

Cdc37 interacting proteins

(other than Hsp90)

Clients	Interaction	Reference	Evidence
AKT (Protein Kinase B)	Biochemical	Basso et al. (2002) J. Biol. Chem. 277: 39858	Endogenous Akt IPs with Hsp90 and Cdc37. Cdc37 can bind Akt directly, not affected by Hsp90 inhibitors.
Androgen receptor	Genetic	Fliss et al. (1997) Mol. Biol. Cell 8: 2501	Yeast <i>cdc37-34</i> has decreased activation of heterologous AR
	Biochemical	Rao et al.(2001) J. Biol. Chem. 276: 5814	Human Cdc37 binds to ligand-binding domain of AR in vitro, partially Hsp90-dependent. N-terminal domain (1-173) is dominant negative
Aurora B	Genetic & Biochemical	Lange et al. (2002) EMBO J. 21: 5364	Mammalian & Drosophila Cdc37, inactivation of Hsp90 or Cdc37 reduces Aurora B levels, Aurora B or Cdc37 RNAi phenotypes are almost indistinguishable. Co-IP
B-Raf	Biochemical	Vaughan et al. (2006) Mol. Cell 23: 697; Grbovic et al. (2006) Proc. Natl. Acad. Sci. USA 103, 57	Co-IP
Cak1	Genetic	Mort-Bontemps-Soret et al. (2002) Mol. Genet. Genomics 267: 447	Synthetic lethal screen
	Genetic	Farrell & Morgan (2000) Mol. Cell. Biol. 20: 749	Yeast <i>cdc37-1</i> has reduced Cak1 level and activity. Cdc37 stabilises Cak1 after translation
Cdc2	Genetic & Biochemical	Turnbull et al. (2006) J. Cell Sci. 119: 292	S. pombe Cdc2 fails to associate with cyclin in <i>cdc37</i> mutant strain; genetic interactions and co-IP.
	Biochemical	García-Morales et al. (2007) Oncogene 26: 7185	Mammalian co-IP
Cdc5	Genetic	Mort-Bontemps-Soret et al. (2002) Mol. Genet. Genomics 267: 447	Synthetic lethal screen
Cdc7	Genetic	Mort-Bontemps-Soret et al. (2002) Mol. Genet. Genomics 267: 447	Synthetic lethal screen
Cdc15	Genetic	S. cerevisiae: Mort-Bontemps-Soret et al. (2002) Mol. Genet. Genomics 267: 447 / S. pombe (=Cdc7) Liang and Fantes (2007) Euk. Cell 6: 1089	Synthetic lethal screen (and kinase assay in S. pombe)
Cdc25c	Biochemical	García-Morales et al. (2007) Oncogene 26: 7185	Co-IP in mammalian cells
Cdc28	Genetic	Gerber et al. (1995) Proc. Natl. Acad. Sci. USA 92: 4651	Yeast <i>cdc37-1</i> mutant affects Cdc28/cyclin complex formation and function
	Genetic	Farrell & Morgan (2000) Mol. Cell. Biol. 20: 749	Yeast Cdc37 stabilises Cdc28 after translation
	Genetic & Biochemical	Mort-Bontemps-Soret et al. (2002) Mol. Genet. Genomics 267: 447	Yeast CDC37 is a multi-copy suppressor of <i>cdc28</i> . yeast two-hybrid interaction between Cdc37 C-terminus and Cdc28 N-terminus
Cdk2	Biochemical	Prince et a. (2005) Biochem. 44: 15287	pull-down assays
Cdk4	Biochemical	Dai et al. (1996) J. Biol. Chem. 271: 22030	Immunoprecipitation with mammalian Cdc37 and Hsp90
	Biochemical	Stepanova et al. (1996) Genes & Dev. 10: 1491	Mammalian co-IP (preferentially without cyclin) with Hsp90
	Biochemical	Stepanova et al. (2000) Mol. Cell. Biol. 20: 4462	CDC37 transgenic mice develop mammary tumours, i.e. can function as an oncogene. Can co-operate with Cyclin D1 or with c-myc in transformation of tissue. See also Schwarze et al. (2003) Cancer Res. 63: 4614.
	Biochemical	Lamphere et al. (1997) Oncogene 14: 1999	Yeast 2-hybrid with human Cdc37. GST-Cdc37 co-IP
Cdk6	Biochemical	Lamphere et al. (1997) Oncogene 14: 1999	GST-Cdc37 co-IP
Cdk9	Biochemical	O'Keeffe et al. (2000) J. Biol. Chem. 275: 279	co-IP with Cdk9 before assembly with cyclin T1
Cdk11	Biochemical	Mikolajczyk and Nelson (2004) Biochem. J. 384: 461	co-IP
CKII (casein kinase II)	Genetic	McCann & Glover (1995) Mol. Biol. Cell (Supp.) 6: 133a	Multi-copy suppressor
	Biochemical	Kimura et al. (1997) Genes & Dev. 11: 1775	in vitro chaperone assay with yeast Cdc37
	Genetic	Bandhakavi et al. (2003) J. Biol. Chem. 278:2829	Cdc37 required for CKII function and CKII for Cdc37 phosphorylation
Crk1	Genetic & Biochemical	Ni et al. (2004) FEBS Lett. 561: 233	Candida Crk1; 2-hybrid, co-IP, and genetic evidence.
DAPK	Biochemical	Citri et al. (2006) J. Biol. Chem. 281: 14361	co-IP
EGF receptor mutant	Biochemical	Lavitoire et al. (2003) J. Biol. Chem. 278: 5292	co-IP
Fused	Biochemical	Kise et al. (2006) Biochem. Biophys. Res. Com. 351: 78	co-IP
β-Galactosidase	Biochemical	Kimura et al. (1997) Genes & Dev. 11: 1775	in vitro chaperone assay with yeast Cdc37
Gcn2	Genetic	Donzé & Picard (1999) Mol. Cell. Biol. 19: 8422	<i>cdc37</i> mutant yeast strain grows poorly upon amino acid starvation
Glucocorticoid receptor	Genetic	Fliss et al. (1997) Mol. Biol. Cell 8: 2501	Yeast <i>cdc37-34</i> has slightly decreased activation of heterologous GR at non-permissive temperature.
Harc	Biochemical	Roiniotis et al. (2005) Biochem. 44: 6662	Harc and Cdc37 form both homodimers and heterodimers
Hog1	Genetic & Biochemical	Hawle et al. (2007) Eukaryot. Cell 6: 521	Hog1 function affected by Cdc37 phosphorylation mutant in yeast; co-IP
Hck (src family kinase)	Genetic & Biochemical	Scholz et al. (2000) Mol. Cell. Biol. 20: 6984	Human Cdc37 overexpression partially suppresses tsHck499F phenotype, co-IP, Hck kinase domain necessary for binding
HRI	Biochemical	Hartson et al. (2000) Biochem. 39: 7631	Human Cdc37 co-IP, maturation intermediates of HRI recruit Cdc37 to Hsp90 heterocomplex
	Biochemical	Shao et al. (2001) J. Biol. Chem. 276: 206	Human Cdc37 associates with nascent HRI co-translationally and persists during maturation and activation, specifically with immature or inactive forms and not with active or repressed forms
IKK (IκB kinase)	Biochemical	Chen et al. (2002) Mol. Cell 9: 401; Bouwmeester et al. (2004) Nat. Cell Biol. 6:97	Human Cdc37 co-IP, in vitro pull downs, direct binding through the kinase domain. Geldanamycin disrupts complex formation and recruitment to receptor.
IRAK-1	Biochemical	De Nardo et al. (2005) J. Biol. Chem. 280: 9813	co-IP
JAK1	Biochemical	Shang and Tomasi (2006) J. Biol. Chem. 281: 1876	co-IP
Kin28	Genetic	Valay et al. (1995) J. Mol. Biol. 249: 535	Synthetic lethal
Ksr	Biochemical	Sundaram et al. (1999) Mol. Cell. Biol. 19: 5523	part of a larger chaperone complex
Lck (src family kinase)	Biochemical	Hartson et al. (2000) Biochem. 39: 7631	Co-IP with human Cdc37
Lkb1	Biochemical	Boudeau et al. (2003) Biochem. J. 370: 849; Nony et al. (2003) Oncogene 22: 9165	Co-IP
LRRK2	Biochemical	Gloeckner et al. (2006) Hum. Mol. Genet. 15: 223; Wang et al. (2008) J. Neurosci. 28: 3384.	co-IP
Luciferase (firefly)	Biochemical	Kimura et al. (1997) Genes & Dev. 11: 1775	in vitro chaperone assay with yeast Cdc37
MEKK1/MEKK3	Biochemical	Bouwmeester et al. (2004) Nat. Cell Biol. 6:97	TAP purification
MLK3	Biochemical	Zhang et al. (2004) J. Biol. Chem. 279: 19457	co-IP
MPS1	Genetic	Schutz et al. (1997) J. Cell Biol. 136: 969	multi-copy suppressor of <i>mps1-1</i> & synthetic lethal (with <i>cdc37-1</i>)
NIK	Biochemical	Bouwmeester et al. (2004) Nat. Cell Biol. 6:97	TAP purification
p38	Biochemical	Ota et al. (2010) Circ. Res. 106:1404	Interaction of recombinant proteins
PDGF receptor α	Biochemical	Matei et al. (2007) J. Biol. Chem. 282:445	co-IP
Pink1	Biochemical	Weihofen et al. (2008) Hum. Mol. Genet. 17:602	co-IP
PKCα	Biochemical	Brajenovic et al. (2004) J. Biol. Chem. 279: 12804	TAP purification
PKC (all types)	Biochemical	Gould et al. (2009) J. Biol. Chem. 284: 4921	co-IP
Raf	Biochemical	Perdew et al. (1997) Biochem. 36: 3600	Mammalian Cdc37 IP
	Biochemical	Stancato et al. (1993) J. Biol. Chem. 268: 21711; Wartmann & Davis (1994) J. Biol. Chem. 269: 6695	Mammalian Cdc37 IP, and Hsp90
	Biochemical	Silverstein et al. (1998) J. Biol. Chem. 273: 20090	Mammalian Cdc37 co-IP, Cdc37 directly binds Raf kinase domain, separate from TPR domain protein heterocomplexes
	Biochemical	Grammatikakis et al. (1999) Mol. Cell. Biol. 19: 1661	Human Cdc37 co-IP, N-terminus of Cdc37 binds Raf1, C-terminus of Cdc37 binds Hsp90, N-terminal 1-163 is dominant negative for Raf activation
RET/PTC1	Biochemical	Marsee et al. (2004) J. Biol. Chem. 279: 43990	co-IP
Reverse Transcriptase (Hepadnavirus)	Biochemical	Wang et al. (2002) J. Biol. Chem. 277: 24361	Human Cdc37 IP and pull downs, specific, direct binding in vitro and in vivo, and C-terminally truncated Cdc37 bound more strongly

Ryk	Biochemical	Lyu et al. (2009) J. Biol. Chem. 284: 12940	co-IP
Sevenless	Genetic	Cutforth & Rubin (1994) Cell 77: 1027	In Drosophila a genetic link between Sevenless signaling & CDC37, HSP83 & CDC37, p34cdc2 & CDC37
Spc1 (SAPK)	Genetic & Biochemical	Tatebe & Shiozaki (2003) Mol. Cell. Biol. 23: 5132	S. pombe: accumulation and phosphorylation of stress kinase Spc1 is lower in <i>cdc37</i> mutant; co-IP; Cdc37 requirement may be independent of Hsp90.
Slit2	Genetic & Biochemical	Hawle et al. (2007) Eukaryot. Cell 6: 521	Hog1 function affected by Cdc37 phosphorylation mutant in yeast; co-IP, increased for phosphorylated (activated) form of Slit2
v-Src	Biochemical Genetic Genetic Biochemical	Brugge (1986) Curr. Top. Microbiol. Immunol. 123: 1 Dey et al. (1996) Mol. Biol. Cell 7: 1405 Kimura et al. (1997) Genes & Dev. 11: 1775 Perdew et al. (1997) Biochem. 36: 3600	Mammalian Cdc37 co-IP, with Hsp90 Yeast <i>cdc37-34</i> & <i>cdc37-17</i> mutants have decreased src activity but protein level unaffected Yeast <i>cdc37-1</i> had decreased src activity. Genetic link between <i>HSC82</i> & <i>HSP82</i> with <i>CDC37</i> Mammalian Cdc37 IP
Ste11	Genetic & Biochemical	Abbas-Terki et al. (2000) FEBS Lett. 467:111	Cdc37 mutant has low Ste11 activity. Pull downs and co-IP
TAK1	Biochemical	Bouwmeester et al. (2004) Nat. Cell Biol. 6:97	TAP purification
Tau	Biochemical	Jinwal et al. (2011) J. Biol. Chem. 286: 16976	Co-IP
TBK1	Biochemical	Bouwmeester et al. (2004) Nat. Cell Biol. 6:97	TAP purification
ULK1	Biochemical	Behrends et al. (2010) Nature 466: 68	Co-IP
ULK2	Biochemical	Behrends et al. (2010) Nature 466: 69	Co-IP
Ydj1	Genetic	Mort-Bontemps-Soret et al. (2002) Mol. Genet. Genomics 267: 447	Synthetic lethal screen
ZAP70	Genetic	Matsuda et al. (1999) J. Biol. Chem. 274: 34515	Rat Cdc37 overexpression restores expression of ZAP70 mutant (protein tyrosine kinase involved in signal transduction through the T-cell receptor)

A non-proteinaceous interactor

Hyaluronan (glycosaminoglycan)	Biochemical	Grammatikakis et al. (1995) J. Biol. Chem. 270: 16198	immunoselection for hyaluronan-binding proteins identified chicken Cdc37 homologue. Cdc37 contains glycosaminoglycan-binding motif
---------------------------------------	-------------	---	--

Hsp90 co-chaperones	Reference	Evidence
Sti1/Hop	Hartson et al. (2000) Biochem. 39: 7631 Abbas-Terki et al. (2002) Biol. Chem. 383: 1335	Very small fraction of Cdc37 appeared as a constituent of mammalian Hop machinery In yeast <i>cdc37-34</i> and <i>Δsti1</i> are synthetically lethal, Sti1 binds GST-Cdc37 in vitro, endogenous proteins co-IP, can interact directly in the absence of Hsp90
FKBP52	Hartson et al. (2000) Biochem. 39: 7631	Cdc37 associates with FKBP52-containing heterocomplexes
PP5	Shao et al. (2002) Biochem. 41: 6770	PP5 coexists with Cdc37 within Hsp90 heterocomplexes (containing immature HRI), PP5-HRI interaction is mediated through Hsp90
Cyclophilin-40/Cpr7	Hartson et al. (2000) Biochem. 39: 7631 Abbas-Terki et al. (2002) Biol. Chem. 383: 1335	Cdc37 associates with Cyclophilin-40 containing heterocomplexes in retic. lysate Endogenous Cdc37 co-IPs with GST-Cpr7 in yeast
p23	Hartson et al. (2000) Biochem. 39: 7631	Small fraction of human Cdc37 pool coadsorbs with anti-p23. p23 occurs in one or more preexisting heterocomplexes with Cdc37. Cdc37 & p23 interaction not direct (via Hsp90)

For more genetic and biochemical interactions of yeast Cdc37, see <http://www.yeastgenome.org>; for yeast 2-hybrid interactions of *C. elegans* Cdc37 (W08F4.8), see Li et al. (2004) Science 303, 540. See also Millson et al. (2004) Cell Stress Chap. 9, 359; for Drosophila http://biodata.mshri.on.ca/fly_grid/Servlet/SearchPage.
For survey of *CDC37* requirement for kinome (differentially for protection of nascent chains and folding) in yeast, see Mandal et al. (2007) J. Cell Biol. 176, 319.