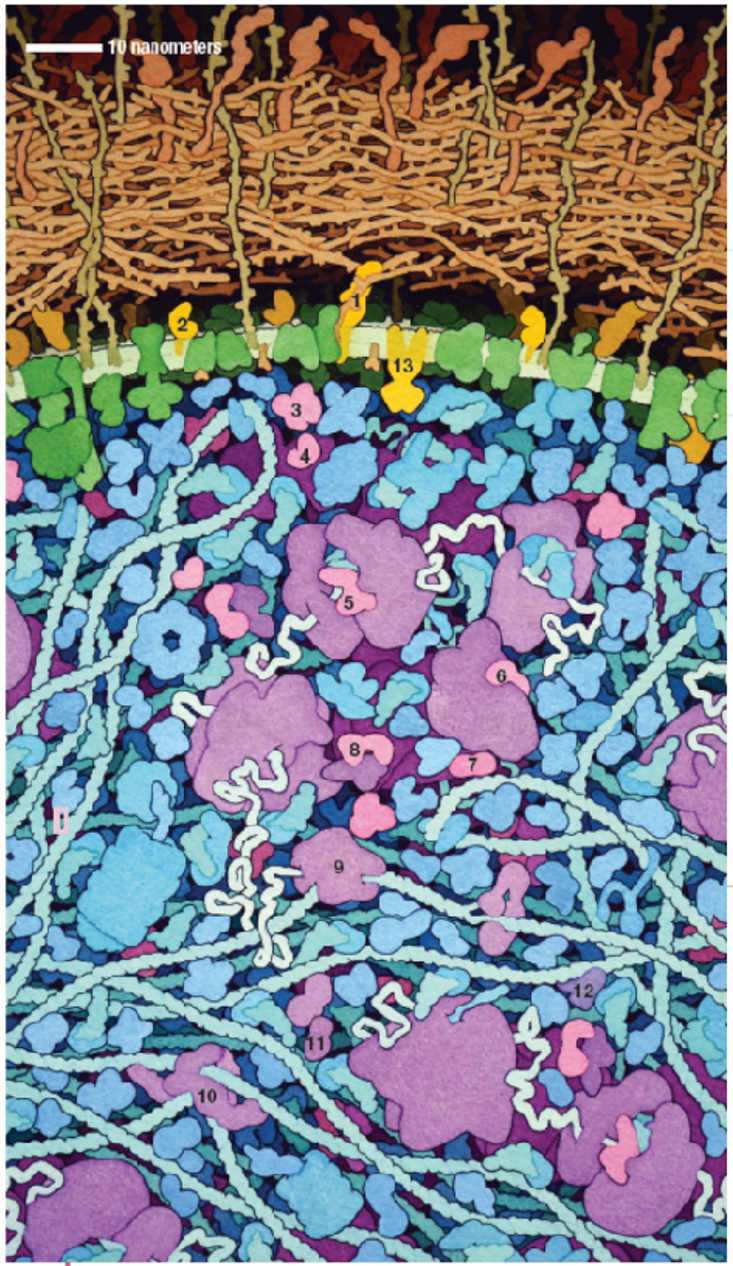
How bacteria evolve resistance to antibiotics.

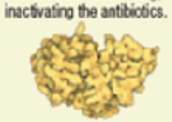


CELL WALL: essential protective layer composed of a crosslinked network of peptidoglycan chains

BETA-LACTAM ANTIBIOTICS such as penicillin and methicillin, contain an extremely reactive beta-lactam ring that attacks PBPs (penicillin-binding proteins) that build the cell wall.

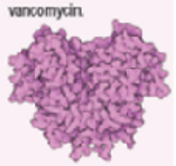
1 1mwu
PBP2a is a mutated form of PBP. It binds weakly to beta-lactam antibiotics (red), so it can cross-link the peptidoglycan chains in the presence of antibiotics.

2 1pio
Beta-lactamases break the reactive beta-lactam ring, inactivating the antibiotics.

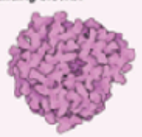


VANCOMYCIN sequesters the building blocks of the cell wall so that they can no longer be crosslinked to form a tough protective layer.

3 1e4e
VanA builds the new type of building block that does not bind vancomycin.



4 1r44
VanX breaks down any of the original building blocks.



CELL MEMBRANE: filled with protein pumps and enzymes that build the cell wall

DETECTING AND AVERTING DANGER

Cells use **REPRESSOR PROTEINS** to regulate the genes involved in resistance, so that the proteins are made only when needed.

12 2d45
The **MecI repressor** regulates the gene that encodes PBP2a.

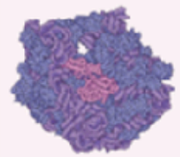
MULTIDRUG RESISTANT TRANSPORTERS are expressed by bacteria when toxins are detected.

13 2dnj
Sav1866 uses a scissor-like motion to transport antibiotics across the cell membrane.

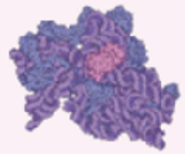
CYTOPLASM: filled with DNA, ribosomes, enzymes, and other proteins key to bacterial life cycle

MACROLIDES and **AMINOGLYCOSIDES** attack ribosomes, blocking manufacture of new proteins.

5 3j9y
TetM protein displaces the macrolide erythromycin, restoring the ribosome to its normal function.

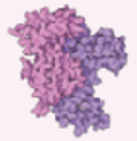


6 4ox9
rRNA Methyltransferases modify ribosomal RNA, providing resistance against aminoglycosides like streptomycin

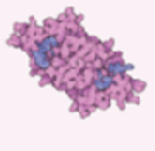


FUSIDIC ACID glues elongation factor G (EF-G) to ribosomes, stalling protein synthesis.

8 2mzw
FusB protein binds to EF-G and protects it from fusidic acid.



7 1bc4
Aminoglycoside acetyltransferases modify antibiotics, making them unable to bind to ribosomes.

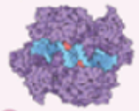


RIFAMPICIN, QUINOLINES and **ANTIFOLATES** attack essential enzymes in bacteria.

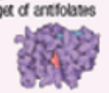
Resistance occurs through mutations that block the antibiotic binding but allow the enzyme to function.

9 5uhc
RNA Polymerase
Target of rifampicin

10 2k6f
Topoisomerase
Target of quinolines



11 2w9s
Dihydrofolate Reductase
Target of antifolates

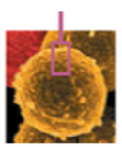


Superbugs!

ANTIBIOTICS are one of the miracles of modern medicine, allowing us to fight infections by pathogenic bacteria. Antibiotics attack essential molecular machines in bacteria, stopping or slowing their action, ultimately slowing growth or killing the cell.

RESISTANCE to antibiotics is posing a new danger to our health care. Infections by resistant bacteria are difficult to treat as they evolved proteins that destroy or modify antibiotics, or evade the drugs.

EVOLUTION of resistance is very fast in bacteria as they multiply rapidly to generate large populations. Antibiotics can kill susceptible strains, leaving resistant ones to proliferate.



Scanning electron micrograph of methicillin-resistant *Staphylococcus aureus* by NIAID used under CC BY 2.0

Superbugs such as MRSA (METHICILLIN-RESISTANT *STAPHYLOCOCCUS AUREUS*), shown in full on the EM-scan on the left and in detail in the illustration above, have found ways to evade almost all current antibiotics. Medical researchers are now using protein structures to search for new ways to fight them.

Use the PDB IDs (*e.g.*, 4ox9) to explore the resistance proteins shown in this poster in 3D and access more educational materials about antimicrobial resistance:

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