National Food Institute

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Antibiotics: mode of action and mechanisms of resistance.

By

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What are antibiotics?

Original definition:

Naturally occurring microbial products

Today:

Any agent used to treat systemic infections

Mechanisms of antibiotics

- Bacteriostatic
- Bactericidal

Bacteriostatic antibiotics

- Tetracyclines
- Spectinomycin
- Sulphonamides
- Macrolides
- Chloramphenicol
- Trimethoprim

Bactericidal antibiotics

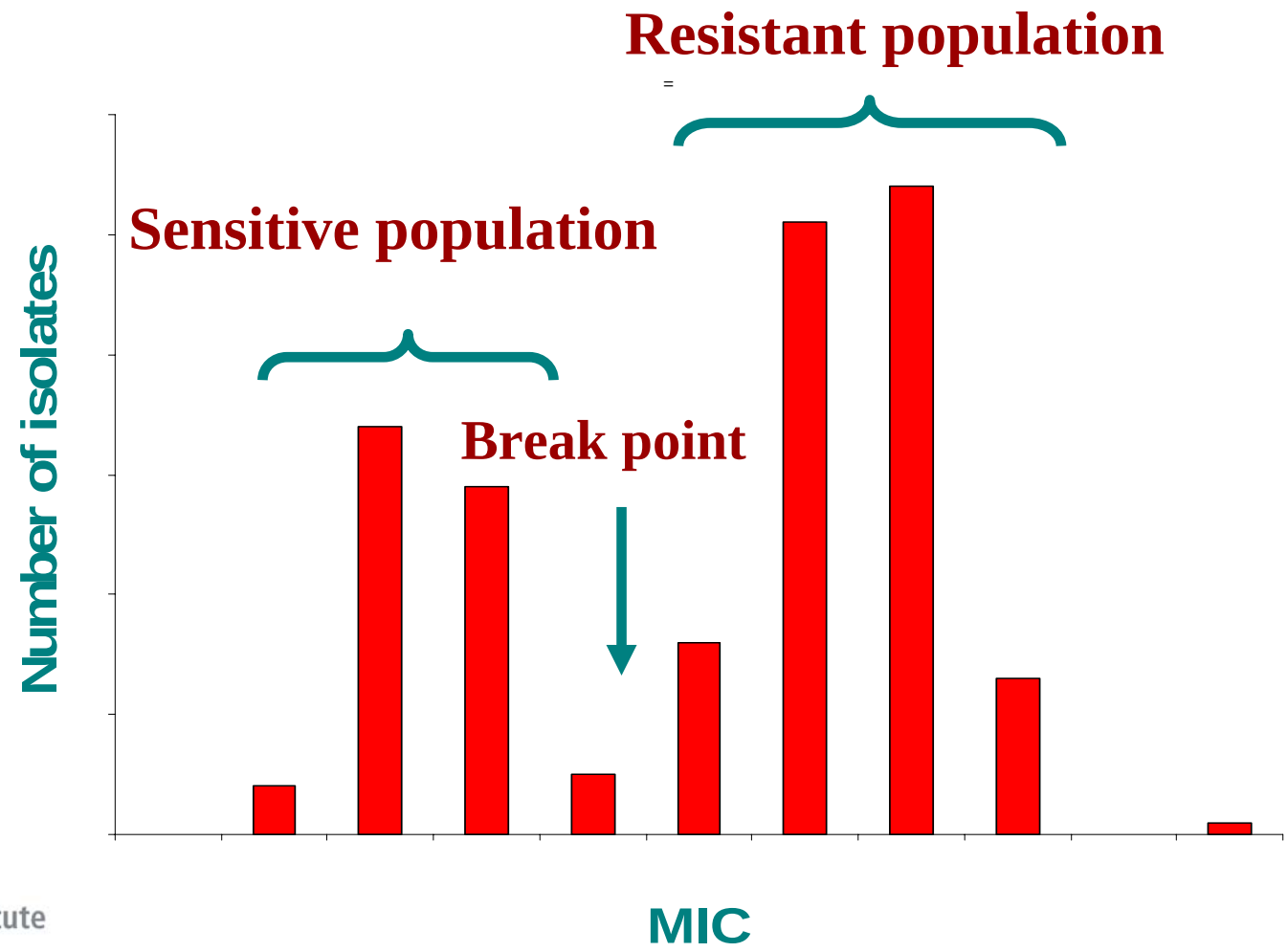
- Penicillins
- Cephalosporins
- Fluoroquinolones (Ciprofloxacin)
- Glycopeptides (Vancomycin)
- Monobactams
- Carbapenems

What is antimicrobial resistance I?

The ability of a microorganism to survive at a given concentration of an antimicrobial agent at which the normal <u>population</u> of the microorganism would be killed

This is called the "Epidemiological breakpoint".

Population distribution

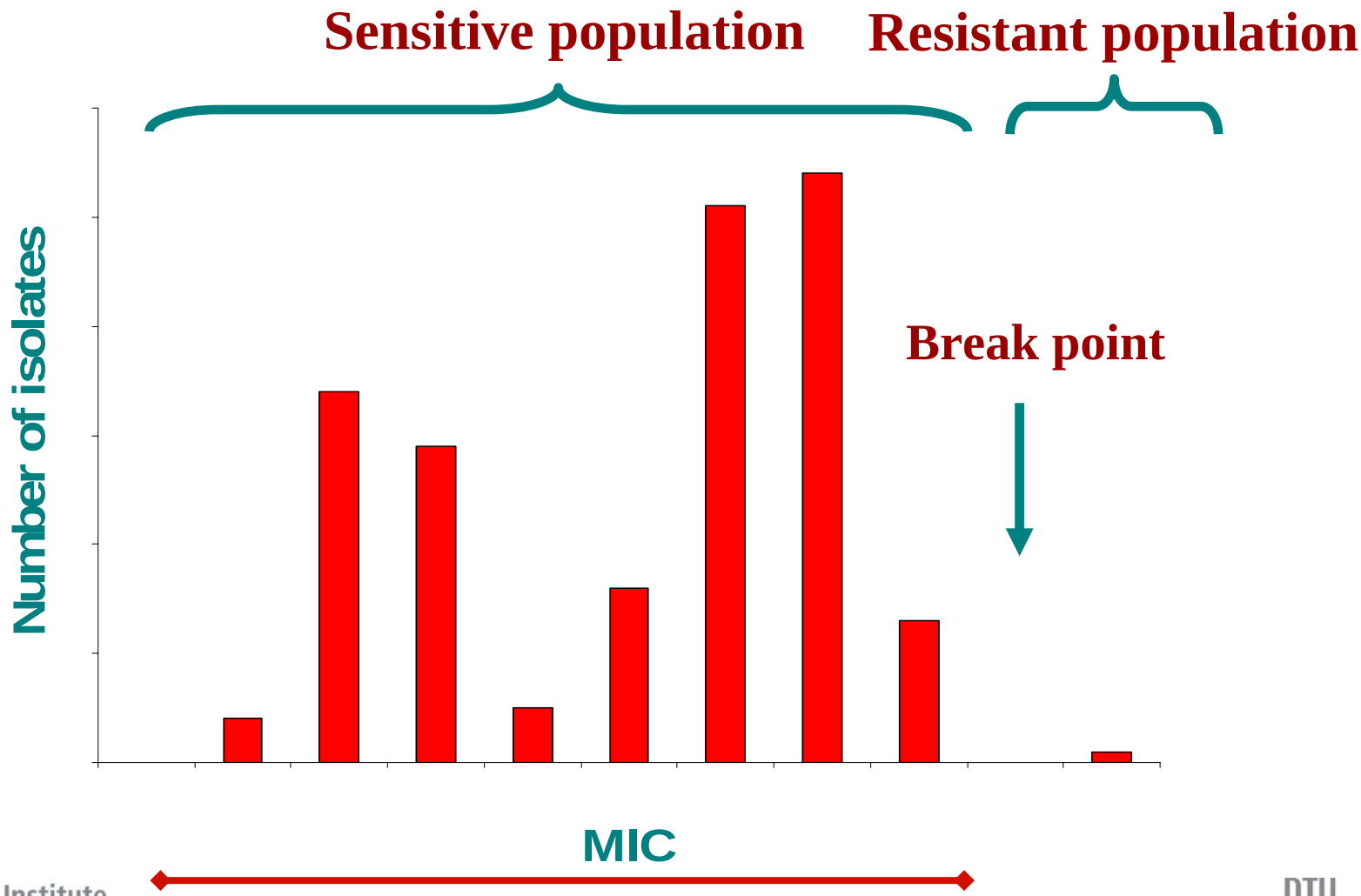


What is antimicrobial resistance II?

The ability of a microorganism to survive treatment with a clinical concentration of an antimicrobial agent in the body.

This is called the "Clinical breakpoint".

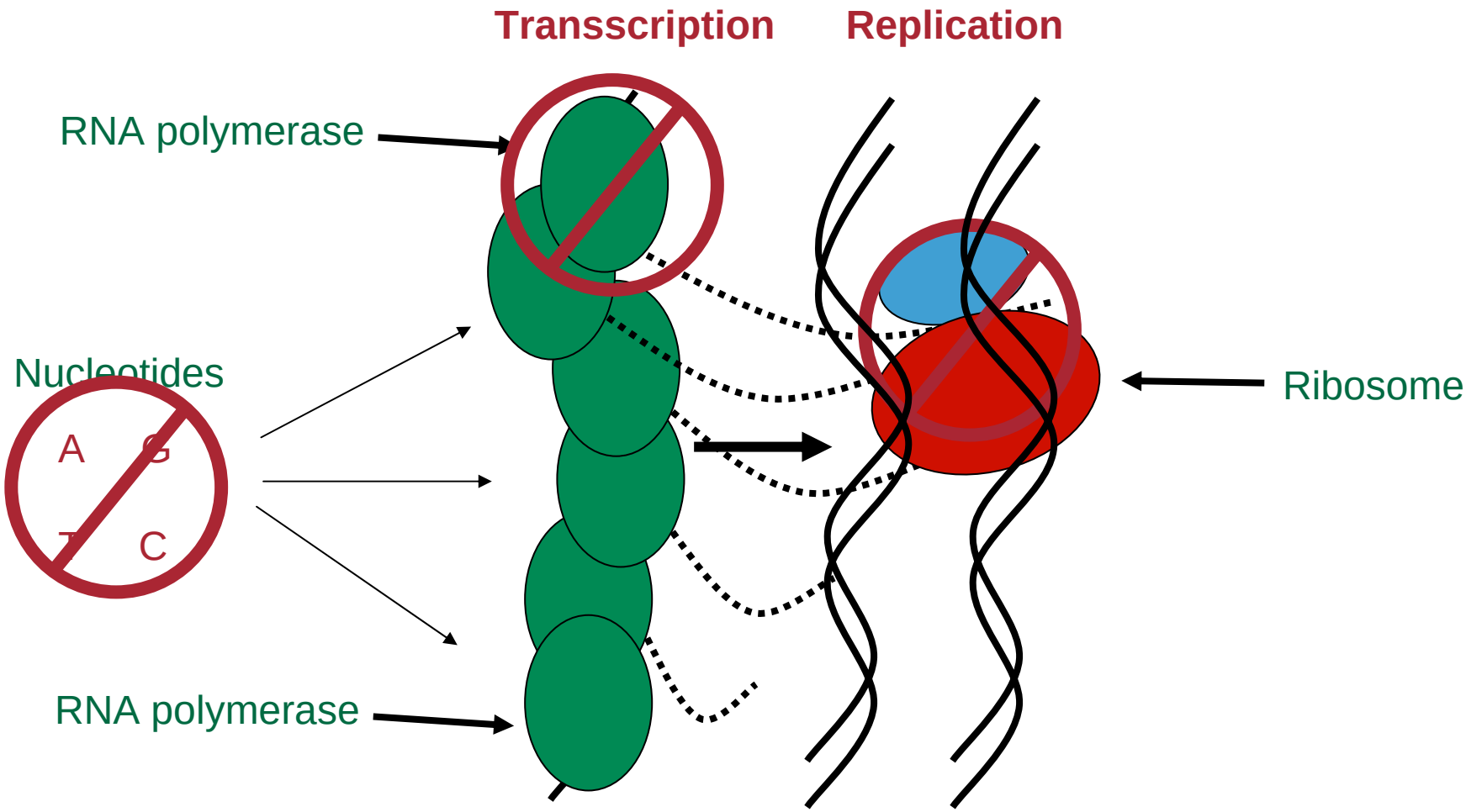
Population distribution



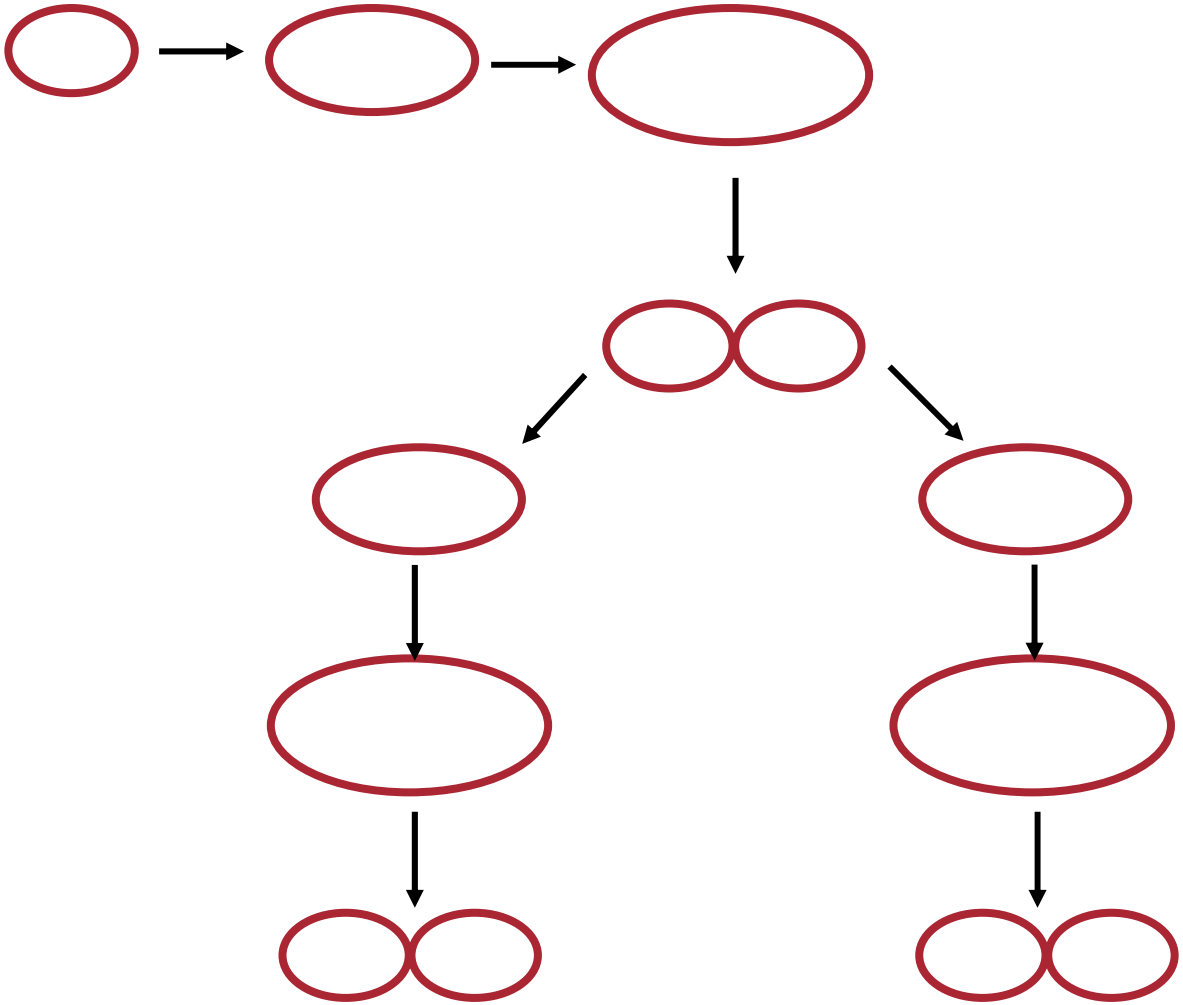
Antibiotics: 3 modes of action

- Inhibitors of DNA synthesis and replication
- Inhibitors of bacterial protein synthesis
- Inhibitors of bacterial cell wall synthesis

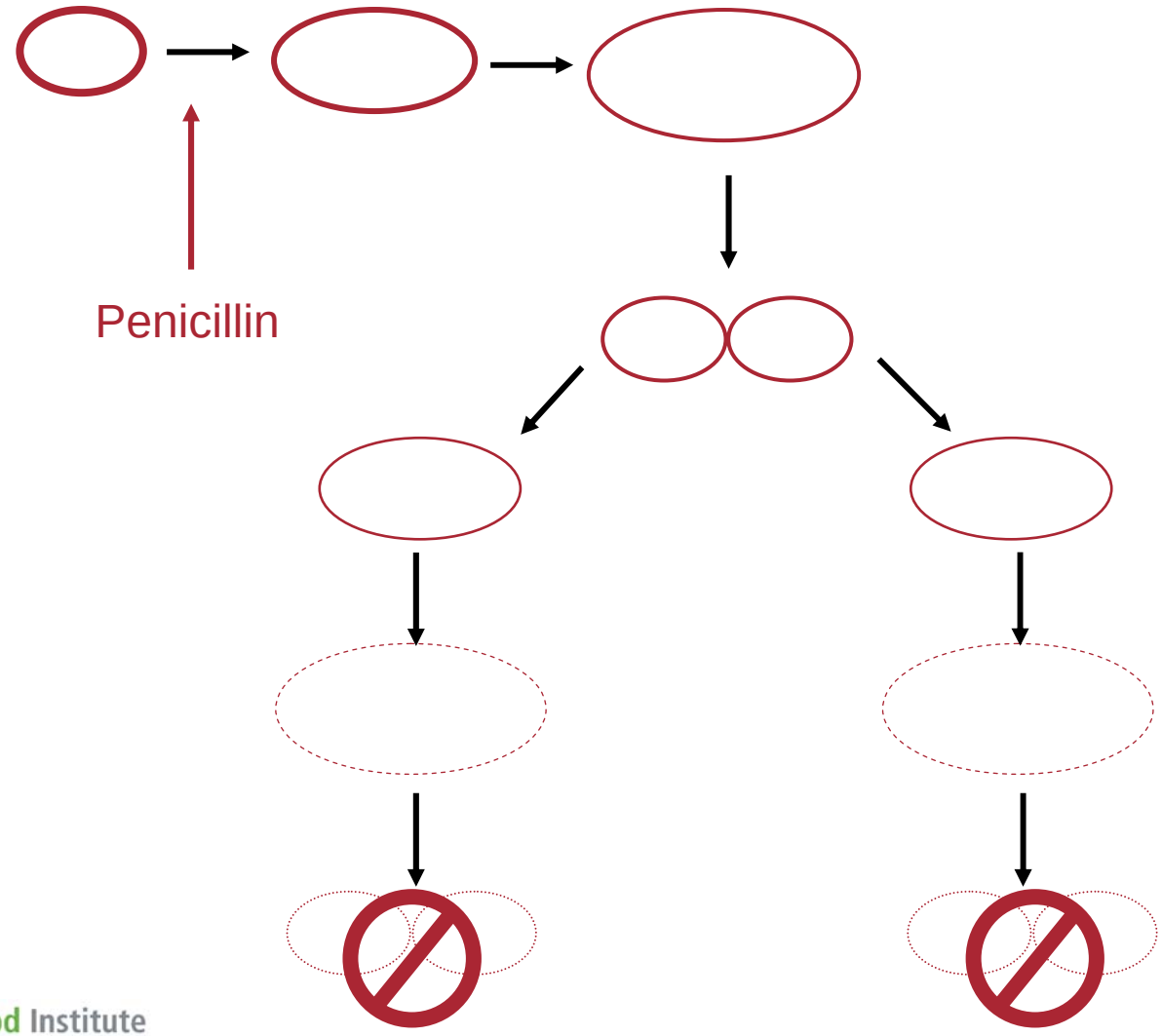
Inhibitors of DNA and protein synthesis



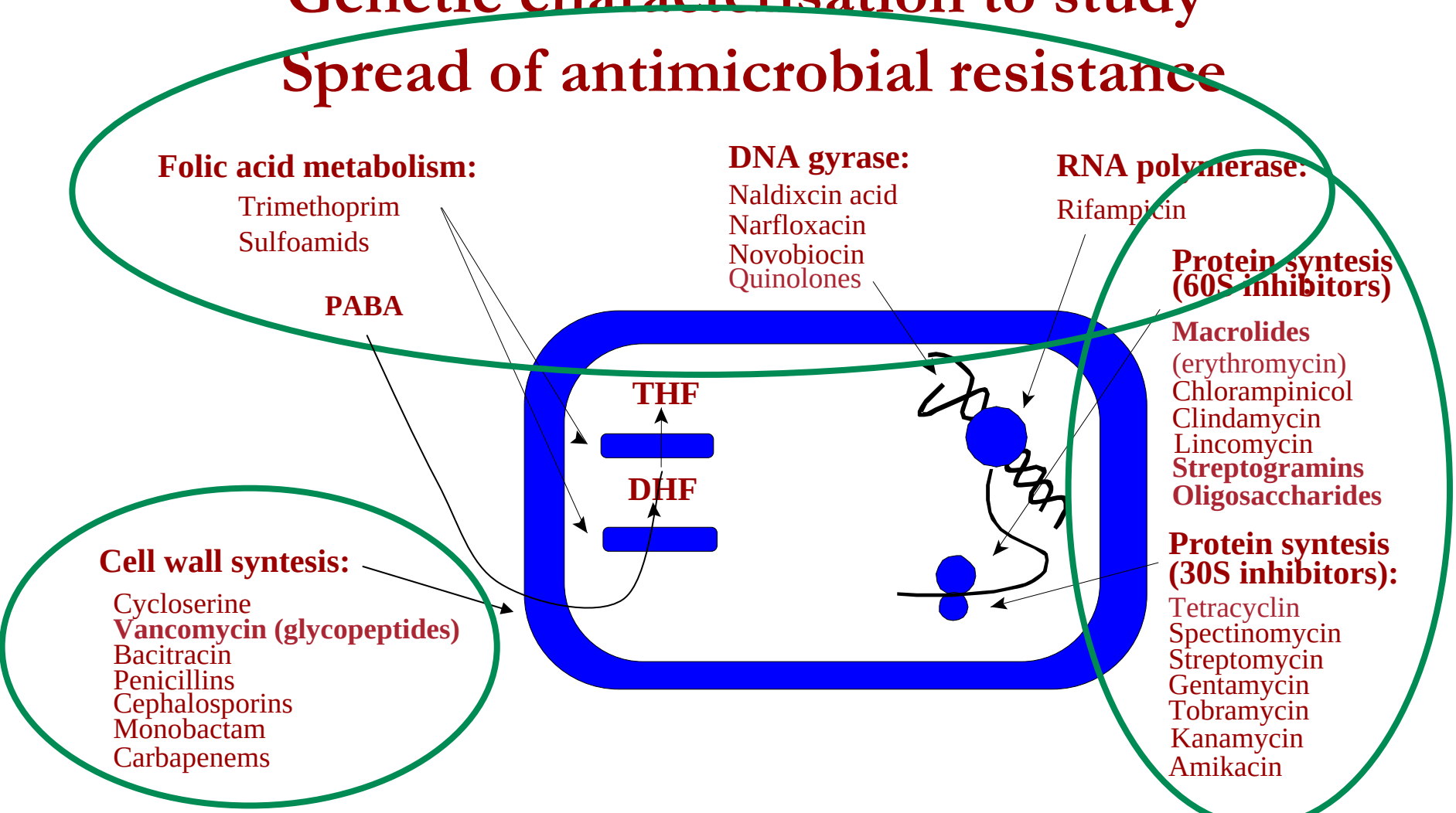
Inhibition of cell wall synthesis



Inhibition of cell wall synthesis



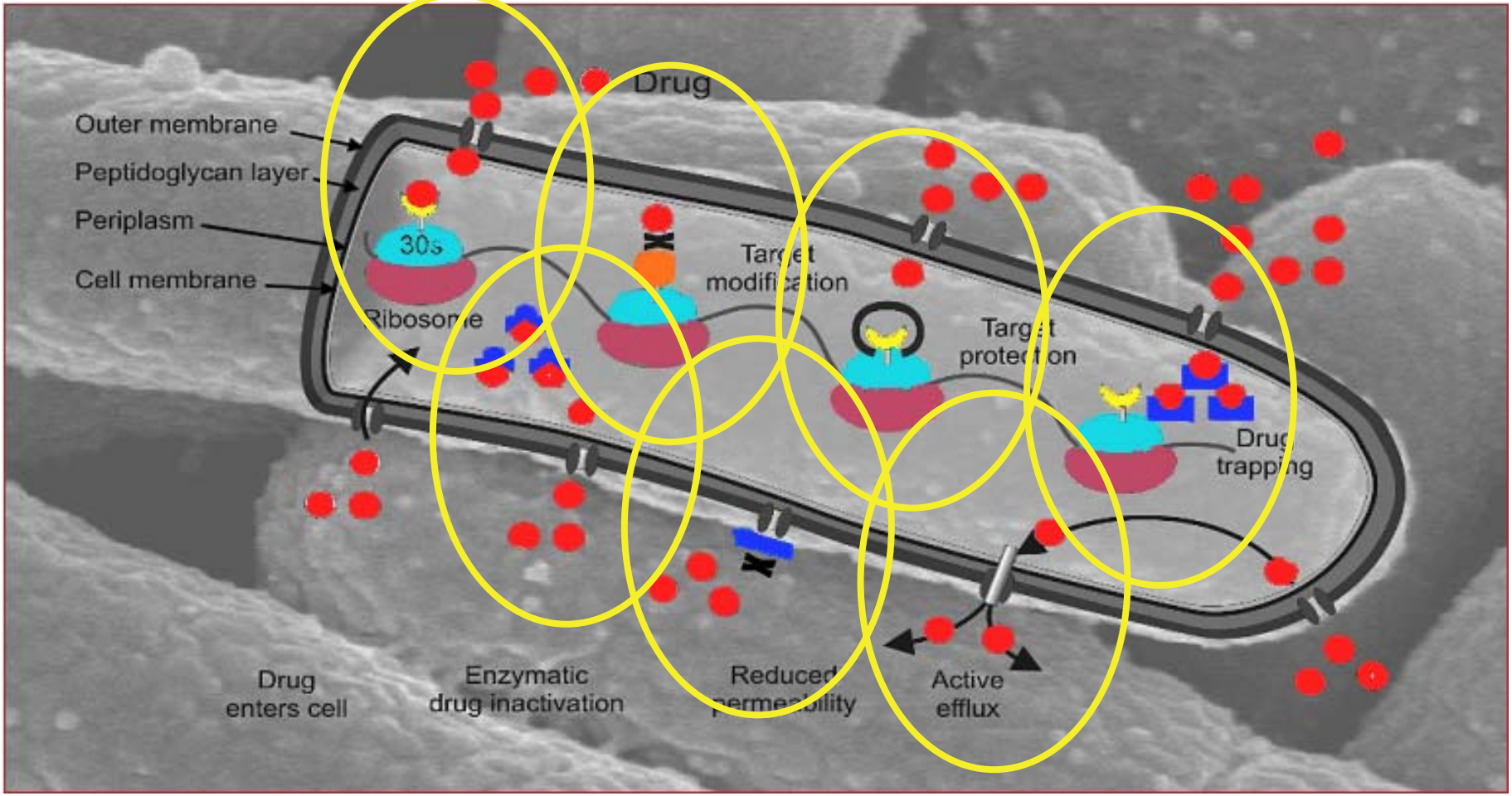
Genetic characterisation to study Spread of antimicrobial resistance



(**PABA=** p-aminobenzocis acid, **DHF=** dihydrofolate, **THF=** tetrahydrofolate (essential for growth of bacteria))

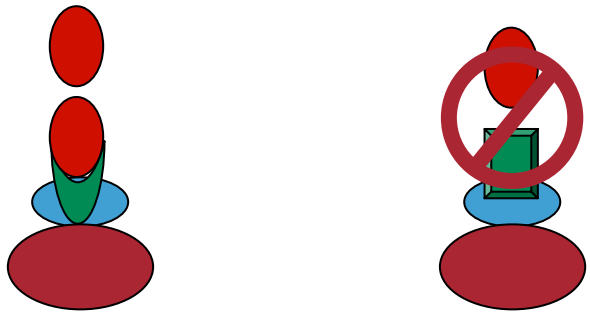
Targets in the bacterium

Antibiotics: Modes of resistance



Resistance mechanisms I

- Point mutations in target genes/influx pumps



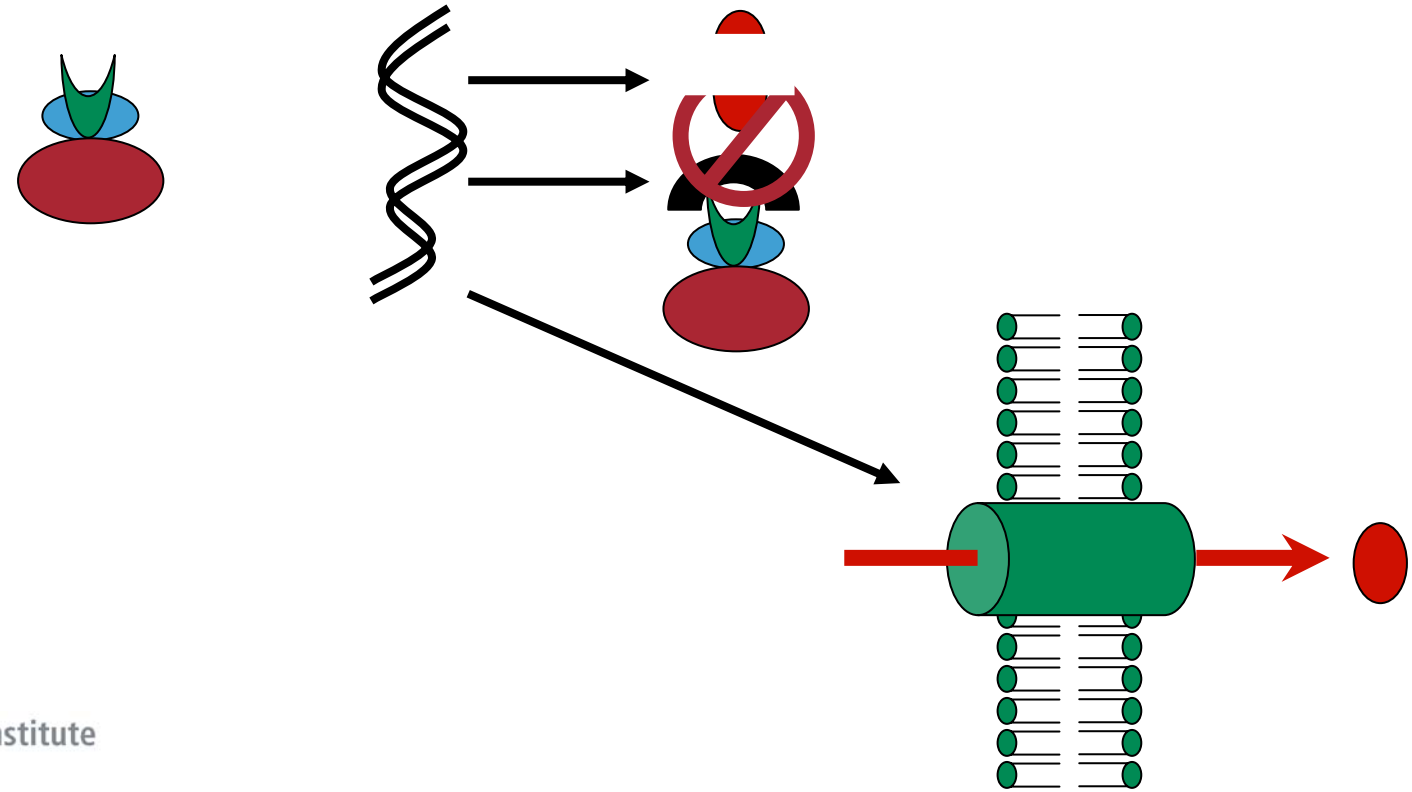
Genetic variations/Point mutations

DNA gyrase –quinolone resistance

Chromosomal mutations rarely spread horizontally

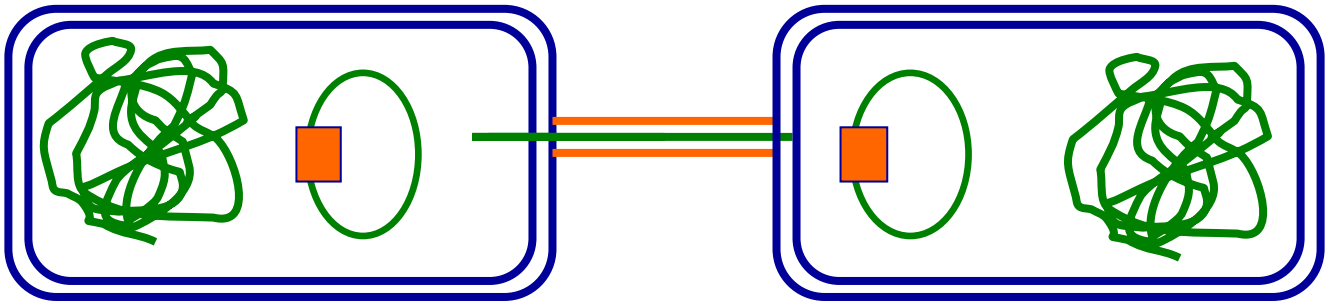
Resistance mechanisms II

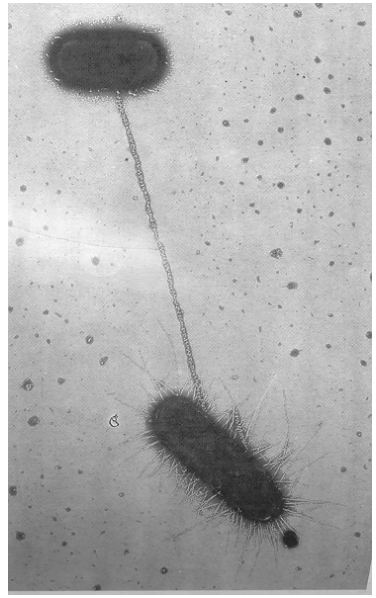
- Acquired genes



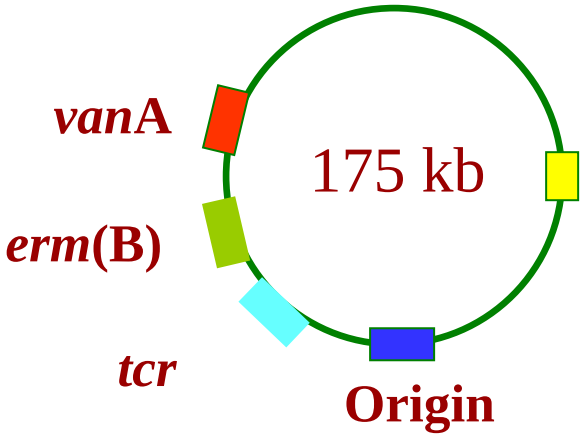
Acquisition of resistance

E. coli/ salmonella





Co-selection of resistance



tcr=Transferable copper resistance

Usage of copper or erythromycin selects for presence of vancomycin resistance

Antimicrobials and resistance problems

Emerging problems

- Fluoroquinolones-resistant *Salmonella*
- 3rd gen. Cephalosporin-resistant *E. coli/Salmonella (ESBL)*
- Carbapenemase producing *Klebsiella*
- Fluoroquinolone- and macrolide-resistant *Campylobacter*
- Vancomycin resistant enterococci (VRE)
- (Multiresistant *E. coli*)
- MRSA in animals (report of high prevalence of MR*SA* in pigs initially in the Netherlands - now also found in many other countries).