Supplementary Material

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S1 The clinical characteristics of the families with known genetic forms of dystonia

Family	Clinical information	Gene
Families with DYT classified Mendelian forms of dystonia		
DYS-5	TR, M, CS AO infancy: involuntary head movements, 20s: left side dystonia, gait abnormalities, facial grimacing, jerking of the trunk and limbs, 20s: generalized dystonia, ACE-R 54/91, MMSE: 22/28 right pallidotomy AE 30s: generalized dystonia, dysphagia, dysarthria cMRI: normal	HPCA
DYS-56	TR Patient II.1, M AO: 60s AE 70s: dystonic hand tremor, MCI Patient II.3, M AO: 60s AE 70s: CD, MCI Patient II.4, F AO: 50s AE 60s: CD, MCI	TSPOAP1
DYS-66	TR, M, CS AO: Childhood AE: 20s, generalized dystonia	PRKRA
DYS-72	TR M AO: birth, febrile seizure, permanent tremor of the UL AE; 30s, myoclonus dystonia, cMRI: mega cisterna magna	SGCE

DYS-86	TR, M AO; 20s, generalized dystonia, DBS, AE 20s: CD	PRKRA
DYS-96	TR, M AO; childhood, left dystonic hand tremor, articulation difficulties, low speech volume AE: 20s, choreatic movements predominating in the UL, cervico-truncal dystonic postures, right sided rigidity, slow horizontal eye saccades cMRI: normal	KMT2B
DYS-98	TR, CS <u>Patient IV.3, M</u> AO: 20s, AE 30s : left arm dystonia, CD, cMRI: normal <u>Patient IV.6 M</u> AO : 30s: BSP, CD AE 30s , segmental dystonia, cMRI : normal	AOPEP
DYS-125	TR/BG <u>Patient III.5, F</u> AO: childhood, action tremor of the UL, AO: 50s, BSP, MCI (MMSE 21/30) <u>Patient IV.1, F</u> AO: childhood, involuntary paroxysmal non-epileptic movements including ataxia, choreoathetosis and dystonic postures, learning disabilities, IQ51 (normal>85) cMRI: normal, CSF/blood glucose ratio: 0,56 mg/dL, CSF lactate concentration: low-normal (1,28 mmol/L) AE 10-20 years: in average two episodes of paroxysmal, mainly exercise-induced dyskinesia per month lasting from several up to 20 minutes. ACE-R: deficits in fluency (6/14), but nearly normal cognition (attention 18/18, memory 19/26, language 22/26, visuospatial 14/16, total 79/100, cut-off 83/100)	SLC2A1
DYS-134	TR, M AO: 40s, writer's cramp, tremor of the right UL, symptoms fully disappear after alcohol consumption AE: 40s: action and postural tremor of the right hand, rapid fatiguing of effort with repetitive motor tasks resulting in dystonic postures, particularly during writing	GCH1

DYS-139	TR, M, CS AO: childhood, paroxysmal movement disorder, LL dystonia AE: 20s, generalized dystonia cMRI: normal	HPCA
DYS-148	TR Patient III.2, M AO: childhood , AE 30s: right hand-forearm dystonia, mainly manifest as WC Patient III.3, F AO: 20s, seizures (2x) without evident cause, AE: 30s, normal Patient III.4, M AO: childhood , AE: 20s: spasmodic dysphonia, mild CD	THAP1
Families with uncommon forms of dystonia		
DYS-68	TR, F, CS AO 50s: BSP, AE 50s: generalized dystonia, loss of weight Testing of plasma amino acids revealed elevated glycine.	PCCB
DYS-69	TR, F AO: birth AE: childhood, dystonic truncal posture, dyskinesic permanent movements of the UL, walking difficulties	CACNA1A
DYS-71	TR Patient III.1, M AO: childhood, involuntarily, repetitive twisting movements of the back, severe retrocollis, mild dysarthria, hyporeflexia, 21s: cervico-laryngeal cramps and permanent feeling of retching. restless, aggressive behaviour, incoherent speech, hallucinations, diagnosis of psychosis AE: 20s: truncal dystonia, irregular retrocollis, ataxia, choreoathetotic movements of the UL, ACE-R at 42/100 (cut-off 83/100), cMRI: small, non-specific right parietal T_2-hyperintensity in the white matter Patient III.2, M	ALDH5A1

	AO: 10-20 years, AE 20s: dysarthria, CD 4-hydroxybutyric aciduria present in both patients.	
DYS-147	Patient V.3 F TR, F, CS AO: childhood , right-sided hemi-dystonia associated with involuntary movements, levodopa-responsive for several years, 33y: left pallidotomy AE: 30s, DBS, dysarthria, LL dystonia and hyperreflexia, right predominant bradykinesia and rigidity, anxiety, MMSE 15/30	PARK2

AO: age at onset AE: age at examination, y: years, CS: consanguinity of the parents, M: male, F: female, TR: Turkey, BG: Bulgaria, ACE-R: Addenbrooke Cognitive Examination revised, MMSE: Mini Mental State Examination, cMRI: cerebral Magnetic Resonance Imaging, Sd: syndrome, WC: writer's cramp, DBS: deep brain stimulation, LL: lower limbs, UL: upper limbs, CD: cervical dystonia, MCI: mild cognitive impairment, BSP: blepharospasm.

S2 The detailed clinical characteristics of the families with Prioritized Variants in the genes with CEN based evidence

Family number	Clinical information	Candidate genes
DYS-4	TR Patient III.1 F, AO: childhood , AE: 20s Patient III.2 F, AO: birth, AE: 10-20 years paroxysmal movement disorder including intermittent ataxia, choreoathetosis, dystonia	PNP
DYS-11	TR , CS, F	TBC1D8

	neonatal jaundice, motor development delay AO: infancy, foot twisting, childhood: dystonic posture LL, walking distance 500m, 10y: involuntary spasms occurring in the foot, legs, trunk or also in the oromandibular region, brisk tendon reflexes, striatal toe, no cognitive impairment AE 20s: generalized dystonia, important improvement with levodopa cMRI: normal	
DYS-26	TR, CS, M lingual titubation (AO: childhood) alopecia (AO: 20s) AO 20s: WC AE 30s: WC, rest tremor, panic attacks	PRDM15
DYS-37	TR, CS, F AO: childhood, right hand dystonia AE: 10-20 years, hallucination, anxiety, neck, truncal and arm dystonia cMRI: T2 bilateral hypotensities in globus pallidus internus ACE-R: 71/100; MMSE 26/30	*ANGEL1* *ABTB2* *NPC1L1* *DLST*
DYS-53	TR, M AO: childhood , AE childhood , right foot dystonia, walking difficulties, improvement with levodopa	TBC1D32
DYS-54	TR, CS, M AO: childhood, right arm dystonia generalized dystonia, 20s: DBS AE: 20s, generalized dystonia, dysphonia	DZIP3 CEP120
DYS-55	TR <u>Patient V.5</u> AO: juvenile, CD, AE: 30s, generalized dystonia, hand tremor	MCM4

	cMRI: normal Patient V.6 AO: 10-15 years, CD, AE: 30s, segmental dystonia cMRI: normal	
DYS-80	TR, M AO: childhood, right hand dystonia AE: 10s: WC, myoclonic dystonia	CCNT1 SH3TC2*
DYS-110	TR, F AO: 40s, CD, head tremor AE: 60s, CD, head and hand tremor	*TUBAL3* *DENND3* *DSG4* *ADGRD1*

*: Corresponding variant has been previously reported.

S3 The detailed clinical characteristics of the families with variants in the genes without supporting evidence

Family	**Clinical information**	**Candidate genes**
DYS-13	TR, F AO 30s: CD AE 40s: CD, depression cMRI: normal	*SHKBP1*
DYS-18	TR, M AO: juvenile, hand tremor AE: 20s, WC, exhaustible bilateral nystagmus, action tremor, rigidity cMRI (21s): mild cerebellar atrophy	TBC1D2B
DYS-26	TR, CS, M AO: childhood AE 30s: WC, rest tremor, panic attacks	*UMODL1* *ZNF79*
DYS-41	TR/BG, F AO 20s: left leg tremor, muscle cramps AE 20s: left leg dystonia, generalized bradykinesia, amimia, tremor cMRI: normal	*SCNN1D*
DYS-70	TR, CS, M AO: childhood AE: juvenile	*ARID1B* *HUWE1*

	exercice induced mouvements cMRT: normal	
DYS-74	TR, F AO 30s: CD AE 30s: generalized dystonia, dysarthria cMRI: normal	*SLFN14*
DYS-82	TR, CS, M AO: childhood , right hand tremor/dystonia juvenile onset: DBS AE: juvenile, generalized dystonia	*HEATR5B*
DYS-91	TR, CS, F AO: 20s, CD 20s: left thalamotomy cCT: normal AE: 40s, tremor generalized dystonia	*DNAH11*
DYS-97	TR, CS, M AO: infantile, generalized choreatic movements Febrile seizure AE: juvenile, generalized dystonia cMRI: normal	*FBXO10* *ICAM3*
DYS-111	TR, F AO 40s: dystonic tremor UL AE 40s: mild rigidity/bradykinesia, generalized dystonic tremor cMRI: normal	*PDF* *STAB1* *PLEKHG4*
DYS-146	TR, CS, M AO: childhood, left hand tremor, epilepsy AE 40s: left hemidystonia with tremor cMRI : normal	*CABIN1* *KCNJ8* *EPHB4*

AO; age at onset, AE; age at examination, y; years, CS; consanguinity of the parents, M; male, F; female, TR; Turkey, BG; Bulgaria, cMRI; cerebral Magnetic Resonance Imaging, Sd; syndrome, DBS; deep brain stimulation, CD; cervical dystonia

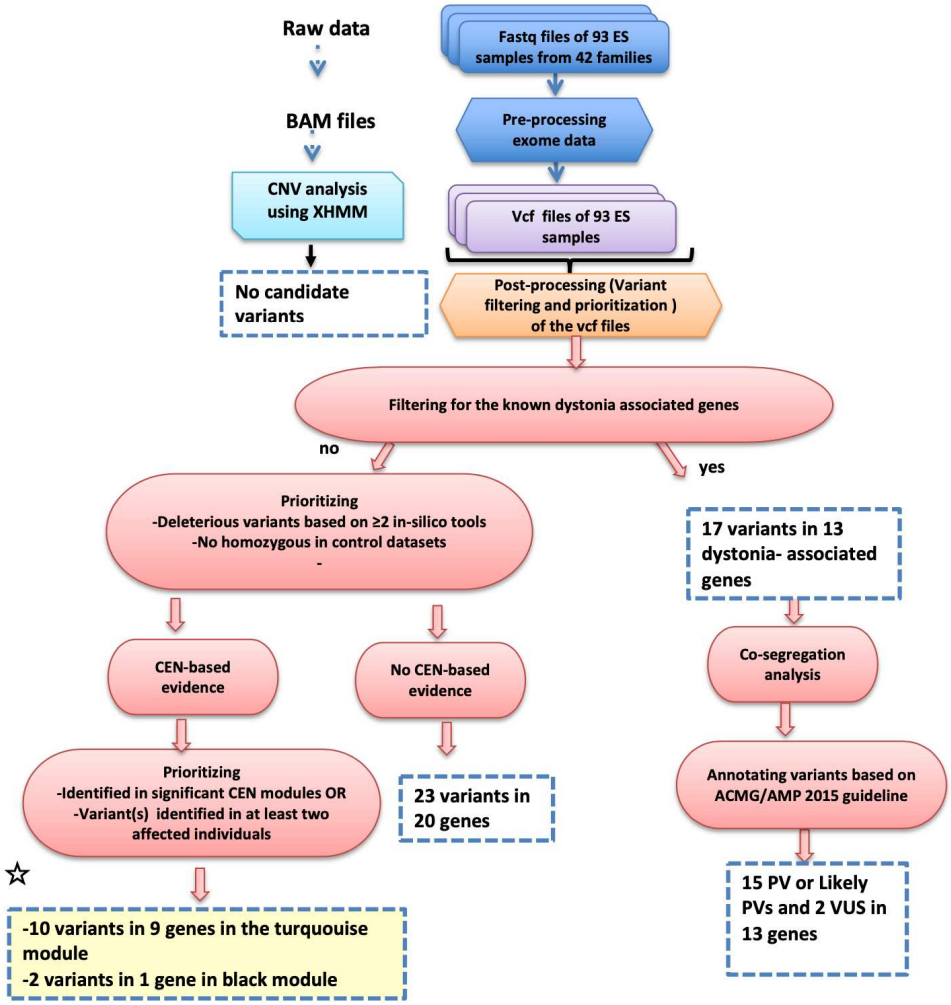
S4 The detailed clinical characteristics of the families with no genetic cause identified in the study

Family	Origin	Sex	CS	Clinical presentation
DYS-3	TR	F	yes	AO: juvenile, rapid onset dystonia AE 20s: severe generalized dystonia cMRI: normal
DYS-28	TR	F, F	no	Patient III.3: AO : juvenile, cervical dystonia AE 60s: segmental dystonia Patient III.6: AO : childhood, cervical dystonia

				AE 40s, segmental dystonia
DYS-62	TR/ TKM	M	no	AO: childhood: cervical dystonia, several myoclonia/tremor AE 30s: myoclonus dystonia, suicide attempt
DYS-95	TR	F	no	AO: infantile, dystonic postures, micrognathism neonatal jaundice, motor development delay AE: childhood, generalized dystonia cMRI: normal
DYS-126	TR	F	no	AO 40s: cervical dystonia AE 50s : cervical dystonia, mild head tremor
DYS-143	TR	M	no	AO childhood , dystonic and ballistic movements left arm AE juvenile, segmental dystonia cMRI: normal
DYS-150	TR	M	no	AO 20s: rapid onset dystonia AE 20s: generalized dystonia cMRI: normal

AO; age at onset, AE; age at examination, y; years, CS; consanguinity of the parents, M; male, F; female, TR; Turkey, TKM; Turkmenistan, cMRI; cerebral Magnetic Resonance Imaging

S5 Genetic screening strategy



S5.1 Systematic illustration of the workflow. The figure illustrates the systematic screening approach conducted to analyze the 42 dystonia families from Turkey.

S6 ES Data Processing

Briefly, ES was performed using in-solution technology from Agilent (SureSelectXT Human All Exon V5) as per manufacturers' protocols at Cegat[1]. High-throughput sequencing was

carried out by the HiSeq 2500 Illumina platform with 2×100 bp. Sequence alignment to the human reference genome (UCSC GRCh37/hg19) was performed using the Burrows-Wheeler Alignment Tool[2]. Picard tools[3] were used for marking duplicates, and GATK (GATKtools-3.8) was employed for local realignment, base quality recalibration, and variant calling approaches based on the GATK best practices[4]. Runs of homozygosity were identified using H3M2[5].

After generating callsets, we proceeded with genotype refinement and variant prioritization approaches by using KGGSeq[6].

After confirming the mode of inheritance of the affected families based on the inbreeding coefficient values, the variants were filtered for (1) the confirmed mode of inheritance, (2) minor allele frequency (MAF ≤ 0.01) based on 1kg201305, dbsnp138, dbsnp141, ESP5400, ESP6500EA, ESP6500AA, GnomAD and in-house databases.

Structural modeling analysis was performed using I-TASSER server[7]. In essence, XHMM uses principal component analysis (PCA) for normalization and a hidden Markov model (HMM) to detect and to genotype copy number variations (CNVs) from normalized read-depth data from targeted sequencing experiments.

Our pipeline uses the BAM files from the preprocessing step of the ES data as input files and subsequently runs GATK to calculate raw depth-of-coverage values across the exome, followed by the first filter step, PCA, the second filter step, and lastly, calls the CNVs by using the standard HMM Viterbi algorithm, which provides the most likely copy-number state given all the sample's read-depth data and fixed HMM parameters.

S7 Statistical analyses

The statistical analyses were performed using R version 4.1.1. Statistical association between the groups and the disease-associated variables were calculated using Fisher's exact

test and comparisons between the groups on continuous data was done using the Kruskal Wallis test. The statistical analysis of the overlap between the dystonia associated genes and the genes identified in the modules was performed using Fisher's exact test. The Benjamini Hochberg and Bonferroni methods were used to correct the p values.

S8 Data Processing of the CEN Data

Correlation networks were constructed using Transcript Per Million values (GTEx_Analysis_2016-01-15_v7_RNASeQCv1.1.8_gene_tpm.gct.gz) corresponding to the BG region and CRBL regions from GTEX, and log2 converted Reads Per Kilobase of transcript per Million (RPKM) values (resids.PUTM.8.rds) corresponding to the putamen region from UKBEC. UKBEC data corresponding to the putamen region of the brain was pre-processed as described in the study by Guelfi et al[8].Modules were identified using the hierarchical clustering method as per the instructions of the weighted correlation network analysis (WGCNA) R package of R (version 3.5.1). After clustering of the samples, no outlier was detected in the BG and the CRBL regions, however, one outlier (A653_1302) detected in the putamen region. After extracting the outliers and filtering the lowly expressed genes we proceeded with 17394 genes from 432 samples in the BG data, 18253 genes from 175 samples in the CRBL data, and 20886 genes from 104 samples in the putamen data. To construct the networks based on approximate scale-free topology, we chose the soft thresholding power β as 12, 10, 7 and the minimum module size as 30, 60 and 30 for the BG, CRBL and putamen datasets, respectively. For each module the module membership value cut off was +0.75 or -0.75 (Supplementary Material S19 and S20).

Based on the overlap between the dystonia-associated genes and the genes in the modules the significant modules were identified. In the BG region of the Gtex dataset only turquoise module was found to be statistically enriched for the dystonia-associated genes and to be involving our

candidate genes. In the CRBL region of the Gtex data no candidate gene was identified in the significant module and in the putamen region of the UKBEC data no significant module was detected.

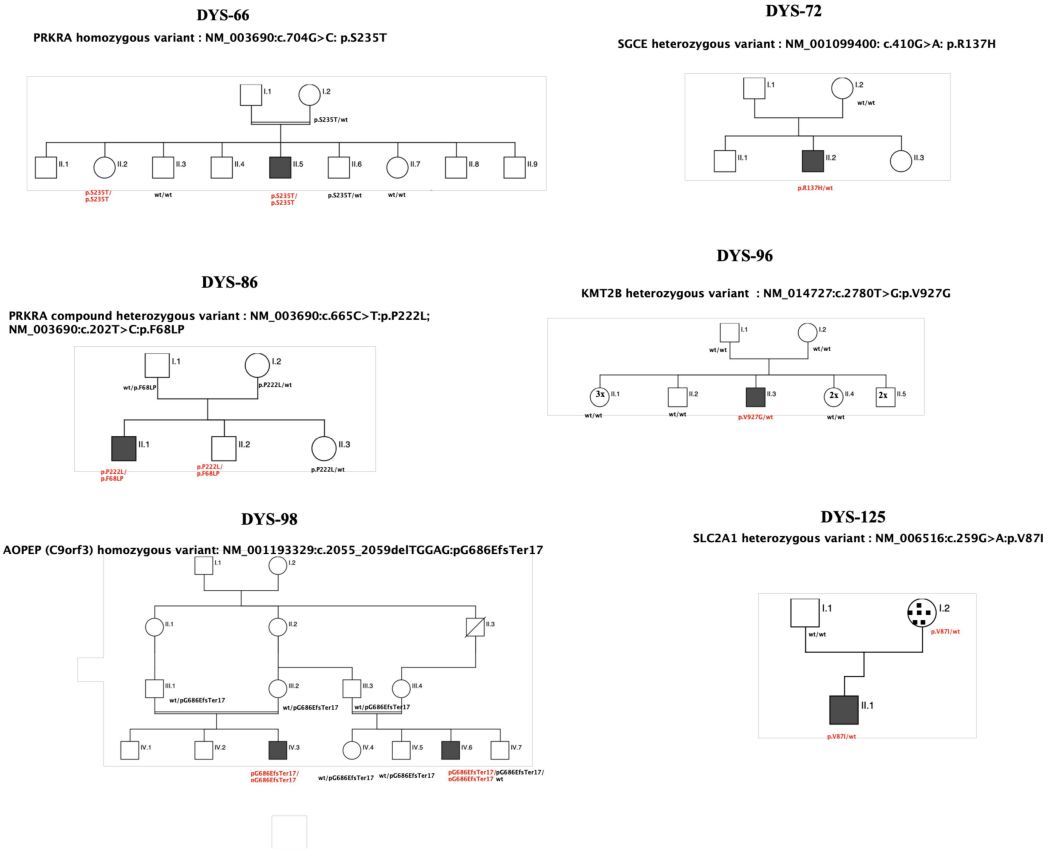
Gene Set Enrichment and Over-representation Analysis

We performed GSEO analysis using the HTSanalyzeR[9] package (version 2.32.0) of R. We set the minimum gene-set size to 10 and used the default values of the remaining parameters.

Protein-Protein Interaction Analysis

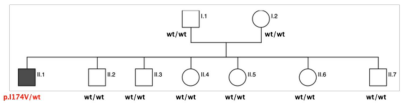
Protein-protein interaction (PPI) and co-localization of the proteins of interest were further investigated using Cytoscape 3.8.0[10] based on the GeneMANIA[11] network.

S9 Pedigrees of the Families with Findings in the Dystonia Associated Genes



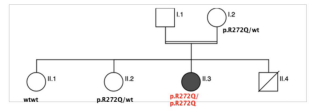
DYS-134

GCH1 heterozygous variant : NM_000161:c.520A>G:p.I174V



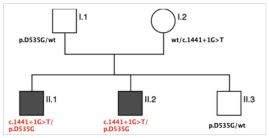
DYS-68

PCCB homozygous variant : NM_000532:c.815G>A:p.R272Q



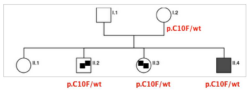
DYS-71

ALDH5A1 compund heterozygous variants : NM_170740:c.1441+1G>T; NM_170740:c.1604A>G:p.D535G



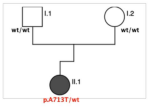
DYS-148

THAP1 heterozygous variant : NM_018105:c.29G>T:p.C10F



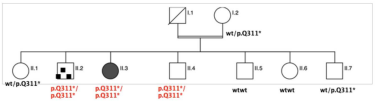
DYS-69

CACNA1A heterozygous variant :NM_023035:c.2137G>A:p.A713T



DYS-147

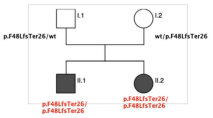
PARK2 homozygous variant :NM_004562:c.931C>T:p.Q311*



S10 Pedigrees of the families with Prioritized Variants in the Candidate Genes with CEN-based evidence

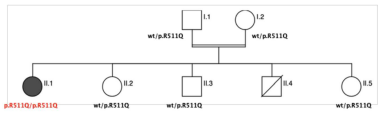
DYS-4

PNP compound heterozygous variant: NM_000270:c.141del:p.F48LfsTer26 / NM_000270:c.637G>A:p.G213R/



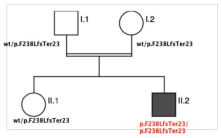
DYS-11

TBC1D8 homozygous variant: NM_001102426:c.1532G>A:p.R511Q



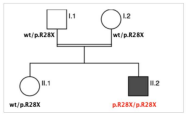
DYS-26

PRDM15 homozygous variant: NM_022115:c.712del:p.F238LfsTer23



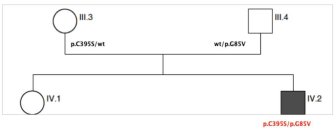
DYS-37

ANGEL1 homozygous variant: NM_015305:c.82C>T:p.R28X



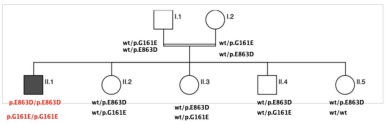
DYS-53

TBC1D32 compound heterozygous variants: NM_152730:c.1184G>C:p.C395S/ NM_152730:c.254G>T:p.G85V



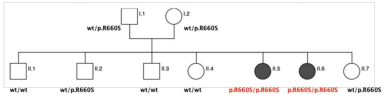
DYS-54

DZIP3 homozygous variant: NM_014648:c.2589G>C:p.E863D
CEP120 homozygous variant: NM_153223:c.482G>A:p.G161E



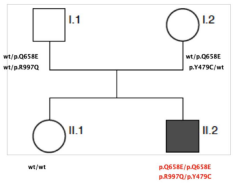
DYS-55

MCM4 homozygous variant: NM_005914:c.1980G>C:p.R660S



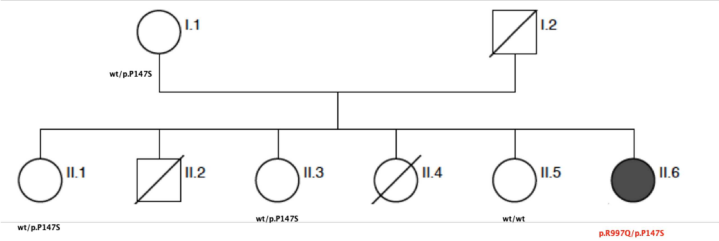
DYS-80

CCNT1 homozygous variant: NM_001240: c.1972C>G: p.Q658E
SH3TC2 compound heterozygous variants: NM_024577:c.2990G>A:p.R997Q/ NM_024577:c.1436A>G:p.Y479C

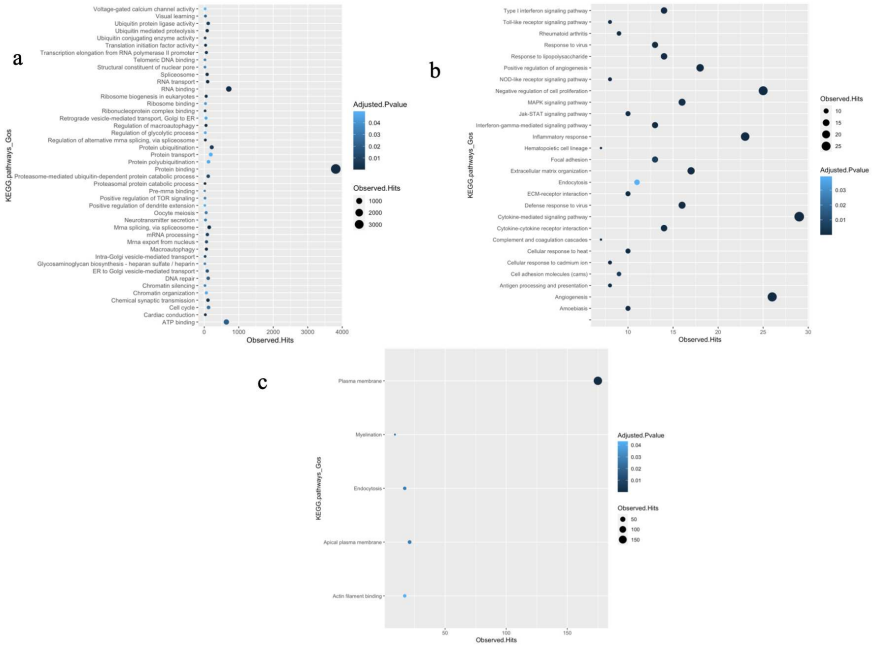


DYS-111

PDF homozygous variant: NM_022341:c.439C>T:p.P147S



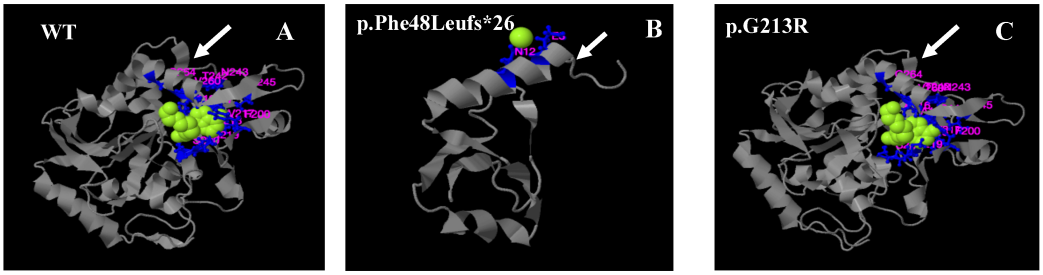
S11 The associated pathways identified in four modules based on the GSEO analysis



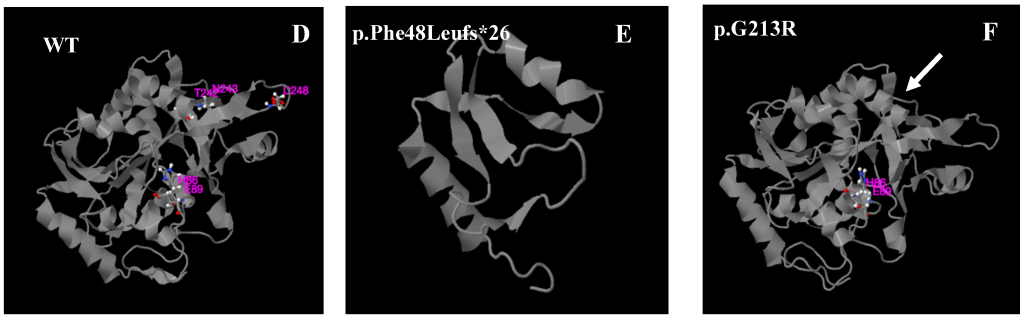
The dotplots represent the overrepresented pathways based on the enriched genes in the (a) turquoise module and (b) black module involving the *PNP* gene, and (c) brown module involving the *AOPEP* gene.

S12 Structural modeling of the pathogenic variants identified in the family DYS-4

Ligand binding sites



Enzyme active sites



Structural modeling showed that the mutated (p.Phe48Leufs*26, p.G123R) PNP lack of the essential ligand binding sites (B,C) as well as the enzyme active sites (E,F), compared to the wild type protein (A,D).White arrow indicates the affected sites of the protein models.

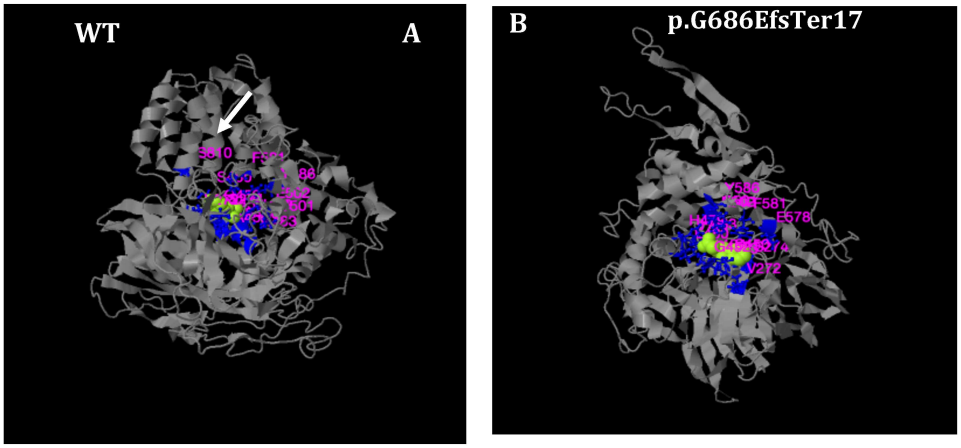
S13 *MCM4* associated reported phenotype

MCM4 gene has previously been associated with immunodeficiency 54 (MIM 609981) that was described in independent families with the same PV from Irish traveller community presenting with recurrent viral infections, decreased number of natural killer (NK) cells and glucocorticoid deficiency, without neurological disturbances except for delayed cognitive development in only one family[12,13]. In this study, none of the symptoms associated with NK

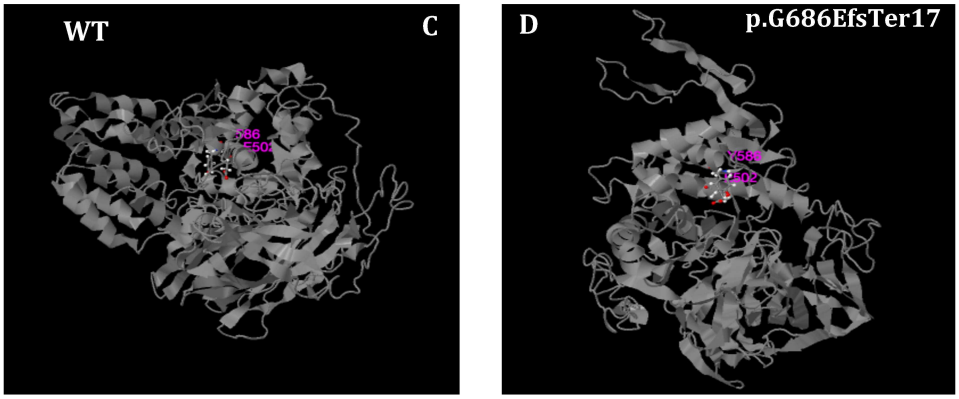
cells and glucocorticoid deficiency except for isolated dystonia in the affected cases of the family DYS-55 with MCM4 PVs was observed.

S14 Structural modeling of the pathogenic variants identified in the family DYS-98

Ligand binding sites

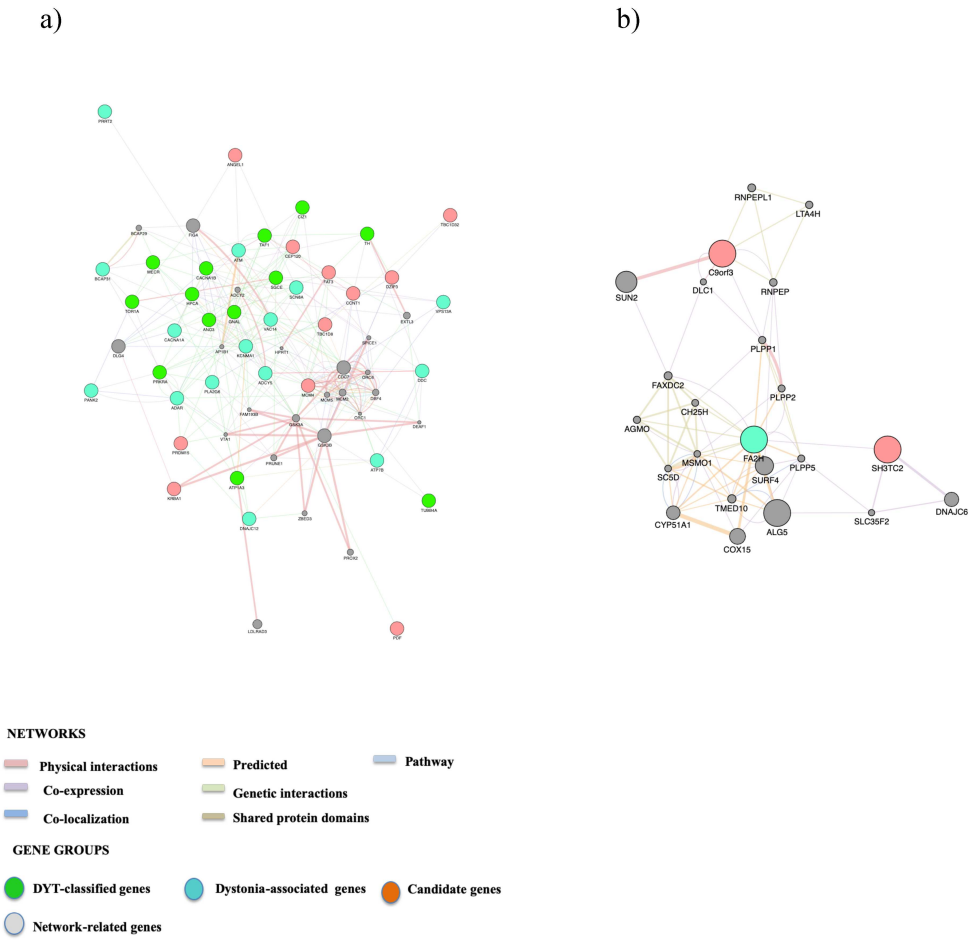


Enzyme active sites



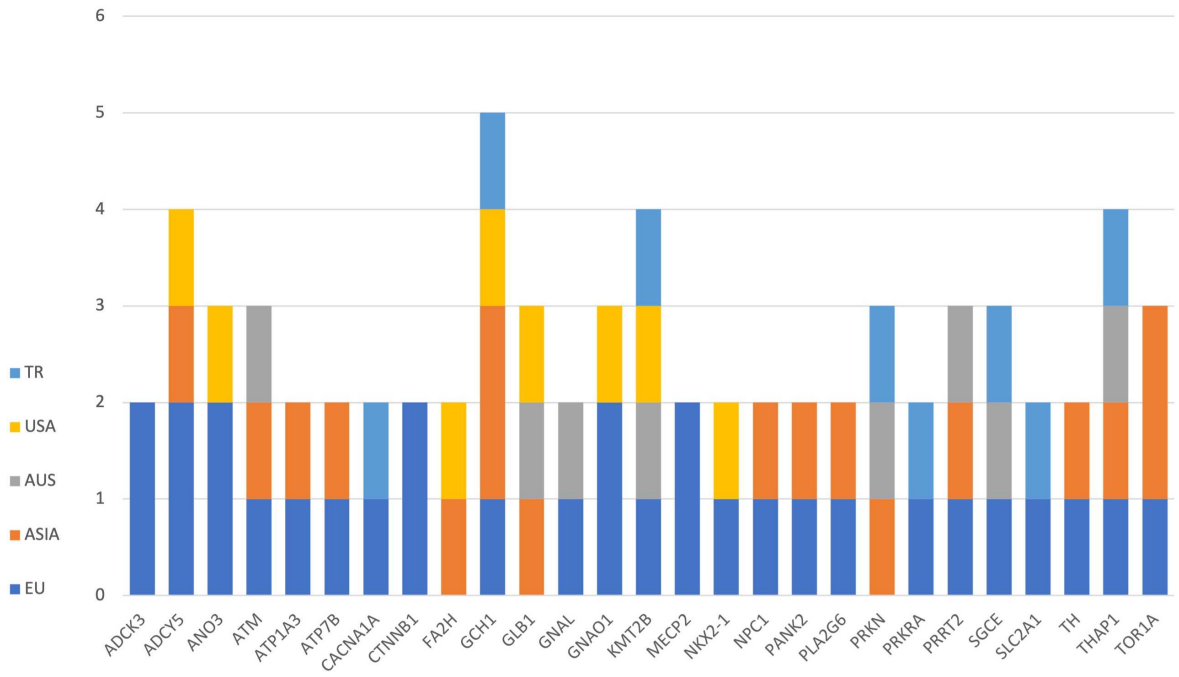
Structural modeling showed that the mutated (pG686EfsTer17) AP-O lack of one of the essential ligand binding sites (indicated by an arrow) (A, B). No major difference was detected in the enzyme active sites (C, D), compared to the wild type protein.

S15 GeneMANIA networks of the genes in particular modules



The representation of some of the interesting protein-protein interactions in the GeneMania modules. The PPI network generated based on the genes form the turquoise module identified in the BG region of Gtex dataset. b) The PPI network generated based on the genes from the brown module identified in the BG region of Gtex dataset. This network involves the *AOPEP(C9orf3)* gene. In the figure green nodes represent the DYT categorized dystonia associated genes, blue nodes represent dystonia associated genes, orange nodes represent our candidate genes and grey nodes represent the network associated genes.

S16 Common Genes Reported in Studies from Different Populations



Representation of common genes reported in so far reported studies from different populations. Reported genes have been indicated as per study: EU; including mainly European populations[14,15,16,17], ASIA; including Asian populations[18,19,20], AUS; including Australian

population[20], USA; including American population[21], TR; including Turkish population reported in this study.

S17 The characteristics of the variants without CEN- based evidence

Gene symbol	Variant	Zygosity	GnomAD MAF[a] hom1/het/hom2	CADD[b], SIFT, PolyPhen, mutation t@sting, M-CAP/S-CAP[c]	Interaction partner	Reported Disease[d]	Neurological impairment in mouse models[e]	Family	PLI[f]	Expression in brain[g]
GLDC	NM_000170:c.2402G>T:p.S801I*[22]	HT (De-novo)	0	24.9, D, PD, DC, PP	-	-	-	DYS-19	0	L
SCNN1D	NM_001130413:c.1657A>G:p.R553G	HT (De-novo)	0	11.6, T, NA, P, DC	- -	- -	- -	DYS-41	0	M
SLFN14	NM_001129820:c.1513A>T:p.K505X	HM	0	38, NA, NA, DC, NA				DYS-74		
HEATR5B	NM_019024:c.1475A>G:p.N492S	HT (De-novo)	0.00003657 4/109392/0	21.4, T, B, DC, LB	-	-	-	DYS-82	0	M
ADGRD1	NM_198827:c.278G>T:p.C93F	HT (De-novo)	0	23.7, D, B, DC, PP	-	-	-	DYS-110	0	L
NPC1L1	NM_013389:c.2293C>T: P765S	HM	0	17, T, NA, P, PP	-	-	-	DYS-37	0	L
DLST	NM_001933:c.442+25A>G	HM	0.000009144 1/109366/0	19, NA, NA, DC, PP	-	-	-		0.48	M
ABTB2	NM_145804:c.2966G>A: p.R989Q	HM	0.0002899 34/117268/0	23, D, B, DC, PP	-	-	Increased grip strength $Abtb2^{tm1a(KOMP)Wtsi}/Abtb2^{tm1a(KOMP)Wtsi}$		0	L
FBXO10	NM_012166:c.1954A>G:p.M652V	CH	0	11.79, T, B, DC, PP	-	-	-	DYS-97	0	L
FBXO10	NM_012166:c.1609G>A:p.V537I	CH	0.0001270 15/118152/0	25.2, T, PD, DC, PP						
TUBAL3	NM_024803:c.178T>C:p.F60L	HT (De-novo)	0.00001828 2/109408/0	24.4, D, PD, DC, PP	-	-	-	DYS-110	0	L

PLEKHG4	NM_001129728:c.2966A>G:p.N989S	HM	0.00007523 29/119634/0	21.8, T, B, P, LB	-	-	-	DYS-111	0	L
STAB1	NM_015136:c.526C>T:p.R176C	CH	0.00006653 8/120244/0	19, T, P, P, PP	-	-	-		0	L
STAB1	NM_015136:c.1796C>T:p.A599V	CH	0.00001676 2/119336/0	25.3, D, D, DC, PP						
EPHB4	NM_004444:c.1692G>C:p.R564S	HM	0.000009140 1/109404/0	27, T, PD, DC, NA	-	-	-	DYS-146	0	L
KCNJ8	NM_004982:c.263C>G:p.A88G	HM	0.0001828 20/109406/0	21.3, T, B, DC, PP	-	-	-		0.29	L
CABIN1	NM_012295:c.5245G>A:p.D1749N	HM	0.0001957 23/117550/0	19.1, T, B, DC, PP	-	-	-		0	M
Suggested Phenotypic Expansion Genes										
ITGA7	NM_001144996:c.3274C>T:p.R1092X	CH	0.00003327 4/120234/0	44, NA, NA, DC, NA	-	Muscular dystrophy, congenital, due to ITGA7 deficiency (MIM 613204)	-	DYS-41	0	M
ITGA7	NM_001144996:c.772C>T:p.L258F	CH	0.00004666 5/107162/0	25.2, D, PP, DC, PP	-	-	-			
HUWE1	NM_031407:c.10400A>T:p.N3467I:	HeM	0	38, D, PD, DC, PP	-	Mental retardation, X-linked syndromic, Turner type (MIM 300706)	-	DYS-70	1	M
DNAH11	NM_001277115:c.10967G>A:p.R3656H	HM	0.00001847 2/108294/0	22.4, NA, NA, DC, PP	-	Ciliary dyskinesia, primary, 7, with or without situs inversus (MIM 611884)	-	DYS-91	0	L
DSG4	NM_177986:c.3047C>T:p.T1016I	HT (De-novo)	0	16.5, NA, NA, DC, LB	-	Hypotrichosis 6 (MIM 607903)	-	DYS-110	0	No expression

TBC1D2B	NM_144572:c.1978C>T:p.R660C	HM	0	28.1, D, D, DC, PP, 0.96381	-	Neurodevelopmental disorder with seizures and gingival overgrowth (MIM 619323)	-	DYS-18	0	M

The table indicates the identified genes without CEN based supporting evidence. Some of the identified genes in this group have been shown to be causing variety of impairments in the mouse model studies. [a]: GnomAD based MAF and allele counts, wt: Homozygous reference, het: Heterozygous, hom: Homozygous alternate, MAF: Minor allele frequency. [b]: CADD score of >15 indicates deleteriousness for the variant. [c]: M-CAP is a pathogenicity classifier for rare missense variants and S-CAP for the splicing variants. [d]:OMIM and literature findings were indicated if the mode of inheritance of the associated disease is compatible. * HGMD report of the variant. [e]: HMDC based mouse model information. [f]: Based on the ExAc consortium computed data, pLI, probability that a gene is intolerant to a loss-of-function mutation (pLI>=0.9 are extremely loss-of-function intolerant). [g]: Expression levels based on the GTEx portal. H: Highly-expressed, M: Moderately-expressed, N: Not-expressed. B; benign, PD; possibly deleterious, D; deleterious, T; Tolerated, LB; likely-benign, PP; possibly pathogenic, NA; not available, DC; disease-causing, P; polymorphism, HM; homozygous, CH; compound heterozygous, H; heterozygous

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