U.S. National Library of Medicine
National Center for Biotechnology Information

NLM Citation: Storey E. Spinocerebellar Ataxia Type 15 – RETIRED CHAPTER, FOR HISTORICAL REFERENCE ONLY. 2006 May 30 [Updated 2014 Jun 12]. In: Adam MP, Feldman J, Mirzaa GM, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2024.
Bookshelf URL: https://www.ncbi.nlm.nih.gov/books/

Spinocerebellar Ataxia Type 15 – RETIRED CHAPTER, FOR HISTORICAL REFERENCE ONLY

Synonym: SCA15

Elsdon Storey, DPhil, FRACP[1]

Created: May 30, 2006; Updated: June 12, 2014.

Summary

NOTE: THIS PUBLICATION HAS BEEN RETIRED. THIS ARCHIVAL VERSION IS FOR HISTORICAL REFERENCE ONLY, AND THE INFORMATION MAY BE OUT OF DATE.

Clinical characteristics

Spinocerebellar ataxia type 15 (SCA15) is characterized by slowly progressive gait and limb ataxia, often in combination with ataxic dysarthria, titubation, upper limb postural tremor, mild hyperreflexia, gaze-evoked nystagmus, and impaired vestibuloocular reflex gain. Onset is between ages seven and 72 years, usually with gait ataxia but sometimes with tremor. Affected individuals remain ambulatory for ten to 54 years after symptom onset. Mild dysphagia usually after two or more decades of symptoms has been observed in members of multiple affected families and movement-induced oscillopsia has been described in one member of an affected family.

Diagnosis/testing

The diagnosis of SCA15 should be considered in individuals in whom the diagnoses of SCA5, SCA6, SCA8, SCA11, SCA12, SCA14, and SCA27 have been excluded by molecular genetic testing (if available) and who fulfill the clinical diagnostic criteria for SCA15.

ITPR1 is the only gene known to be associated with SCA15. Neuroimaging reveals atrophy of the rostral and dorsal vermis of the cerebellum with mild atrophy of the cerebellar hemispheres.

Management

Treatment of manifestations: Physical and occupational therapy; management of neurogenic dysphagia, if it occurs.

Author Affiliation: 1 Director, Van Cleef Roet Centre for Nervous DiseasesHead, Department of NeuroscienceDepartment of Medicine (Neuroscience)Monash UniversityMelbourne, Victoria, Australia; Email: elsdon.storey@monash.edu.

Prevention of secondary complications: Aids for walking and home modifications to help prevent falls; prevention/treatment of osteoporosis to reduce fracture risk.

Surveillance: Follow up by a neurologist with consultation from physiatrists and physical and occupational therapists every two or three years.

Agents/circumstances to avoid: Limit alcohol intake to lessen the risk of falls.

Genetic counseling

SCA15 is inherited in an autosomal dominant manner. If a parent of the proband is affected, the risk to each sib is 50%. Prenatal testing for pregnancies at increased risk is possible through laboratories offering either testing for the gene of interest or custom testing.

Diagnosis

Clinical Diagnosis

The diagnosis of spinocerebellar ataxia type 15 (SCA15) should be considered in individuals with the following findings:

- Very slowly progressive ataxia (e.g., still independently ambulant after 20-30 years of symptoms)
- No other neurologic signs beyond postural and kinetic tremor (which are common and may be the presenting features) and mild hyperreflexia (typically without spasticity, but occasionally with extensor plantar responses)
- Family history consistent with autosomal dominant inheritance

Additional findings may include the following:

- Gaze-evoked nystagmus (sometimes transient only) in approximately 80% of affected individuals
- Impaired vestibuloocular reflex gain (even to the point of producing movement-induced oscillopsia in a minority) in approximately 50% of members of the two families in which it has been tested
- Postural head and/or truncal tremor in a minority (probably <30%) of affected individuals
- Upper-limb postural tremor that may occasionally occur early in the disease course or, rarely, be the presenting feature
- Orolingual dyskinesias, perioral myokymia, and chorea (reported in one family each)
- Cognitive impairment noted in two families; it is not clear that this extends beyond the mild (mainly executive) dysfunction common to most cerebellar disorders [Schmahmann & Sherman 1998].

Brain MRI. Neuroimaging typically reveals atrophy of the rostral and dorsal vermis of the cerebellum. The cerebellar hemispheres may appear normal or be mildly atrophic. The brain stem and cerebral hemispheres are unaffected.

Note: One affected Italian individual with cognitive impairment had bifrontoparietal atrophy; however, it is not certain whether this was attributable to SCA15 or another coexistent process.

Neurophysiology. Nerve conduction studies are typically normal, although minor slowing of sural sensory and median motor conduction velocity was noted in members of one Japanese pedigree.

Molecular Genetic Testing

Gene. *ITPR1* is the only gene known to be associated with SCA15 [van de Leemput et al 2007].

Table 1. Molecular Genetic Testing Used in Spinocerebellar Ataxia Type 15

Gene [1]	Method	Proportion of Probands with a Pathogenic Variant Identified by Method
ITPR1	Sequence analysis [2]	1/23
	Deletion/duplication analysis [3]	22/23

1. See Table A. Genes and Databases for chromosome locus and protein. See Molecular Genetics for information on variants.
2. Sequence analysis detects variants that are benign, likely benign, of uncertain significance, likely pathogenic, or pathogenic. Variants may include missense, nonsense, and splice site variants and small intragenic deletions/insertions; typically, exon or whole-gene deletions/duplications are not detected. For issues to consider in interpretation of sequence analysis results, click here.
3. Testing that identifies exon or whole-gene deletions/duplications not detectable by sequence analysis of the coding and flanking intronic regions of genomic DNA. Methods used may include a range of techniques such as quantitative PCR, long-range PCR, multiplex ligation-dependent probe amplification (MLPA), and chromosomal microarray (CMA) that includes this gene/chromosome segment.

Testing Strategy

Establishing the diagnosis in a proband. The diagnosis of SCA15 should be considered in individuals in whom the diagnoses of SCA5, SCA6, SCA8, SCA11, SCA12, SCA14, and SCA27 have been excluded by molecular genetic testing (if available) and who fulfill the clinical diagnostic criteria for SCA15.

Serial single-gene testing. Because 96% of *ITPR1* pathogenic variants are exon or whole-gene deletions that are not detected by sequence analysis, molecular genetic testing begins with deletion/duplication analysis followed by sequence analysis if a deletion is not identified. The combination of deletion analysis and sequence analysis has identified a pathogenic variant in every individual tested to date whose family demonstrates linkage to *ITPR1* [Obayashi et al 2012, Storey & Gardner 2012].

Multigene panel. Another strategy for molecular diagnosis of a proband suspected of having SCA15 is use of a multigene panel that includes genes known to cause ataxias. These panels vary by methods used and genes included; thus, the ability of a panel to detect a pathogenic variant in any given individual also varies. See Differential Diagnosis. For an introduction to multigene panels click here. More detailed information for clinicians ordering genetic tests can be found here.

Clinical Characteristics

Clinical Description

Clinical information on spinocerebellar ataxia type 15 (SCA15) is based on findings in 67 affected individuals from 20 families: the index pedigree (an Australian family of Anglo-Celtic descent [Storey et al 2001]), three Japanese pedigrees [Hara et al 2008, Iwaki et al 2008], six French pedigrees [Marelli et al 2011], five German pedigrees [Synofzik et al 2011], three Italian pedigrees [Di Gregorio et al 2010, Castrioto et al 2011], one UK pedigree [Novak et al 2010], and one Australian pedigree [Author, unpublished]. Although two other British pedigrees and one other Japanese pedigree have also been identified, clinical descriptions are limited to mention of the presence of pure, slowly progressive ataxia in all three pedigrees and additionally truncal tremor and pyramidal features in the Japanese pedigree.

Onset in all 67 affected individuals was between ages seven and 72 years. SCA15 typically presents with very slowly progressive gait ataxia, often in combination with ataxic dysarthria. Head and/or truncal tremor with or without upper-extremity tremor is seen in fewer than 30%. It may begin simultaneously with (or even occasionally precede) gait ataxia. Deterioration in handwriting, motion-induced instability (e.g., on escalators), and myoclonus were the first symptoms in one individual each.

Progression of SCA15 is notably slow. All nine affected members of the two Australian pedigrees remained independently ambulant after an average of 31 years of symptoms (range 10-54 years); of these nine, two used canes. Most of the affected members of one Japanese pedigree were ambulant 20 years after onset; in another, one affected individual required a wheelchair when assessed after 40 years of symptoms. After ten years of gait ataxia, two affected individuals from the Australian pedigree were able to perform tandem gait, but were unable to hop on one foot within a 30-cm (1 foot) square; one had minor difficulties on the half-turn. All 13 members of the French pedigrees remained independently ambulatory after an average of 22 years (range 6-43 years); of these, two with an average duration of symptoms of 42 years used unilateral supports. Eight of ten members of the German pedigrees were ambulatory after an average of nine years; of these, one used a crutch after 19 years of symptoms.

Two of nine members of the two Australian pedigrees, two of nine members of the six French pedigrees in whom it was ascertained, four of ten members of the five German pedigrees, and five of nine members of two of the Italian pedigrees in whom it was ascertained reported mild dysphagia that typically developed after two or more decades of symptoms. One Australian family member reported onset of a movement-induced oscillopsia 40 years after initial symptoms of movement-induced unsteadiness.

Life-threatening complications such as severe bulbar dysfunction have not become evident during the disease course. From the limited clinical information available, cognition does not typically appear to be affected. While cognitive impairment has been noted in two families, this may represent the mild executive dysfunction commonly seen in many cerebellar disorders.

Genotype-Phenotype Correlations

A Japanese family with a single-nucleotide variant c.3176C>T [Hara et al 2008] had a progressive course and has been classified as SCA15.

Contiguous gene deletions of 3p26. Some individuals with SCA15 have larger microdeletions that encompass portions of both *ITPR1* and *SUMF1*, a gene that causes autosomal recessive multiple sulfatase deficiency. Such individuals are at risk of developing features of SCA15 but are not at risk of having features of multiple sulfatase deficiency, unless the nondeleted homologue of *SUMF1* contains a pathogenic variant [Obayashi et al 2012, Storey & Gardner 2012].

Penetrance

The penetrance is unknown. Based on the even segregation ratio in older generations of the known SCA15 pedigrees, penetrance is likely to be high or complete in these families. The late age of onset in some cases (≤72 years) may confound attempts to establish penetrance. Apparently unaffected parents of three affected sibs were reported in one Japanese pedigree, although detailed information on the parents was not available [Obayashi et al 2012]. Based on pedigree analysis, a parent who would have been predicted to have a pathogenic variant in one of the German families died young (age 31) and was asymptomatic at the time of death, potentially concealing disease development [Synofzik et al 2011].

Anticipation

First-hand information from each member of the 22 parent-offspring pairs for whom age of onset information is available [Storey et al 2009, Di Gregorio et al 2010, Marelli et al 2011, Synofzik et al 2011] reveals that onset was an average of nine years younger in the offspring than the parents; however, information is inadequate to support or refute anticipation. The age of onset in affected children ranged between 40 years earlier to 34 years later than their affected parent.

Note: The molecular mechanism of most pathogenic variants (i.e., deletion) does not suggest that anticipation is likely.

Nomenclature

The sole family in which SCA16 was originally described has now been shown by molecular genetic testing to have SCA15; therefore, the designation SCA16 has been subsumed by SCA15.

The designation SCA16 is currently an "empty" term, as are SCA9 and SCA24 [van de Leemput et al 2007, Gardner 2008, Iwaki et al 2008].

Prevalence

Preliminary information from Ganesamoorthy et al [2009] suggests that approximately 2%-3% of Australian familial ataxias can be attributed to SCA15 after molecular genetic testing has ruled out SCA1, SCA2, SCA3, SCA6, and SCA7, which together are responsible for approximately 50% of dominantly inherited ataxias in Australia.

In a German series of 56 families with autosomal dominant ataxias in whom the SCA conditions caused by trinucleotide repeat expansion (SCA1, SCA2, SCA3, SCA6, SCA7, SCA8, SCA12, SCA17, and dentatorubral-pallidoluysian atrophy [DRPLA]) and SCA conditions caused by other pathogenic variant types (SCA10, SCA11, SCA14 and SCA27) had been excluded, five (9%) families had SCA15. The rate among all dominant SCA conditions was 1.8% [Synofzik et al 2011].

An Italian series of 60 pedigrees segregating an autosomal dominant SCA phenotype, in which testing for SCA1, SCA2, SCA3, SCA6, SCA7, SCA8, SCA10, SCA12, and DRPLA was negative, reported one family with SCA15 (1.7%) [Di Gregorio et al 2010].

A French series of 333 pedigrees segregating an autosomal dominant SCA phenotype, in which testing for SCA1, SCA2, SCA3,SCA 6, SCA7, SCA17, and DRPLA was negative and for which testing in some pedigrees was also negative for SCA5, SCA10, SCA11, SCA12, SCA13, SCA14, and SCA28, revealed six pedigrees with SCA15 – a rate of 1.8% [Marelli et al 2011].

A Japanese series of 74 pedigrees (with at least 2 affected members) with SCA, in which SCA1, SCA2, SCA3, SCA6, SCA31, and DRPLA had been excluded, reported one pedigree with SCA15, for a rate of 1.4% [Obayashi et al 2012].

Genetically Related (Allelic) Disorders

SCA29. The locus for a dominantly inherited congenital non-progressive ataxia with cognitive impairment in a large Australian pedigree overlaps that of SCA15 [Dudding et al 2004]. This pedigree and a similar Canadian family have now been shown to have different single-nucleotide variants in *ITPR1* [Huang et al 2012]. This allelic disorder has been assigned the name SCA29.

Differential Diagnosis

The differential diagnosis of SCA15 is that of a (relatively) pure, slowly progressive, dominantly inherited ataxia, perhaps with early tremor. SCA5, SCA6, SCA8, SCA11, SCA12, SCA14, SCA19/22, SCA21, SCA23, SCA26, SCA27, SCA28, and SCA30 may also fall into this category [Schöls et al 2004, Stevanin et al 2004, Verbeek et al 2004, Manto 2005, van de Warrenburg et al 2005, Cagnoli et al 2006, Storey et al 2009]. Some of these disorders can be excluded by molecular genetic testing, if available. SCA8 and SCA30, in particular, may result in phenotypes almost identical to SCA15. Clinical differentiation of SCA15 from SCA5, SCA11, SCA19/22, SCA21, SCA23, SCA26, and SCA27 may also be impossible, based on the reported details of these disorders.

Head tremor, if present in addition, is more strongly suggestive of SCA15 (than of the other types of inherited ataxia). The disease course is more aggressive in SCA1, SCA2, and SCA3, and SCA2 is also characterized by clinically obvious slow saccades (not seen in SCA15). Also, approximately 60% of individuals with SCA15 display gaze-evoked nystagmus, which is rare in SCA2.

The radiologic picture of SCA15 is that of a pure cerebellar atrophy, which may also be seen in SCA4, SCA5, SCA6, SCA8, SCA10, SCA11, SCA14, SCA18, SCA21, SCA22, SCA23, SCA25, SCA28, and SCA30 [Stevanin et al 2004, Verbeek et al 2004, Manto 2005, Cagnoli et al 2006, Storey et al 2009]. Some of these disorders can be excluded by molecular genetic testing, if available.

The clinical characteristics of the other hereditary ataxias can be found in Hereditary Ataxia Overview.

Management

Evaluations Following Initial Diagnosis

To establish the extent of disease and needs in an individual diagnosed with spinocerebellar ataxia type 15 (SCA15), the following evaluations are recommended:

- Clinical evaluation
- MRI to determine the pattern and extent of cerebellar atrophy and confirm the absence of extracerebellar changes
- Consultation with a clinical geneticist and/or genetic counselor

Treatment of Manifestations

Education for affected individuals and their families is the cornerstone of management.

Physical and occupational therapy, as used for ataxic syndromes of any etiology, may be employed.

Although neither exercise nor physical therapy has been shown to stem the progression of incoordination or muscle weakness, individuals should maintain activity.

To date significant dysphagia has not been an issue for individuals with SCA15; however, if significant dysphagia were to develop, a speech pathologist expert in the management of neurogenic dysphagia should be asked to help guide management.

Prevention of Secondary Complications

Secondary complications are unlikely in the early years of the disease.

Weight control is important because obesity can exacerbate difficulties with ambulation and mobility.

Later, risk of falls can be reduced via appropriate gait aids and home modifications; if falls are frequent, a personal alarm system may be required.

To limit the likelihood of fractures resulting from falls, bone density should be estimated and osteoporosis treated if present.

Surveillance

Follow up by a neurologist with consultation from physiatrists and physical and occupational therapists every two or three years is appropriate.

Agents/Circumstances to Avoid

Because individuals with ataxic syndromes in general have abnormal sensitivity to the motor effects of alcohol, it is reasonable to limit alcohol intake to lessen the risk of falls.

Evaluation of Relatives at Risk

See Genetic Counseling for issues related to testing of at-risk relatives for genetic counseling purposes.

Therapies Under Investigation

Search ClinicalTrials.gov in the US and EU Clinical Trials Register in Europe for access to information on clinical studies for a wide range of diseases and conditions. Note: There may not be clinical trials for this disorder.

Other

Treatment of symptomatic tremor has not been reported in SCA15. At least in the Australian pedigrees, tremor did not cause major functional disability.

Genetic Counseling

Genetic counseling is the process of providing individuals and families with information on the nature, mode(s) of inheritance, and implications of genetic disorders to help them make informed medical and personal decisions. The following section deals with genetic risk assessment and the use of family history and genetic testing to clarify genetic status for family members; it is not meant to address all personal, cultural, or ethical issues that may arise or to substitute for consultation with a genetics professional. —ED.

Mode of Inheritance

Spinocerebellar ataxia type 15 is inherited in an autosomal dominant manner.

Risk to Family Members

Parents of a proband. All individuals diagnosed to date with SCA15 have an affected parent.

Sibs of a proband. If a parent of the proband is affected (which thus far has always been the case), the risk to the sibs is 50%.

Offspring of a proband. Each child of an individual with SCA15 is at a 50% risk of inheriting the *ITPR1* pathogenic variant.

Other family members of a proband. The risk to other family members depends on the status of the proband's parents. If a parent is affected, the parent's family members may be at risk.

Related Genetic Counseling Issues

Family planning

- The optimal time for determination of genetic risk and discussion of the availability of prenatal/preimplantation genetic testing is before pregnancy.
- It is appropriate to offer genetic counseling (including discussion of potential risks to offspring and reproductive options) to young adults who are affected or at risk.

DNA banking. Because it is likely that testing methodology and our understanding of genes, pathogenic mechanisms, and diseases will improve in the future, consideration should be given to banking DNA from probands in whom a molecular diagnosis has not been confirmed (i.e., the causative pathogenic mechanism is unknown). For more information, see Huang et al [2022].

Prenatal Testing and Preimplantation Genetic Testing

Once the *ITPR1* pathogenic variant has been identified in an affected family member, prenatal and preimplantation genetic testing for SCA15 are possible.

Differences in perspective may exist among medical professionals and within families regarding the use of prenatal testing. While most centers would consider use of prenatal testing to be a personal decision, discussion of these issues may be helpful.

Resources

GeneReviews staff has selected the following disease-specific and/or umbrella support organizations and/or registries for the benefit of individuals with this disorder and their families. GeneReviews is not responsible for the information provided by other organizations. For information on selection criteria, click here.

- **Ataxia UK**
  United Kingdom
  Phone: 0800 995 6037; +44 (0) 20 7582 1444 (from abroad)
  Email: help@ataxia.org.uk
  www.ataxia.org.uk
- **euro-ATAXIA (European Federation of Hereditary Ataxias)**
  United Kingdom
  Email: lporter@ataxia.org.uk
  www.euroataxia.org
- **National Ataxia Foundation**
  Phone: 763-553-0020
  Fax: 763-553-0167
  Email: naf@ataxia.org
  www.ataxia.org
- **Spanish Ataxia Federation (FEDAES)**
  Spain
  Phone: 601 037 982
  Email: info@fedaes.org
  fedaes.org
- **CoRDS Registry**
  Sanford Research
  Phone: 605-312-6300
  CoRDS Registry

Molecular Genetics

Information in the Molecular Genetics and OMIM tables may differ from that elsewhere in the GeneReview: tables may contain more recent information. —ED.

Table A. Spinocerebellar Ataxia Type 15: Genes and Databases

Gene	Chromosome Locus	Protein	Locus-Specific Databases	HGMD	ClinVar
ITPR1	3p26.1	Inositol 1,4,5-trisphosphate receptor type 1	ITPR1 database	ITPR1	ITPR1

Data are compiled from the following standard references: gene from HGNC; chromosome locus from OMIM; protein from UniProt. For a description of databases (Locus Specific, HGMD, ClinVar) to which links are provided, click here.

Table B. OMIM Entries for Spinocerebellar Ataxia Type 15 (View All in OMIM)

147265	INOSITOL 1,4,5-TRIPHOSPHATE RECEPTOR, TYPE 1; ITPR1
606658	SPINOCEREBELLAR ATAXIA 15; SCA15

Gene structure. *ITPR1*, encoding inositol 1,4,5-triphosphate receptor type 1, has 58 exons. Eleven spliced and two unspliced mRNAs putatively encode valid proteins. For a detailed summary of gene and protein information, see Table A, **Gene**.

Pathogenic variants. The known pathogenic variants almost all involve deletion of part or all of *ITPR1*, often in association with partial deletion of the adjacent gene *SUMF1* [van de Leemput et al 2007, Hara et al 2008, Iwaki et al 2008]. Known variants include deletion of the following:

- Exons 1-10 of *ITPR1* and 1-3 of *SUMF1*
- Exons 1-40 of *ITPR1* and 1-3 of *SUMF1*
- Exons 1-44 of *ITPR1* and 1-3 of *SUMF1*
- Exons 1-48 of *ITPR1* without any deletion of *SUMF1*
- All of *ITPR1* with exon 1 of *SUMF1*

A p.Pro1059Leu pathogenic variant (disturbing a highly conserved residue) has also been presumptively linked with a Japanese SCA15 pedigree [Hara et al 2008]. See Table 2.

Table 2. Selected *ITPR1* Pathogenic Variants

DNA Nucleotide Change	Predicted Protein Change	Reference Sequences
c.3176C>T [1]	p.Pro1059Leu	NM_002222.4 NP_002213.4
Partial- and whole-gene deletions; see **Pathogenic variants**	Deletions of varying length	

Variants listed in the table have been provided by the author. *GeneReviews* staff have not independently verified the classification of variants.
GeneReviews follows the standard naming conventions of the Human Genome Variation Society (varnomen.hgvs.org). See Quick Reference for an explanation of nomenclature.
1. Hara et al [2008]

Normal gene product. The archetypal protein is 2758 residues in length (Q14643.3). Isoform NP_002213.4 is shorter with 2695 amino acid residues. The proteins form a homotetramer. The C-terminal domains form an intracellular transmembrane channel that mediates calcium release from the endoplasmic reticulum following binding by inositol 1,4,5-trisphosphate receptor type 1. The cytoplasmic N-terminal domain contains the inositol 1,4,5-trisphosphate receptor type 1 binding domain. The protein is particularly abundant in Purkinje cells, but is also found in other brain areas apparently unaffected in SCA15 including CA1 hippocampus, striatum, and cerebral cortex.

Abnormal gene product. Given that deletions of part or all of *ITPR1* are the most frequent causes of SCA15, it is presumed that the pathogenic mechanism is haploinsufficiency.

Chapter Notes

Author Notes

Professor Storey is a neurologist to the Neurogenetics Clinics at the Alfred, and Royal Melbourne Hospitals, Melbourne, Victoria, Australia.

Revision History

- 25 April 2024 (ma) Chapter retired: outdated
- 12 June 2014 (me) Comprehensive update posted live
- 21 April 2011 (cd) Revision: molecular genetic testing available clinically
- 10 December 2009 (me) Comprehensive update posted live
- 30 May 2006 (me) Review posted live
- 7 February 2006 (es) Original submission

References

Literature Cited

Cagnoli C, Mariotti C, Taroni F, Seri M, Brussino A, Michielotto C, Grisoli M, Di Bella D, Migone N, Gellera C, Di Donato S, Brusco A (2006) SCA 28, a novel form opf autosomal dominant cerebellar ataxia on chromosome 18p11.22-q11.2. Brain 129:235-42 PubMed PMID: 16251216.

Castrioto A, Prontera P, Di Gregorio E, Rossi V, Parnetti L, Rossi A, Donti E, Brusco A, Calabresi P, Tambasco N (2011) A novel spinocerebellar ataxia type 15 family with involuntary movements and cognitive decline. Eur J Neurol 18:1263-5 PubMed PMID: 21382133.

Di Gregorio E, Orsi L, Godani M, Vaula G, Jensen S, Salmon E, Ferrari G, Squadrone S, Abete MC, Cagnoli C, Brussino A, Brusco A (2010) Two Italian families with ITPR1 gene deletion presenting a broader phenotype of SCA 15. Cerebellum. 9:115-23 PubMed PMID: 20082166.

Dudding TE, Friend K, Schofield PW, Lee S, Wilkinson IA, Richards RI (2004) Autosomal dominant congenital non-progressive ataxia overlaps with the SCA15 locus. Neurology 63:2288-92 PubMed PMID: 15623688.

Ganesamoorthy D, Bruno DL, Schoumans J, Storey E, Delatycki MB, Zhu D, Wei MK, Nicholson GA, McKinlay Gardner RJ, Slater HR (2009) Development of a multiplex ligation-dependent probe amplification assay for diagnosis and estimation of the frequency of spinocerebellar ataxia type 15. Clin Chem 55:1415-8 PubMed PMID: 19423733.

Gardner RJM (2008) "SCA 16" is really SCA 15. J Med Genet 45:192 PubMed PMID: 18310270.

Hara K, Shiga A, Nozaki H, Mitsui J, Takahashi Y, Ishiguro H, Yomono H, Kurisaki H, Goto J, Ikeuchi T, Tsuji S, Nishizawa M, Onodera O (2008) Total deletion and a mis-sense mutation of ITPR1 in Japanese SCA15 families. Neurology 71:547-51 PubMed PMID: 18579805.

Huang L, Chardon JW, Carter MT, Friend KL, Dudding TE, Schwartzentruber J, Zou R, Schofield PW, Douglas S, Bulman DE, Boycott KM. Missense mutations in ITPR1 cause autosomal dominant congenital nonprogressive spinocerebellar ataxia. Orphanet J Rare Dis. 2012;7:67. PubMed PMID: 22986007.

Huang SJ, Amendola LM, Sternen DL. Variation among DNA banking consent forms: points for clinicians to bank on. J Community Genet. 2022;13:389-97. PubMed PMID: 35834113.

Iwaki A, Kawano Y, Miura S, Shibata H, Matsuse D, Li W, Furuya H, Ohyagi Y, Taniwaki T, Kira J, Fukumaki Y (2008) Heterozygous deletion of ITPR1, but not SUMF1, in spinocerebellar ataxia type 16. J Med Genet 45:32-5 PubMed PMID: 17932120.

Manto MU (2005) The wide spectrum of spinocerebellar ataxias (SCAs). Cerebellum 4:2-6 PubMed PMID: 15895552.

Marelli C, van de Lemput J, Johnson JO, Tison F, Thauvin-Robinet C, Picard F, Tranchant C, Hernandez DG, Huttin B, Boulliat J, Sangla I, Marescaux C, Brique S, Dollfus H, Arepalli S, Benatru I, Ollagnon E, Forlani S, Hardy J, Stevanin G, Dürr A, Singleton A, Brice A (2011) SCA15 due to large ITPR1 deletions in a cohort of 333 white families with dominant ataxia. Arch Neurol 68:637-43 PubMed PMID: 21555639.

Novak MJU, Sweeney MG, Li A, Treacy C, Chandrashekar HS, Giunti P, Goold RG, Davis MB, Houlden H, Tabrizi SJ (2010) An ITPR1 gene deletion causes spinocerebellar ataxia 15/16: a genetic, clinical and radiological description. Mov Disord 25:2176-82 PubMed PMID: 20669319.

Obayashi M, Ishikawa K, Izumi Y, Takahashi M, Niimi Y, Sato N, Onodera O, Kaji R, Nishizawa M, Mizusawa H. (2012) Prevalence of inositol 1,4,5-triphosphate receptor type 1 gene deletion, the mutation for spinocerebellar ataxia type 15, in Japan screened by gene dosage. J Hum Genet 57:202-6 PubMed PMID: 22318346.

Schmahmann JD, Sherman JC. The cerebellar cognitive affective syndrome. Brain. 1998;121:561-79. PubMed PMID: 9577385.

Schöls L, Bauer P, Schmidt T, Schulte T, Riess O (2004) Autosomal dominant cerebellar ataxias: clinical features, genetics, and pathogenesis. Lancet Neurol 3:291-304 PubMed PMID: 15099544.

Stevanin G, Bouslam N, Thobois S, Azzedine H, Ravaux L, Boland A, Schalling M, Broussolle E, Durr A, Brice A (2004) Spinocerebellar ataxia with sensory neuropathy (SCA25) maps to chromosome 2p. Ann Neurol 55:97-104 PubMed PMID: 14705117.

Storey E, Bahlo M, Fahey MC, Sisson S, Lueck C, Gardner RJM (2009) A new dominantly-inherited pure cerebellar ataxia, SCA 30. J Neurol Neurosurg Psychiatry 80:408-11 PubMed PMID: 18996908.

Storey E, Gardner RJ, Knight MA, Kennerson ML, Tuck RR, Forrest SM, Nicholson GA (2001) A new autosomal dominant pure cerebellar ataxia. Neurology 57:1913-5 PubMed PMID: 11723290.

Storey E, Gardner RJM. Spinocerebellar ataxia type 15. In: Subramony SH, Durr A, eds. *Ataxic Disorders - Handbook of Clinical Neurology Series*. Vol 103. 3 ed. Amsterdam: Elsevier Science; 2012:561-5.

Synofzik M, Beetz C, Bauer C, Bonin M, Sanchez-Ferrero E, Schmitz-Hübsch T, Wüllner U, Nägele T, Riess O, Schöls L, Bauer P (2011) Spinocerebellar ataxia type 15: diagnostic assessment, frequency, and phenotypic features. J Med Genet 48:407-12 PubMed PMID: 21367767.

van de Leemput J, Chandran J, Knight MA, Holtzclaw LA, Scholz S, Cookson MR, Houlden H, Gwinn-Hardy K, Fung HC, Lin X, Hernandez D, Simon-Sanchez J, Wood NW, Giunti P, Rafferty I, Hardy J, Storey E, Gardner RJ, Forrest SM, Fisher EM, Russell JT, Cai H, Singleton AB (2007) Deletion at ITPR1 underlies ataxia in mice and spinocerebellar ataxia 15 in humans. PLoS Genet 3:e108 PubMed PMID: 17590087.

van de Warrenburg BP, Sinke RJ, Kremer B (2005) Recent advances in hereditary spinocerebellar ataxias. J Neuropathol Exp Neurol 64:171-80 PubMed PMID: 15804048.

Verbeek DS, van de Warrenburg BP, Wesseling P, Pearson PL, Kremer HP, Sinke RJ (2004) Mapping of the SCA23 locus involved in autosomal dominant cerebellar ataxia to chromosome region 20p13-12.3. Brain 127:2551-7 PubMed PMID: 15306549.

License