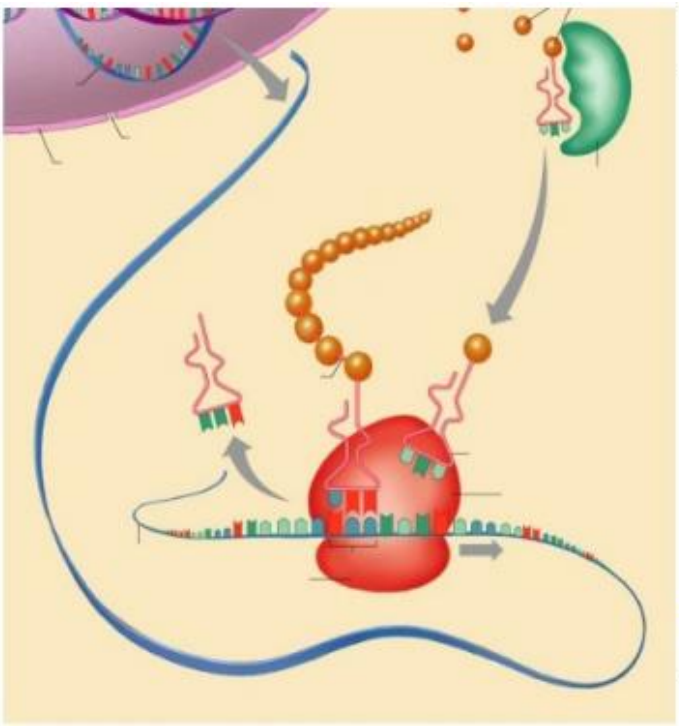
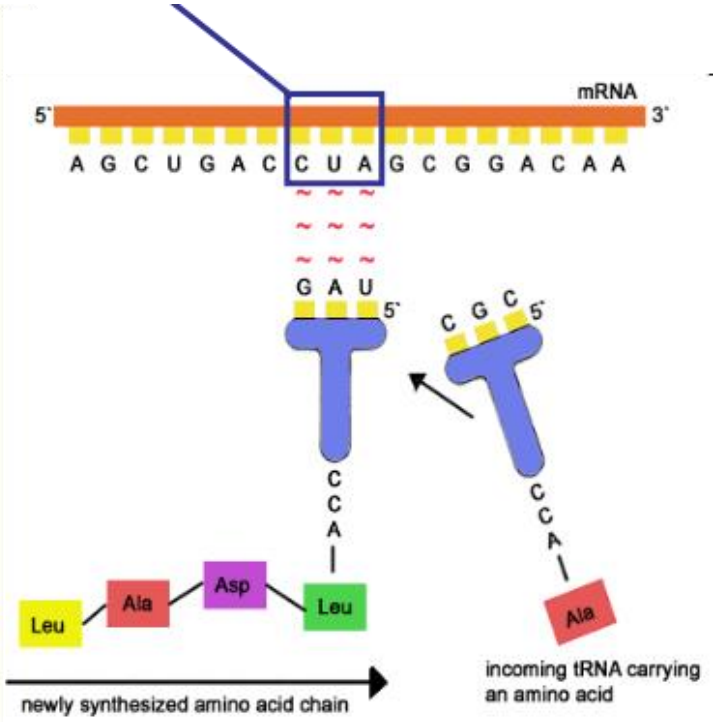
Translation or Protein Synthesis

Every three mRNA nucleotides (**codon**) specify an amino acid





tRNA have an **anticodon** region that specifically binds to its codon

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

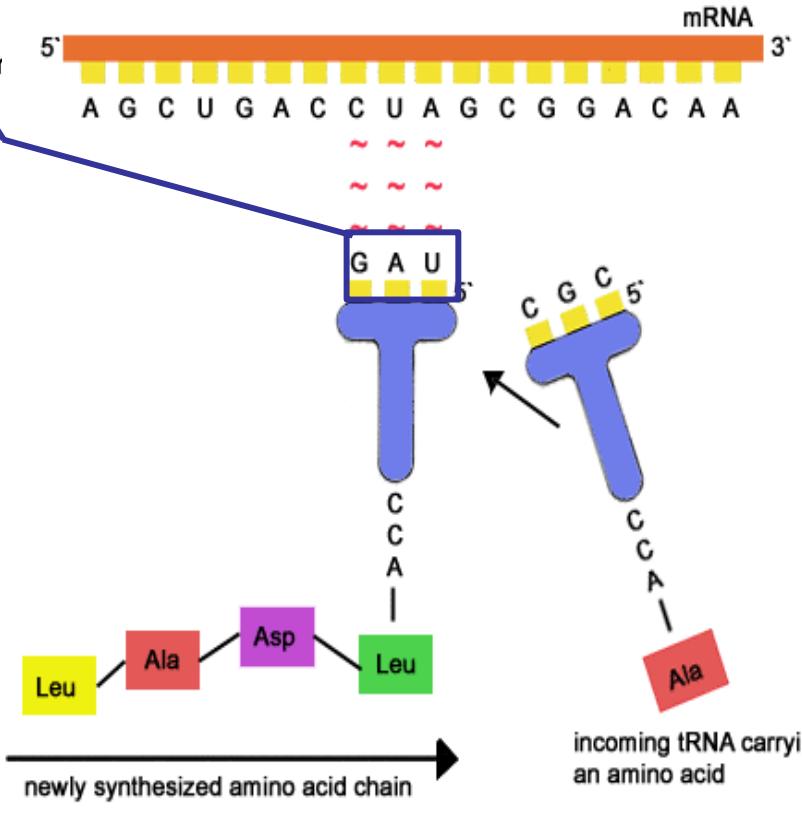
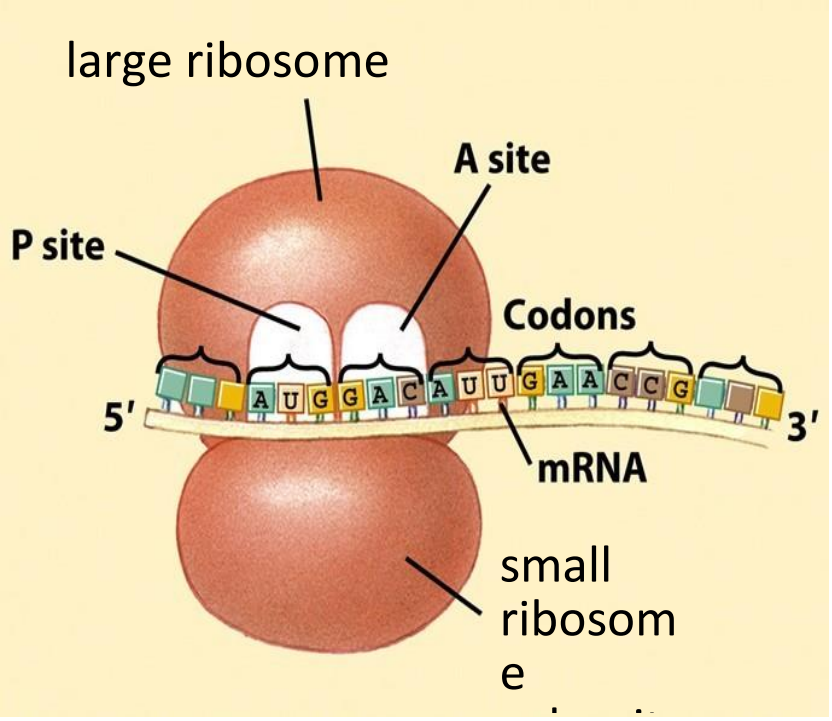


Figure 7-8 Microbiology, 7/e



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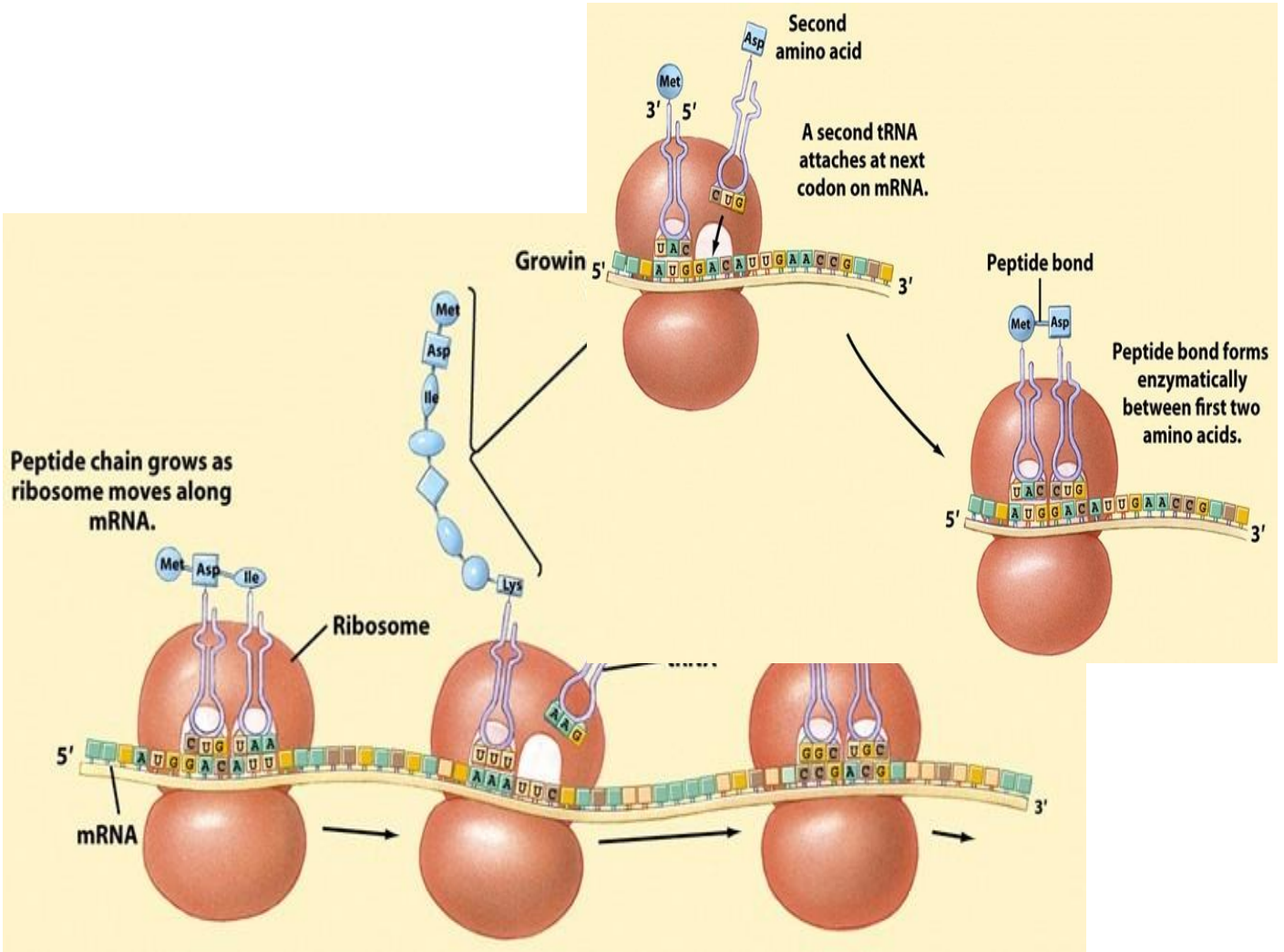


Translation:

Initiation

mRNA binds to a ribosome, and the transfer RNA corresponding to the START codon binds to this complex. Ribosomes are composed of 2 subunits (large and small), which come together when the messenger RNA attaches during the initiation process.

Elongation

Elongation: the ribosome moves down the messenger RNA, adding new amino acids to the growing polypeptide chain. The ribosome has 2 sites for binding transfer RNA. The first RNA with its attached amino acid binds to the first site, and then the transfer RNA corresponding to the second codon bind to the second site. The ribosome then removes the amino acid from the first transfer RNA and attaches it to the second amino acid. At this point, the first transfer RNA is empty: no attached amino acid, and the second transfer RNA has a chain of 2 amino acids attached to it.

Termination

The elongation cycle repeats as the ribosome moves down the messenger RNA, translating it one codon and one amino acid at a time.

The process repeats until a STOP codon is reached.

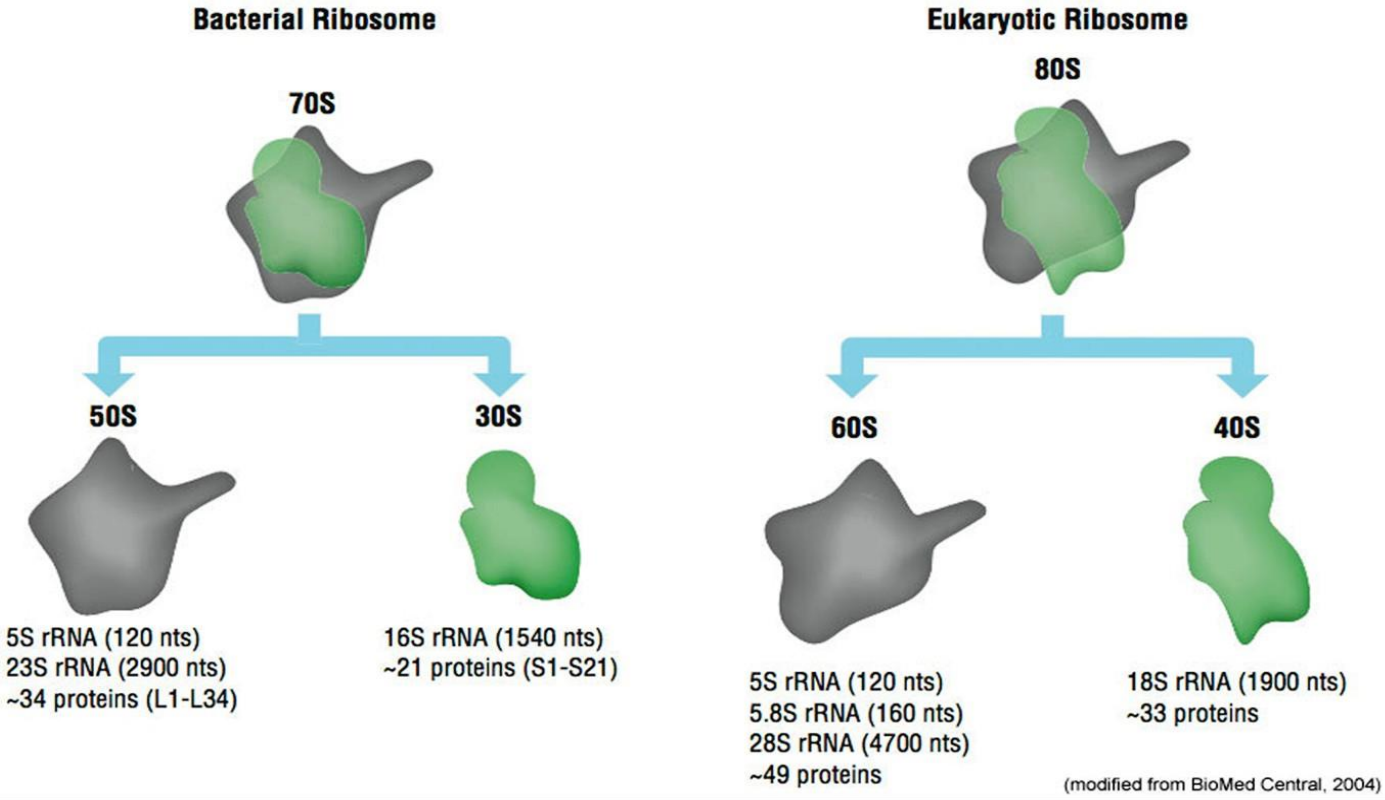
INHIBITOR OF PROTEIN SYNTHESIS

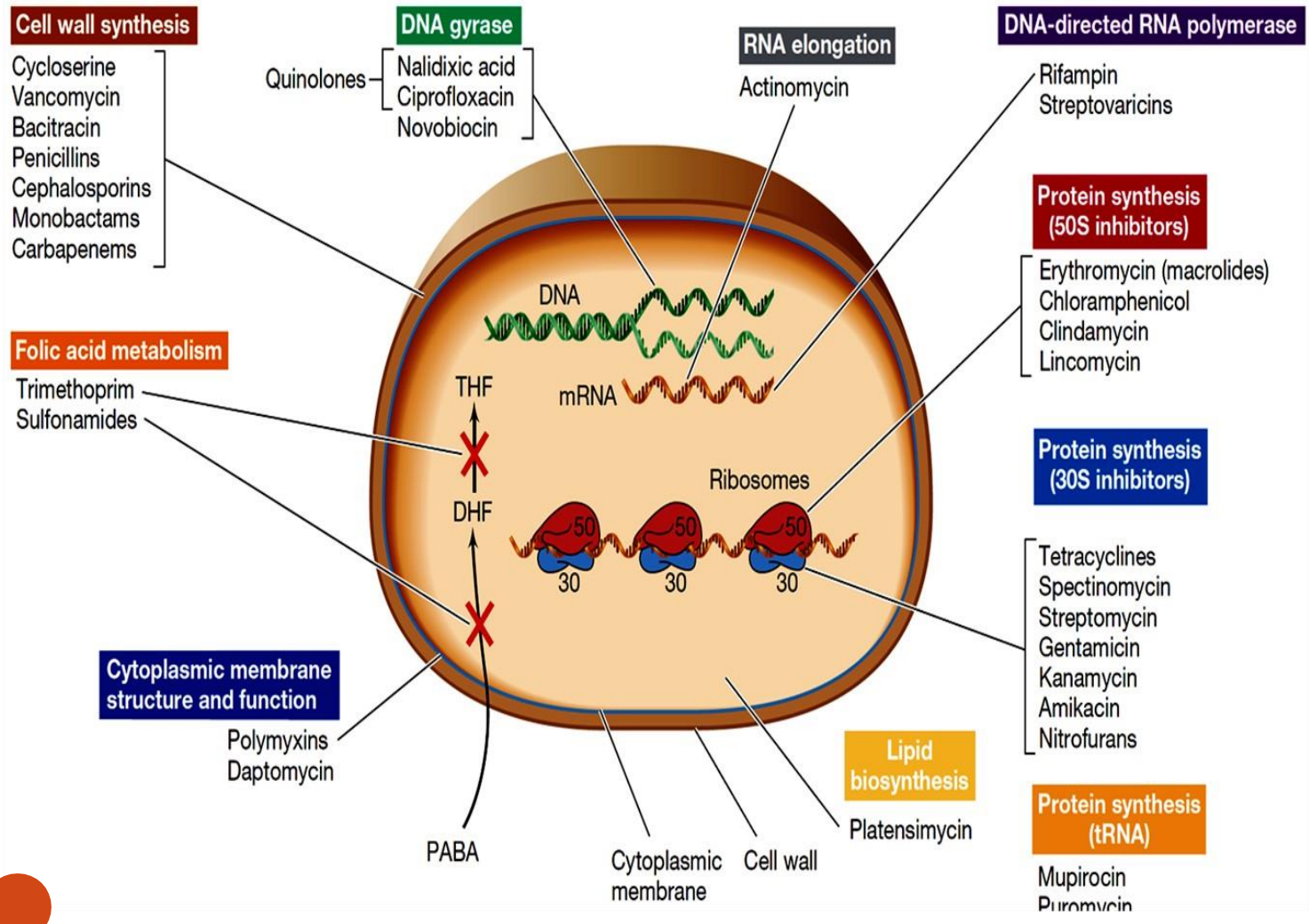
A protein synthesis inhibitor is a substance that stops or slows the growth or proliferation of bacterial cells by disrupting the processes to the generation of new proteins by targeting the bacterial ribosome.

Protein synthesis inhibitors usually act at the ribosome level, taking advantage of the major differences between prokaryotic and eukaryotic ribosome structures.

Protein synthesis inhibitors work at different stages of prokaryotic mRNA translation into proteins like initiation, elongation (including aminoacyl tRNA entry, proofreading, peptidyl transfer, and ribosomal translocation), and termination.

Ribosomes


Bacterial Ribosome
70S
50S
30S
5S rRNA (120 nts)
23S rRNA (2900 nts)
~34 proteins (L1-L34)
16S rRNA (1540 nts)
~21 proteins (S1-S21)
Eukaryotic Ribosome
80S
60S
40S
5S rRNA (120 nts)
5.8S rRNA (160 nts)
28S rRNA (4700 nts)
~49 proteins
18S rRNA (1900 nts)
~33 proteins
(modified from BioMed Central, 2004)


Cell wall synthesis
Cycloserine
Vancomycin
Bacitracin
Penicillins
Cephalosporins
Monobactams
Carbapenems
DNA gyrase
Quinolones
Nalidixic acid
Ciprofloxacin
Novobiocin
RNA elongation
Actinomycin
DNA-directed RNA polymerase
Rifampin
Streptovaricins
Protein synthesis (50S inhibitors)
Erythromycin (macrolides)
Chloramphenicol
Clindamycin
Lincomycin
Folic acid metabolism
Trimethoprim
Sulfonamides
DNA
mRNA
THF
DHF
Ribosomes
50
30
Protein synthesis (30S inhibitors)
Tetracyclines
Spectinomycin
Streptomycin
Gentamicin
Kanamycin
Amikacin
Nitrofurans
Cytoplasmic membrane structure and function
Polymyxins
Daptomycin
PABA
Cytoplasmic membrane
Cell wall
Lipid biosynthesis
Platensimycin
Protein synthesis (tRNA)
Mupirocin
Puromycin

CLASSIFICATION OF PROTEIN INHIBITOR

1 TETRACYCLINES

- Demeclocycline DECLOMYCIN
- Doxycycline VIBRAMYCIN
- Minocycline MINOCIN
- Tetracycline SUMYCIN

2 GLYCYLCYCLINES

- Tigecycline TYGACIL

3 AMINOGLYCOSIDES

- Amikacin AMIKIN, OTHERS
- Gentamicin GARAMYCIN
- Neomycin NEO-FRADIN
- Streptomycin STREPTOMYCIN
- Tobramycin TOBREX

4 MACROLIDES/KETOLIDES

- Azithromycin ZITHROMAX
- Clarithromycin BIAXIN
- Erythromycin E-MYCIN
- Telithromycin KETEK

5 OTHERS

- Chloramphenicol CHLOROMYCETIN
- Clindamycin CLEOCIN
- Linezolid ZYVOX
- Quinupristin/Dalfopristin SYNERCID