Poster Presentation

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Paip1 and Paip2: conformational modulators of PABP

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Translation is regulated in cells. Key among the different stages of translation, translation initiation is controlled by regulatory interactions of eIFs and also translation regulatory proteins interacting with eIFs and PABP. PABP-interacting protein (Paip) 1 and 2 have been identified as regulatory proteins affecting the rate of translation initiation through their interactions with PABP. These interactions are mediated by the PABP interacting Motifs (PAM) 1 and 2 of Paips. Paip1 enhances the rate of translation while Paip2 suppresses it. To further understand their mechanisms of actions, here, we have studied the interactions of PABP RRMs with the PAM1 regions of Paip1 and 2. Compared to Paip1, affinity measurements using ITC show that Paip2 binds to PABP with higher affinity. While Paip2 dissociates poly(A) from PABP RRMs, Paip1 can not compete with poly(A) binding to PABP. Our binding studies show that Paip1 increases eIF4G-binding to PABP RRM1-2, supporting its stimulatory role in translation. Upon binding, Paip1 and Paip2 affect the conformation of the PABP RRMs differently. Compared to RRMs Paip1, the complex of RRMs Paip2 has a compact conformation. Our data suggest that Paip1 and Paip2 regulate PABP function through modulating its conformation, stimulating its incorporation in the pre-initiation complex, or sequestering it from translational machinery.

Keywords: conformational changes, Translational regulators, SAXS