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Dynamic complexes, folding and phase separation of disordered proteins in biological regulation

The intrinsically disordered 4E-BP2 interacts tightly with eIF4E in a dynamic complex to inhibit translation initiation. The dynamic complex enables kinase access for phosphorylation-induced folding of 4E-BP2, leading to loss of binding. The disordered N-terminal residues of Ddx4, an RNA DEAD-box helicase involved in formation of germ granules in sperm development, facilitate phase separation. Post-translation modification of Ddx4, as well a number of other modulators, regulate the phase separation to control this membrane-less cellular organization. Both are examples of the key roles of disorder and various transitions (folding, phase separation) in regulation of biological function.