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PROTEIN SYNTHESIS INHIBITOR

BY

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

A ribosome is a biological machine that utilizes protein dynamics on nanoscales to translate RNA into proteins. While a broad interpretation of this definition could be used to describe nearly any antibiotic, in practice, it usually refers to substances that act at the ribosome level (either the ribosome

itself or the translation factor), taking advantages of the major differences between prokaryotic and eukaryotic ribosome structures.

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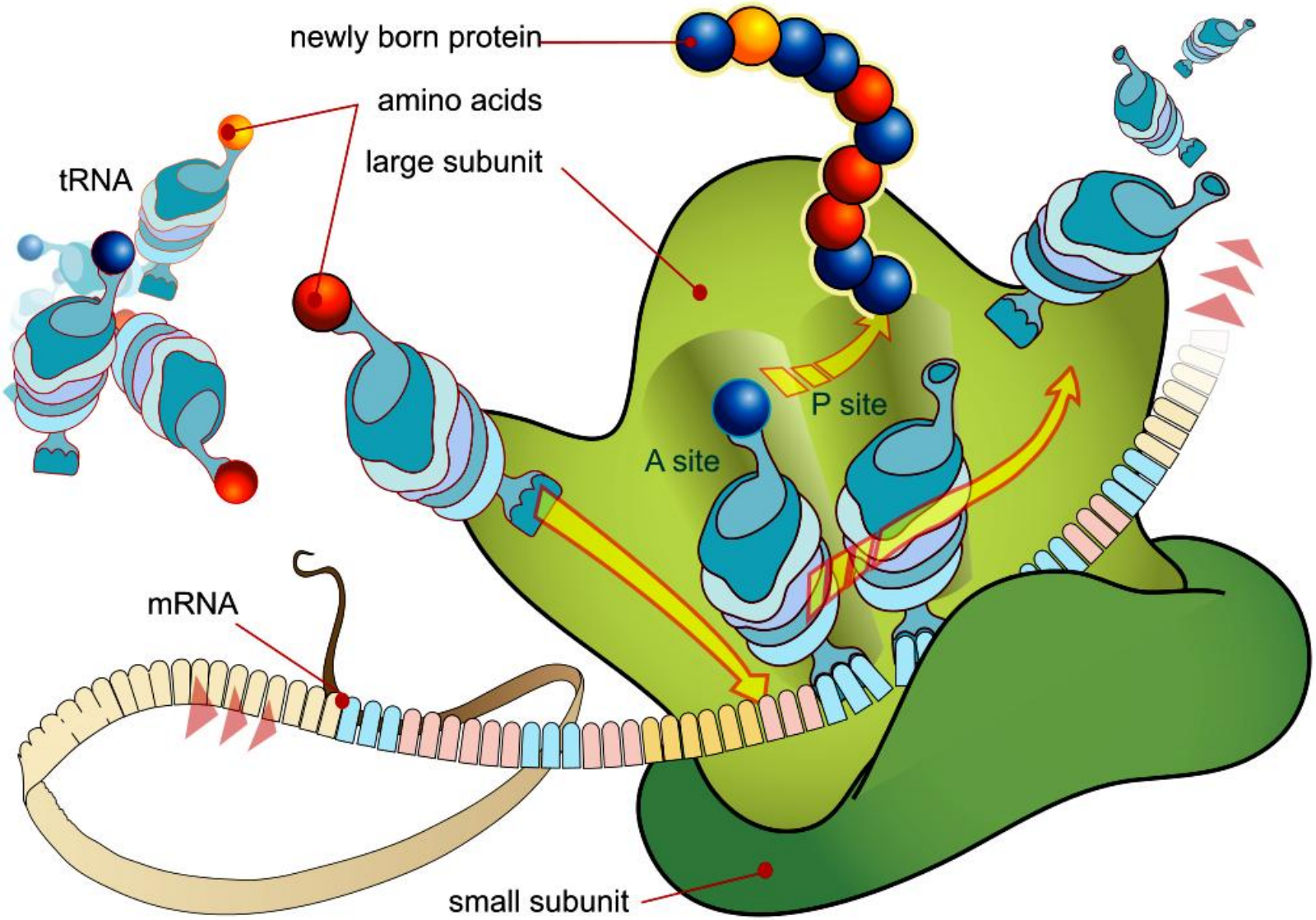

Mechanism:

In general, 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 as follows:

- Rifamycin inhibits prokaryotic DNA transcription into mRNA by inhibiting DNA-dependent RNA polymerase by binding its beta-subunit.

Initiation

- Linezolid acts at the initiation stage, probably by preventing the formation of the initiation complex, although the mechanism is not fully understood.

Ribosome assembly

- Aminoglycosides prevent ribosome assembly by binding to the prokaryotic 30S ribosomal subunit.

Aminoacyl tRNA entry

- Tetracyclines and Tigecycline (a glycylcycline related to tetracyclines) block the A site on the ribosome, preventing the binding of aminoacyl tRNAs.

Proofreading

- Aminoglycosides, among other potential mechanisms of action, interfere with the proofreading process, causing increased rate of error in synthesis with premature termination.

Peptidyl transfer

- Chloramphenicol blocks the peptidyl transfer step of elongation on the 50S ribosomal subunit in both bacteria and mitochondria.
- Macrolides (as well as inhibiting *ribosomal translocation* and other potential mechanisms) bind to the 50s ribosomal subunits, inhibiting *peptidyl transfer*.
- Quinupristin/dalfopristin act synergistically, with dalfopristin, enhancing the binding of quinupristin, as well as

inhibiting *peptidyl transfer*. Quinupristin binds to a nearby site on the 50S ribosomal subunit and prevents elongation of the polypeptide, as well as causing incomplete chains to be released.

- Geneticin, also called G418, inhibits the elongation step in both prokaryotic and eukaryotic ribosomes.

Ribosomal translocation

- Macrolides, clindamycin and aminoglycosides (with all these three having other potential mechanisms of action as well), have evidence of inhibition of ribosomal translocation.
- Fusidic acid prevents the turnover of elongation factor G (EF-G) from the ribosome.
- Ricin inhibits elongation by enzymatically modifying an rRNA of the eukaryotic 60S ribosomal subunit.

Termination

- Macrolides and clindamycin (both also having other potential mechanisms) cause premature dissociation of the peptidyl-tRNA from the ribosome.
- Puromycin has a structure similar to that of the tyrosinyl aminoacyl-tRNA. Thus, it binds to the ribosomal A site and participates in peptide bond formation, producing peptidyl-puromycin. However, it does not engage in

translocation and quickly dissociates from the ribosome, causing a premature termination of polypeptide synthesis.

- Streptogramins also cause premature release of the peptide chain.

Protein synthesis inhibitors of unspecified mechanism

- Retapamulin
- Mupirocin
- Fusidic acid

Binding site

The following antibiotics bind to the 30S subunit of the ribosome:

- Aminoglycosides
- Tetracyclines

The following antibiotics bind to the 50S ribosomal subunit:

- Chloramphenicol
- Clindamycin

- Linezolid (an oxazolidinone)
- Macrolides
- Telithromycin
- Streptogramins
- Retapamulin

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THANK YOU