Fusidic Acid Resistance and Sensitivity in Ribosomal Elongation Factor G

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Elongation factor G (EF-G) catalyzes translocation in protein synthesis on the ribosome. EF-G is inhibited by Fusidic acid (FA), a commonly used antibiotic. Structural information on FA binding to EF-G has not yet been available.

We present three crystal structures of two mutant EF-G factors; G16V, highly FA sensitive, and T84A, highly FA resistant. The crystal structures provide a first insight into the conformational changes induced by GTP binding and how this affects FA binding. These structural conformations show the general importance of the interface of domain G, III and V as a key component of the FA binding site and the specific role of Phe90 as a gatekeeper and conformational regulator. We provide an explanation on how EF-G is able to discriminate between GDP and GTP.

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