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Atomic resolution structures in nuclear transport

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Abstract

There are currently at least 53 structures of components of nuclear transport in the Protein Databank. In addition to providing critical insights into molecular mechanisms of nuclear transport, these atomic resolution structures provide a large body of information that could guide biochemical and cell biological analyses involving nuclear transport proteins. This paper catalogs 53 crystal and NMR structures of nuclear transport proteins, with the emphasis on providing information useful for mutagenesis and overexpression of recombinant proteins.

1. Introduction

High resolution structures of macromolecular complexes are necessary to understand molecular mechanisms of cellular processes. The importance of structures is particularly evident in the cellular process of nucleocytoplasmic transport. The nuclear transport machinery consists of a large number of proteins that include components of the nuclear pore complex (nucleoporins), transport factors that recognize import or export substrates (Karyopherins/Importins/Exportins and TAP), Ran, its transporter NTF2 and its regulators, RanBP1, RanGAP and RanGEF. Macromolecular interactions in nuclear transport are complex. Each protein generally contacts multiple macromolecular ligands, binding to different partners in the cytoplasm versus the nucleus. Partner-switching in the different subcellular compartments is also frequently accompanied with large conformational changes in the proteins. High resolution structures of nuclear transport complexes have been crucial in revealing how a transport factor recognizes its ligands and how structural plasticity plays a central role in the different steps of nuclear import and export.

High resolution structures that have been determined in nuclear transport include those of Kapβs, Kapαs, Ran and its regulators RanGAP, RanGEF, RanBP1 and NTF2, mRNA export factor TAP and nucleoporins. The list of Kapβ structures includes nine Kapβ1/Impβ structures (unliganded, Ran-, substrate- and nucleoporin-complexes), two Kapβ2/Transportin structures, two Cse1 structures and a structure of a small Crm1 fragment. A large number of Kapα structures are available, including nine of mouse Kapα and five of the yeast homolog Kap60p, providing insight into the recognition of a variety of classical-NLSs and also nucleoporins such as Nup50 and Nup2p. Ran, its regulators RanBP1, NTF2, RanGAP and RanGEF as well as complexes involving these proteins are also well represented with a total of 12 structures. Structures in mRNA export include eight structures of TAP or its yeast homolog Mex67p, and finally, there are currently five structures of individual nucleoporin domains.

Other than their important roles in revealing molecular mechanisms of cellular processes, high resolution structures of macromolecular complexes also provide tremendous resources and tools for biochemical and cell biological experimental design. Structures could provide critical guidance in mutagenesis studies, especially when the aim is to disrupt specific interactions. Structure determination efforts, which require large amounts of proteins

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Table 1
Crystal structures of Kapβ1 complexes

Structure	PDB-ID	Ref.	Organism	Resolution (Å)	Protein constructs in crystals	Residues in model	Domains/motifs	Contact residues (molecule 1)	Contact residues (molecule 2)	Contact type	Disruptive interface mutants
Kap95p-RanGTP	2BKU	[1]	Kap95p: yeast	2.7	Kap95p: 1–861	Kap95p: 1–861	β1: HEAT repeats	Kap95p:	Ran:		Ran: K37D/K152A binds Kap95p, but is unable to displace IBB
								I14	L75	HP*	
			Ran: dog		Ran: 1–176	Ran: 9–176		K66	D77	Polar	
								N67	D77	Polar	
								E164	R110	Polar	
								E288	R140	Polar	
								E295	R140	Polar	
								E295	K141	Polar	
								W345	R140	HP*	
								N515	N156	Polar	
								Q570	R29	Polar	
								E615	K37	Polar	
								D616	K37	Polar	
								D617	K152	Polar	
								Q650	K37	Polar	
Kapβ1-RanGppNHp	1IBR	[2]	β1: human	2.3	β1: 1–462	β1 (chain B): 2–459	β1: HEAT repeats	β1:	Ran:		
								L59	V111	HP*	
			Ran: human		Ran: 1–216			K62	D77	Polar	
						β1 (chain D): 2–439		K68	D107	Polar	
								D160	R110	Polar	
								R232	E113	Polar	
						Ran: 9–176		E281	R140	Polar	
								E281	K141	Polar	
								D288	R140	Polar	
								D338	R166	Polar	
Kapβ1	1GCJ	[3]	Mouse	2.6	1–449	1–449	HEAT repeats				
Kapβ1-IBB$_{Kap\alpha}$	1QGK	[4]	β1: human	2.5	β1: 1–867	β1: 1–867	β1: HEAT repeats	β1:	α:		β1:
								E281	R13	Polar	W864 (∼35-fold)
					α: 11–54	α: 11–54	α: IBB	D288	R13	Polar	
								D339	K20	Polar	W864/W342
								D340	K20	Polar	W864/W430
								W342	R13	HP*	W864/W472
								W342	L14	HP*	(∼400-fold)
								K346	F17	HP*	
								V350	R13	HP*	W342/W430/W864
								M388	K18	HP*	W342/W472/W864
								D426	K18	Polar	W430/W472/W864
								T427	K18	Polar	(∼950-fold)
								W430	K18	HP*	
	1QGR			2.3	β1: 1–867	β1: 1–614, 621–867		N469	N19	Polar	[5]
								W472	N19	HP*	
					α: 11–54			W472	K22	HP*	
						α: 27–54		E530	R31	Polar	
								R593	N35	Polar	
								D627	R28	Polar	
								D627	R31	Polar	
								M630	I32	HP*	
								D676	R39	Polar	
								E767	K43	Polar	
								D824	R51	Polar	
								W864	R51	HP*	
								W864	V53	HP*	

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