STRUCTURAL AND THERMODYNAMIC COMPARISON BETWEEN THE NUCLEAR IMPORT RECEPTOR IMPORTIN-α FROM DIFFERENT FAMILIES

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Cellular compartments allow the separation of the genetic material and transcriptional machinery of the nucleus from the translational and metabolic processes of the cytoplasm. Transport of proteins through nuclear pore is facilitated by nucleo-cytoplasmic transport factors termed importins. The best characterized nuclear import pathway requires positively charged sequence(s) within the cargo protein, known as classical nuclear localization (NLS) sequence which binds to the importin-α (Impα) protein. Structures of Impα from different organisms (yeast, rice, mouse and human) have been determined, revealing that this receptor posses a conserved structural scaffold. However, some studies have also demonstrated that the Impα mechanism of action may vary significantly for different organisms or for different isoforms from the same organism. Thus, in this work we performed a structural and thermodynamic comparison between two families of Impα (types α1 and α2) to the same NLS peptides in order to define specificities of the Impα from Mus musculus (MmImpα - type α2) and the Impα from Neurospora crassa filamentous fungus (NcImpα - type α1) which it was recently solved by us. The crystal structures of MmImpα and NcImpα complexed to SV40NLS peptide and thermodynamic assays using a Isothermal Titration Calorimeter were used for this study. The comparison of these data with previous studies on Impα proteins led us to demonstrate that NcImpα possess specific features that are distinct from MmImpα but exhibits important similarities to rice Impα, particularly at the minor NLS binding site. The differences between different Impα proteins may result from the phylogenetic distance among the proteins and the functions of each protein family in organism development, which results in differences in affinities for NLSs.

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