



Figure S1. Illustration of GSK3B mediated phosphorylation. Frat2 can significantly increase GSK3B mediated phosphorylation of Tau by binding to GSK3B. GSK3B: kinases; Tau: substrate; Frat2: kinase binding protein.

Table S1. Numbers of positive and negative data of different kinases in four hierarchical levels

Kinase name	Positive number	Negative number
Kinase level		
CDC2	122	1649
PKCa	110	1608
Ck2alpha	91	1619
Erk2(MAPK1)	82	1700
Erk1(MAPK3)	77	1705
ATM	58	1765
CDK2	53	1720
GSK3B	44	1766
p38a(MAPK14)	44	1741
PLK1	39	1784
CaMK2a	27	1777
BARK1	27	1772
PDK1	24	1799
AurA	22	1801
MAPKAPK2	20	1803
SRC	88	377
LCK	43	419
SYK	35	431
EGFR	34	432
ABL1(Abl)	32	434
FYN	25	438
LYN	27	435
INSR	27	439
Subfamily level		
CDC2	173	1602
ERK1	118	1659
Alpha	116	1597
ATM	58	1758

p38	52	1730
PLK1	39	1777
BARK	30	1765
MAPKAPK	21	1795
SrcA	88	378
SrcB	64	402
Family level		
PKC	248	1575
CDK	243	1580
MAPK	230	1593
CK2	204	1619
PIKK	88	1735
GRK	63	1760
GSK	58	1765
CAMK2	46	1777
PLK	40	1783
Aur	39	1784
PDK1	24	1799
MAPKAPK	22	1801
Src	173	293
Syk	46	420
EGFR	39	427
INSR	37	429
Abl	33	433
Group level		
CMGC	719	1104
AGC	660	1163
CAMK	164	1659
Other	158	1665
Atypical	95	1728
TK	452	14

Table S3. Performance comparison with iGPS and NetworKIN at kinase level.

Kinase	iGPS		NetworKIN		Proposed			
					Medium (Sp>90%)		High (Sp>99%)	
	<i>Sn</i> (%)	<i>Sp</i> (%)	<i>Sn</i> (%)	<i>Sp</i> (%)	<i>Sn</i> (%)	<i>Sp</i> (%)	<i>Sn</i> (%)	<i>Sp</i> (%)
Ck2a1	0	100	93.41	92.28	94.51	94.75	79.12	99.26
CDC2	58.20	95.33	0.81	99.82	87.70	95.39	33.61	99.82
PKCA	29.09	95.83	50.00	93.97	73.64	96.21	57.27	99.07
MAPK1	58.54	92.06	1.22	99.59	71.95	95.94	25.61	99.71
MAPK3	53.25	92.73	2.60	99.65	68.83	95.01	20.78	99.71
ATM	94.83	98.98	96.55	96.83	98.28	96.94	84.48	99.15
CDK2	64.15	91.74	98.11	76.63	98.11	90.64	77.36	99.07
GSK3B	27.27	98.75	29.55	95.53	81.82	95.98	54.55	99.26
MAPK14	61.36	90.41	25.00	93.34	84.09	98.10	65.91	99.20
PLK1	97.44	97.59	0	99.78	76.92	98.21	17.95	99.83
PDK1	75.00	98.72	37.50	99.89	95.83	99.11	83.33	99.94
BARK1	55.56	99.21	-	-	77.78	98.65	62.96	99.27
CAMK2A	0	100	22.22	99.16	62.96	95.55	40.74	99.38
SRC	35.23	73.21	5.68	97.35	45.45	97.35	21.45	99.20
LCK	46.51	79.24	2.33	96.66	60.47	96.90	20.93	99.05
SYK	94.29	85.85	5.71	100	82.86	98.84	17.14	100
EGFR	76.47	81.71	14.71	98.15	79.41	96.99	41.18	99.31
FYN	56.00	71.00	8.00	97.03	72.00	97.26	60.00	99.09
ABII	56.25	89.86	9.37	96.31	68.75	98.85	59.38	99.31
LYN	55.56	71.26	3.70	96.78	81.48	95.17	62.96	99.31
INSR	88.89	86.33	66.67	32.35	96.30	98.18	74.07	99.09

-: not available

Table S4. Performance comparison with IGPS at subfamily, family and group hierarchical levels.

kinase	IGPS		Proposed	
	Sn(%)	Sp(%)	Sn(%)	Sp(%)
Subfamily:				
Alpha	-	-	56.03	99.06
ATM	-	-	86.21	99.32
BARK	-	-	83.33	99.43
CDC2	-	-	63.01	99.06
ERK1	-	-	53.39	99.04
MAPKAPK	-	-	47.62	99.28
P38	-	-	48.08	99.13
PLK1	-	-	64.10	99.04
SrcA	-	-	18.18	99.21
SrcB	-	-	32.81	99.00
Family:				
GRK	63.49	99.66	76.19	99.72
PDK1	100.0	0.00	95.83	99.61
PIKK	96.59	94.76	97.73	96.71
CAMK2	30.43	95.78	47.83	99.04
PKC	30.24	95.56	48.79	99.05
MAPKAPK	68.18	97.67	72.73	97.72
CDK	62.14	93.42	63.79	98.92
CK2	57.35	98.09	77.94	99.01
GSK	60.35	94.16	67.24	97.22
MAPK	58.26	91.78	60.43	98.18
Aur	100.0	0.00	76.92	99.33
PLK*	97.50	97.36	75.00	98.82
Abl	57.58	90.07	66.67	99.08
EGFR	76.92	74.01	87.18	97.42
InsR	86.49	87.88	89.19	98.37
Src	48.56	80.55	50.29	93.17
Syk	91.30	87.62	80.43	95.71
Group:				
AGC	57.42	91.83	59.24	96.73
Atypical	92.63	94.04	93.68	96.64
Other*	87.34	83.96	74.05	90.03
CMGC	49.10	95.02	58.28	99.00
TK	-	-	64.82	92.86
CAMK	-	-	33.54	99.04

-: not available

Table S5. Enrichment analysis of proteins associated with selected PPIs for kinase GSK3B.

Category	Term	PValue	Benjamini	FDR
GOTERM_BP_FAT	GO:0005977~glycogen metabolic process	1.17E-05	0.008024	0.01755
GOTERM_BP_FAT	GO:0006073~cellular glucan metabolic process	1.31E-05	0.004508	0.019685
GOTERM_BP_FAT	GO:0044042~glucan metabolic process	1.31E-05	0.004508	0.019685
GOTERM_BP_FAT	GO:0006112~energy reserve metabolic process	2.68E-05	0.00616	0.040375
INTERPRO	IPR003659:Plexin/semaphorin/integrin	2.96E-05	0.002825	0.036848
GOTERM_BP_FAT	GO:0044264~cellular polysaccharide metabolic process	6.18E-05	0.010613	0.092936
GOTERM_BP_FAT	GO:0005976~polysaccharide metabolic process	8.52E-05	0.011712	0.128256
SP_PIR_KEYWORDS	glycogen biosynthesis	2.95E-04	0.023878	0.35675
PIR_SUPERFAMILY	PIRSF001238:cyclic amidohydrolases (dihydroorotase, allantoinase)	3.81E-04	0.015862	0.351714
GOTERM_BP_FAT	GO:0006006~glucose metabolic process	3.82E-04	0.043084	0.574033
GOTERM_BP_FAT	GO:0009250~glucan biosynthetic process	8.72E-04	0.064779	1.304604
GOTERM_BP_FAT	GO:0005978~glycogen biosynthetic process	8.72E-04	0.064779	1.304604
GOTERM_BP_FAT	GO:0019318~hexose metabolic process	0.00107	0.065037	1.598703
GOTERM_BP_FAT	GO:0042254~ribosome biogenesis	0.001506	0.083112	2.242956
GOTERM_BP_FAT	GO:0005996~monosaccharide metabolic process	0.002031	0.102448	3.014839
GOTERM_BP_FAT	GO:0015980~energy derivation by oxidation of organic compounds	0.002757	0.119436	4.071431
KEGG_PATHWAY	hsa04360:Axon guidance	0.002833	0.151706	2.782874
GOTERM_BP_FAT	GO:0033692~cellular polysaccharide biosynthetic process	0.004955	0.19307	7.205018
GOTERM_BP_FAT	GO:0022613~ribonucleoprotein complex biogenesis	0.006097	0.220088	8.795399
GOTERM_MF_FAT	GO:0008466~glycogenin glucosyltransferase activity	0.007688	0.809723	9.323882
GOTERM_BP_FAT	GO:0019853~L-ascorbic acid biosynthetic process	0.008115	0.256462	11.54413
GOTERM_BP_FAT	GO:0006091~generation of precursor metabolites and energy	0.008683	0.260157	12.30395
GOTERM_BP_FAT	GO:0016051~carbohydrate biosynthetic process	0.009368	0.266347	13.21199
PIR_SUPERFAMILY	PIRSF000465:glycogenin (glycosyl transferase)	0.01025	0.194557	9.094911
GOTERM_BP_FAT	GO:0000271~polysaccharide biosynthetic process	0.014368	0.36527	19.57701
UP_SEQ_FEATURE	glycosylation site:O-linked (Glc...)	0.018954	0.615871	22.56322
GOTERM_MF_FAT	GO:0035251~UDP-glucosyltransferase activity	0.030406	0.963822	32.40224
UP_SEQ_FEATURE	nucleotide phosphate-binding region:NADP	0.030968	0.740287	34.31944
INTERPRO	IPR002495:Glycosyl transferase, family 8	0.031265	0.490389	32.64065
GOTERM_CC_FAT	GO:0005730~nucleolus	0.03186	0.978786	31.00416
GOTERM_BP_FAT	GO:0034637~cellular carbohydrate biosynthetic process	0.032006	0.608037	38.7202
GOTERM_MF_FAT	GO:0046527~glucosyltransferase activity	0.034142	0.917055	35.63253
SP_PIR_KEYWORDS	glycoprotein	0.04676	0.674358	44.04851