

Table S1. Mammalian effectors of Cdc42

Gene name	Function	References
ACK/TNK2	Actin organization	Manser et al., 1993
Borg1/CDC42EP2	Actin organization, cell shape	Hirsch et al., 2001; Joberty et al., 1999; Joberty et al., 2001
Borg2/CDC42EP3	Actin organization, cell shape	Hirsch et al., 2001; Joberty et al., 1999; Joberty et al., 2001
Borg3/CDC42EP5	Actin organization, cell shape	Hirsch et al., 2001; Joberty et al., 1999; Joberty et al., 2001
Borg4/CDC42EP4	Actin organization	Hirsch et al., 2001; Joberty et al., 1999
Borg5/CDC42EP1	Actin organization	Hirsch et al., 2001; Joberty et al., 1999
CEP2	Pseudopodia formation	Hirsch et al., 2001
CEP5	Pseudopodia formation	Hirsch et al., 2001
CIP4/TRIP10	Actin organization	Aspenstrom, 1997
Daam1	Actin organization	Aspenstrom et al., 2006
FMNL1	Actin organization	Seth et al., 2006
IFN2	Trafficking – trancytosis.	Madrid et al., 2010
FMNL2	Actin organization	Block et al., 2012
IQGAP1	Cell morphology and motility	Kuroda et al., 1996
IQGAP2	Actin organization	Kuroda et al., 1996; LeCour et al., 2016
IQGAP3	Actin organization	Kuroda et al., 1996
IRSp53/BAIAP2	Actin organization – filopodia induction	Krugmann et al., 2001
mDia2/DRF2	Actin organization	Alberts et al., 1998
mDia3	Actin organization	Yasuda et al., 2004
Mig-6/RALT	Regulates cell migration	Jiang et al., 2016
MEKK1/MAP3K1	JNK and ERK pathway activation	Fanger et al., 1997
MLK2/MAP3K10	JNK and ERK pathway activation; microtubules	Nagata et al., 1998
MLK3 /MAP3K11	JNK activation, microtubules	Nagata et al., 1998
MEKK4/MAP3K4	CSBP2 and JNK activation	Fanger et al., 1997

MRCK α /CDC42BPA	Actomyosin regulation	Leung et al., 1998
MRCK β /CDC42BPB	Actomyosin regulation	Leung et al., 1998
MRCK γ /CDC42BPG	Actomyosin regulation	Leung et al., 1998
MSE55	Actin organization	Burbelo et al., 1999
N-WASP/WASL	Actin organization	Miki et al., 1998
PAK1	Actin organization, apoptosis	Manser et al., 1994
PAK2	Apoptosis, inhibition of cell growth	Gatti et al., 1999
PAK3	Dendrite development	Bagrodia et al., 1998
PAK4	Actin organization, adherens junction, adhesion, migration	Abo et al., 1998
PAK5	Neurite development, microtubule stability	Dan et al., 2002
PAK6	Actin organization, motility, adherens junction	Lee et al., 2002
PAR6A	Cell polarity	Joberty et al., 2000
PAR6B	Cell polarity	Joberty et al., 2000
PAR6G	Cell polarity	Joberty et al., 2000; Johansson et al., 2000
PIK3R1/p85 α	Actin regulation, growth, motility, trafficking	Cheung et al., 2014
PLD1/phospholipase D1	Phosphatidic acid levels, cytoskeleton	Walker et al., 2000
RPS6KB1/S6 kinase	Cell growth and proliferation	Chou and Blenis, 1996
SPEC1/CDC42SE1	Actin organization, cell shape	Pirone et al., 2000
SPEC2/CDC42SE2	Actin organization, cell shape	Pirone et al., 2000
USP6/TRE17	Trafficking	Masuda-Robens et al., 2003
WASP	Actin organization	Symons et al., 1996

Table S2. Cdc42 GEFs and GAPs in mammals.**Guanine nucleotide exchange factors (GEFs)**

Gene name	Function	Reference
ARHGEF4/Asef	Dbl family of Rho GEFs – associated with lamellipodia and membrane ruffles.	Gotthardt and Ahmadian, 2007; Itoh et al., 2008; Kawasaki et al., 2007
ARHGEF6/Cool-2	Dbl family of Rho GEFs – associated with PAK function.	Baird et al., 2005
ARHGEF7/βPix/Cool-1	Dbl family of Rho GEFs – associated with PAK function in focal adhesion complexes in COS cells. Also associates with Scribble to regulate epithelial morphogenesis.	Bagrodia et al., 1998; Eastburn et al., 2012; Manser et al., 1998
ARHGEF15/Vsm-RhoGEF/Ephexin5	Dbl family of Rho GEFs – mediates VEGF-induced retinal angiogenesis.	Kusuhara et al., 2012
CLG	Dbl family of Rho GEFs – promotes growth in NIH 3T3 cells.	Himmel et al., 2002
DBL3	Dbl family of Rho GEFs – regulates epithelial junction position and apical differentiation.	Hart et al., 1991; Zihni et al., 2014
DBS	Dbl family of Rho GEFs – Schwann cell and tumor-derived, human breast epithelial cells migration.	Liu et al., 2009; Yamauchi et al., 2005
DOCK2	CDM family of Rho GEFs – regulates neutrophil motility and polarity.	Kunisaki et al., 2006; Kwofie and Skowronski, 2008
DOCK6	CDM family of Rho GEFs – regulates neurite outgrowth in mouse N1E-115 neuroblastoma cells, and axon extension in dorsal root ganglion neurons.	Miyamoto et al., 2013; Miyamoto et al., 2007
DOCK7	CDM family of Rho GEFs – induces dendritic pseudopodia in human cancer cell lines.	Yamamoto et al., 2013
DOCK9/Zizimin 1	CDM family of Rho GEFs – induces filopodia in NIH-3T3 cells and dendrite growth in rat hippocampal neurons.	Kuramoto et al., 2009; Kwofie and Skowronski, 2008; Meller et al., 2002
ECT2	Dbl family of Rho GEFs – promotes glioma cell migration and invasion. Actomyosin remodeling during cell division. Promotes PKCζ activity in MDCK cells to regulate junction maturation.	Fortin et al., 2012; Liu et al., 2004; Rosa et al., 2015
FGD1	Dbl family of Rho GEFs – induces the formation of filopodia in NIH-3T3 cells. Linked to faciogenital dysplasia and to F-actin morphogenesis through Arp2/3.	Hou et al., 2003; Zheng et al., 1996
FGD2	Dbl family of Rho GEFs – associated with early endosomes and membrane ruffles.	Huber et al., 2008
FGD3	Dbl family of Rho GEFs – induces broad sheet-like protrusions in HeLa cells.	Hayakawa et al., 2008
FGD4/FAB	Dbl family of Rho GEFs – associates with F-actin. Induces filopodia like protrusions NIH-3T3.	Obaishi et al., 1998

FGD5/FYVE	Dbl family of Rho GEFs – associated with Cdc42 activation at the cell–cell contacts in HUVECS cells.	Ando et al., 2013
FRG	Dbl family of Rho GEFs – associated with nectin-based adhesion at the adherens junction in MDCK cells.	Fukuhara et al., 2004; Miyamoto et al., 2003
ITSN1	Dbl family of Rho GEFs -Associated to F-actin remodeling during exocytosis in neuroendocrine cells. Involved in tethering endocytic proteins to the sites of endocytosis.	Koh et al., 2004; Malacombe et al., 2006
ITSN2	Dbl family of Rho GEFs - Localized at the centrosome in MDCK spheroids. Promotes central lumen formation by regulating spindle orientation in MDCK spheroid. Regulates asymmetric meiotic divisions in mammalian oocyte through F-actin (WASp) regulation. WASp-binding protein associated with the endocytic pathway in T lymphocytes.	McGavin et al., 2001; Rodriguez-Fraticelli et al., 2010; Zhang et al., 2017
TUBA/KIAA1010/DNM BP/ArhGEF36	Dbl family of Rho GEFs - Localized at the tight junction through ZO1 in Caco-2cells, and in the vicinity of the apical membrane in MDCK spheroids. Enterocyte polarity, lumen formation, tight junction integrity and ciliogenesis.	Baek et al., 2016; Kovacs et al., 2011; Otani et al., 2006; Qin et al., 2010
Vav3	Dbl family of Rho GEFs - Involved in integrin-mediated signaling, wound healing, angiogenesis and neurite outgrowth.	Zeng et al., 2000

GTPase-activating proteins

Gene name	Function	Reference
ARHGAP17/Rich1/ Nadrin/Cdc42GAP	Localizes at the adherens junction and basal end of the tight junction in MDCK cells. Linked to epithelial junction regulation in MDCK spheroids and in the mouse intestine. Linked to transcellular transport in the intestine epithelium, in mice. Associated with endocytic actin capping proteins. Regulates exocytosis in neurons.	Harada et al., 2000; Lee et al., 2016; Richnau and Aspenstrom, 2001; Wells et al., 2006
ARHGAP31/CdGAP	Regulates embryonic vascular development in mice. Regulates lamellipodia formation NIH 3T3 cells and directional membrane protrusions of migrating osteosarcoma cells.	Caron et al., 2016; Lamarche-Vane and Hall, 1998
ARHGAP33/NOMA-GAP	Regulates neurite formation and extension through PAK signaling.	Rosario et al., 2007
DLC1/START-GAP1	Localized in focal adhesions in Hela cells. Regulates cell motility in cancer cell lines.	Healy et al., 2008
DLC2/START-GAP2	Localized in focal adhesions in Hela cells. Associated to hepatocarcinogenesis.	Ching et al., 2003; Kawai et al., 2009
RLIP	F-actin cytoskeleton regulation during <i>Xenopus</i> gastrulation.	Jullien-Flores et al., 1995
RACGAP1	Regulate the migration of hepatocyte-derived cells.	Wang et al., 2011

SH3BP1	Localized at the adherens junction and basal end of the tight junction. Regulator of junction assembly and epithelial morphogenesis in Caco-2 spheroids.	Elbediwy et al., 2012
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