Arg[1809] substitution in neurofibromin: further evidence of a genotype-phenotype correlation in neurofibromatosis type 1.

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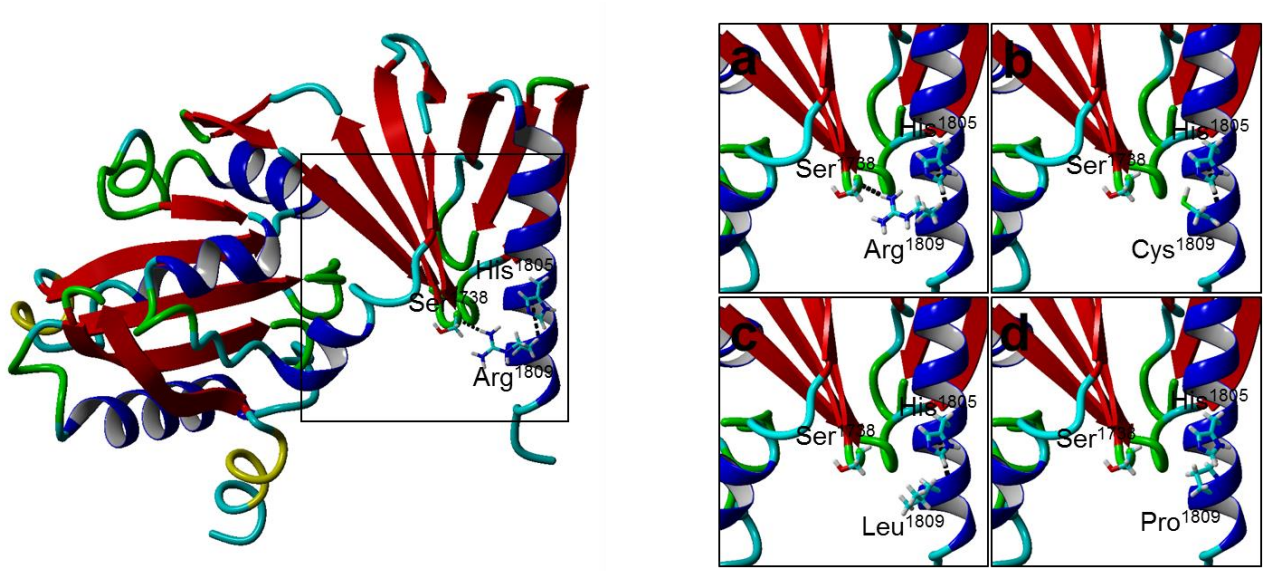
Supplementary Information

Supplementary Table 1 – *Clinical features of the 16 patients from six families with different Arg[1809] substitutions.*

Clinical features	5425C>T (Arg1809Cys)										5426G>T (Arg1809Leu)				5426G>C (Arg1809Pro)	Total	Total (*Pinna et al*)
	Family 1					*Family 2*		*Family 3*			*Family 4*			*Family 5*	*Family 6*		
	II.4	II.6	II.7	III.4	III.5	II.3	III.1	III.3	III.4	IV.4	II.2	III.1	III.2				
Age yrs (at the last examination)	41	39	32	13	11	54	11	40	37	5	40	5	3	15	12		
Sex	M	F	M	F	M	F	F	F	M	M	F	M	F	F	F	6M/9F	5M/9F
CALS	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	15/15	14/14
Freckling	+ (very mild)	+ (very mild)	-	+ (very mild)	+ (very mild)	+ (diffuse)	+	NA	-	+ (very mild)	+ (mild)	-	-	-	-	8/14	9/10
Lisch nodules	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0/15	0/10
Cutaneous NF	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0/15	0/13
Subcutaneous NF	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0/15	0/13
External plexiform NF	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0/15	0/13
Optic pathway glioma	NA	-	NA	NA	NA	NA	-	-	NA	-	NA	NA	NA	NA	-	0/5	0/11
Learning difficulties	-	-	-	-	-	-	-	-	+	-	+	-	-	+	+	4/15	1/13
Other neoplasias	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0/15	0/11
Short stature (≤-2 SD)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0/15	1/10
Macrocephaly	-	-	+	-	+ (relative)	-	-	NA	+ (relative)	-	+ (relative)	+ (relative)	+	-	+	7/14	2/10
Thoracic anomalies	-	PC	PE	PE	PE, SW	PE	-	NA	PE	-	PE	-	-	-	-	7/14	3/11
Scoliosis (non-dystrophic)	-	-	-	+	-	+	+	-	-	-	-	-	-	+	-	4/15	2/10
Pulmonary valve stenosis	-	-	NA	-	-	-	-	-	-	-	-	-	-	-	NA	0/13	0/10
Other cardiac defects	NA	-	NA	ASD	-	-	-	NA	NA	-	NA	-	-	-	NA	1/8	NA
Other NS features	SN, LSPH, WSN	HD,SSDC	SN, SPC, E	-	SN, SSDC, WSN	SSDC	SSDC	NA	SSDC	-	HD, LSPH, H, BNT, MJL, SSDC	CF, S, SSDC, MJL, FF	H, BNT,T, SSDC, KK, MJL, FF	FF	NA		
Lipomas	+	-	+	-	-	+	-	NA	+	-	+	-	-	-	-	5/14	NA
Others	X, CMS, P	X	X, CMS, LLI, UH		Na, Ma, FF, SRC, LRP	Piv, EDAA	Piv		X, Piv	JIE, Ne, SuN, PP	CMS, D, EK, POF, SA, LLI, TD	TD, UH, SuN	SA, AD, SuN	Ne, Pil	O		

Abbreviations: -, negative; +, positive; AD, abdominal diastasis; ASD, atrial septal defect; BNT, bulbous nasal tip; CF, coarse facies; CMS, Campbell de Morgan spots; D, dolichocolon; E, exophthalmos; EDAA, eating disorders in adult age; EK, ectopic kidney; F, female; FF, flat feet; H, hypertelorism; HD, hypokinetic dysphonia; JIE, juvenile idiopathic epilepsy; KK, knock knees; LLI, leg length inequality; LRP, lichen ruber planus; LSPH, low-set posterior hairline; M, male; Ma, malocclusion; MJL, mild joint laxity; NA, not available; Ne, nevus anemicus; NF, neurofibromas; O, osteopenia; P, psoriasis; PC, pectus carinatum; PE, pectus excavatum; Pil, pilomatrixoma; Piv, phototype IV; POF, premature ovarian failure; PP, postaxial polydactyly; S, scaphocephaly; SA, sacral appendix; SN, short neck; SPC, single palmar creases; SRC, single renal cyst; SSDC, soft skin-deep palm and sole creases; SuN, supernumerary nipples; SW, scapular winging; T, turricephaly; TD, tooth decay; UH, umbilical hernia; WSN, wide-set nipples; X, xanthelasma.



Supplementary Figure S1 - *3D homology-modeling*

Sec/PH-like bipartite model (RefSeq: NP_000258.1 residues 1560-1816; RCS-PDB: 2Q4D) was generated for wild-type (left) and mutant forms. The zoomed boxes (right) highlight H-bonds involving the residue at position 1809: (a) the wild-type Arg^{1809} forms H-bonds with Ser^{1738} and His^{1805}. H-bond with Ser^{1738} is lost with Cys^{1809} (b) or Leu^{1809} (c) substitutions, while both H-bonds are lost with Pro^{1809} substitution (d).