Scientific Research Publishing

Open Journal of Pathology, 2026, 16(4), 167-176
https://www.scirp.org/journal/ojpathology
ISSN Online: 2164-6783
ISSN Print: 2164-6775

Friedreich's Ataxia: Is It a True Single Gene Disease?

Andrey Frolov[1], Teja Bhimavarapu[1], Grace Shallert[1], Miguel A. Guzman[2], John R. Martin III[1*]

[1]Center for Anatomical Science and Education, Department of Surgery, Saint Louis University School of Medicine, St. Louis, MO, USA
[2]Department of Pathology, Saint Louis University School of Medicine, St. Louis, MO, USA
Email: *john.martin@health.slu.edu

How to cite this paper: Frolov, A., Bhimavarapu, T., Shallert, G., Guzman, M.A. and Martin, J.R. III (2026) Friedreich's Ataxia: Is It a True Single Gene Disease? *Open Journal of Pathology*, **16**, 167-176.
https://doi.org/10.4236/ojpathology.2026.164018

Received: June 25, 2026
Accepted: August 10, 2026
Published: August 13, 2026

Abstract

Friedreich's ataxia (FRDA) is the most common form of hereditary ataxia. The disease affects multiple organs and manifests with progressive ataxia, scoliosis, cardiomyopathy, and diabetes. FRDA is believed to occur due to a mutation in a single gene, frataxin (*FXN*), despite its incomplete genotype-phenotype correlation. *FXN* encodes an essential mitochondrial protein regulating cellular energy production and iron homeostasis. To gain novel insights into FRDA molecular underlining, this study examined, postmortem, a putative link between phenotypic features and genetic mutations in an FRDA body donor. A 34-year-old female with reported FRDA and comorbidities such as heart failure and type I diabetes was evaluated using a multimodal approach. External examination revealed cavovarus foot deformity, and MRI showed levoscoliosis. Histological examination of the interventricular septum demonstrated cardiac hypertrophy, while examination of the cerebellar dentate nucleus revealed a significant loss of large neuronal cells. These findings were consistent with the FRDA diagnosis and prompted a search for additional genes potentially contributing to the disease. Whole exome sequencing (WES) using the Illumina next-generation sequencing (NGS) platform revealed 77 genes with rare (minor allele frequency, MAF ≤ 0.01) and 67 with low-frequency (0.01 < MAF < 0.05) pathological/deleterious variants. Functional annotation identified a number of genes closely relevant to the donor's FRDA phenotype, including *ELF2*, *SYNE1*, *ZNF512B*, *CLCN1*, *HSPG2*, *NEB*, *OBSCN*, and *BMP10* (rare variants); *ARMC9*, *GRID2IP*, *VWA5B1*, *MYO18B*, and *SGCD* (low-frequency variants). These genes, together with *FXN*, may contribute to the phenotypic variability and multisystem manifestations of FRDA, thereby pointing toward its polygenic underlining.

Keywords

Friedreich's Ataxia, Cavovarus Foot Deformity, Levoscoliosis, Cardiac Hypertrophy, Whole Exome Sequencing, Next Generation Sequencing, Polygenic Underlining

1. Introduction

Friedreich's ataxia (FRDA) is the most common form of hereditary ataxia, caused primarily by a homozygous GAA trinucleotide repeat expansion in the first intron of the *FXN* gene, leading to reduced production of frataxin, a mitochondrial protein essential for iron-sulfur cluster formation and cellular energy metabolism [1]. More recently, it has been reported that *FXN* gene expression can also be regulated post-transcriptionally through the microRNA (miR-124) targeting an altered 3'-untranslated region (3'-UTR) of the *FXN* messenger RNA [2]. Frataxin deficiency results in mitochondrial dysfunction, oxidative stress, and impaired energy production, affecting primarily the central and peripheral nervous systems (CNS and PNS) as well as cardiovascular and endocrine systems. Genetic testing for modified *FXN* provides a definitive FRDA diagnosis (NIH NIDS). Clinically, FRDA presents in late childhood or early adolescence with progressive gait ataxia, areflexia, and dysarthria, and may progress to scoliosis, muscle weakness, diabetes, and hypertrophic cardiomyopathy [3]. As a multisystem disorder, FRDA demonstrates significant variability in disease severity and progression [4]. The variability in disease onset, progression, and organ involvement suggests the influence of additional genetic or molecular modifiers. This study examines a rare adult case of FRDA through a multifaceted approach integrating magnetic resonance imaging (MRI), anatomical dissection, histological analysis, and whole exome sequencing (WES). By identifying modified genes besides *FXN* with rare and low-frequency pathological/deleterious variants and correlating them with anatomical findings, this study aims to explore the role of genetic modifiers in shaping the multisystem phenotype of FRDA.

2. Methods

2.1. Human Cadaveric Body Procurement

The body of a 34-year-old female was received through the Saint Louis University (SLU) Gift Body Program with signed informed consent. The available medical history reported FRDA diagnosis at the age of 10, congestive heart failure, type 1 diabetes mellitus, scoliosis, acid reflux, muscle spasms, atrophy of the feet, and wheelchair dependence since adolescence. The cause of death was acute respiratory failure secondary to congestive heart failure.

2.2. Magnetic Resonance Imaging

Magnetic resonance imaging (MRI) was performed at the SSM Health Saint Louis

University Hospital as previously described [5].

2.3. Anatomical Dissection

Removal of the brain and heart followed the dissection procedures in Grant's Dissector, 16th edition [6]. After their removal, the specimens were submerged in a 10% neutrally buffered formalin solution for approximately eight weeks.

2.4. Histochemical Staining

The heart was sectioned transversely from the midventricular line to the apex, while the brain was sliced coronally into 10 mm sections. Regions of each specimen were removed, dehydrated, paraffin-embedded, sectioned (4 - 5 μm), and stained with hematoxylin and eosin (H & E) according to standard procedures of the Advanced Spatial Biology and Research Histology Facility (Department of Pathology, SLU School of Medicine).

2.5. Light Microscopy

Images were obtained with a Leica Leitz DMRB light microscope equipped with a DFC7000 T camera and controlled by the Neurolucida software (MBF Bioscience, Williston, VT, USA) using the 4×, 10×, 20×, and 63× objectives. Contours were manually traced in Neurolucida using the continuous tracing tool. Six representative regions of the cardiac interventricular septum were selected, and contours were drawn around cardiomyocytes with a visible nucleus. Cells extending beyond the region boundaries were excluded. The average cardiomyocyte cross-sectional area was then calculated. For the dentate nucleus, neurons with a visible nucleus were selected, and contours were manually drawn around each neuronal soma. Neuronal soma area measurements were subsequently obtained.

2.6. Genetic Screening

The postmortem genetic screening by WES was conducted by Novogene (Sacramento, CA) to a 50× depth of coverage on the Illumina HiSeq 2500 NGS platform. The respective bioinformatics analysis, including detection of genes with rare (minor allele frequency, MAF ≤ 0.01) and low-frequency (0.01 < MAF < 0.05) pathological/deleterious genetic variants and their functional annotation, was performed as previously described [7]. By virtue of detecting mutations in the DNA coding regions (exons), WES in the current study was not aimed at identifying canonical *FXN* GAA repeat expansions in the donor's DNA non-coding regions (introns).

3. Results

3.1. Pathological Examination

External body examination revealed cavovarus foot deformity (**Figure 1(A)**), while MRI demonstrated the existence of levoscoliosis and the presence of a foreign metal object (**Figure 1(B)**), which was identified during anatomical dissection as

an implantable cardioverter-defibrillator (ICD). The latter would be consistent with ventricular tachycardia (VT) being present in the donor. Since cardiomyopathy is one of the possible underlining causes of VT, the histopathological analysis of the donor's heart was performed. H & E-stained heart interventricular septum revealed hypertrophic cardiomyocytes with irregular contours, size variability, and large, rectangular, so-called "box-car" nuclei (**Figure 2(A)**). A total of 415 cardiomyocytes were counted with a mean cross-sectional area of 2304 μm^2 (range, 212 - 9780 μm^2) vs. a normal mean of 249 μm^2 [8]. The putative CNS pathology underlining FRDA's key neurological symptoms was probed by histopathological analysis of the cerebellum. H & E-stained cerebellar dentate nucleus showed predominantly small neuronal cell bodies (**Figure 2(B)**). A total of 754 neurons were counted in the right and left dentate nuclei, with a mean diameter of 17 μm (range, 9.4 - 29.1 μm). Only 2% of neurons exceeded 25 μm in diameter, whereas 98% were <25 μm, indicating a significant loss of large neurons. In the normal dentate nucleus, approximately 70% of neurons are large, and depletion of this population is a well-recognized pathologic feature of dentate degeneration and cerebellar disease [9] [10].

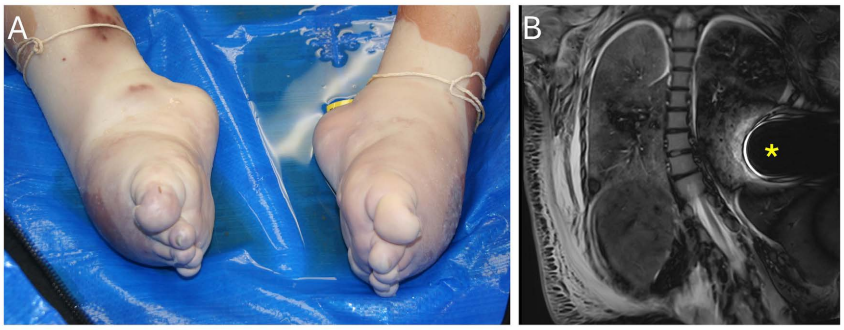

Figure 1. Anatomical findings in the FRDA body donor. (A) External examination demonstrating bilateral cavovarus foot deformity. (B) Coronal MRI illustrating levoscoliosis. The yellow asterisk denotes the implantable cardioverter-defibrillator in the left upper chest.

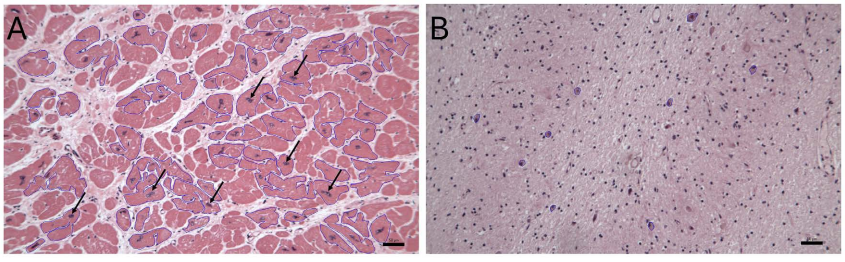

Figure 2. Histopathological findings in the FRDA body donor. Representative H&E-stained sections used for morphometric analysis. (A) Cardiac tissue demonstrating cardiomyocyte hypertrophy, with blue tracings outlining analyzed cardiomyocytes. Enlarged nuclei with squared nuclear contours ("box-car nuclei"), a characteristic feature of cardiomyocyte hypertrophy, are indicated by black arrows. (B) Cerebellar dentate nucleus showing predominance of small neurons and loss of large neurons, consistent with dentate nucleus degeneration in Friedreich ataxia; blue tracings outline analyzed neuronal cell bodies. Scale bars = 50 μm.

3.2. Genetic Analysis

Using a very stringent, five-step analytical algorithm where the last three steps included consecutive filtering of genetic variants through SIFT, PolyPhen_2-HDIV, and PROVEAN databases [7], 77 genes with rare (R) and 67 genes with low-frequency (LF) pathological/deleterious mutations were identified. Those genes were then manually grouped into 9 functional categories most relevant to the present case: Development, Neurodevelopment, Bone/Cartilage Development, Muscle Development/Function, Mitochondrial Function, Cilia Development/Function, Immunity/Inflammation, Neurological Diseases, and Cardiovascular Diseases (Table 1 and Table 2). These categories were chosen based on the FRDA diagnosis and its associated comorbidities reported in the medical history of the body donor, the most relevant physiological pathways potentially affected in the donor, as well as on the results of the respective pathological examination (see above).

Table 1. Genes with rare pathological/deleterious variants that are most relevant to the present case.

Categories	Genes
Development	*CYS1*, *DPH6*, *ESRP1*, *FAT1*, *HAAO*, *IMPG2*, *LAMB1*, *LAMC3*, *LTB SNX17 P2*, *NKX2-3*, *NUP58*, *OR6C76*, *SKIV2L*, *SLC49A3*, *SNX17*, *USH1C*, *USH2A*, *ZNF594*
Neurodevelopment	*BAHCC1*, *COL6A6*, *DENND5A*, *EPHA8*, *GABRD*, *GCFC2*, *GRK6*, *KIF17*, *LAMB1*, *LAMC3*, *ME2*, *SLC49A3*, *SNX17*, *SYPL2*, *TIAM2*
Bone/Cartilage Development	*DPH6*, *HAAO*, *HSPG2*, *LTBP2*, *RNASE11*, *TMUB1*, *ZNF594*
Muscle Development/Function	*BMP10*, *CLCN1*, *HSPG2*, *MYF6*, *NEB*, *OBSCN*, *SYNE1*
Cilia Development/Function	*AGR3*, *KIF17*
Mitochondrial Function/Energy Metabolism	*AK1*, *DLD*
Immunity/Inflammation	*GRK6*, *HAAO*, *HLA-DQB1*, *HLA-DRB5*, *MRPL9*, *MXRA5*, *NKX2-3*, *RFX5*, *SDK1*, *SKIV2L*, *SYPL2*, *UACA*
Neurological Diseases	*DENND5A*, *ELF2*, *GABRD*, *GCFC2*, *GRK6*, *SLC8A3*, *SYNE1*, *ZNF512B*
Cardiovascular Diseases	*BMP10*, *SDK1*

Table 2. Genes with low-frequency pathological/deleterious variants that are most relevant to the present case.

Categories	Genes
Development	*ADGRF3*, *ARMC3*, *COL4A4*, *CYP4A22*, *HIP1R*, *IFT8*, *IQCE*, *LRP2*, *MYO18B*, *OR5K1*, *RDH11*, *TBX15*, *YY1AP1*

Continued

Neurodevelopment	*ABHD14A*, *ARMC9*, *CHRNA10*, *GFAP*, *GRID2IP*, *HELB*, *HIP1R*, *LRP2*, *PRODH2*, *SZT2*, *VWA5B1*, *VWA5B1*, *ZNF620*
Bone/Cartilage Development	*IQCE*, *LECT2*, *P3H1*, *TCIRG*
Muscle Development/Function	*ABHD14A*, *MYO18B*, *SGCD*
Cilia Development/Function	*ARMC9*, *DNAH2*, *DNAH3*, *FAM166A*, *HIP1R*, *TEKT4*, *TTC21A*
Mitochondrial Function/Energy Metabolism	*RFESD*, *SGIP1*
Immunity/Inflammation	*BPIFB*, *CHIA CYP4F2*, *DSG3*, *LECT2*, *PADI4*, *PKP3*, *PRKN*, *SIGIRR*, *TNIP3*
Neurological Diseases	*ARMC9*, *GFAP*, *GRID2IP*, *PRKN*, *PRODH2*, *VWA5B1*, *ZNF620*
Cardiovascular Diseases	*ABHD14A*, *GPAT3*, *HFE*, *LRP2*, *PRKN*, *SGCD*

4. Discussion

The multifaceted evaluation of the donor's body using external examination, MRI, gross anatomical dissection, and histopathological analysis revealed several phenotypical features often associated with FRDA: cavovarus foot deformity, scoliosis, cardiac hypertrophy, which likely resulted in hypertrophic cardiomyopathy, and cerebellar degeneration. Because each of these phenotypical features could have been produced by mutated genes other than *FXN*, the existence of such auxiliary genes was probed by WES of the donor's DNA.

In both functionally annotated WES datasets, R and LF, the most notable was the presence of mutated genes associated with ataxia-*ELF2* (R) [11], *SYNE1*(R) [12], *ARMC9* (LF) [13], and *GRID2IP* (LF) [14]—with all of them being linked to ataxia types underlined by cerebellar pathology. The latter was consistent with the pathological changes in the cerebellum observed in the present case. Besides the altered genes linked to specific ataxia types, there were two mutated genes, *ZNF512B* (R) and *VWA5B1* (LF), known to be associated with neurological diseases, respectively, amyotrophic lateral sclerosis [15] and Niemann-Pick Type C2 (GeneCards), whose symptoms, including ataxia, overlap with FRDA.

The cavovarus foot deformity and levoscoliosis in the donor's body could be linked to a number of mutated genes known to regulate bone and limb development—*HAAO* (R), *RNASE11* (R), *TMUB1* (R), *ZNF594* (R), *IQCE* (LF), and *P3H1* (LF)—where *ZNF594* was particularly linked to scoliosis [16]. The latter skeletal deformity could also be associated with a number of modified genes present in the Muscle Development/Function category (R)—*CLCN1* [17], *HSPG2* [18] [19], *NEB* [20], *OBSCN* [21], and *SYNE1* [22]—where *SYNE1* reveals its pleiotropic nature by its association with both ataxia (see above) and scoliosis. Two additional genes linked to scoliosis were found in the LF dataset: *MYO18B* [22] and *SGCD* [23].

The identified cardiac hypertrophy could have an input from two modified genes, *BMP10* (R) [24] [25] and *SGCD* (LF) [26]. Interestingly, cardiac hypertrophy and scoliosis may be linked together via the modified *SGCD* gene [23] [26].

5. Conclusion

Our data are consistent with a hypothesis that FRDA, in addition to the primary modified *FXN* gene, may have an auxiliary polygenic component.

Acknowledgements

We are grateful to all individuals and their families for their invaluable contribution to the SLU Gift Body Program. We also like to thank Dr. Paul Cliften (Genome Technology Access Center, Washington University in St. Louis, St. Louis, MO, USA) for his expert assistance with the bioinformatics analysis, as well as Vasiliki Grammatopoulou (Advanced Spatial Biology and Research Histology Facility, Department of Pathology, SLU School of Medicine) for her skillful help with the histology slides preparation.

Limitations

The study was performed with one participant, thereby requiring further validation of its results by using a large cohort of patients and/or the respective clinical database(s).

Funding

This study was supported by the Center for Anatomical Science and Education, SLU School of Medicine.

Author Contributions

Concept and design: John R. Martin III and Andrey Frolov.
Acquisition, analysis, or interpretation of data: John R. Martin III, Andrey Frolov, Teja Bhimavarapu, Grace Shallert, and Miguel A. Guzman.
Critical review of the manuscript for important intellectual content: John R. Martin III, Teja Bhimavarapu, Grace Shallert, and Miguel A. Guzman.
Supervision: John R. Martin III.
Drafting of the manuscript: Andrey Frolov.
All authors have read and approved the final version of the manuscript.

Ethics Statement

Throughout the study, no living human subjects were used. The cadaveric body used in the study was received through the SLU Gift Body Program with signed informed consent from the donor. The SLU Gift Body Program abides by all rules set forth by the Uniform Anatomical Gift Act (UAGA). All work with the cadavers, as well as with any material procured from the deceased bodies, is exempt from the Institutional Review Board approval as long as the identity of the de-

ceased individual is not revealed.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] Koeppen, A.H. (2011) Friedreich's Ataxia: Pathology, Pathogenesis, and Molecular Genetics. *Journal of the Neurological Sciences*, **303**, 1-12. https://doi.org/10.1016/j.jns.2011.01.010

[2] Bandiera, S., Cartault, F., Jannot, A.S., Hatem, E., Girard, M., Rifai, L., *et al.* (2013) Genetic Variations Creating MicroRNA Target Sites in the FXN 3'-UTR Affect Frataxin Expression in Friedreich Ataxia. *PLOS ONE*, **8**, e54791. https://doi.org/10.1371/journal.pone.0054791

[3] Delatycki, M.B. and Bidichandani, S.I. (2019) Friedreich Ataxia—Pathogenesis and Implications for Therapies. *Neurobiology of Disease*, **132**, Article ID: 104606. https://doi.org/10.1016/j.nbd.2019.104606

[4] Reetz, K., Dogan, I., Hilgers, R.D., Giunti, P., Mariotti, C., Durr, A., *et al.* (2016) Progression Characteristics of the European Friedreich's Ataxia Consortium for Translational Studies (EFACTS): A 2 Year Cohort Study. *The Lancet Neurology*, **15**, 1346-1354. https://doi.org/10.1016/s1474-4422(16)30287-3

[5] Frolov, A., Vanka, D., Roumany, H., Guzman, M.A. and III, J.R.M. (2026) Deciphering Concurrent Tuberous Sclerosis Complex and Bipolar Disorder with a Genetic Approach. *Open Journal of Pathology*, **16**, 136-147. https://doi.org/10.4236/ojpathology.2026.162015

[6] Detton, A.J. (2017) Grant's Dissector. 16 Edition, Walters Kluwer.

[7] Frolov, A., Guzman, M.A., Hayat, G. and Martin, J.R. (2024) Two Cases of Sporadic Amyotrophic Lateral Sclerosis with Contrasting Clinical Phenotypes: Genetic Insights. *Cureus*, **16**, e56023. https://doi.org/10.7759/cureus.56023

[8] Koeppen, A.H., Ramirez, R.L., Becker, A.B., Bjork, S.T., Levi, S., Santambrogio, P., *et al.* (2015) The Pathogenesis of Cardiomyopathy in Friedreich Ataxia. *PLOS ONE*, **10**, e0116396. https://doi.org/10.1371/journal.pone.0116396

[9] Fukutani, Y., Nakamura, I., Matsubara, R., Kobayashi, K. and Isaki, K. (1996) Pathology of the Cerebellar Dentate Nucleus in Sporadic Olivopontocerebellar Atrophy: A Morphometric Investigation. *Journal of the Neurological Sciences*, **137**, 103-108. https://doi.org/10.1016/0022-510x(95)00303-j

[10] Ristanović, D., Milošević, N.T., Stefanović, B.D., Marić, D.L. and Rajković, K. (2010) Morphology and Classification of Large Neurons in the Adult Human Dentate Nucleus: A Qualitative and Quantitative Analysis of 2D Images. *Neuroscience Research*, **67**, 1-7. https://doi.org/10.1016/j.neures.2010.01.002

[11] Ahmad, H., Requena, T., Frejo, L., Cobo, M., Gallego-Martinez, A., Martin, F., *et al.* (2018) Clinical and Functional Characterization of a Missense ELF2 Variant in a CANVAS Family. *Frontiers in Genetics*, **9**, Article 85. https://doi.org/10.3389/fgene.2018.00085

[12] Gros-Louis, F., Dupré, N., Dion, P., Fox, M.A., Laurent, S., Verreault, S., *et al.* (2006) Mutations in SYNE1 Lead to a Newly Discovered Form of Autosomal Recessive Cerebellar Ataxia. *Nature Genetics*, **39**, 80-85. https://doi.org/10.1038/ng1927

[13] Van De Weghe, J.C., Rusterholz, T.D.S., Latour, B., Grout, M.E., Aldinger, K.A., Shaheen, R., *et al.* (2017) Mutations in ARMC9, Which Encodes a Basal Body Protein,

Cause Joubert Syndrome in Humans and Ciliopathy Phenotypes in Zebrafish. *The American Journal of Human Genetics*, **101**, 23-36. https://doi.org/10.1016/j.ajhg.2017.05.010

[14] Tolve, M., Tutas, J., Özer-Yildiz, E., Klein, I., Petzold, A., Fritz, V.J., *et al.* (2025) The Endocytic Adaptor AP-2 Maintains Purkinje Cell Function by Balancing Cerebellar Parallel and Climbing Fiber Synapses. *Cell Reports*, **44**, Article ID: 115256. https://doi.org/10.1016/j.celrep.2025.115256

[15] Tetsuka, S., Morita, M., Iida, A., Uehara, R., Ikegawa, S. and Nakano, I. (2013) ZNF512B Gene Is a Prognostic Factor in Patients with Amyotrophic Lateral Sclerosis. *Journal of the Neurological Sciences*, **324**, 163-166. https://doi.org/10.1016/j.jns.2012.10.029

[16] Dicks, A.R., Maksaev, G.I., Harissa, Z., Savadipour, A., Tang, R., Steward, N., *et al.* (2023) Skeletal Dysplasia-Causing TRPV4 Mutations Suppress the Hypertrophic Differentiation of Human iPSC-Derived Chondrocytes. *eLife*, **12**, e71154. https://doi.org/10.7554/elife.71154

[17] Skalova, D., Zidkova, J., Vohanka, S., Mazanec, R., Musova, Z., Vondracek, P., *et al.* (2013) *CLCN1* Mutations in Czech Patients with Myotonia Congenita, *in Silico* Analysis of Novel and Known Mutations in the Human Dimeric Skeletal Muscle Chloride Channel. *PLOS ONE*, **8**, e82549. https://doi.org/10.1371/journal.pone.0082549

[18] Baschal, E.E., Wethey, C.I., Swindle, K., Baschal, R.M., Gowan, K., Tang, N.L.S., *et al.* (2015) Exome Sequencing Identifies a Rare *HSPG2* Variant Associated with Familial Idiopathic Scoliosis. *G3 Genes|Genomes|Genetics*, **5**, 167-174. https://doi.org/10.1534/g3.114.015669

[19] Tuncay, I.O., Lee, E.K., Gustafson, A., Lee, Y., Jung, D., Koh, J., *et al.* (2025) Whole Genome Sequencing in Adolescent Idiopathic Scoliosis Cohort Implicates Multiple Biological Pathways. *npj Genomic Medicine*, **10**, Article No. 67. https://doi.org/10.1038/s41525-025-00520-5

[20] Huang, J., Zhang, C., Li, J., Wang, H., Cui, X., Wang, J., *et al.* (2024) Nemaline Myopathy with Scoliosis: A Case Report. *Frontiers in Pediatrics*, **12**, Article 1413096. https://doi.org/10.3389/fped.2024.1413096

[21] Xiao, F., Cai, M.Y., Yang, B.Y., Gu, W.D., Wang, L.L., Wu, H.Y., *et al.* (2026) Gene-Based Burden Testing Implicates Four Novel Susceptibility Genes Associated with Isolated Short Stature in Pediatric Patients. *World Journal of Pediatrics*, **22**, 362-371. https://doi.org/10.1007/s12519-026-01021-w

[22] Latypova, X., Creadore, S.G., Dahan-Oliel, N., Gustafson, A.G., Wei-Hung Hwang, S., Bedard, T., *et al.* (2021) A Genomic Approach to Delineating the Occurrence of Scoliosis in Arthrogryposis Multiplex Congenita. *Genes*, **12**, Article 1052. https://doi.org/10.3390/genes12071052

[23] Sakhaei, A. and Mohammadi-Asl, J. (2026) Clinical and Genetic Analysis of Limb-Girdle Muscular Dystrophy Type 2F with a Novel SGCD Mutation: A Case Report. *Cell Journal*, **27**, 1-10.

[24] Nakano, N., Hori, H., Abe, M., Shibata, H., Arimura, T., Sasaoka, T., *et al.* (2007) Interaction of BMP10 with TCAP May Modulate the Course of Hypertensive Cardiac Hypertrophy. *American Journal of Physiology-Heart and Circulatory Physiology*, **293**, H3396-H3403. https://doi.org/10.1152/ajpheart.00311.2007

[25] Sun, S., Yang, S., Zhang, N., Yu, C., Liu, J., Feng, W., *et al.* (2023) *Astragalus* Polysaccharides Alleviates Cardiac Hypertrophy in Diabetic Cardiomyopathy via Inhibiting the BMP10-Mediated Signaling Pathway. *Phytomedicine*, **109**, Article ID: 154543. https://doi.org/10.1016/j.phymed.2022.154543

[26] Sakamoto, A., Ono, K., Abe, M., Jasmin, G., Eki, T., Murakami, Y., *et al.* (1997) Both

Hypertrophic and Dilated Cardiomyopathies Are Caused by Mutation of the Same Gene, δ-Sarcoglycan, in Hamster: An Animal Model of Disrupted Dystrophin-Associated Glycoprotein Complex. *Proceedings of the National Academy of Sciences of the United States of America*, **94**, 13873-13878.
https://doi.org/10.1073/pnas.94.25.13873