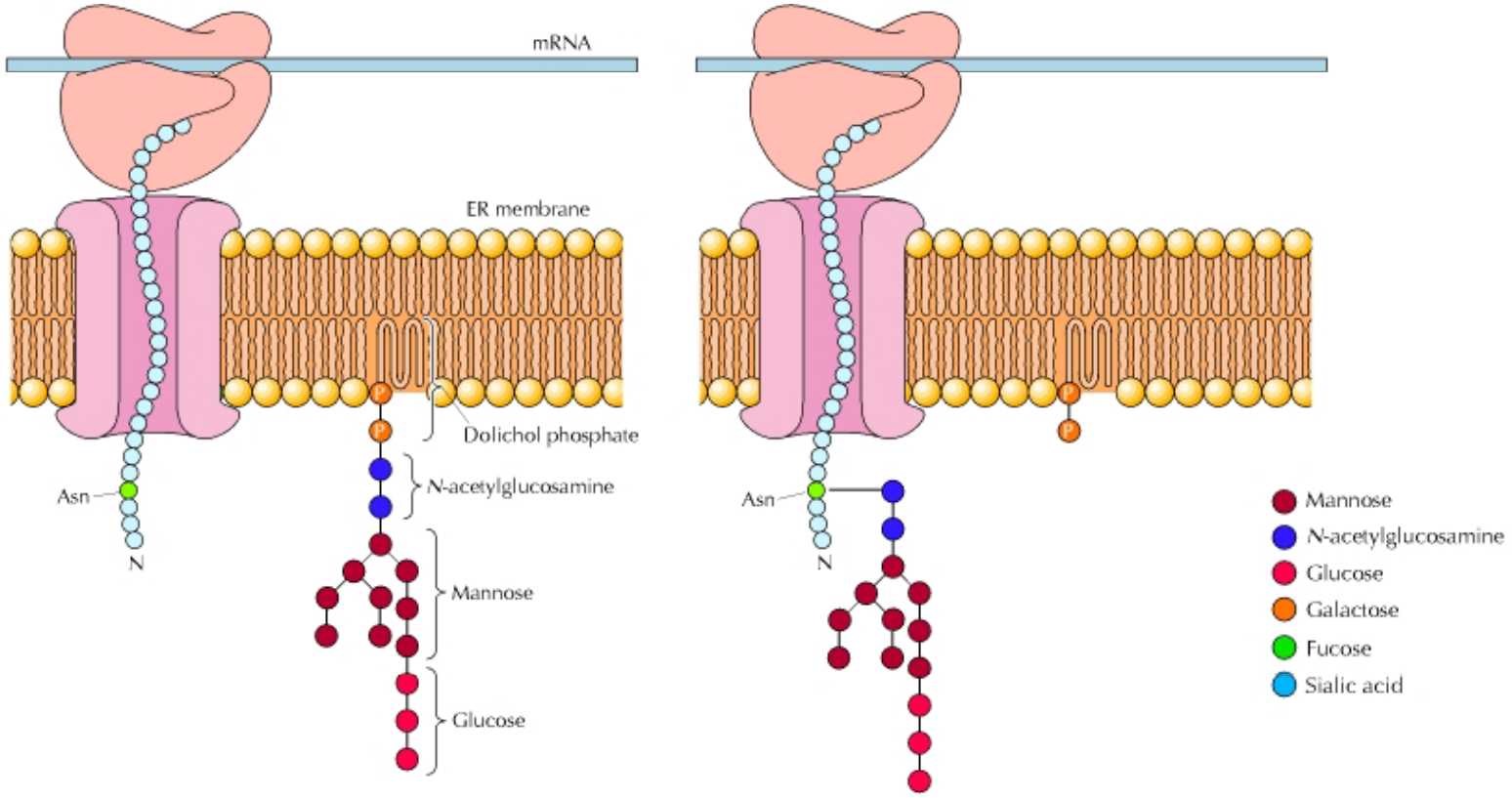
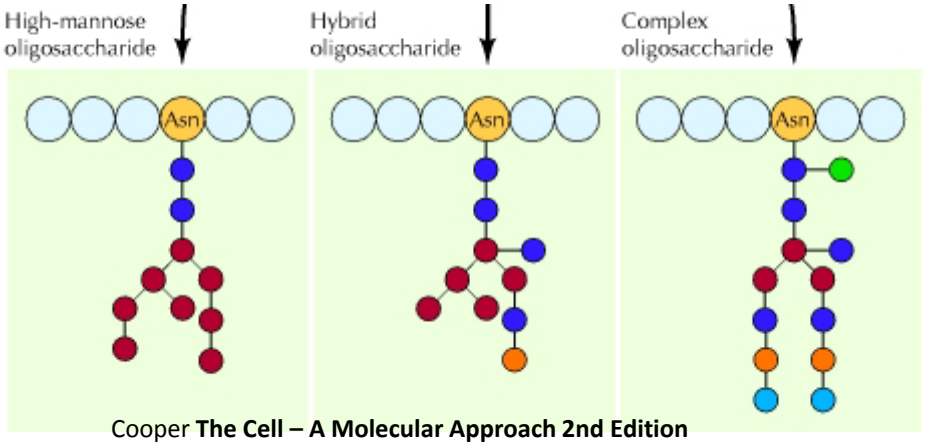
Gycosylation



Addition of an oligosaccharide consisting of 14 sugar residues to a growing polypeptide chain in the ER.

Various oligosaccharides form from further modifications of the common 14-sugar. Both in the ER and GA.



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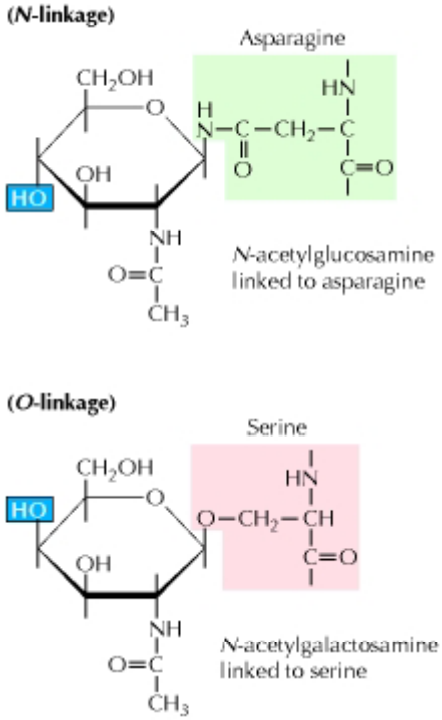
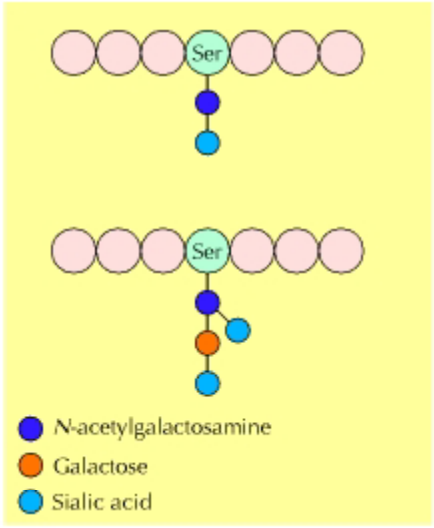
Gycosylation





N-linked glycoproteins are attached to asparagine
O-linked glycoproteins are attached to either serine or threonine

O-linked oligosaccharides usually consist of only a few carbohydrate residues, which are added one sugar at a time within the GA.

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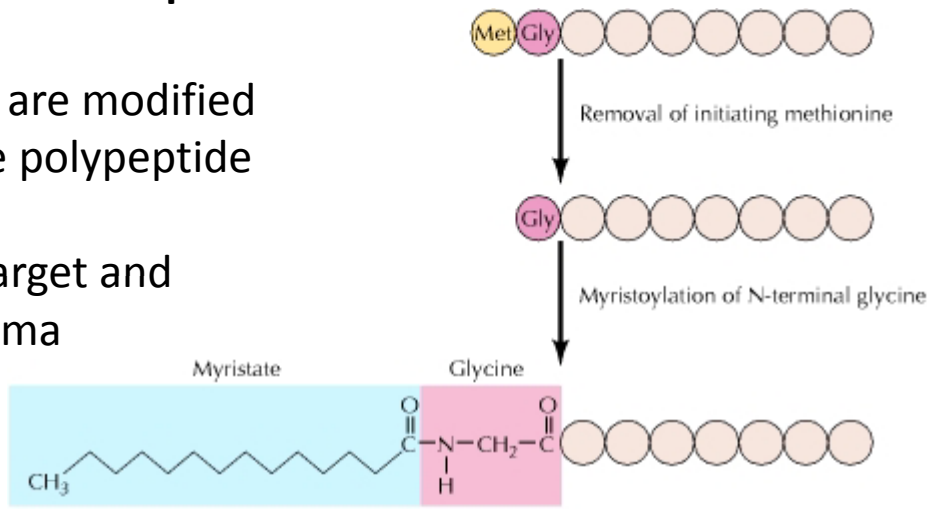
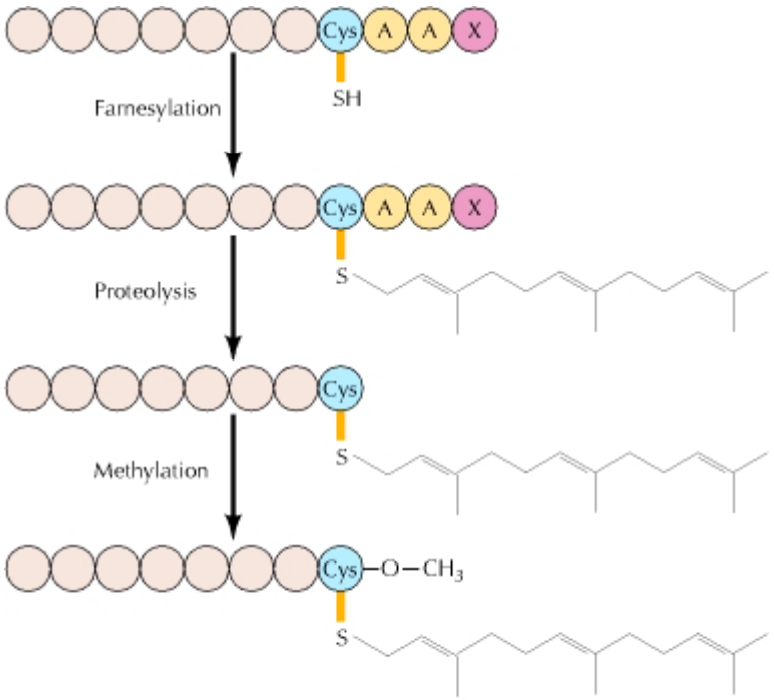
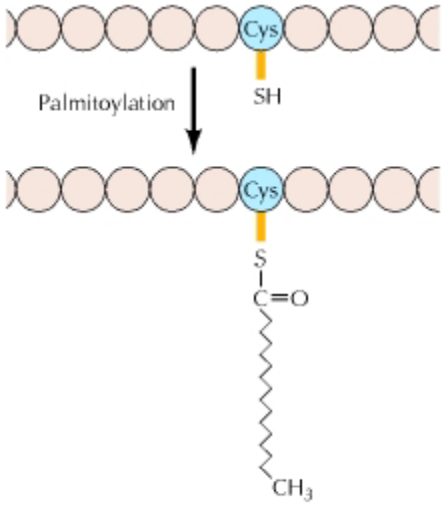
Attachment of Lipids

Some proteins in eukaryotic cells are modified by the attachment of lipids to the polypeptide chain.

These modifications frequently target and anchor these proteins to the plasma membrane







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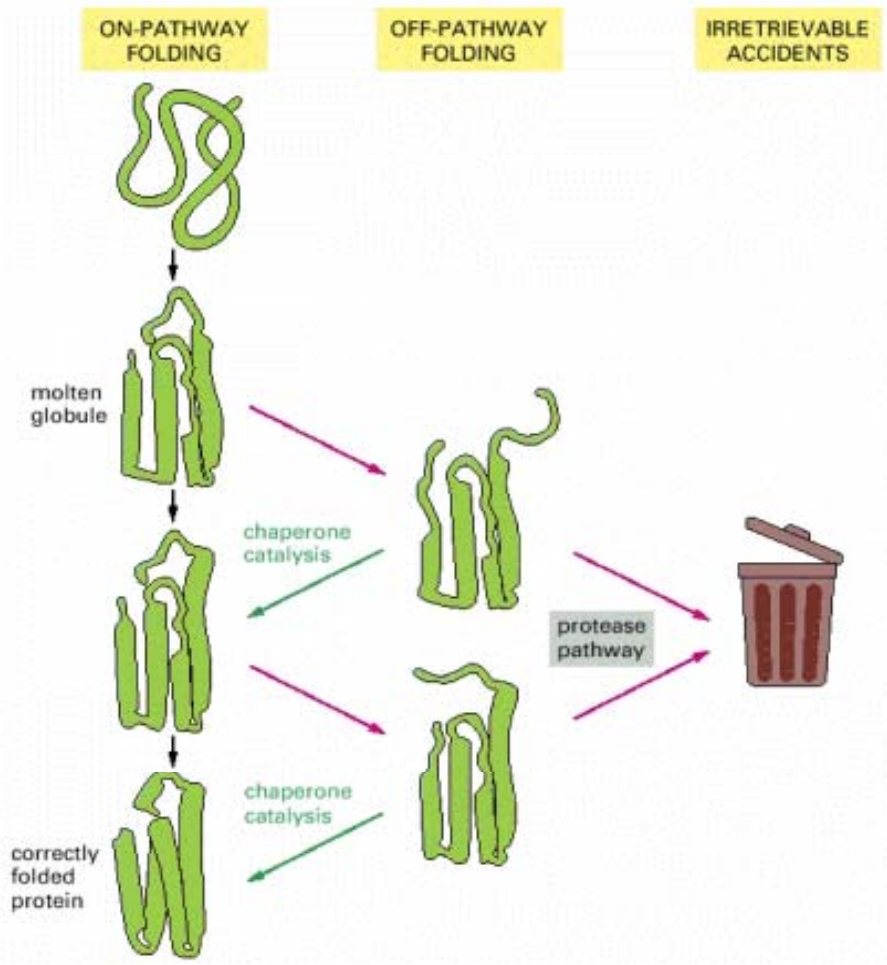
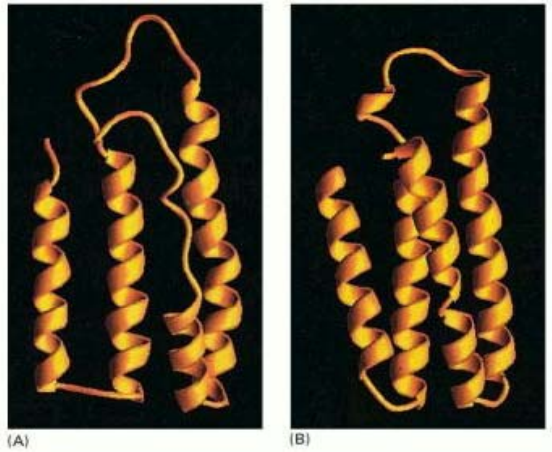
Protein folding



Each domain of a newly synthesized protein rapidly attains a “molten globule” state. Subsequent folding occurs more slowly and by multiple pathways, often involving the help of a molecular chaperone.

cytochrome b_{562}



molten globule final folded form

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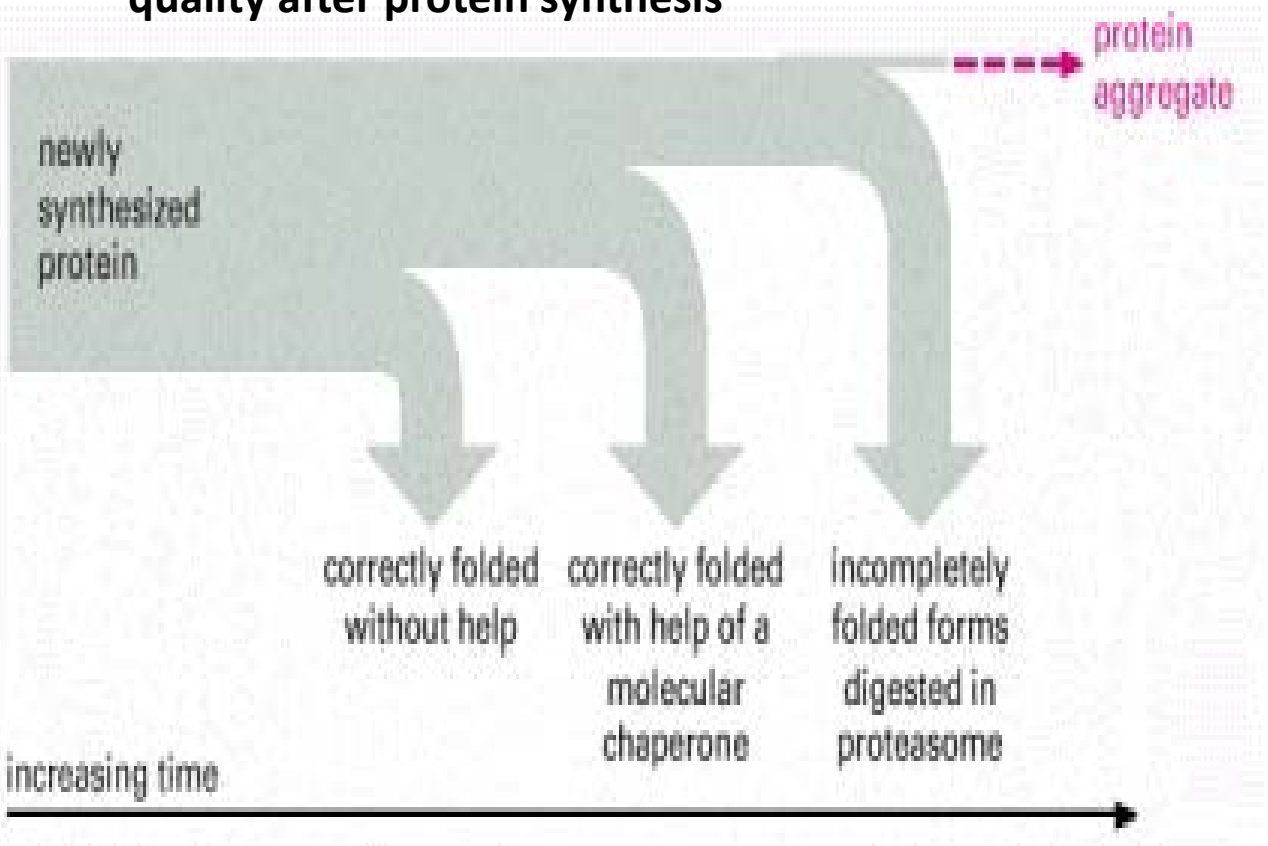
The cellular mechanisms that monitor protein quality after protein synthesis



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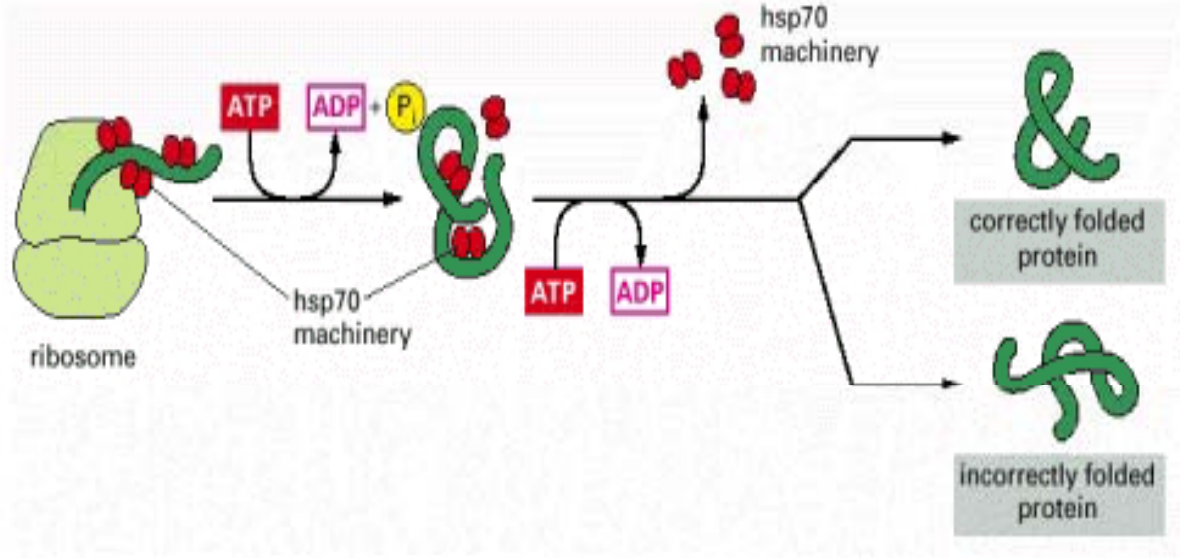
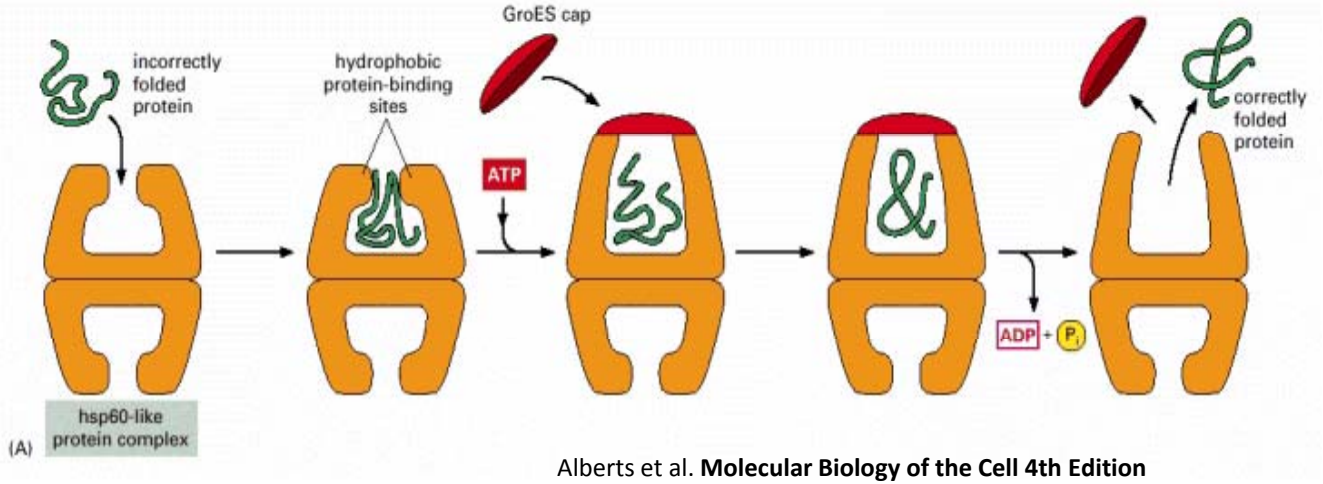
newly synthesized protein sometimes folds correctly on its own.
Incompletely folded proteins are helped to refold by molecular chaparones:
-first by a family of hsp70 proteins
-then by hsp60-like proteins
-abnormally folded proteins are transferred to a proteasome for complete destruction.

The hsp70 family of molecular chaperones



The hsp60 family of molecular chaperones



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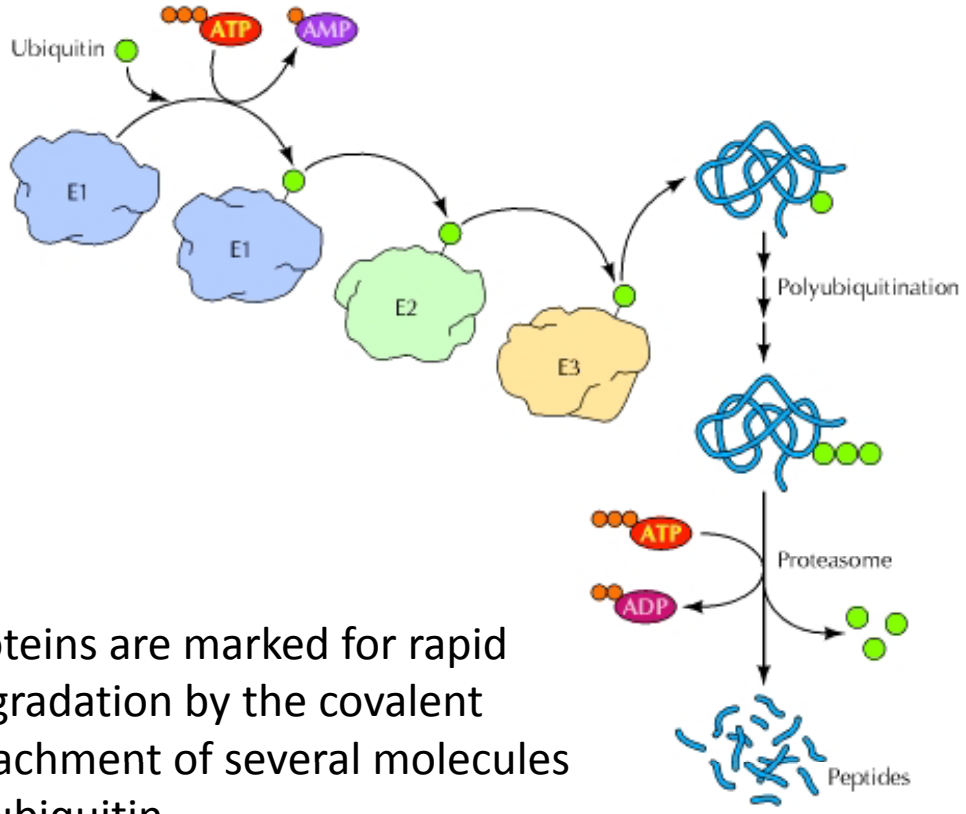
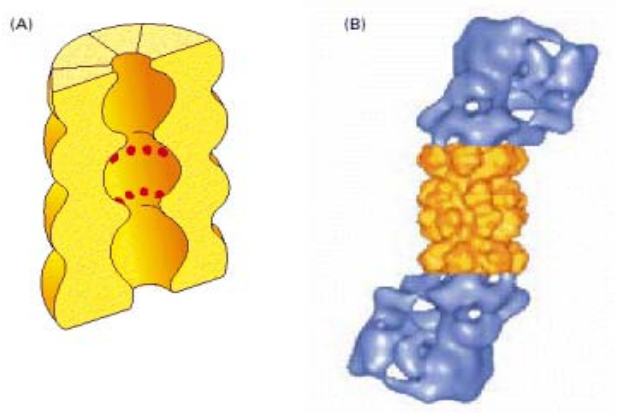
Protein Degradation

The ubiquitin-proteasome pathway





Proteins are marked for rapid degradation by the covalent attachment of several molecules of ubiquitin

The proteasome
– the central 20S cylinder has the active sites of the proteases .
- The 19S cap selectively binds those proteins that have been marked for unfolds their polypeptide chains

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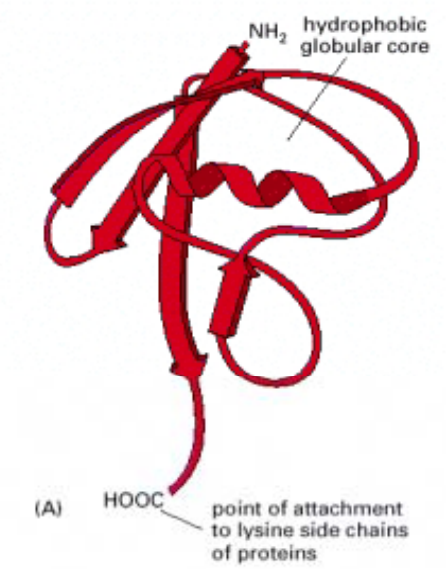
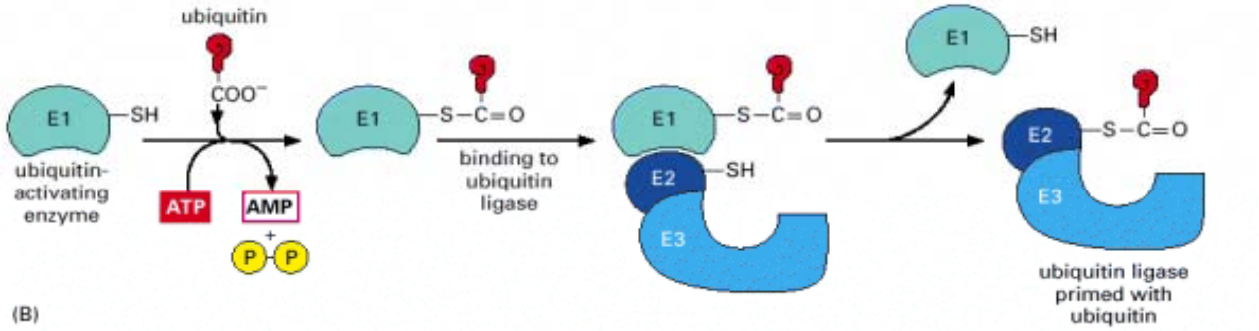
Ubiquitin is activated on E1, also known as the ubiquitin-activating enzyme, then is transferred to a set of E2 molecules.
The E2s exist as complexes with an even larger family of E3 molecules.





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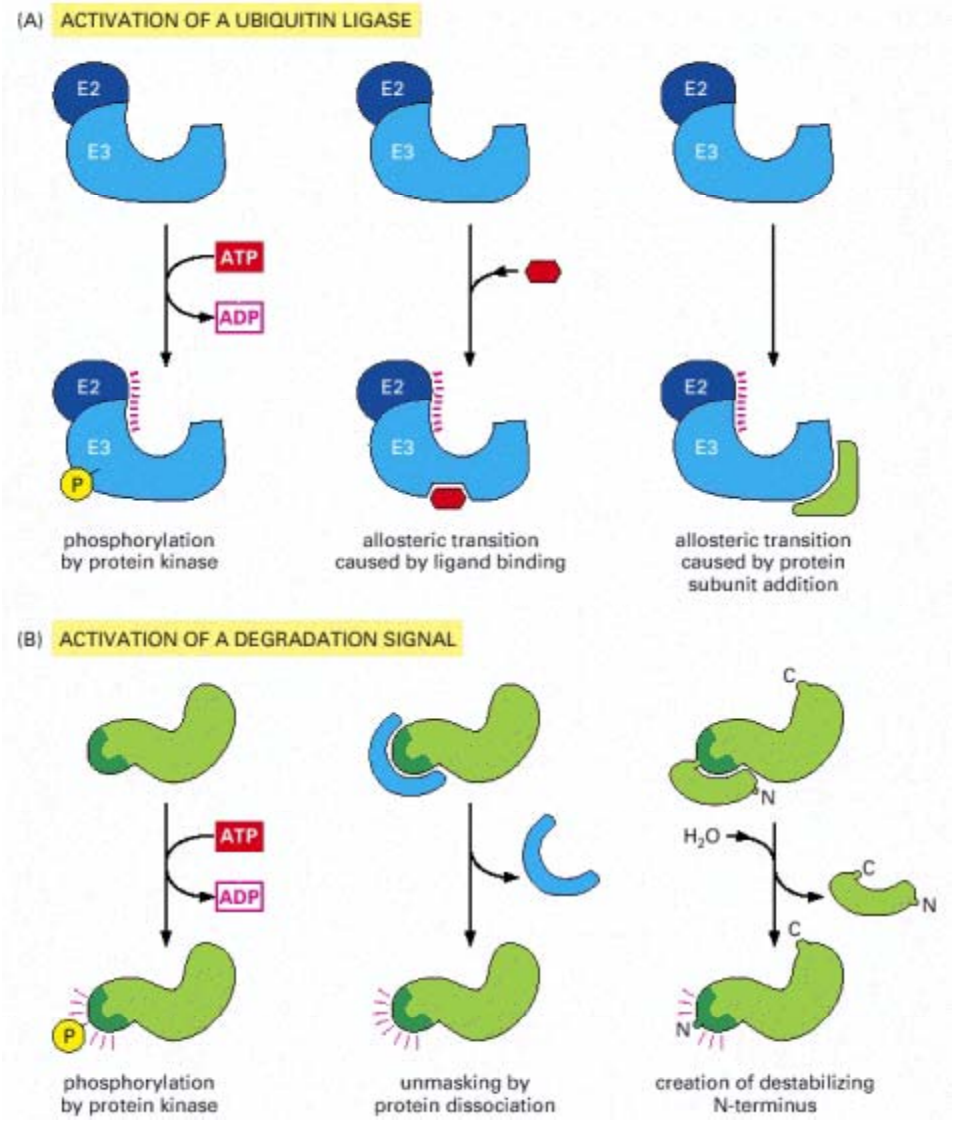
In a mammalian cell there are roughly 300 distinct E2-E3 complexes, each of which recognizes a different degradation signal on a target protein.

Two general ways of inducing the degradation of a specific protein



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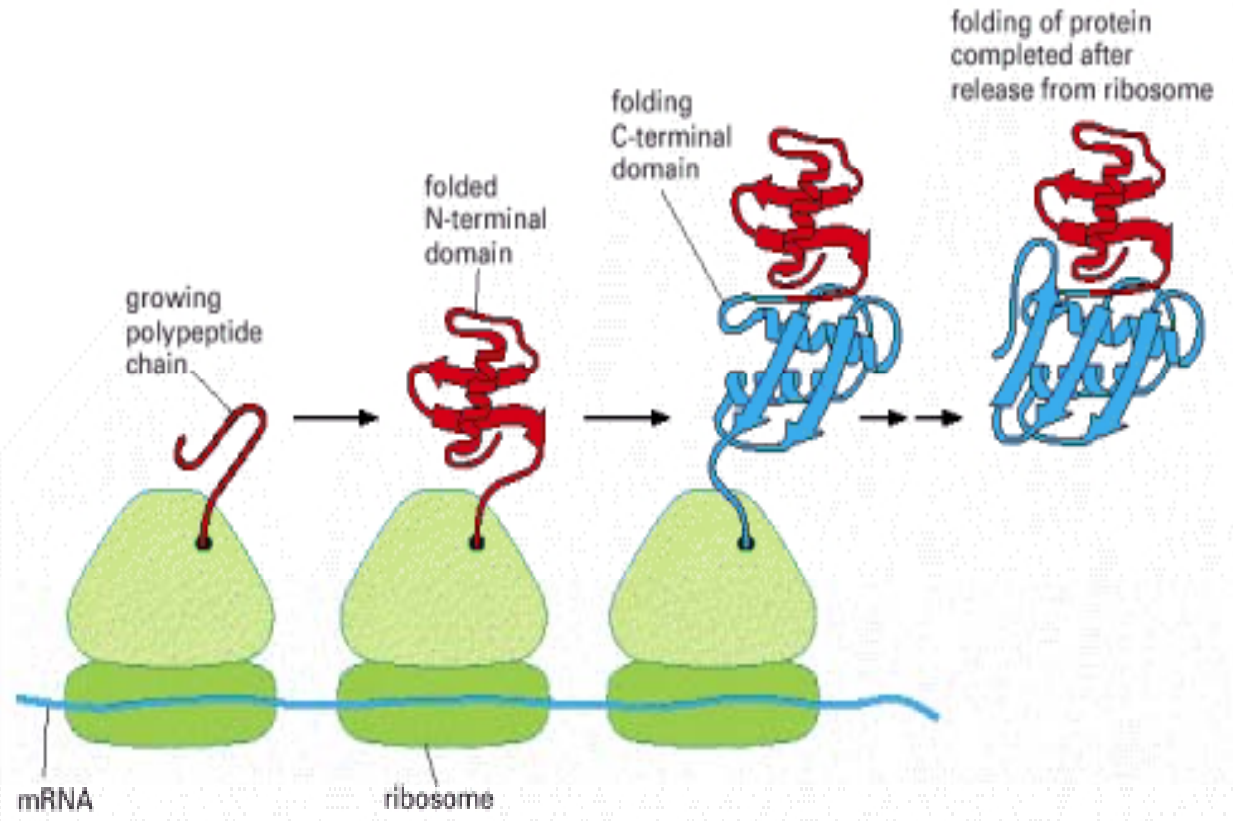
Protein folding



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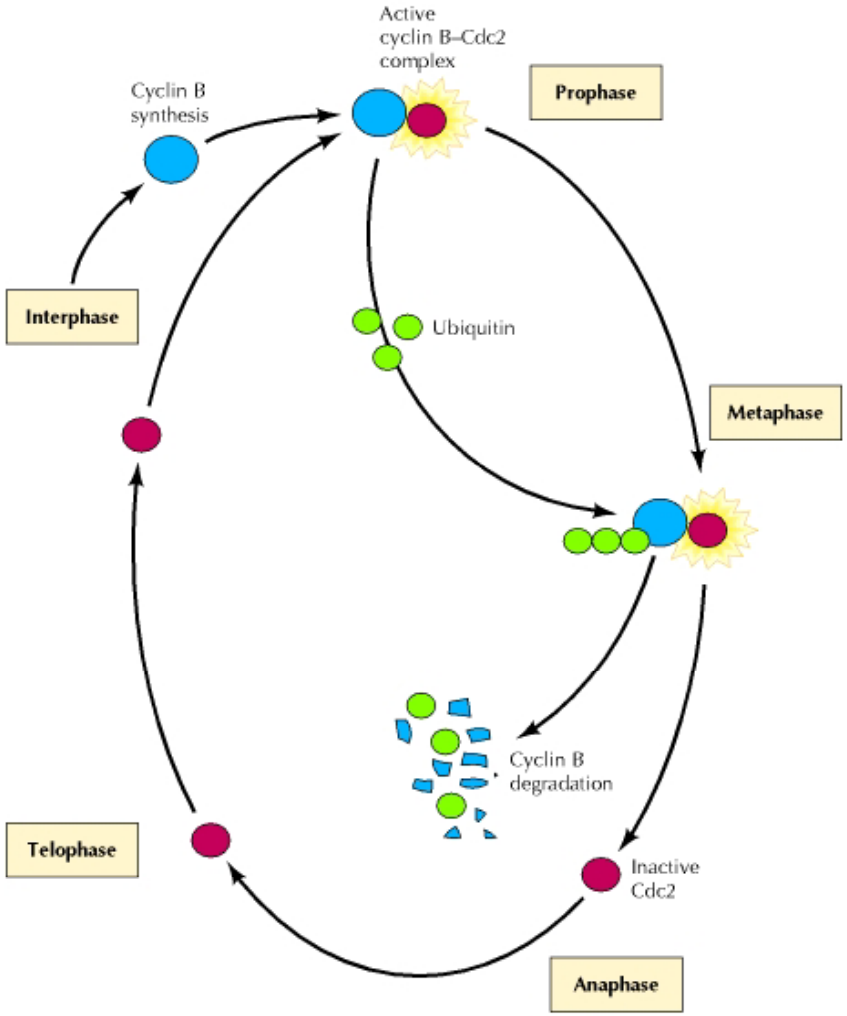
Co-translational folding of a protein The N-terminal domain folds first, while the C-terminal domain is still being synthesized

Cyclin degradation during the cell cycle



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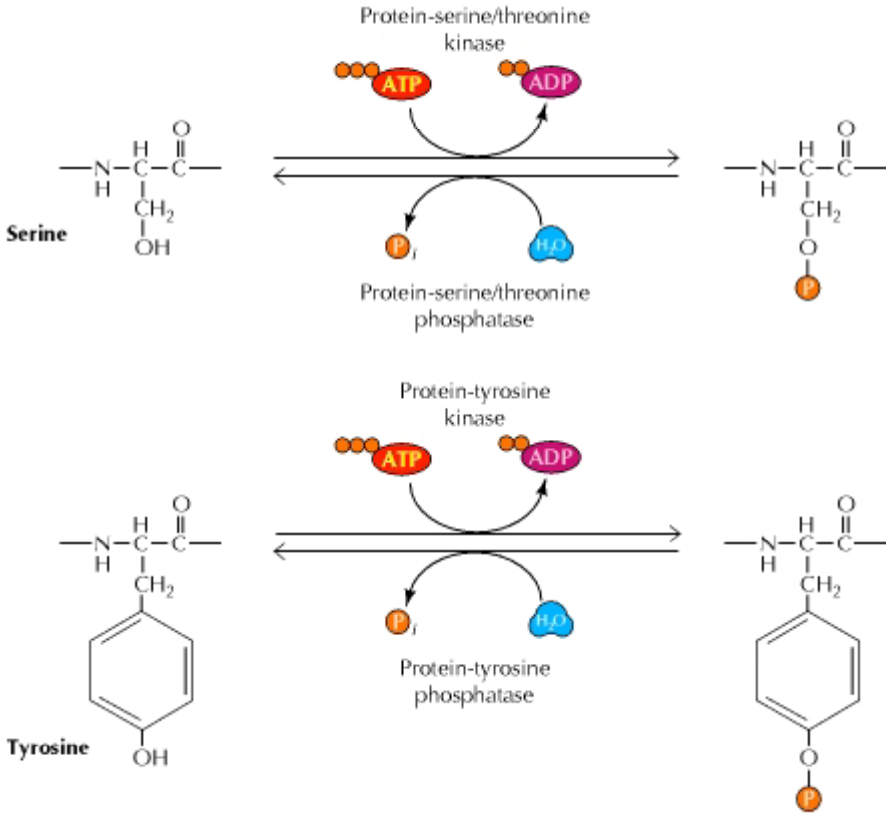
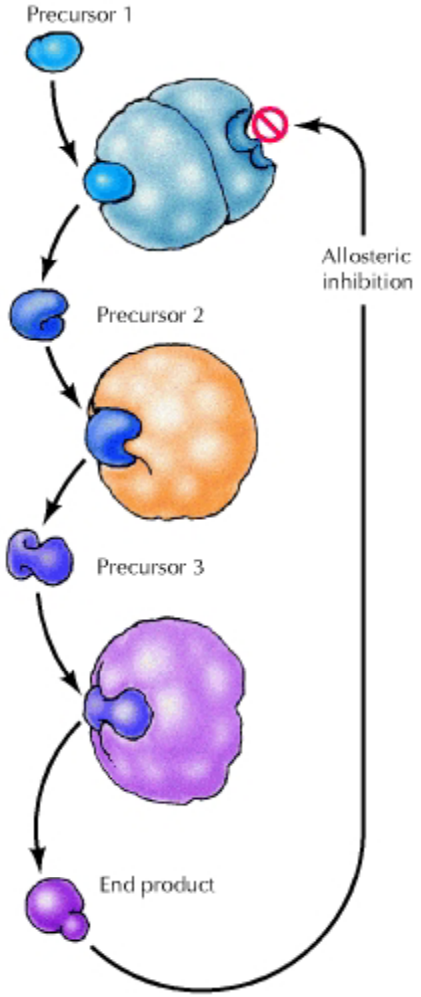
The progression of eukaryotic cells through the division cycle is controlled in part by the synthesis and degradation of cyclin B

Regulation of Protein Function



Protein kinases and phosphatases



Feedback inhibition

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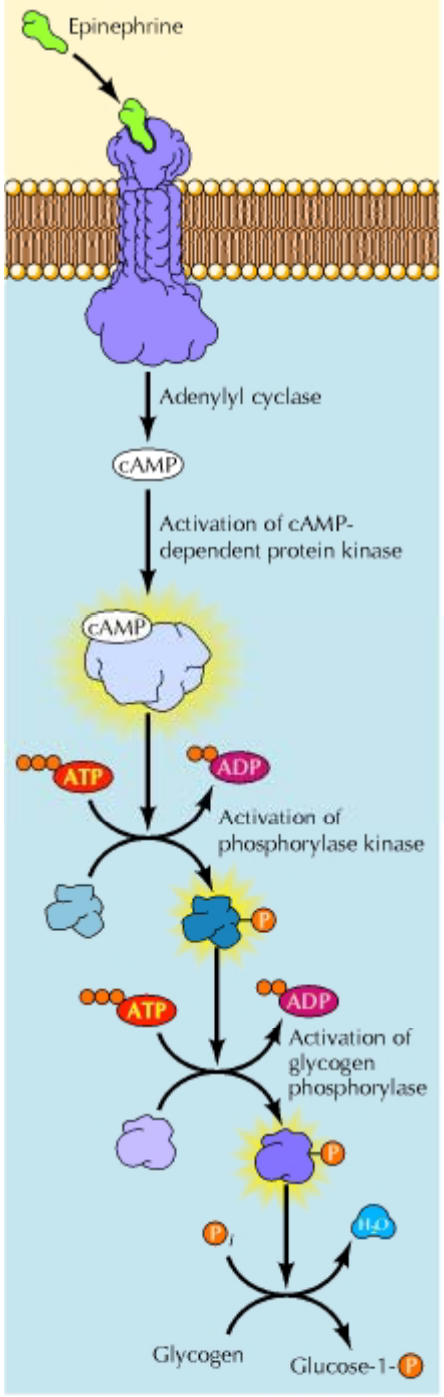
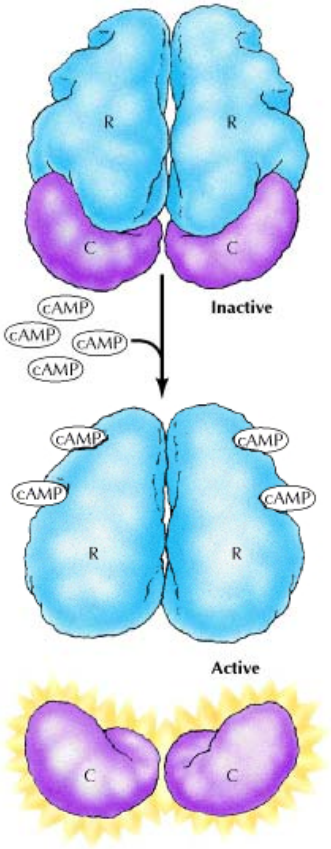


Regulation of glycogen breakdown by protein phosphorylation



cAMP-dependent protein kinase - the enzyme consists of two regulatory (R) and two catalytic (C) subunits.
Cyclic AMP binds to the regulatory subunits, inducing a conformational change that leads to their dissociation from the catalytic subunits

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