Table S1: Summary of Integrative Structure Determination of Molecular architecture of the yeast Mediator complex (PDBDEV00000003)

1. Model Composition	
Entry composition	- med6: Chain A (295 residues) - med8: Chain B (223 residues) - med11: Chain C (115 residues) - med17: Chain D (687 residues) - med18: Chain E (307 residues) - med20: Chain F (210 residues) - med22: Chain G (121 residues) - med4: Chain H (284 residues) - med7: Chain I (222 residues) - med9: Chain J (149 residues) - med31: Chain K (127 residues) - med21: Chain L (140 residues) - med10: Chain M (157 residues) - med1: Chain N (566 residues) - med14: Chain O (1082 residues) - med19: Chain P (220 residues) - med2: Chain Q (436 residues) - med3: Chain R (401 residues) - med5: Chain S (1146 residues) - med15: Chain T (1094 residues) - med16: Chain U (986 residues) - med6: Chain A (295 residues) - med8: Chain B (223 residues) - med11: Chain C (115 residues) - med17: Chain D (687 residues) - med18: Chain E (307 residues) - med20: Chain F (210 residues) - med22: Chain G (121 residues) - med4: Chain H (284 residues) - med7: Chain I (222 residues) - med9: Chain J (149 residues) - med31: Chain K (127 residues) - med21: Chain L (140 residues) - med10: Chain M (157 residues) - med1: Chain N (566 residues) - med14: Chain O (1082 residues) - med19: Chain P (220 residues) - med2: Chain Q (436 residues) - med3: Chain R (401 residues) - med5: Chain S (1146 residues) - med15: Chain T (1094 residues) - med16: Chain U (986 residues) - med6: Chain A (295 residues) - med8: Chain B (223 residues) - med11: Chain C (115 residues) - med17: Chain D (687 residues) - med18: Chain E (307 residues) - med20: Chain F (210 residues) - med22: Chain G (121 residues) - med4: Chain H (284 residues) - med7: Chain I (222 residues) - med9: Chain J (149 residues) - med31: Chain K (127 residues) - med21: Chain L (140 residues) - med10: Chain M (157 residues) - med1: Chain N (566 residues)

	- med14: Chain O (1082 residues) - med19: Chain P (220 residues) - med2: Chain Q (436 residues) - med3: Chain R (401 residues) - med5: Chain S (1146 residues) - med15: Chain T (1094 residues) - med16: Chain U (986 residues) - med6: Chain A (295 residues) - med8: Chain B (223 residues) - med11: Chain C (115 residues) - med17: Chain D (687 residues) - med18: Chain E (307 residues) - med20: Chain F (210 residues) - med22: Chain G (121 residues) - med4: Chain H (284 residues) - med7: Chain I (222 residues) - med9: Chain J (149 residues) - med31: Chain K (127 residues) - med21: Chain L (140 residues) - med10: Chain M (157 residues) - med1: Chain N (566 residues) - med14: Chain O (1082 residues) - med19: Chain P (220 residues) - med2: Chain Q (436 residues) - med3: Chain R (401 residues) - med5: Chain S (1146 residues) - med15: Chain T (1094 residues) - med16: Chain U (986 residues)
Datasets used for modeling	- Experimental model, PDB ID: 4GWP - Comparative model, template PDB ID: Not listed - Comparative model, template PDB ID: Not listed - Experimental model, PDB ID: 3FBI - Experimental model, PDB ID: Not listed - Experimental model, PDB ID: 1YKH - Experimental model, PDB ID: Not listed - Experimental model, PDB ID: 4BZK - Comparative model, template PDB ID: Not listed - Mass Spectrometry data, MSV000079237 - CX-MS data, Linker name: DSS, Number of cross-links: 359 cross-links - 3DEM volume, EMDB ID: EMD-2634 - 3DEM volume, EMDB ID: Not listed - 3DEM volume, EMDB ID: Not listed - 3DEM volume, EMDB ID: Not listed - 3DEM volume, EMDB ID: Not listed
2. Representation	
Atomic structural coverage	10%
Number of rigid bodies, flexible units	12, 50
	- A: - - B: - - C: - - D: - - E: - - F: - - G: - - H: 37-127:Comparative model/None. - I: 12-84:Experimental model/None, 112-

Rigid bodies	206:Experimental model/None. - J: 65-149:Comparative model/None. - K: 19-110:Experimental model/None. - L: 2-128:Experimental model/None. - M: - - N: - - O: - - P: - - Q: - - R: - - S: - - T: - - U: 8-49:Comparative model/None, 94-150:Comparative model/None, 165-174:Comparative model/None, 231-406:Comparative model/None, 437-476:Comparative model/None, 503-538:Comparative model/None.
Flexible units	- A: 1-60, 61-82, 83-192, 193-295. - B: 1-22, 23-173, 174-181, 182-214, 215-223. - C: 1-3, 4-115. - D: 123-181, 182-371, 372-377, 378-661, 662-669, 670-687, 1-122. - E: 1-1, 2-110, 111-157, 158-301, 302-307. - F: 1-1, 2-210. - G: 1-121. - H: 1-36, 128-284. - I: 1-11, 85-111, 207-222. - J: 1-64. - K: 1-18, 111-127. - L: 1-1, 129-140. - M: 1-157. - N: 1-566. - O: 1-1082. - P: 1-220. - Q: 1-436. - R: 1-401. - S: 1-1146. - T: 1-1094. - U: 50-93, 151-164, 175-230, 407-436, 477-502, 539-986.
Resolution	Rigid bodies: 1 residue per bead. Flexible regions: 10 residues per bead.
3. Restraints	
Physical principles	Excluded volume and Sequence connectivity.
Experimental data	- CrossLinkRestraint: 359 cross-links, DSS - EM3DRestraint: 29, Gaussian mixture models - EM3DRestraint: 49, Gaussian mixture models
4. Validation	
Sampling validation	
Clustering algorithm ,*clustering feature*	None, RMSD
Number of ensembles	4

Number of models in ensembles	142, 192, 39, 126
Model precision (uncertainty of models)	19.519Å, 21.833Å, 25.289Å, 21.061Å
Quality of data	-
Assessment of atomic segments	-
Fit of the model to information used to compute it	
Fit of the model to information not used to compute it	
5. Methodology and Software	
Method	Sampling
Name	Replica exchange Monte Carlo
Details	
Software	- Integrative Modeling Platform (IMP) (version develop-0a5706e202) - IMP PMI module (version 67456c0) - Protein Prospector (version 5.13.1) - Situs (version 2.7) - Phyre2 (version 2.0)