

Resistance to macrolides and lincosamides (main causes of resistance, efflux)

'*Macrolides*' (erythromycin, clarithromycin, azithromycin) and '*lincosamides*' (lincomycin and clindamycin) have some similar properties, such as antimicrobial activity, mechanisms of action and [[Antibiotic resistance | resistance]]. '*Ketolides*' are a new class of erythromycin-derived antibiotics that act against macrolide-resistant strains. ^[1]

Macrolides

Macrolide resistance

There are four mechanisms resistance:

- '*reduced outer membrane permeability*,' (eg *Enterobacteriaceae*, *Pseudomonas spp.*, *Acinetobacter spp.* are naturally resistant);
- '*pump efflux*,' (eg *msr (A)* gen *S. aureus* a *mef (A)* gen *S. pneumoniae* and *GAS*);
- '*alteration of 23S rRNA by adenine methylation*.' This confers resistance to type B macrolides, lincosamides and streptogramins and is referred to as the '*MLS_B phenotype*.' It is encoded by genes *erm* (erythromycin ribosomal methylase);
- enzymatic inactivation by phosphotransferases, mediated by "mph" genes. The hydrolysis of the macrocyclic lactone is encoded by the esterase genes *ere (A)* and *ere (B)* on the plasmids.

MLS_B resistance

Also known as inducible resistance. Macrolides, lincosamides, and type B streptogramin antibiotics (MLS) bind to *50S Ribosomes bacteria*. Some bacteria (eg, staphylococci, streptococci, and enterococci) with inducible erythromycin resistance also makes them resistant to other MLS_B agents in the presence of erythromycin. The enzyme methylase is not induced by lincosamides or streptogramins, which therefore remain active in the absence of macrolides. More than 20 *erm* genes encode MLS_B resistance and are becoming more common in GAS and pneumococci. ^[1]

Lincosamides

This group of antibiotics includes *lincomycin* 'and' '*clindamycin*'. *Lincomycin* was isolated from "*Streptomyces lincolnensis*" in 1962. *Clindamycin* has better oral bioavailability and increased bacterial efficacy compared to *lincomycin*. Although not chemically related to erythromycin, many of the biological properties of lincosamides are similar to macrolides.

Resistance

There are several mechanisms of resistance:

- '*changes in 50S ribosomal proteins*' at the receptor site condition resistance to macrolides and lincosamides;
- '*change in the 23S subunit by adenine methylation*' leads to the MLS_B phenotype and conditions resistance to macrolides, lincosamides and type B streptogramins. This MLS_B phenotype is encoded by the '*erm*' (erythromycin ribosomal methylase) genes;
- '*reduced membrane permeability in G-species*,' (eg *Enterobacteriaceae*, *Pseudomonas spp.*, *Acinetobacter spp.*) ^[1]

Resources used

1. TOROK, E. MORAN, E., COOKE, F. : *Oxford Handbook of Infectious Diseases and Microbiology*. (Oxford Medical Handbooks). ISBN-10: 019967132X ISBN-13: 978-0199671328.