Published in final edited form as:

Methods. 2006 August ; 39(4): 342–355. doi:10.1016/j.ymeth.2006.06.015.

Atomic resolution structures in nuclear transport

Katherine E. Süel, Ahmet E. Cansizoglu, and Yuh Min Chook*

Department of Pharmacology, University of Texas Southwestern Medical Center at Dallas, 6001 Forest Park, Dallas, TX 75390-9041, USA

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 Kap β s, Kap α s, Ran and its regulators RanGAP, RanGEF, RanBP1 and NTF2, mRNA export factor TAP and nucleoporins. The list of Kap β structures includes nine Kap β 1/Imp β structures (unliganded, Ran-, substrate- and nucleoporin-complexes), two Kap β 2/Transportin structures, two Cse1 structures and a structure of a small Crm1 fragment. A large number of Kap α structures are available, including nine of mouse Kap α 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 also provide very useful information about overexpression and purification of recombinant proteins.

This paper strives to catalog a comprehensive list of high resolution structures (mostly crystal structures) in nuclear transport in Tables 1–6 and Figs. 1–6. We have tabulated information about the identity of successful protein constructs for each structure as well as residues that are observed in those structures, to guide production of recombinant proteins. Many proteins involved in nuclear transport contain multiple modular and globular domains (such as TAP and nucleoporins), and knowledge of where individual domains begin and end obtained from the structures will allow design of protein constructs to optimize both folding and function of those domains. In contrast to the common globular proteins, both Kap α and Kap β proteins contain multiple HEAT/ARM repeats such that these proteins are either elongated or spiral-shape. More importantly, every single HEAT repeat helix in these proteins contributes to the extended hydrophobic cores of the proteins. Thus, it is not trivial to generate deletion mutants involving HEAT/ARM repeats without interfering with the folding or solubility of the proteins. Structures of karyopherin fragments summarized here should provide information on the few deletion mutants that have been overexpressed successfully. Many of the structures tabulated in this paper are those of complexes of two or more proteins. These structures are very informative as they reveal the chemical and physical nature of the contact interfaces. We have also included contact residues in individual binding partners seen in structures of complexes, and also information on published interface mutants that disrupt specific protein–protein interactions. Such structural and biochemical data should aid significantly in mutagenesis analysis especially to disrupt specific functions in this large group of proteins.

2. Concluding remarks

We have summarized 53 structures of Kap β s, Kap α s, Ran and its regulators RanGAP, RanGEF, RanBP1 and NTF2, mRNA export factor TAP and nucleoporins. The information provided should be useful for both overexpression of recombinant proteins as well as for analysis and experimental manipulation of specific interactions of the proteins. We look forward to many more structure of nuclear transport proteins in the future, especially to complexes of different Kap β s with their substrates to understand NLS/NES specificity in the different pathways and also to structures of nucleoporin subcomplexes to understand the assembly of the nuclear pore complex and mechanism of translocation through the pore.

References

1. Lee SJ, Matsuura Y, Liu SM, Stewart M. Nature. 2005; 435:693–696. [PubMed: 15864302]
2. Vetter IR, Arndt A, Kutay U, Gorlich D, Wittinghofer A. Cell. 1999; 97:635–646. [PubMed: 10367892]
3. Lee SJ, Imamoto N, Sakai H, Nakagawa A, Kose S, Koike M, Yamamoto M, Kumasaka T, Yoneda Y, Tsukihara T. J. Mol. Biol. 2000; 302:251–264. [PubMed: 10964573]
4. Cingolani G, Petosa C, Weis K, Muller CW. Nature. 1999; 399:221–229. [PubMed: 10353244]
5. Koerner C, Guan T, Gerace L, Cingolani G. J. Biol. Chem. 2003; 278:16216–16221. [PubMed: 12594203]
6. Cingolani G, Bednenko J, Gillespie MT, Gerace L. Mol. Cell. 2002; 10:1345–1353. [PubMed: 12504010]

7. Lee SJ, Sekimoto T, Yamashita E, Nagoshi E, Nakagawa A, Imamoto N, Yoshimura M, Sakai H, Chong KT, Tsukihara T, Yoneda Y. *Science*. 2003; 302:1571–1575. [PubMed: 14645851]
8. Bayliss R, Littlewood T, Stewart M. *Cell*. 2000; 102:99–108. [PubMed: 10929717]
9. Bayliss R, Littlewood T, Strawn LA, Wentz SR, Stewart M. *J. Biol. Chem.* 2002; 277:50597–50606. [PubMed: 12372823]
10. Liu SM, Stewart M. *J. Mol. Biol.* 2005; 349:515–525. [PubMed: 15878174]
11. Chook YM, Blobel G. *Nature*. 1999; 399:230–237. [PubMed: 10353245]
12. Lee BJ, Cansizoglu AE, Stiel KE, Louis TH, Zhang Z, Chook YM. *Cell*. 2006; 126:543–558. [PubMed: 16901787]
13. Cook A, Fernandez E, Lindner D, Ebert J, Schlenstedt G, Conti E. *Mol. Cell*. 2005; 18:355–367. [PubMed: 15866177]
14. Matsuura Y, Stewart M. *Nature*. 2004; 432:872–877. [PubMed: 15602554]
15. Petosa C, Schoehn G, Askjaer P, Bauer U, Moulin M, Steuerwald U, Soler-Lopez M, Baudin F, Mattaj JW, Muller CW. *Mol. Cell*. 2004; 16:761–775. [PubMed: 15574331]
16. Kobe B. *Nat. Struct. Biol.* 1999; 6:388–397. [PubMed: 10201409]
17. Fontes MR, Teh T, Kobe B. *J. Mol. Biol.* 2000; 297:1183–1194. [PubMed: 10764582]
18. Fontes MR, Teh T, Toth G, John A, Pavo I, Jans DA, Kobe B. *Biochem. J.* 2003; 375:339–349. [PubMed: 12852786]
19. Chen MH, Ben-Efraim I, Mitrousis G, Walker-Kopp N, Sims PJ, Cingolani G. *J. Biol. Chem.* 2005; 280:10599–10606. [PubMed: 15611084]
20. Fontes MR, Teh T, Jans D, Brinkworth RI, Kobe B. *J. Biol. Chem.* 2003; 278:27981–27987. [PubMed: 12695505]
21. Lanford RE, Butel JS. *Cell*. 1984; 37:801–813. [PubMed: 6086146]
22. Kalderon D, Richardson WD, Markham AF, Smith AE. *Nature*. 1984; 311:33–38. [PubMed: 6088992]
23. Colledge WH, Richardson WD, Edge MD, Smith AE. *Mol. Cell. Biol.* 1986; 6:4136–4139. [PubMed: 3025638]
24. Matsuura Y, Stewart M. *EMBO J.* 2005; 24:3681–3689. [PubMed: 16222336]
25. Conti E, Uy M, Leighton L, Blobel G, Kuriyan J. *Cell*. 1998; 94:193–204. [PubMed: 9695948]
26. Conti E, Kuriyan J. *Struct. Fold Des.* 2000; 8:329–338.
27. Matsuura Y, Lange A, Harreman MT, Corbett AH, Stewart M. *EMBO J.* 2003; 22:5358–5369. [PubMed: 14532109]
28. Stewart M, Kent HM, McCoy AJ. *J. Mol. Biol.* 1998; 284:1517–1527. [PubMed: 9878368]
29. Renault L, Nassar N, Vetter I, Becker J, Klebe C, Roth M, Wittinghofer A. *Nature*. 1998; 392:97–101. [PubMed: 9510255]
30. Renault L, Kuhlmann J, Henkel A, Wittinghofer A. *Cell*. 2001; 105:245–255. [PubMed: 11336674]
31. Lounsbury KM, Richards SA, Carey KL, Macara IG. *J. Biol. Chem.* 1996; 271:32834–32841. [PubMed: 8955121]
32. Azuma Y, Seino H, Seki T, Uzawa S, Klebe C, Ohba T, Wittinghofer A, Hayashi N, Nishimoto T. *J. Biochem. (Tokyo)*. 1996; 120:82–91. [PubMed: 8864848]
33. Azuma Y, Renault L, Garcia-Ranea JA, Valencia A, Nishimoto T, Wittinghofer A. *J. Mol. Biol.* 1999; 289:1119–1130. [PubMed: 10369786]
34. Hillig RC, Renault L, Vetter IR, Drell T, Wittinghofer A, Becker J. *Mol. Cell*. 1999; 3:781–791. [PubMed: 10394366]
35. Geyer JP, Doker R, Kremer W, Zhao X, Kuhlmann J, Kalbitzer HR. *J. Mol. Biol.* 2005; 348:711–725. [PubMed: 15826666]
36. Vetter IR, Nowak C, Nishimoto T, Kuhlmann J, Wittinghofer A. *Nature*. 1999; 398:39–46. [PubMed: 10078529]
37. Seewald MJ, Korner C, Wittinghofer A, Vetter IR. *Nature*. 2002; 415:662–666. [PubMed: 11832950]

38. Bernier-Villamor V, Sampson DA, Matunis MJ, Lima CD. Cell. 2002; 108:345–356. [PubMed: 11853669]
39. Reverter D, Lima CD. Nature. 2005; 435:687–692. [PubMed: 15931224]
40. Bullock TL, Clarkson WD, Kent HM, Stewart M. J. Mol. Biol. 1996; 260:422–431. [PubMed: 8757804]
41. Stewart M, Kent HM, McCoy AJ. J. Mol. Biol. 1998; 277:635–646. [PubMed: 9533885]
42. Clarkson WD, Corbett AH, Paschal BM, Kent HM, McCoy AJ, Gerace L, Silver PA, Stewart M. J. Mol. Biol. 1997; 272:716–730. [PubMed: 9368653]
43. Bayliss R, Leung SW, Baker RP, Quimby BB, Corbett AH, Stewart M. EMBO J. 2002; 21:2843–2853. [PubMed: 12065398]
44. Bayliss R, Ribbeck K, Akin D, Kent HM, Feldherr CM, Gorlich D, Stewart M. J. Mol. Biol. 1999; 293:579–593. [PubMed: 10543952]
45. Liker E, Fernandez E, Izaurralde E, Conti E. EMBO J. 2000; 19:5587–5598. [PubMed: 11060011]
46. Ho DN, Coburn GA, Kang Y, Cullen BR, Georgiadis MM. Proc. Natl. Acad. Sci. USA. 2002; 99:1888–1893. [PubMed: 11854490]
47. Grant RP, Hurt E, Neuhaus D, Stewart M. Nat. Struct. Biol. 2002; 9:247–251. [PubMed: 11875519]
48. Grant RP, Neuhaus D, Stewart M. J. Mol. Biol. 2003; 326:849–858. [PubMed: 12581645]
49. Fribourg S, Braun IC, Izaurralde E, Conti E. Mol. Cell. 2001; 8:645–656. [PubMed: 11583626]
50. Fribourg S, Conti E. EMBO Rep. 4:699–703. [PubMed: 12835756]
51. Handa N, Murayama K, Kukimoto M, Hamana H, Uchikubo C, Takemoto T, Terada T, Shirouzu M, Yokoyama S. to be published.
52. Hodel AE, Hodel MR, Griffis ER, Hennig KA, Ratner GA, Xu S, Powers MA. Mol. Cell. 2002; 10:347–358. [PubMed: 12191480]
53. Robinson MA, Park S, Sun ZY, Silver PA, Wagner G, Hogle JM. J. Biol. Chem. 2005; 280:35723–35732. [PubMed: 16105837]
54. Berke IC, Boehmer T, Blobel G, Schwartz TU. J. Cell Biol. 2004; 167:591–597. [PubMed: 15557116]
55. Weirich CS, Erzberger JP, Berger JM, Weis K. Mol. Cell. 2004; 16:749–760. [PubMed: 15574330]

Fig. 1. Structures of Kapβ1/Impβ complexes. Kapβ1 proteins are shown as red ribbons. Substrates IBB (blue) and SREBP2 (orange) are drawn as cylinders and ribbons, PTHrP as a yellow ribbon. Ran is shown in green and nucleoporin peptides in blue (Nsp1p and the GLFG peptide drawn as stick figure and nup1p as cylinder/ribbon). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this paper.)

Fig. 2.

Structures of Kap β 2/Transportin complexes, Cse1p complexes and a Crm1 fragment. In the two Kap β 2 complexes, both Kap β 2 (red) and Ran (green) are shown as cylinders/ribbons and substrate M9NLS is shown as a cyan ribbon. Cse1p and Crm1 are both shown as purple cylinders/ribbons, and Ran (green) and Kap α (yellow) in the Cse1p-Ran-Kap α complex as ribbons. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this paper.)

Fig. 3. Structures of mouse Kap α and yeast Kap60p complexes. Mouse Kap α s are all drawn as green ribbons and yeast Kap60p as blue ribbons. With the exception of Nup50p (red ribbon), all other ligands are shown as stick figures. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this paper.)

Fig. 4.

Structures of complexes involving Ran, NTF2, RanGAP and RanGEF. All 11 structures are shown as ribbon diagrams, with Ran in green, RanGAP in magenta, RCC1 RanGEF in blue, NTF2 in red, and RanBD1 or RanBP1-domain in gold (RanGppNHp-RBD1; 1RRP) and grey (RanGppNHp-RanBD1-RanGAP; 1K5D). RanGAP ligands, UBC9 is in aquamarine, SUMO is light brown and a fragment of Nup358 is in light green.

Fig. 5.

Structures of mRNA export factor TAP. TAP, Mex67p, p15 and MTR2p are all drawn as ribbons, and FG nucleoporin peptides are shown as stick figures. Domains of TAP and its yeast homolog Mex67p are in purple, p15 and its homolog Mtr2p are in red, and nucleoporin peptides in light green. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this paper.)

Fig. 6.
Structures of nucleoporin domains.

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: I14	Ran:	HP *	Ran: K37D/K152A binds Kap95p, but is unable to displace IBB
Kapβ1-RanGppNHP	IIBR	[2]	β1: human	2.3	β1: 1–462	β1 (chain B): 2–459	β1: HEAT repeats	β1: L59	Ran:	HP *	
Kapβ1	IGCJ	[3]	Mouse	2.6	1–449	1–449	HEAT repeats	D77	R111	Polar	

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
Kapβ1-IBB _{Kapα}	1Q GK	[4]	β1; human	2.5	β1: 1–867 α: 11–54	β1: 1–867 α: 11–54	β1: HEAT repeats α: IBB	β1: E281 D288 D339 D340 W342 W342 K346 V350 M388 D426 T427 W430 N469 W472 W472 E530 R593 D627 D627 M630 D676 E767 D824 W864 W864	α: R13 R13 K20 K20 R13 L14 F17 R13 K18 K18 K18 N19 N19 K22 R31 N35 R28 R31 I32 R39 K43 R51 R51 V53	Polar Polar Polar Polar HP [*] HP [*] HP [*] HP [*] Polar Polar HP [*] Polar Polar Polar HP [*] Polar Polar Polar HP [*] HP [*]	β1: W864 (~35-fold) W864/W342 W864/W430 W864/W472 (~400-fold) W342/W430/W864 W342/W472/W864 W430/W472/W864 (~950-fold) [5]
Kapβ1-PTHrP	1M5N	[6]	Human	2.9	β1: 1–485	β1: 1–485	β1: HEAT repeats	β1: I295	PTHrP: K93	HP [*]	

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
Kapβ1-SREBP-2	1UKL	[7]	β1: mouse	3.0	β1: 1–876	β1: 1–876	β1: HEAT repeats	W430	P86	HP [*]	
								W472	K89	HP [*]	
			SREBP-2: human	SREBP-2: 343–403	SREBP-2: 343–403	β1: SREBP-2: HEAT repeats	β1:				
							I295	Y379 (D)	HP [*]		
							F752	Y376 (C)	HP [*]		
Kapβ1-Nsp1p I	1F59	[8]	β1: human	2.8	β1: 1–442	β1: 1–440	β1: HEAT repeats	β1:	FxFG:		β1: I178D
								L174	F16	HP [*]	
			Nsp1p: yeast	Nsp1p: 497–608	FxFG: Nsp1p 8–20 and 41–48	I178	F16	HP [*]			
						F217	F14	HP [*]			
						F217	F16	HP [*]			
Kapβ1-GLFG	1O6O	[9]	β1: human	2.8	β1: 1–442	β1: 2–440	β1: HEAT repeats	I218	F16	HP [*]	
								Y255	F46	HP [*]	
			GLFG: Synthetic peptide	GLFG peptide: 1DSGGLFGSK9	GLFG: 4–7	GLFG: 9–14	β1: HEAT repeats	β1:	GLFG:		β1: I178D
								L174	F6	HP [*]	
								T175	L5	HP [*]	

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
			nup1p: yeast		1–861	1–861	HEAT repeats	L181	F1008	HP [*]	F977D/F987D
					nup1p: 963–1076	nup1p: 974–1012		I182	P1004	HP [*]	
								I182	F1008	HP [*]	
								V185	F1008	HP [*]	
								Y224	I1007	HP [*]	
								Y224	F1008	HP [*]	
								M226	F987	HP [*]	
								Q227	N986	Polar	
								Q227	F987	HP [*]	
								C230	I985	HP [*]	
								C230	F987	HP [*]	
								Y262	F987	HP [*]	
								M263	F977	HP [*]	
								Y268	P979	HP [*]	
								L270	P983	HP [*]	
								L270	I985	HP [*]	
								F317	F977	HP [*]	

^{*} HP, Hydrophobic contact.

Crystal structures of Kapβ2, Csel complexes and a Crml fragment

Table 2

Structure	PDB-ID	Ref.	Organism	Resolution (Å)	Protein constructs in crystals	Residues in model	Domains/ motifs	Contact residues (mol. 1)	Contact residues (mol. 2)	Contact residues (mol. 3)	Contact type	Disruptive interface mutants
Kapβ2-RanGppnhp	1QBK	[11]	β2: human	3.0	β2: 1–890	β2:	β2:	β2:	Ran:			
			Ran: human		Ran: 1–216	3–152, 158–166, 170–890	HEAT repeats	I114	R110		HP*	
								S165	R110		Polar	
								E275	K141		Polar	
						Ran:		E278	K141		Polar	
						8–197		I315	P172		HP*	
								E332	N154		Polar	
								R336	D148		Polar	
								P337	Y155		HP*	
								W373	N143		Polar	
								E682	K127		Polar	
Kapβ2-M9NLS	2H4M	[12]	β2: human	3.1	β2: 1–336-GSGSGS-368–890	β2: 6–36, 44–77, 57–73, 80–319, 368–890	β2: HEAT repeats	β2: R805	M9NLS: N268		Polar	β2: W460A/ W730A
								K765	Q269		Polar	
								E809, I773	F273		HP*	
								W730	P275		HP*	
								T766	M276		HP*	
								T547	N280		Polar	M9NLS:
								F584, E588,	F281		HP*	G274A/
								V643			HP*	P288A/
								A505, T506,	R284		Polar	Y289A
								E509, D543,			Polar	
								T547			Polar	
								L419, I457,	P288		HP*	
								W460			HP*	
								A380, A381,	Y289		HP*	
								D384, L419,			HP*	
Kapβ2-M9NLS from hnRNP A1, human			M9NLS: from hnRNP A1, human		M9NLS: 257–305		M9NLS: extended					

Structure	PDB-ID	Ref.	Organism	Resolution (Å)	Protein constructs in crystals	Residues in model	Domains/ motifs	Contact residues (mol. 1)	Contact residues (mol. 2)	Contact residues (mol. 3)	Contact type	Disruptive interface mutants
									E506	K130	Polar	
									E511	K132	Polar	
CrmI	1W9C	[15]	Human	2.3	707–1034	707–1027	HEAT repeats					

Crystal structures of Kapα complexes

Table 3

Structure	PDB-ID	Ref.	Organism	Resolution (Å)	Protein constructs in crystals	Residues in model	Domains/motifs	Contact residues (mol. 1)	Contact residues (mol. 2)	Contact interface type	Disruptive interface mutants								
Kapα	1IAL	[16]	Mouse	2.5	1–529	44–54, 70–496	Armadillo domain (ARM), IBB	ARM	IBB										
								T151	K49	Polar									
								T155	K49	Polar									
								D192	K49	Polar									
								D270	Q46	Polar									
Kapα-SV40 monopartite NLS	1EJL	[17]	Kapα: mouse	2.8	α: 70–529 SV40: 126–132	α: 72–497 sv40: 126–132	α: ARM	α:	SV40:										
								W142	K131	HP [*]									
								T155	K128	Polar									
								D192	K128	Polar									
								T328	K128	Polar									
								E354	K131	Polar									
								S360	K129	Polar									
								E396	K129	Polar									
								W399	K129	HP [*]									
								Kapα-SV40 CN	1QIT	[18]	Kapα: mouse	2.5	α: 70–529 SV40: 110–132	α: 70–496 SV40: 123–133 127–134	α: ARM	α:	SV40:		
																T155	K128	Polar	
D192	K128	Polar																	
E396	R130	Polar																	
Kapα-phospho-SV40CN	1QIS	[18]	Kapα: Mouse	2.3	α: 70–529 SV40: 110–132	α: 64–497 SV40: 119–133 128–132	α: ARM	α:	SV40:										
								T155	K128	Polar									
								D192	K128	Polar									
								E396	R130	Polar									

Structure	PDB-ID	Ref.	Organism	Resolution (Å)	Protein constructs in crystals	Residues in model	Domains/ motifs	Contact residues (mol. 1)	Contact residues (mol. 2)	Contact type	Disruptive interface mutants
monopartite											
NLS					PLSCR1: 257–266	PLSCR1: 257–266		E107	H262	Polar	
								W142	K261	HP *	
								W142	W263	HP *	
								T155	K258	Polar	
								W184	I299	HP *	
								W184	K261	HP *	
								D192	K258	Polar	
Kapα-nucleoplasmin bipartite NLS	1EJY	[17]	Kapα: mouse	2.9	α: 70–529	α: 72–497	α: ARM	α:	NLS:		
					Nucleoplasmin: 155–170	Nucleoplasmin: 155–170		T155	K167	Polar	
								D192	K167	Polar	
								W231	K168	HP *	
								S360	R156	Polar	
								E396	R156	Polar	
Kapα-NIN2 bipartite NLS	1PJN	[20]	Kapα: mouse	2.5	α: 70–529	α: 72–496	α: ARM	α:	NIN2:		SV40:
								W142	K554	HP *	K128
			NIN2: <i>Xenopus</i> , peptide		NIN2: 533–556	NIN2: 535–555		N146	S553	Polar	[21–23]
								T155	K551	Polar	
								Q181	K554	Polar	
								S276	K547	Polar	
								Y277	K547	HP *	
								T322	K539	Polar	
								T328	K537	Polar	
								S360	R538	Polar	
								E396	R538	Polar	

Structure	PDB-ID	Ref.	Organism	Resolution (Å)	Protein constructs in crystals	Residues in model	Domains/ motifs	Contact residues (mol. 1)	Contact residues (mol. 2)	Contact type	Disruptive interface mutants
Kapα-nup50	2C1M	[24]	RB: human peptide	2.2	RB: 859–879	RB: 859–878	α.: ARM	Q181	R877	Polar	
								D192	K874	Polar	
								Y277	K871	Polar	
								T328	K861	Polar	
								E396	R862	Polar	
Kapα-nup50	2C1M	[24]	Kapα: mouse	2.2	α.: 70–529	α.: 75–498	α.: ARM	α.:	Nup50:		Nup50p: R38A/ R45D
								K240	E9	Polar	
								L307	W15	HP *	
								T328	K3	Polar	
								K348	D16	Polar	
								S360	R4	Polar	
								K392	E7	Polar	
								E396	R4	Polar	
								D471	R45	Polar	
								E474	R45	Polar	
								E493	K41	Polar	
Kap60p	1BK5	[25]	Kap60p: yeast	2.2	Kap60p: 88–530	Kap60p: 89–509	Kap60p: ARM				
Kap60p-SV40 monopartite NLS	1BK6	[25]	Kap60p: yeast	2.8	Kap60p: 88–530	Kap60p: 89–509	Kap60p: ARM	Kap60p: W153	SV40: K131	HP *	Kap60p: N157A/ D203K
								T166	K128	Polar	
								Q192	K131	Polar	
								W195	K129	HP *	
								D203	K128	Polar	
								W237	K127	HP *	
								E272	K129	Polar	
								D276	K127	Polar	
								D331	K127	Polar	
								E402	K128	Polar	

Structure	PDB-ID	Ref.	Organism	Resolution (Å)	Protein constructs in crystals	Residues in model	Domains/ motifs	Contact residues (mol. 1)	Contact residues (mol. 2)	Contact type	Disruptive interface mutants
Kap60 p- <i>c-myc</i> monopartite NLS	1EE4	[26]	Kap60p: yeast <i>c-myc</i> : human peptide	2.1	Kap60p: 88–530 <i>c-myc</i> : 319–329	Kap60p: 87–509 <i>c-myc</i> : 320–328 323–326	Kap60p: ARM	Kap60p: NLS: T166 W195 D203 D276 T334 S366 E402	NLS: K323 K326 K323 R324 K323 R324 R324	Polar HP* Polar Polar Polar Polar Polar	
Kap60p- Nucleopalsmin bipartite NLS	1EE5	[26]	Kap60p: yeast Nucleoplasmin: <i>Xenopus</i> peptide	2.4	Kap60p: 88–530 Nucleoplasmin: 154–172	Kap60p: 90–506 Nucleoplasmin: 153–171	Kap60p: ARM	Kap60p: W195 D203 W237 W279 T334 S366 E402	NLS: K170 K167 K168 K162 K155 R156 R156	HP* Polar HP* HP* Polar Polar Polar	
Kap60p -nup2p	1UN0 (2C1T)	[27] [24]	Kap60p: yeast nup1p: yeast	2.6	Kap60p: 88–530 Nup1p: 1–51	Kap60p: 88–526 Nup1p: 36–51	Kap60p: ARM Nup1p: N-terminal Kap60p Binding domain and NPC targeting domain	Kap60p: S240 N241 D276 W279 W363 E402	Nup1p: R47 R47 R47 K45 K40 R38	Polar Polar Polar HP* HP* Polar	

* HP, Hydrophobic contact.

Structures of Ran and NTF2 complexes

Table 4

Structure	PDB-ID	Ref.	Organism	Method	Resolution (Å)	Protein constructs in crystals	Residues in model	Domains/ motifs	Contact residues (mol. 1)	Contact residues (mol. 2)	Contact residues (mol. 3)	Contact type	Disruptive interface mutants
RanGDP	1BYU	[28]	Canine	Crystal	2.15	1–216	A: 2–216 B: 5–208	G-domain					
RanGDP Q69L	3RAN	[28]	Canine	Crystal	2.3	1–216	5–205	G-domain					
RCC1	1A12	[29]	Human	Crystal	1.7	1–421	21–421	7-Bladed propeller					
Ran-RCC1	1I2M	[30]	Ran: human RCC1: human	Crystal	1.8	Ran: 1–216 RCC1:	Ran: 8–31, 37–177 RCC1:	Ran: G-domain RCC1:	Ran: K71 R76	RCC1: H304 E334		Polar Polar Polar Polar Polar Polar Polar	Ran: G19V [31] RCC1: D128A, D182A, H304A [32,33]
RanGAP (malp)	1YRG	[34]	<i>S. pombe</i>	Crystal	2.66	1–387	2–344	LRR					
RanBD2 of RanBP2	1XKE	[35]	human	NMR		2028–2154 (RanBP2)	2028–2154 (RanBP2)	PH					
Ran-GppNHp-RanBD1	1RRP	[36]	Ran: human RanBD1 of Ran BP2: human	Crystal	2.9	Ran: 1–216 RanBD1 of Ran BP2:	Ran: (A) 8–211 (C): 8–187	RanBD1: PH Ran: G-domain	Ran: F11 F11 R29	RanBD1: V21 V22 E59		HP * HP * Polar	

Structure	PDB-ID	Ref.	Organism	Method	Resolution (Å)	Protein constructs in crystals	Residues in model	Domains/ motifs	Contact residues (mol. 1)	Contact residues (mol. 2)	Contact residues (mol. 3)	Contact residues (mol. 4)	Contact type	Disruptive interface mutants
Ran-GDP-RanBP1-RanGAP	1K5G	[37]	Ran: human	Crystal	3.1	Ran: 1–216	Ran: 8–213	RanGAP: LRR	L201	K111			HP*	
									L201	V121			HP*	
									D213	K54			Polar	
									D213	R141			Polar	
Ran-GDP-RanBP1-RanGAP	1K5G	[37]	RanBP1: human	Crystal	3.1	RanBP1: 1–201	RanBP1: 22–167	RanGAP: LRR	D18	R168			Polar	
									L43	I79			HP*	
									D128	R200			Polar	
									K130	D225			Polar	
									K130	L255			HP*	
									V9		L33		HP*	
									R29		E69		Polar	
									N55		E35		Polar	
									R56		E35		Polar	
									W163		F27		HP*	
Ran-GDP-RanBP1-RanGAP	1K5G	[37]	RanGAP: Yeast (<i>S. pombe</i>)	Crystal	3.1	RanGAP: 1–386	RanGAP: 2–345	RanGAP: LRR	K167		D24		Polar	
									K167		Q26		Polar	
									L168		I30		HP*	
									I169		V31		HP*	
									I169		L33		HP*	
									V177		I38		HP*	
									L201		K111		HP*	
									L201		V121		HP*	
									D213		K54		Polar	
									D213		R141		Polar	
Ubc9-RanGAP1	1KPS	[38]	Ubc9: human	Crystal	2.5	Ubc9: 1–159	Ubc9: 3–158	RanGAP1:	Ubc9:	RanGAP1:				
									K74	E528			Polar	

Structure	PDB-ID	Ref.	Organism	Method	Resolution (Å)	Protein constructs in crystals	Residues in model	Domains/ motifs	Contact residues (mol. 1)	Contact residues (mol. 2)	Contact residues (mol. 3)	Contact residues (mol. 4)	Contact type	Disruptive interface mutants
RanGAP1: mouse														
SUMO-1- RanGAP1- Ubc9- Nup358/ RanBP2	1Z5S	[39]	Human	Crystal	3.0	SUMO-1: 18–97 RanGAP1: 419–587 Ubc9: 1–158 Nup358: 2631–2695	RanGAP1: 434–589 RanGAP1: 432–587 Ubc9: 2–157	RanBP2: E3 ligase domain	SUMO-1: R63 Q92 K39 R54	RanGAP1: E122 E526	Ubc9: R104 E122 K74	Nup358: D2631 E2637 E2675 D2673 D2676	HP* Polar Polar Polar Polar Polar Polar Polar Polar	
NTF2	1OUN	[40]	Rat	Crystal	1.6	1–127	(A): 2–126 (B): 4–124							
NTF2-RanGDP	1A2K	[41]	NTF2: rat Ran: canine	Crystal	2.5	NTF2: 1–127 Ran: 1–216	NTF2: 4–127 Ran: (C) 8–206 (D) 8–204	Ran: G-protein domain	NTF2: W41 E42 F61 I64 L89 D92 D94 F119	Ran: F72 R76 F72 F72 F72 K71 K71 F72			HP* Polar HP* HP* HP* Polar Polar HP*	NTF2: E42K, D92/94N [42] Ran: Q69L [28]
NTF2 N77Y-FxFG	1GYB	[43]	Yeast	Crystal	1.9	NTF2: 1–125	NTF2:		NTF2 (A):	FxFG (A):				NTF2:

Structure	PDB-ID	Ref.	Organism	Method	Resolution (Å)	Protein constructs in crystals	Residues in model	Domains/ motifs	Contact residues (mol. 1)	Contact residues (mol. 2)	Contact residues (mol. 3)	Contact type	Disruptive interface mutants
							3–124 (A and B) 5–124 (C and D)		F5	F43		HP [*]	Q43/45D
									P73	F43		HP [*]	W7A [44]
									P73	F45		HP [*]	
									NTF2(B): FxFg(B):				
									E34	F45		HP [*]	
									M36	F43		HP [*]	
									M36	F45		HP [*]	
									Q43	F43		HP [*]	
									F115	F45		HP [*]	

^{*} HP, Hydrophobic contact.

Structures of mRNA export complexes

Table 5

Structure	PDB-ID	Ref.	Organism	Method	Resolution (Å)	Protein constructs in crystals	Residues in model	Domains/motifs	Contact residues (mol. 1)	Contact residues (mol. 2)	Contact type	Disruptive interface mutants
TAP-RBD (LRR)	1FO1	[45]	Human	Crystal	2.9	102–372	123–191, 203–362	Partially disordered RNP domain and LRR domains				
TAP-RBD (RNP)	1FT8	[45]	Human	Crystal	3.15	102–372	119–198, 205–362	RNP domains and LRR domains				
TAP-novel RBD (native)	1KOH	[46]	Human	Crystal	3.8	96–372	A: 105–362 B: 201–367 C: 105–362 D: 201–372	RNP and LRR domains				
Tap/NXF1-C-term	1GO5	[47]	Human	NMR		551–619	551–619	UBA-like domain				
TAP-UBA-FXFG	1OAI	[48]	Human	Crystal	1	TAP: 561–619 FXFG: DSGFSFGSK	TAP: 561–619 FXFG: 10–18	TAP: UBA-like domain	TAP: M580 W584 K587 C588 A602 L606 E611 P613	FG: F15 F15 F15 F15 F15 F15 F13 F13	HP* HP* HP* HP* HP* HP* HP* HP*	TAP: C588
TAP-p15	1JKG	[49]	TAP: human	Crystal	1.9	TAP: 371–619	TAP: 370–423, 431–555	TAP: UBA-like domain NTF2-like domain	TAP: R440	p15: D76		TAP: D482R

Structure	PDB-ID	Ref.	Organism	Method	Resolution (Å)	Protein constructs in crystals	Residues in model	Domains/motifs	Contact residues (mol. 1)	Contact residues (mol. 2)	Contact type	Disruptive interface mutants
TAP-p15-FG	1JN5	[49]	p15: human	Crystal	2.8	p15: 2–140	p15: 1–240	p15: NTF2-like domain	K446 D482 I518 F535	E18 R134 V80 C96	Polar Polar HP* HP*	I518R
TAP-p15-FG	1JN5	[49]	p15: human	Crystal	2.8	371–619	371–422, 430–555	NTF2-like domain domain,	L383 L386 P521 L527	F1810 F1810 F1810 F1810	HP* HP* HP* HP*	L383R, L386R, W594A
Mex67-Mtr2	1OF5	[50]	Mex67: <i>Saccharomyces cerevisiae</i> Mtr2: <i>S. cerevisiae</i>	Crystal	2.8	Mex67: 264–407, 436–488 Mtr2: 1–184	Mex67: 268–315, 354–107, 436–488 Mtr2: 14–106, 141–177	NTF2-like domain	Mex67: D446 T466 E385	Mtr2: S148 N99 N170	Polar Polar Polar	

* HP, Hydrophobic contact.

Table 6

Structures of nucleoporins

Structure	PDB-ID	Ref.	Organism	Method	Resolution (Å)	Protein constructs in crystals	Residues in model	Domains/motifs
Nup35	1WWH	[51]	Mouse	Crystal	2.70	149–267	169–249	Mppn domain
c-Nup98 autoprotease domain	1KO6	[52]	Human	Crystal	3.00	710–870	712–870	Auto-proteolytic/pore-targeting
c-Nup116p	2AIV	[53]	Yeast	NMR		967–1113	967–1113	Pore-targeting
n-Nup133	1XKS	[54]	Human	Crystal	2.35	67–514	75–162, 170–201, 206–251, 270–177	7-Bladed β-propeller
n-Nup159p	1XIP	[55]	Yeast	Crystal	2.5	2–387	2–347, 362–381	7-Bladed β-propeller