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Kinetics of Chain Motions within the disordered eIF4E-BP2 protein

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Intrinsically disordered proteins (IDPs) play critical roles in regulatory protein interactions. Cap-dependent translation initiation is regulated by the interaction of eukaryotic initiation factor 4E (eIF4E) with disordered eIF4E binding proteins (4E-BPs) in a phosphorylation dependent manner. Fluorescence correlation and time-resolved anisotropy spectroscopies were used to detect and assess sequence-specific local chain motions of 4E-BP2 upon phosphorylation and upon binding to eIF4E.

Nanosecond scale dynamics of 4E-BP2 was observed by correlation spectroscopy, and it was tentatively assigned to intrachain contact formation process. Our data suggests that multi-phosphorylation of the protein slows down the proximal chain motions and also modulates the kinetics of distal regions. Rotational correlation times and wobbling cone angles extracted for different segments of the 4E-BP2 protein provide a quantitative picture of the rigidity of the protein at different sites and can also be used as a probe to evaluate the binding to eIF4E. We show that the region near the position 73 in the sequence has highest binding affinity to eIF4E. Data acquired under high denaturant conditions, in 6 M guanidinium chloride, indicates that this IDP behaves differently than a random coil model.

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