

Additional File 3 Top 20 predicted interacting protein pairs (from PU4 and PU0) not present in existing experimental data sets (KNOWN2).

Top 1	Protein A	Protein B
	STK6_HUMAN	PLK1_HUMAN
Molecular function GO term	GO:0004672;protein kinase activity; GO:0005515;protein binding	GO:0004674;protein serine/threonine kinase activity; GO:0005515;protein binding
Biological process GO term	GO:0006468;protein amino acid phosphorylation; GO:0007049;cell cycle; GO:0007051;spindle organization and biogenesis; GO:0007067;mitosis; GO:0031647;regulation of protein stability; GO:0048015;phosphoinositide-mediated signaling	GO:0000074;regulation of progression through cell cycle; GO:0007067;mitosis; GO:0008283;cell proliferation
UniProt functional keyword matching	3D-structure ATP-binding Kinase Nucleotide-binding Phosphorylation Serine/threonine-protein kinase Transferase	
Cell-cycle stage	G2/M	
OMIM ID	602687	602098

Top 2	Protein A	Protein B
	ORC1_HUMAN	MCM4_HUMAN
Molecular function GO term	GO:0003677;DNA binding; GO:0005515;protein binding	GO:0005515;protein binding; GO:0005524;ATP binding
Biological process GO term	GO:0006270;DNA replication initiation	GO:0006260;DNA replication
UniProt functional keyword matching	ATP-binding; DNA replication; DNA-binding; Nuclear protein; Nucleotide-binding; Polymorphism	
Cell-cycle stage	G1/S	
OMIM ID	601902	602638

Top 3	Protein A	Protein B
	MCM6_HUMAN	MCM5_HUMAN
Molecular function GO term	GO:0005524;ATP binding; GO:0042802;identical protein binding	GO:0005515;protein binding
Biological process GO term	O:0006260;DNA replication	GO:0000074;regulation of progression through cell cycle; GO:0006260;DNA replication
UniProt functional keyword matching	ATP-binding; DNA replication; DNA-binding; Nuclear protein; Nucleotide-binding; Polymorphism; Transcription; Transcription regulation	
Cell-cycle stage	G1/S	
OMIM ID	601806	602696

Top 4	Protein A	Protein B
	MCM4_HUMAN	MCM5_HUMAN
Molecular function GO term	GO:0005515;protein binding; GO:0005524;ATP binding	GO:0005515;protein binding
Biological process GO term	GO:0006260;DNA replication	GO:0000074;regulation of progression through cell cycle; GO:0006260;DNA replication
UniProt functional keyword matching	ATP-binding; DNA replication; DNA-binding; Nuclear protein; Nucleotide-binding; Polymorphism; Transcription; Transcription regulation	
Cell-cycle stage	G1/S	
OMIM ID	602638	602696

Top 5	Protein A	Protein B
	ORC1_HUMAN	MCM6_HUMAN
Molecular function GO term	GO:0003677;DNA binding; GO:0005515;protein binding	GO:0005524;ATP binding; GO:0042802;identical protein binding
Biological process GO term	GO:0006270;DNA replication initiation	GO:0006260;DNA replication
UniProt functional keyword matching	ATP-binding; DNA replication; DNA-binding; Nuclear protein; Nucleotide-binding; Polymorphism	
Cell-cycle stage	G1/S	
OMIM ID	601902	601806

Top 6	Protein A	Protein B
	PRI1_HUMAN	RFC4_HUMAN
Molecular function GO term	GO:0003896;DNA primase activity	GO:0005515;protein binding
Biological process GO term	GO:0006269;DNA replication, synthesis of RNA primer	GO:0006260;DNA replication; GO:0006271;DNA strand elongation; GO:0006281;DNA repair; GO:0048015;phosphoinositide-mediated signaling
UniProt functional keyword matching	DNA replication; Polymorphism	
Cell-cycle stage	S	
OMIM ID	176635	102577

Top 7	Protein A	Protein B
	CDC7_HUMAN	PRI1_HUMAN
Molecular function GO term	GO:0004674;protein serine/threonine kinase activity; GO:0005515;protein binding	GO:0003896;DNA primase activity
Biological process GO term	GO:0000082;G1/S transition of mitotic cell cycle; GO:0006270;DNA replication initiation; GO:0007089;traversing start control point of mitotic c...; GO:0008285;negative regulation of cell proliferation	GO:0006269;DNA replication, synthesis of RNA primer
UniProt functional keyword matching	Polymorphism; Transferase	
Cell-cycle stage	S	
OMIM ID	603311	603078

Top 8	Protein A	Protein B
	RFC2_HUMAN	PRI1_HUMAN
Molecular function GO term	GO:0005515;protein binding; GO:0005524;ATP binding	GO:0003896;DNA primase activity
Biological process GO term		GO:0006269;DNA replication, synthesis of RNA primer
UniProt functional keyword matching	DNA replication; Polymorphism	
Cell-cycle stage	S	
OMIM ID	600404	176635

Top 9	Protein A	Protein B
	SMC4_HUMAN	KINH_HUMAN
Molecular function GO term	GO:0005524;ATP binding; GO:0046982;protein heterodimerization activity	GO:0003777;microtubule motor activity
Biological process GO term	GO:0007001;chromosome organization and biogenesis; GO:0007076;mitotic chromosome condensation	GO:0007018;microtubule-based movement
UniProt functional keyword matching	ATP-binding; Coiled coil; Nucleotide-binding	
Cell-cycle stage	G2	
OMIM ID	601902	601806

Top 10	Protein A	Protein B
	H2BQ_HUMAN	TOP1_HUMAN
Molecular function GO term	GO:0003677;DNA binding	GO:0003917;DNA topoisomerase type I activity
Biological process GO term	GO:0006334;nucleosome assembly	
UniProt functional keyword matching	DNA-binding	
Cell-cycle stage	M/G1	
OMIM ID	601831	126420

Top 11	Protein A	Protein B
	IMB1_HUMAN	H2BQ_HUMAN
Molecular function GO term	GO:0005515;protein binding; GO:0008139;nuclear localization sequence binding; GO:0008270;zinc ion binding	GO:0003677;DNA binding
Biological process GO term	GO:0000060;protein import into nucleus, translocation; GO:0006607;NLS-bearing substrate import into nucleus	GO:0006334;nucleosome assembly
UniProt functional keyword matching	Nuclear protein	
Cell-cycle stage	M/G1	
OMIM ID	602738	601831

Top 12	Protein A	Protein B
	PRI2_HUMAN	RFC4_HUMAN
Molecular function GO term	GO:0003896;DNA primase activity	GO:0005515;protein binding
Biological process GO term	GO:0006269;DNA replication, synthesis of RNA primer	GO:0006260;DNA replication; GO:0006271;DNA strand elongation; GO:0006281;DNA repair; GO:0048015;phosphoinositide-mediated signaling
UniProt functional keyword matching	DNA replication	
Cell-cycle stage	S	
OMIM ID	176636	102577

Top 13	Protein A	Protein B
	PRI2_HUMAN	RFC2_HUMAN
Molecular function GO term	GO:0003896;DNA primase activity	GO:0005515;protein binding; GO:0005524;ATP binding
Biological process GO term	GO:0006269;DNA replication, synthesis of RNA primer	
UniProt functional keyword matching	Alternative splicing; DNA replication	
Cell-cycle stage	S	
OMIM ID	176636	600404

Top 14	Protein A	Protein B
	PRI1_HUMAN	RFA2_HUMAN
Molecular function GO term	GO:0003896;DNA primase activity	GO:0003697;single-stranded DNA binding; GO:0005515;protein binding
Biological process GO term	GO:0006269;DNA replication, synthesis of RNA primer	GO:0006261;DNA-dependent DNA replication
UniProt functional keyword matching	DNA replication; Polymorphism	
Cell-cycle stage	S	
OMIM ID	176635	179836

Top 15	Protein A	Protein B
	HMGB2_HUMAN	H2AX_HUMAN
Molecular function GO term	GO:0003690;double-stranded DNA binding; GO:0003697;single-stranded DNA binding; GO:0003700;transcription factor activity; GO:0008301;DNA bending activity	GO:0003677;DNA binding; GO:0005515;protein binding
Biological process GO term	GO:0006260;DNA replication; GO:0006268;DNA unwinding during replication; GO:0006281;DNA repair; GO:0006288;base-excision repair, DNA ligation; GO:0006325;establishment and/or maintenance of chromat...; GO:0006334;nucleosome assembly; GO:0006357;regulation of transcription from RNA polyme...; GO:0048015;phosphoinositide-mediated signaling	GO:0007001;chromosome organization and biogenesis; GO:0006334;nucleosome assembly
UniProt functional keyword matching		
Cell-cycle stage	G2	
OMIM ID	163906	

Top 16	Protein A	Protein B
	H2AX_HUMAN	CHK2_HUMAN
Molecular function GO term	GO:0003677;DNA binding; GO:0005515;protein binding	GO:0005515;protein binding; GO:0004674;protein serine/threonine kinase activity
Biological process GO term	GO:0007001;chromosome organization and biogenesis; GO:0006334;nucleosome assembly	GO:0000077;DNA damage checkpoint; GO:0006974;response to DNA damage stimulus
UniProt functional keyword matching		
Cell-cycle stage	G2	
OMIM ID		604373

Top 17	Protein A	Protein B
	IMDH1_HUMAN	ERBB3_HUMAN
Molecular function GO term	GO:0003938;IMP dehydrogenase activity	GO:0005006;epidermal growth factor receptor activity; GO:0005515;protein binding; GO:0046982;protein heterodimerization activity
Biological process GO term		GO:0006468;protein amino acid phosphorylation; GO:0007165;signal transduction
UniProt functional keyword matching	3D-structure; Alternative splicing	
Cell-cycle stage		
OMIM ID	146690	190151

Top 18	Protein A	Protein B
	RASH_HUMAN	ERBB3_HUMAN
Molecular function GO term	GO:0008022;protein C-terminus binding	GO:0005006;epidermal growth factor receptor activity; GO:0005515;protein binding; GO:0046982;protein heterodimerization activity
Biological process GO term	GO:0000074;regulation of progression through cell cycle; GO:0006935;chemotaxis; GO:0007166;cell surface receptor linked signal transduction; GO:0009887;organ morphogenesis	GO:0006468;protein amino acid phosphorylation; GO:0007165;signal transduction
UniProt functional keyword matching	3D-structure; Membrane; Nucleotide-binding	
Cell-cycle stage		
OMIM ID	190020	190151

Top 19	Protein A	Protein B
	FRK_HUMAN	TEC_HUMAN
Molecular function GO term	GO:0004715;non-membrane spanning protein tyrosine kinase activity	GO:0004715;non-membrane spanning protein tyrosine kinase activity
Biological process GO term	GO:0000074;regulation of progression through cell cycle; GO:0006468;protein amino acid phosphorylation; GO:0008285;negative regulation of cell proliferation	GO:0006468;protein amino acid phosphorylation; GO:0007243;protein kinase cascade
UniProt functional keyword matching	ATP-binding; Kinase; Nucleotide-binding; Phosphorylation; SH2 domain; SH3 domain; Transferase; Tyrosine-protein kinase	
Cell-cycle stage		
OMIM ID	606573	600583

Top 20	Protein A	Protein B
	RHOC_HUMAN	ERBB3_HUMAN
Molecular function GO term	GO:0003924;GTPase activity; GO:0004871;signal transducer activity	GO:0005006;epidermal growth factor receptor activity; GO:0005515;protein binding; GO:0046982;protein heterodimerization activity
Biological process GO term	GO:0043123;positive regulation of I-kappaB kinase/NF-kappaB cascade	GO:0006468;protein amino acid phosphorylation; GO:0007165;signal transduction
UniProt functional keyword matching	3D-structure; Membrane; Nucleotide-binding	
Cell-cycle stage		
OMIM ID	165380	190151