Supplementary Table 1 | Modeling of yeast TFIIH subunits, domains and regions.

Subunit / Chain ID	Domain	Residue range (yeast)	Initial model	PDB-template for initial model	Modeling algorithm	Changes to initial model	Density assigned in Extended Data Figure 4c / Color
Rad3 / 0	N-terminus	1-17	not modeled	-	-	-	yes / yellow
Rad3 / 0	Lobe 1	18-108, 204-248, 441-484	homology-/ *ab-initio* model	2VSF:A	I-Tasser		-
Rad3 / 0	FeS cluster	109-203	homology-/ *ab-initio* model	2VSF:A	I-Tasser		-
Rad3 / 0	ARCH	249-293, 327-425, 429-440	(1) *de-novo* modeling of α-helices	-	Gorgon	MDFF and manual corrections, PHENIX geometry minimization	-
			(2) homology-/ *ab-initio* model	α-helix PDB from Gorgon, 5IVW:W, 5IVW:A, 5IY9:W	I-Tasser		-
Rad3 / 0	ARCH linker	294-326	poly-alanine model	-	-		-
Rad3 / 0	Lobe 2	485-723	homology-/ *ab-initio* model	2VSF:A	I-Tasser		-
Rad3 / 0	C-terminus	724-778	not modeled	-	-	-	yes / yellow
Tfb1 / 1	PHD	1-121	yeast NMR-structure	1Y5O:A	-	PHENIX geometry minimization	-
Tfb1 / 1	PH-linker	122-175	not modeled	-	-	-	no
Tfb1 / 1	BSD1	176-218	homology-/ *ab-initio* model	2DII:A	I-Tasser		-
Tfb1 / 1	Linker	219-251	poly-alanine model loop	-	-		-
Tfb1 / 1	BSD2	252-294	homology-/ *ab-initio* model	2DII:A	I-Tasser	MDFF and manual corrections, PHENIX geometry minimization	-
Tfb1 / 1	Linker	295-307	poly-alanine model loop	-	-		-
Tfb1 / 1	Rad3 anchor (α-Helix 1)	308-330	poly-alanine model α-helix	-	-		-
Tfb1 / 1	Linker	331-353	poly-alanine model loop	-	-		-
Tfb1 / 1	Rad3 anchor (α-Helix 2)	369-394	poly-alanine model α-helix	-	-		-
Tfb1 / 1	Ridge	395-464	not modeled	-	-	-	partially / purple
Tfb1 / 1	Tfb4 anchor (α-Helix 1)	465-483	poly-alanine model α-helix	-	-	MDFF and manual corrections, PHENIX geometry	-
Tfb1 / 1	Linker	484-494	poly-alanine model loop	-	-		-

Tfb1 / 1	Tfb4 anchor (α-Helix 2)	495-519	poly-alanine model α-helix	-	-	minimization	-
Tfb1 / 1	Linker	520-543	not modeled	-	-	-	no
Tfb1 / 1	3-helix bundle	544-639	(1) *ab-initio* model	-	QUARK	MDFF and manual corrections, PHENIX geometry minimization	-
			(2) homology-/ *ab-initio* model	PDB output from QUARK 2W6D:A, 1WRD:A, 4M70:A, 5F8P:A,	I-Tasser		
Tfb1 / 1	C-terminus	640-643	not modeled	-	-	-	no
Tfb2 / 2	N-terminus	1-2	not modeled	-	-	-	no
Tfb2 / 2	α	3-40	poly-alanine model α-helix	-	-		-
Tfb2 / 2	HTH-1	41-113	homology-/ *ab-initio* model	1U2W:A	SWISS		-
Tfb2 / 2	α	114-131	poly-alanine model loop	-	-	MDFF and manual corrections, PHENIX geometry minimization	-
Tfb2 / 2	α	132-159	poly-alanine model α-helix/loop	-	-		-
Tfb2 / 2	HTH-2	160-194	homology-/ *ab-initio* model	2MC3:A	SWISS		-
Tfb2 / 2	HTH-2	195-213	poly-alanine model α-helix	-	-		-
Tfb2 / 2	HTH-3	214-281	homology-/ *ab-initio* model	5BOX:A	SWISS		-
Tfb2 / 2	Linker	282-336	not modeled	-	-	-	no
Tfb2 / 2	Clutch	337-419	poly-alanine model α-helix/β-sheet (partially)	-	-	MDFF and manual corrections, PHENIX geometry minimization	-
Tfb2 / 2	Linker	420-432	not modeled	-	-	-	yes / blue
Tfb2 / 2	Dimerization domain	433-450	poly-alanine model α-helix	-	-	MDFF and manual corrections, PHENIX geometry minimization	-
Tfb2 / 2	Dimerization domain	451-508	yeast crystal structure	3DGP:A	-	PHENIX geometry minimization	-
Tfb2 / 2	C-terminus	509-513	not modeled	-	-	-	no
Tfb3 / 3	N-terminus	1-7	not modeled	-	-	-	no

Tfb3 / 3	RING	8-70	homology-/ *ab-initio* model	1G25:A, 3M62:A	I-Tasser		-
Tfb3 / 3	ARCH anchor	71-145	(1) *ab-initio* model	-	QUARK	MDFF and manual corrections, PHENIX geometry minimization	-
			(2) homology/ *ab-initio* model	PDB output from QUARK; 2W6D:A, 3NIX:A, 5EQZ:A, 2EWF:A	I-Tasser		
Tfb3 / 3	C-terminus	146-321	not modeled	-	-	-	no
Tfb4 / 4	N-terminus	1-21	not modeled	-	-	-	no
Tfb4 / 4	vWA	22-88	homology-/ *ab-initio* model	4PN7:A, 4CRN:X, 4PLA:A, 4OKU:A, 5IY9:3	I-Tasser	MDFF and manual corrections, PHENIX geometry minimization	-
Tfb4 / 4	vWA insertion	89-97	poly-alanine model loop	-	-		-
Tfb4 / 4	vWA insertion	98-102	not modeled	-	-	-	no
Tfb4 / 4	vWA insertion	103-114	poly-alanine model loop	-	-		-
Tfb4 / 4	vWA	115-256	homology-/ *ab-initio* model	4PN7:A, 4CRN:X, 4PLA:A, 4OKU:A, 5IY9:3	I-Tasser	MDFF and manual corrections, PHENIX geometry minimization	-
Tfb4 / 4	Linker	257-273	poly-alanine model loop	-	-		-
Tfb4 / 4	eZnF / C-terminus	274-323	homology-/ *ab-initio* model	3LRQ:D	Robetta		-
Tfb4 / 4	C-terminus	324-338	not modeled	-	-	-	no
Tfb5 / 5	N-terminus	1	not modeled	-	-	-	no
Tfb5 / 5	Dimerization domain	2-64	yeast crystal structure	3DGP:B	-	PHENIX geometry minimization	-
Tfb5 / 5	C-terminus	65-68	poly-alanine model loop	-	-	MDFF and manual corrections, PHENIX geometry minimization	-
Tfb5 / 5	C-terminus	69-72	not modeled	-	-	-	no
Ssl1 / 6	unstructured NTE	1-73	not modeled	-	-	-	no
Ssl1 / 6	α	74-122	not modeled	-	-	-	yes / green
Ssl1 / 6	vWA	123-308	yeast crystal structure	4WFQ:A	-	PHENIX geometry minimization	-

SsI1 / 6	Linker	309-324	poly-alanine model loop	-	-		-
SsI1 / 6	eZnF	325-372	homology-/ *ab-initio* model	1NNQ:A	Robetta	MDFF and manual corrections, PHENIX geometry minimization	-
SsI1 / 6	α	373-386	poly-alanine model α-helix	-	-		-
SsI1 / 6	RING	387-457	homology-/ *ab-initio* model	1Z60:A	Robetta		-
				1Z60:A	SWISS		
SsI1 / 6	C-terminus	458-461	not modeled	-	-	-	no
SsI2 / 7	NTE	1-110	-	-	-	-	no
SsI2 / 7	Clutch and DRD	111-362	not modeled	-	-	-	yes / pink
SsI2 / 7	Lobe 1	363-425	homology-/ *ab-initio* model	2FWR:A	SWISS		-
SsI2 / 7	Lobe 1	426-451	homology model / poly-alanine model	-	-	MDFF and manual corrections, PHENIX geometry minimization	-
SsI2 / 7	Lobe 1	452-462	homology-/ *ab-initio* model	2FWR:A	SWISS		-
SsI2 / 7	Lobe 1	463-481	poly-alanine model α-helix/loop	-	-		-
SsI2 / 7	Lobe 1	482-548	homology-/ *ab-initio* model	2FWR:A	SWISS		-
SsI2 / 7	Lobe 2	549-691	homology-/ *ab-initio* model	4ERN:A	Robetta		-
SsI2 / 7	Lobe 2	692-702	poly-alanine model α-helix/loop	-	-	MDFF and manual corrections, PHENIX geometry minimization	-
SsI2 / 7	Lobe 2	703-712	homology-/ *ab-initio* model	4ERN:A	Robetta		-
SsI2 / 7	Extension	713-770	homology-/ *ab-initio* model	4ERN:A	Robetta		-
SsI2 / 7	C-Terminus	771-843	not modeled	-	-	-	no

TFIIE / W	E-bridge	259-266	poly-alanine model β-strand	-	-	MDFF and manual corrections, PHENIX geometry minimization	-
TFIIE / W	E-bridge	267-289	poly-alanine model α-helix	-	-		-
TFIIE / W	E-floater	349-373	poly-alanine model α-helix	-	-		-
TFIIE / W	Acidic peptide	407-417	*homo sapiens* NMR structure	2RNR:A	-	amino acid replacement MDFF, PHENIX geometry minimization	-

Supplementary Table 2 | Compilation of published BS3- and SBAT-crosslinking information.

a.

Study	Link type	Protein 1	Protein 2	Residue 1	Residue 2	Distance (Å)	Used for modeling	Remark
Robinson 2016	intra	Rad3	Rad3	30	476	16.4	x	-
Murakami 2013, Luo 2016, Robinson 2016	intra	Rad3	Rad3	30	481	14.8	x	-
Luo 2015	intra	Rad3	Rad3	81	673	19.5	x	-
Robinson 2016	intra	Rad3	Rad3	95	125	39.0	-	-
Murakami 2013, Luo 2015, Robinson 2016	intra	Rad3	Rad3	112	125	5.9	x	-
Robinson 2016	intra	Rad3	Rad3	112	132	10.7	x	-
Robinson 2016	intra	Rad3	Rad3	112	142	24.0	x	-
Robinson 2016	intra	Rad3	Rad3	112	180	16.0	x	-
Murakami 2013, Luo 2015, Robinson 2016	intra	Rad3	Rad3	112	605	19.6	x	-
Luo 2015	intra	Rad3	Rad3	122	125	8.6	x	-
Luo 2015, Robinson 2016	intra	Rad3	Rad3	122	132	9.4	x	-
Luo 2015	intra	Rad3	Rad3	125	588	26.2	x	-
Luo 2015	intra	Rad3	Rad3	144	276	27.1	x	-
Luo 2015	intra	Rad3	Rad3	144	281	18.5	x	-
Luo 2015	intra	Rad3	Rad3	173	68	17.3	x	-
Robinson 2016	intra	Rad3	Rad3	183	112	15.0	x	-
Robinson 2016	intra	Rad3	Rad3	188	180	11.6	x	-
Luo 2015	intra	Rad3	Rad3	228	68	9.7	x	-
Luo 2015, Robinson 2016	intra	Rad3	Rad3	336	343	10.5	x	-
Luo 2015, Robinson 2016	intra	Rad3	Rad3	347	343	6.2	x	-
Luo 2015	intra	Rad3	Rad3	357	372	13.7	x	-
Luo 2015, Robinson 2016	intra	Rad3	Rad3	364	372	11.7	x	-
Luo 2015	intra	Rad3	Rad3	447	476	11.9	x	-
Luo 2015	intra	Rad3	Rad3	447	636	24.9	x	-
Luo 2015	intra	Rad3	Rad3	476	30	16.3	x	-
Luo 2015	intra	Rad3	Rad3	476	481	16.4	x	-
Robinson 2016	intra	Rad3	Rad3	476	636	28.4	x	-
Robinson 2016	intra	Rad3	Rad3	490	476	37.6	-	low score
Robinson 2016	intra	Rad3	Rad3	490	636	43.2	-	-
Luo 2015	intra	Rad3	Rad3	499	489	24.5	x	-
Robinson 2016	intra	Rad3	Rad3	588	636	44.9	-	-
Luo 2015, Robinson 2016	intra	Rad3	Rad3	605	125	18.4	x	-
Luo 2015	intra	Rad3	Rad3	605	588	21.4	x	-
Luo 2015, Robinson 2016	intra	Rad3	Rad3	605	636	24.3	x	-
Luo 2015	intra	Rad3	Rad3	673	112	38.0	-	-
Luo 2015	intra	Rad3	Rad3	673	125	39.6	-	low score
Luo 2015	intra	Rad3	Rad3	673	489	10.2	x	-
Robinson 2016	intra	Rad3	Rad3	673	490	7.1	x	-
Luo 2015	intra	Rad3	Rad3	673	588	24.4	x	-
Luo 2015	intra	Rad3	Rad3	673	636	42.8	-	-
Luo 2015	intra	Rad3	Rad3	695	481	16.0	x	-
Luo 2015	intra	Rad3	Rad3	695	490	12.0	x	-
Luo 2015	intra	Rad3	Rad3	695	673	15.5	x	-
Luo 2015	inter	Rad3	Ssl2	499	372	29.2	x	-
Robinson 2016	inter	Rad3	Tfb1	180	334	14.3	x	-
Luo 2015	intra	Ssl1	Ssl1	139	201	17.4	x	-
Luo 2015	intra	Ssl1	Ssl1	139	205	14.7	x	-
Luo 2015	intra	Ssl1	Ssl1	197	201	7.2	x	-
Robinson 2016	intra	Ssl1	Ssl1	312	321	24.9	x	-
Murakami 2013, Luo 2015, Robinson 2016	intra	Ssl1	Ssl1	397	414	17.4	x	-
Murakami 2013, Luo 2015	intra	Ssl1	Ssl1	397	420	15.3	x	-
Murakami 2013, Luo 2015, Robinson 2016	intra	Ssl1	Ssl1	414	420	4.6	x	-
Luo 2015	intra	Ssl1	Ssl1	433	397	10.6	x	-
Robinson 2016	inter	Ssl1	Tfa1	201	284	21.9	x	-
Luo 2015	inter	Ssl1	Tfb1	201	101	54.8	-	-
Robinson 2016	inter	Ssl1	Tfb1	201	238	33.2	-	positional variants
Luo 2015	inter	Ssl1	Tfb2	197	415	29.2	x	-
Murakami 2013, Luo 2015, Robinson 2016	inter	Ssl1	Tfb2	201	415	27.4	x	-
Murakami 2013, Luo 2015, Robinson 2016	inter	Ssl1	Tfb2	201	418	22.1	x	-
Luo 2015, Robinson 2016	inter	Ssl1	Tfb2	201	419	22.4	x	-
Luo 2015	inter	Ssl1	Tfb4	197	173	34.0	-	-
Luo 2015	inter	Ssl1	Tfb4	197	207	27.4	x	-
Murakami 2013, Luo 2015, Robinson 2016	inter	Ssl1	Tfb4	315	319	17.8	x	-
Robinson 2016	inter	Ssl1	Tfb4	321	319	11.4	x	-
Murakami 2013, Luo 2015, Robinson 2016	inter	Ssl1	Tfb4	321	323	10.5	x	-
Murakami 2013, Luo 2015, Robinson 2016	inter	Ssl1	Tfb4	397	95	20.8	x	-
Murakami 2013, Luo 2015	inter	Ssl1	Tfb4	414	95	23.2	x	-
Robinson 2016	inter	Ssl2	Rpb5	472	94	18.1	x	-
Luo 2015	intra	Ssl2	Ssl2	523	372	25.7	x	-
Luo 2015	intra	Ssl2	Ssl2	766	624	22.3	x	-
Robinson 2016	inter	Ssl2	Tfa2	472	277	62.7	-	only 1 spectral count
Luo 2015	inter	Ssl2	Tfb2	734	415	19.6	x	-
Robinson 2016	inter	Tfa1	Tfb1	355	186	13.2	x	-
Murakami 2013, Robinson 2016	inter	Tfa1	Tfb1	366	179	12.7	x	-
Murakami 2013, Robinson 2016	inter	Tfa1	Tfb1	367	581	19.2	x	-
Luo 2015	inter	Tfb1	Rad3	73	125	83.1	-	low score
Luo 2015	inter	Tfb1	Rad3	101	95	87.3	-	-
Luo 2015	inter	Tfb1	Rad3	120	125	60.0	-	low score
Robinson 2016	inter	Tfb1	Rad3	334	183	14.4	x	-
Robinson 2016	inter	Tfb1	Rad3	334	588	13.7	x	-
Luo 2015	inter	Tfb1	Rad3	335	112	13.4	x	-
Luo 2015	inter	Tfb1	Rad3	335	588	16.1	x	-
Luo 2015	inter	Tfb1	Rad3	376	125	24.0	x	-
Luo 2015	inter	Tfb1	Rad3	390	588	10.3	x	-
Robinson 2016	inter	Tfb1	Rpb1	73	1093	116.7	-	only 1 spectral count, low score
Luo 2015	inter	Tfb1	Ssl1	120	201	33.2	-	-
Luo 2015, Robinson 2016	inter	Tfb1	Ssl1	238	205	21.4	x	-

Luo 2015	inter	Tfb1	Ssl1	246	205	26.7	x	-
Robinson 2016	inter	Tfb1	Ssl1	255	201	28.7	x	-
Murakami 2013, Luo 2015, Robinson 2016	inter	Tfb1	Ssl1	255	205	18.6	x	-
Robinson 2016	inter	Tfb1	Tfa1	587	367	24.9	x	-
Luo 2015	intra	Tfb1	Tfb1	47	101	11.5	x	-
Robinson 2016	intra	Tfb1	Tfb1	47	112	9.8	x	-
Robinson 2016	intra	Tfb1	Tfb1	57	65	24.3	x	-
Robinson 2016	intra	Tfb1	Tfb1	73	65	15.8	x	-
Murakami 2013, Luo 2015, Robinson 2016	intra	Tfb1	Tfb1	73	70	9.0	x	-
Robinson 2016	intra	Tfb1	Tfb1	73	71	6.5	x	-
Luo 2015	intra	Tfb1	Tfb1	73	120	30.5	x	-
Robinson 2016	intra	Tfb1	Tfb1	83	47	15.8	x	-
Murakami 2013, Luo 2015, Robinson 2016	intra	Tfb1	Tfb1	83	70	11.7	x	-
Luo 2015	intra	Tfb1	Tfb1	83	71	13.0	x	-
Luo 2015	intra	Tfb1	Tfb1	83	291	41.3	-	-
Luo 2015, Robinson 2016	intra	Tfb1	Tfb1	101	112	16.1	x	-
Luo 2015, Robinson 2016	intra	Tfb1	Tfb1	101	120	28.4	x	-
Luo 2015	intra	Tfb1	Tfb1	101	335	62.1	-	-
Robinson 2016	intra	Tfb1	Tfb1	112	65	14.0	x	-
Luo 2015, Robinson 2016	intra	Tfb1	Tfb1	120	65	21.6	x	-
Luo 2015	intra	Tfb1	Tfb1	120	70	21.7	x	-
Murakami 2013, Robinson 2016	intra	Tfb1	Tfb1	120	246	16.2	x	-
Luo 2015	intra	Tfb1	Tfb1	120	279	14.8	x	-
Luo 2015	intra	Tfb1	Tfb1	120	291	24.3	x	-
Murakami 2013, Robinson 2016	intra	Tfb1	Tfb1	171	574	23.1	x	-
Murakami 2013	intra	Tfb1	Tfb1	171	581	22.1	x	-
Robinson 2016	intra	Tfb1	Tfb1	227	179	20.7	x	-
Robinson 2016	intra	Tfb1	Tfb1	227	255	14.4	x	-
Luo 2015, Robinson 2016	intra	Tfb1	Tfb1	227	267	20.6	x	-
Luo 2015	intra	Tfb1	Tfb1	238	101	31.7	-	low score
Robinson 2016	intra	Tfb1	Tfb1	238	120	26.3	x	-
Murakami 2013, Luo 2015, Robinson 2016	intra	Tfb1	Tfb1	238	255	11.2	x	-
Robinson 2016	intra	Tfb1	Tfb1	238	279	23.5	x	-
Luo 2015	intra	Tfb1	Tfb1	246	101	20.7	x	-
Murakami 2013, Luo 2015, Robinson 2016	intra	Tfb1	Tfb1	246	255	17.6	x	-
Luo 2015	intra	Tfb1	Tfb1	246	276	26.1	x	-
Luo 2015, Robinson 2016	intra	Tfb1	Tfb1	246	279	19.5	x	-
Luo 2015	intra	Tfb1	Tfb1	246	291	16.3	x	-
Robinson 2016	intra	Tfb1	Tfb1	255	186	28.9	x	-
Robinson 2016	intra	Tfb1	Tfb1	255	300	23.9	x	-
Robinson 2016	intra	Tfb1	Tfb1	268	279	14.8	x	-
Murakami 2013, Luo 2015, Robinson 2016	intra	Tfb1	Tfb1	268	324	15.2	x	-
Robinson 2016	intra	Tfb1	Tfb1	268	334	35.2	-	only 1 spectral count
Luo 2015	intra	Tfb1	Tfb1	276	291	19.5	x	-
Luo 2015	intra	Tfb1	Tfb1	291	70	39.9	-	-
Luo 2015, Robinson 2016	intra	Tfb1	Tfb1	291	295	5.9	x	-
Luo 2015, Robinson 2016	intra	Tfb1	Tfb1	291	300	10.4	x	-
Robinson 2016	intra	Tfb1	Tfb1	291	324	20.3	x	-
Luo 2015	intra	Tfb1	Tfb1	300	335	37.9	-	low score
Robinson 2016	intra	Tfb1	Tfb1	300	384	23.6	x	-
Luo 2015, Robinson 2016	intra	Tfb1	Tfb1	324	267	15.9	x	-
Luo 2015, Robinson 2016	intra	Tfb1	Tfb1	324	384	11.9	x	-
Luo 2015	intra	Tfb1	Tfb1	335	384	19.6	x	-
Luo 2015	intra	Tfb1	Tfb1	335	390	22.3	x	-
Luo 2015	intra	Tfb1	Tfb1	376	384	12.3	x	-
Robinson 2016	intra	Tfb1	Tfb1	384	268	20.4	x	-
Luo 2015	intra	Tfb1	Tfb1	384	295	17.1	x	-
Luo 2015	intra	Tfb1	Tfb1	498	508	15.0	x	-
Luo 2015	intra	Tfb1	Tfb1	508	501	10.2	x	-
Murakami 2013, Luo 2015, Robinson 2016	intra	Tfb1	Tfb1	508	515	9.9	x	-
Luo 2015	inter	Tfb1	Tfb3	291	10	51.1	-	low score
Luo 2015	inter	Tfb1	Tfb4	83	323	95.4	-	-
Robinson 2016	inter	Tfb1	Tfb4	101	323	92.4	-	only 1 spectral count, low score
Luo 2015	inter	Tfb1	Tfb4	120	323	68.0	-	-
Murakami 2013, Robinson 2016	intra	Tfb1	Tfb4	171	319	23.2	x	-
Luo 2015	inter	Tfb1	Tfb4	483	108	6.8	x	-
Murakami 2013, Luo 2015, Robinson 2016	intra	Tfb2	Tfb2	238	262	12.4	x	-
Luo 2015, Robinson 2016	intra	Tfb2	Tfb2	415	419	6.5	x	-
Murakami 2013, Luo 2015, Robinson 2016	inter	Tfb2	Tfb5	495	6	8.9	x	-
Murakami 2013, Luo 2015, Robinson 2016	intra	Tfb2	Tfb5	506	6	18.1	x	-
Luo 2015	inter	Tfb3	Rad3	10	125	44.7	-	-
Luo 2015	inter	Tfb3	Rad3	17	125	50.0	-	low score
Robinson 2016	inter	Tfb3	Rad3	119	276	17.7	x	-
Luo 2015, Robinson 2016	intra	Tfb3	Tfb3	17	57	11.8	x	-
Luo 2015	intra	Tfb3	Tfb3	27	65	16.4	x	-
Luo 2015	intra	Tfb3	Tfb3	61	67	14.9	x	-
Luo 2015	intra	Tfb3	Tfb3	86	67	16.9	x	-
Murakami 2013	intra	Tfb3	Tfb3	94	132	17.2	x	-
Murakami 2013, Luo 2015	intra	Tfb3	Tfb3	119	132	8.7	x	-
Luo 2015	intra	Tfb3	Tfb3	141	65	29.5	x	-
Luo 2015	intra	Tfb3	Tfb3	141	67	26.0	x	-
Luo 2015	intra	Tfb3	Tfb3	141	132	14.0	x	-
Luo 2015	inter	Tfb4	Ssl1	108	397	42.3	-	-
Luo 2015, Robinson 2016	inter	Tfb4	Tfb2	108	238	24.6	x	-
Murakami 2013, Luo 2015, Robinson 2016	intra	Tfb4	Tfb4	84	138	19.4	x	-
Luo 2015	intra	Tfb4	Tfb4	95	108	23.6	x	-
Murakami 2013, Luo 2015, Robinson 2016	intra	Tfb4	Tfb4	95	138	29.4	x	-
Murakami 2013, Luo 2015, Robinson 2016	intra	Tfb4	Tfb4	131	138	15.9	x	-
Luo 2015, Robinson 2016	intra	Tfb4	Tfb4	165	207	14.8	x	-
Murakami 2013, Luo 2015, Robinson 2016	intra	Tfb4	Tfb4	173	207	10.1	x	-
Luo 2015	intra	Tfb4	Tfb4	319	323	6.6	x	-
Luo 2015	intra	Tfb4	Tfb4	321	323	5.7	x	-

Luo 2015	inter	Tfb5	Ssl1	6	201	73.2	-	-
Luo 2015	inter	Tfb5	Ssl2	60	721	17.0	x	-
Robinson 2016	intra	Tfb5	Tfb5	46	6	13.7	x	-
Robinson 2016	intra	Tfb5	Tfb5	60	51	14.4	x	-

b.

Study	Link type	Protein 1	Protein 2	Residue 1	Residue 2
Robinson 2016	inter	Tfa1	Ssl2	301	711
Robinson 2016	intra	Tfa1	Tfa1	284	295
Robinson 2016	intra	Tfa1	Tfa1	286	301
Robinson 2016	inter	Tfa1	Tfb2	295	415
Murakami 2013	inter	Tfa1	Tfb2	301	427

a. TFIIH crosslinks from previous studies[10,24,25] utilizing BS3 and SBAT and respective Cα-distances within the PIC-cMed model obtained in this study. Crosslinks used to verify various TFIIH regions are indicated. For details also refer to main text and Methods.

b. TFIIH crosslinks from previous studies[10,24,25] that were located up to 12 residues from the next residue modeled in our study. These crosslinks were additionally used to confirm TFIIH regions. For details also refer to **Extended Data Fig. 6**.

Supplementary Table 3 | Newly obtained EDC-crosslinks.

a.

PIC-cMed components	Total number of crosslinks	Number of crosslinks mappable on the PIC-cMed structure
Total crosslinks	262	158
Inter-protein crosslinks		
Total	109	65
Pol II – Pol II	18	15
Pol II – TFIIB	8	4
Pol II – TFIIE	8	3
Pol II – TFIIF	4	2
Pol II – TFIIH	4	0
Pol II – cMed	2	2
TFIIA – TFIIA	2	2
TFIIA – TFIIE	1	0
TFIIA – TBP	1	0
TFIIB – TBP	1	0
TFIIA – TFIIF	3	0
TFIIE – TFIIE	1	0
TFIIE – TFIIF	2	1
TFIIF – TFIIF	14	9
TFIIE – TFIIH	11	10
TFIIH – TFIIH	19	13
TFIIH – cMed	3	0
cMed – cMed	7	4
Intra-protein crosslinks		
Total	153	93
Pol II	35	34
TFIIA	4	3
TFIIB	5	4
TBP	8	0
TFIIE	3	3
TFIIF	22	6
TFIIH	59	34
cMed	17	9

b.

Link type	Protein 1	Protein 2	Residue 1	Residue 2	Total Count	Score	Distance (Å)	Alternative residue
Intra	Ccl1	Ccl1	45	286	2	3,93	NA	-
Intra	Kin28	Kin28	32	37	2	6,72	NA	-
Intra	Med1	Med1	375	389	1	8,88	NA	-
Intra	Med1	Med1	377	389	1	8,01	NA	-
Intra	Med14	Med14	420	544	2	3,84	7.8	418
Intra	Med14	Med14	539	544	2	10,84	8.0	-
Intra	Med17	Med17	386	416	1	9,73	9.5	413
Intra	Med17	Med17	386	418	2	13,55	NA	-
Intra	Med17	Med17	418	427	3	11,05	NA	-
Intra	Med17	Med17	419	427	2	15,78	NA	-
Intra	Med17	Med17	421	427	2	23,03	5.2	424
Intra	Med17	Med17	579	608	1	3,74	12.6	-
Intra	Med17	Med17	581	608	12	18,05	13.1	580
Inter	Med17	Med22	548	118	1	5,51	9.6	-
Inter	Med17	Med22	608	105	4	11,67	5.4	-
Inter	Med17	Med22	608	106	1	15,05	8.6	-
Inter	Med17	Med22	608	109	3	11,46	7.4	-
Inter	Med17	Med7	75	191	1	4,83	NA	-
Inter	Med17	Med7	78	191	1	7,28	NA	-
Intra	Med20	Med20	2	187	1	3,69	13.2	-
Intra	Med20	Med20	10	183	3	4,31	8.0	-
Intra	Med21	Med21	107	113	1	8,04	10.0	-
Intra	Med4	Med4	34	39	2	14,65	NA	-
Intra	Med7	Med7	93	103	3	8,82	NA	-
Intra	Med8	Med8	189	210	2	3,31	NA	-
Inter	Med9	Med4	117	26	1	4,75	NA	-
Inter	Med9	Rpb1	88	977	3	4,77	9.9	-
Inter	Med9	Rpb1	99	918	6	5,74	15.9	-
Inter	Rad3	Med7	389	1	2	9,7	NA	-
Intra	Rad3	Rad3	68	225	8	10,59	13.3	-
Intra	Rad3	Rad3	132	269	1	12,46	23.4	-
Intra	Rad3	Rad3	268	336	2	3,21	10.1	-
Intra	Rad3	Rad3	269	336	2	8,01	13.7	-
Intra	Rad3	Rad3	276	389	3	7,67	15.8	-
Intra	Rad3	Rad3	276	394	1	3,91	24.3	-
Intra	Rad3	Rad3	281	389	35	14,94	12.8	-
Intra	Rad3	Rad3	336	340	6	18,42	5.9	-
Intra	Rad3	Rad3	578	605	2	5,13	11.8	-
Intra	Rad3	Rad3	605	608	1	12,22	8.9	-
Intra	Rad3	Rad3	605	674	1	3,3	28.7	-
Intra	Rad3	Rad3	613	673	3	6,58	11.7	-
Intra	Rad3	Rad3	636	640	4	4,69	6.0	-
Inter	Rad3	Tfb1	112	340	2	7,25	13.6	-
Inter	Rad3	Tfb1	605	340	1	4,94	7.0	-
Inter	Rad3	Tfb1	605	345	3	10,12	16.7	-
Inter	Rad3	Tfb1	605	346	1	5,3	17.8	-
Inter	Rad3	Tfb3	336	77	18	15,55	9.8	-
Inter	Rad3	Tfb3	343	74	3	8,51	8.9	-
Intra	Rpb1	Rpb1	39	49	11	10,7	7.0	-
Intra	Rpb1	Rpb1	186	193	4	9,02	4.3	197
Intra	Rpb1	Rpb1	186	195	5	8,77	4.3	197
Intra	Rpb1	Rpb1	368	398	5	5,71	10.2	-
Intra	Rpb1	Rpb1	724	728	3	3,73	6.0	-
Intra	Rpb1	Rpb1	833	1102	13	13	9.0	-

Intra	Rpb1	Rpb1	951	1290	1	9,74	9.9	-
Intra	Rpb1	Rpb1	1093	1074	13	6,87	24.9	-
Intra	Rpb1	Rpb1	1093	1309	3	6,16	10.0	-
Intra	Rpb1	Rpb1	1132	1206	12	10,42	10.2	-
Inter	Rpb1	Rpb11	368	8	6	15,99	16.8	-
Inter	Rpb1	Rpb2	481	987	1	6,02	10.7	-
Inter	Rpb1	Rpb2	483	987	8	5,53	6.4	-
Inter	Rpb1	Rpb2	486	979	6	5,71	12.3	-
Inter	Rpb1	Rpb2	486	1102	6	6,34	8.3	-
Inter	Rpb1	Rpb2	1144	262	47	6,27	13.0	-
Inter	Rpb1	Rpb5	945	201	5	9,17	8.4	-
Inter	Rpb1	Rpb7	2	65	1	12,31	15.6	3
Inter	Rpb1	Rpb9	1253	20	1	8,65	12.6	1254
Inter	Rpb1	Tfa1	193	71	4	6,95	19.2	197
Inter	Rpb1	Tfa1	195	71	11	7,88	19.2	197
Inter	Rpb1	Tfa1	196	71	10	4,21	19.2	197
Inter	Rpb10	Rpb12	68	33	2	7,14	9.1	65
Inter	Rpb10	Rpb12	68	50	8	10,54	18.8	65
Intra	Rpb11	Rpb11	14	20	2	12,22	14.6	-
Intra	Rpb11	Rpb11	16	20	1	10,23	9.1	-
Intra	Rpb11	Rpb11	20	36	3	16,04	8.4	-
Intra	Rpb11	Rpb11	26	38	3	3,29	24.9	-
Intra	Rpb12	Rpb12	58	68	1	4,44	17.2	65
Inter	Rpb2	Rpb1	507	833	3	13,1	NA	-
Inter	Rpb2	Rpb1	979	485	3	4,68	10.4	-
Intra	Rpb2	Rpb2	99	183	5	7,89	12.6	-
Intra	Rpb2	Rpb2	131	134	3	15,45	9.9	-
Intra	Rpb2	Rpb2	133	138	1	6,14	17.0	-
Intra	Rpb2	Rpb2	227	262	2	6,32	11.7	-
Intra	Rpb2	Rpb2	239	507	1	9,19	NA	-
Intra	Rpb2	Rpb2	246	468	2	4,57	19.2	467
Intra	Rpb2	Rpb2	391	393	1	5,15	5.5	-
Intra	Rpb2	Rpb2	393	621	1	4,57	9.9	-
Intra	Rpb2	Rpb2	886	908	14	8,94	8.8	-
Intra	Rpb2	Rpb2	886	909	1	6,4	9.3	-
Intra	Rpb2	Rpb2	923	934	4	6,1	12.2	-
Intra	Rpb2	Rpb2	924	934	1	4,61	12.1	-
Intra	Rpb2	Rpb2	1057	1061	1	5,25	6.2	-
Inter	Rpb2	Tfg2	441	279	4	7,24	4.7	-
Inter	Rpb2	TFIIB	438	108	2	3,19	27.9	-
Inter	Rpb2	TFIIB	438	112	2	5,73	25.8	-
Inter	Rpb2	TFIIB	921	224	3	8,51	NA	-
Inter	Rpb2	TFIIB	922	224	8	12,19	NA	-
Inter	Rpb2	TFIIB	923	155	3	7,88	23.9	-
Inter	Rpb3	Rpb10	149	67	1	3,23	10.3	65
Inter	Rpb3	Rpb11	137	118	51	15,25	NA	-
Inter	Rpb3	Rpb11	266	84	2	11,79	9.9	265
Inter	Rpb3	Rpb11	266	88	1	8,84	12.3	265
Intra	Rpb3	Rpb3	90	160	4	12,77	11.5	-
Intra	Rpb4	Rpb4	127	142	2	9,93	6.1	-
Intra	Rpb4	Rpb4	131	142	13	17,27	8.2	-
Intra	Rpb5	Rpb5	161	172	5	8,86	9.5	-
Intra	Rpb5	Rpb5	191	194	1	16,46	5.9	-
Intra	Rpb5	Rpb5	194	201	6	7,2	23.0	-
Inter	Rpb6	Rpb5	62	171	4	11,2	NA	-
Intra	Rpb6	Rpb6	112	123	20	6,75	9.6	-
Inter	Rpb9	Tfg1	9	400	6	16,92	8.4	-
Intra	Ssl1	Ssl1	262	303	3	10,3	10.7	-
Intra	Ssl1	Ssl1	387	430	8	4,45	9.5	-
Inter	Ssl1	Tfa1	201	270	2	5,16	19.0	-
Inter	Ssl1	Tfa1	201	275	2	4,32	14.3	-
Inter	Ssl1	Tfa1	205	270	1	5,04	14.6	-
Inter	Ssl1	Tfa1	205	275	2	9,84	15.2	-
Inter	Ssl1	Tfb4	401	95	9	25,87	13.1	-
Inter	Ssl1	Tfb4	439	165	16	7,22	9.8	-
Inter	Ssl1	Tfb4	441	165	7	8,88	14.7	-
Inter	Ssl1	Tfb4	446	165	2	4,76	15.2	-
Inter	Ssl2	Med7	520	1	4	18,53	NA	-
Inter	Ssl2	Ssl1	351	52	1	3,64	NA	-
Intra	Ssl2	Ssl2	46	65	2	6,51	NA	-
Intra	Ssl2	Ssl2	90	334	6	13,37	NA	-
Intra	Ssl2	Ssl2	228	304	4	4,61	NA	-
Intra	Ssl2	Ssl2	510	520	2	10,53	25.1	-
Intra	Ssl2	Ssl2	510	521	2	3,71	23.7	-
Intra	Ssl2	Ssl2	617	624	1	6,12	10.7	-
Intra	Ssl2	Ssl2	758	827	2	3,71	NA	-
Intra	Ssl2	Ssl2	762	791	3	5,79	NA	-
Intra	Ssl2	Ssl2	762	827	2	3,82	NA	-
Intra	Ssl2	Ssl2	768	827	1	3,28	NA	-
Intra	Ssl2	Ssl2	774	835	1	3,53	NA	-
Intra	TBP	TBP	2	27	1	6,94	NA	-
Intra	TBP	TBP	2	44	1	7,29	NA	-
Intra	TBP	TBP	2	188	2	6,77	NA	-
Intra	TBP	TBP	27	35	3	4,88	NA	-
Intra	TBP	TBP	27	47	2	10,36	NA	-
Intra	TBP	TBP	47	52	1	3,83	NA	-
Intra	TBP	TBP	47	54	2	4,22	NA	-
Intra	TBP	TBP	47	108	1	9,2	NA	-
Inter	Tfa1	Rpb1	222	188	10	3,21	NA	-
Inter	Tfa1	Rpb1	222	193	18	11,9	NA	-
Inter	Tfa1	Rpb1	222	195	16	9,64	NA	-
Inter	Tfa1	Rpb1	222	196	47	9,75	NA	-
Intra	Tfa1	Tfa1	1	195	2	11,53	10.7	4,194
Inter	Tfa1	Tfb1	345	189	2	6,08	11.7	349
Inter	Tfa1	Tfb1	347	189	1	6,74	11.7	349
Inter	Tfa1	Tfb1	349	189	14	9,55	11.7	-
Inter	Tfa1	Tfb1	350	189	11	9,59	12.6	-
Inter	Tfa2	Rpb1	294	193	1	4,4	NA	-
Inter	Tfa2	Tfa1	294	195	3	9,73	NA	-

Intra	Tfa2	Tfa2	140	149	5	7,23	15.7	-
Intra	Tfa2	Tfa2	273	277	1	6,41	6.1	-
Inter	Tfa2	Tfg2	133	335	2	6,42	8.3	-
Inter	Tfb1	Tfa1	57	411	1	3,4	8.3	-
Inter	Tfb1	Tfa1	57	412	1	3,44	9.4	-
Intra	Tfb1	Tfb1	65	118	2	11,74	17.7	-
Intra	Tfb1	Tfb1	118	279	3	8,85	11.2	-
Intra	Tfb1	Tfb1	166	173	2	3,86	6.3	168
Intra	Tfb1	Tfb1	268	320	7	15,09	12.4	-
Intra	Tfb1	Tfb1	291	305	2	5,17	10.0	-
Intra	Tfb1	Tfb1	322	324	7	11,97	5.3	-
Inter	Tfb1	Tfb4	458	43	1	3,13	NA	-
Inter	Tfb1	Tfb4	636	323	8	15,83	14.4	-
Inter	Tfb2	Tfa1	449	301	7	11,53	NA	-
Intra	Tfb2	Tfb2	168	175	19	21,6	7.0	-
Inter	Tfb2	Tfb4	326	166	1	7,8	NA	-
Inter	Tfb2	Tfb5	449	51	9	12,01	12.0	-
Inter	Tfb2	Tfb5	463	1	2	7,28	7.5	2
Inter	Tfb3	Med6	154	143	4	8,37	NA	-
Inter	Tfb3	Rad3	156	357	5	6,45	NA	-
Inter	Tfb3	Rpb4	25	1	1	5,51	NA	-
Inter	Tfb3	Rpb4	226	186	32	13,88	NA	-
Inter	Tfb3	Rpb4	235	186	1	4,72	NA	-
Inter	Tfb3	Rpb7	220	134	1	3,57	NA	-
Inter	Tfb3	Ssl2	44	69	7	6,68	NA	-
Intra	Tfb3	Tfb3	27	40	1	4,1	5.8	-
Intra	Tfb3	Tfb3	57	204	1	4,11	NA	-
Intra	Tfb3	Tfb3	80	121	11	17,24	7.0	-
Intra	Tfb3	Tfb3	94	154	2	5,27	NA	-
Intra	Tfb3	Tfb3	94	156	1	3,39	NA	-
Intra	Tfb3	Tfb3	159	163	2	7,5	NA	-
Intra	Tfb3	Tfb3	180	192	4	7,51	NA	-
Intra	Tfb3	Tfb3	180	226	1	5,66	NA	-
Intra	Tfb3	Tfb3	181	192	1	6,38	NA	-
Intra	Tfb3	Tfb3	182	192	3	6,44	NA	-
Intra	Tfb3	Tfb3	182	226	3	8,35	NA	-
Intra	Tfb3	Tfb3	192	204	2	8,81	NA	-
Intra	Tfb3	Tfb3	192	207	5	9,96	NA	-
Intra	Tfb3	Tfb3	192	210	1	8,02	NA	-
Intra	Tfb3	Tfb3	204	235	1	5,41	NA	-
Intra	Tfb3	Tfb3	207	235	2	8,48	NA	-
Intra	Tfb3	Tfb3	226	265	1	5,4	NA	-
Intra	Tfb4	Tfb4	84	127	5	5	12.1	-
Intra	Tfb4	Tfb4	84	128	16	5,86	8.4	-
Intra	Tfb4	Tfb4	89	102	1	9,98	15.0	103
Intra	Tfb4	Tfb4	102	123	2	10,97	9.1	103
Intra	Tfb4	Tfb4	102	127	1	7,97	10.9	103
Intra	Tfb4	Tfb4	108	123	7	14,01	10.8	-
Intra	Tfb4	Tfb4	108	127	10	11,52	14.4	-
Inter	Tfb5	Ssl2	6	46	2	3,24	NA	-
Inter	Tfg1	Tfa1	91	269	1	3,89	NA	-
Intra	Tfg1	Tfg1	60	68	4	16,07	NA	-
Intra	Tfg1	Tfg1	60	69	3	12,16	NA	-
Intra	Tfg1	Tfg1	89	97	2	5,16	NA	-
Intra	Tfg1	Tfg1	274	411	1	12,18	NA	-
Intra	Tfg1	Tfg1	274	416	1	9,12	NA	-
Intra	Tfg1	Tfg1	280	289	8	15,2	NA	-
Intra	Tfg1	Tfg1	281	289	1	9,22	NA	-
Intra	Tfg1	Tfg1	411	419	2	9,31	7.6	415
Intra	Tfg1	Tfg1	658	671	5	14,2	NA	-
Intra	Tfg1	Tfg1	658	672	3	11,72	NA	-
Intra	Tfg1	Tfg1	671	704	2	8,68	NA	-
Inter	Tfg1	Tfg2	93	99	1	4,99	5.8	97
Inter	Tfg1	Tfg2	93	103	7	13,91	10.7	97
Inter	Tfg1	Tfg2	94	103	3	6,24	10.7	97
Inter	Tfg1	Tfg2	97	94	1	5,98	15.9	-
Inter	Tfg1	Tfg2	97	99	16	6,18	5.8	-
Inter	Tfg1	Tfg2	100	94	2	3,47	6.4	-
Inter	Tfg1	Tfg2	125	130	5	14,97	9.1	-
Inter	Tfg1	Tfg2	126	130	35	17,99	6.1	-
Inter	Tfg1	Tfg2	126	132	5	14,32	10.0	-
Inter	Tfg2	Rpb1	2	196	1	6,84	NA	-
Inter	Tfg2	Rpb1	186	196	3	8,63	NA	-
Inter	Tfg2	Tfg1	100	91	1	3,15	NA	-
Inter	Tfg2	Tfg1	103	92	7	15,12	NA	-
Inter	Tfg2	Tfg1	110	91	1	4,9	NA	-
Inter	Tfg2	Tfg1	114	91	1	3,2	NA	-
Inter	Tfg2	Tfg1	194	411	1	4,8	NA	-
Intra	Tfg2	Tfg2	23	54	1	12,75	NA	-
Intra	Tfg2	Tfg2	31	206	1	3,28	NA	-
Intra	Tfg2	Tfg2	38	142	2	5,73	NA	-
Intra	Tfg2	Tfg2	38	206	1	6,03	NA	-
Intra	Tfg2	Tfg2	54	141	6	15,33	11.5	58,138
Intra	Tfg2	Tfg2	54	142	5	9,35	11.5	58,138
Intra	Tfg2	Tfg2	79	245	1	5,75	15.5	244
Intra	Tfg2	Tfg2	80	114	1	3,59	13.6	110
Intra	Tfg2	Tfg2	126	130	1	4,38	10.1	-
Intra	Tfg2	Tfg2	308	357	1	9,57	NA	-
Intra	Tfg2	Tfg2	356	360	1	4,04	NA	-
Inter	TFIIB	Rpb2	100	470	2	9,2	NA	
Inter	TFIIB	Rpb2	184	865	8	3,85	14.2	-
Inter	TFIIB	Rpb2	224	923	4	5,8	NA	-
Inter	TFIIB	TBP	343	241	2	3,82	NA	-
Intra	TFIIB	TFIIB	75	147	1	3,12	NA	-
Intra	TFIIB	TFIIB	88	155	5	11,85	9.8	-
Intra	TFIIB	TFIIB	103	108	1	5,13	9.3	-
Intra	TFIIB	TFIIB	155	219	4	6,87	14.8	218
Intra	TFIIB	TFIIB	160	217	1	12,22	12.3	-
Inter	Toa1	TBP	169	110	2	3,83	NA	-

Inter	Toa1	Tfg2	23	2	2	17,06	NA	-
Inter	Toa1	Tfg2	24	2	1	12,39	NA	-
Inter	Toa1	Tfg2	26	2	1	15,32	NA	-
Intra	Toa1	Toa1	44	48	1	5,18	5.0	47
Intra	Toa1	Toa1	144	167	2	4,02	NA	-
Inter	Toa1	Toa2	2	101	7	11,21	12.1	104
Inter	Toa1	Toa2	45	21	17	10,62	8.7	-
Inter	Toa2	Tfa2	24	20	2	7,93	NA	-
Intra	Toa2	Toa2	2	42	2	5,4	9.6	5
Intra	Toa2	Toa2	59	88	9	15,94	4.8	-

a. Summary and statistics of EDC-crosslinks in the PIC-cMed complex obtained in this study.
b. List of single EDC-crosslinks. 'Total Count' refers to sum of spectral counts originating from both replicates and 'score' refers to highest detected score value (Methods). Cα distances are indicated if structural information was available within a range of 4 residues from the cross-linked residue. Several crosslinks were used to guide TFIIE density interpretation and to confirm TFIIE-TFIIH interactions. For details also refer to main text and **Extended Data Fig. 6**.

Supplementary Table 4 | Adaptation and extension of yeast cPIC and cMed models.

Factor/Subunit / Chain ID	Initial Model	PDB-template for initial model	Modeling algorithm	Changes to initial model
Pol II / A-L	yeast high resolution EM structure	5FYW:A-L	-	rigid body fit of clamp region (residues 1-346 in chain A) and peripheral regions in Rpb3 (residues 22-44, 73-97), Rpb6 (residues 72-154), Rpb8 (residues 2-146), Rpb9 (residues 20-43, 55-117) and Rpb12 (residues 26-65); MDFF correction of stalk (chain D, G), PHENIX geometry minimization
TFIIA / U-V	yeast high resolution EM structure	5FYW:U-V	-	rigid body fit, PHENIX geometry minimization
TFIIB / M	yeast high resolution EM structure	5FYW:M	-	extension by residues 59-123 based on PDB 4bbr:M; MDFF correction of this range, PHENIX geometry minimization
TBP / O	yeast high resolution EM structure	5FYW:O	-	PHENIX geometry minimization
TFIIE / W-X	homology model	5GPY:A-B	I-Tasser SWISS	MDFF correction of homology model, PHENIX geometry minimization
TFIIF / Q-R	yeast high resolution EM structure	5FYW:Q-R	-	rigid body fit of residues 329-415 in chain Q and residues 58-244 in chain R; extension of linker (residues 245-250) in chain R, PHENIX geometry minimization

cMed model originates from *S. cerevisiae* homology model of PDB 5n9j (Nozawa et. al, 2017) and was subjected to alterations listed below; complete cMed model was subjected to PHENIX geometry minimization routine

Factor/Subunit / Chain ID	Initial Model	PDB-template for initial model	Modeling algorithm	Changes to initial model
Med4 / h	homology model	5N9J:H	-	extension of α-helix in residue range 118-126; *de-novo* modeling of α-helix in residue range 130-145; MDFF correction of homology model
Med7 / i	yeast crystal structure	1YKE:A	-	extension of α-helix in residue range 206-211; MDFF correction of homology model
Med14 / l	homology model	5N9J:L	-	truncation of residues 341-345; MDFF correction of homology model
Med21 / j	yeast crystal structure	1YKE:B	-	extension of α-helix in residue range 128-138; MDFF correction of homology model
Med31 / o	yeast crystal structure	3FBI:B	-	truncation of residues 94-110; replacement by *de-novo* modeled α-helix (SSE predicted); MDFF correction of homology model