

STRUCTURAL AND EVOLUTIONARY STUDIES OF IMPORTIN-ALPHA AND ITS INTERACTIONS WITH NLS PEPTIDES.

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Importin-alpha (ImpA) recognizes clusters of basic amino acids known as nuclear localization sequences (NLS) to transport proteins into the nucleus. Several ImpA isoforms have been described displaying cargo preferences in vitro and in vivo. Crystal structures of native mammalian ImpA and complexed with monopartite and bipartite NLSs peptides have been solved by us. (Kobe, 1999, Fontes et al., 2000, 2003) Studies of ImpA-NLSs interactions would provide information for the development of ligands capable of distinguish isoforms leading to applications on diagnostics and drugs. In this work we present a phylogenetic analysis of ImpA family using representative Eukarya protein sequences whose provided a phylogenetic tree with remarkable independent duplication events in Metazoa and Viridiplantae. We also present Molecular Dynamics (MD) studies, using Gromacs 3.3.1 software, with the crystallographic data from N-terminally truncated native ImpA and ImpA SV40 NLS peptide / nucleoplasmin NLS peptide complexes (PDBs 1IEJL, 1EJY) to observe the stability of the native N-terminally truncated ImpA native structure and interactions between the ImpA and NLSs peptides. Different equilibrium states were observed after 5ns of simulation time resulting on different structures. The MD of complex ImpA/NLS peptides led to a final state close to the crystallographic structure, while the MD of the native ImpA had significant changes. Support by FAPESP, CNPq, CAPES/PRODOC, FUNDUNESP.