Patient-Gender/Age	Family history	MM severity*	MM location	Associated disorders	Functional disability	*NTN1* mutation
1.9-M/18	Yes	2	H, FA, A	Alopecia, Irritable bowel syndrome	Difficulties in fine bimanual activities; Contralateral hand pain while writing	p.Cys601Arg
1.4-F/43	Yes	1	H, Ft	Temperature regulation issues, Irritable bowel syndrome	None	p.Cys601Arg
1.11-F/44	Yes	2	H, FA	Schizophrenia, Drug addiction	Difficulties in fine bimanual activities	p.Cys601Arg
1.1-M/81	Yes	0	0	Hypertension, Drug addiction	0	p.Cys601Arg
2.3-F/23	Yes	3	H, FA, UA, S	Temperature regulation issues	Difficulties in fine bimanual activities	p.Ile518del
2.2-M/54	Yes	3	H, FA, UA, S	Diabetes type 2	Difficulties in fine bimanual activities	p.Ile518del
2.1-M/84	Yes	3	H, FA, UA, S	Diabetes type 2	Difficulties in fine bimanual activities	p.Ile518del
3-M/60	No	3	H, Ft	0	None	p.Cys601Ser
4-M/10	No	3	H, FA > Ft	Benign stereotypies	Clumsiness and poor coordination, Difficulties in fine bimanual activities	0
5-M/41	No	3	H, FA, A	0	Painful contralateral contractions during effortful voluntary movement	0
6-F/23	No	3	H, FA > Ft, L	0	Difficulties in fine bimanual and bipedal activities	0
7-F/52	No	3	H	0	Poor coordination, Difficulties in fine bimanual activities	0
8-M/33	No	3	H	0	Difficulties in fine bimanual activities, pain in both hands	0
9- F/10	No	3	H, FA	0	Difficulties in fine bimanual activities, General clumsiness	0
10-M/41	No	3	H, FA, Ft	0	Difficulties in fine bimanual activities	0
11-F/30	No	3	H, FH	0	Difficulties in bimanual activities; Occasional pain after prolonged manual activities	0
12-M/8	Yes	4	H, FA > Ft	0	Difficulties in fine bimanual and bipedal activities, Poor coordination	0
13-M/52	Yes	ND	ND	ND	ND	0
14-F/35	No	3	H	lymphoma	Difficulties in fine bimanual activities	0
15-F/55	No	3	H, FA	0	Difficulties in fine bimanual activities	0
16-F/69	No	3	H	Multiple system atrophy	Difficulties in fine bimanual activities	0
2514-M/46	No	2	H, FA	0	Difficulties in fine bimanual activities	0
2565-M/30	Yes	2	H, FA, Ft	0	Difficulties in fine bimanual activities	0
2615-M/14	Yes	2	H, FA	0	Difficulties in fine bimanual activities	0
2717-M/4	No	3	H, FA	0	Clumsiness and poor coordination, Difficulties in bimanual activities	0
2889-F/55	Yes	3	H, FA	0	Difficulties in fine bimanual activities	0
2957-M/63	No	2	H, FA	0	None	0
2959-F/47	No	2	H, FA, A	0	None	0
2961-F/26	No	2	H, FA	0	Difficulties in fine bimanual activities	0
2997-M/35	No	1.5	H, FA	0	Difficulties in fine bimanual activities	0
3182-M/31	Yes	1.5	H, FA	0	Difficulties in fine bimanual activities	0

Supplemental Table 1: Characteristics and mutational analysis results of the patients.

MM, Mirror Movement; H, Hands; FA, Forearms; A, Arms; UA, Upper Arms; S, Shoulder; L, leg; Ft, Feet; M, male; F, female; ND, not determined.

*according to the Woods and Teuber MM severity scale: (0. No MM; 1. Barely discernible but repetitive MM; 2. Either slight but sustained MM, or stronger, but briefer MM; 3. Strong and sustained repetitive MM; 4. MM equal to that observed in the intended hand).

ID	Mean coverage (X)	10X Coverage (%)	SNP Nb	SNP Hom	SNP Htz	Insertion	Deletion	Indels Htz	Indels Hom	Indels known	Indels new	nTi	nTv	TiTvRatio
1.4	72	95	35947	13635	22312	1350	1367	1679	1050	1675	1058	26181	9697	2.7
1.9	103	96	36218	13895	22323	1424	1457	1801	1119	1749	1154	26422	9745	2.71
4	83	95	35963	14209	21754	1403	1367	1672	1117	1724	1066	26070	9826	2.65
5	70	94	35777	14071	21706	1341	1302	1587	1061	1633	1023	25904	9799	2.64
6	73	94	35328	13628	21700	1341	1304	1608	1055	1635	1037	25712	9560	2.69
7	68	94	36178	13920	22258	1316	1365	1637	1043	1673	1026	26352	9778	2.7
8	71	95	35786	13936	21850	1396	1435	1753	1093	1739	1107	26002	9734	2.67
9	72	95	35685	14163	21522	1398	1373	1645	1136	1691	1087	25897	9718	2.66
10	80	95	36471	14132	22339	1403	1384	1748	1067	1719	1085	26532	9870	2.69
11	72	95	35990	14001	21989	1353	1381	1673	1073	1665	1086	26197	9722	2.69
12	79	95	35842	14169	21673	1397	1367	1689	1094	1703	1075	26077	9700	2.69
13	64	95	40738	14412	26326	1566	1583	2011	1143	1833	1320	29702	10958	2.71
14	82	95	35853	13652	22201	1393	1352	1688	1077	1686	1080	26034	9743	2.67
15	78	95	36050	13758	22292	1404	1354	1656	1121	1702	1080	26165	9823	2.66
16	75	95	36205	13918	22287	1347	1343	1632	1067	1687	1014	26360	9787	2.69

Supplemental Table 2: Exomes processed by the French group

ID, Identity; Nb, Number; Hom, Homozygous; Htz, Heterozygous; Indels, Insertion-Deletions; nTi, number of transitions; nTv, number of transversions.

ID	Mean Coverage (X)	10X Coverage (%)	Capture Platform	Total Bases Mapped to Target	Total SNPs	Novel SNPs (not in dbSNP)	dbSNP TiTv	Novel TiTv	Total Indels	Novel Indels (not in dbSNP)
2514	52.4	92.5	SureSelect V4	2682320093	74701	1105	2.234278	1.232323	8052	790
2565	50.65	92.8	SureSelect V4	2592597643	75669	1198	2.256987	1.162455	8172	832
2615	51.21	92.9	SureSelect V4	2621307329	75992	1097	2.261977	1.093511	8282	853
2.3	50.64	93.5	SureSelect V4	2592300649	76154	1166	2.240902	1.183521	8339	890
2717	46.41	92.8	SureSelect V4	2375721529	76876	1192	2.275513	1.120996	8433	893
2889	29.45	92.9	SureSelect V4	1507629107	73660	1078	2.257866	1.427928	8162	839
2957	48.84	97.4	SureSelect V4	2500028036	83712	1096	2.244933	1.255144	9727	985
2959	65.91	98.3	SureSelect V4	3373948057	98431	1605	2.216063	1.276596	11452	1214
2961	46.58	96.7	SureSelect V4	2384574653	83221	1253	2.237283	1.382129	9654	1094
2997	37.84	95.9	SureSelect V4	1936811261	81263	1801	2.253439	1.595101	9364	1060
3182	97.85	98.3	SureSelect V5+UTR	7291420217	171102	7257	2.262025	1.211826	20793	2483

Supplemental Table 3: Exomes processed in New Zealand.

ID, Identity; dbSNP, Single Nucleotide Polymorphism Database; TiTv, ratio of number of transitions on number of transversions; Indels, Insertion-Deletions.

Supplemental Table 4 (see excel file): List of all variants remaining after the first stage of variant filtering for each subject.

Chr: chromosome; het: heterozygote; hom: homozygote; SIFT: Sorting Intolerant From Tolerant : http://sift.bii.a-star.edu.sg; PolyPhen-2: Polymorphism Phenotyping v2: http://genetics.bwh.harvard.edu/pph2/; ExAC; 1000Genome : http://www.internationalgenome.org ; EVS: Exome Variant Server : http://evs.gs.washington.edu/EVS/

Chr	Position	Transcript Consequence	Protein Consequence	Protein Domain	Impact	SIFT	PolyPhen-2	CADD Raw score	CADD PHRED	REVEL	Allele Frequency	Allele Count	Allele Number
17	8925896	c.206C>T	p.Thr69Ile	Nter	missense	Deleterious	Possibly damaging	5.749786	27.0	0.830	0.00009246	1	10816
17	8926031	c.341C>T	p.Pro114Leu	Nter	missense	Deleterious	Possibly damaging	5.700206	26.8	0.569	0.00001902	1	29092
17	8926106	c.416G>T	p.Gly139Val	Nter	missense	Deleterious	Probably damaging	5.977892	27.8	0.898	0.00001115	1	89648
17	8926139	c.449A>T	p.Gln150Leu	Nter	missense	Deleterious	Possibly damaging	5.820223	27.2	0.704	0.00001026	1	97504
17	8926175	c.485A>G	p.Tyr162Cys	Nter	missense	Deleterious	Probably damaging	4.220402	23.9	0.498	0.00001953	2	55990
17	8926196	c.506G>T	p.Arg169Leu	Nter	missense	Deleterious	Possibly damaging	4.972482	25.1	0.433	0.000009484	1	57638
17	8926199	c.509C>T	p.Thr170Met	Nter	missense	Deleterious	Probably damaging	6.733971	32	0.646	0.00005667	1	57882
17	8926207	c.517C>T	p.Pro173Ser	Nter	missense	Deleterious	Probably damaging	6.167530	28.5	0.887	0.00001875	2	58416
17	8926217	c.527T>G	p.Phe176Cys	Nter	missense	Deleterious	Probably damaging	5.475417	26.2	0.846	0.000009351	1	58572
17	8926250	c.560G>T	p.Arg187Leu	Nter	missense	Deleterious	Possibly damaging	5.123830	25.4	0.438	0.000009871	1	101308
17	8926259	c.569G>A	p.Arg190His	Nter	missense	Deleterious	Probably damaging	6.620844	32	0.490	0.00001005	1	99518
17	8926261	c.571G>A	p.Ala191Thr	Nter	missense	Deleterious	Probably damaging	5.576961	26.4	0.514	0.00001009	1	54564
17	8926273	c.583A>C	p.Lys195Gln	Nter	missense	Deleterious	Probably damaging	5.441114	26.1	0.541	0.00001046	1	52700
17	8926280	c.590A>G	p.Asn197Ser	Nter	missense	Deleterious	Possibly damaging	3.975681	23.6	0.493	0.00001067	1	93724
17	8926281	c.591C>A	p.Asn197Lys	Nter	missense	Deleterious	Probably damaging	5.749865	27.0	0.402	0.00001072	1	93264
17	8926290	c.600G>T	p.Glu200Asp	Nter	missense	Deleterious	Probably damaging	5.742261	26.9	0.499	0.00001102	1	90714
17	8926310	c.620A>G	p.His207Arg	Nter	missense	Deleterious	Possibly damaging	3.203209	22.7	0.782	0.00001236	1	80904
17	8926396	c.706C>T	p.Pro236Ser	Nter	missense	Deleterious	Probably damaging	6.304876	29.2	0.707	0.00003744	1	26708
17	8926435	c.745G>T	p.Val249Leu	Nter	missense	Deleterious	Possibly damaging	6.440602	29.8	0.492	0.00004662	1	21450
17	8926448	c.758G>A	p.Arg253His	Nter	missense	Deleterious	Probably damaging	7.193163	34	0.906	0.00004781	1	20918
17	8926502	c.812C>G	p.Ser271Trp	Nter	missense	Deleterious	Probably damaging	7.086665	33	0.766	0.00004817	1	8430
17	8926537	c.847G>A	p.Gly283Ser	Nter	missense	Deleterious	Probably damaging	7.101435	33	0.851	0.00004998	1	20008
17	8926597	c.907G>A	p.Val303Met	EGF-1	missense	Deleterious	Possibly damaging	3.423483	23.0	0.212	0.0001132	2	17666
17	9066135	c.1024A>T	p.Asn342Tyr	EGF-2	missense	Deleterious	Possibly damaging	4.658115	24.5	0.450	0.000008431	1	65274
17	9066153	c.1042C>T	p.Arg348Trp	EGF-2	missense	Deleterious	Probably damaging	7.426418	34	0.550	0.00002510	2	65500

17	9066154	c.1043G>A	p.Arg348Gln	EGF-2	missense	Deleterious	Probably damaging	5.670526	26.7	0.290	0.00003343	4	65550
17	9066162	c.1051C>A	p.Arg351Ser	EGF-2	missense	Deleterious	Probably damaging	5.316330	25.8	0.439	0.000008338	1	65660
17	9066163	c.1052G>A	p.Arg351His	EGF-2	missense	Deleterious	Probably damaging	7.323722	34	0.403	0.00003335	3	65672
17	9066177	c.1066C>A	p.Leu356Ile	EGF-2	missense	Deleterious	Probably damaging	5.697370	26.8	0.214	0.000008323	1	65782
17	9066180	c.1069T>C	p.Tyr357His	EGF-2	missense	Deleterious	Probably damaging	5.891008	27.4	0.383	0.000008322	1	65794
17	9066181	c.1070A>G	p.Tyr357Cys	EGF-2	missense	Deleterious	Probably damaging	5.645314	26.6	0.295	0.000008323	1	65778
17	9066186	c.1075C>T	p.Leu359Phe	EGF-2	missense	Deleterious	Probably damaging	6.301429	29.1	0.217	0.000008325	1	65758
17	9066195	c.1084C>T	p.Arg362Cys	EGF-2	missense	Deleterious	Probably damaging	7.821538	35	0.488	0.000008346	1	119818
17	9066196	c.1085G>A	p.Arg362His	EGF-2	missense	Deleterious	Probably damaging	7.397351	34	0.420	0.00005010	3	65584
17	9066203	c.1092C>A	p.Ser364Arg	EGF-2	missense	Deleterious	Probably damaging	5.740789	26.9	0.543	0.000008418	1	118794
17	9066203	c.1092C>G	p.Ser364Arg	EGF-2	missense	Deleterious	Probably damaging	5.238930	25.6	0.543	0.000008418	1	118794
17	9066220	c.1109A>G	p.Asn370Ser	EGF-2	missense	Deleterious	Possibly damaging	2.670347	20.6	0.292	0.00001722	2	116120
17	9066238	c.1127C>T	p.Ala376Val	EGF-2	missense	Deleterious	Probably damaging	7.111793	34	0.322	0.000009226	1	108390
17	9066277	c.1166G>A	p.Arg389His	EGF-2	missense	Deleterious	Probably damaging	7.545972	34	0.528	0.00001940	2	103068
17	9066304	c.1193G>A	p.Arg398Gln	EGF-2	missense	Deleterious	Probably damaging	7.786678	35	0.238	0.00001139	1	87764
17	9083175	c.1259C>A	p.Thr420Asn	EGF-3	missense	Deleterious	Probably damaging	6.674780	32	0.388	0.000008252	1	66580
17	9083198	c.1282G>A	p.Gly428Ser	EGF-3	missense	Deleterious	Probably damaging	7.646026	35	0.629	0.000008255	1	121132
17	9083205	c.1289C>T	p.Thr430Met	EGF-3	missense	Deleterious	Probably damaging	7.510121	34	0.548	0.00006606	3	66532
17	9083228	c.1312G>A	p.Ala438Thr	EGF-3	missense	Deleterious	Probably damaging	7.469702	34	0.403	0.00004137	3	66432
17	9083253	c.1337C>T	p.Ser446Phe	EGF-3	missense	Deleterious	Probably damaging	7.184709	34	0.547	0.000008382	1	119308
17	9083253	c.1337C>G	p.Ser446Cys	EGF-3	missense	Deleterious	Probably damaging	6.581699	31	0.479	0.000008382	1	65760
17	9086251	c.1376C>T	p.Pro459Leu	-	missense	Deleterious	Possibly damaging	5.205918	25.5	0.296	0.00001648	1	66728
17	9124502	c.1429A>G	p.Lys477Glu	NTR	missense	Deleterious	Possibly damaging	6.384467	29.5	0.331	0.000008240	1	66722
17	9124529	c.1456A>G	p.Asn486Asp	NTR	missense	Deleterious	Possibly damaging	4.360267	24.1	0.196	0.000008238	1	66734
17	9124539	c.1466A>G	p.Lys489Arg	NTR	missense	Deleterious	Probably damaging	4.519314	24.3	0.230	0.0001400	1	66728
17	9124540	c.1467G>C	p.Lys489Asn	NTR	missense	Deleterious	Possibly damaging	4.895699	24.9	0.203	0.000008238	1	121388
17	9124552	c.1479G>C	p.Lys493Asn	NTR	missense	Deleterious	Possibly damaging	5.799589	27.1	0.174	0.000008240	1	66714
17	9124559	c.1486+6_1486+9del	p.?	NTR	splice donor	-	-	-	-	-	0.000008241	1	121342
17	9142968	c.1498C>T	p.His500Tyr	NTR	missense	Deleterious	Possibly damaging	4.943501	25.0	0.175	0.00001674	2	65632

17	9143028	c.1558G>A	p.Val520Met	NTR	missense	Deleterious	Probably damaging	6.932315	33	0.332	0.000008345	1	119838
17	9143029	c.1559T>C	p.Val520Ala	NTR	missense	Deleterious	Possibly damaging	5.663844	26.7	0.375	0.000008348	1	65616
17	9143034	c.1567_1569del	p.Gln523del	NTR	inframe deletion	-	-	-	-	-	0.000008360	1	119622
17	9143061	c.1591G>C	p.Gly531Arg	NTR	missense	Deleterious	Probably damaging	7.157872	34	0.608	0.00003343	4	65546
17	9143136	c.1666C>G	p.Leu556Val	NTR	missense	Deleterious	Probably damaging	4.584348	24.4	0.426	0.000008738	1	63198
17	9143185	c.1715C>G	p.Ala572Gly	NTR	missense	Deleterious	Possibly damaging	4.846049	24.8	0.224	0.00001030	1	97054
17	9143215	c.1745G>T	p.Arg582Leu	NTR	missense	Deleterious	Possibly damaging	7.532915	34	0.246	0.00005168	4	42850
17	9143269	c.1799A>C	p.Lys600Thr	NTR	missense	Deleterious	Probably damaging	5.526176	26.3	0.146	0.00002017	1	49582
17	9143280	c.1810G>A	p.Ala604Thr	Cter	missense	Deleterious	Possibly damaging	4.280305	24.0	0.114	0.00007407	2	13192

Supplemental Table 5: List of rare *NTN1* variants present in ExAC (allele frequency<0.1%) and predicted pathogenic by both SIFT and PolyPhen-2.

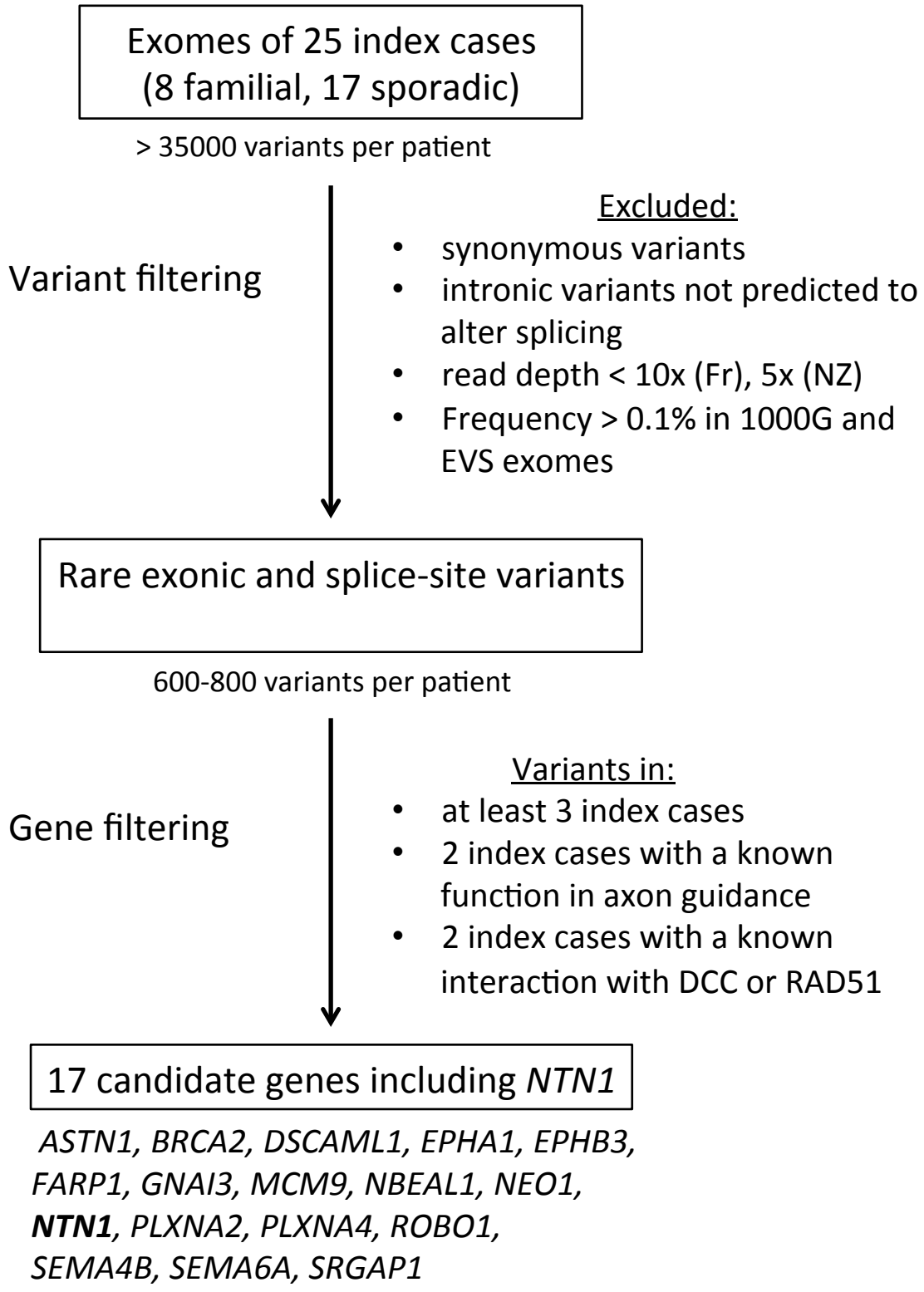
Chr, chromosome; Nter, Laminin N-Terminal domain; EGF-1, Laminin EGF-like 1 domain; EGF-2, Laminin EGF-like 2 domain; EGF-3, Laminin EGF-like 3 domain; NTR, Netrin domain; Cter, C-terminal domain; PolyPhen-2, Polymorphism Phenotyping v2; ExAC, Exome Aggregation Consortium: http://exac.broadinstitute.org; CADD score, Combined Annotation Dependent Depletion: http://cadd.gs.washington.edu/; REVEL, Rare Exome Variants Ensemble Learner: https://sites.google.com/site/revelgenomics/.

NTN1-2A_For	GGACTTTGGGGGAGAGAGG
NTN1-2A_Rev	TGCGTGGAGTAGAACTGGAA
NTN1-2B_For	ACCTACGTGAGCCTGCAGTT
NTN1-2B_Rev	CTTCTTGGCTTCGCAGAGAG
NTN1-3_For	TGCTAGTGGAGAAGGGAGGA
NTN1-3_Rev	CCCCTTTGTTTTGGCTTACA
NTN1-4_For	ATCGCTGCTCTTCCTCCAG
NTN1-4_Rev	CGACACAGTGAGACTCAACCA
NTN1-5_For	GTCTGTGCTGGGCTCATTCT
NTN1-5_Rev	ACCCAGGATGCCACTCATAC
NTN1-6_For	AGGCCTCTGGCTATTTAGGG
NTN1-6_Rev	ATCGGTCACAGGGTCTTCAC
NTN1-7_For	TGTTAGCAGGTGGGGGTCTA
NTN1-7_Rev	CGTCTCTGCTCTGGAAGGAG

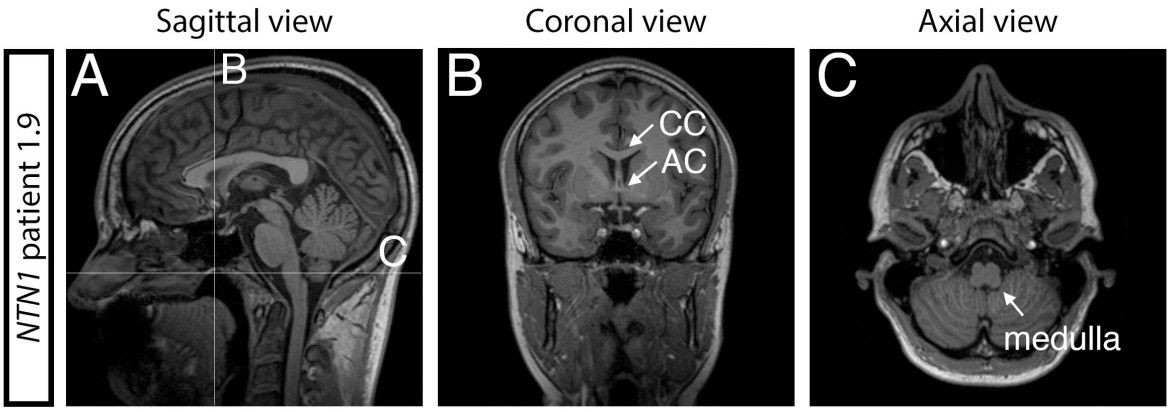
Supplemental Table 6: Primers used to amplify the coding and flanking regions of *NTN1*.

NTN1-human-C601R_For	GCTAGGCCTTCTTGCGCTTGCCCTTCTTCTC
NTN1-human-C601R_Rev	GAGAAGAAGGGCAAGCGCAAGAAGGCCTAGC
NTN1-mouse-C601R_For	GCTAGGCCTTCTTGCGCTTGCCCTTCTTCTC
NTN1-mouse-C601R_Rev	GAGAAGAAGGGCAAGCGCAAGAAGGCCTAGC
NTN1-human-I518del_For	CCCTGCTTATACACGGAGATGTTCACCGTGAACT
NTN1-human-I518del_Rev	AGTTCACGGTGAACATCTCCGTGTATAAGCAGGG
NTN1-mouse-I518del_For	CCTGCTTGTACACGGAGATGTTCACGGTGAAC
NTN1-mouse-I518del_Rev	GTTCACCGTGAACATCTCCGTGTACAAGCAGG
NTN1-human-C601S_For	CGCTAGGCCTTCTTGGACTTGCCCTTCTTCT
NTN1-human-C601S_Rev	AGAAGAAGGGCAAGTCCAAGAAGGCCTAGCG
NTN1-mouse-C601S_For	CGCTAGGCCTTCTTGGACTTGCCCTTCTTCT
NTN1-mouse-C601S_Rev	AGAAGAAGGGCAAGTCCAAGAAGGCCTAGCG

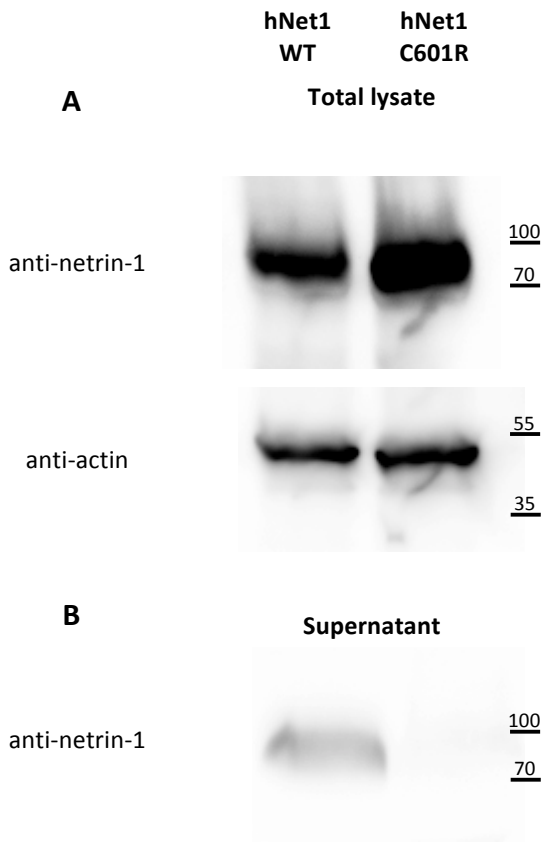
Supplemental Table 7: Primers used to introduce the 3 mutations by site-directed mutagenesis in *NTN1* construct.



Supplemental Figure 1: Flow chart of the exome data analysis and list of the 17 candidate genes.



Supplemental Figure 2: Anatomical images of the central nervous system of *NTN1* patient 1.9 harbouring a C601R mutation. (A) Sagittal section; (B) coronal section; (C) horizontal section (planes indicated in A). Note the presence of normal corpus callosum (CC), anterior commissure (AC) and medulla in *NTN1* patient 1.9.



Supplemental Figure 3: HEK293 cells were transfected with human WT and mutated netrin-1 **(A, B)** plasmids and grown for 48 hours. Western blot showed the presence of the WT and mutated proteins in total lysates at the expected molecular weight **(A)** but the absence of the mutated proteins in the supernatant, contrary to WT **(B)**. Antibodies were anti-netrin-1 (A, B) and anti-actin (A). The experiments were replicated 3 times (n=3).