Homologous Recombination Deficiency (HRD) Assays in Patients with High-Grade Epithelial Ovarian Cancer. Cancers (Basel). 2023; 15: 23. doi: 10.3390/cancers15235525.

14. Gutiérrez-Zepeda B.M., Gómez-Del Toro M.M., et al. The VEGFA rs3025039 Variant Is a Risk Factor for Breast Cancer in Mexican Women. Int J Mol Sci. 2024; 18: 10172. doi: 10.3390/ijms251810172.

15. Gu D., Wang M. VEGF 936C>T polymorphism and breast cancer risk: evidence from 5,729 cases and 5,868 controls. Breast Cancer Res Treat. 2011; 2: 489-493. doi: 10.1007/s10549-010-0991-z.

16. Huang D., Ke L., Cui H., et al. Efficacy and safety of VEGF/VEGFR inhibitors for platinum-resistant ovarian cancer: a systematic review and meta-analysis of randomized controlled trials. BMC Women's Health. 2024; 1: 34. doi: 10.1186/s12905-023-02879-y.

17. James R, Ramesh G, Krishnamoorthy L, et al. Prevalence of +405G>C,−1154G>A Vascular Endothelial Growth Factor Polymorphism in Breast Cancer. Ind J Clin Biochem. 2014; 21-28. doi: 10.1007/s12291-013-0307-2

18. Janardhan B, Vaderhobli S, Bhagat R, et al. Investigating impact of Vascular Endothelial Growth Factor Polymorphisms in Epithelial Ovarian Cancers: A Study in the Indian Population. PLoS One. 2015; 7: 0131190. doi: 10.1371/journal.pone.0131190.

19. Kapahi R., Manjari M., Sudan, Uppal M.S., et al. Association of+405C>G and+936C>T Polymorphisms of th Vascular Endothelial Growth Factor Gene with Sporadic Breast Cancer in North Indians. Asian Pacific Journal of Cancer Prevention. 2014. No. 1. P. 257-263. doi:10.7314/apjcp.2014.15.1.257.

20. Kim Y.H., Kim M.A., Park I.A., et al. VEGF polymorphisms in early cervical cancer susceptibility, angiogenesis, and survival. Gynecol Oncol. 2010. No. 2. P. 232-236. doi: 10.1016/j.ygyno.2010.07.035

21. Li Y, Wang Y, Kang S, et al. Association of vascular endothelial growth factor gene polymorphisms with susceptibility to epithelial ovarian cancer. Int J Gynecol Cancer. 2010. No. 5. P. 717-723. doi: 10.1111/igc.0b013e3181dbd32b.

22. Li Z, Wang Y, Liu C, et al. Association between VEGF single nucleotide polymorphism and breast cancer in the Northern China Han population. Breast Cancer Res Treat. 2021. No. 186. P. 149-156. doi: 10.1007/s10549-020-06024-3

23. Madrid-Paredes A., Casado-Combreras M.A., Pérez-Ramírez C., et al. Association of ABCB1 and VEGFA gene polymorphisms with breast cancer susceptibility and prognosis. Pathology-Research and Practice. 2020. No. 4. P. 152860. doi: 10.1016/j.prp.2020.152860

24. Rahoui J., Laraqui A., Sbitti Y., et al. Investigating the association of vascular endothelial growth factor polymorphisms with breast cancer: a Moroccan case–control study. Med Oncol. 2014. No. 31. P. 193. doi: 10.1007/s12032-014-0193-3

25. Rezaei M., Hashemi M., Sanaei S., et al. Association Between Vascular Endothelial Growth Factor Gene Polymorphisms with Breast Cancer Risk in an Iranian Population. Breast Cancer: Basic and Clinical Research. 2016. No. 10. P. 85–91. doi:10.4137/BCBCr.s39649.

26. VEGFA vascular endothelial growth factor A [Homo sapiens (human)]. [Electronic resource]. Date of update: 14.09.2025. URL: https://www.ncbi.nlm.nih.gov/gene/7422 (Accessed: 22.10.2025).

27. Wang Y., Huang Q., Liu J., et al. Vascular endothelial growth factor A polymorphisms are associated with increased risk of coronary heart disease: a meta-analysis. Oncotarget. 2017. No. 8. P. 30539-30551. doi: 10.18632/oncotarget.15546.

28. Zhang Y., Yu YF, Wang JZ, Jia H. Vascular endothelial growth factor +405G/C and -2578C/A polymorphisms and breast cancer risk: a meta-analysis. Genet Mol Res. 2015 Aug 3;14(3):8909-18. doi: 10.4238/2015.August.3.14. PMID: 26345822.

29. Zidi S, Stayoussef M, Gazouani E. Relationship of common vascular endothelial growth factor polymorphisms and haplotypes with the risk of cervical cancer in Tunisians. Cytokine. 2014. No.1. P. 108-112. doi:10.1016/j.cyto.2014.11.009.

S.K. Kononova

DOI 10.25789/YMJ.2025.92.24

УДК 616-009.26

APPROACHES TO THE TREATMENT OF AUTOSOMAL DOMINANT SPINOCEREBELLAR ATAXIAS

This article is devoted to prospects for treating neurodegenerative diseases caused by dynamic mutations, based on published studies searching for therapeutic approaches to spinocerebellar ataxias. Although these diseases are incurable, research results show that some medications and physiotherapy can alleviate symptoms of cerebellar ataxia. Thanks to progress in the study of spinocerebellar ataxias in recent years, there is considerable hope that gene-therapy methods can be developed that will slow disease progression or even halt it.

Keywords: spinocerebellar ataxia, dynamic mutations, treatment, gene therapy, physiotherapy

For citation: Kononova S.K. Approaches to the treatment of autosomal dominant spinocerebellar ataxias. Yakut Medical Journal. 2025; 92(4): 103-107. https://doi.org/10.25789/YMJ.2025.92.24

Introduction. Autosomal dominant spinocerebellar ataxias (ADSCA) represent a large heterogeneous group of hereditary ataxias, currently including about 40 types that differ by geno-phenotypic manifestations [18, 55]. ADSCAs are numbered chronologically as the genes responsible for the disease are discovered; for example, SCA47 was recently described by Gennarino V. et al., 2018 [5,30]. The most studied are SCA1, SCA2, SCA3, SCA6, SCA7, SCA17. Certain ADSCA forms are known to be concentrated in particular world populations: SCA1 in the Yakut population [3,31,63]; SCA2 in the Indian population [56]; SCA3 in Portuguese, Brazilian and Chinese populations [27].

Characteristic clinical signs of ADSCA are slowly or rapidly progressive dysarthria, oculomotor disorders and gait ataxia, and impaired coordination. The cerebellum, brainstem and spinal cord undergo neurodegeneration [1].

A common feature of all ADSCA subtypes is the presence of an unstable (dynamic) mutation caused by expansion of CAG repeats in the coding region of a gene, leading to formation of a polyglutamine (polyQ) tract in the encoded protein [43,55]. There is a relationship between age at onset and severity of neurological symptoms and the size of the polyQ-repeats expansion [45]. The expanded polyglutamine tract causes synthesis of a misfolded, aggregation-prone protein which, at advanced stages of aggregation, disrupts regulation of gene expression at the transcriptional level and leads to disturbance of neuronal homeostasis [26].

Table 1. Various ADSCA diseases with polyglutamine mutations.

The Republic of Sakha (Yakutia) is a region with the highest accumulation

KONONOVA Sardana Kononovna – PhD in Biological Sciences, chief researcher, head of the Department of the YSC CMP, email: konsard@rambler.ru, ORCID: 0000-0002-2143-0021

of autosomal-dominant ataxia type 1 (SCA1). Epidemiological, population, molecular-genetic and bioethical studies of this socially significant neurodegenerative disease have been conducted earlier [3,31,63].

Currently there is no treatment for hereditary neurodegenerative diseases with polyglutamine mutations, but it is necessary to discuss directions for improving patient condition.

At present there are three main therapeutic approaches to ADSCA:

- symptomatic treatment using known pharmaceutical agents [18,38];
- gene methods or gene-edited products to reduce toxic consequences of polyglutamine mutations [22,27,43];
- neurorehabilitation [14].

Most studies related to SCA pathogenesis are carried out using populations of transgenic mice that overexpress mutant and normal transgenes (the latter as controls) [6]. In addition, studies are performed directly in Purkinje cells of mice with gene knock-outs using genetic vectors carrying large segments of the human gene with expanded polyglutamine sequences and regulatory elements [6,32,43].

Studies on the Use of Certain Pharmacological Agents in ADSCA Therapy. The main cellular disturbances in the cerebellum (Bergmann glia, Purkinje cells) targeted by therapeutic strategies are:

- disrupted expression and function of ion channels and receptors [32];
- excitotoxicity, where excessive accumulation of glutamate in the extracellular space (synaptic cleft) causes toxicity to neurons [2,33];
- decreased levels of potassium-calcium channels in Purkinje cells [19].

Studies of 3,5-dimethyladamantane-1-amine (memantine) for possible neuroprotective effects and synaptic plasticity with long-term use in SCA1 model mice (Belozor et al., 2024) showed that memantine increases expression of amino-acid transporter proteins, thereby reducing reverse glutamate uptake and enhancing signaling within Purkinje cells. It is claimed that memantine reduces anatomical signs of neurodegeneration in SCA1 model mice and partially ameliorates the ataxic phenotype; at the same time it also affects cerebellar plasticity and impairs motor learning. The authors suggest that clinical use of memantine in SCA1 may be complicated by its suppression of cortical plasticity [2,38,46].

Kalla R. & Strupp M., 2019, in recent studies showed the promise of obtaining a neuroprotective effect in SCA1 treatment with 4-aminopyridine. In SCA1 mouse models motor activity was disrupted due to decreased electrical activity (firing rate) in Purkinje cells, their dysfunction and atrophy. Nonselective blockade of voltage-dependent potassium channels with 4-aminopyridine increased Purkinje cell excitability, partially protected against cell atrophy and improved motor behavior of the animals [8,36].

Over the last ten years there has been intensive research and clinical trials of the amino acid derivative acetyl-DL-leucine in symptomatic therapy of different SCA types. Acetyl-DL-leucine regulates the membrane potential of Purkinje cells by interacting with membrane phospholipids. In a series of clinical trials across different research groups, modified acetyl-DL-leucine improved ataxia and dysarthria in patients with SCA1, SCA2, SCA3, SCA6 [54,64,65].

Another therapeutic strategy is studying mechanisms of autophagy in the cell, by which excess or damaged proteins and organelle structures are degraded by enzymes and removed from the cell; this may become a new approach to ADSCA therapy. It has been shown that enhancing autophagy in cells of mouse models reduced neurodegeneration and eased the course of SCA3 [10,41]. For example, in SCA3 excessive polyglutamine repeat length causes misfolding of ataxin-3 and formation of aggregates that disrupt cellular processes, cause cellular toxicity and degeneration [42,60]. This protein is toxic; one of the main pathways for degradation of misfolded proteins is autophagy [42]. Burnett et al. suggest that the ubiquitin–proteasome pathway, where ataxin-3 is involved, plays a key role in the development of neurodegenerative diseases characterized by misfolding and aggregation of proteins [13]. The deubiquitinating active ataxin-3 is widely expressed in the brain. The polyQ domain of ataxin-3 binds the Beclin-1 (BECN1) protein, which initiates autophagy [42,44].

Cellular repair systems and mitochondrial energy production become active under caloric restriction. Food shortage engages protective systems of the organism and activates autophagy. The beneficial effects of fasting observed in mice remain to be confirmed in patients with neurodegenerative diseases [59,60]. The well-known protein sirtuin 1 (SIRT1) induces autophagy and suppresses neuroinflammation. In a study by Zhu L. et al., 2025, the dietary supplement resveratrol was shown, via activation of SIRT1, to influence core mechanisms of neurodegeneration. As a result of SIRT1 activation by resveratrol, oxidative stress, mitochondrial dysfunction and protein aggregation decrease, while neuronal survival and function and neuroinflammation improve [35].

The widely consumed and well-known compound 1,3,7-trimethylpurine-2,6-dione (caffeine) has recently been studied as an effective protective agent in some neurodegenerative disorders. Caffeine is a nonselective antagonist of adenosine receptors (A2A). These receptors participate in synaptic viability, neuroinflammation and neuronal apoptosis. Inactivation of A2A receptors reduces neurodegeneration, making caffeine a potential therapeutic candidate for neurodegenerative diseases [11,47].

Potential Gene-Therapy Methods for Neurodegenerative Diseases. Gene-therapy strategies are developing along several directions:

- regulation of gene expression using RNA interference with small interfering RNAs (siRNAs), short hairpin RNAs (shRNAs) and microRNAs (miRNAs) to target and degrade mRNA molecules. Gene silencing occurs via a multiprotein ribonucleoprotein complex [29,53];
- application of targeted therapies based on antisense oligonucleotides (ASOs) [58];
- gene editing using CRISPR/Cas9 (clustered regularly interspaced short palindromic repeats / associated nuclease 9) [22].

Table 2 presents results of gene-therapy methods for some types of SCAs; as a rule these are at the stage of studies in genetically modified model organisms and have not reached clinical trials. Wide use of various regulatory microRNAs is due to their universality and ability to induce or inhibit gene expression (transcription, translation, processing, etc.) [4,7,25,37,50]. The goal of gene therapy in SCA is to inhibit or remove the expanded gene region that encodes the toxic protein. Animal-model studies have shown encouraging results: reduced levels of toxic proteins, decreased degeneration of cerebellar cells, alleviation of motor deficit and overall improvement in neuropathological measures [4,7,25,37,50].

The CRISPR-Cas9 system was discovered and obtained from Streptococcus pyogenes as an adaptive bacterial immune system for protection against viruses; in this system CRISPR and guide RNAs work together with Cas proteins [9]. It turned out that this system is very convenient not only for various genomic modifications in research, but also for

Table 1

Various ADSCA diseases with polyglutamine mutations [30]

name	gene	locus	protein	repeats	number of repeats of normal alleles	number of repeats of intermediate alleles	number of repeats
SCA1	*ATXN1*	6p22.3	Ataxin-1	$(CAG)_n (CAT)_n (CAG)_n$	of pathological alleles	36-38	39-91
SCA2	*ATXN2*	12q24.12	Ataxin-2	$[CAG_n CAA (CAG)_n]_n$	14-31	32	33-500
SCA3	*ATXN3*	14q32.12	Ataxin-3	CAG2 CAA AAG CAA $(CAG)_n$	11-44	45-59	60-87
SCA6	*CACNA1A*	19p13.13	CACNA1A	(CAG)n	4-18	19	20-33
SCA7	*ATXN7*	3p14.1	Ataxin-7	(CAG)n	4-19	28-33	34-460
SCA17	*TBP*	6q27	TBP	[(CAG)n (CAA)n (CAG)n]	25-40	-	41-66

Note. (CAG)n – cytosine-adenine-guanine repeats; CAT – cytosine-adenine-thymine stop codon; CAA – cytosine-adenine-adenine-stop codons; AAG – adenine-adenine-guanine-stop codon.

gene therapy via selective targeting of the eukaryotic cell genome [39]. Delivery of CRISPR-Cas9 components into target cells occurs as a ribonucleoprotein consisting of the Cas9 protein and an sgRNA — single-guide RNA [9,21,39].

A case of deleting the coding poly-Q region using CRISPR/Cas9 gene-editing was described by Ouyang S. et al., 2018. For the first time the authors provided preliminary data for CRISPR/Cas9 editing in SCA3 in the ATXN3 gene and showed the possibility of using a pair of single-guide RNAs to delete the expanded polyglutamine region of the gene [22].

In the study by He et al., 2021, in induced pluripotent stem cells (iPSCs) derived from a patient with SCA3, using paired single-guide RNAs and a homology-directed repair strategy, they successfully repaired 74 CAG expansions in exon 10 of ATXN3, leading to specific and effective suppression of mutant ataxin-3 protein expression [23]. Using CRISPR/Cas9 with homology-directed repair, Song et al., 2022 developed effective approaches for one-step genetic correction of patient-derived SCA3 iPSCs. They later advanced their research by developing disease models in disease-relevant neurons differentiated to cerebellar phenotypes [24]. The study by Pappadà et al., 2022 allowed development and validation of a therapeutic approach using CRISPR/Cas9 for fibroblasts obtained from patients with SCA1. This sgRNA/Cas9 method effectively reduced production of both normal and mutant ATXN1 protein [52].

Neurorehabilitation as an Adjunctive Therapy for SCA. Researchers conducting clinical studies in neurodegenerative diseases suggest that cerebellar changes are associated with significant cognitive and affective deficits in ADSCA patients due to degeneration of the cerebellum and its connections [17,61,62].

Antal, 2022 described in detail non-invasive brain stimulation methods for studying brain function in healthy people and the possibility of improving cognitive processes using these methods [40]. Methods such as transcranial magnetic stimulation (TMS) and transcranial direct-current stimulation (tDCS) are used to accelerate neuropsychological or psychiatric rehabilitation by modulating neuroplasticity. In TMS protocols, a coil placed over the scalp delivers a brief high-amplitude current generating a magnetic pulse that induces a brief electric current on the brain surface beneath the coil. At sufficient intensity a single

Table 2

Examples of gene therapy for some SCAs [30]

disease	method	model system	effect
SCA1	Created microRNA containing siRNA	mice SCA1 K1	Improvement of neuropathology parameters and reduction of ATXN 1 protein levels by 58-72% [50].
SCA2	AON: decreased levels of ataxin-2 protein	mice ATXN2 , BAC-Q72 SCA2	A 75% reduction in ATXN2 protein levels in mouse brain Purkinje cells and significant improvement in motor phenotype [7].
SCA3	shRNA: allele-specific downregulation	rats SCA3	Reduction of neuropathological abnormalities [4]
SCA6	miRNA-3191-5p	mice SCA6 K1	Alleviation of motor deficits and Purkinje cell degeneration [37]
SCA7	miRNA-124	Cells N2A and mice SCA7	80% reduction in ATXN7 protein levels [25]
SCA3	CRISPR/Cas9	Neurons derived from patient-specific immunopluropatent stem cells	Successful removal of the polyQ coding region [22]

Note. AON – antisense oligonucleotide; iPSCs – immunopluropatent stem cells; mi RNA – short RNA; si RNA – short interfering RNA; sh RNA – short hairpin RNA

TMS pulse elicits highly synchronized action potentials in the target area (Fig. 1). Ten or more minutes can lead to modulatory effects that extend the period of stimulation for many minutes or hours, with more pronounced behavioral effects often observed immediately after the end of stimulation [51].

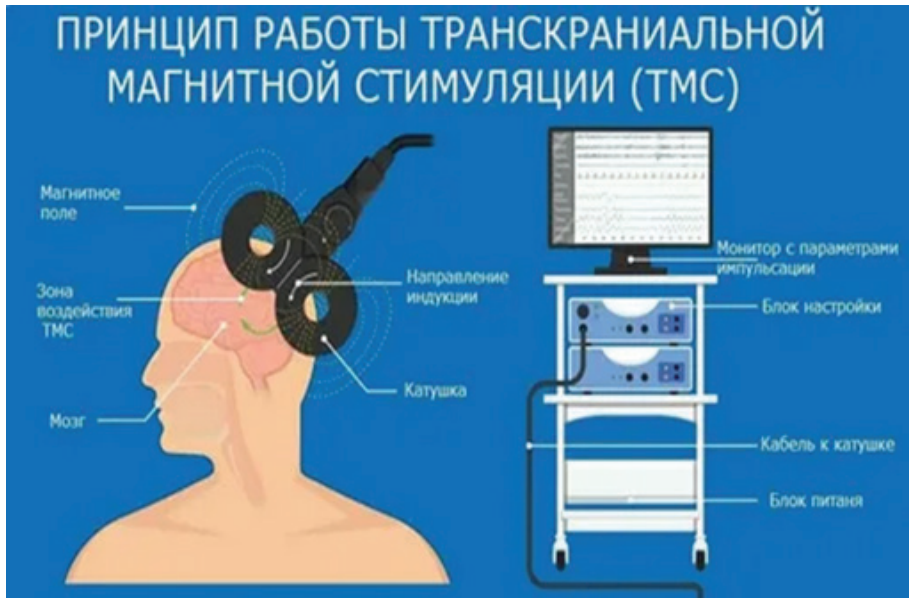
Some data indicate TMS effectiveness in treating core symptoms and cognitive functions in various neurological and neuropsychiatric disorders, as well as in improving behavioral and socio-affective deficits [16,30].

Farzan F. et al., 2013 provide evidence for cerebellar stimulation as a treatment strategy for degenerative cerebellar ataxia. Observed improvements in physical function, gait kinematics and coordinated muscle contraction, as well as cerebellar–cortical interactions, were fairly convincing. However, the authors noted that the study lacked control participants and control conditions, and they emphasized the need for further controlled studies to examine the effects of TMS in SCA patients [15].

The aim of the study by Maas et al., 2022 was to determine whether a two-week regimen of daily cerebellar tDCS sessions reduces ataxia and severity of nonmotor symptoms and whether it changes cerebello–M1 connectivity in individuals with spinocerebellar ataxia type 3 (SCA3). Change in the Scale for the Assessment and Rating of Ataxia (SARA) after two weeks was the primary endpoint. After the final stimulation session both groups showed significant short-term improvements in several motor, cognitive functions and patient-reported outcomes, but no treatment effect in favor of active tDCS was found. Some patients in the intervention group showed sustained reduction in SARA scores for six or even twelve months, indicating individual variability in treatment response [16].

The main adjunctive neurorehabilitation method for patients with cerebellar ataxia is therapeutic physical exercise (physiotherapy), so mechanisms by which aerobic training and balance exercises improve cerebellar ataxia symptoms have been studied more closely.

In Burciu, 2013, postural and clinical assessments as well as structural magnetic resonance imaging were performed before and after training. The main results were: first, training improved balance measures in patients with cerebellar damage. Second, unlike the control group, patients showed a significant increase in gray-matter volume in the dorsal premotor cortex after training. Third,



Transcranial magnetic stimulation

associated with training there was an increase in cerebellar gray-matter volume that was more pronounced in the control group than in patients [12].

Recent studies provide evidence that intensive motor training can be effective in degenerative ataxia: coordination training — via physiotherapy or game-based exercises — benefits ataxia patients; improvements result from remediation of ataxia-specific deficits rather than nonspecific changes; maintenance of training effects depends on continued training; even patients with progressive neurodegeneration benefit from these treatments. This research asserted that intensive aerobic training is safe for people with cerebellar ataxia, with high participant engagement and adherence. Home aerobic training for people with cerebellar ataxia may be more effective against ataxia than balance training, because aerobic exercise may induce neuroplastic changes in the degenerating cerebellum [28,34,49,57].

Conclusion. There is currently intensive growth of ADSCA gene-therapy related research. Animal studies have shown promising results: reduced levels of toxic proteins, decreased degeneration of cerebellar cells, alleviation of motor deficits and overall improvement in neuropathology.

On the one hand, these diseases are incurable, but on the other hand studies show that known pharmaceuticals, dietary supplements, noninvasive transcranial neuromodulation and physiotherapy are alternative treatment options and can alleviate ataxia symptoms.

Thanks to progress in SCA research in recent years, there is strong hope that therapies can be developed that will slow disease progression or even halt it.

Авторы заявляют об отсутствии конфликта интересов.

References

1. Gorbunova V.N., Baranov V.S. Vvedenie v molekulyarnuyu diagnostiku i genoterapiyu nasledstvennyh zabolevanij [Introduction to molecular diagnostics and gene therapy of hereditary diseases]. Special'naya literature [Special literature], 1997. 278 p. (In Russ.).]

2. Belozor O.S., Vasiliev A.A., Mileyko A.G., et al. 3,5-Dimetil-adamantan-1-amin vosstanavlivaet kratkovremennuyu sinapticheskuyu plastichnost' posredstvom izmeneniya funkcii transportyorov vozbuzhdayushchih aminokislot u model'nyh myshej so spinocerebellyarnoj ataksiej 1 tipa [3,5-Dimethyl-adamantane-1-amine restores short-term synaptic plasticity by changing the function of excitatory amino acid transporters in model mice with type 1 spinocerebellar ataxia]. Annaly klinicheskoj i eksperimental'noj nevrologii [Annals of Clinical and Experimental Neurology. 2024; 18 (1): 63-71 (In Russ.).] DOI: https://doi.org/10.54101/ACEN.2024.1.7

3. Kononova S.K. Vnedrenie geneticheskih tekhnologij v prakticheskoe zdravoohranenie Yakutii na primere spinocerebellyarnoj ataksii 1 tipa v kontekste translyacionnoj mediciny The introduction of genetic technologies into practical healthcare in Yakutia on the example of type 1 spinocerebellar ataxia in the context of translational medicine. Yakutskij medicinskij zhurnal [Yakut Medical Journal. 2022; 3 (79): 103-107 (In Russ.).]

4. Alves S., Nascimento-Ferreira I., Auregan G., et al. Allele-specific RNA silencing of mutant ataxin-3 mediates neuroprotection in a rat model of Machado-Joseph disease. PLoS One. 2008; 3(10): e3341. doi: 10.1371/journal.pone.0003341.

5. Gennarino V.A., Palmer E.E., McDonell L.M., et al. A Mild PUM1 Mutation Is Associated with Adult-Onset Ataxia, whereas Haploinsuffi-

ciency Causes Developmental Delay and Seizures. Cell. 2018 Feb 22;172(5):924-936.e11. doi: 10.1016/j.cell.2018.02.006.

6. Switonski P.M., Szlachcic W.J., Krzyzosiak W.J., et al. A new humanized ataxin-3 knock-in mouse model combines the genetic features, pathogenesis of neurons and glia and late disease onset of SCA3/MJD. Neurobiol Dis. 2015;73:174-88. doi: 10.1016/j.nbd.2014.09.020.

7. Scoles D.R., Meera P., Schneider M.D., et al. Antisense oligonucleotide therapy for spinocerebellar ataxia type 2. Nature. 2017;544(7650):362-366. doi: 10.1038/nature22044.

8. Hourez R., Servais L., Orduz D., et al. Aminopyridines correct early dysfunction and delay neurodegeneration in a mouse model of spinocerebellar ataxia type 1. J Neurosci. 2011; 31(33):11795-807. doi: 10.1523/JNEUROSCI.0905-11.2011.

9. Makarova K.S., Grishin N.V., Shabalina S.A., et al. A putative RNA-interference-based immune system in prokaryotes: computational analysis of the predicted enzymatic machinery, functional analogies with eukaryotic RNAi, and hypothetical mechanisms of action. Biol Direct. 2006;1(1):1–26. doi: 10.1186/1745-6150-1-7.

10. Palmer J.E., Wilson N., Son S.M., et al. Autophagy, aging, and age-related neurodegeneration / Neuron. 2025;113(1):29-48. doi: 10.1016/j.neuron.2024.09.015.

11. Pohanka M., Borea P.A., Varani K., et al. A(2A) Adenosine Receptor Antagonists in Neurodegenerative Diseases. Curr Med Chem. 2022;29(24):4138-4151. doi:10.2174/0929867328666211129122550.

12. Burciu R.G., N. Fritsche, O. Granert, et al. Brain changes associated with postural training in patients with cerebellar degeneration: a voxel-based morphometry study. J Neurosci. 2013;33(10):4594-604. doi: 10.1523/JNEUROSCI.3381-12.2013.

13.Burnett B, Li F, Pittman RN. The polyglutamine neurodegenerative protein ataxin-3 binds polyubiquitylated proteins and has ubiquitin protease activity. Hum Mol Genet. 2003;12(23):3195-205. doi: 10.1093/hmg/ddg344.

14. Cardoso SV, Fernandes SR, Tomás MT. Therapeutic Importance of Exercise in Neuroplasticity in Adults with Neurological Pathology: Systematic Review. Int J Exerc Sci. 2024;17(1):1105-1119. doi: 10.70252/VZWF7949.

15. Farzan F., Wu Y., Manor B., et al. Cerebellar TMS in treatment of a patient with cerebellar ataxia: evidence from clinical, biomechanics and neurophysiological assessments. Cerebellum. 2013;12(5):707-12. doi: 10.1007/s12311-013-0485-8.

16. Maas M., Teerenstra S, Toni I., et al. Cerebellar Transcranial Direct Current Stimulation in Spinocerebellar Ataxia Type 3: a Randomized, Double-Blind, Sham-Controlled Trial. RPPW. Neurotherapeutics. 2022;19(4):1259-1272. doi: 10.1007/s13311-022-01231-w.

17. Ciricugno A., Oldrati V., Cattaneo Z., et al. Cerebellar Neurostimulation for Boosting Social and Affective Functions: Implications for the Rehabilitation of Hereditary Ataxia Patients. Cerebellum. 2024;23(4):1651-1677. doi: 10.1007/s12311-023-01652-z.

18. Szpisjak L., Zadori D., Klivenyi P., et al. Clinical Characteristics and Possible Drug Targets in Autosomal Dominant Spinocerebellar Ataxias. CNS Neurol Disord Drug Targets. 2019;18(4):279-293. doi: 10.2174/1871527318666190311155846

19. Gruol D.L., Netzeband J.G., Quina L.A., et al. Contribution of L-type channels to Ca2+ regulation of neuronal properties in early developing purkinje neurons. Cerebellum. 2005;4(2):128-39. doi: 10.1080/14734220510007969.

20. To W.T., De Ridder D., Jr. Hart J., et al. Changing Brain Networks Through Non-invasive Neuromodulation. Front Hum Neurosci. 2018 ;12:128. doi: 10.3389/fnhum.2018.00128.

21. Gowing G, Svendsen S, Svendsen CN. Ex vivo gene therapy for the treatment of neurological disorders. Progr Brain Res. 2017; 230:99–132. doi: 10.1016/bs.pbr.2016.11.003.

22. Ouyang S, Xie Y, Xiong Z, et al. CRISPR/Cas9-Targeted Deletion of Polyglutamine in Spinocerebellar Ataxia Type 3-Derived Induced Pluripotent Stem Cells. Stem Cells Dev. 2018;27(11):756-770. doi: 10.1089/scd.2017.0209.

23. He L., Wang S., Peng L., et al. CRISPR/Cas9 mediated gene correction ameliorates abnormal phenotypes in spinocerebellar ataxia type 3 patient-derived induced pluripotent stem cells. Transl Psychiatry. 2021;11(1):479. doi: 10.1038/s41398-021-01605-2.

24. Song G., Ma Y., Gao X., et al. CRISPR/Cas9-mediated genetic correction reverses spinocerebellar ataxia 3 disease-associated phenotypes in differentiated cerebellar neurons. Life Med. 2022;1(1):27–44. doi: 10.1093/lifemedi/lnac020.

25. Tan J.Y., Vance K.W., Varela M.A., et al. Cross-talking noncoding RNAs contribute to cell-specific neurodegeneration in SCA7. Nat Struct Mol Biol. 2014;21(11):955-961. doi: 10.1038/nsmb.2902.

26. Schaffar G., Breuer P., Boteva P., et al. Cellular toxicity of polyglutamine expansion proteins: mechanism of transcription factor deactivation. Mol Cell. 2004;15(1):95-105. doi: 10.1016/j.molcel.2004.06.029.

27. Déglon N. Gene editing as a therapeutic strategy for spinocerebellar ataxia type-3// Rev Neurol (Paris). 2024;180(5):378-382. doi: 10.1016/j.neurol.2024.03.003.

28. Cabanas-Valdés R., Fernández-Lago H., Peláez-Hervás S., et al. Effect of a Home-Base Core Stability Exercises in Hereditary Ataxia. A Randomized Controlled Trial. A Pilot Randomized Controlled Trial. Mov Disord Clin Pract. 2024;11(6):666-675. doi: 10.1002/mdc3.14036.

29. Frédérick PM, Simard MJ. Regulation and different functions of the animal microRNA-induced silencing complex. Wiley Interdiscip Rev RNA. 2022;13(4):e1701. doi: 10.1002/wrna.1701.

30. Buijsen R.A.M., Toonen L.J.A., Gardiner S.L., et al. Genetics, Mechanisms, and Therapeutic Progress in Polyglutamine Spinocerebellar Ataxias. Neurotherapeutics. 2019 ;16(2):263-286. doi: 10.1007/s13311-018-00696-y.

The full version of the list of references is in the editorial office.