The crystal structure of elongation factor G

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Protein synthesis on the ribosome is aided by a number of protein factors that bind transiently to the ribosome during the different phases of protein synthesis. There are three elongation factors: EF-Tu, EF-Ts and EF-G. EF-G catalyses the translocation of the messenger RNA and the tRNA:s with the effect that a new codon becomes exposed for interaction with the next tRNA. EF-G is a GTPase which binds GTP and when the GTP is hydrolysed the factor with bound GDP adopts another conformation. EF-G with GTP binds to the ribosome and causes translocation and it dissociates from the ribosome after GTP hydrolysis.

We have solved the structure of EF-G from *Thermus thermophilus* without bound nucleotide to 2.8Å resolution. The space group is $P2_12_12_1$ and the cell dimensions are a=75.59Å, b=105.96Å, and c=116.43Å (1). Data from native crystals and a large number of derivatives were collected using a Siemens area detector mounted on a rotating anode. The electron density was very hard to interpret until one of the derivatives was recollected at station 9.5 at Daresbury laboratory optimizing the anomalous dispersion. The clarity of the resulting electron density map was significantly improved permitting more than 90% of the 691 residues to be traced (2). The structure has been refined using XPLOR. Attempts to extend the resolution at Daresbury have so far been unsuccessful.

EF-G has the molecular dimensions 118x60x50Å and consists of five domains. Domain 1 is the G domain which binds GTP/GDP. It is a version of the Rossmann fold with very similar structure to other GTPases such as EF-Tu (3, 4), p21 ras (5) and transducin (6). Contrary to other GTPases EF-G has a subdomain (G') of about 90 residues on one side of the G domain. Domain 2 corresponds closely to domain 2 of EF-Tu both in folding and in its interactions with the G domain. The surprising thing is that those two domains of the empty structure of EF-G compares best with EF-Tu in complex with a GTP analogue in this respect. Domains 3, 4 and 5 do not correspond to domains found so far in other G proteins. However domains 3 and 5 have the same fold as several ribosome proteins as well as a number of other RNA binding proteins. This fold has been described as a double split $\beta-\alpha-\beta$ (7).

The so called effector loop and much of domain 3 are hardly visible indicating large flexibility. These regions are thus of particular interest in trying to understand the conformational changes that are related to EF-G's function. X-ray studies of other conformations are also in progress in our laboratories.

References

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