

SUPPLEMENTARY INFORMATION

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Functional Category	Partner	Function	Reference	NF1 domain	Boundary
Intracellular trafficking	LRPPRC	Complex in RNA granules, trafficking	(Arun et al., 2013)	TBD	1095-1176
	Kinesin-1	vesicle transport, APP?	(Hakimi et al., 2002)	Protein complex with NF1	Not known
	APP	Melanosome transport?	(De Schepper et al., 2006)	Full length GRD	1198-1530
Cytoskeletal interaction	LIMK2	Serine-threonine kinase; Rho/ROCK actin cytoskeletal remodeling	(Vallee et al., 2012)	SecPH, Full length	1545-1816
	Tubulin	Microtubules; inhibits NF1 Ras-GAP activity	(Bollag et al., 1993)	TBD (N-term GRD)	1095-1175
Neuronal Differentiation	VCP	AAA (ATPase); dendritic spine formation	(Wang et al., 2011)	Sec14PH/LRD	1545-1950
	CRMP-2	neurite outgrowth	(Patrakitkomjorn et al., 2008)	CTD	2260-2818
Cell adhesion	FAK (Focal adhesion kinase)	Cell adhesion	(Kweh et al., 2009)	CTD	2205-2785
Ubiquitination	ETEA	UBA/UBX protein	(Phan et al., 2010)	GRD	1176-1552
	SAG/CUL1/FBXW7	SCF E3 ubiquitin ligase complex/ubiquitination	(Tan et al., 2011)	CTD	2180-2840
	Cullin 3	E3 ubiquitin ligase complex/Ubiquitination	(Hollstein and Cichowski, 2013)	Full length NF1, protein complex	Not known
Membrane localization	Phospholipids	membrane localization?	(Welti et al., 2007)	SEC14	1570-1699
	Caveolin-1	Localization and Ras/FAK/Akt signaling	(Boyanapalli et al., 2006)	Full length	Not known
	Syndecan	heparan sulfate proteoglycan	(Hsueh et al., 2001)	GRD, SBD?	1356-1562, 2616-2812
Cell signaling	DDAH	NO/NOS regulator	(Tokuo et al., 2001)	Mostly CTD, also CSRD	2620-2818 543-909
	14-3-3	Negatively regulates NF1-GAP activity	(Feng et al., 2004)	CTD	2260-2818
	Ras	Signaling	(Ballester et al., 1990, Martin et al., 1990, Xu et al., 1990)	Full length, GRD	1198-1530
Membrane localization	Spred1	Downregulation of Ras activity	(Stowe et al., 2012)	Not known	Not known

- Arun V, Wiley JC, Kaur H, Kaplan DR, Guha A (2013) A novel neurofibromin (NF1) interaction with the leucine-rich pentatricopeptide repeat motif-containing protein links neurofibromatosis type 1 and the French Canadian variant of Leigh's syndrome in a common molecular complex. *Journal of neuroscience research* 91:494-505.
- Ballester R, Marchuk D, Boguski M, Saulino A, Letcher R, Wigler M, Collins F (1990) The NF1 locus encodes a protein functionally related to mammalian GAP and yeast IRA proteins. *Cell* 63:851-859.
- Bollag G, McCormick F, Clark R (1993) Characterization of full-length neurofibromin: tubulin inhibits Ras GAP activity. *The EMBO journal* 12:1923-1927.
- Boyanapalli M, Lahoud OB, Messiaen L, Kim B, Anderle de Sylor MS, Duckett SJ, Somara S, Mikol DD (2006) Neurofibromin binds to caveolin-1 and regulates ras, FAK, and Akt. *Biochemical and biophysical research communications* 340:1200-1208.
- De Schepper S, Boucneau JM, Westbroek W, Mommaas M, Onderwater J, Messiaen L, Naeyaert JM, Lambert JL (2006) Neurofibromatosis type 1 protein and amyloid precursor protein interact in normal human melanocytes and colocalize with melanosomes. *The Journal of investigative dermatology* 126:653-659.
- Feng L, Yunoue S, Tokuo H, Ozawa T, Zhang D, Patrakitkomjorn S, Ichimura T, Saya H, Araki N (2004) PKA phosphorylation and 14-3-3 interaction regulate the function of neurofibromatosis type I tumor suppressor, neurofibromin. *FEBS letters* 557:275-282.
- Hakimi MA, Speicher DW, Shiekhattar R (2002) The motor protein kinesin-1 links neurofibromin and merlin in a common cellular pathway of neurofibromatosis. *The Journal of biological chemistry* 277:36909-36912.
- Hollstein PE, Cichowski K (2013) Identifying the Ubiquitin Ligase complex that regulates the NF1 tumor suppressor and Ras. *Cancer discovery* 3:880-893.
- Hsueh YP, Roberts AM, Volta M, Sheng M, Roberts RG (2001) Bipartite interaction between neurofibromatosis type I protein (neurofibromin) and syndecan transmembrane heparan sulfate proteoglycans. *The Journal of neuroscience : the official journal of the Society for Neuroscience* 21:3764-3770.
- Kweh F, Zheng M, Kurenova E, Wallace M, Golubovskaya V, Cance WG (2009) Neurofibromin physically interacts with the N-terminal domain of focal adhesion kinase. *Molecular carcinogenesis* 48:1005-1017.
- Martin GA, Viskochil D, Bollag G, McCabe PC, Crosier WJ, Haubruck H, Conroy L, Clark R, O'Connell P, Cawthon RM, et al. (1990) The GAP-related domain of the neurofibromatosis type 1 gene product interacts with ras p21. *Cell* 63:843-849.
- Patrakitkomjorn S, Kobayashi D, Morikawa T, Wilson MM, Tsubota N, Irie A, Ozawa T, Aoki M, Arimura N, Kaibuchi K, Saya H, Araki N (2008) Neurofibromatosis type 1 (NF1) tumor suppressor, neurofibromin, regulates the neuronal differentiation of PC12 cells via its associating protein, CRMP-2. *The Journal of biological chemistry* 283:9399-9413.
- Phan VT, Ding VW, Li F, Chalkley RJ, Burlingame A, McCormick F (2010) The RasGAP proteins Ira2 and neurofibromin are negatively regulated by Gpb1 in yeast and ETEA in humans. *Molecular and cellular biology* 30:2264-2279.
- Stowe IB, Mercado EL, Stowe TR, Bell EL, Oses-Prieto JA, Hernandez H, Burlingame AL, McCormick F (2012) A shared molecular mechanism underlies the human rasopathies Legius syndrome and Neurofibromatosis-1. *Genes Dev* 26:1421-1426.
- Tan M, Zhao Y, Kim SJ, Liu M, Jia L, Saunders TL, Zhu Y, Sun Y (2011) SAG/RBX2/ROC2 E3 ubiquitin ligase is essential for vascular and neural development by targeting NF1 for degradation. *Dev Cell* 21:1062-1076.
- Tokuo H, Yunoue S, Feng L, Kimoto M, Tsuji H, Ono T, Saya H, Araki N (2001) Phosphorylation of neurofibromin by cAMP-dependent protein kinase is regulated via a cellular association of N(G),N(G)-dimethylarginine dimethylaminohydrolase. *FEBS letters* 494:48-53.
- Vallee B, Doudeau M, Godin F, Gombault A, Tchalikian A, de Tauzia ML, Benedetti H (2012) Nf1 RasGAP inhibition of LIMK2 mediates a new cross-talk between Ras and Rho pathways. *PLoS One* 7:e47283.
- Wang HF, Shih YT, Chen CY, Chao HW, Lee MJ, Hsueh YP (2011) Valosin-containing protein and neurofibromin interact to regulate dendritic spine density. *J Clin Invest* 121:4820-4837.
- Welti S, Fraterman S, D'Angelo I, Wilm M, Scheffzek K (2007) The sec14 homology module of neurofibromin binds cellular glycerophospholipids: mass spectrometry and structure of a lipid complex. *Journal of molecular biology* 366:551-562.
- Xu GF, O'Connell P, Viskochil D, Cawthon R, Robertson M, Culver M, Dunn D, Stevens J, Gesteland R, White R, et al. (1990) The neurofibromatosis type 1 gene encodes a protein related to GAP. *Cell* 62:599-608.