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POTASSIUM CHANNEL-RELATED DEVELOPMENTAL AND EPILEPTIC ENCEPHALOPATHIES: FROM FUNCTIONAL MECHANISMS TO PRECISION THERAPEUTICS

A narrative review focused on KCNQ2, KCNA2, KCNT1, and KCNB1

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Abstract

Potassium channels are central regulators of neuronal resting membrane potential, action-potential repolarization, firing adaptation, and neurotransmitter release. Pathogenic variants in potassium-channel genes can produce a broad neurodevelopmental spectrum, ranging from self-limited epilepsy to severe developmental and epileptic encephalopathies (DEEs). Importantly, the direction of channel dysfunction cannot be inferred reliably from the clinical phenotype alone: loss-of-function, gain-of-function, dominant-negative, and mixed effects may converge on epilepsy through cell-type- and circuit-specific mechanisms. This narrative review examines four potassium channelopathies especially relevant to pediatric DEE and precision neurology—KCNQ2, KCNA2, KCNT1, and KCNB1. We integrate electroclinical phenotypes, functional mechanisms, genotype-phenotype correlations, conventional antiseizure treatment, and emerging mechanism-based therapies. KCNQ2 illustrates the clinical value of early molecular diagnosis, with sodium-channel blockers showing high effectiveness in loss-of-function neonatal epilepsies and recent multicenter data associating earlier treatment with earlier seizure offset and more favorable developmental trajectories. KCNA2 demonstrates the need for functional stratification because gain-of-function variants may respond to 4-aminopyridine. KCNT1-related epilepsy remains therapeutically challenging; quinidine has inconsistent clinical effectiveness, while antisense oligonucleotide strategies are supported by preclinical studies. KCNB1-related disorders combine epilepsy with prominent cognitive, language, and behavioral morbidity and currently lack a validated gene-specific therapy.

Across these disorders, functional testing, natural-history cohorts, patient-centered outcomes, and trial-ready registries are essential for moving from gene diagnosis to disease modification. Potassium channelopathies provide a model for precision medicine in pediatric neurology in which treatment selection should increasingly integrate phenotype, variant mechanism, developmental timing, and evidence level rather than gene name alone.

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Keywords: developmental and epileptic encephalopathy; potassium channel; KCNQ2; KCNA2; KCNT1; KCNB1; precision medicine; genetic epilepsy; antisense oligonucleotide; pediatric neurology.

1. Introduction

Developmental and epileptic encephalopathies are severe neurodevelopmental disorders in which developmental impairment reflects the combined effects of the underlying etiology and epileptic activity. Genomic testing has transformed their classification: disorders once grouped only by age at seizure onset, seizure type, or electroencephalographic pattern can now be stratified by molecular pathway and, increasingly, by variant-specific functional effect. Ion-channel disorders are particularly instructive because the molecular defect is directly connected to neuronal excitability, yet the relationship between channel current and network behavior is often non-linear.

Potassium channels constitute the most diverse ion-channel family in the nervous system. They participate in repolarization, resting membrane potential, spike-frequency adaptation, axonal conduction, and synaptic release. Among pediatric DEEs, KCNQ2, KCNA2, KCNT1, and KCNB1 illustrate recurring precision-medicine problems: marked allelic heterogeneity, overlap between epilepsy and developmental phenotypes, imperfect prediction of functional effect from sequence data, and an emerging but uneven therapeutic pipeline.

This review asks how functional mechanism can be translated into earlier diagnosis and more rational treatment. The topic is timely because potassium-channel disorders increasingly sit at the intersection of molecular diagnosis, functional neurophysiology, and therapeutic development. The Channelopathies 2026 scientific program at Institut Imagine is mentioned only as a contemporary indicator of field organization and research priorities; it is not used as evidence for biological mechanisms, clinical efficacy, or therapeutic recommendations.

2. Scope and literature approach

This article is a focused narrative review rather than a systematic review or meta-analysis. For the revised manuscript, the literature was updated through 22 September 2026 using PubMed/MEDLINE and targeted searches of publisher-indexed records. Search concepts

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combined KCNQ2, KCNA2, KCNT1, and KCNB1 with developmental and epileptic encephalopathy, epilepsy, gain of function, loss of function, dominant negative, trafficking, functional study, precision medicine, sodium-channel blocker, 4-aminopyridine, quinidine, antisense oligonucleotide, gene therapy, natural history, SUDEP, and patient-centered outcomes. English-language peer-reviewed human studies, functional studies, clinically relevant preclinical studies, systematic or authoritative reviews, and seminal older reports were eligible. Priority was given to studies informing electroclinical phenotype, genotype-phenotype relationships, functional direction, treatment response, safety, natural history, or translational readiness. The search was structured but non-systematic; therefore, a PRISMA flow diagram and a prospectively logged deduplicated record count were not generated. The final cited evidence set was selected iteratively for relevance, recency, primary-data support, and representation across all four genes. When reports were discordant, the manuscript retained the disagreement and favored direct primary evidence over conference material or narrative inference.

Therapeutic evidence is labeled using a pragmatic hierarchy: (1) Clinical evidence - replicated cohort data or controlled clinical evidence; (2) Limited clinical evidence - retrospective series, small prospective studies, or multiple observational reports; (3) Anecdotal evidence - isolated case reports; (4) Translational evidence - functional rescue with limited patient exposure; and (5) Preclinical evidence - cellular or animal-model evidence only. Evidence maturity is gene-specific and uneven; KCNQ2 currently has the strongest clinical actionability signal among the four disorders reviewed. The Channelopathies 2026 program is retained only as contextual evidence of contemporary research priorities and is not used to support therapeutic effectiveness.

3. Why potassium channel dysfunction can produce epilepsy

A simplistic model predicts that loss of an outward potassium current should increase excitability and that gain of potassium current should suppress firing. Human channelopathies show why this model is incomplete. The effect of a variant depends on neuronal population, subcellular localization, heteromeric assembly, voltage dependence, gating kinetics, developmental expression, and whether inhibitory or excitatory neurons are preferentially affected.

Excess potassium conductance in inhibitory interneurons may reduce inhibitory network output and paradoxically promote seizures. Gain-of-function potassium variants can therefore be epileptogenic.

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Variant pathogenicity classification and functional classification are related but distinct. A variant may satisfy accepted criteria for pathogenicity without its precise functional direction being established. Functional classification should distinguish loss-of-function (LOF), gain-of-function (GOF), dominant-negative effects, altered trafficking or expression, and mixed effects, interpreted in the relevant biological context. Patch-clamp studies, patient-derived neuronal models, animal models, and computational approaches can inform therapeutic direction, but individualized functional testing remains research-based and is not routinely available for every patient or variant. In clinical practice, recurrent variants with established functional data should be distinguished from variants for which only molecular pathogenicity is known.

4. KCNQ2-related developmental and epileptic encephalopathy

KCNQ2 encodes the Kv7.2 subunit, a major component of the neuronal M-current. Pathogenic KCNQ2 variants produce a spectrum from self-limited neonatal epilepsy to severe neonatal-onset DEE. The severe phenotype typically begins in the first days of life with frequent focal tonic, clonic, or asymmetric seizures, often accompanied by a markedly abnormal EEG background that may include burst-suppression. Seizures can later improve substantially, while developmental disability, hypotonia or spasticity, movement abnormalities, and impaired communication may persist.

The KCNQ2 spectrum demonstrates the importance of variant mechanism. Haploinsufficiency or other LOF mechanisms are common in self-limited neonatal epilepsy, whereas severe DEE is enriched for de novo missense variants affecting functionally critical channel regions. Phenotype, however, cannot be assigned from variant type alone.

Treatment evidence is stronger for KCNQ2 than for the other channelopathies considered here. Retrospective studies repeatedly report effectiveness of sodium-channel blockers, particularly carbamazepine, phenytoin, and oxcarbazepine. A 2026 international multicenter cohort of 282 individuals further supported carbamazepine and oxcarbazepine as highly effective therapies in LOF KCNQ2 disorders; initiation within the first month was associated with earlier seizure offset and more favorable neurodevelopmental trajectories. These observational data do not establish that early treatment itself caused the developmental difference, because variant severity and other biological factors contribute to outcome heterogeneity. Severe impairment can occur despite early seizure control.

Direct Kv7 modulation is a second precision strategy. Ezogabine/retigabine, a Kv7 channel opener, has been associated with seizure reduction and caregiver-reported developmental

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improvements in a small retrospective KCNQ2-DEE cohort. Newer Kv7 modulators are under development, but pediatric gene-specific evidence remains limited.

5. KCNA2-related encephalopathy

KCNA2 encodes Kv1.2, a voltage-gated potassium-channel subunit expressed prominently in axonal compartments and in both excitatory and inhibitory neurons. Pathogenic variants cause a continuum that includes DEE, generalized or focal epilepsy, episodic or progressive ataxia, dysarthria, spasticity, movement abnormalities, and intellectual disability. Cohort and functional studies demonstrate strong GOF, LOF with dominant-negative behavior, altered trafficking, and mixed effects. Importantly, variants affecting the same residue can produce opposite functional consequences, reinforcing that sequence location or phenotype alone cannot reliably predict therapeutic direction.

KCNA2 is one of the clearest examples of mechanism-guided targeted channel modulation in genetic epilepsy. In selected GOF KCNA2 encephalopathy, 4-aminopyridine can counter excessive Kv1.2 current. Functional rescue and multicenter n-of-1 clinical experience support improvement in seizures, gait, ataxia, alertness, cognition, or speech in a subset of appropriately selected patients; however, treatment should not be generalized to LOF or functionally unresolved variants. Longer-term evidence remains limited, and movement, coordination, communication, cognition, and quality of life should be measured alongside seizure outcomes.

Emerging KCNA2 strategies include mechanism-specific modulation and experimental gene-silencing approaches. These remain translational or preclinical and should not be presented as established disease-modifying therapy. Recent functional work and adult follow-up reports broaden the recognized genotype-phenotype spectrum and emphasize longitudinal assessment of ataxia and movement phenotypes.

6. KCNT1-related epilepsy and DEE

KCNT1 encodes the sodium-activated potassium channel KNa1.1 (Slack/Slo2.2). Pathogenic variants are associated with a spectrum extending from sleep-related hypermotor epilepsy to severe DEEs, most notably epilepsy of infancy with migrating focal seizures. Affected infants may develop very frequent focal seizures that migrate between hemispheres, autonomic manifestations, developmental stagnation or regression, hypotonia, and profound disability.

Many pathogenic KCNT1 variants produce GOF, although exceptions emphasize the need to avoid assuming mechanism solely from gene identity. Quinidine became an early precision-

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guided candidate because it can inhibit KCNT1 current. Primary clinical evidence is heterogeneous: early case reports described benefit in selected patients, whereas a randomized trial and a prospective neonatal EIMFS series did not demonstrate consistent seizure reduction. Achievable central nervous system exposure, variant-specific pharmacology, drug interactions, QT prolongation, and other cardiac toxicities constrain use. Quinidine therefore remains an individualized, specialist-supervised option rather than an established gene-specific therapy.

Gene-silencing strategies are mechanistically compelling for selected GOF disease. In mouse models, Kcnt1-directed antisense oligonucleotides have reduced target expression and partially corrected molecular abnormalities. These findings are preclinical; correction of current or molecular signatures in experimental systems must not be interpreted as demonstrated clinical effectiveness. Human efficacy, dosing, developmental timing, delivery, durability, and safety remain unresolved.

7. KCNB1-related neurodevelopmental disorders

Functional consequences are heterogeneous and can include altered current density, gating, trafficking, dominant-negative effects, and, in selected variants, gain of function. A single validated gene-directed antiseizure drug has not emerged, so current treatment remains largely phenotype-driven. A 2025 case report described approximately 90% seizure reduction after vagus nerve stimulation in a child with KCNB1-related DEE; however, VNS optimization occurred alongside fenfluramine, creating an important confounder that prevents attribution of the full response to VNS. The report therefore supports multimodal management rather than gene-specific VNS efficacy.

Functional consequences are heterogeneous and can include altered current density, gating, trafficking, and dominant-negative effects. A single gene-directed antiseizure drug has not yet emerged. Current treatment is therefore largely phenotype-driven. A 2025 case report described approximately 90% seizure reduction after vagus nerve stimulation in a child with KCNB1-related DEE, illustrating the potential role of multimodal treatment while not establishing gene-specific efficacy.

KCNB1 is a reminder that seizure frequency is an incomplete outcome measure. Cognitive, language, behavioral, and psychiatric morbidity may be the dominant burden for patients and families.

A practical precision approach can be organized into five steps: define the electroclinical syndrome and urgency; establish molecular diagnosis with accepted pathogenicity classification; determine whether functional direction is already established, infer it

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cautiously when appropriate, and avoid equating pathogenicity with GOF/LOF status; select therapy according to the strongest available evidence while separating standard care from experimental intervention; and measure developmental, behavioral, motor, sleep, autonomic, and family-centered outcomes in addition to seizures.

For KCNQ2, early recognition of a LOF-associated neonatal epilepsy may prioritize sodium-channel blockers as mechanism-informed antiseizure therapy. For KCNA2 GOF, 4-aminopyridine represents targeted channel modulation. For KCNT1 GOF, direct inhibition is mechanistically rational but clinically inconsistent, while gene silencing remains preclinical. For KCNB1, mechanistic heterogeneity and limited targeted evidence currently favor individualized symptomatic management and trial enrollment. These categories should not be conflated: mechanism-informed antiseizure therapy, targeted channel modulation, and molecular disease-modifying therapy represent different levels of therapeutic specificity and evidence maturity.

For KCNQ2, early recognition of a LOF-associated neonatal epilepsy may prioritize sodium-channel blockers. For KCNA2 GOF, 4-aminopyridine may be rational. For KCNT1 GOF, direct inhibition or gene silencing is conceptually aligned with disease mechanism, although current evidence is insufficient for routine gene-directed therapy. For KCNB1, mechanistic heterogeneity and limited targeted evidence currently favor individualized symptomatic management and trial enrollment.

Therapeutic development in DEE spans three distinct levels: mechanism-informed use of conventional antiseizure medicines; targeted modulation of the abnormal channel; and molecular disease-modifying approaches such as antisense oligonucleotides, RNA-based regulation, gene replacement, or gene editing. Small molecules are scalable and reversible but may lack selectivity. ASOs may reduce toxic GOF transcripts but require central nervous system delivery and remain preclinical for the potassium-channel disorders discussed here. Gene replacement or editing is conceptually attractive in selected mechanisms but remains emerging rather than established clinical therapy, with major challenges involving dosage sensitivity, cell-type targeting, off-target effects, delivery, and developmental timing.

Precision therapy in DEE is expanding from repurposed small molecules toward channel-selective modulators, antisense oligonucleotides, RNA-based regulation, and gene replacement or editing strategies. Small molecules are scalable and reversible but may lack selectivity.

ASOs can reduce toxic GOF transcripts but require repeated central nervous system delivery. Gene replacement is more intuitive for haploinsufficiency but faces dosage sensitivity, cell-type targeting, and developmental timing.

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Rare DEEs pose predictable trial-design problems: small populations, heterogeneous variants, severe baseline developmental impairment, and outcomes that matter differently to families. Seizure burden may also change spontaneously with age; uncontrolled before/after comparisons can therefore overestimate treatment effects. Prospective, age-stratified natural-history cohorts and registries are essential to define expected seizure trajectories, developmental milestones, movement and behavioral features, mortality, and clinically meaningful change thresholds before interventional trials begin.

Patient-centered outcomes should be co-developed with families and advocacy organizations. A therapy that modestly reduces seizures but meaningfully improves alertness, sleep, communication, motor function, autonomy, or caregiver burden may still be clinically important. Contemporary channelopathy initiatives emphasize collaboration among clinicians, researchers, registries, and patient groups; such initiatives are useful for identifying research priorities but do not constitute evidence of therapeutic efficacy.

Rare DEEs pose predictable trial-design problems: small populations, heterogeneous variants, changing seizure burden with age, severe baseline developmental impairment, and outcomes that matter differently to families. Natural-history studies and registries can define age-dependent seizure trajectories, developmental milestones, movement and behavioral features, mortality, and clinically meaningful change thresholds before an interventional trial begins.

Severe genetic epilepsies carry mortality risks that extend beyond seizure counts. SUDEP, status epilepticus, aspiration, respiratory complications, autonomic dysfunction, and treatment toxicity require proactive surveillance. For the four genes reviewed here, comparative gene-specific SUDEP rates are not sufficiently established to support direct risk ranking; this discussion therefore refers primarily to DEE-wide mortality and safety considerations. KCNT1 cohorts have reported high mortality and SUDEP in severe phenotypes, but risk estimates remain phenotype- and cohort-dependent. Cardiac assessment is particularly relevant when therapies themselves can alter cardiac electrophysiology, as with quinidine.

11. SUDEP, systemic manifestations, and longitudinal care

Severe genetic epilepsies carry mortality risks that extend beyond seizure counts. SUDEP, status epilepticus, aspiration, respiratory complications, autonomic dysfunction, and treatment toxicity require proactive surveillance. Cardiac assessment is particularly relevant when therapies themselves can alter cardiac electrophysiology, as with quinidine.

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The evidence base is uneven across genes and remains limited by retrospective design, small samples, publication bias, inconsistent functional testing, heterogeneous outcome definitions, variable treatment timing, and incomplete natural-history controls. KCNQ2 currently has the strongest treatment-actionability signal; KCNA2 has compelling mechanism-specific but smaller clinical experience; KCNT1 has biologically rational but inconsistent targeted pharmacology and preclinical ASO work; and KCNB1 remains predominantly phenotype-driven. A reported response in a rare-disease case series should not be equated with established efficacy, and in-vitro or animal-model correction does not guarantee clinical benefit.

12. Limitations and research priorities

The evidence base remains limited by retrospective design, small samples, publication bias, inconsistent functional testing, heterogeneous outcome definitions, and variable treatment timing. A reported response in a rare-disease case series should not be equated with established efficacy. Similarly, in-vitro correction of channel current does not guarantee clinical benefit.

Potassium channel-related DEEs illustrate the transition of pediatric epilepsy from syndrome-based treatment toward mechanism-aware precision medicine. KCNQ2 provides the strongest current clinical example, with observational evidence supporting early molecular diagnosis and early sodium-channel blocker use in relevant LOF disorders while not proving developmental causality. KCNA2 demonstrates how functional studies can identify a pharmacological direction for selected GOF disease. KCNT1 shows both the promise and limitations of repurposed channel blockade and motivates preclinical gene-silencing strategies. KCNB1 highlights the need to target neurodevelopmental and behavioral morbidity as rigorously as seizures.

13. Conclusion

Potassium channel-related DEEs illustrate the transition of pediatric epilepsy from syndrome-based treatment toward mechanism-aware precision medicine. KCNQ2 already provides clinically actionable evidence supporting early molecular diagnosis and early sodium-channel blocker treatment in relevant LOF disorders. KCNA2 demonstrates how functional studies can identify a pharmacological direction for GOF disease.

KCNT1 shows both the promise and limitations of repurposed channel blockade and motivates gene-silencing approaches. KCNB1 highlights the need to target neurodevelopmental and behavioral morbidity as rigorously as seizures.

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The next phase of the field will depend on linking variant function to treatment, building trial-ready natural-history cohorts, and defining outcomes that matter to patients and families. Gene diagnosis is the beginning of precision care, not its endpoint.

Table 1. Comparative precision-medicine map of four potassium channelopathies

Gene	Channel	Typical severe phenotype	Functional pattern	Current clinical signal	Emerging strategy	Key caution	Evidence level
KCNQ2	Kv7.2	Neonatal-onset DEE	Often LOF; severe missense can be complex	Early CBZ/OXC; PHT also reported	Kv7 openers	Development may remain impaired; observational developmental associations are not causal	Limited clinical evidence (multicenter observational cohorts)
KCNA2	Kv1.2	DEE with epilepsy and ataxia	GOF, LOF/dominant-negative, trafficking, mixed	4-aminopyridine for selected GOF disease	Mechanism-specific modulation; experimental gene silencing	Requires functional classification; long-term data limited	Translational / limited clinical evidence
KCNT1	KNa1.1 / Slack	EIMFS and other severe DEEs	Frequently GOF; exceptions exist	Quinidine: inconsistent response	KCNT1-lowering ASO	Cardiac safety, CNS exposure, variant-specific response	Limited/negative clinical evidence for quinidine; preclinical ASO evidence
KCNB1	Kv2.1	DEE / developmental encephalopathy	Heterogeneous gating/trafficking; DN or GOF in selected variants	No validated gene-specific drug	Model-based screening; precision trials	Non-seizure morbidity is major; VNS case confounded by concurrent therapy	Anecdotal for VNS; preclinical/translational for targeted strategies

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Data availability: No new dataset was generated. All information analyzed is available in the cited peer-reviewed literature. The Channelopathies 2026 program is cited only as contextual material describing contemporary research priorities.

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Use of artificial intelligence: During manuscript revision, generative artificial intelligence (OpenAI ChatGPT) was used for language editing, organizational assistance, and preparation of revision text. All scientific claims, references, interpretations, and final wording were reviewed and verified by the author, who takes full responsibility for the content.

References

1. Allen NM, Weckhuysen S, Gorman K, et al. Genetic potassium channel-associated epilepsies: clinical review of the Kv family. Eur J Paediatr Neurol. 2020;24:105-116. doi:10.1016/j.ejpn.2019.12.002.
2. Barcia G, Fleming MR, Deligniere A, et al. De novo gain-of-function KCNT1 channel mutations cause malignant migrating partial seizures of infancy. Nat Genet. 2012;44:1255-1259.
3. Miceli F, Soldovieri MV, Joshi N, Weckhuysen S, Cooper EC, Taglialatela M. KCNQ2-related disorders. In: GeneReviews. University of Washington, Seattle.
4. Millichap JJ, Park KL, Tsuchida T, et al. KCNQ2 encephalopathy: delineation of the electroclinical phenotype and treatment response. Neurology. 2014;82:368-370. doi:10.1212/WNL.0000000000000060.
5. Pisano T, Numis AL, Heavin SB, et al. Early and effective treatment of KCNQ2 encephalopathy. Epilepsia. 2015;56:685-691. doi:10.1111/epi.12984.
6. Kim HJ, Yang D, Kim SH, et al. Clinical characteristics of KCNQ2 encephalopathy. Brain Dev. 2021;43:244-250. PMID:32917465.
7. Jadhav T, Bouffler SE, Innes E, et al. KCNQ2 neonatal epilepsy: impact of prompt diagnosis and treatment, and early predictors of outcome severity. Epilepsia Open. 2026;11(3):949-961. doi:10.1002/epi4.70266. PMID:42081271.

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Received: 12/09/2026 - **Accepted:22/09/2026**
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DOI: 10.66104/xdyksp91
Pages: 1-13

8. Millevert C, et al. Early sodium channel blocker initiation is associated with better outcomes in KCNQ2 disorders. Brain. 2026. doi:10.1093/brain/awag277. PMID:42610455.

9. Millichap JJ, Miceli F, De Maria M, et al. Ezogabine impacts seizures and development in patients with KCNQ2 developmental and epileptic encephalopathy. Epilepsia. 2023. doi:10.1111/epi.17627.

10. Syrbe S, Hedrich UBS, Riesch E, et al. De novo loss- or gain-of-function mutations in KCNA2 cause epileptic encephalopathy. Nat Genet. 2015;47:393-399.

11. Hedrich UBS, Lauxmann S, Wolff M, et al. 4-Aminopyridine is a promising treatment option for patients with gain-of-function KCNA2-encephalopathy. Sci Transl Med. 2021;13(609):eaaz4957. doi:10.1126/scitranslmed.aaz4957. PMID:34516822.

12. Bonardi CM, Heyne HO, Fiannacca M, et al. KCNT1-related epilepsies and epileptic encephalopathies: phenotypic and mutational spectrum. Brain. 2021;144:3635-3650.

13. Sun F, Wang H, Wu J, et al. Molecular profiling of mouse models of loss or gain of function of the KCNT1 (Slack) potassium channel and antisense oligonucleotide treatment. Biomolecules. 2024;14(11):1397. doi:10.3390/biom14111397.

14. Bar C, Kuchenbuch M, Barcia G, et al. Expanding the genetic and phenotypic relevance of KCNB1 variants in developmental and epileptic encephalopathies: 27 new patients and overview of the literature. Hum Mutat. 2020;41:69-80. PMID:31513310.

15. Sayanagi T, Kosugi K, Ogawa E, et al. Vagus nerve stimulation in KCNB1-related developmental and epileptic encephalopathy: a case of seizure reduction and review of literature. Epilepsy Behav Rep. 2025;32:100826. doi:10.1016/j.ebr.2025.100826.

16. Xie C, Yin F, Kessi M, Peng J. Potassium channelopathies and precision medicine approaches in epilepsy: a systematic review of personalized treatment strategies. Curr Neuropharmacol. 2026. doi:10.2174/011570159X407197251204124232.

17. Wang J, et al. Precision therapies for genetic epilepsies in 2025: promises and pitfalls. Epilepsia Open. 2025. doi:10.1002/epi4.70065.

18. Guerrini R, Conti V, Mantegazza M, Balestrini S, Galanopoulou AS, Benfenati F. Developmental and epileptic encephalopathies: from genetic heterogeneity to phenotypic continuum. Physiol Rev. 2023;103(1):433-513. doi:10.1152/physrev.00063.2021. PMID:35951482.

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Pages: 1-13

19. Zhao T, Wang L, Chen F. Potassium channel-related epilepsy: pathogenesis and clinical features. Epilepsia Open. 2024;9(3):891-905. doi:10.1002/epi4.12934.

20. Channelopathies 2026 - Institut Imagine. Scientific program, 24-26 September 2026, Paris, France. Contextual source only; not used as evidence of therapeutic efficacy.

21. Masnada S, Hedrich UBS, Gardella E, et al. Clinical spectrum and genotype-phenotype associations of KCNA2-related encephalopathies. Brain. 2017;140(9):2337-2354. doi:10.1093/brain/awx184.

22. Mínguez-Viñas T, Prakash V, Wang K, et al. Two epilepsy-associated variants in KCNA2 (KV1.2) at position H310 oppositely affect channel functional expression. J Physiol. 2023;601(23):5367-5389. doi:10.1113/JP285052. PMID:37883018.

23. Mikati MA, Jiang YH, Carboni M, et al. Quinidine in the treatment of KCNT1-positive epilepsies. Ann Neurol. 2015;78(6):995-999. doi:10.1002/ana.24520.

24. Mullen SA, Carney PW, Roten A, et al. Precision therapy for epilepsy due to KCNT1 mutations: a randomized trial of oral quinidine. Neurology. 2018;90:e67-e72. doi:10.1212/WNL.0000000000004769.

25. Numis AL, Nair U, Datta AN, et al. Lack of response to quinidine in KCNT1-related neonatal epilepsy. Epilepsia. 2018;59(10):1889-1898. doi:10.1111/epi.14551. PMID:30182418.

26. Kuchenbuch M, Barcia G, Chemaly N, et al. KCNT1 epilepsy with migrating focal seizures shows a temporal sequence with poor outcome, high mortality and SUDEP. Brain. 2019;142:2996-3008. doi:10.1093/brain/awz240.

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