Productive and Non-productive Binding of Polyketides to the Ribosome Large Subunit

Rita Berisio[a], Maya Amit[b], David Baram[b], Joerg Harms[c], Anat Bashan[b], Harly Hansen[c], Frank Schluenzen[c], Ada Yonath[b], *[a]IBB, CNR, Naples, Italy. [b]Weizmann Institute, Rehovot, Israel. [c]Max Planck Institut, Hamburg, Germany.* E-mail: rberisio@chemistry.unina.it

Since the early days of ribosome research, the principal reaction of protein biosynthesis was localized in the large ribosomal subunit. Protein biosynthesis may be hampered by the occlusion of the exit tunnel, through which proteins emerge. This tunnel has a non-uniform diameter and contains grooves and cavities [1]. Crystal structures of complexes of the large ribosomal subunit from the eubacterium *Deinococcus radiodurans* with various polyketides (troleandomycin, telithromycin, rapamycin)[2,3] have shown that the exit tunnel is able to bind them with different fashions and that only some of those are capable to induce protein inactivation. We show that, among the three polyketides here analysed, rapamycin binds to a tunnel crevice that is located aside the typical macrolide-binding pocket and cannot occlude the exit tunnel. These structural results constitute the first example of a non-inactivating binding to the ribosome, thus suggesting that a necessary requirement for efficient antibiotic activity of macrolide-like compounds is their binding to the ribosome exit tunnel, in a manner that efficiently blocks the tunnel. Implications of polyketides binding to the ribosome large subunit will be discussed in the poster.

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