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Structural insight into the eIF2-eIF2B interaction

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eIF2B (eukaryotic initiation factor 2B) is a key regulator of translation initiation. It catalyzes guanine nucleotide exchange on eIF2, which delivers the methionylated initiator tRNA to the 40S ribosomal subunit. This exchange reaction is inhibited by the stress-induced phosphorylation of the eIF2 alpha subunit, which leads to global repression of cellular protein synthesis. eIF2B is composed of five subunits. The catalytic gamma/epsilon subcomplex is responsible for nucleotide exchange, while the regulatory alpha/beta/delta subcomplex discriminates the phosphorylation status of the eIF2 alpha subunit. We established a bacterial expression system for eIF2B, and determined its crystal structure at 3.2 Å resolution. The crystal structure revealed that eIF2B is a decamer containing two molecules of each subunit. The hexameric regulatory subcomplex is formed by the trimerization of one alpha-alpha homodimer unit and two beta-delta heterodimer units, and two catalytic subcomplexes are individually connected to the regulatory subcomplex through two beta-delta heterodimer units. Photo-cross-linking analyses showed that the N-terminal domain of the eIF2 alpha subunit, which bears the phosphorylation site, is recognized by a composite surface formed by the eIF2B alpha, beta, and delta subunits. Based on these results, we report structural insights into the interaction between eIF2 and eIF2B.

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