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 enteccocci) 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 MLSB 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 MLSB phenotype and conditions resistance to macrolides, lincosamides and type B streptogramins. This MLSB 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.*