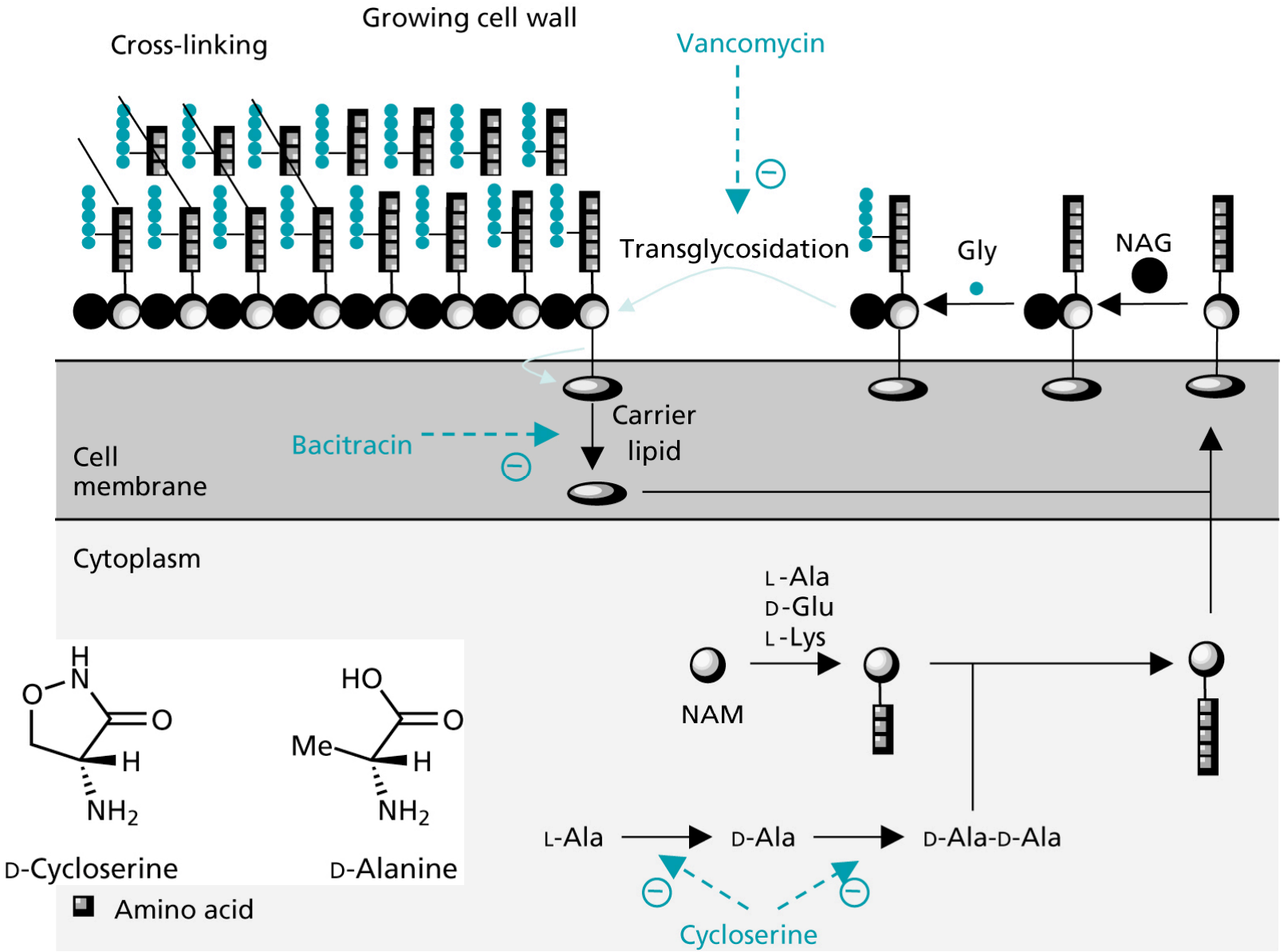
Topic 8-2 Other Antibiotics

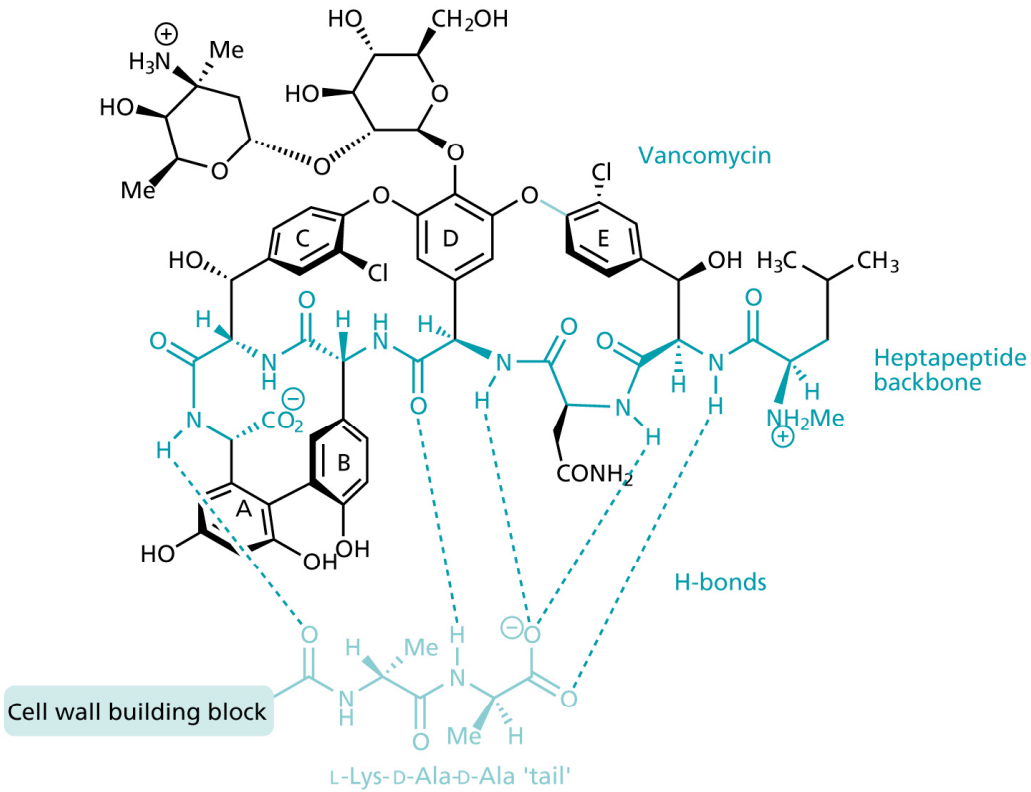
Ch 16 Patrick

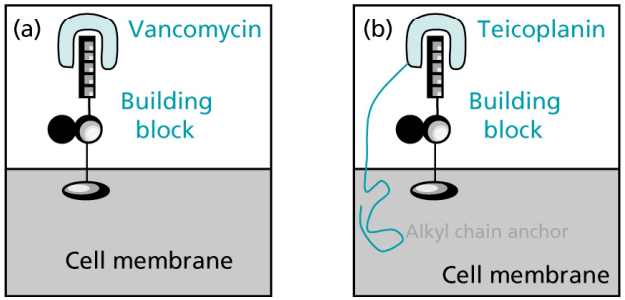
P157- Infectious disease chapter- Corey

Other cell wall inhibitors

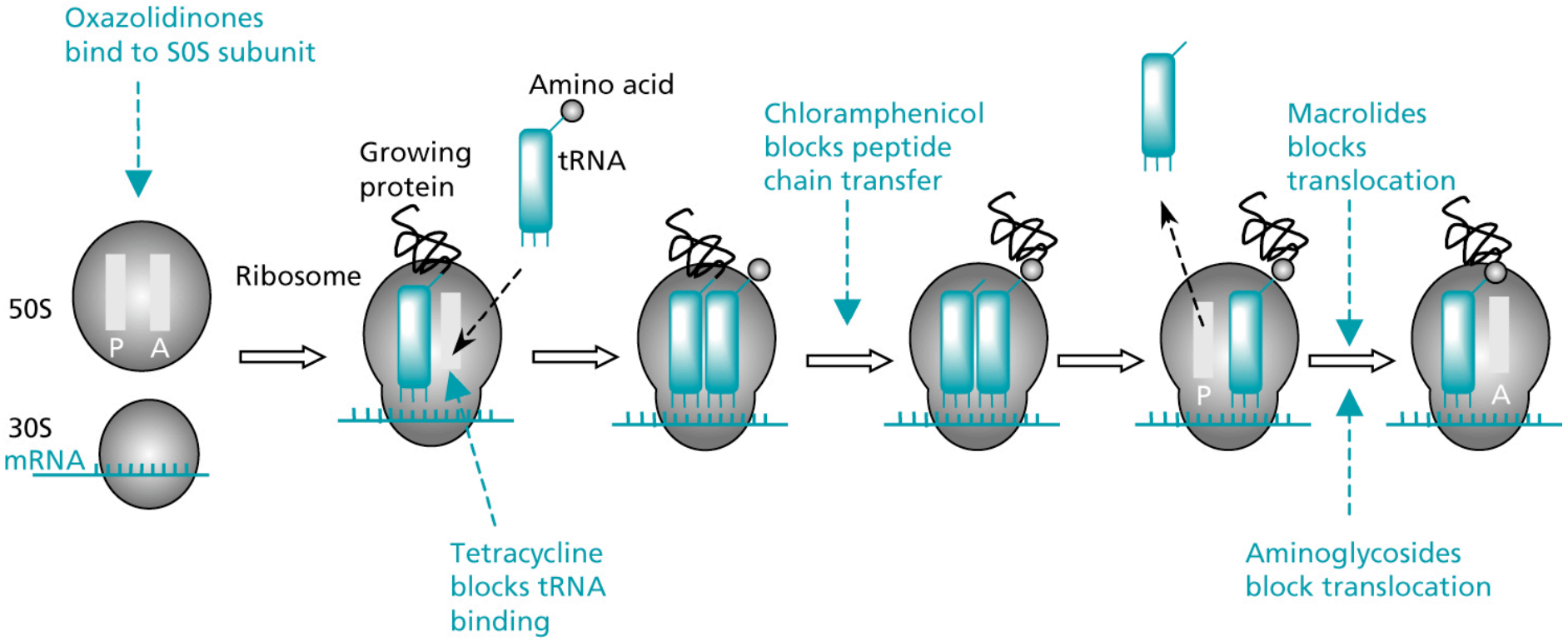


Vancomycin

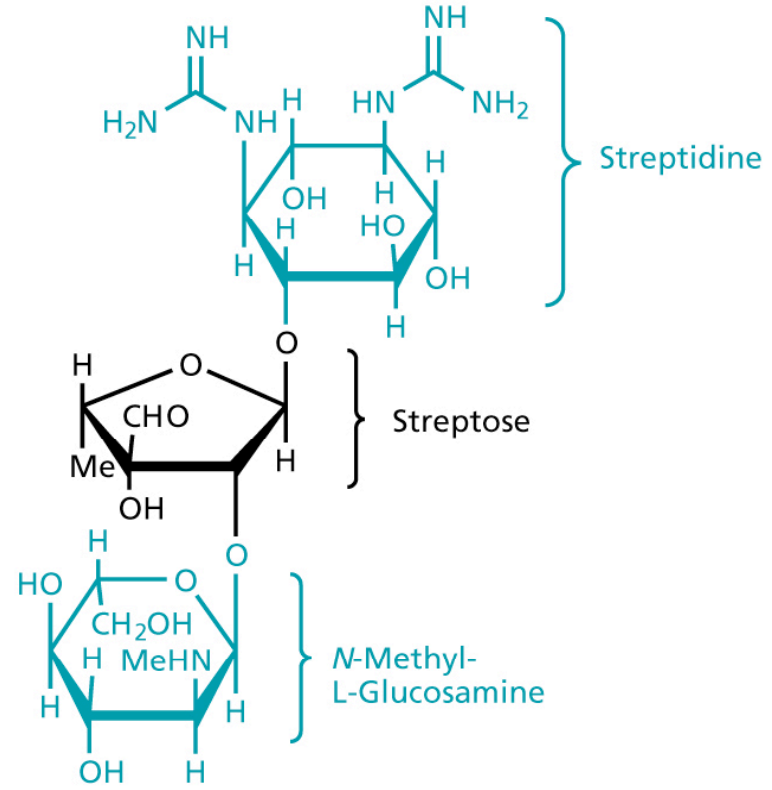

Vancomycin
Heptapeptide backbone
H-bonds
Cell wall building block
L-Lys-D-Ala-D-Ala 'tail'


(a)
Vancomycin
Building block
Cell membrane
(b)
Teicoplanin
Building block
Alkyl chain anchor
Cell membrane

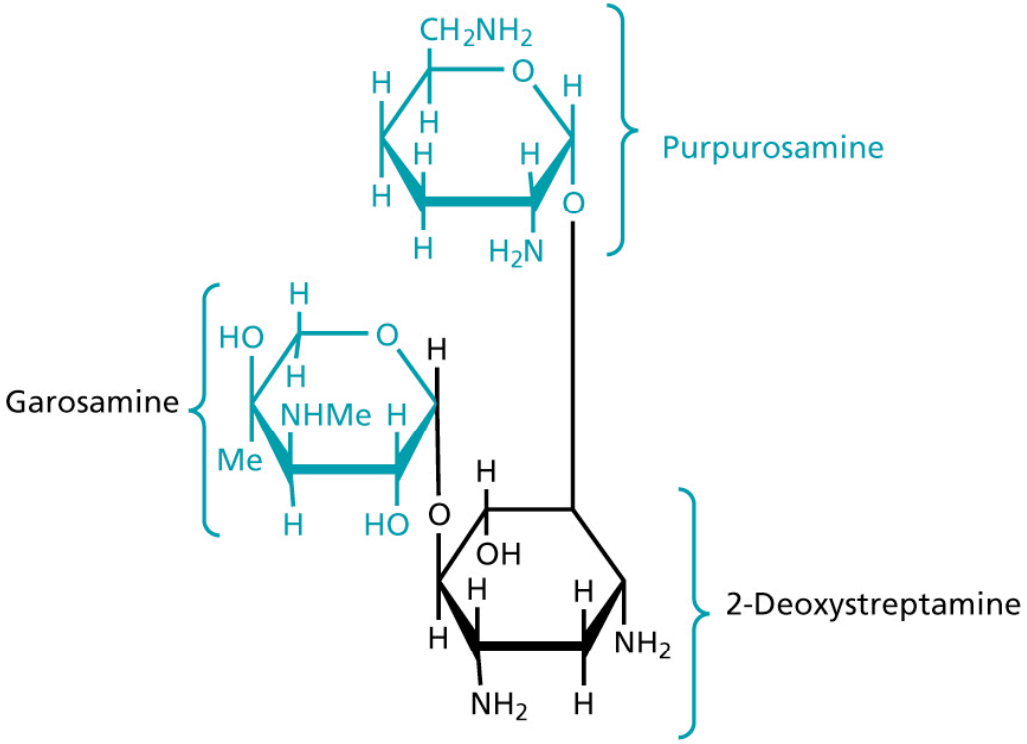
Protein synthesis inhibitors



Protein synthesis translation inhibitors

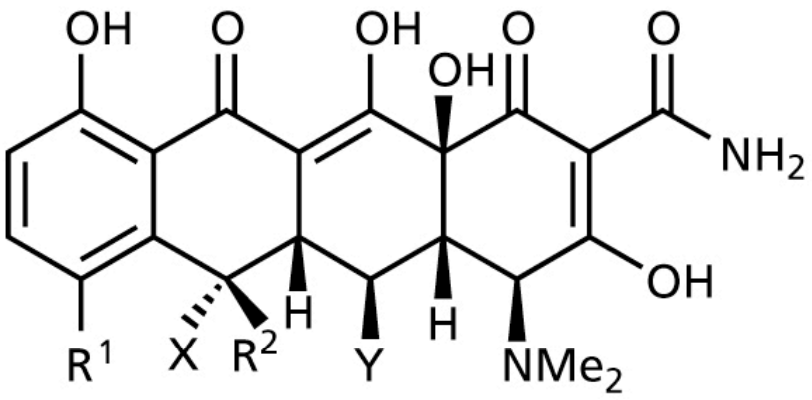


Streptomycin (from *Streptomyces griseus*)

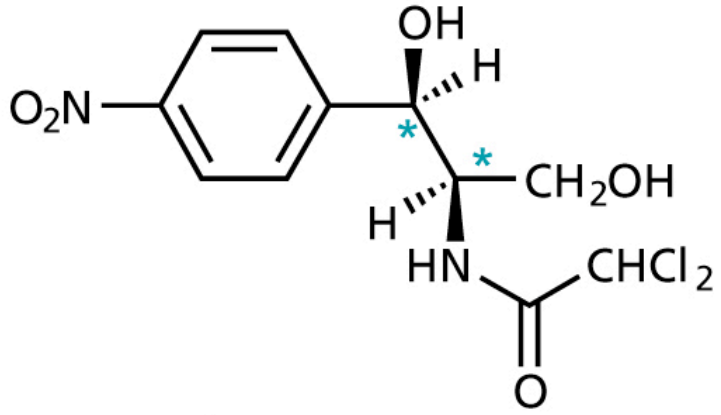


Gentamicin C1a

Protein synthesis translation inhibitors

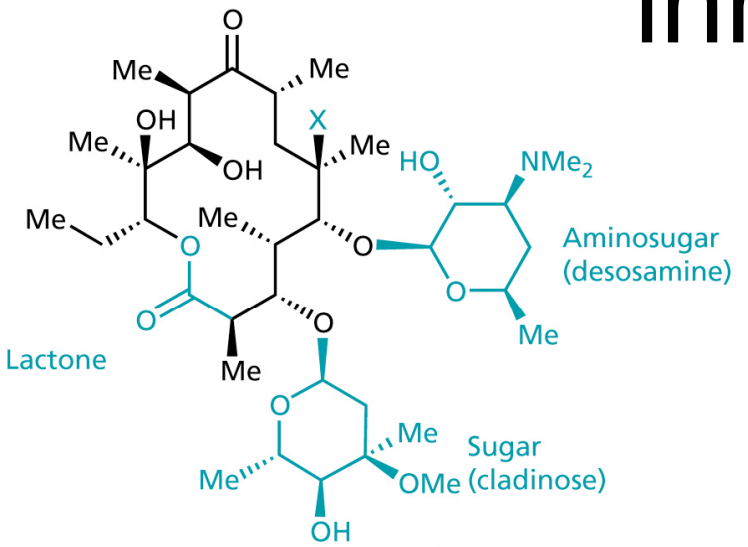


Chlortetracyclin (Aureomycin) (R^1 = Cl, R^2 = MeX = OH, Y = H)
Tetracycline (R^1 = H, R^2 = MeX = OH, Y = H)
Doxycycline (Vibramycin) (R^1 = H, R^2 = MeX = H, Y = OH)
Demeclocycline (R^1 = Cl, R^2 = H, X = OH, Y = H)

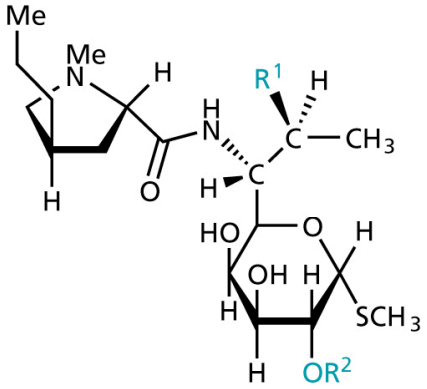


Chloramphenicol

Protein synthesis translation inhibitors



Erythromycin; X = OH
Clarithromycin; X = OMe

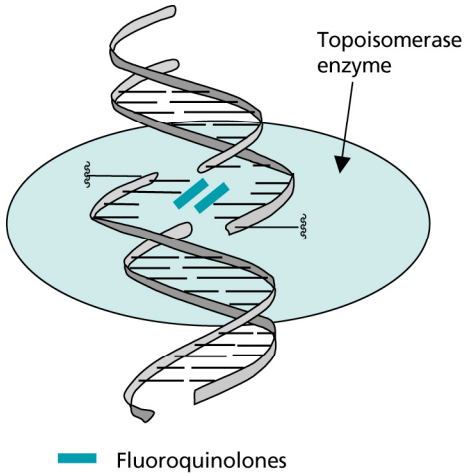


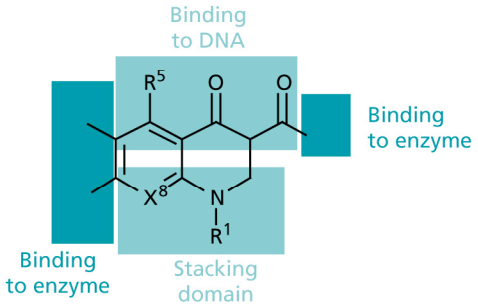
Lincomycin $R^1 = OH$, $R^2 = H$
Clindamycin $R^1 = Cl$, $R^2 = H$
Clindamycin phosphate $R^1 = Cl$, $R^2 = PO_3^{2-}$

Erythromycin

- Binds 50S ribosome
- Low toxicity
- Enteric coated to prevent acid damage(ketal formation)

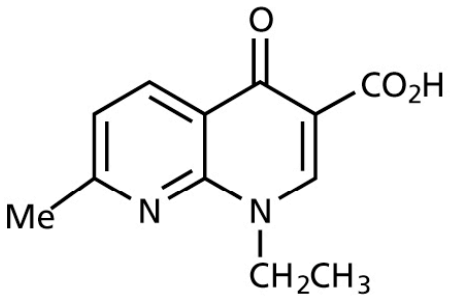
Transcription and replication inhibitors



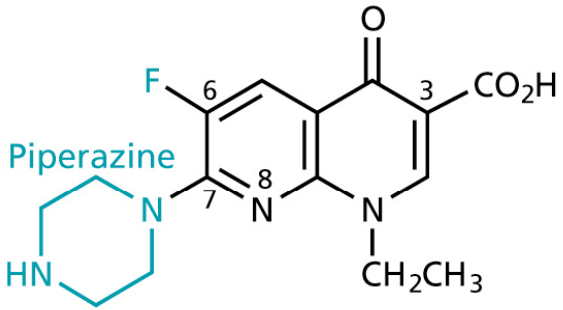


Quinoline antibiotics

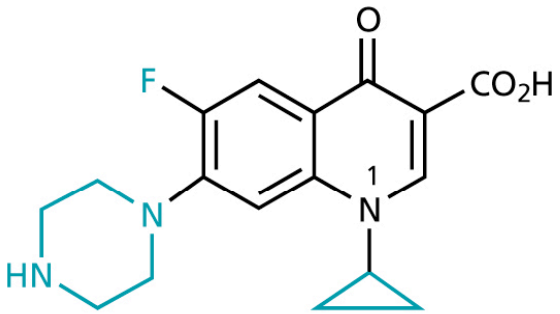
- Topo inhibitors
- Gr + and Gr- esp *Pseudomona*
- Cipro is one of the best broad spectrum antibiotics
- Used for resistant strains
- Resistance forms due to efflux pumps mostly



Nalidixic acid



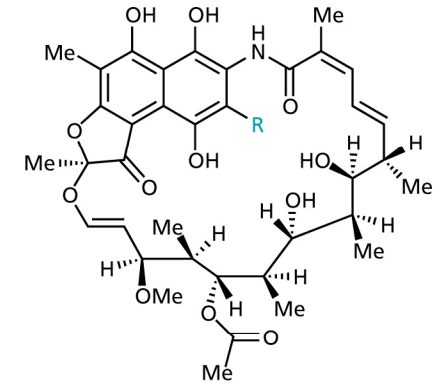
Enoxacin

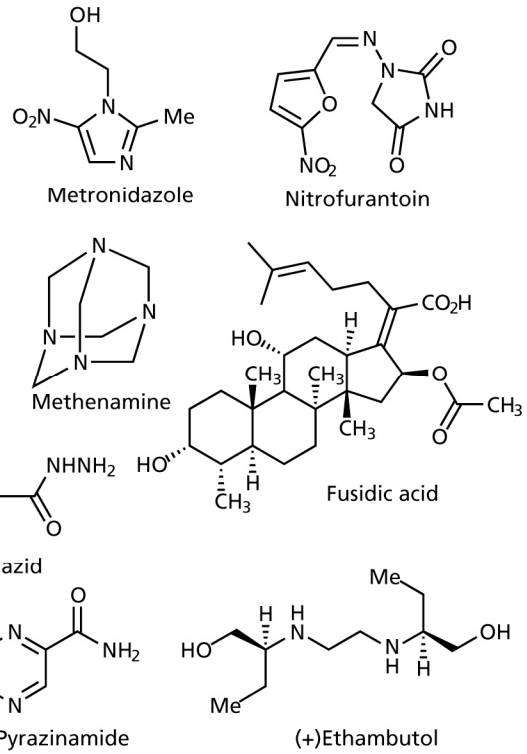


Ciprofloxacin

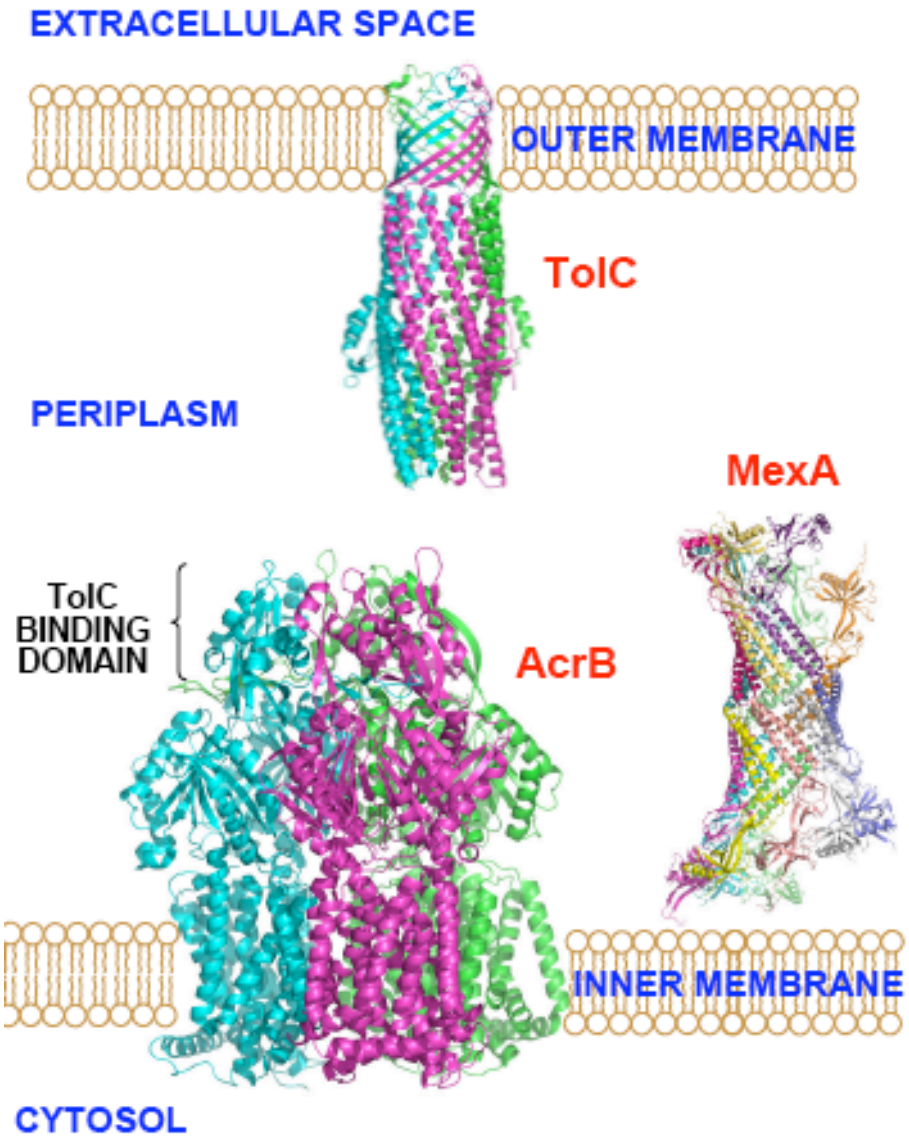
Rifamycins

- RNA polymerase inhibitor, Gr+ activity
- Used for tuberculosis, leprosy and resistant bacterial strains
- Can adversely effect other drugs (like HIV protease) by inducing CYP3A



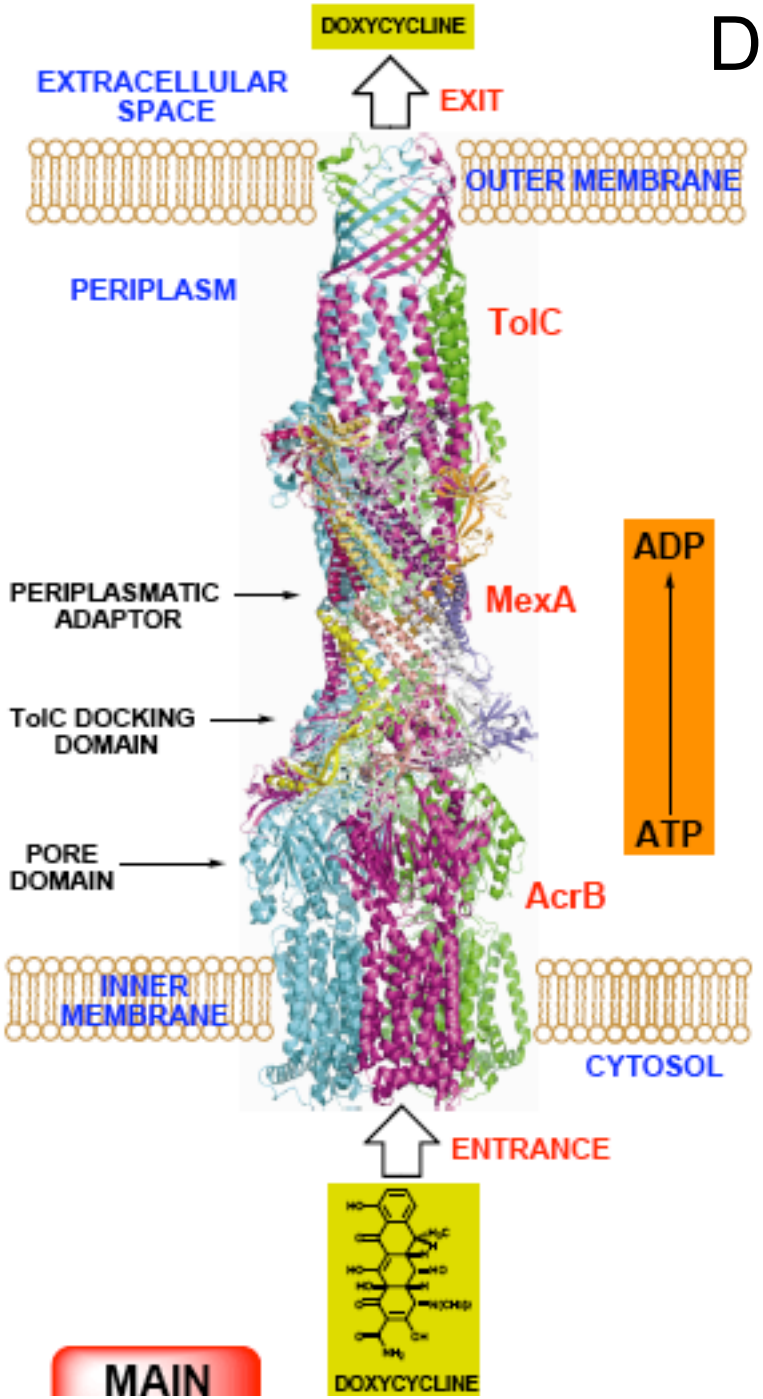


Drug resistance pumps



A representation of the structures of the three drug efflux pump components (resting state), proteins TolC, MexA and AcrB. TolC is barrel-shaped; its upper α-barrel domain is embedded in the outer membrane and forms an exit channel to the extracellular space. The lower β-barrel domain extends into the periplasmatic space. AcrB is a trimeric protein at the inner membrane that provides entry from the cytosol. MexA is a periplasmatic adaptor, linking TolC and ArcB when the efflux pump is in its fully assembled functioning form.

Drug resistance pump assembled!



This image is a representation of the fully assembled drug efflux pump, connecting the intracellular with the extracellular space. The MexA periplasmatic adaptor fills the gap between AcrB and TolC so there is no opening of the channel into the periplasm. The substrate enters the AcrB assembly and exits into the extracellular space through the opening of the TolC.