Kirromycin and pulvomycin bind to different sites on the elongation-factor Tu from E. coli

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The function of the prokaryotic elongation-factor Tu is regulated by guanosine nucleotides, which induce different conformations of the protein. These different conformational states can be assessed by ^{1}H-NMR spectroscopy and their different activities by functional assays.

The antibiotics kirromycin and pulvomycin are known to interfere with the natural function of EF-Tu by altering the conformation of EF-Tu. Our ^{1}H-NMR experiments demonstrate that these alterations can in part be explained in such a manner, that kirromycin makes EF-Tu·GDP look more like EF-Tu·GTP {1} and that pulvomycin makes EF-Tu·GTP more EF-Tu·GDP like. This explains, why EF-Tu·GDP, which normally cannot bind aminoacyl-tRNAs, can do so in the presence of kirromycin {2} and mutatis mutandis, that EF-Tu·GTP, which normally interacts with aminoacyl-tRNAs does not in the presence of pulvomycin {3}. In the presence of both pulvomycin and kirromycin binding of aminoacyl-tRNAs to EF-Tu·GDP or EF-Tu·GTP is precluded, demonstrating that pulvomycin has a dominant effect over kirromycin with respect to this reaction. Kirromycin induces a strong GTPase activity in EF-Tu {2}, pulvomycin, however, only a weak one. Excess pulvomycin can suppress the strong GTPase activity induced by kirromycin, while excess kirromycin over pulvomycin leads to a moderate increase in the GTPase activity of EF-Tu.

These experiments are interpreted such that kirromycin and pulvomycin have different sites on EF-Tu, and that pulvomycin can replace kirromycin in its site; kirromycin, however, cannot replace pulvomycin in its respective site. We are currently carrying out circular dichroism measurements and analytical ultracentrifugation studies using a synthetic boundary cell to prove this model.

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{2} G. Chinali, H. Wolf & A. Parmeggiani (1977) Eur.J.Biochem. 75, 55-65
{3} H. Wolf, D. Assmann & E. Fischer (1978) Proc.Natl.Acad.Sci.USA 75, 5324-5328

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