Supplementary Materials

Table I

2ptcE		1l9hA		1bz0AB		101m		1gpaA		1g5yB		1kzkA	
All memb	Repr	All memb	Repr	All memb	Repr	All memb	Repr	All memb	Repr	All memb	Repr	All memb	Repr
30E	30E	57A	57A	98	14A	14	24	163A	90A	307B	307B	85A	23A
46E	46E	67A	67A	99	15B	42	26	166A	163A	353B	309B	87A	28A
138E	53E	261A	73A	103	42A	69	42	182A	166A	420B	324B		32A
141E	138E	265A	122A	131	65A	71	69	273A	179A	424B	330B		50A
189E	141E	268A	253A	141	65B	89	71	277A	180A	426B	352B		85A
194E	189E	293A	268A	145	66A	104	72	608A	184A		421B		87A
212E	194E	301A	293A		68B	107	89		185A		426B		
213E	212E	312A	296A		70B	131	104		194A		431B		
227A	213E		301A		71B		138		196A		438B		
228A	227E		302A		85B				250A		443B		
	228E		312A		98A				269A				
					101A				271A				
					106A				273A				
					110B				277A				
					128A				568A				
									608A				

Table I List of predicted interconnectivity determinants (ICD) and conserved interconnectivity determinants (CICD) for each protein family in our study.

Table II

2ptc		1l9h		101m		1gpa	
CICDs	CONSERVED	CICDs	CONSERVED	CICDs	CONSERVED	CICDs	CONSERVED
Gln30	GLY19	Leu57	MET1	**Trp14**	VAL1	Phe163	ALA54
Leu46	CYS22	**Lys67**	ASN2	**Lys42**	LEU2	**Phe166**	THR70
Ile138	SER32	**Phe261**	GLY3	**Leu69**	GLU6	**Trp182**	TYR84
Trp141	CYS42	**Trp265**	THR4	**Ala71**	TRP7	Glu273	SER86
Asp189	GLY43	**Tyr268**	GLU5	**Leu89**	VAL10	Arg277	GLU88
Asp194	**LEU46**	**Phe293**	GLY6	**Leu104**	LEU11	**Lys608**	TYR90
Ile212	TRP51	**Tyr301**	PHE9	**Ile107**	**TRP14**		GLY92
Val213	VAL52	**Gln312**	TYR10	**Met131**	LYS16		LEU95
Val227	SER54		PRO12		VAL17		ASN97
Tyr228	ALA55		ASN15		GLU18		GLU126
	ALA56		GLY18		ASP20		ASP128
	HIS57		PRO23		HIS24		ALA129
	CYS58		PRO27		GLY25		LEU131

	VAL65		GLN28		LEU32		GLY132
	LEU67		TYR29		PHE33		ASN133
	GLY69		TYR30		HIS36		GLY134
	HIS91		LEU31		PRO37		GLY135
	PRO92		LEU40		GLU38		LEU136
	ASP102		ALA42		THR39		GLY137
	MET104		TYR43		LEU40		ARG138
	LEU105		MET44		GLU41		LEU139
	VAL118		PHE45		**LYS42**		ALA140
	CYS136		LEU47		PHE43		ALA141
	SER139		ILE48		LYS47		CYS142
	GLY140		GLY51		LYS50		ASP145
	TRP141		PRO53		MET55		SER146
	GLY142		ASN55		SER58		ALA148
	CYS157		PHE56		LEU61		THR149
	CYS168		THR58		LYS63		GLY156
	ILE176		LEU59		GLY65		TYR157
	MET180		VAL61		VAL68		GLY158
	CYS182		THR62		**LEU69**		TYR161
	CYS191		LYS66		**ALA71**		GLY164
	ASP194		**LYS67**		LEU72		**PHE166**
	SER195		LEU68		GLY73		GLN168
	GLY196		ARG69		LEU76		GLN175
	GLY197		PRO71		LYS77		GLU177
	PRO198		LEU72		LYS78		ASP180
	VAL199		ASN73		GLY80		**TRP182**
	CYS201		TYR74		ALA84		LEU183
	GLY211		ILE75		**LEU89**		GLU190
	VAL213		LEU77		ALA90		GLY204
	SER214		ASN78		SER92		VAL206
	GLY216		LEU79		HIS93		ASP227
	CYS220		PHE85		ALA94		ARG242
	PRO225		MET86		LYS96		TRP244
	TRP237		GLY90		HIS97		ASN258
	ILE238		PHE91		LYS98		GLY260
	THR241		THR94		ILE99		LEU279
	ASN245		SER98		PRO100		TYR280
			TYR102		LYS102		ASP283
			PHE103		TYR103		GLY288
			GLY106		**LEU104**		LEU291
			GLY109		GLU105		ARG292
			CYS110		**ILE107**		LEU293
			GLU113		SER108		GLN295
			GLY114		ILE111		GLU296
			PHE116		HIS119		GLN336
			ALA117		PHE123		ASN338

			THR118		ALA130		ASP339
			GLY120		**MET131**		THR340
			GLY121		ALA134		HIS341
			GLU122		LEU135		PRO342
			LEU125		GLU136		GLU348
			TRP126		LEU137		LEU353
			LEU128		PHE138		ASP355
			VAL129		ARG139		ALA364
			LEU131		ASP141		THR375
			GLU134		ALA143		ASN376
			ARG135		TYR146		HIS377
			VAL138		LEU149		THR378
			CYS140		GLY150		GLU382
			LYS141		GLY153		ALA383
			PRO142				LEU384
			ASN145				GLU385
			PHE146				ARG398
			ARG147				ILE403
			PHE148				ILE406
			HIS152				MET441
			ALA153				ALA442
			GLY156				LEU444
			TRP161				ASN453
			MET163				GLY454
			ALA164				VAL455
			CYS167				HIS459
			PRO171				SER460
			GLY174				PRO476
			TRP175				PHE479
			SER176				ASN481
			ARG177				THR483
			TYR178				ASN484
			ILE179				GLY485
			PRO180				THR487
			GLY182				ARG489
			GLN184				ARG490
			CYS185				TRP491
			SER186				LEU499
			CYS187				LYS538
			GLY188				LYS542
			ASN200				PHE563
			SER202				ASP564
			PHE203				LYS568
			VAL204				ARG569
			TYR206				HIS571
			MET207				TYR573

			PHE208				LYS574
			HIS211				ARG575
			PHE212				GLN576
			PRO215				ASN579
			PHE221				PRO600
			CYS222				GLY607
			TYR223				**LYS608**
			GLY224				ALA609
			LEU226				ALA610
			VAL230				PRO611
			LYS231				TYR613
			ALA233				ALA616
			ALA235				LYS617
			THR243				ILE619
			GLN244				ILE620
			ALA246				ILE626
			GLU247				ASN631
			GLU249				ASP633
			VAL250				VAL642
			ARG252				PHE644
			MET253				TYR648
			VAL254				VAL650
			MET257				ALA653
			PHE261				PRO658
			LEU262				ASP661
			CYS264				SER663
			TRP265				GLN665
			PRO267				ILE666
			TYR268				SER667
			ALA269				THR668
			VAL271				ALA669
			ALA272				GLY670
			ILE275				GLU672
			PHE276				ALA673
			GLN279				SER674
			GLY280				GLY675
			PHE283				THR676
			PRO285				GLY677
			PHE287				ASN678
			MET288				MET679
			THR289				LYS680
			PRO291				ASN684
			PHE293				GLY685
			PHE294				LEU687
			ALA295				ILE689
			LYS296				GLY690

			TYR301				THR691
			ASN302				ASP693
			PRO303				GLY694
			ILE305				ALA695
			TYR306				ASN696
			ILE307				GLU698
			ASN310				GLY704
			GLN312				ASN707
			ARG314				PHE711
			CYS316				GLY712
			GLY324				VAL718
			ASN326				ASP769
			VAL345				ASP776
							TYR780
							TRP797
							PHE811
							SER812
							SER813
							ASP814
							ARG815
							ILE817
							TYR820
							ILE824
							TRP825

1bz0			**1g5y**		**1kzk**	
CICDs	**CONSERVED (CHAIN A)**	**CONSERVED (CHAIN B)**	**CICDs**	**CONSERVED**	**CICDs**	**CONSERVED**
Phe98	VAL1	VAL1	**Glu307**	VAL232	Ile85	PRO1
Lys99	LEU2	HIS2	Leu353	CYS269	**Arg87**	PRO9
His103	SER3	LEU3	Leu420	LEU276		LEU23
Arg141	ASP6	THR4	Ala424	ALA283		ASP25
Gln131	LYS7	GLU7	**Arg426**	PHE289		THR26
Tyr145	TRP14	LYS8		ASP296		GLY27
	GLY18	VAL11		GLN297		ALA28
	TYR24	LEU14		LEU300		GLY49
	GLY25	TRP15		TRP305		GLY52
	ALA28	LYS17		**GLU307**		PRO81
	LEU29	VAL18		LEU308		GLY86
	GLU30	ASN19		LEU309		**ARG87**
	ARG31	VAL20		VAL354		PHE99
	PHE33	VAL23		ASP363		
	PRO37	GLY24		GLU366		
	THR38	GLY25		ARG371		
	THR39	GLU26		ALA372		

	LYS40	LEU28		ASP379		
	THR41	GLY29		ARG393		
	TYR42	ARG30		LEU400		
	PHE43	LEU31		ARG414		
	PRO44	LEU32		LEU419		
	PHE46	VAL34		LEU422		
	HIS50	TYR35		PRO423		
	GLY51	PRO36		LEU425		
	SER52	TRP37		**ARG426**		
	GLN54	THR38		GLY443		
	VAL55	GLN39		PRO458		
	HIS58	ARG40				
	GLY59	PHE42				
	LYS61	SER44				
	VAL62	PHE45				
	ALA65	GLY46				
	LEU66	LEU48				
	ALA69	SER49				
	ASP74	ALA53				
	PRO77	MET55				
	LEU83	ASN57				
	SER84	LYS59				
	ASP85	VAL60				
	LEU86	LYS61				
	HIS87	ALA62				
	ALA88	HIS63				
	LYS90	GLY64				
	LEU91	LYS65				
	VAL93	LYS66				
	ASP94	VAL67				
	PRO95	LEU68				
	VAL96	PHE71				
	ASN97	SER72				
	PHE98	GLY74				
	LYS99	LEU75				
	LEU100	LEU78				
	LEU101	ASP79				
	HIS103	LEU81				
	LEU105	LYS82				
	LEU106	THR84				
	VAL107	PHE85				
	THR108	LEU88				
	ALA110	SER89				
	PHE117	GLU90				
	THR118	LEU91				
	PRO119	HIS92				
	ALA120	CYS93				

	HIS122	LEU96				
	ALA123	HIS97				
	SER124	VAL98				
	ASP126	ASP99				
	LYS127	PRO100				
	PHE128	GLU101				
	VAL132	ASN102				
	THR134	PHE103				
	VAL135	LEU105				
	LEU136	LEU106				
	SER138	GLY107				
	LYS139	ASN108				
	TYR140	VAL109				
	ARG141	LEU110				
		VAL111				
		CYS112				
		VAL113				
		LEU114				
		ALA115				
		PHE118				
		GLY119				
		LYS120				
		GLU121				
		PHE122				
		THR123				
		PRO124				
		GLN127				
		ALA128				
		ALA129				
		GLN131				
		LYS132				
		VAL133				
		VAL134				
		ALA135				
		GLY136				
		VAL137				
		ALA138				
		ALA140				
		LEU141				
		ALA142				
		HIS143				
		LYS144				
		TYR145				
		HIS146				

Table II Comparison between the CICDs and sequence conserved residues for each protein family. CICD residues, which are sequence conserved, are shown in bold type characters. Solvent accessible residues are indicated with dark grey shading.

Table III

Protein	PDB ID	Predicted residues	Clustering
acylphosphatase	**1aps**	**11**	**--**
serine proteinase inhibitor CI-2	**2ci2**	67 **80**	Yes
major cold shock protein	**1mjc**	**21** 32 **67**	Yes
tenascin	**1ten**	833 **835** 837 **871** **873**	Yes
prolactin	**1f6f**	176 **180**	Yes

Table III CICD residues corresponding to five examples of non-allosteric proteins. Experimentally verified key residues for protein folding are shown in bold characters. The predicted CICDs form clusters belonging to the protein folding nuclei. Experimental data for these proteins was obtained as follows: 1mjc (de Bono *et al*, 2005), 1f6f (Sami *et al*, 1999), 1ten (Mirny & Shakhnovich, 1999), 1aps (Vendruscolo *et al*, 2002), 2ci2 (Dokholyan *et al*, 2005).

Figure 1

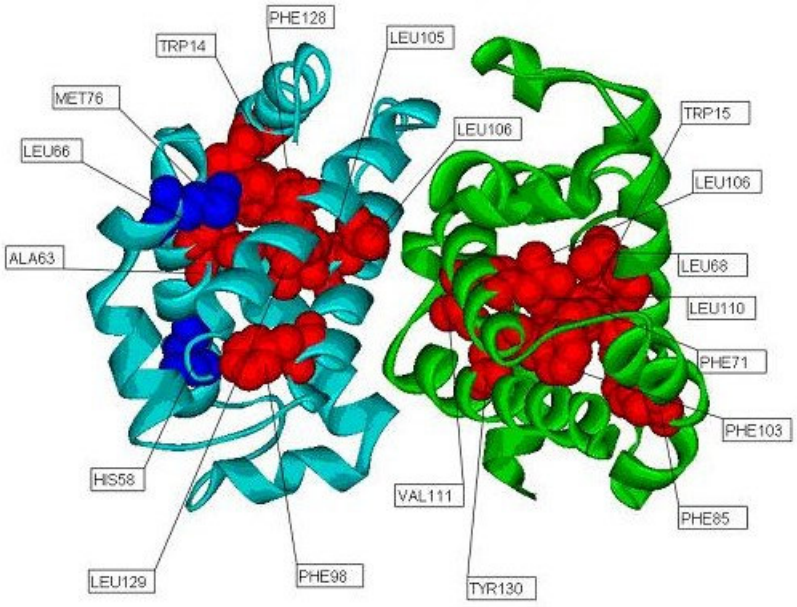

Figure 1 CICD residues of the T and R state structures of the alpha-beta homodimer of human hemoglobin depicted in the oxygenated state (R state)**.** The two subunits are colored in blue and green (alpha and beta, respectively). The CICD residues predicted that overlap in both states (T and R) are shown in red. CICD residues only predicted in R state are depicted in blue.

Figure 2a

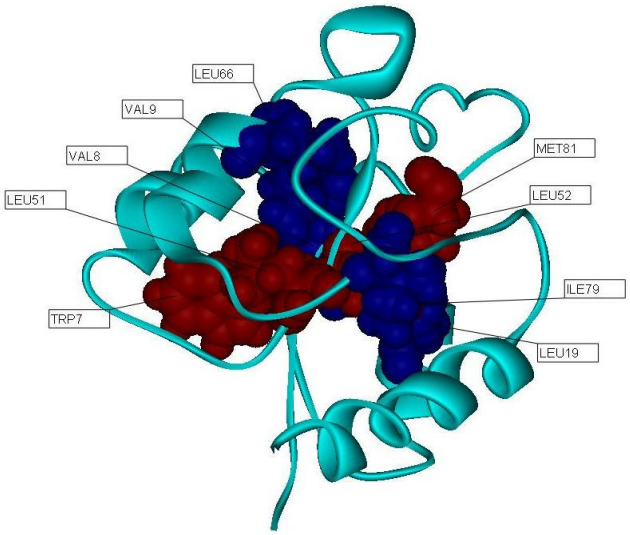

Figure 2b

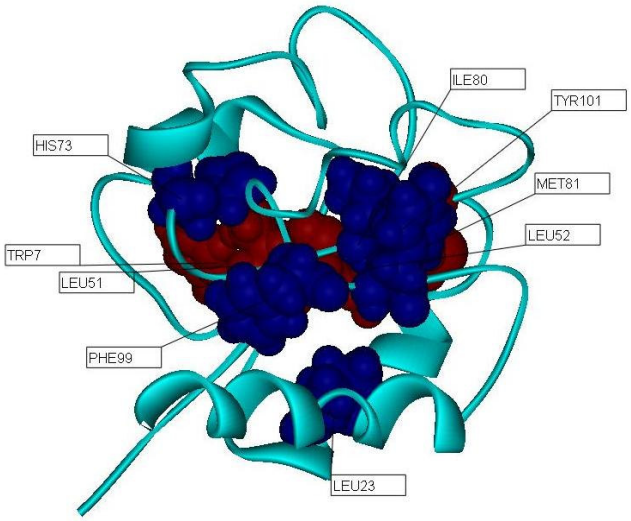

Figure 2(a) Representation of the inactive state of the Nitrogen regulator I protein (NtrC, PDB ID 1dc7). The central residues in both states are shown in red. The residues predicted only in the inactive state are depicted in blue. **(b)** Mapping of the central residues onto the active state of the NtrC (PDB ID 1dc8). The central residues in both states are shown in red. The residues predicted only in the inactive state are depicted in blue.

Figure 3

2ptcE

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1hj8A      IVGGYECKAY SQPHQVSLN. SGYHFCGGSL VNENWVVSAA HCYKSRVEVR
1h4wA      IVGGYTCEEN SLPYQVSLN. SGSHFCGGSL ISEQWVVSAA HCYKTRIQVR
1mctA      IVGGYTCAAN SIPYQVSLN. SGSHFCGGSL INSQWVVSAA HCYKSRIQVR
1tawA      IVGGYTCGAN TVPYQVSLN. SGYHFCGGSL INSQWVVSAA HCYKSGIQVR
1tpaE      IVGGYTCGAN TVPYQVSLN. SGYHFCGGSL INSQWVVSAA HCYKSGIQVR
2ptcE      IVGGYTCGAN TVPYQVSLN. SGYHFCGGSL INSQWVVSAA HCYKSGIQVR
1trnA      IVGGYNCEEN SVPYQVSLN. SGYHFCGGSL INEQWVVSAG HCYKSRIQVR
3tgiE      IVGGYTCQEN SVPYQVSLN. SGYHFCGGSL INDQWVVSAA HCYKSRIQVR


1hj8A      LGEHNIKVTE GSEQFISSSR VIRHPNYSSY NIDNDIMLIK LSKPATLNTY
1h4wA      LGEHNIKVLE GNEQFINAVK IIRHPKYNRD TLDNDIMLIK LSSPAVINAR
1mctA      LGEHNIDVLE GNEQFINAAK IITHPNFNGN TLDNDIMLIK LSSPATLNSR
1tawA      LGEDNINVVE GNEQFISASK SIVHPSYNSN TLNNDIMLIK LKSAASLNSR
1tpaE      LGEDNINVVE GNEQFISASK SIVHPSYNSN TLNNDIMLIK LKSAASLNSR
2ptcE      LGEDNINVVE GNEQFISASK SIVHPSYNSN TLNNDIMLIK LKSAASLNSR
1trnA      LGEHNIEVLE GNEQFINAAK IIRHPQYDRK TLNNDIMLIK LSSRAVINAR
3tgiE      LGEHNINVLE GNEQFVNAAK IIKHPNFDRK TLNNDIMLIK LSSPVKLNAR


1hj8A      V..QPVALPT SCAPAGTMCT VSGWGNTMSS .TADSNKLQC LNIPILSYSD
1h4wA      V..STISLPT APPAAGTECL ISGWGNTLSF GADYPDELKC LDAPVLTQAE
1mctA      V..ATVSLPR SCAAAGTECL ISGWGNTKSS GSSYPSLLQC LKAPVLSNSS
1tawA      V..ASISLPT SCASAGTQCL ISGWGNTKSS GTSYPDVLKC LKAPILSTSS
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1tpaE      V..ASISLPT SCASAGTQCL ISGWGNTKSS GTSYPDVLKC LKAPILSDSS
2ptcE      V..ASISLPT SCASAGTQCL ISGWGNTKSS GTSYPDVLKC LKAPILSDSS
1trnA      V..STISLPT APPATGTKCL ISGWGNTASS GADYPDELQC LDAPVLSQAK
3tgiE      V..ATVALPS SCAPAGTQCL ISGWGNTLSS GVNEPDLLQC LDAPLLPQAD

1hj8A      CNNSYPGMIT NAMFCA.YLE G.KDSCQGDS GGPVVCNGEL QGVVSWGYGC
1h4wA      CKASYPGKIT NSMFCV.GLE G.GDSCQRDS GGPVVCNGQL QGVVSWGHGC
1mctA      CKSSYPGQIT GNMICV.FLQ G.KDSCQGDS GGPVVCNGQL QGIVSWGYGC
1tawA      CKSAYPGQIT SNMFCA.YLE G.KDSCQGDS GGPVVCSGKL QGIVSWGSGC
1tpaE      CKSAYPGQIT SNMFCA.YLE G.KDSCQGDS GGPVVCSGKL QGIVSWGSGC
2ptcE      CKSAYPGQIT SNMFCA.YLE G.KDSCQGDS GGPVVCSGKL QGIVSWGSGC
1trnA      CEASYPGKIT SNMFCV.FLE G.KDSCQGDS GGPVVCNGQL QGVVSWGDGC
3tgiE      CEASYPGKIT DNMVCV.GLE G.GDSCQGDS GGPVVCNGEL QGIVSWGYGC

1hj8A      .EPGNPGVYA KVCIFNDWLT STMASY.
1h4wA      .AKNRPGVYT KVYNYVDWIK DTIAANS
1mctA      .QKNKPGVYT KVCNYVNWIQ QTIAAN.
1tawA      .QKNKPGVYT KVCNYVSWIK QTIASN.
1tpaE      .QKNKPGVYT KVCNYVSWIK QTIASN.
2ptcE      .QKNKPGVYT KVCNYVSWIK QTIASN.
1trnA      .QKNKPGVYT KVYNYVKWIK NTIAANS
3tgiE      .APDNPGVYT KVCNYVDWIQ DTIAAN.
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1l9hA

```
1l9hA      MNGTEGPNFY VPFSNKTGVV RSPFEAPQYY LAEPWQFSML AAYMFLLIML
1f88A      MNGTEGPNFY VPFSNKTGVV RSPFEAPQYY LAEPWQFSML AAYMFLLIML
1hzxA      MNGTEGPNFY VPFSNKTGVV RSPFEAPQYY LAEPWQFSML AAYMFLLIML
1ln6A      .......... .......... .......... .........L AAYMFLLIML

1l9hA      GFPINFLTLY VTVQHKKLRT PLNYILLNLA VADLFMVFGG FTTTLYTSLH
1f88A      GFPINFLTLY VTVQHKKLRT PLNYILLNLA VADLFMVFGG FTTTLYTSLH
1hzxA      GFPINFLTLY VTVQHKKLRT PLNYILLNLA VADLFMVFGG FTTTLYTSLH
1ln6A      GFPINFLTLY VTVQHKKLRT PLNYILLNLA VADLFMVFGG FTTTLYTSLH

1l9hA      GYFVFGPTGC NLEGFFATLG GEIALWSLVV LAIERYVVVC KPMSNFRFGE
1f88A      GYFVFGPTGC NLEGFFATLG GEIALWSLVV LAIERYVVVC KPMSNFRFGE
1hzxA      GYFVFGPTGC NLEGFFATLG GEIALWSLVV LAIERYVVVC KPMSNFRFGE
1ln6A      GYFVFGPTGC NLEGFFATLG GEIALWSLVV LAIERYVVVC KPMSNFRFGE

1l9hA      NHAIMGVAFT WVMALACAAP PLVGWSRYIP EGMQCSCGID YYTPHEETNN
1f88A      NHAIMGVAFT WVMALACAAP PLVGWSRYIP EGMQCSCGID YYTPHEETNN
1hzxA      NHAIMGVAFT WVMALACAAP PLVGWSRYIP EGMQCSCGID YYTPHEETNN
1ln6A      NHAIMGVAFT WVMALACAAP PLVGWSRYIP EGMQCSCGID YYTPHEETNN

1l9hA      ESFVIYMFVV HFIIPLIVIF FCYGQLVFTV KEAAA..... ATTQKAEKEV
1f88A      ESFVIYMFVV HFIIPLIVIF FCYGQLVFTV KEAAA....S ATTQKAEKEV
1hzxA      ESFVIYMFVV HFIIPLIVIF FCYGQLVFTV KEAAA..... ATTQKAEKEV
1ln6A      ESFVIYMFVV HFIIPLIVIF FCYGQLVFTV KEAAAQQQES ATTQKAEKEV
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```
1l9hA      TRMVIIMVIA FLICWLPYAG VAFYIFTHQG SDFGPIFMTI PAFFAKTSAV
1f88A      TRMVIIMVIA FLICWLPYAG VAFYIFTHQG SDFGPIFMTI PAFFAKTSAV
1hzxA      TRMVIIMVIA FLICWLPYAG VAFYIFTHQG SDFGPIFMTI PAFFAKTSAV
1ln6A      TRMVIIMVIA FLICWLPYAG VAFYIFTHQG SDFGPIFMTI PAFFAKTSAV

1l9hA      YNPVIYIMMN KQFRNCMVTT LCCGKNPLGD ...STTVSKT ETSQVAPA
1f88A      YNPVIYIMMN KQFRNCMVTT LCCGKNP... ...STTVSKT ETSQVAPA
1hzxA      YNPVIYIMMN KQFRNCMVTT LCCGKNPLGD ...STTVSKT ETSQVAPA
1ln6A      YNPVIYIMMN KQFRNCMVTT LCCGKNPLGD DEASTTVSKT ETSQVAPA
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1bz0A

```
1bz0A      VLSPADKTNV KAAWGKVGAH AGEYGAEALE RMFLSFPTTK TYFPHF.DLS
1hdaA      VLSAADKGNV KAAWGKVGGH AAEYGAEALE RMFLSFPTTK TYFPHF.DLS
1fhjA      VLSPADKTNI KSTWDKIGGH AGDYGGEALD RTFQSFPTTK TYFPHF.DLS
1hbhA      SLSDKDKAAV RALWSKIGKS ADAIGNDALS RMIVVYPQTK TYFSHWPDVT
1hbrA      MLTAEDKKLI QQAWEKAASH QEEFGAEALT RMFTTYPQTK TYFPHF.DLS
1hv4A      VLSAADKTNV KGVFSKISGH AEEYGAETLE RMFTAYPQTK TYFPHF.DLQ
1hdsA      VLSAANKSNV KAAWGKVGGN APAYGAQALQ RMFLSFPTTK TYFPHF.DLS
2pghA      VLSAADKANV KAAWGKVGGQ AGAHGAEALE RMFLGFPTTK TYFPHF.NLS
1gcvA      AFTACEKQTI GKIAQVLAKS PEAYGAECLA RLFVTHPGSK SYFEYK.DYS

1bz0A      HGSAQVKGHG KKVADALTNA VAHVDDMPNA LSALSDLHAH KLRVDPVNFK
1hdaA      HGSAQVKGHG AKVAAALTKA VEHLDDLPGA LSELSDLHAH KLRVDPVNFK
1fhjA      PGSAQVKAHG KKVADALTTA VAHLDDLPGA LSALSDLHAY KLRVDPVNFK
1hbhA      PGSPHIKAHG KKVMGGIALA VSKIDDLKTG LMELSEQHAY KLRVDPANFK
1hbrA      PGSDQVRGHG KKVLGALGNA VKNVDNLSQA MAELSNLHAY NLRVDPVNFK
1hv4A      HGSAQIKAHG KKVVAALVEA VNHIDDIAGA LSKLSDLHAQ KLRVDPVNFK
1hdsA      HGSAQQKAHG QKVANALTKA QGHLNDLPGT LSNLSNLHAH KLRVNPVNFK
2pghA      HGSDQVKAHG QKVADALTKA VGHLDDLPGA LSALSDLHAH KLRVDPVNFK
1gcvA      AAGAKVQVHG GKVIRAVVKA AEHVDDLHSH LETLALTHGK KLLVDPQNFP

1bz0A      LLSHCLLVTL AAHLPAEFTP AVHASLDKFL ASVSTVLTSK YR
1hdaA      LLSHSLLVTL ASHLPSDFTP AVHASLDKFL ANVSTVLTSK YR
1fhjA      LLSHCLLVTL ACHHPTEFTP AVHASLDKFF TAVSTVLTSK YR
1hbhA      ILNHCILVVI STMFPKEFTP EAHVSLDKFL SGVALALAER YR
1hbrA      LLSQCIQVVL AVHMGKDYTP EVHAAFDKFL SAVSAVLAEK YR
1hv4A      FLGHCFLVVV AIHHPSALTA EVHASLDKFL CAVGTVLTAK YR
1hdsA      LLSHSLLVTL ASHLPTNFTP AVHANLNKFL ANDSTVLTSK YR
2pghA      LLSHCLLVTL AAHHPDDFNP SVHASLDKFL ANVSTVLTSK YR
1gcvA      MLSECIIVTL ATHLT.EFSP DTHCAVDKLL SAICQELSSR YR
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1bz0B

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1bz0B      VHLTPEEKSA VTALWGKVNV DEVGGEALGR LLVVYPWTQR FFESFGDLST
1fhjB      VHLTAEEKSL VSGLWGKVNV DEVGGEALGR LLIVYPWTQR FFDSFGDLST
2pghB      VHLSAEEKEA VLGLWGKVNV DEVGGEALGR LLVVYPWTQR FFESFGDLSN
1hbhB      VEWTDKERSI ISDIFSHMDY DDIGPKALSR CLIVYPWTQR HFSGFGNLYN
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1hbrB      VHWTAEEKQL ITGLWGKVNV AECGAEALAR LLIVYPWTQR FFASFGNLSS
1hv4B      VHWSAEEKQL ITGLWGKVNV ADCGAEALAR LLIVYPWTQR FFSSFGNLSS
1hdsB      .MLTAEEKAA VTGFWGKVDV DVVGAQALGR LLVVYPWTQR FFQHFGNLSS
1hdaB      .MLTAEEKAA VTAFWGKVKV DEVGGEALGR LLVVYPWTQR FFESFGDLST
1gcvB      VHWTQEERDE ISKTFQGTDM KTVVTQALDR MFKVYPWTNR YFQKRTDF..

1bz0B      PDAVMGNPKV KAHGKKVLGA FSDGLAHLDN LKGTFATLSE LHCDKLHVDP
1fhjB      PDAVMSNAKV KAHGKKVLNS FSDGLKNLDN LKGTFAKLSE LHCDKLHVDP
2pghB      ADAVMGNPKV KAHGKKVLQS FSDGLKHLDN LKGTFAKLSE LHCDQLHVDP
1hbhB      AEAIIGNANV AAHGIKVLHG LDRGVKNMDN IAATYADLST LHSEKLHVDP
1hbrB      PTAILGNPMV RAHGKKVLTS FGDAVKNLDN IKNTFSQLSE LHCDKLHVDP
1hv4B      PTAILGNPMV RAHGKKVLTS FGDAVKNLDN IKNTFAQLSE LHCDKLHVDP
1hdsB      AGAVMNNPKV KAHGKRVLDA FTQGLKHLDD LKGAFAQLSG LHCNKLHVNP
1hdaB      ADAVMNNPKV KAHGKKVLDS FSNGMKHLDD LKGTFAALSE LHCDKLHVDP
1gcvB      ........RS SIHAGIVVGA LQDAVKHMDD VKTLFKDLSK KHADDLHVDP

1bz0B      ENFRLLGNVL VCVLAHHFGK EFTPPVQAAY QKVVAGVANA LAHKYH
1fhjB      ENFKLLGNVL VCVLAHHFGK EFTPQVQAAY QKVVAGVANA LAHKYH
2pghB      ENFRLLGNVI VVVLARRLGH DFNPDVQAAF QKVVAGVANA LAHKYH
1hbhB      DNFKLLSDCI TIVLAAKMGH AFTAETQGAF QKFLAVVVSA LGKQYH
1hbrB      ENFRLLGDIL IIVLAAHFSK DFTPECQAAW QKLVRVVAHA LAR...
1hv4B      ENFRLLGDIL IIVLAAHFAK EFTPDCQAAW QKLVRVVAHA LARKYH
1hdsB      QNFRLLGNVL ALVVARNFGG QFTPNVQALF QKVVAGVANA LAHKYH
1hdaB      ENFKLLGNVL VVVLARNFGK EFTPVLQADF QKVVAGVANA LAHRYH
1gcvB      GSFHLLTDCI IVELAYLRKD CFTPHIQGIW DKFFEVVIDA ISKQYH
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101m

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1EMY__     .GLSDGEWEL VLKTWGKVEA DIPGHGETVF VRLFTGHPET LEKFDKFKHL
1J52_A     MVLSEGEWQL VLHVWAKVEA DVAGHGQDIL IRLFKSHPET LEKFDRFKHL
1LHT__     .GLSDDEWNH VLGIWAKVEP DLSAHGQEVI IRLFQLHPET QERFAKFKNL
1MBA__     XSLSAAEADL AGKSWAPVFA NKNANGLDFL VALFEKFPDS ANFFADFKG.
1MBS__     .GLSDGEWHL VLNVWGKVET DLAGHGQEVL IRLFKSHPET LEKFDKFKHL
1MWC_A     .GLSDGEWQL VLNVWGKVEA DVAGHGQEVL IRLFKGHPET LEKFDKFKHL
1MYT__     .....ADFDA VLKCWGPVEA DYTTMGGLVL TRLFKEHPET QKLFPKFAGI
2MM1__     .GLSDGEWQL VLNVWGKVEA DIPGHGQEVL IRLFKGHPET LEKFDRFKHL
101M__     MVLSEGEWQL VLHVWAKVEA DVAGHGQDIL IRLFKSHPET LEKFDRVKHL
1GJN_A     .GLSDGEWQQ VLNVWGKVEA DIAGHGQEVL IRLFTGHPET LEKFDKFKHL

1EMY__     KTEGEMKASE DLKKQGVTVL TALGGILKKK ...GHHEAEI QPLAQSHATK
1J52_A     KTEAEMKASE DLKKHGVTVL TALGAILKKK ...GHHEAEL KPLAQSHATK
1LHT__     TTIDALKSSE EVKKHGTTVL TALGRILKQK ...NNHEQEL KPLAESHATK
1MBA__     KSVADIKASP KLRDVSSRIF TRLNEFVNNA ANAGKMSAML SQFAKEH...
1MBS__     KSEDDMRRSE DLRKHGNTVL TALGGILKKK ...GHHEAEL KPLAQSHATK
1MWC_A     KSEDEMKASE DLKKHGNTVL TALGGILKKK ...GHHEAEL TPLAQSHATK
1MYT__     .AQADIAGNA AISAHGATVL KKLGELLKAK ...GSHAAIL KPLANSHATK
2MM1__     KSEDEMKASE DLKKHGATVL TALGGILKKK ...GHHEAEI KPLAQSHATK
101M__     KTEAEMKASE DLKKHGVTVL TALGAILKKK ...GHHEAEL KPLAQSHATK
1GJN_A     KTEAEMKASE DLKKHGTVVL TALGGILKKK ...GHHEAEL KPLAQSHATK
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1EMY__     HKIPIKYLEF ..ISDAIIHV LQSKHPAEFG ADAQGAMKKA LELFRNDIAA
1J52_A     HKIPIKYLEF ..ISEAIIHV LHSRHPGNFG ADAQGAMNKA LELFRKDIAA
1LHT__     HKIPVKYLEF ..ICEIIVKV IAEKHPSDFG ADSQAAMKKA LELFRNDMAS
1MBA__     VGFGVGSAQF ENVRSMFPGF VASVAAPPAG ADA..AWTKL FGLIIDALKA
1MBS__     HKIPIKYLEF ..ISEAIIHV LHSKHPAEFG ADAQAAMKKA LELFRNDIAA
1MWC_A     HKIPVKYLEF ..ISEAIIQV LQSKHPGDFG ADAQGAMSKA LELFRNDMAA
1MYT__     HKIPINNFKL ..ISEVLVKV MHEKAGLDAG ..GQTALRNV MGIIIADLEA
2MM1__     HKIPVKYLEF ..ISEAIIQV LQSKHPGDFG ADAQGAMNKA LELFRKDMAS
101M__     HKIPIKYLEF ..ISEAIIHV LHSRHPGNFG ADAQGAMNKA LELFRKDIAA
1GJN_A     HKIPIKYLEF ..ISDAIIHV LHSKHPGDFG ADAQGAMTKA LELFRNDIAA

1EMY__     KYKELGFQG
1J52_A     KYKELGYQG
1LHT__     KYKEFGFQG
1MBA__     AGA......
1MBS__     KYKELGFHG
1MWC_A     KYKELGFQG
1MYT__     NYKELGFSG
2MM1__     NYKELGFQG
101M__     KYKELGYQG
1GJN_A     KYKELGFQG
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1gpaA

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1em6A      .......... .......... .......... .....ENVAE LKKSFNRHLH
1gpaA      .......... .......... ...RKQISVR GLAGVENVTE LKKNFNRHLH
1ygpA      TRRLTGFLPQ EIKSIDTMIP LLSRALWNKH QVKKFNKAED FQDRFIDHVE
1qm5A      .......... .......... .......... .SQPIFNDKQ FQEALSRQWQ

1em6A      FTLVKDRNVA TTRDYYFALA HTVRDHLVGR WIRTQQHYYD KCPKRVYYLS
1gpaA      FTLVKDRNVA TPRDYYFALA HTVRDHLVGR WIRTQQHYYE KDPKRIYYLS
1ygpA      TTLARSLYNC DDMVAYEAAS MSIRDNLVID WNKTQQKFTT RDPKRVYYLS
1qm5A      RYGLNSAAEM TPRQWWLAVS EALAEMLRAQ P....FAKPV ANQRHVNYIS

1em6A      LEFYMGRTLQ NTMINLGLQN ACDEAIYQLG LDIEELEEIE EDAGLGNGGL
1gpaA      LEFYMGRTLQ NTMVNLALEN ACDEATYQLG LDMEELEEIE EDAGLGNGGL
1ygpA      LEFLMGRALD NALINMK... .....IPELG FKLEDVLDQE PDAGLGNGGL
1qm5A      MEFLIGRLTG NNLLNLGWYQ DVQDSLKAYD INLTDLLEEE IDPALGNGGL

1em6A      GRLAACFLDS MATLGLAAYG YGIRYEYGIF NQKIRDGWQV EEADDWLRYG
1gpaA      GRLAACFLDS MATLGLAAYG YGIRYEFGIF NQKICGGWQM EEADDWLRYG
1ygpA      GRLAACFVDS MATEGIPAWG YGLRYEYGIF AQKIIDGYQV ETPDYWLNSG
1qm5A      GRLAACFLDS MATVGQSATG YGLNYQYGLF RQSFVDGKQV EAPDDWHRSN

1em6A      NPWEKSRPEF MLPVHFYGKV EHTNTGTKWI DTQVVLALPY DTPVPGYMNN
1gpaA      NPWEKARPEF TLPVHFYGRV EHTSQGAKWV DTQVVLAMPY DTPVPGYRNN
1ygpA      NPWEIERNEV QIPVTFYGYV DRP....TWI GGERVLAVAY DFPVPGFKTS
1qm5A      YPWFRHNEAL DVQVGIGGKV TKD...GRWE PEFTITGQAW DLPVVGYRNG
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1em6A      TVNTMRLWSA RAPG...... ....DYIQAV LDRNLAENIS RVLYPNDNFF
1gpaA      VVNTMRLWSA KAPNDFNLKD FNVGGYIQAV LDRNLAENIS RVLYPNDNFF
1ygpA      NVNNLRLWQA RPTTEFDLNK FNNGDYKNSV AQQQRAESIT AVLYPNDNFA
1qm5A      VAQPLRLWQA THAHPFDLTK FNDGDFLRAE QQGINAEKLT KVLYPNDNHT

1em6A      EGKELRLKQE YFVVAATLQD IIRRFKAS.. .......TVF DAFPDQVAIQ
1gpaA      EGKELRLKQE YFVVAATLQD IIRRFKSSKF GCRDPVRTNF DAFPDKVAIQ
1ygpA      QGKELRLKQQ YFWCAASLHD ILRRFKKSK. .......RPW TEFPDQVAIQ
1qm5A      AGKKLRLMQQ YFQCACSVAD ILRRHHLAGR ........KL HELADYEVIQ

1em6A      LNDTHPALAI PELMRIFVDI EKLPWSKAWE LTQKTFAYTN HTVLPEALER
1gpaA      LNDTHPSLAI PELMRVLVDL ERLDWDKAWE VTVKTCAYTN HTVIPEALER
1ygpA      LNDTHPTLAI VELQRVLVDL EKLDWHEAWD IVTKTFAYTN HTVMQEALEK
1qm5A      LNDTHPTIAI PELLRVLIDE HQMSWDDAWA ITSKTFAYTN HTLMPEALER

1em6A      WPVDLVEKLL PRHLEIIYEI NQKHLDRIVA LFPKDVDRLR RMSLIEEEGS
1gpaA      WPVHLLETLL PRHLQIIYEI NQRFLNRVAA AFPGDVDRLR RMSLVEEGAV
1ygpA      WPRRLFGHLL PRHLEIIYDI NWFFLEDVAK KFPKDVDLLS RISIIEENSP
1qm5A      WDVKLVKGLL PRHMQIINEI NTRFKTLVEK TWPGDEKVWA KLAVVHD...

1em6A      KRINMAHLCI VGSHAVNGVA KIHSDIVKTK VFKDFSELEP DKFQNKTNGI
1gpaA      KRINMAHLCI AGSHAVNGVA RIHSEILKKT IFKDFYELEP HKFQNKTNGI
1ygpA      ERQRMAFLAI VGSHKVNGVV ELHSELIKTT IFKDFIKFYP SKFVNVTNGI
1qm5A      KQVHMANLCV VGGFAVNGVA ALHSDLVVKD LFPEYHQLWP NKFHNVTNGI

1em6A      TPRRWLLLCN PGLAELIAEK IGEDYVKDLS QLTKLHSFLG DDVFLRELAK
1gpaA      TPRRWLVLCN PGLAEIIAER IGEEYISDLD QLRKLLSYVD DEAFIRDVAK
1ygpA      TPRRWLKQAN PSLAKLISET LNEEYLLDMA KLTQLEKYVE DKEFLKKWNQ
1qm5A      TPRRWIKQCN PALAALLDKS LQKEWANDLD QLINLEKFAD DAKFRDQYRE

1em6A      VKQENKLKFS QFLETEYKVK INPSSMFDVQ VKRIHEYKRQ LLNCLHVITM
1gpaA      VKQENKLKFA AYLEREYKVH INPNSLFDVQ VKRIHEYKRQ LLNCLHVITL
1ygpA      VKLNNKIRLV DLIKKENDGV DIDDTLFDMQ VKRIHEYKRQ QLNVFGIIYR
1qm5A      IKQANKVRLA EFVKVRTGIE INPQAIFDIQ IKRLHEYKRQ HLNLLHILAL

1em6A      YNRIKKDP.. .FVPRTVIIG GKAAPGYHMA KMIIKLITSV ADVVNNDPMV
1gpaA      YNRIKKEPNK FVVPRTVMIG GKAAPGYHMA KMIIKLITAI GDVVNHDPVV
1ygpA      YLAMKNEVAR KYPRKVSIFG GKSAPGYYMA KLIIKLINCV ADIVNNDESI
1qm5A      YKEIRENPQA DRVPRVFLFG AKAAPGYYLA KNIIFAINKV ADVINNDPLV

1em6A      GSKLKVIFLE NYRVSLAEKV IPATDLSEQI STAGTEASGT GNMKFMLNGA
1gpaA      GDRLRVIFLE NYRVSLAEKV IPAADLSEQI STAGTEASGT GNMKFMLNGA
1ygpA      EHLLKVVFVA DYNVSKAEII IPASDLSEHI STAGTEASGT SNMKFVMNGG
1qm5A      GDKLKVVFLP DYCVSAAEKL IPAADISEQI STAGKEASGT GNMKLALNGA

1em6A      LTIGTMDGAN VEMAEEAGEE NLFIFGMRID DVAALDKKGY EAKEYYEALP
1gpaA      LTIGTMDGAN VEMAEEAGEE NFFIFGMRVE DVDRLDQRGY NAQEYYDRIP
1ygpA      LIIGTVDGAN VEITREIGED NVFLFGNLSE NVEELRYNHQ YHPQDL...P
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1qm5A      LTVGTLDGAN VEIAEKVGEE NIFIFGHTVE QVKAILAKGY DPVKWRKKDK


1em6A      ELKLVIDQID NGFFSPKQPD LFKDIINMLF Y..HDRFKVF ADYEAYVKCQ
1gpaA      ELRQIIEQLS SGFFSPKQPD LFKDIVNMLM H..HDRFKVF ADYEEYVKCQ
1ygpA      SLDSVLSYIE ..QFSPENPN EFKPLVDSIK H..GDYYLVS DDFESYLATH
1qm5A      VLDAVLKELE SGKYSDGDKH AFDQMLHSIG KQGGDPYLVM ADFAAYVEAQ


1em6A      DKVSQLYMNP KAWNTMVLKN IAASGKFSSD RTIKEYAQNI WNVEPS....
1gpaA      ERVSALYKNP REWTRMVIRN IATSGKFSSD RTIAQYAREI WGVEPSRQRL
1ygpA      ELVDQEFHNQ REWLKKSVLS LANVGFFSSD RCIEEYSDTI WNVEPVT...
1qm5A      KQVDVLYRDQ EAWTRAAILN TARCGMFSSD RSIRDYQARI WQAKR.....


1em6A      ...
1gpaA      PAP
1ygpA      ...
1qm5A      ...
PileUp
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1g5yB

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1g5yB      .......... PVERILEAEL AVEPKTETYV EA........ NM........
1fm6D      ..PESADLRA LAKHLYDSYI KSFPLTKAKA RAILTGKTTD KSPFVIYDMN
1dkfB      .....PEVGE LIEKVRKAHQ ETFPA..... .LC...QLGK YTT....SEQ
1k74D      ..PESADLRA LAKHLYDSYI KSFPLTKAKA RAILTGKTTD KSPFVIYDMN
1uhlB      ...MSPEQLG MIEKLVAAQQ QCNRRS.... .F........ ..........
1xv9B      PVQLSKEQEE LIRTLLGAHT RHMGTMFEQF VQF...RPPA HLFIHHQPLP
1rdtD      ..AESADLRA LAKHLYDSYI KSFPLTKAKA RAILTGKTTD KSPFVIYDMN


1g5yB      .........G LNPSSP.... .....NDPVT NICQAADKQL FTLVEWAKRI
1fm6D      SLMMGEDKIK FKHITPLQEQ SKEVAIRIFQ GCQFRSVEAV QEITEYAKSI
1dkfB      .......... .........R VSLD.IDLWD KFSELSTKCI IKTVEFAKQL
1k74D      SLMMGEDKIK FKHITPLQEQ SKEVAIRIFQ GCQFRSVEAV QEITEYAKSI
1uhlB      .......... .......... .EAR.QQRFA HFTELAIVSV QEIVDFAKQL
1xv9B      .......... .........T LAPV.LPLVT HFADINTFMV LQVIKFTKDL
1rdtD      SLM....... .......... ..EVAIRIFQ GCQFRSVEAV QEITEYAKSI


1g5yB      PHFSELPLDD QVILLRAGWN ELLIASFSHR SIAVKDGILL .ATGLHVHR.
1fm6D      PGFVNLDLND QVTLLKYGVH EIIYTMLASL MNK..DGVLI SEGQGFMTRE
1dkfB      PGFTTLTIAD QITLLKAACL DILILRICTR YTPEQDTMTF .SDGLTLNR.
1k74D      PGFVNLDLND QVTLLKYGVH EIIYTMLASL MNK..DGVLI SEGQGFMTRE
1uhlB      PGFLQLSRED QIALLKTSAI EVMLLETSRR YNPGSESIT. ...DFSYNR.
1xv9B      PVFRSLPIED QISLLKGAAV EICHIVLNTT FCLQTQNFLC ..GPLRYTI.
1rdtD      PGFVNLDLND QVTLLKYGVH EIIYTMLASL MNK..DGVLI SEGQGFMTRE


1g5yB      NSAHSA.GVG AIFDRVLTEL VSKMRDMQMD KTELGCLRAI VLFNPDSKGL
1fm6D      FLKSLRKPFG DFMEPKFE.F AVKFNALELD DSDLAIFIAV IILSGDRPGL
1dkfB      TQMHNAGFGP .LTDLVFA.F ANQLLPLEMD DAETGLLSAI CLICGDRQDL
1k74D      FLKSLRKPFG DFMEPKFE.F AVKFNALELD DSDLAIFIAV IILSGDRPGL
1uhlB      EDFAKAGLQV EFINPIFE.F SRAMNELQLN DAEFALLIAI SIFSADRPNV
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1xv9B      EDGARVGFQV EFLELLFH.F HGTLRKLQLQ EPEYVLLAAM ALFSPDRPGV
1rdtD      FLKSLRKPFG DFMEPKFE.F AVKFNALELD DSDLAIFIAV IILSGDRPGL


1g5yB      SNPAEVEALR EKVYASLEAY CKHK..YPEQ PGRFAKLLLR LPALRSIGLK
1fm6D      LNVKPIEDIQ DNLLQALELQ LKLN..HPES SQLFAKLLQK MTDLRQIVTE
1dkfB      EQPDRVDMLQ EPLLEALKVY VRKR..RPSR PHMFPKMLMK ITDLRSISAK
1k74D      LNVKPIEDIQ DNLLQALELQ LKLN..HPES SQLFAKLLQK MTDLRQIVTE
1uhlB      QDQLQVERLQ HTYVEALHAY VSIH..HPHD RLMFPRMLMK LVSLRTLSSV
1xv9B      TQRDEIDQLQ EEMALTLQSY IKGQQRRPRD RFLYAKLLGL LAELRSINEA
1rdtD      LNVKPIEDIQ DNLLQALELQ LKLN..HPES SQLFAKLLQK MTDLRQIVTE


1g5yB      CLEHLFFFKL IGDTPIDTFL MEMLEAPH.
1fm6D      HVQLLQVIKK TETDMSLHPL LQEIYKDLY
1dkfB      GAERVITLKM E..IPGSMPP LIQEMLEN.
1k74D      HVQLLQVIKK TETDMSLHPL LQEIYKDLY
1uhlB      HSEQVFALRL Q..DKKLPPL LSEIWDV..
1xv9B      YGYQIQHIQ. G..LSAMMPL LQEICS...
1rdtD      HVQLLQVIKK TETDMSLHPL LQEIYKDLY
PileUp
```

1kzkA

```
1KZK_A     .....PQITL WKRPLVTIRI GGQLKEALLD TGADDTVLEE MNLPGK....
1HSI_A     .....PQFSL WKRPVVTAYI EGQPVEVLLD TGADDSIVAG IELGNN....
1YTG_A     .....PQITL WKRPLVTIRI GGQLKEALLD TGADDTVLEE MNLPGK....
3FIV_A     YNKVGTTTTL EKRPEILIFV NGYPIKFLLN TGADITILNR RDFQVKNSIE
2HPE_A     .....PQFSL WKRPVVTAYI EGQPVEVLLD TGADDSIVAG IELGNN....
1HII_A     .....PQFSL WKRPVVTAYI EGQPVEVLLD TGADDSIVAG IELGNN....


1KZK_A     .WKPKMIGGI GGFIKVRQYD QIPVEICGHK AIGTVLVGPT PV........
1HSI_A     .YSPKIVGGI GGFINTKEYK NVEIEVLNKK VRATIMTGDT PI........
1YTG_A     .WKPKMIGGI GGFIKVRQYD QIPVEICGHK AIGTVLVGPT PV........
3FIV_A     NGRQNMIG.V GGGKRGTNYI NVHLEIRDEN YKTQXIFGNV CVLEDNSLIQ
2HPE_A     .YSPKIVGGI GGFINTLEYK NVEIEVLNKK VRATIMTGDT PI........
1HII_A     .YSPKIVGGI GGFINTKEYK NVEIEVLNKK VRATIMTGDT PI........


1KZK_A     NIIGRNLLTQ IGCTLNF
1HSI_A     NIFGRNILTA LGMSLNL
1YTG_A     NIIGRNLLTQ IGCTLNF
3FIV_A     PLLGRDNMIK FNIRLVM
2HPE_A     NIFGRNILTA LGMSLNL
1HII_A     NIFGRNILTA LGMSLNL
```

Figure 3 Structural alignments of the seven studied families.

Figure 4

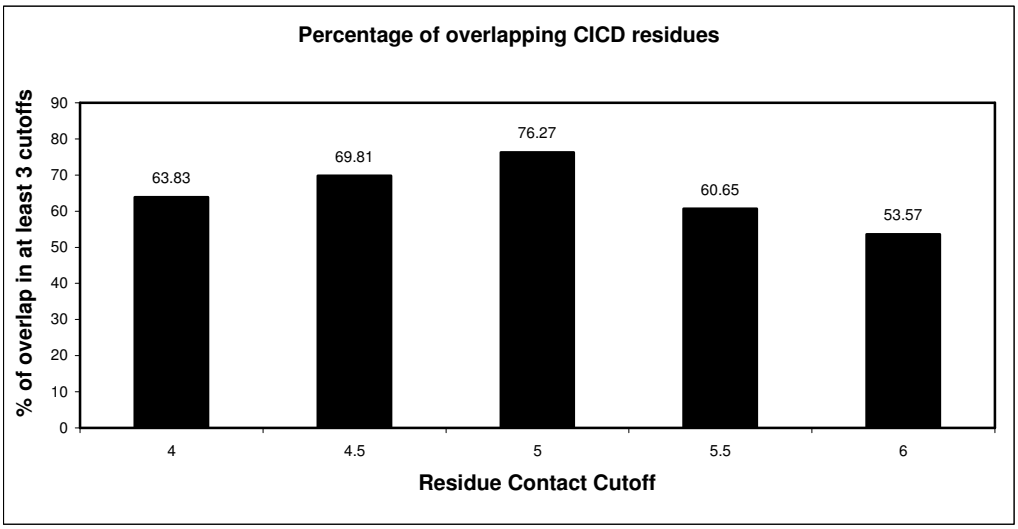
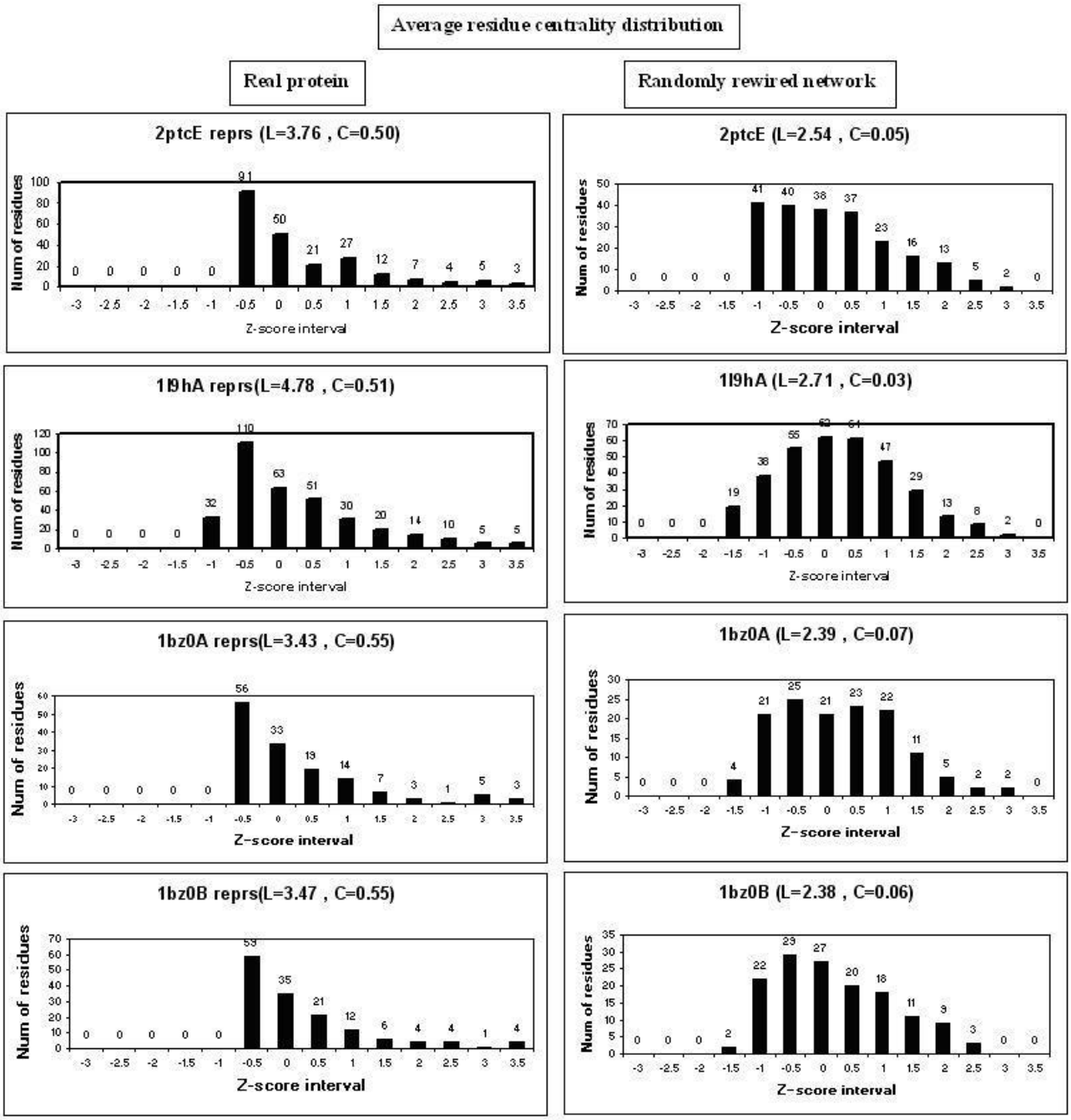


Figure 4 Percentage of overlapping CICD residues for different residue contact cutoff values (4, 4.5, 5, 5.5, 6). We considered overlapping CICD residues as those positions predicted in at least three cutoffs. Notice that the highest percentage of overlapping corresponds to 5 Å.

Figure 5


Average residue centrality distribution
Real protein
Randomly rewired network
2ptcE reprs (L=3.76 , C=0.50)
2ptcE (L=2.54 , C=0.05)
1l9hA reprs(L=4.78 , C=0.51)
1l9hA (L=2.71 , C=0.03)
1bz0A reprs(L=3.43 , C=0.55)
1bz0A (L=2.39 , C=0.07)
1bz0B reprs(L=3.47 , C=0.55)
1bz0B (L=2.38 , C=0.06)
Num of residues
Z-score interval

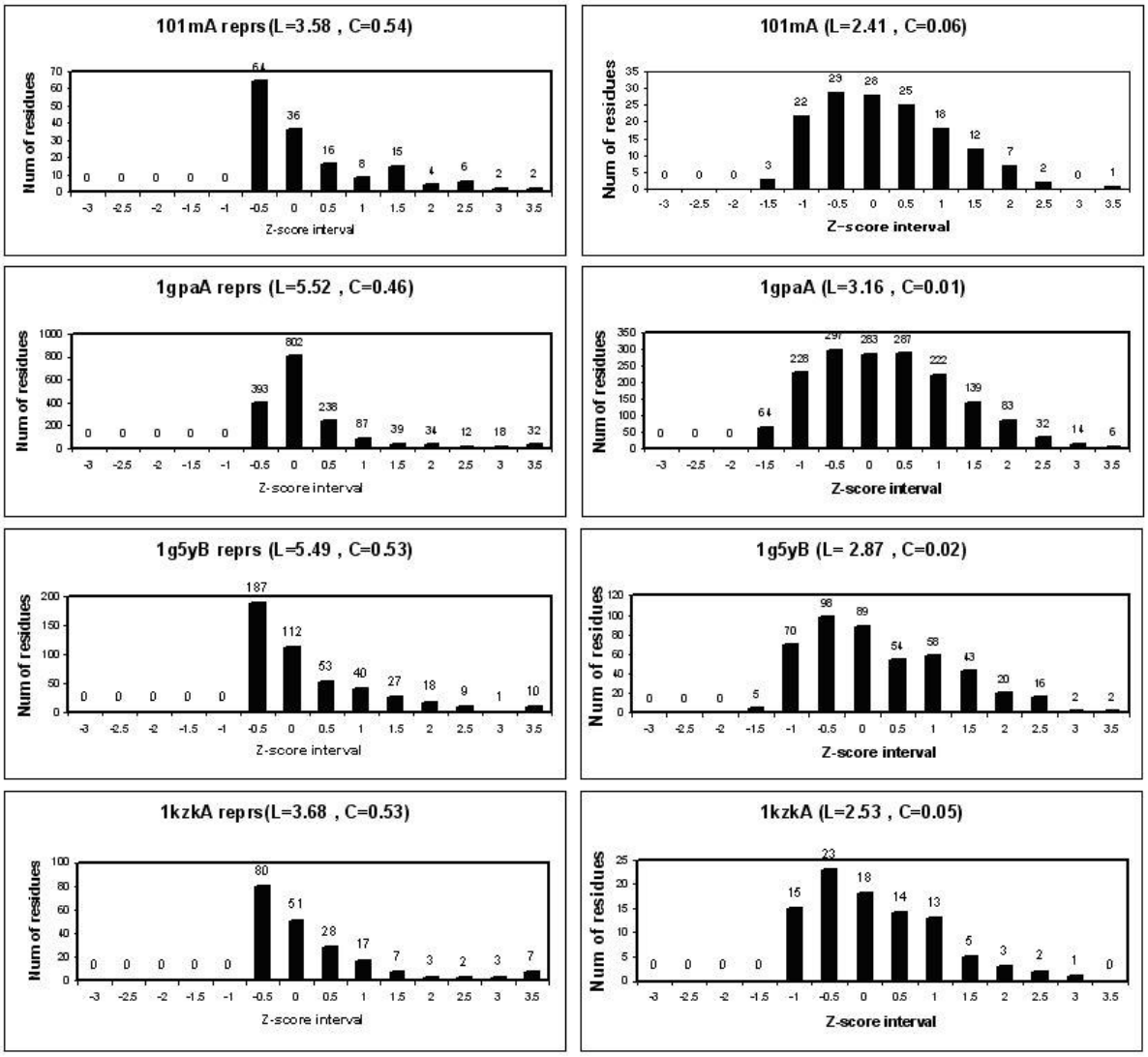
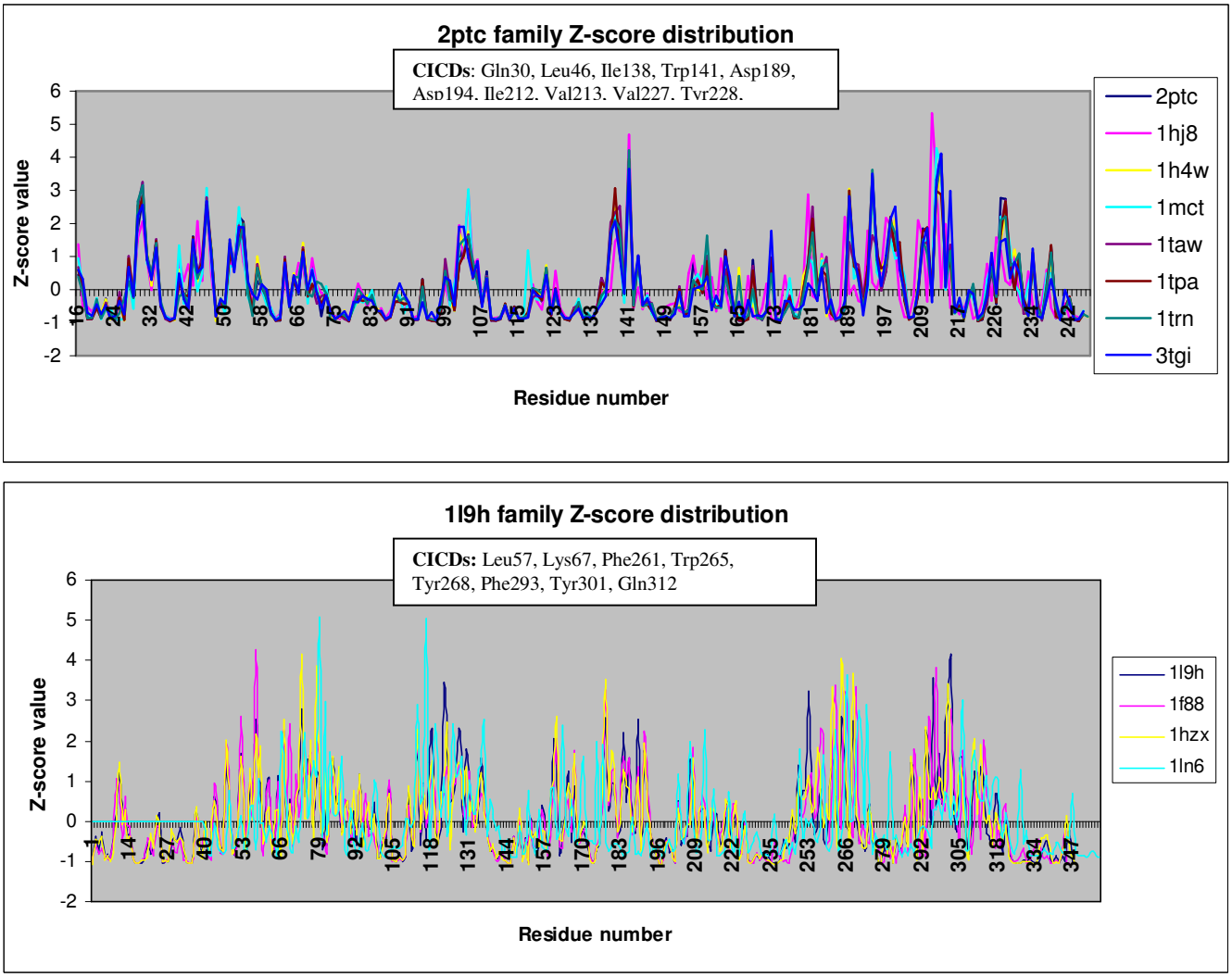
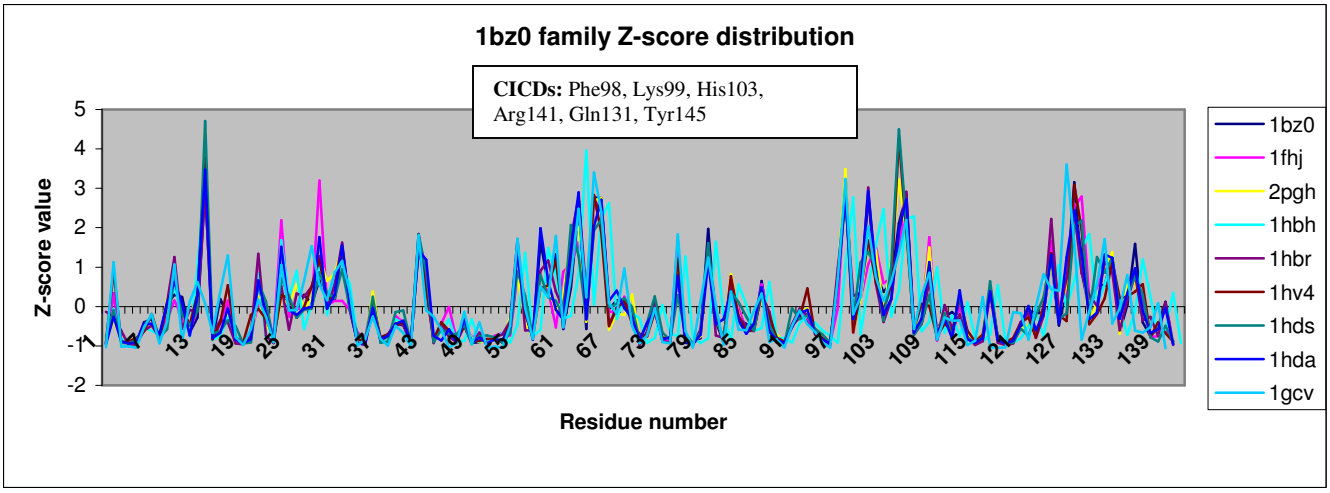
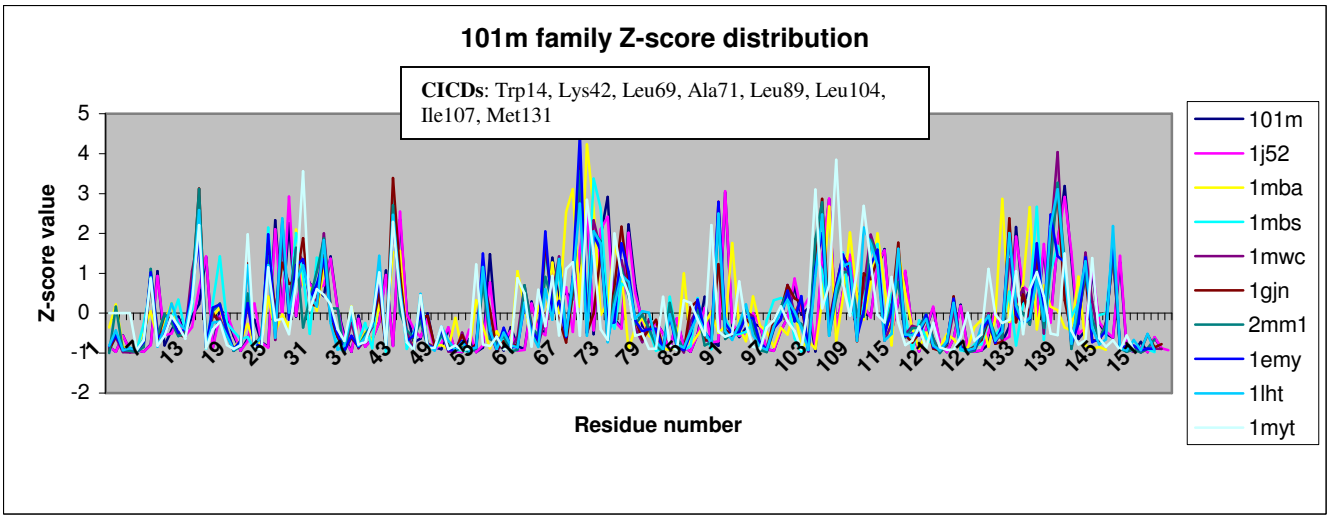


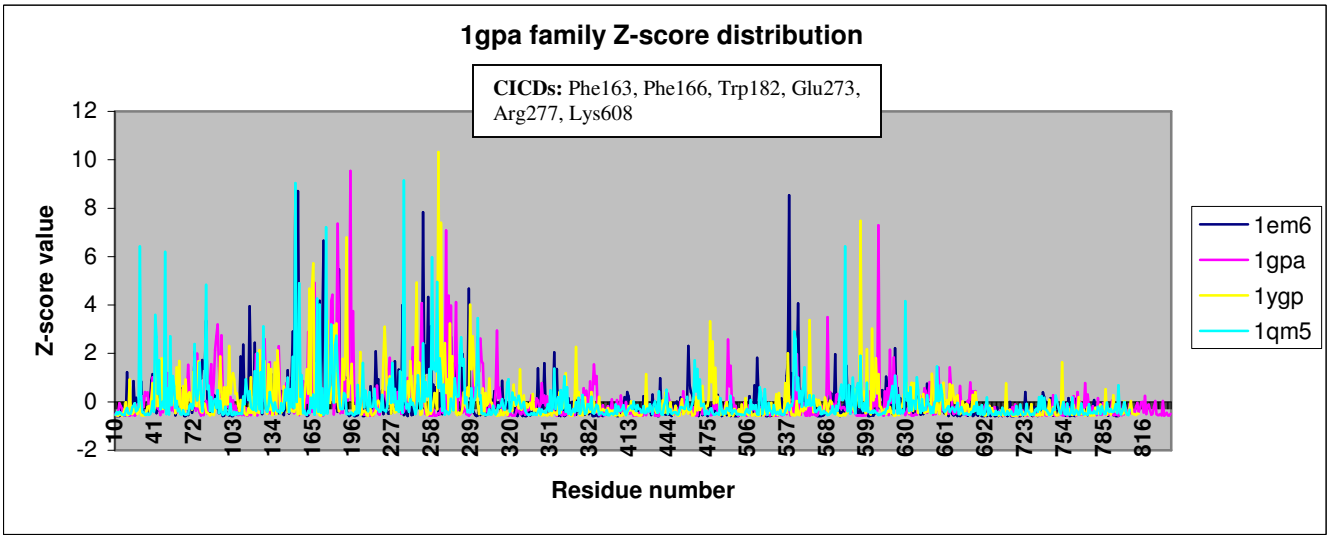
Figure 5 Averaged residue centrality distributions for each family representative protein and its corresponding randomly rewired network. The network clustering coefficient and characteristic path length are indicated in each case.

Figure 6


2ptc family Z-score distribution
CICDs: Gln30, Leu46, Ile138, Trp141, Asp189, Asp194. Ile212. Val213. Val227. Tyr228.
Z-score value
Residue number
2ptc
1hj8
1h4w
1mct
1taw
1tpa
1trn
3tgi
1l9h family Z-score distribution
CICDs: Leu57, Lys67, Phe261, Trp265, Tyr268, Phe293, Tyr301, Gln312
Z-score value
Residue number
1l9h
1f88
1hzx
1ln6


1bz0 family Z-score distribution
CICDs: Phe98, Lys99, His103, Arg141, Gln131, Tyr145
Z-score value
Residue number
1bz0
1fhj
2pgh
1hbh
1hbr
1hv4
1hds
1hda
1gcv


101m family Z-score distribution
CICDs: Trp14, Lys42, Leu69, Ala71, Leu89, Leu104, Ile107, Met131
Z-score value
Residue number
101m
1j52
1mba
1mbs
1mwc
1gjn
2mm1
1emy
1lht
1myt


1gpa family Z-score distribution
CICDs: Phe163, Phe166, Trp182, Glu273, Arg277, Lys608
Z-score value
Residue number
1em6
1gpa
1ygp
1qm5

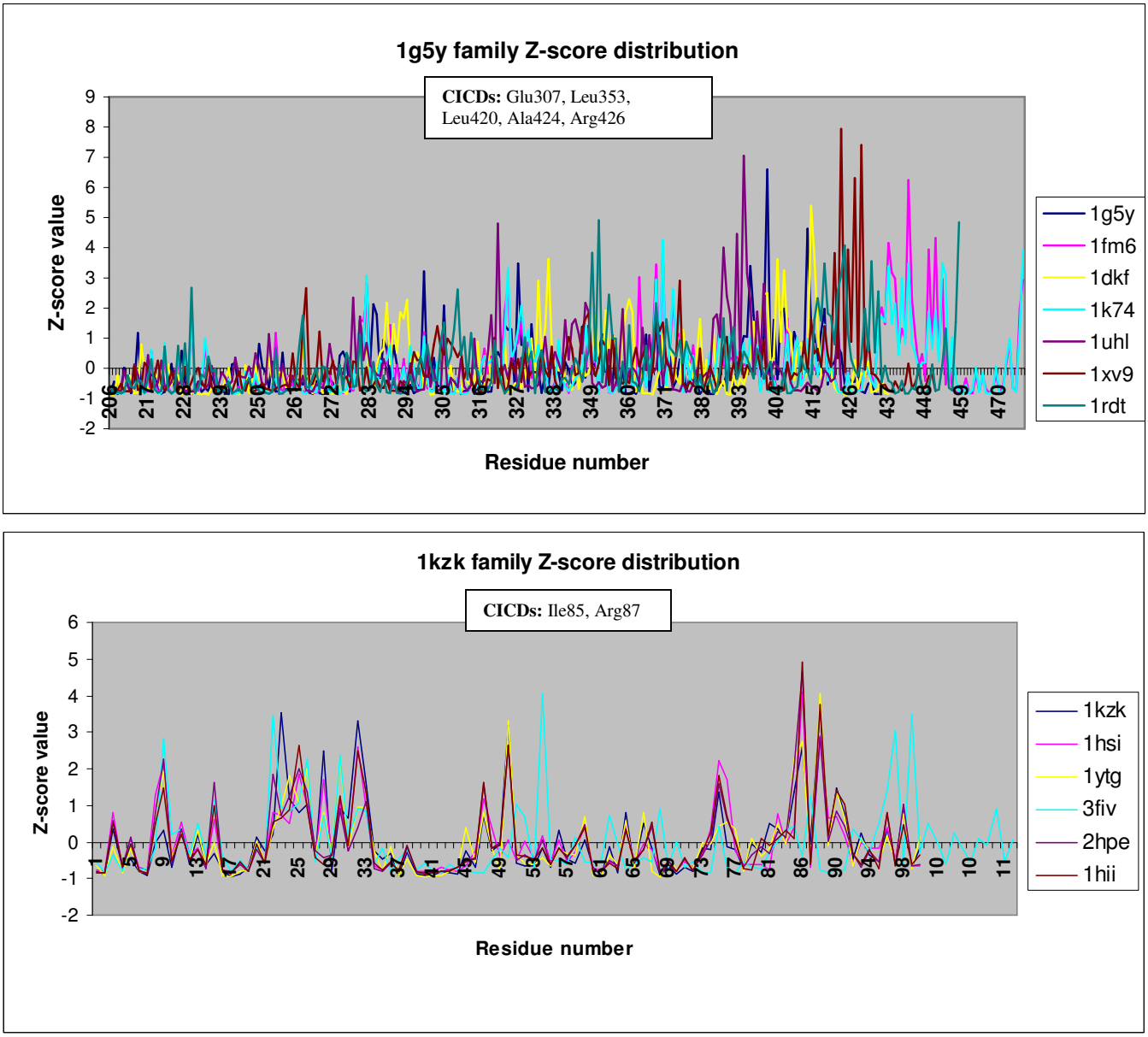


Figure 6 Residue centrality z-score distributions for all the members of the seven studied families. In each case, the distribution of each family member is depicted in a different color. The CICD residues are indicated.