

Supplementary Table 1. Neurofibromin key residues involved in protein structure and protein-protein associations.

Domain	Residue	Binding partner	Mutation	Effect in protein	Ref
N-terminal region	103	PKC	R>K	Nd	49
	105	PKC	D>N	Nd	49
	108	PKC	M>I	Nd	49
	114	PKC	L>M	Nd	49
	116	PKC	E>*	Truncated protein → loss of functional GRD and CSRD domains	49
	131	PKC	A>S	Nd	49
	225	PKC	E>Rfs/6	Truncated protein → non functional	49
Interdomain region	304	PKC	R>*	Improper functioning of PKC phosphorylation	84
	315		Q>Q		84
	316		L>M		84
	335		N>N		84
CSRD	777	Ras	W>R	Reduction of RasGAP activity	48
	844-848	DDAH1	Missense	Severe phenotypes	36
Interdomain region	991	Nd	MΔ	Reduction of protein stability	36
	1084	Nd	P>R		36
TBD	1095-1097 (KYF)	Nd	Nd	Degradation	48
	1098-1100 (TLF)	Nd	Nd		48
GRD	1276	Ras	R>E	Reduction of RasGAP activity	48
	1423		K>E		48
PH	1719-1736	5-HT6	Δ	Defects in 5-HT6 activity	82
	1746-1750		Δ		82
	1748		R>A		82
	1750		K>A, Δ		82
	1809	Ras	R>G	Reduction of RasGAP activity	48
HLR	1825-2428	Nd	Nd	Lower risk of OPG	52
	1834	NF1	L>R	Dimerization	38
	2104		L>R		48
	1849	Nd	R>Q	Dimerization Reduction of protein stability	48 48
Interdomain region	1869	Ras	G>S	Reduction of RasGAP activity	48
	2067		L>P	Reduction of RasGAP activity and protein stability	48
CTD	T2554	14-3-3	S/T> A	Significantly decreased binding activity with 14-3-3	55
	S2576				55
	S2578				55
	S2580				55
	S2813				55

Supplementary Table 2. Neurofibromin posttranslational modifications.

Domain	Residue	Modification	Protein	Effect in neurofibromin	Ref
N-Terminal region	Nd	Phosphorylation	PKC α	Proteasomal degradation	104
			Hyperactivated PKC α	Destabilization, role in sporadic tumorigenesis	104
	Nd		PKC β	Nd	105
	Nd		PKC ϵ	Recruitment to lipid rafts Increase of RasGAP activity	50, 51
	Nd		PKC ζ	Nd	22
CSRD	T586	Phosphorylation	PKA α	Allosteric activation of GRD domain	54
	S818				54
	S876				54
	C622/C632	Palmitoylation	Nd	Presumably stabilization of tridimensional structure	51
	C673/680				51
	C714/721				51
	C845				Nd
TBD	1095-1097 KYF	Ubiquitination	Nd	Degradation of the protein	59
	1098-1100 TLF		Nd		59
GRD	1176-1552	Ubiquitination	FAF2 (ETEA)	Ub-dependent proteolysis	72
	C1365	Palmitoylation	Nd	Weaker RasGAP activity in GRD nf1 type II	51
SEC14-PH	K1634	SUMOylation		Role in Ras-GAP activity	83
	K1731				83
CTD	T2554	Phosphorylation	PKA	Association with 14-3-3, leading to a negative regulation of GAP activity	55
	Y2556		CK2		55
	S2576		PKA		55
	S2578				55
	S2580				55
	S2813				55
	Nd	Ubiquitination	HAF	Proteasomal degradation during hypoxia	149
Nd	Nd	Ubiquitination	Cul3 E3 ligase	Proteasomal degradation	149