

P010 Restricting the conformational dynamics of the ribosome by aminoglycoside antibiotics

Gromadski K. B., Holtkamp W., Rodnina M. V.

Institute of Physical Biochemistry, University of Witten/Herdecke, 58448 Witten, Germany

Recognition of aminoacyl-tRNA (aa-tRNA) on the ribosome is a key reaction of the elongation cycle that determines both speed and fidelity of translation. The accuracy of decoding is controlled by local conformational changes at the decoding site that leads to a global change in the structure of the 30S and activates GTP hydrolysis in EF-Tu. The rearrangements induced by cognate codon recognition are mimicked by aminoglycoside antibiotic paromomycin. Paromomycin accelerates the GTPase activation step in the near-cognate ternary complex up to the cognate value, while GTP hydrolysis in the cognate complex remains high and rate-limited by the preceding codon recognition step. Similar functional effects are found in the presence of hygromycin B, another aminoglycoside antibiotic which binds close to the decoding center although it does not induce rearrangements similar to those observed with paromomycin. Streptomycin induces global closing movements of the 30S subunit by connecting the shoulder to the central part of the subunit. Streptomycin alters the rates of GTP hydrolysis by EF-Tu in a reciprocal way on cognate and near-cognate codons, resulting in almost identical rates of GTP hydrolysis and virtually complete loss of selectivity. The data suggest the importance of conformational dynamics of the ribosome for the accuracy of the tRNA selection.