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Supplemental Data

Targeted High-Throughput Sequencing Identifies Mutations in *atlastin-1* as a Cause of Hereditary Sensory Neuropathy Type I

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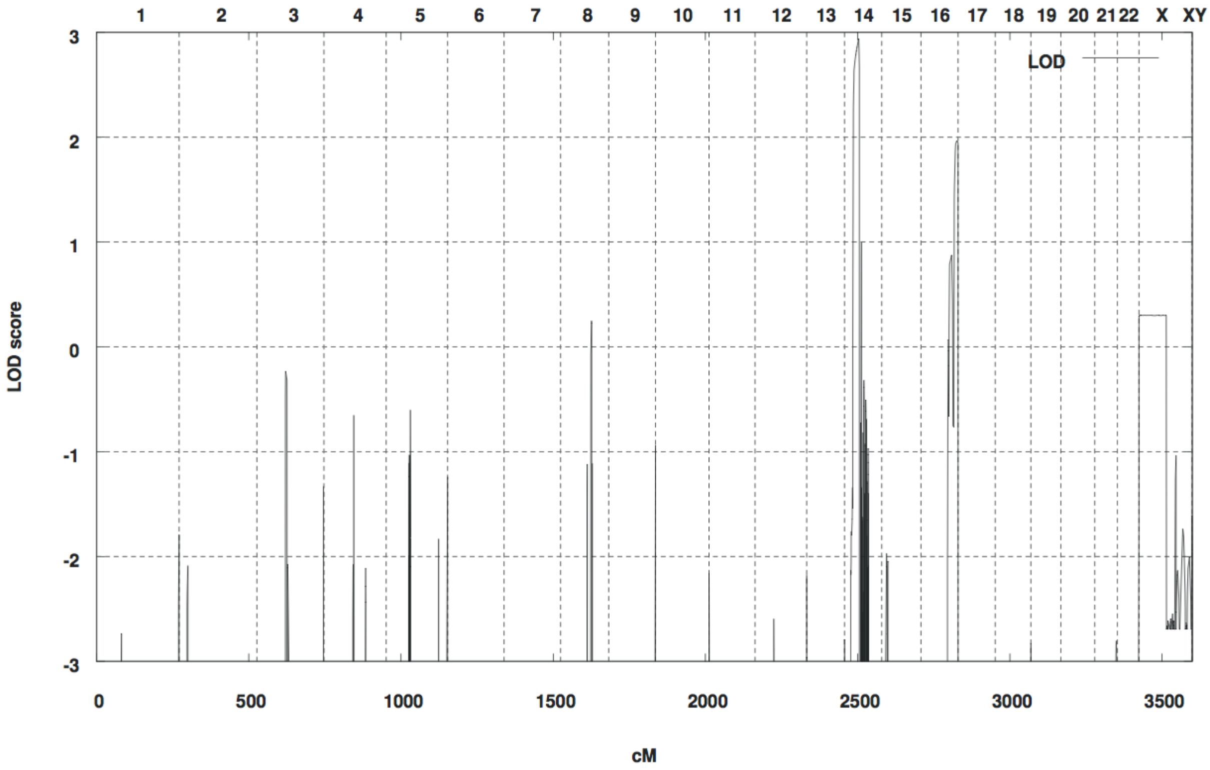


Figure S1. Mapping a HSN 1 locus.
The graph represents a parametric LOD score on the y axis in relation to genetic position on the x axis. Human chromosomes are concatenated from p-ter (left) to q-ter (right) on the x axis, and the genetic distance is given in cM. This scan identified a single region on chromosome 14 segregating with the disease based on the hypothesis of autosomal dominant inheritance and 100 % penetrance of the mutation.

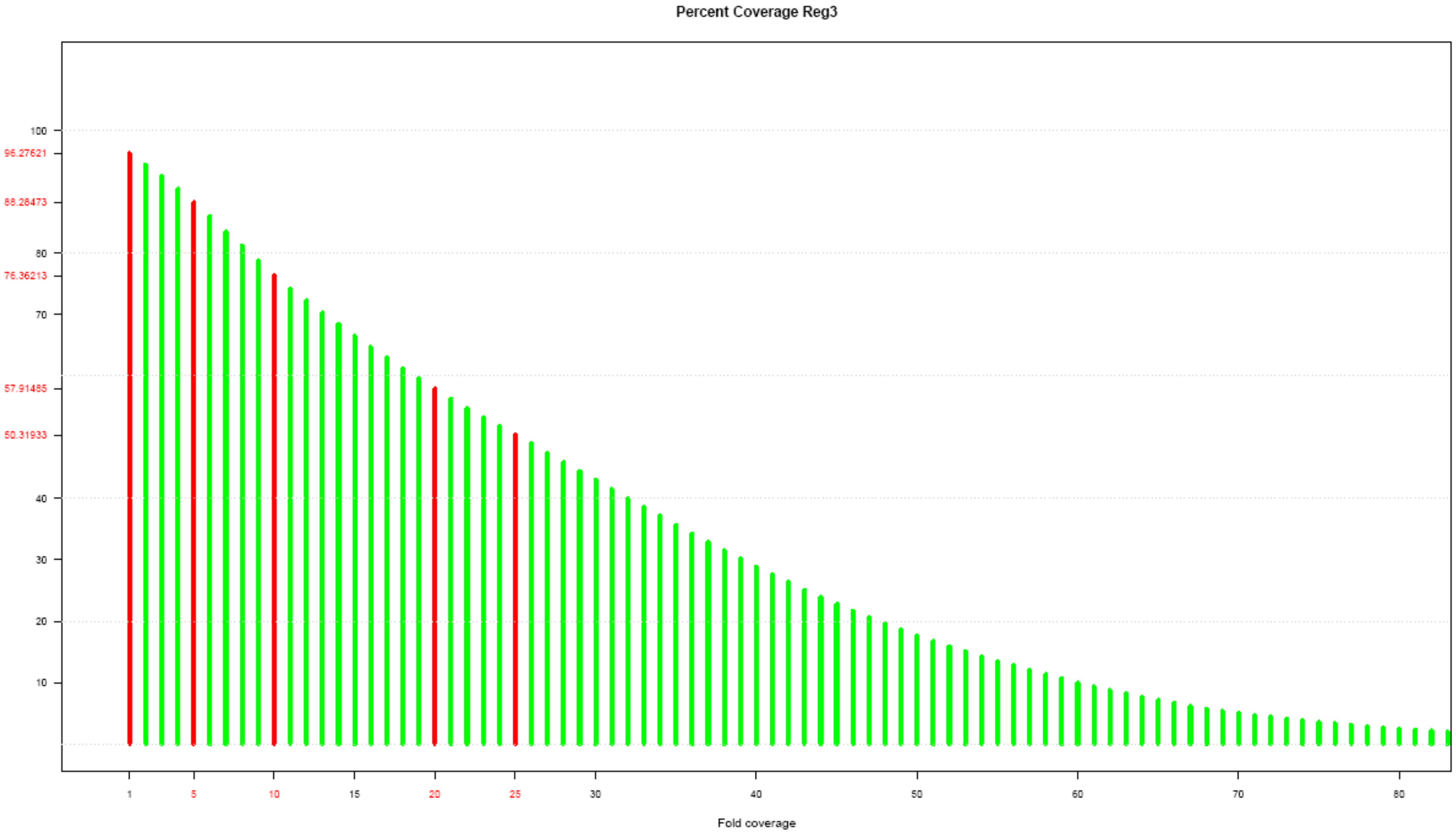
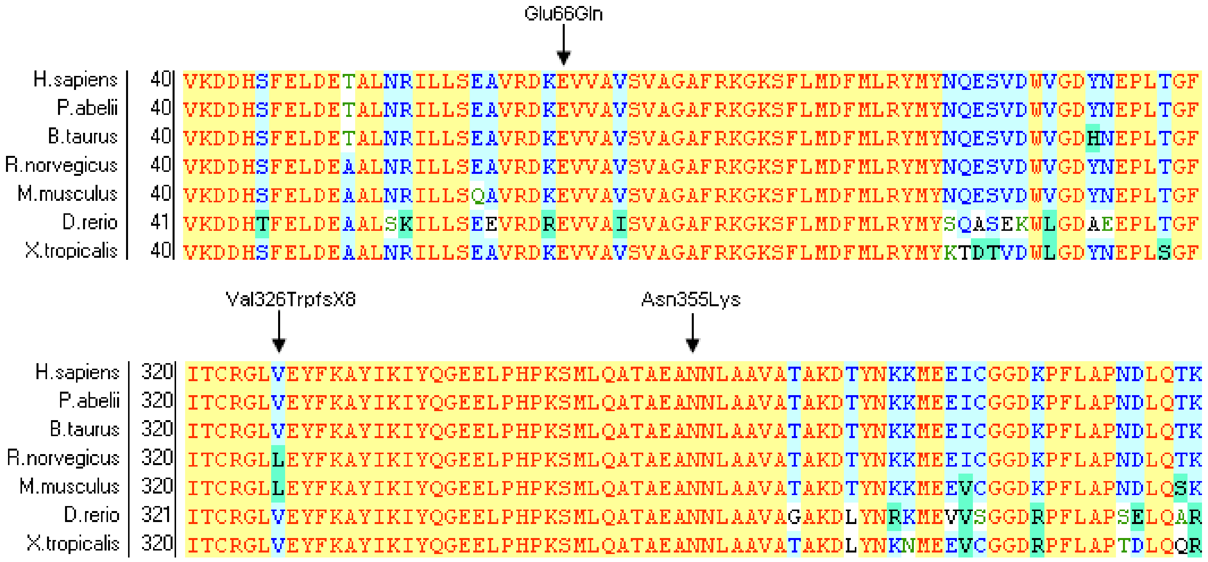


Figure S2. Sequence coverage of the disease linked interval (chr.14: bp 41,334,596- 55,611,787). Captured DNA was sequenced to a calculated average depth of 30-fold. De-facto coverage (observed) was determined at the per nucleotide level. The x-axis indicates the calculated coverage per target nucleotide and the y-axis represents the percentage of sequenced target nucleotides. Red bars highlight the observed sequencing depth of 25-, 20-, 10-, 5- and 1-fold. 76.36% of the target nucleotides were sequenced to a minimum depth of 10-fold.



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H.sapiens    | 40 | VKDDHSFELDETALNRILLSEAVRDKEVVAVSVAGAFRKGKSFLMDFMLRYMYNQESVDWVGDYNEPLTGF
P.abelii     | 40 | VKDDHSFELDETALNRILLSEAVRDKEVVAVSVAGAFRKGKSFLMDFMLRYMYNQESVDWVGDYNEPLTGF
B.taurus     | 40 | VKDDHSFELDETALNRILLSEAVRDKEVVAVSVAGAFRKGKSFLMDFMLRYMYNQESVDWVGDHNEPLTGF
R.norvegicus | 40 | VKDDHSFELDEAALNRILLSEAVRDKEVVAVSVAGAFRKGKSFLMDFMLRYMYNQESVDWVGDYNEPLTGF
M.musculus   | 40 | VKDDHSFELDEAALNRILLSQAVRDKEVVAVSVAGAFRKGKSFLMDFMLRYMYNQESVDWVGDYNEPLTGF
D.rerio      | 41 | VKDDHTFELDEAALSKILLSEEVRDREVVAISVAGAFRKGKSFLMDFMLRYMYSQASEKWLGDAEEPLTGF
X.tropicalis | 40 | VKDDHSFELDEAALNRILLSEAVRDKEVVAVSVAGAFRKGKSFLMDFMLRYMYKTDTVDWLGDYNEPLSGF

H.sapiens    | 320 | ITCRGLVEYFKAYIKIYQGEELPHPKSMLQATAEANNLAAVATAKDTYNKKMEEICGGDKPFLAPNDLQTK
P.abelii     | 320 | ITCRGLVEYFKAYIKIYQGEELPHPKSMLQATAEANNLAAVATAKDTYNKKMEEICGGDKPFLAPNDLQTK
B.taurus     | 320 | ITCRGLVEYFKAYIKIYQGEELPHPKSMLQATAEANNLAAVATAKDTYNKKMEEICGGDKPFLAPNDLQTK
R.norvegicus | 320 | ITCRGLLEYFKAYIKIYQGEELPHPKSMLQATAEANNLAAVATAKDTYNKKMEEICGGDKPFLAPNDLQTK
M.musculus   | 320 | ITCRGLLEYFKAYIKIYQGEELPHPKSMLQATAEANNLAAVATAKDTYNKKMEEVCGGDKPFLAPNDLQSK
D.rerio      | 321 | ITCRGLVEYFKAYIKIYQGEELPHPKSMLQATAEANNLAAVAGAKDLYNRKMEVVSGGDRPFLAPSELQAR
X.tropicalis | 320 | ITCRGLVEYFKAYIKIYQGEELPHPKSMLQATAEANNLAAVATAKDLYNKNMEEVCGGDRPFLAPTDLQQR
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Figure S3. Evolutionary conservation of the atlastin-1 protein.
The atlastin-1 amino acid sequence was compared to its orthologues and paralogues with VectorNTI software. *H. sapiens* (NP_056999.2), *P. abelii* (orangutan; NP_001126926.1), *B. taurus* (bovine; NP_001029803.1), *R. norvegicus* (NP_001009831.1.), *M. musculus* (NP_848743.1), *D. rerio* (zebrafish; NP_001139172.1), *X. tropicalis* (frog; NP_001072222.1). The arrows indicate mutation sites found in exons 2, 9 and 11. Amino acid residues numbers are at the left.

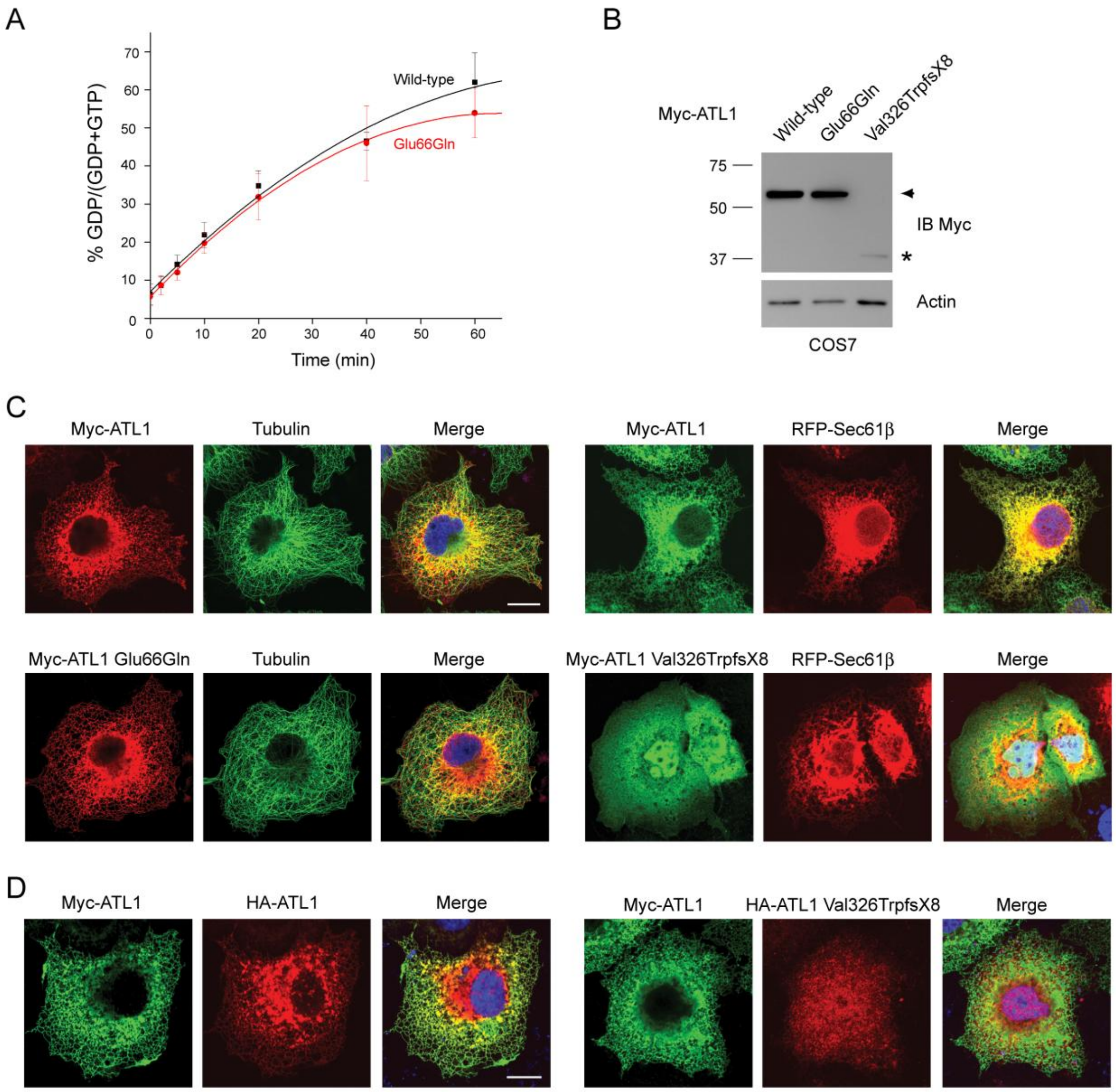


Figure S4. ER morphology upon overexpression of the Glu66Gln and the Val326TrpfsX8 atlastin-1 mutants

Neither Glu66Gln atlastin-1 nor Val326TrpfsX8 atlastin-1 disrupt ER morphology upon overexpression.

(A) Wild-type or Glu66Gln atlastin-1 (ATL1) were immunopurified from COS7 cells, and GTP hydrolysis *in vitro* plotted as a function of time (means ± SD).

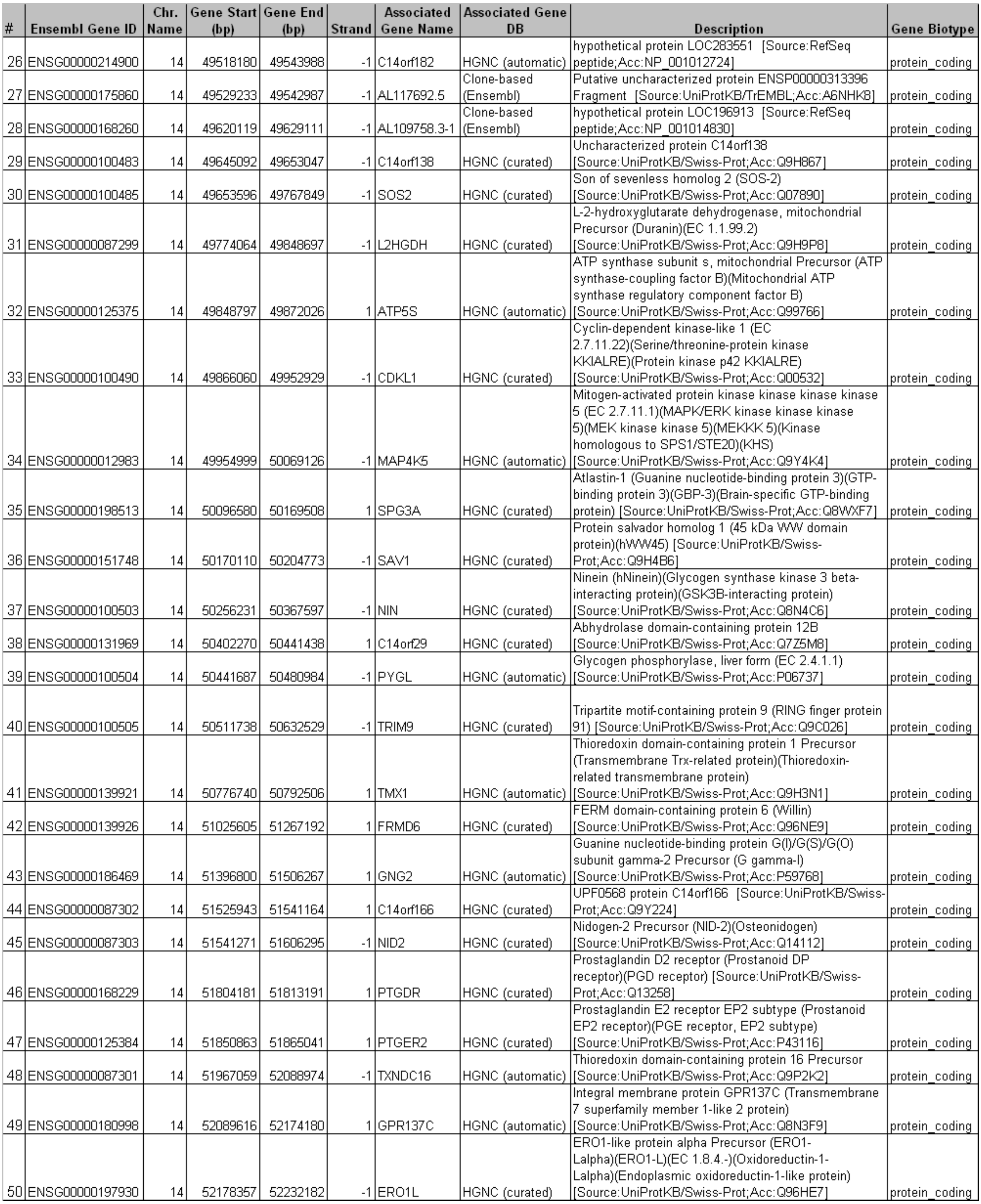
(B) COS7 cells transfected with Myc-tagged wild-type, Glu66Gln (arrowhead) or Val326TrpfsX8 atlastin-1 (asterisk) were immunoblotted (IB) for Myc-epitope. Actin levels were monitored as a control for protein loading. Migrations of molecular mass standards are at the left.

(C) COS7 cells were transfected with Myc-tagged wild-type or Glu66Gln atlastin-1 (left panels) and immunostained for Myc-epitope (red) and β-tubulin (green). Myc-tagged wild-type atlastin-1 and Val326TrpfsX8 atlastin-1 were co-transfected with the ER marker RFP-Sec61β (red; right panels) and immunostained for Myc-epitope (green). Merged images are at the right of each panel set with DAPI nuclear staining (blue) included.

(D) COS7 cells were co-transfected with Myc-tagged wild-type and either HA-tagged wild-type atlastin-1 (left panels) or Val326TrpfsX8 atlastin-1 (right panels) and immunostained for Myc-epitope (green) and HA-epitope (red). Merged images are at the right, with DAPI nuclear staining included. Bars, 20 µm.

#	Ensembl Gene ID	Chr. Name	Gene Start (bp)	Gene End (bp)	Strand	Associated Gene Name	Associated Gene DB	Description	Gene Biotype
1	ENSG00000165379	14	41146523	41443498	1	LRFN5	HGNC (curated)	Leucine-rich repeat and fibronectin type-III domain-containing protein 5 Precursor [Source:UniProtKB/Swiss-Prot;Acc:Q96NI6]	protein_coding
2	ENSG00000189139	14	44043295	44046232	-1	C14orf155	HGNC (curated)	Fibrous sheath CABYR-binding protein [Source:UniProtKB/Swiss-Prot;Acc:Q5H9T9]	protein_coding
3	ENSG00000179476	14	44436257	44446210	1	C14orf28	HGNC (automatic)	Uncharacterized protein C14orf28 (Dopamine receptor-interacting protein 1) [Source:UniProtKB/Swiss-Prot;Acc:Q4W4Y0]	protein_coding
4	ENSG00000179454	14	44463298	44500929	-1	KLHL28	HGNC (curated)	Kelch-like protein 28 (BTB/POZ domain-containing protein 5) [Source:UniProtKB/Swiss-Prot;Acc:Q9NXS3]	protein_coding
5	ENSG00000198718	14	44501166	44613384	1	FAM179B	HGNC (curated)	Protein FAM179B [Source:UniProtKB/Swiss-Prot;Acc:Q9Y4F4]	protein_coding
6	ENSG00000185246	14	44623080	44654554	1	PRPF39	HGNC (curated)	Pre-mRNA-processing factor 39 (PRP39 homolog) [Source:UniProtKB/Swiss-Prot;Acc:Q86UA1]	protein_coding
7	ENSG00000214921	14	44638408	44640897	1	AL121809.6-1	Clone-based (Ensembl)	Putative uncharacterized protein ENSP00000382190 Fragment [Source:UniProtKB/TrEMBL;Acc:A8MXI1]	protein_coding
8	ENSG00000100442	14	44654856	44674272	-1	FKBP3	HGNC (curated)	FK506-binding protein 3 (EC 5.2.1.8)(Peptidyl-prolyl cis-trans isomerase)(PPIase)(Rotamase)(25 kDa FKBP)(FKBP-25)(Rapamycin-selective 25 kDa immunophilin) [Source:UniProtKB/Swiss-Prot;Acc:Q00688]	protein_coding
9	ENSG00000214919	14	44665321	44670589	-1	AL121809.6-2	Clone-based (Ensembl)	Putative uncharacterized protein ENSP00000382186 Fragment [Source:UniProtKB/TrEMBL;Acc:A8MU49]	protein_coding
10	ENSG00000187790	14	44674900	44739835	1	FANCM	HGNC (automatic)	Fanconi anemia group M protein (Protein FACM)(EC 3.6.1.-)(ATP-dependent RNA helicase FANCM)(Fanconi anemia-associated polypeptide of 250 kDa)(FAAP250)(Protein Hef ortholog) [Source:UniProtKB/Swiss-Prot;Acc:Q8IYD8]	protein_coding
11	ENSG00000129534	14	44742144	44792146	-1	C14orf106	HGNC (curated)	Mis18-binding protein 1 (P243) [Source:UniProtKB/Swiss-Prot;Acc:Q6P0N0]	protein_coding
12	ENSG00000165496	14	46190045	46190689	-1	RPL10L	HGNC (automatic)	60S ribosomal protein L10-like [Source:UniProtKB/Swiss-Prot;Acc:Q96L21]	protein_coding
13	ENSG00000139915	14	46379045	47213703	-1	MDGA2	HGNC (curated)	MAM domain-containing glycosylphosphatidylinositol anchor protein 2 Precursor (MAM domain-containing protein 1) [Source:UniProtKB/Swiss-Prot;Acc:Q7Z553]	protein_coding
14	ENSG00000213741	14	49113809	49122844	-1	RPS29	HGNC (curated)	40S ribosomal protein S29 [Source:UniProtKB/Swiss-Prot;Acc:P62273]	protein_coding
15	ENSG00000125385	14	49113809	49122844	-1	AL139099.3-2	Clone-based (Ensembl)	Putative uncharacterized protein ENSP00000346229 [Source:UniProtKB/TrEMBL;Acc:A6NBZ9]	protein_coding
16	ENSG00000165501	14	49135165	49151705	1	PPIL5	HGNC (curated)	Peptidylprolyl isomerase-like 5 (LRR-repeat protein 1)(LRR-1)(4-1BB-mediated-signaling molecule)(4-1BBlrr) [Source:UniProtKB/Swiss-Prot;Acc:Q96L50]	protein_coding
17	ENSG00000165502	14	49155159	49157099	-1	RPL36AL	HGNC (curated)	60S ribosomal protein L36a-like [Source:UniProtKB/Swiss-Prot;Acc:Q969Q0]	protein_coding
18	ENSG00000168282	14	49157239	49159948	1	MGAT2	HGNC (curated)	Alpha-1,6-mannosyl-glycoprotein 2-beta-N-acetylglucosaminyltransferase (EC 2.4.1.143)(Mannoside acetylglucosaminyltransferase 2)(N-glycosyl-oligosaccharide-glycoprotein N-acetylglucosaminyltransferase II)(Beta-1,2-N-acetylglucosaminyltransferase II)(GlcNAc-T II)(GNT-II) [Source:UniProtKB/Swiss-Prot;Acc:Q10469]	protein_coding
19	ENSG00000165506	14	49161642	49171698	-1	C14orf104	HGNC (curated)	Protein kintoun [Source:UniProtKB/Swiss-Prot;Acc:Q9NVR5]	protein_coding
20	ENSG00000100479	14	49180028	49224685	-1	POLE2	HGNC (automatic)	DNA polymerase epsilon subunit 2 (DNA polymerase II subunit 2)(EC 2.7.7.7)(DNA polymerase epsilon subunit B) [Source:UniProtKB/Swiss-Prot;Acc:P56282]	protein_coding
21	ENSG00000197776	14	49229610	49289610	1	KLHDC1	HGNC (curated)	Kelch domain-containing protein 1 [Source:UniProtKB/Swiss-Prot;Acc:Q8N7A1]	protein_coding
22	ENSG00000165516	14	49304537	49319606	1	KLHDC2	HGNC (curated)	Kelch domain-containing protein 2 (Hepatocellular carcinoma-associated antigen 33)(Host cell factor homolog LCP)(Host cell factor-like protein 1)(HCLP-1) [Source:UniProtKB/Swiss-Prot;Acc:Q9Y2U9]	protein_coding
23	ENSG00000165525	14	49320282	49389289	-1	SDCCAG1	HGNC (curated)	Serologically defined colon cancer antigen 1 (Antigen NY-CO-1) [Source:UniProtKB/Swiss-Prot;Acc:O60524]	protein_coding
24	ENSG00000197502	14	49370560	49381302	-1	AL627171.1-1	Clone-based (Ensembl)	Putative uncharacterized protein ENSP00000351653 Fragment [Source:UniProtKB/TrEMBL;Acc:A6NP80]	protein_coding
25	ENSG00000165527	14	49429486	49433522	1	ARF6	HGNC (curated)	ADP-ribosylation factor 6 [Source:UniProtKB/Swiss-Prot;Acc:P62330]	protein_coding

Table S1. List of sequence-capture protein-encoding target genes (n=75) located within the linkage region (chr14: bp41,334,596 – 55,611,787).

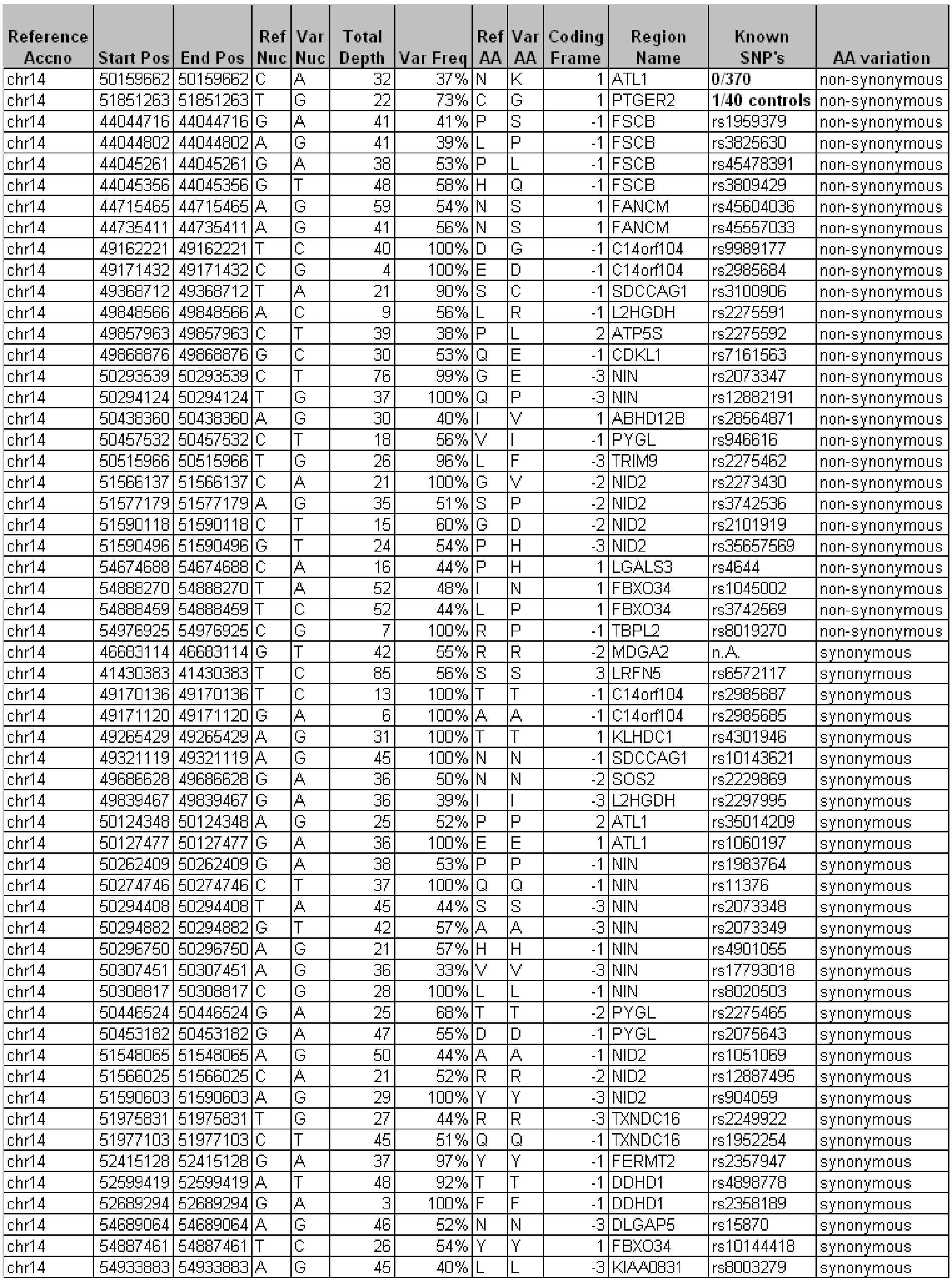


#	Ensembl Gene ID	Chr. Name	Gene Start (bp)	Gene End (bp)	Strand	Associated Gene Name	Associated Gene DB	Description	Gene Biotype
26	ENSG00000214900	14	49518180	49543988	-1	C14orf182	HGNC (automatic)	hypothetical protein LOC283551 [Source:RefSeq peptide;Acc:NP_001012724]	protein_coding
27	ENSG00000175860	14	49529233	49542987	-1	AL117692.5	Clone-based (Ensembl)	Putative uncharacterized protein ENSP00000313396 Fragment [Source:UniProtKB/TrEMBL;Acc:A6NHK8]	protein_coding
28	ENSG00000168260	14	49620119	49629111	-1	AL109758.3-1	Clone-based (Ensembl)	hypothetical protein LOC196913 [Source:RefSeq peptide;Acc:NP_001014830]	protein_coding
29	ENSG00000100483	14	49645092	49653047	-1	C14orf138	HGNC (curated)	Uncharacterized protein C14orf138 [Source:UniProtKB/Swiss-Prot;Acc:Q9H867]	protein_coding
30	ENSG00000100485	14	49653596	49767849	-1	SOS2	HGNC (curated)	Son of sevenless homolog 2 (SOS-2) [Source:UniProtKB/Swiss-Prot;Acc:Q07890]	protein_coding
31	ENSG00000087299	14	49774064	49848697	-1	L2HGDH	HGNC (curated)	L-2-hydroxyglutarate dehydrogenase, mitochondrial Precursor (Duranin)(EC 1.1.99.2) [Source:UniProtKB/Swiss-Prot;Acc:Q9H9P8]	protein_coding
32	ENSG00000125375	14	49848797	49872026	1	ATP5S	HGNC (automatic)	ATP synthase subunit s, mitochondrial Precursor (ATP synthase-coupling factor B)(Mitochondrial ATP synthase regulatory component factor B) [Source:UniProtKB/Swiss-Prot;Acc:Q99766]	protein_coding
33	ENSG00000100490	14	49866060	49952929	-1	CDKL1	HGNC (curated)	Cyclin-dependent kinase-like 1 (EC 2.7.11.22)(Serine/threonine-protein kinase KKIALRE)(Protein kinase p42 KKIALRE) [Source:UniProtKB/Swiss-Prot;Acc:Q00532]	protein_coding
34	ENSG00000012983	14	49954999	50069126	-1	MAP4K5	HGNC (automatic)	Mitogen-activated protein kinase kinase kinase kinase 5 (EC 2.7.11.1)(MAPK/ERK kinase kinase kinase 5)(MEK kinase kinase 5)(MEKKK 5)(Kinase homologous to SPS1/STE20)(KHS) [Source:UniProtKB/Swiss-Prot;Acc:Q9Y4K4]	protein_coding
35	ENSG00000198513	14	50096580	50169508	1	SPG3A	HGNC (curated)	Atlastin-1 (Guanine nucleotide-binding protein 3)(GTP-binding protein 3)(GBP-3)(Brain-specific GTP-binding protein) [Source:UniProtKB/Swiss-Prot;Acc:Q8WXF7]	protein_coding
36	ENSG00000151748	14	50170110	50204773	-1	SAV1	HGNC (curated)	Protein salvador homolog 1 (45 kDa WW domain protein)(hWW45) [Source:UniProtKB/Swiss-Prot;Acc:Q9H4B6]	protein_coding
37	ENSG00000100503	14	50256231	50367597	-1	NIN	HGNC (curated)	Ninein (hNinein)(Glycogen synthase kinase 3 beta-interacting protein)(GSK3B-interacting protein) [Source:UniProtKB/Swiss-Prot;Acc:Q8N4C6]	protein_coding
38	ENSG00000131969	14	50402270	50441438	1	C14orf29	HGNC (curated)	Abhydrolase domain-containing protein 12B [Source:UniProtKB/Swiss-Prot;Acc:Q7Z5M8]	protein_coding
39	ENSG00000100504	14	50441687	50480984	-1	PYGL	HGNC (automatic)	Glycogen phosphorylase, liver form (EC 2.4.1.1) [Source:UniProtKB/Swiss-Prot;Acc:P06737]	protein_coding
40	ENSG00000100505	14	50511738	50632529	-1	TRIM9	HGNC (curated)	Tripartite motif-containing protein 9 (RING finger protein 91) [Source:UniProtKB/Swiss-Prot;Acc:Q9C026]	protein_coding
41	ENSG00000139921	14	50776740	50792506	1	TMX1	HGNC (automatic)	Thioredoxin domain-containing protein 1 Precursor (Transmembrane Trx-related protein)(Thioredoxin-related transmembrane protein) [Source:UniProtKB/Swiss-Prot;Acc:Q9H3N1]	protein_coding
42	ENSG00000139926	14	51025605	51267192	1	FRMD6	HGNC (curated)	FERM domain-containing protein 6 (Willin) [Source:UniProtKB/Swiss-Prot;Acc:Q96NE9]	protein_coding
43	ENSG00000186469	14	51396800	51506267	1	GNG2	HGNC (automatic)	Guanine nucleotide-binding protein G(I)/G(S)/G(O) subunit gamma-2 Precursor (G gamma-I) [Source:UniProtKB/Swiss-Prot;Acc:P59768]	protein_coding
44	ENSG00000087302	14	51525943	51541164	1	C14orf166	HGNC (curated)	UPF0568 protein C14orf166 [Source:UniProtKB/Swiss-Prot;Acc:Q9Y224]	protein_coding
45	ENSG00000087303	14	51541271	51606295	-1	NID2	HGNC (curated)	Nidogen-2 Precursor (NID-2)(Osteonidogen) [Source:UniProtKB/Swiss-Prot;Acc:Q14112]	protein_coding
46	ENSG00000168229	14	51804181	51813191	1	PTGDR	HGNC (curated)	Prostaglandin D2 receptor (Prostanoid DP receptor)(PGD receptor) [Source:UniProtKB/Swiss-Prot;Acc:Q13258]	protein_coding
47	ENSG00000125384	14	51850863	51865041	1	PTGER2	HGNC (curated)	Prostaglandin E2 receptor EP2 subtype (Prostanoid EP2 receptor)(PGE receptor, EP2 subtype) [Source:UniProtKB/Swiss-Prot;Acc:P43116]	protein_coding
48	ENSG00000087301	14	51967059	52088974	-1	TXNDC16	HGNC (automatic)	Thioredoxin domain-containing protein 16 Precursor [Source:UniProtKB/Swiss-Prot;Acc:Q9P2K2]	protein_coding
49	ENSG00000180998	14	52089616	52174180	1	GPR137C	HGNC (automatic)	Integral membrane protein GPR137C (Transmembrane 7 superfamily member 1-like 2 protein) [Source:UniProtKB/Swiss-Prot;Acc:Q8N3F9]	protein_coding
50	ENSG00000197930	14	52178357	52232182	-1	ERO1L	HGNC (curated)	ERO1-like protein alpha Precursor (ERO1-Lalpha)(ERO1-L)(EC 1.8.4.-)(Oxidoreductin-1-Lalpha)(Endoplasmic oxidoreductin-1-like protein) [Source:UniProtKB/Swiss-Prot;Acc:Q96HE7]	protein_coding

Table S1. continued

#	Ensembl Gene ID	Chr. Name	Gene Start (bp)	Gene End (bp)	Strand	Associated Gene Name	Associated Gene DB	Description	Gene Biotype
51	ENSG00000100519	14	52243668	52264463	1	PSMC6	HGNC (curated)	26S protease regulatory subunit S10B (Proteasome 26S subunit ATPase 6)(Proteasome subunit p42) [Source:UniProtKB/Swiss-Prot;Acc:P62333]	protein_coding
52	ENSG00000198252	14	52266675	52311409	1	STYX	HGNC (curated)	Serine/threonine/tyrosine-interacting protein (Protein tyrosine phosphatase-like protein) [Source:UniProtKB/Swiss-Prot;Acc:Q8WUJ0]	protein_coding
53	ENSG00000100522	14	52311662	52328133	-1	GNPNAT1	HGNC (curated)	Glucosamine 6-phosphate N-acetyltransferase (EC 2.3.1.4)(Phosphoglucosamine transacetylase)(Phosphoglucosamine acetylase) [Source:UniProtKB/Swiss-Prot;Acc:Q96EK6]	protein_coding
54	ENSG00000073712	14	52393736	52487460	-1	PLEKHC1	HGNC (curated)	Fermitin family homolog 2 (Pleckstrin homology domain-containing family C member 1)(Kindlin-2)(Mitogen-inducible gene 2 protein)(MIG-2) [Source:UniProtKB/Swiss-Prot;Acc:Q96AC1]	protein_coding
55	ENSG00000214855	14	52479391	52483939	-1	AL352979.4	Clone-based (Ensembl)	Putative uncharacterized protein ENSP00000382076 Fragment [Source:UniProtKB/TrEMBL;Acc:A8MVM4]	protein_coding
56	ENSG00000100523	14	52580436	52689750	-1	DDHD1	HGNC (curated)	Phospholipase DDHD1 (EC 3.1.1.-)(DDHD domain-containing protein 1)(Phosphatidic acid-preferring phospholipase A1 homolog)(PA-PLA1) [Source:UniProtKB/Swiss-Prot;Acc:Q8NEL9]	protein_coding
57	ENSG00000125378	14	53486204	53493279	-1	BMP4	HGNC (curated)	Bone morphogenetic protein 4 Precursor (BMP-4)(BMP-2B) [Source:UniProtKB/Swiss-Prot;Acc:P12644]	protein_coding
58	ENSG00000100526	14	53933476	53956682	1	CDKN3	HGNC (curated)	Cyclin-dependent kinase inhibitor 3 (EC 3.1.3.48)(EC 3.1.3.16)(CDK2-associated dual-specificity phosphatase)(Kinase-associated phosphatase)(Cyclin-dependent kinase-interacting protein 2)(Cyclin-dependent kinase interactor 1) [Source:UniProtKB/Swiss-Prot;Acc:Q16667]	protein_coding
59	ENSG00000214854	14	53938646	53968772	-1	AL049778.3	Clone-based (Ensembl)		protein_coding
60	ENSG00000100528	14	53956590	53977898	-1	CNIH	HGNC (curated)	Protein cornichon homolog (T-cell growth-associated molecule 77)(TGAM77) [Source:UniProtKB/Swiss-Prot;Acc:O95406]	protein_coding
61	ENSG00000197045	14	54010959	54025494	-1	GMFB	HGNC (curated)	Glia maturation factor beta (GMF-beta) [Source:UniProtKB/Swiss-Prot;Acc:P60983]	protein_coding
62	ENSG00000100532	14	54046310	54075317	1	CGRRF1	HGNC (curated)	Cell growth regulator with RING finger domain protein 1 (Cell growth regulatory gene 19 protein)(RING finger protein 197) [Source:UniProtKB/Swiss-Prot;Acc:Q99675]	protein_coding
63	ENSG00000020577	14	54104387	54325595	1	SAMD4A	HGNC (automatic)	Sterile alpha motif domain-containing protein 4A [Source:UniProtKB/Swiss-Prot;Acc:Q9UPU9]	protein_coding
64	ENSG00000131979	14	54378476	54439292	-1	GCH1	HGNC (curated)	GTP cyclohydrolase 1 (EC 3.5.4.16)(GTP cyclohydrolase I)(GTP-CH-I) [Source:UniProtKB/Swiss-Prot;Acc:P30793]	protein_coding
65	ENSG00000198554	14	54476692	54563557	-1	WDHD1	HGNC (curated)	WD repeat and HMG-box DNA-binding protein 1 (Acidic nucleoplasmic DNA-binding protein 1)(And-1) [Source:UniProtKB/Swiss-Prot;Acc:O75717]	protein_coding
66	ENSG00000180008	14	54563594	54585957	1	SOCS4	HGNC (curated)	Suppressor of cytokine signaling 4 (SOCS-4)(Suppressor of cytokine signaling 7)(SOCS-7) [Source:UniProtKB/Swiss-Prot;Acc:Q8WXH5]	protein_coding
67	ENSG00000168175	14	54588110	54606665	1	MAPK1IP1L	HGNC (automatic)	MAPK-interacting and spindle-stabilizing protein-like (Mitogen-activated protein kinase 1-interacting protein 1-like) [Source:UniProtKB/Swiss-Prot;Acc:Q8NDC0]	protein_coding
68	ENSG00000131981	14	54665574	54681874	1	LGALS3	HGNC (automatic)	Galectin-3 (Galactose-specific lectin 3)(Mac-2 antigen)(IgE-binding protein)(35 kDa lectin)(Carbohydrate-binding protein 35)(CBP 35)(Laminin-binding protein)(Lectin L-29)(L-31)(Galactoside-binding protein)(GALBP) [Source:UniProtKB/Swiss-Prot;Acc:P17931]	protein_coding
69	ENSG00000126787	14	54684601	54728149	-1	DLGAP5	HGNC (curated)	Disks large-associated protein 5 (DAP-5)(Disks large-associated protein DLG7)(Discs large homolog 7)(Hepatoma up-regulated protein)(HURP) [Source:UniProtKB/Swiss-Prot;Acc:Q15398]	protein_coding
70	ENSG00000178974	14	54807832	54890080	1	FBXO34	HGNC (automatic)	F-box only protein 34 [Source:UniProtKB/Swiss-Prot;Acc:Q9NWN3]	protein_coding
71	ENSG00000126775	14	54902863	54948329	-1	KIAA0831	HGNC (automatic)	Uncharacterized protein KIAA0831 [Source:UniProtKB/Swiss-Prot;Acc:Q6ZNE5]	protein_coding
72	ENSG00000182521	14	54950733	54977074	-1	TBPL2	HGNC (curated)	TATA box-binding protein-like protein 2 (TBP-like protein 2)(TATA box-binding protein-related factor 3)(TBP-related factor 3) [Source:UniProtKB/Swiss-Prot;Acc:Q6SJ96]	protein_coding
73	ENSG00000186615	14	55113662	55116581	-1	C14orf33	HGNC (automatic)	Putative uncharacterized protein C14orf33 [Source:UniProtKB/Swiss-Prot;Acc:Q86SY8]	protein_coding
74	ENSG00000126777	14	55116678	55221054	1	KTN1	HGNC (curated)	Kinectin (Kinesin receptor)(CG-1 antigen) [Source:UniProtKB/Swiss-Prot;Acc:Q86UP2]	protein_coding
75	ENSG00000177350	14	55302716	55304187	1	AL355773.4	Clone-based (Ensembl)	Putative 60S ribosomal protein L13a-like MGC87657 [Source:UniProtKB/Swiss-Prot;Acc:Q6NVV1]	protein_coding

Table S1. continued



Reference Accno	Start Pos	End Pos	Ref Nuc	Var Nuc	Total Depth	Var Freq	Ref AA	Var AA	Coding Frame	Region Name	Known SNP's	AA variation
chr14	50159662	50159662	C	A	32	37%	N	K	1	ATL1	**0/370**	non-synonymous
chr14	51851263	51851263	T	G	22	73%	C	G	1	PTGER2	**1/40 controls**	non-synonymous
chr14	44044716	44044716	G	A	41	41%	P	S	-1	FSCB	rs1959379	non-synonymous
chr14	44044802	44044802	A	G	41	39%	L	P	-1	FSCB	rs3825630	non-synonymous
chr14	44045261	44045261	G	A	38	53%	P	L	-1	FSCB	rs45478391	non-synonymous
chr14	44045356	44045356	G	T	48	58%	H	Q	-1	FSCB	rs3809429	non-synonymous
chr14	44715465	44715465	A	G	59	54%	N	S	1	FANCM	rs45604036	non-synonymous
chr14	44735411	44735411	A	G	41	56%	N	S	1	FANCM	rs45557033	non-synonymous
chr14	49162221	49162221	T	C	40	100%	D	G	-1	C14orf104	rs9989177	non-synonymous
chr14	49171432	49171432	C	G	4	100%	E	D	-1	C14orf104	rs2985684	non-synonymous
chr14	49368712	49368712	T	A	21	90%	S	C	-1	SDCCAG1	rs3100906	non-synonymous
chr14	49848566	49848566	A	C	9	56%	L	R	-1	L2HGDH	rs2275591	non-synonymous
chr14	49857963	49857963	C	T	39	38%	P	L	2	ATP5S	rs2275592	non-synonymous
chr14	49868876	49868876	G	C	30	53%	Q	E	-1	CDKL1	rs7161563	non-synonymous
chr14	50293539	50293539	C	T	76	99%	G	E	-3	NIN	rs2073347	non-synonymous
chr14	50294124	50294124	T	G	37	100%	Q	P	-3	NIN	rs12882191	non-synonymous
chr14	50438360	50438360	A	G	30	40%	I	V	1	ABHD12B	rs28564871	non-synonymous
chr14	50457532	50457532	C	T	18	56%	V	I	-1	PYGL	rs946616	non-synonymous
chr14	50515966	50515966	T	G	26	96%	L	F	-3	TRIM9	rs2275462	non-synonymous
chr14	51566137	51566137	C	A	21	100%	G	V	-2	NID2	rs2273430	non-synonymous
chr14	51577179	51577179	A	G	35	51%	S	P	-2	NID2	rs3742536	non-synonymous
chr14	51590118	51590118	C	T	15	60%	G	D	-2	NID2	rs2101919	non-synonymous
chr14	51590496	51590496	G	T	24	54%	P	H	-3	NID2	rs35657569	non-synonymous
chr14	54674688	54674688	C	A	16	44%	P	H	1	LGALS3	rs4644	non-synonymous
chr14	54888270	54888270	T	A	52	48%	I	N	1	FBXO34	rs1045002	non-synonymous
chr14	54888459	54888459	T	C	52	44%	L	P	1	FBXO34	rs3742569	non-synonymous
chr14	54976925	54976925	C	G	7	100%	R	P	-1	TBPL2	rs8019270	non-synonymous
chr14	46683114	46683114	G	T	42	55%	R	R	-2	MDGA2	n.A.	synonymous
chr14	41430383	41430383	T	C	85	56%	S	S	3	LRFN5	rs6572117	synonymous
chr14	49170136	49170136	T	C	13	100%	T	T	-1	C14orf104	rs2985687	synonymous
chr14	49171120	49171120	G	A	6	100%	A	A	-1	C14orf104	rs2985685	synonymous
chr14	49265429	49265429	A	G	31	100%	T	T	1	KLHDC1	rs4301946	synonymous
chr14	49321119	49321119	A	G	45	100%	N	N	-1	SDCCAG1	rs10143621	synonymous
chr14	49686628	49686628	G	A	36	50%	N	N	-2	SOS2	rs2229869	synonymous
chr14	49839467	49839467	G	A	36	39%	I	I	-3	L2HGDH	rs2297995	synonymous
chr14	50124348	50124348	A	G	25	52%	P	P	2	ATL1	rs35014209	synonymous
chr14	50127477	50127477	G	A	36	100%	E	E	1	ATL1	rs1060197	synonymous
chr14	50262409	50262409	G	A	38	53%	P	P	-1	NIN	rs1983764	synonymous
chr14	50274746	50274746	C	T	37	100%	Q	Q	-1	NIN	rs11376	synonymous
chr14	50294408	50294408	T	A	45	44%	S	S	-3	NIN	rs2073348	synonymous
chr14	50294882	50294882	G	T	42	57%	A	A	-3	NIN	rs2073349	synonymous
chr14	50296750	50296750	A	G	21	57%	H	H	-1	NIN	rs4901055	synonymous
chr14	50307451	50307451	A	G	36	33%	V	V	-3	NIN	rs17793018	synonymous
chr14	50308817	50308817	C	G	28	100%	L	L	-1	NIN	rs8020503	synonymous
chr14	50446524	50446524	G	A	25	68%	T	T	-2	PYGL	rs2275465	synonymous
chr14	50453182	50453182	G	A	47	55%	D	D	-1	PYGL	rs2075643	synonymous
chr14	51548065	51548065	A	G	50	44%	A	A	-1	NID2	rs1051069	synonymous
chr14	51566025	51566025	C	A	21	52%	R	R	-2	NID2	rs12887495	synonymous
chr14	51590603	51590603	A	G	29	100%	Y	Y	-3	NID2	rs904059	synonymous
chr14	51975831	51975831	T	G	27	44%	R	R	-3	TXNDC16	rs2249922	synonymous
chr14	51977103	51977103	C	T	45	51%	Q	Q	-1	TXNDC16	rs1952254	synonymous
chr14	52415128	52415128	G	A	37	97%	Y	Y	-1	FERMT2	rs2357947	synonymous
chr14	52599419	52599419	A	T	48	92%	T	T	-1	DDHD1	rs4898778	synonymous
chr14	52689294	52689294	G	A	3	100%	F	F	-1	DDHD1	rs2358189	synonymous
chr14	54689064	54689064	A	G	46	52%	N	N	-3	DLGAP5	rs15870	synonymous
chr14	54887461	54887461	T	C	26	54%	Y	Y	1	FBXO34	rs10144418	synonymous
chr14	54933883	54933883	A	G	45	40%	L	L	-3	KIAA0831	rs8003279	synonymous

Table S2. Table of high-confidence sequence variations observed for patient II/6-U. Observed sequence variations (Var Nuc) are listed together with the reference nucleotide (Ref Nuc), number of reads at the respective position (Total Depth; min.>25%), observed variation frequency (Var Freq), resulting amino acid (AA) variation (Ref AA and Var AA), relevant gene annotation (Region/Gene Name, know SNP IDs, mutation type) and status after manual curation of read data.

Primer		Sequence	
ATL1-Ex1fw	5´	TCAGAGTCTGAGCGAACTGC	3´
ATL1-Ex1rv	5´	GTCTCCACAGAAGCAGAAAGTG	3´
ATL1-Ex2fw	5´	TGCACCCAGCATAAAATGAG	3´
ATL1-Ex2rv	5´	CAGAGAAAATTGGTCTGTGTAGTTT	3´
ATL1-Ex3fw	5´	TGAATTTCCTCTGGTCTGCA	3´
ATL1-Ex3rv	5´	CAAAGATCATGCTATAGGATGCTA	3´
ATL1_Ex4fw	5´	GGCATTCATGGCATGTGTAA	3´
ATL1_Ex4rv	5´	CACGAGAACTCGTATGCTAATTG	3´
ATL1-ex5fw	5´	ATTCCATCTCCAGAGCAGGT	3´
ATL1-ex5Rv	5´	GCTGTTCTCTGTTCTCGCTG	3´
ATL1-Ex6fw	5´	ACCTAGAGGGAAAAGTAAATGAAAG	3´
ATL1-Ex6rv	5´	ATTTTGCCTGGAACCAGAAT	3´
ATL1-Ex7fw	5´	TGACATAGCTCCATTCAGGC	3´
ATL1-Ex7rv	5´	TTACACTGGCTTTGAAACCTCT	3´
ATL1-Ex8fw	5´	GTGGCTCCTACGAGTGCTTT	3´
ATL1-Ex8rv	5´	CACAGAGATAAGAAGGTGAGGGT	3´
ATL1-Ex9fw	5´	GGGCAAGGAGAATCATTCAC	3´
ATL1-Ex9rv	5´	ACCTTTGCTCCCATATTATCG	3´
ATL1-Ex10fw	5´	TTTAAGAAGGGCCAGATTGG	3´
ATL1-Ex10rv	5´	AAGAGAATGAAAACCCTTTGGT	3´
ATL1-Ex11fw	5´	AATGTGAACTGCCTGTGGAA	3´
ATL1-Ex11rv	5´	GCCTTCAAAATTGTGCACAC	3´
ATL1-Ex12,13fw	5´	ATAGGGGGTGGAAAGATGTG	3´
ATL1-Ex12,13rv	5´	GGAAAATAGTTGTGTAGGACTTCAC	3´
ATL1-ex14fw	5´	AAACTGGATCCTCTGAGCCA	3´
ATL1-ex14rv	5´	CCCTGCTTAAAGTGGTATGTATTAC	3´
ATL1-Ex15fw	5´	GGGCAAAGTAGAAGCTCACTG	3´
ATL1-Ex15rv	5´	CCAAACGTGGAATATCACATG	3´

Table S3. Primer sequences.