Title: Hyperkalemic Periodic Paralysis *GeneReview* Table 3
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Note: The following information is provided by the author listed above and has not been reviewed by *GeneReviews* staff.

Table 3. Pathogenic Variants in *SCN4A* by Phenotype

Phenotype	Mechanism	Main *SCN4A* Pathogenic Variants
Hyperkalemic periodic paralysis [1] *(topic of this* GeneReview*, included for reference)*	Disrupted slow inactivation	p.Ala204Glu, [2] p.Asn440Lys, p.Ile692Met, p.Ile693Thr, p.Thr704Met, p.Ala1156Thr, p.Met1360Val, p.Arg1448Cys, [3] p.Arg1451Cys, [4] p.Arg1451Leu, [4] "p.Ile1490Leu-p.Met1493Ile," [5] p.Ile1495Phe, p.Ile1495Val, [6] p.Met1592Val [7]
Hypokalemic periodic paralysis (hypoPP)	Proton-selective or cation-selective gating pore current at resting potential	p.Ala204Glu, [2] p.Arg222Gly, p.Arg222Trp, p.Arg222Gln, [8] p.Arg222Trp, [9] p.Arg669His, p.Arg672Cys, p.Arg672Gly, p.Arg672His, p.Arg672Ser, p.Thr704Met, p.Arg1129Gln, p.Arg1132Gln, p.Arg1135His, p.Phe1158Ser, [10] p.Arg1448His, [11] p.Arg1451Leu [4, 12]
Normokalemic periodic paralysis (normoPP)	Gating pore current at depolarized potentials & in slow-inactivated state	p.Arg675Gly, p.Arg675Trp, p.Arg675Gln, [13] p.Thr704Met, [14] p.Met1592Val [7]
Paramyotonia congenita (PMC) [1] (OMIM 168300)	Disrupted fast inactivation & disrupted slow inactivation w/cold	p.Leu266Val, p.Thr704Met, [11] p.Val1293Ile, p.Thr1313Met, p.Asn1366Ser, [15] p.Met1370Val, p.Ile1433Arg, p.Arg1448His, p.Arg1448Cys, p.Arg1448Pro, p.Arg1448Ser, p. Arg1451Cys, [4] p. Arg1451Leu, [4] p.Ile1455Thr, p.Gly1456Glu, p.Val1458Phe, p.Phe1473Ser, p.Phe11705Ile
Sodium channel myotonias known as potassium-aggravated myotonia (SCM/PAM)	Disrupted fast inactivation or enhanced recovery from inactivation	p.Val445Met, p.Leu689Phe, [16] p.Leu796Val, [17] p.Val1293Ile, p.Gly1306Ala, p.Gly1306Val, p.Gly1306Glu, [18] p.Arg1460Gln, [19] p.Arg1463His [20] See footnote 21.
Tremor	Altered ion selectivity	p.Gly1537Ser (pore region) One report [22]
Congenital myasthenic syndrome (CMS)		p.Arg1454Trp, [23] p.Arg1457His, [24] p.Arg1460Gln [16]
Alternating hemiplegia of childhood		p.Met1080Val One report. [25]

1. The clinical overlap of paramyotonia congenita (PMC) and hyperkalemic periodic paralysis (hyperPP) is extensive, and family members with the same pathogenic variant may have a syndrome typical of PMC or hyperPP [Cannon 2018].
2. Kokunai et al [2018]
3. van Osch et al [2018]
4. Poulin et al [2018]
5. Complex allele c.4468_4479del12insCTCCTGGTCATA reported as p.Ile1490Leu-p.Met1493Ile [Bendahhou et al 2000]
6. Quiroga-Carrillo et al [2020]
7. Respiratory paralysis has been described in association with this pathogenic variant [Fu et al 2018]
8. Thor et al [2019]
9. Bayless-Edwards et al [2018]
10. May also be associated with myotonia [Ghovanloo et al 2018].

11. Huang et al [2019]
12. May also be associated with myotonia [Luo et al 2019].
13. Shi et al [2019]
14. Akaba et al [2018]
15. Ke et al [2017]
16. Hata et al [2019]
17. Elia et al [2020]
18. Ritter et al [2021]
19. Elia et al [2019]
20. Brenes et al [2021]
21. p.Gly1306Glu: Glu causes myotonia permanens with neonatal laryngospasms; also other SCM-causing variants (e.g., p.Gly1306Ala) may be responsible for neonatal respiratory insufficiency (i.e. myotonia fluctuans).
22. Bergareche et al [2015]
23. Habbout et al [2016]
24. Arnold et al [2015]
25. Duan et al [2019]

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