

Lecture #19 – 10/19/01 – Dr. Wormington

Additional Features of the Genetic Code

• Codon Redundancy or Degeneracy Reflects the Relative Prevalence of an Amino Acid
e.g., Ser & Leu each have 6 codons whereas Tyr & Asp have only 2 apiece

• Redundant Codons Reduce Potential Deleterious Effects of Mutations

Particularly in 3rd position e.g., CCC, CCU, CCG & CCA All Code for Pro
Therefore, such mutations are *Silent or Synonymous*

• Several "functionally" equivalent Amino Acids Are Encoded by 2/3 matching codons

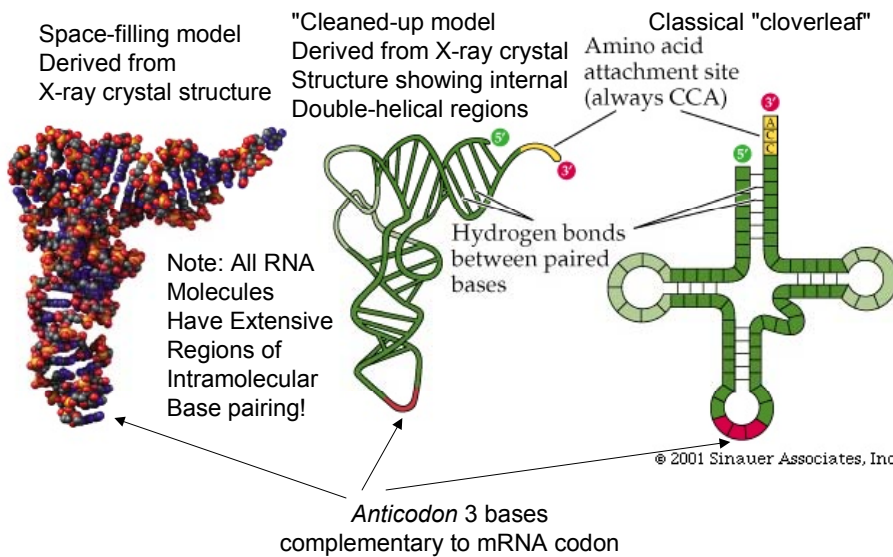
e.g., UUU (Phe), UUA (Leu), AUU (Ile) Are All Hydrophobic Amino Acids
AAA (Lys), AGA (Arg) Are Both Basic Amino Acids

Such Mutations are *Conservative Substitutions* & Unlikely to Affect Protein Function

| | | Second letter | | | | | |
|--------------|---|--|------------------------------------|---|---|------------------|--|
| | | U | C | A | G | | |
| First letter | U | UUU Phenyl-alanine UUC UUA Leucine UUG | UCU Serine UCC UCA UCG | UAU Tyrosine UAC UAA Stop codon UAG Stop codon | UGU Cysteine UGC UGA Stop codon UGG Tryptophan | U C A G | |
| | C | CUU Leucine CUC CUA CUG | CCU Proline CCC CCA CCG | CAU Histidine CAC CAA Glutamine CAG | CGU Arginine CGC CGA CGG | U C A G | |
| | A | AUU Isoleucine AUC AUA AUG Methionine; start codon | ACU Threonine ACC ACA ACG | AAU Asparagine AAC AAA Lysine AAG | AGU Serine AGC AGA Arginine AGG | U C A G | |
| | G | GUU Valine GUC GUA GUG | GCU Alanine GCC GCA GCG | GAU Aspartic acid GAC GAA Glutamic acid GAG | GGU Glycine GGC GGA GGG | U C A G | |

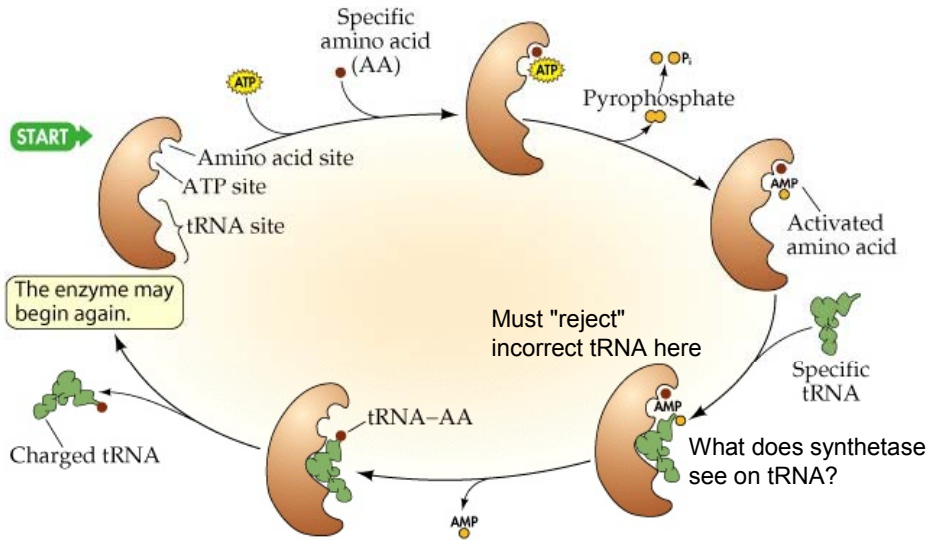
© 2001 Sinauer Associates, Inc.

3 Ways of Depicting Crick's "Adaptor Molecule"
transfer RNA aka tRNA



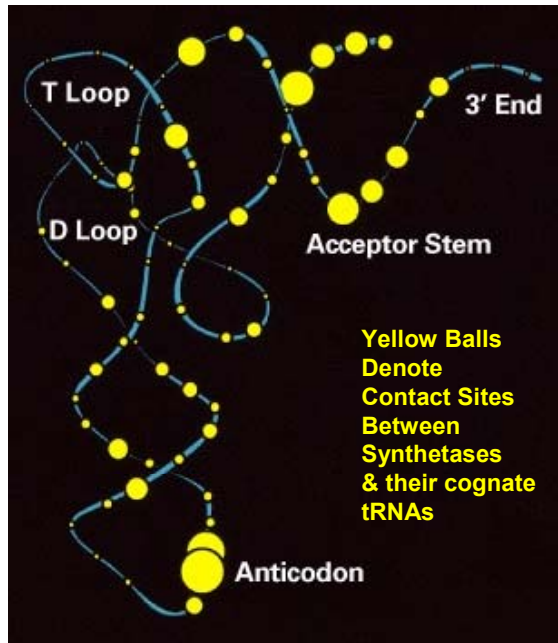
Activating Enzymes = tRNA Synthetases

"Charge" tRNAs with the Correct Amino Acid – Requires ATP • AMP + PP_i • 2P_i
 Charging Provides the **Only** Proofreading Step in Protein Synthesis



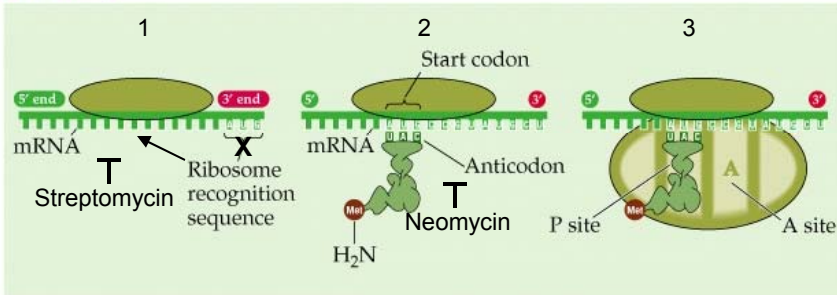
© 2001 Sinauer Associates, Inc.

The "Touchy-Feely" Side of tRNA Synthetases



Translation Initiation – The Big Picture

Initiation



© 2001 Sinauer Associates, Inc.

1. Small Ribosomal Subunit Recruited to mRNA by Binding Sequence *Preceding* AUG
Note: Fig. 12.10(1st step) is incorrect! The Small Ribosomal Subunit does not recognize RNA by binding directly to the 1st AUG! In general, it binds at an upstream recognition site & scans to the 1st AUG.

2. Anticodon of Methionine-Charged tRNA Recognizes AUG Codon

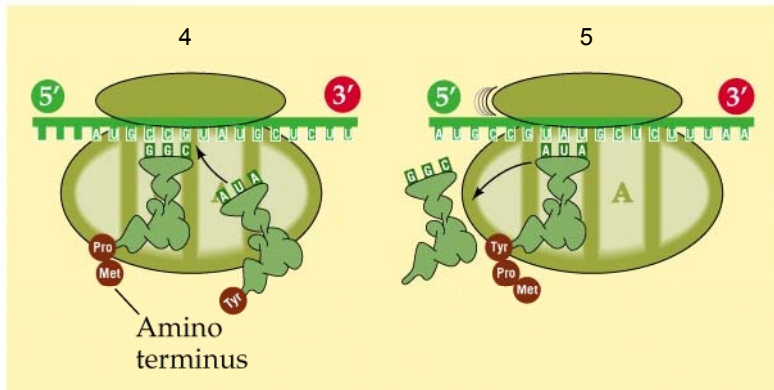
3. Large Ribosomal Subunit Binds - Methionine-tRNA Occupies P site

T = Specific step In Bacterial Translation Inhibited by Antibiotic

Translation Elongation cont'd

Previous Steps Repeated blah, blah, blah

Elongation



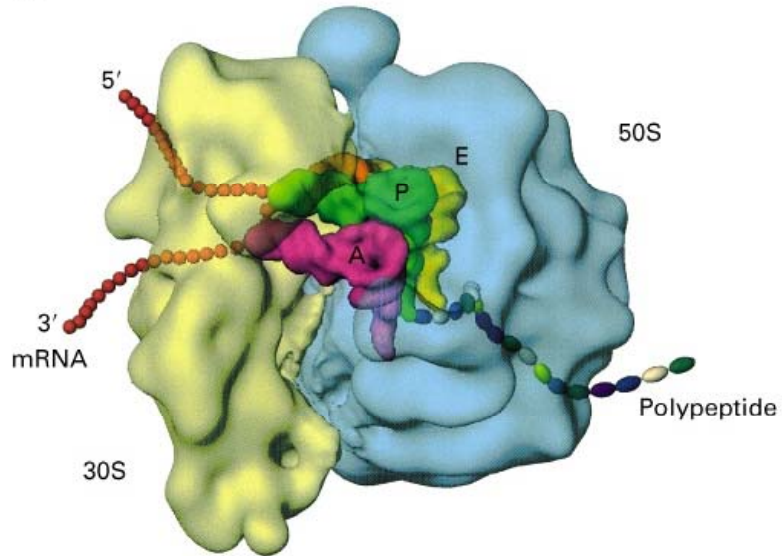
© 2001 Sinauer Associates, Inc.

4. Next amino acid-tRNA (Tyrosine-tRNA) Binds to Its Codon In Empty A Site

5. Peptide Bond Forms Between Tyr & Pro. Free Proline-tRNA Released
 Ribosome translocates to next codon.
 Met-Pro-Tyr-polypeptide attached to Tyr-tRNA moves to P site.

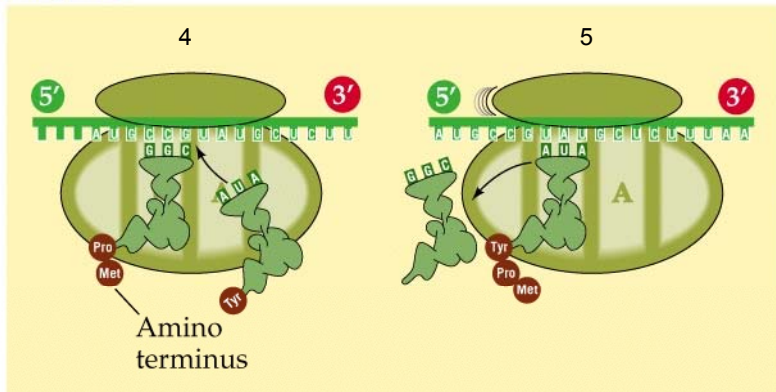
Structure of Ribosome-mRNA Complex During Elongation

(a)



Translation Elongation cont'd
Process repeats until...

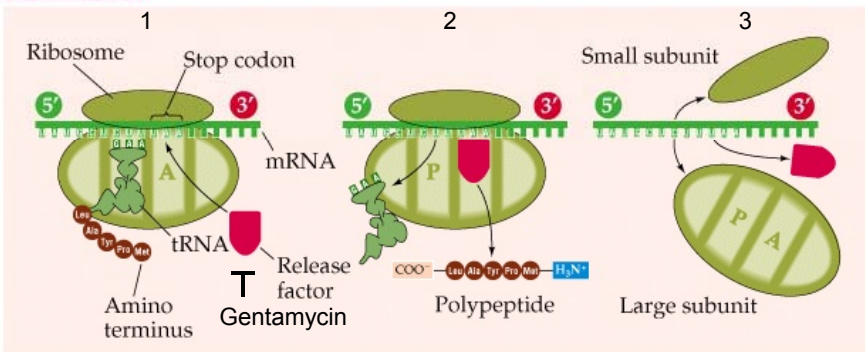
Elongation



© 2001 Sinauer Associates, Inc.

The End! Translation Termination

Termination

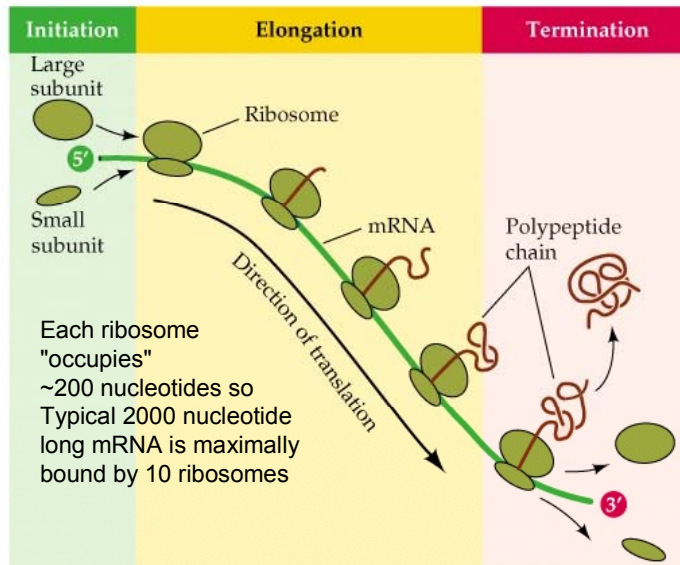


© 2001 Sinauer Associates, Inc.

1. *Release Factor* Recognizes Stop Codon in A Site
2. Release Factor Dissociates Completed Polypeptide from Last tRNA & Releases Both
3. mRNA, Large & Small Ribosomal Subunits All Dissociate From Each Other
Small Ribosomal Subunit Can Re-Bind Same mRNA or Bind "New" mRNA To Reinitiate

T = Step In Bacterial Translation Inhibited by Antibiotic

A Single mRNA Can Be Translated By Several Ribosomes Simultaneously
Generating a *Polyribosome* or *Polysome*



© 2001 Sinauer Associates, Inc.

Ribosome Is "Target-Rich" Environment To Direct Highly Specific Antibiotics
 Numerous rRNA & Protein Targets & Multiple Biochemical Steps
 Basis for Specificity?

12.2 Antibiotics that Inhibit Bacterial Protein Synthesis

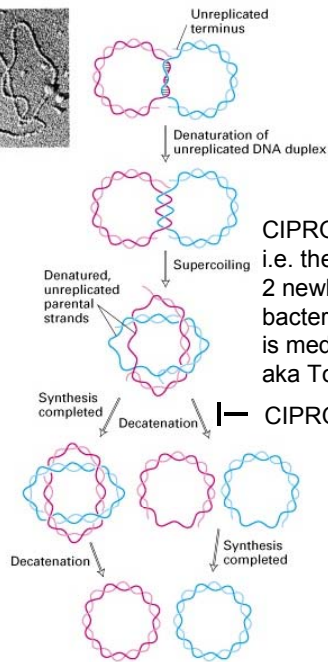
| ANTIBIOTIC | STEP INHIBITED |
|---------------|--------------------------------------|
| Chloromycetin | Formation of peptide bonds |
| Erythromycin | Translocation of mRNA along ribosome |
| Neomycin | Interactions between tRNA and mRNA |
| Streptomycin | Initiation of translation |
| Tetracycline | Binding of tRNA to ribosome |

Gentamycin Interaction between release factor and ribosome

© 2001 Sinauer Associates, Inc.

Note – Ciprofloxacin (CIPRO) does *not* Target the Ribosome
 But, It *does* target.....

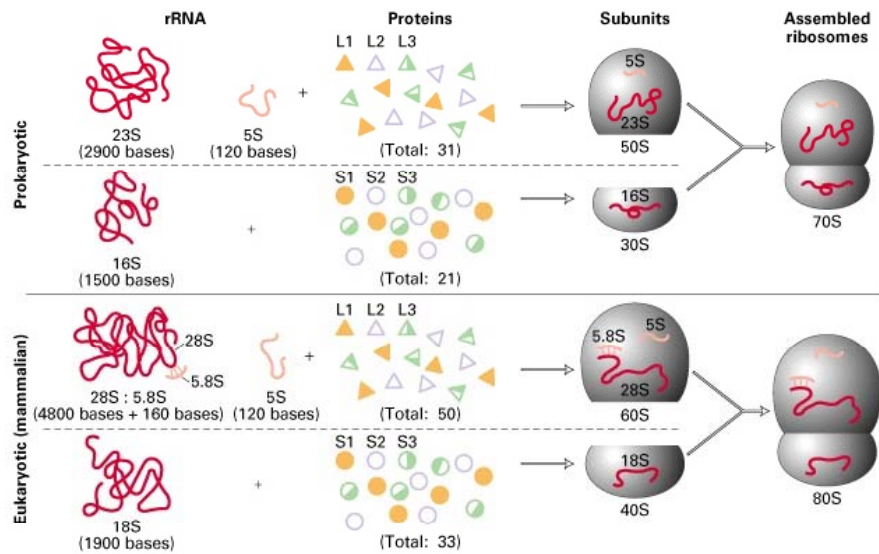
Catenated (Interlocked) circular chromosomes cannot be segregated during cell division



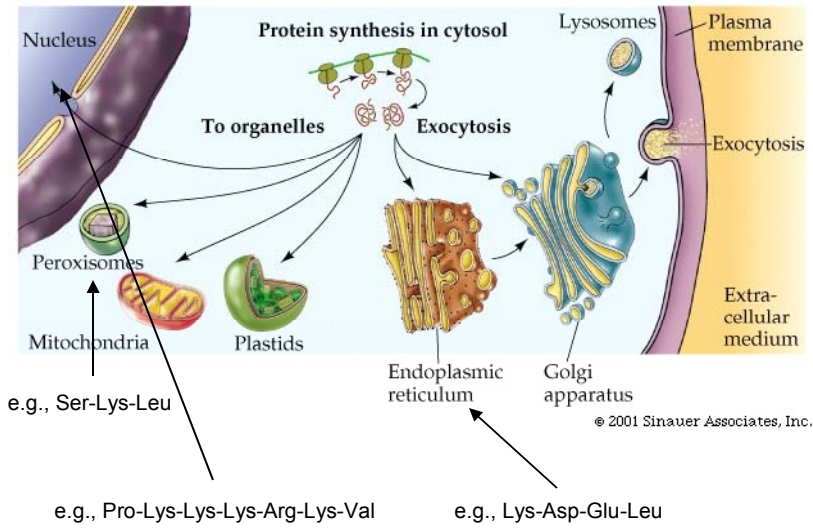
CIPRO inhibits Decatenation
 i.e. the separation of the 2 newly replicated bacterial chromosomes which is mediated by DNA Gyrase aka Topoisomerase

— CIPRO

Different rRNA and Protein Constituents
 Render Prokaryotic (e.g., bacterial), but not Eukaryotic (e.g., human) Ribosomes
 Sensitive to Certain Antibiotics



Specific Amino Acid Sequences Function as “Zip Codes” to Target Proteins
 To Appropriate Organelles & Subcellular Compartments
 Note: >30 Distinct Destinations In Typical Eukaryotic Cell!



Most Proteins Undergo At Least 1 of 3 Major Post-Translational Modifications
 To Regulate Stability, Subcellular Localization and Biological Activity
 As with Protein Localization, Post-Translational Modifications
 Are Directed by Specific Amino Acid Sequences Within Proteins

