

## Supplementary material:

**Table 1:** Docking interactions of amino acid residues of MAPT and CDK5 with interatomic distances.

MAPT	CDK5	RMS (Å)
GLN6 O	ARG217 H	2.38
GLY9 H	GLN273 H	2.22
ARG15 H	GLN282 O	2.42
ARG56 H	ARG156 H	2.64
ALA66 O	SER276 H	2.10
LYS209 H	GLU224 OE2	1.67
THR205 H	PRO228 O	1.36

**Table 2:** Docking interactions of amino acid residues of MAPT and GSK3B with interatomic distances.

MAPT	GSK3B	RMS (Å)
GLY76 H	GLU279 OE2	2.40
THR95 OEG1	GLN273 H	2.63

**Table 3:** Phosphorylation of MAPT with CDK5

Site	Residue	Sequence	Modification state	Kinase type	Score
53	T	IGDTPSL	modified	CDK5	1.0
97	T	KIATPRG	modified	CDK5	1.0
117	T	PAKTPPA	modified	CDK5	1.0
144	S	SPGSPGT	modified	CDK5	1.0
150	S	TPGSRSR	modified	CDK5	1.0
154	T	RSRTPSL	modified	CDK5	1.0
173	T	VVRTPPK	modified	CDK5	1.0
177	S	PPKSPSS	modified	CDK5	1.0
315	S	GDTSPRH	modified	CDK5	1.0
333	S	MVDSPQL	modified	CDK5	1.0
123	T	APKTPPS	modified	CDK5	0.71
147	T	SPGTPGS	modified	CDK5	0.67
288	T	HKLTFRE	modified	CDK5	0.6
159	T	SLPTPPI	modified	CDK5	0.57

**Table 4:** Phosphorylation of MAPT with GSK3B

Site	Residue	Sequence	Modification state	Kinase type	Score
53	T	IGDTPSL	modified	GSK3B	0.78
117	T	PAKTPPA	modified	GSK3B	0.75
95	T	KIATPRG	modified	GSK3B	0.64
315	S	GDTSPRH	modified	GSK3B	0.64
307	S	VYKSPVV	modified	GSK3B	0.56

**Table 5:** ATP interacting residues of CDK5 and GSK3B kinases

Protein kinase	ATP interacting residues
CDK5	2, 3, 6,7, 8, 29, 34, 35, 39, 40, 42, 43, 45, 47, 48, 51, 53, 54, 55, 57, 62, 64, 65, 70, 74, 78, 79, 81, 82, 83, 84, 86, 93, 103, 106, 107, 108, 109, 110, 111, 112, 123, 125, 126, 127, 128, 129, 131, 132, 136, 137, 138, 140, 149, 151, 154, 156, 157, 158, 159, 160, 161, 162, 165, 167, 168, 171, 173, 175, 176.
GSK3B	1, 2, 3,4, 13, 14, 17, 20, 22, 24, 26, 27, 36, 38, 41, 42, 54, 57, 58, 63, 64, 66, 67, 68, 69, 70, 71, 72, 74, 78, 81, 84, 87, 88, 93, 99, 102, 104, 105, 107, 108, 110, 111, 112, 120, 124, 125, 126, 127, 128, 129, 131, 132, 135, 139, 140, 141, 142, 143, 145, 146, 148, 151, 158, 163, 164, 167, 173, 179, 181, 184, 187, 195, 196, 197, 200, 201, 202, 209, 211, 213, 214, 220, 223, 225, 226, 229,231, 232, 233, 235, 236, 241, 246, 248, 253, 259, 261, 264, 269, 270.

**Table 6:** List of amino acid residues in CDK5 and GSK3B which are acting as stabilization centers with MAPT. The stabilization residues also acting as ATP interacting residues are shown in bold.

Protein kinase	Stabilization centers in complex with MAPT
CDK5	4, 5, 6, 13, 14, 17, 18, 19, 26, 27, 28, 29, 30, 31, 32, 47, 50, 56, 58, 59, 61, 62, 63, <b>71,72, 75</b> , 76, 80, 81, 82, 83, 103, 109, 110, 112, 118, 119, <b>120</b> , 121, 128, 129, 130, 137, 138, 142, 143, 144, 145, 146, 166, 169, 171, 179, 181, <b>185</b> , 192, 200, 208, 210, 211, 230, 248, 249, <b>251</b> , 252, 259, 262, <b>282</b> , 286
GSK3B	40,41, <b>42</b> , 43, 44, 52, <b>53</b> , 56, 57, 58, 59, 60, <b>61, 71, 72</b> , 73, <b>74, 75</b> , 82, 83, 84, 85, 86, 87, 88, 89, 103, 104, 106, 108, 109, 111, 112, 113, 114, 115, 116, 117, <b>127</b> , 128, 129, <b>130</b> , 131, 132, 133, 136, 137, 138, 139, 159, 163, 168, 169, 171, 175, 178, 179, 180, 187, <b>188</b> , 189, 190, 193, 197, 198, 203, 204, 205, 214, 225, 232, 240, 258, 266, 268, 283, 324, 333, 342

**Table 7:** List of amino acids acting as stabilizing residues in CDK5 and GSK3B kinases. The stabilizing residues involves in ATP interaction are shown in bold.

Protein kinase	Stabilization residues
CDK5	ALA31, PHE80, ASP86, GLY113, LYS141, LEU142
GSK3B	LYS85, LYS86, LEU130, VAL131, LEU132, LYS197

**Table 8:** The summary of results from the various *insilico* methods

Methods	MAPT and CDK5	MAPT and GSK3B
Protein-Protein docking and interacting residues	7	2
Predicted no. of phosphorylation sites	14	5
Predicated no. of ATP binding sites	70	112
Predicated no. of stabilization centers	69	80
Predicated no. of stabilization residues	6	6