

**Supplemental Table 1: Data collection and refinement statistics for the SET7/9 complexes.**

Protein-Peptide Complex	WT SET7/9		SET7/9 Y305F		SET7/9 Y245A			
	TAF10-K189	TAF10-K189	TAF10-K189me1	TAF10-K189me2	TAF10-K189	TAF10-K189me1	TAF10-K189me2	TAF10-K189me3
<b>RCSB PDB ID</b>	3M53	3M54	3M55	3M56	3M57	3M58	3M59	3M5A
<b>Data Collection</b>								
Beamline	21-ID-G	21-ID-G	21-ID-G	23-ID-D	23-ID-D	23-ID-D	21-ID-G	21-ID-G
Wavelength (Å)	0.9786	0.9786	0.9786	1.0093	1.0093	1.0093	0.9786	0.9786
Space group	<i>P</i> <sub>3</sub> <sup>2</sup> <i>1</i>	<i>P</i> <sub>3</sub> <sup>2</sup> <i>1</i>	<i>P</i> <sub>3</sub> <sup>2</sup> <i>1</i>	<i>P</i> <sub>3</sub> <sup>2</sup> <i>1</i>	<i>P</i> <sub>3</sub> <sup>2</sup> <i>1</i>	<i>P</i> <sub>3</sub> <sup>2</sup> <i>1</i>	<i>P</i> <sub>3</sub> <sup>2</sup> <i>1</i>	<i>P</i> <sub>3</sub> <sup>2</sup> <i>1</i>
Cell dimensions	<i>a</i> = <i>b</i> (Å)	83.75	83.73	83.52	82.95	83.64	83.21	83.50
	<i>c</i> (Å)	96.11	96.05	95.67	95.58	96.05	95.26	95.72
Resolution (Å)	1.85	1.60	1.55	1.65	1.70	1.40	1.70	1.75
Last shell (Å)	(1.92-1.85)	(1.66-1.60)	(1.61-1.55)	(1.71-1.65)	(1.76-1.70)	(1.45-1.40)	(1.76-1.70)	(1.81-1.75)
<i>R</i> <sub>merge</sub> (%) <sup>a</sup>	6.2 (50.6)	5.9 (52.6)	5.3 (38.8)	5.9 (48.6)	5.5 (42.1)	4.8 (43.2)	5.5 (52.7)	8.0 (42.5)
<i>I</i> / $\sigma$ <sup>a</sup>	32.7 (5.0)	32 (4.7)	35.1 (3.2)	30.3 (3.4)	30.9 (3.1)	31.0 (3.6)	32.2 (1.8)	17.9 (3.0)
Reflections	33714	51912	56257	46148	42981	74675	40597	38975
Completeness (%) <sup>a</sup>	100 (100)	99.9 (100)	99.1 (91.8)	99.1 (99.7)	99.1 (96.2)	98.7 (96.7)	95.0 (88.1)	99.9 (99.8)
Redundancy <sup>a</sup>	10.4 (10.5)	10.5 (11.0)	10.2 (5.9)	7.5 (6.0)	7.4 (5.1)	7.4 (5.6)	6.0 (3.3)	6.3 (3.5)
<b>Refinement<sup>b</sup></b>								
No. of reflections	31974	49196	53363	43630	40788	70869	38561	36983
No. of atoms	2248	2303	2362	2324	2262	2521	2296	2197
Protein atoms	1939	1957	1957	1974	1917	2061	1935	1924
Ligand atoms <sup>c</sup>	99	99	81	80	99	103	97	98
Metals and other atoms <sup>d</sup>	0	0	0	0	6	10	27	25
Water	210	247	324	270	240	347	237	150
<i>R</i> <sub>work</sub> / <i>R</i> <sub>free</sub> <sup>e</sup>	19.3 / 22.4	19.8 / 21.9	19.1 / 21.7	19.4 / 22.1	19.6 / 22.1	17.5 / 19.8	18.7 / 20.6	19.6 / 21.0
Average B-factors (Å <sup>2</sup> )								
Overall	32.59	26.34	25.63	26.55	30.45	21.18	27.06	30.20
Protein	31.23	24.80	25.59	24.85	28.88	18.90	25.09	28.87
Ligands <sup>c</sup>	43.81	36.87	30.75	33.51	37.82	23.64	33.64	35.81
Metals/other <sup>d</sup>	-	-	-	-	69.30	35.92	46.30	57.30
Waters	38.81	34.35	36.61	36.92	38.97	33.61	38.19	39.09
Root mean square deviation								
Bond length (Å)	0.015	0.014	0.012	0.014	0.016	0.010	0.016	0.011
Bond Angles (°)	1.474	1.505	1.391	1.514	1.613	1.393	1.522	1.342
MolProbity Score	1.84	1.78	1.55	1.61	1.45	1.36	1.66	1.55
Percentile	78 <sup>th</sup>	68 <sup>th</sup>	85 <sup>th</sup>	84 <sup>th</sup>	93 <sup>rd</sup>	91 <sup>st</sup>	82 <sup>nd</sup>	91 <sup>st</sup>
Resolution range (Å)	1.85 ± 0.25	1.60 ± 0.25	1.55 ± 0.25	1.65 ± 0.25	1.70 ± 0.25	1.40 ± 0.25	1.70 ± 0.25	1.75 ± 0.25
Ramachandran								
Favored (%)	95.58	95.97	95.92	96.31	95.95	97.65	95.55	95.97
Allowed (%)	4.42	4.03	4.08	3.69	4.05	2.35	4.45	4.03
Outliers (%)	0	0	0	0	0	0	0	0

<sup>a</sup> Values in parentheses correspond to the highest-resolution shell. <sup>b</sup> 3M58 was refined using anisotropic temperature-factor refinement; all other structures were refined using isotropic temperature-factor refinement. <sup>c</sup> Ligand atoms include the TAF10 peptide and AdoHcy. <sup>d</sup> Other atoms include glycerol, sulfate ions, or Co atoms in the solvent region. <sup>e</sup>  $R_{work} = \sum ||F_o| - |F_c|| / \sum |F_o|$ ;  $R_{free} = 5\%$  of the total reflections.