

Structural Parameters Influencing the Affinities and Effectiveness of Ribosomal Antibiotics

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Residing in the large ribosomal subunit and stretching from the site of peptide bond formation, to the other end of the particle, the protein exit tunnel provides the path of the emerging nascent proteins. Being of utmost importance for life, the ribosomal tunnel is targeted by a large number of antibiotics, belonging to the macrolide and ketolide families, which bind to a specific pocket made exclusively of RNA and act by blocking the tunnel, thus hampering nascent protein progression.

High-resolution crystal structures of several antibiotics, belonging to the various branches of these families as well as of compounds possessing characteristic properties of both the macrolides and ketolides, allowed parameterization of the specific contributions of the different nucleotides comprising the macrolide binding pocket. Analysis of these structures shed light on basic issues of antibiotics selectivity and provided the structural basis for the mechanisms of antibiotics resistance.

Comparative analysis of antibiotics binding modes to the eubacterial pathogen model, *Deinococcus radiodurans*, and to the archaea *Haloarcula marismortui*, which shares properties with eukaryotes and prokaryotes, showed that despite the overall conservation of the ribosome, phylogenetic and conformational variations in antibiotics binding pocket allow their selectivity, thus facilitating their therapeutical usage.

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