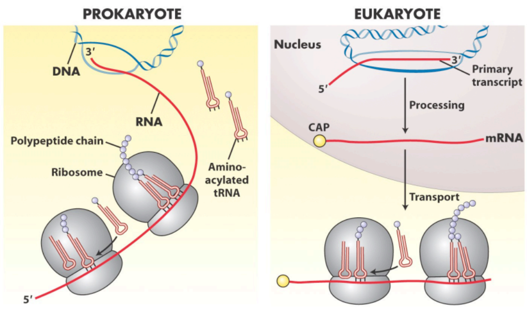
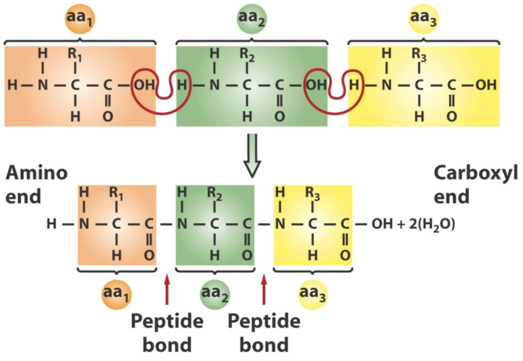
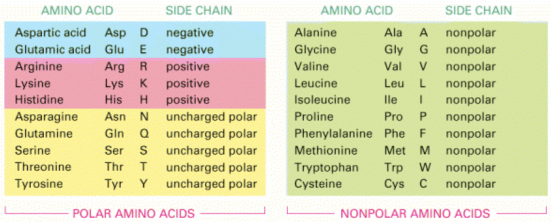

PROKARYOTE
DNA
3′
RNA
Polypeptide chain
Ribosome
Amino-acylated tRNA
5′
EUKARYOTE
Nucleus
3′
5′
Primary transcript
Processing
CAP
mRNA
Transport


aa1
aa2
aa3
H R1 H–N–C–C–OH H O
H R2 H–N–C–C–OH H O
H R3 H–N–C–C–OH H O
Amino end
Carboxyl end
H–N–C–C–N–C–C–N–C–C–OH + 2(H2O)
aa1
aa2
aa3
Peptide bond
Peptide bond

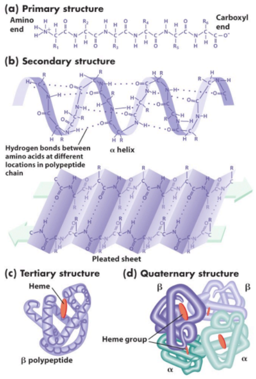


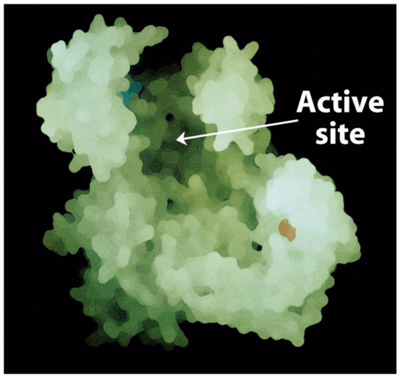
AMINO ACID			SIDE CHAIN
Aspartic acid	Asp	D	negative
Glutamic acid	Glu	E	negative
Arginine	Arg	R	positive
Lysine	Lys	K	positive
Histidine	His	H	positive
Asparagine	Asn	N	uncharged polar
Glutamine	Gln	Q	uncharged polar
Serine	Ser	S	uncharged polar
Threonine	Thr	T	uncharged polar
Tyrosine	Tyr	Y	uncharged polar

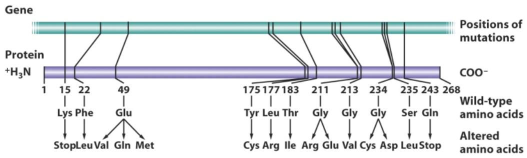
POLAR AMINO ACIDS

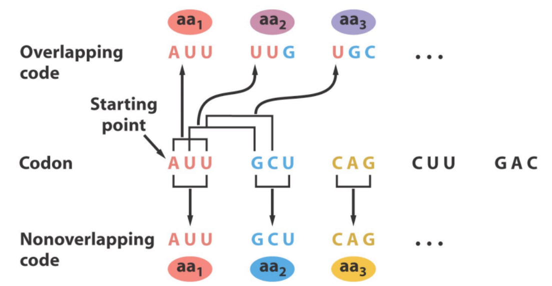
AMINO ACID			SIDE CHAIN
Alanine	Ala	A	nonpolar
Glycine	Gly	G	nonpolar
Valine	Val	V	nonpolar
Leucine	Leu	L	nonpolar
Isoleucine	Ile	I	nonpolar
Proline	Pro	P	nonpolar
Phenylalanine	Phe	F	nonpolar
Methionine	Met	M	nonpolar
Tryptophan	Trp	W	nonpolar
Cysteine	Cys	C	nonpolar

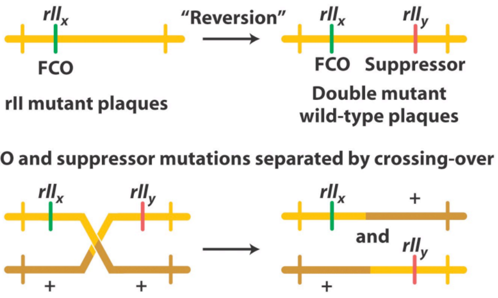
NONPOLAR AMINO ACIDS


(a) Primary structure
Amino end
Carboxyl end
(b) Secondary structure
Hydrogen bonds between amino acids at different locations in polypeptide chain
α helix
Pleated sheet
(c) Tertiary structure
Heme
β polypeptide
(d) Quaternary structure
β
β
Heme group
α
α


Active site


Gene
Positions of mutations
Protein
+H3N
COO−
1 15 22 49 175 177 183 211 213 234 235 243 268
Lys Phe Glu Tyr Leu Thr Gly Gly Gly Ser Gln
Wild-type amino acids
Stop Leu Val Gln Met Cys Arg Ile Arg Glu Val Cys Asp Leu Stop
Altered amino acids


aa1
aa2
aa3
Overlapping code
A U U
U U G
U G C
. . .
Starting point
Codon
A U U
G C U
C A G
C U U
G A C
Nonoverlapping code
A U U
G C U
C A G
. . .
aa1
aa2
aa3

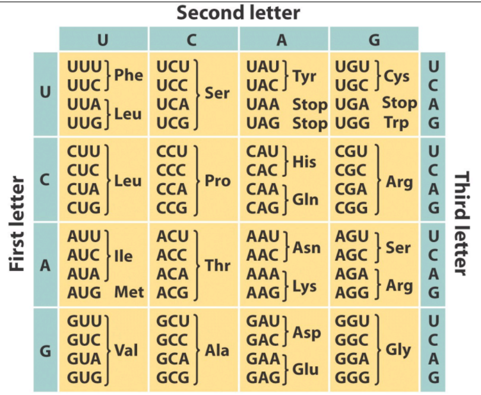

rII x
FCO
rII mutant plaques
"Reversion"
rII x
rII y
FCO
Suppressor
Double mutant wild-type plaques
FCO and suppressor mutations separated by crossing-over
rII x
rII y
+
+
rII x
+
and
rII y
+

WT THE FAT CAT ATE THE BIG RAT

Delete C THE FAT ATA TET HEB IGR AT

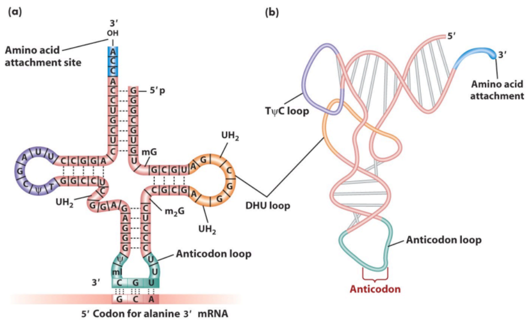
Insert A THE FAT ATA ATE THE BIG RAT

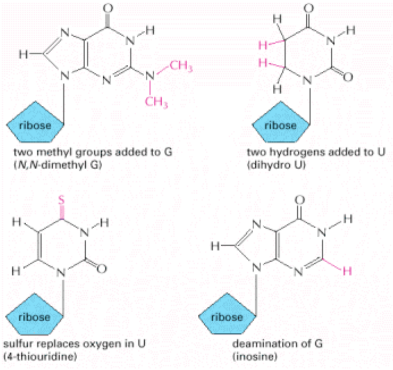
GCA GCC GCG GCU	AGA AGG CGA CGC CGG CGU	GAC GAU	AAC AAU	UGC UGU	GAA GAG	CAA CAG	GGA GGC GGG GGU	CAC CAU	AUA AUC AUU	UUA UUG CUA CUC CUG CUU	AAA AAG	AUG	UUC UUU	CCA CCC CCG CCU	AGC AGU UCA UCC UCG UCU	ACA ACC ACG ACU	UGG	UAC UAU	GUA GUC GUG GUU	UAA UAG UGA
Ala	Arg	Asp	Asn	Cys	Glu	Gln	Gly	His	Ile	Leu	Lys	Met	Phe	Pro	Ser	Thr	Trp	Tyr	Val	stop
A	R	D	N	C	E	Q	G	H	I	L	K	M	F	P	S	T	W	Y	V	

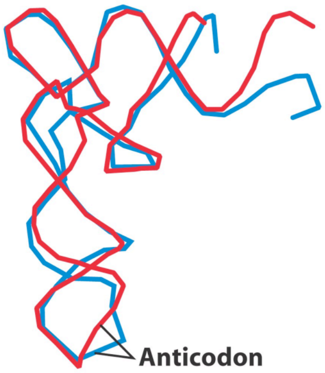


Second letter

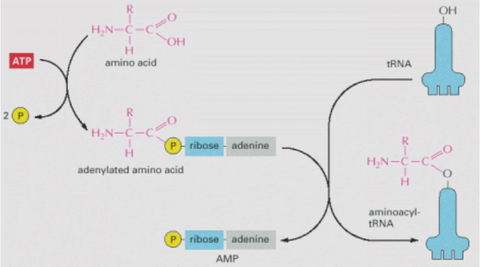
First letter	U	C	A	G	Third letter
U	UUU Phe UUC Phe UUA Leu UUG Leu	UCU Ser UCC Ser UCA Ser UCG Ser	UAU Tyr UAC Tyr UAA Stop UAG Stop	UGU Cys UGC Cys UGA Stop UGG Trp	U C A G
C	CUU Leu CUC Leu CUA Leu CUG Leu	CCU Pro CCC Pro CCA Pro CCG Pro	CAU His CAC His CAA Gln CAG Gln	CGU Arg CGC Arg CGA Arg CGG Arg	U C A G
A	AUU Ile AUC Ile AUA Ile AUG Met	ACU Thr ACC Thr ACA Thr ACG Thr	AAU Asn AAC Asn AAA Lys AAG Lys	AGU Ser AGC Ser AGA Arg AGG Arg	U C A G
G	GUU Val GUC Val GUA Val GUG Val	GCU Ala GCC Ala GCA Ala GCG Ala	GAU Asp GAC Asp GAA Glu GAG Glu	GGU Gly GGC Gly GGA Gly GGG Gly	U C A G

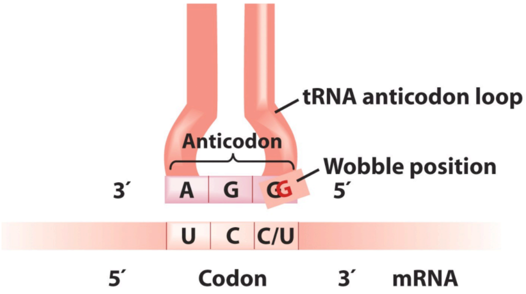

(a)
3′
OH
Amino acid attachment site
5′p
mG
UH2
UH2
m2G
UH2
DHU loop
Anticodon loop
3′
5′ Codon for alanine 3′ mRNA
(b)
5′
3′
Amino acid attachment
TψC loop
Anticodon loop
Anticodon


ribose
two methyl groups added to G
(*N*,*N*-dimethyl G)
ribose
two hydrogens added to U
(dihydro U)
ribose
sulfur replaces oxygen in U
(4-thiouridine)
ribose
deamination of G
(inosine)



Action of amino-acyl tRNA synthetase


ATP
amino acid
2 P
adenylated amino acid
P ribose adenine
tRNA
aminoacyl-tRNA
P ribose adenine
AMP


tRNA anticodon loop
Anticodon
Wobble position
3′
A G G
5′
U C C/U
5′
Codon
3′
mRNA

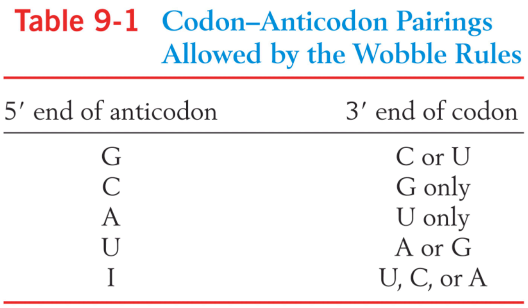


Table 9-1 Codon–Anticodon Pairings Allowed by the Wobble Rules

5′ end of anticodon	3′ end of codon
G	C or U
C	G only
A	U only
U	A or G
I	U, C, or A

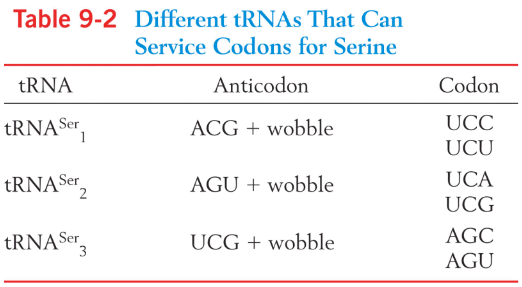
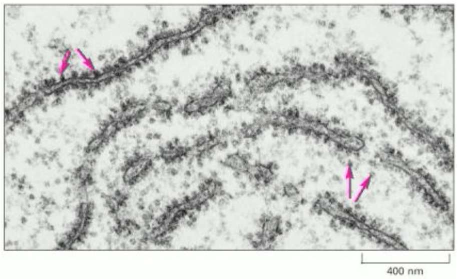
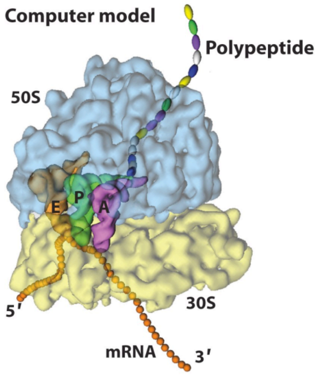


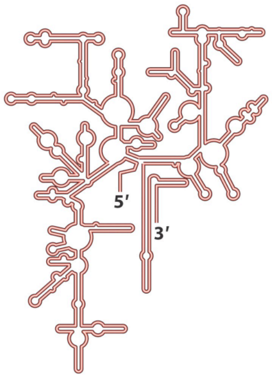
Table 9-2 Different tRNAs That Can Service Codons for Serine

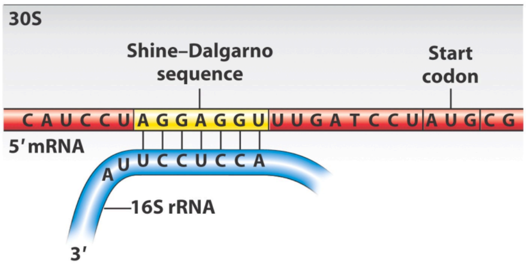
tRNA	Anticodon	Codon
$tRNA^{Ser}_{1}$	ACG + wobble	UCC UCU
$tRNA^{Ser}_{2}$	AGU + wobble	UCA UCG
$tRNA^{Ser}_{3}$	UCG + wobble	AGC AGU

mRNA is translated by ribosomes

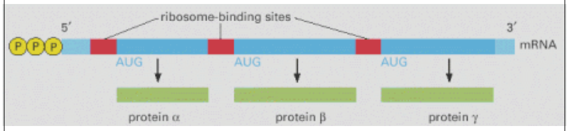


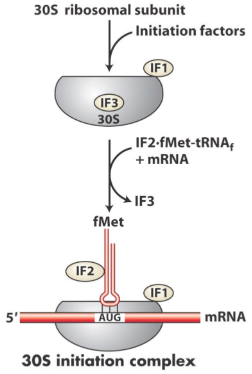

Computer model
Polypeptide
50S
E
P
A
5′
30S
mRNA
3′

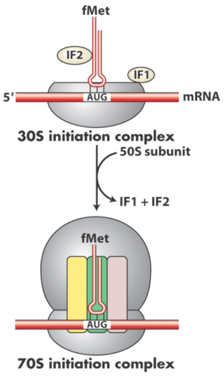


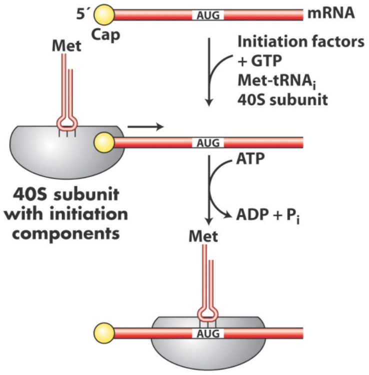

30S
Shine–Dalgarno sequence
Start codon
C A U C C U A G G A G G U U U G A T C C U A U G C G
5′ mRNA
A U U C C U C C A
16S rRNA
3′

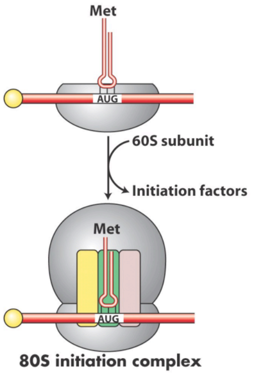
Typical bacterial mRNA molecule - polycistronic

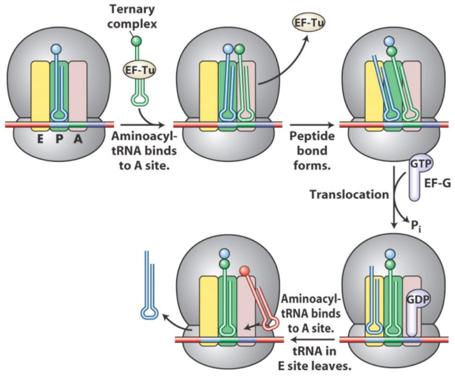

ribosome-binding sites
5′
3′
P P P
mRNA
AUG
AUG
AUG
protein α
protein β
protein γ

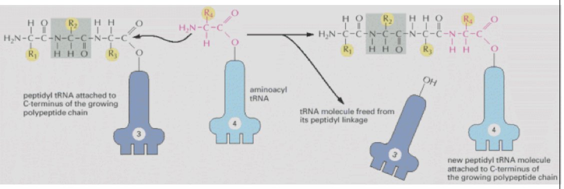

30S ribosomal subunit
Initiation factors
IF1
IF3
30S
IF2-fMet-tRNA$_f$ + mRNA
IF3
fMet
IF2
IF1
5′
AUG
mRNA
30S initiation complex


fMet
IF2
IF1
5′
AUG
mRNA
30S initiation complex
50S subunit
IF1 + IF2
fMet
AUG
70S initiation complex


5′
AUG
mRNA
Cap
Met
Initiation factors
+ GTP
Met-tRNA$_i$
40S subunit
AUG
ATP
40S subunit
with initiation
components
ADP + P$_i$
Met
AUG


Met
AUG
60S subunit
Initiation factors
Met
AUG
80S initiation complex


Ternary
complex
EF-Tu
EF-Tu
E P A
Aminoacyl-
tRNA binds
to A site.
Peptide
bond
forms.
GTP
EF-G
Translocation
P$_i$
GDP
Aminoacyl-
tRNA binds
to A site.
tRNA in
E site leaves.


H₂N
R₁
R₂
R₃
R₄
OH
3
4
3
4

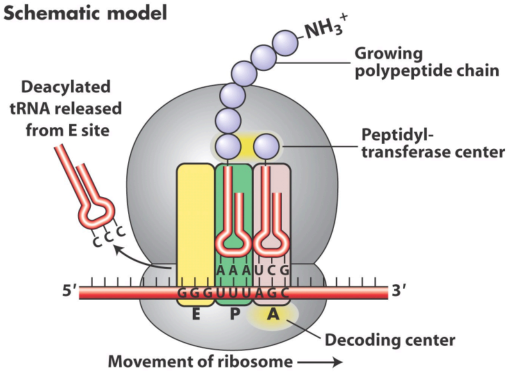
peptidyl tRNA attached to C-terminus of the growing polypeptide chain

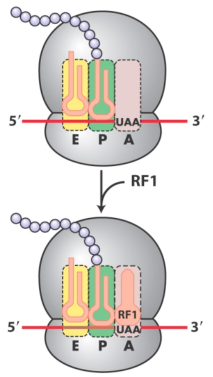
aminoacyl tRNA

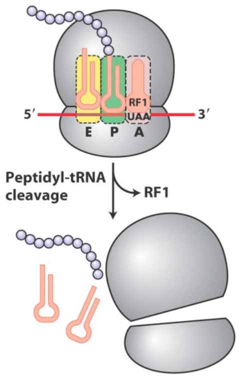
tRNA molecule freed from its peptidyl linkage

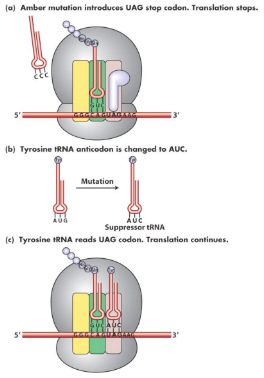
new peptidyl tRNA molecule attached to C-terminus of the growing polypeptide chain

Schematic model


NH$_3^+$
Growing
polypeptide chain
Deacylated
tRNA released
from E site
Peptidyl-
transferase center
C C C
A A A U C G
5′
G G G U U U A G C
3′
E
P
A
Decoding center
Movement of ribosome →


5′
UAA
3′
E
P
A
RF1
5′
RF1
UAA
3′
E
P
A

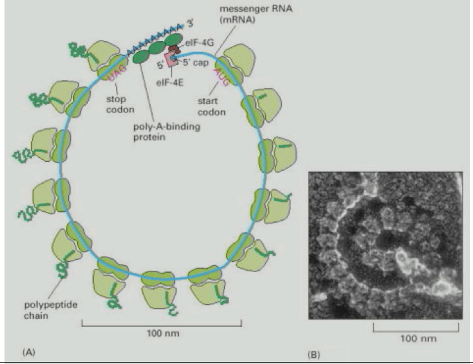

5′
RF1
UAA
3′
E
P
A
Peptidyl-tRNA cleavage
RF1


(a) Amber mutation introduces UAG stop codon. Translation stops.

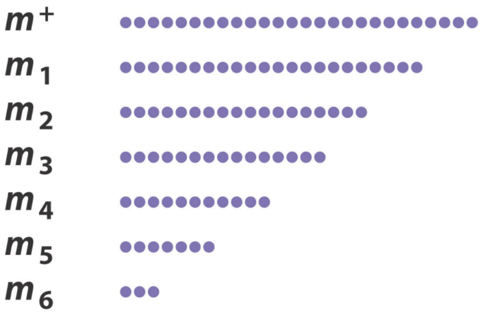
(b) Tyrosine tRNA anticodon is changed to AUC.

(c) Tyrosine tRNA reads UAG codon. Translation continues.
CCC
His
Gly
Gln
GUC
5′
GGGCAGUAGAAG
3′
Tyr
Mutation
AUG
AUC
Suppressor tRNA
His
Gly
Gln
Tyr
GUC
AUC
5′
GGGCAGUAGAAG
3′

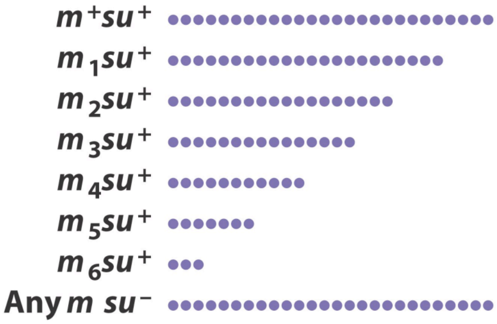
polyribosome


messenger RNA (mRNA)
AAAAAAAAA 3′
eIF-4G
5′
5′ cap
eIF-4E
UAG
AUG
stop codon
start codon
poly-A-binding protein
polypeptide chain
100 nm
(A)
100 nm
(B)

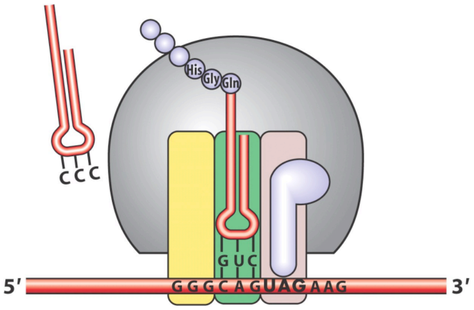
Polypeptide length



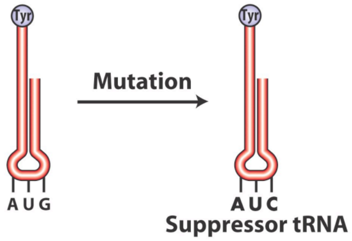
Polypeptide length



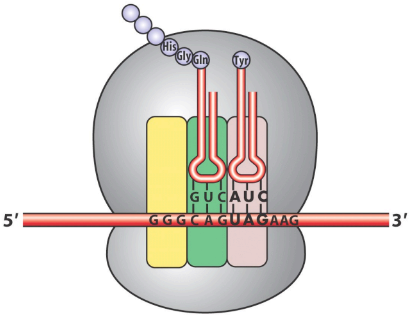
Amber mutation introduces UAG stop codon. Translation stops.

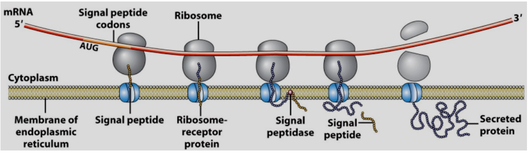

His
Gly
Gln
C C C
G U C
5′
G G G C A G UAG A A G
3′

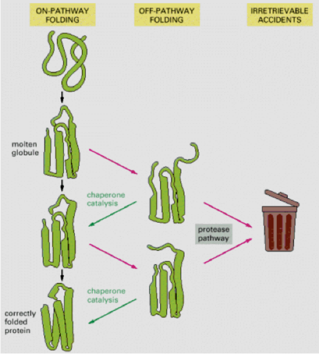
Tyrosine tRNA anticodon is changed to AUC.


Tyr
A U G
Mutation
Tyr
A U C
Suppressor tRNA

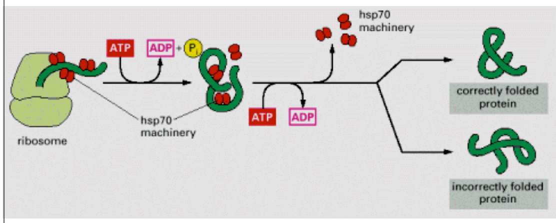
Tyrosine tRNA reads UAG codon. Translation continues.


His
Gly
Gln
Tyr
G U C
A U C
5′
G G G C A G U A G A A G
3′

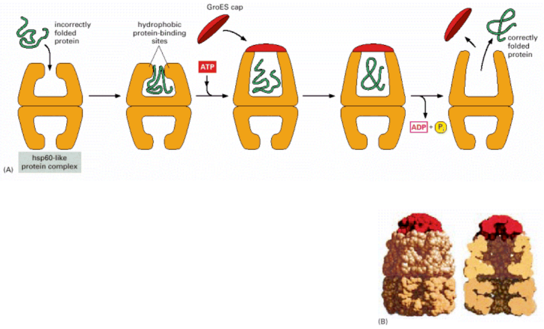

mRNA
5′
Signal peptide codons
AUG
Ribosome
3′
Cytoplasm
Membrane of endoplasmic reticulum
Signal peptide
Ribosome-receptor protein
Signal peptidase
Signal peptide
Secreted protein


ON-PATHWAY FOLDING
OFF-PATHWAY FOLDING
IRRETRIEVABLE ACCIDENTS
molten globule
chaperone catalysis
protease pathway
chaperone catalysis
correctly folded protein

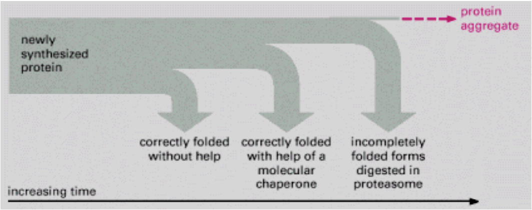
Hsp 70 family of chaperones mecdiate protein folding


ribosome
ATP
ADP
+
P_i
hsp70 machinery
ATP
ADP
hsp70 machinery
correctly folded protein
incorrectly folded protein

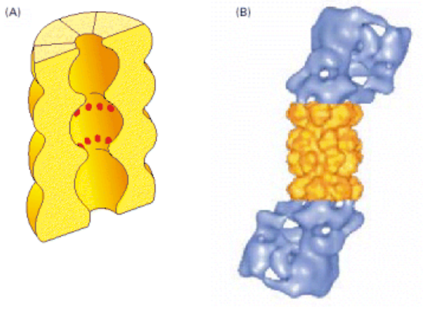
Hsp60, GroEL, TCP1 mediated protein folding


GroES cap
incorrectly folded protein
hydrophobic protein-binding sites
ATP
ADP + P_i
correctly folded protein
hsp60-like protein complex
(A)
(B)

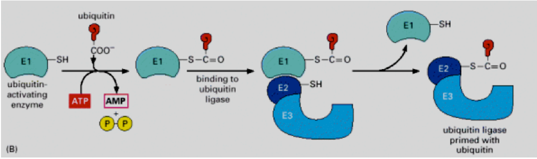
Cellular pathway to monitor protein folding


newly synthesized protein
protein aggregate
correctly folded without help
correctly folded with help of a molecular chaperone
incompletely folded forms digested in proteasome
increasing time

The structure of the proteosome

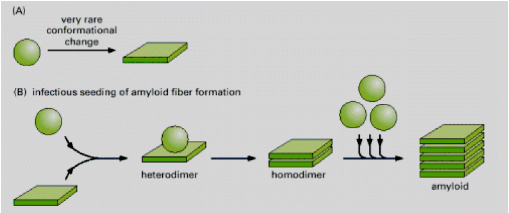


Controlled degredation of proteins - formation of ubiquitin ligase


ubiquitin
COO⁻
E1
—SH
ubiquitin-activating enzyme
ATP
AMP
P P
S—C=O
binding to ubiquitin ligase
E2
E3
ubiquitin ligase primed with ubiquitin
(B)

Model for basis of prion diseases

scrapie (sheep)
Creutzfeldt-Jacob disease (humans)
bovine spongiform encephalopathy (cattle)


(A)
very rare conformational change
(B) infectious seeding of amyloid fiber formation
heterodimer
homodimer
amyloid