

Supplementary Table

Title: Structural Models for the KCNQ1 Voltage-gated Potassium Channel

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Supplementary Table 1. Description of disease-associated mutations within the open and closed state models of KCNQ1.

Amino Acid Mutation	Phenotype	Site Location: Open State	Site Location: Closed State	Surface-Exposed Site? (Open/Closed)	VDW Contacts in Open State (amino acid, subunit letter, residue number)	VDW Contacts in Closed State	Known Properties of this Mutant Probable Overall Defect	Reference
Cys122Tyr	LQTS1	S1, N-terminus	S1, N-terminus	yes/yes	TYR A 125 HIS A 126	VAL A 124 TYR A 125 HIS A 126		(1)
Val133Ile	LQTS1	S1, interface between middle of S1 and end of S4 near S4-S5 linker	S1, interface between S2 and S4	partial/partial	VAL A 129 ILE A 132 LEU A 137 PHE A 167 ARG A 237 HIS A 240 VAL A 241	VAL A 129 ILE A 132 LEU A 137 LEU A 163 ILE A 235 MET A 238		(1;2)
Cys136Phe	LQTS1	S1, oriented towards center of 4 helix bundle of voltage sensor domain	S1, interface between S2 and S4	no/slightly	ILE A 132 LEU A 137 MET A 159 GLU A 160 LEU A 163 ARG A 237	ILE A 132 SER A 140 MET A 159 LEU A 163 ARG A 231 ILE A 235		(1)
Leu137Phe	LQTS1	S1, interacts with both lower region of S4 near S4-S5 linker from same subunit and is part of interface with S5 from different subunit	S1, interface between S2 and S4	partial/yes	VAL A 133 LEU A 134 CYS A 136 ILE A 138 SER A 140 ARG A 237 MET A 238 VAL A 241 ILE B 274 TYR B 278	VAL A 133 LEU A 134 ILE A 138 SER A 140 VAL A 141 PHE A 232 ILE A 235		(3)
Ser140Gly	AF	S1, interacts both with middle of S4 from same subunit and S5 from another subunit	S1, interface with S4	no/no	LEU A 137 SER A 143 THR A 144 GLN A 234 ARG A 237 TYR B 278	CYS A 136 LEU A 137 VAL A 141 MET A 159 ARG A 231 PHE A 232	When expressed alone, loss of function. In presence of E1, shows dramatically enhanced current and rapid activation at all voltages. When expressed with WT and E1, channel properties that are intermediate between mutant/E1 and WT/E1 are observed. When	(4)

						ILE A 235	expressed with E2, rapid channel activation is retained and current is dramatically increased. (4) When expressed alone, similar to wild type in absence of KCNE1 (George, A.F., et al., unpublished) Favors open state in strictly KCNE1-dependent manner.	
Val141Met	AF	S1, interacts with upper part of S5 and beginning of the pore helix, both from adjacent subunit	S1, oriented towards solvent	mostly/yes	ILE A 138 LEU A 142 TYR B 278 TYR B 299	LEU A 137 SER A 140 LEU A 142 PHE A 232	When expressed alone (no E1 or WT), very similar to WT but significantly higher current. When expressed with E1, loses much of its voltage dependence of activation—open at all potentials. Retains K ⁺ selectivity. When co-expressed with E1 and WT, exhibits properties that at intermediate between V141M/E1-only and WT/E1-only. (5) Favors open state in a partially KCNE1-dependent manner.	(5;6)
Thr144Ala	LQTS1	S1, located at C-terminal end of S1, disposed towards the tops of the P-helix and S5 from another subunit	S1, partial interface with S4	slightly/yes	SER A 140 SER A 143 GLN A 234 TYR B 278 TYR B 281 LEU B 282 LYS B 285 TYR B 299	ILE A 145 ARG A 228 PHE A 232		(7)
Glu146Lys	LQTS1	S1-S2 oriented so as to fill up much of the space under the S1-S2 loop	at beginning of very short linking helix between S1 and S2, exposed to solvent	partial/yes	ALA A 149 LEU A 151 LYS B 285	ILE A 145 GLN A 147 ALA A 149 ALA A 150		(3)
Phe157Cys	LQTS1	S2, located near beginning of S2 helix, oriented so that it interacts on one face with the S1-S2 loop	at beginning of S2, interacts with S3-S4 loop	yes/yes	GLY A 154 LEU A 156 ILE A 161	GLY A 154 LEU A 156 GLU A 160 ILE A 161 ILE A 227		(8)
Glu160Lys	LQTS1	S2, located in middle of S1-S4 helical bundle	S2, located in middle of S1-S4 helical bundle	partial/partial	CYS A 136 MET A 159 ILE A 161 VAL A 164 VAL A 212 LEU A 233 ARG A 237	LEU A 156 PHE A 157 MET A 159 ILE A 161 VAL A 164 ILE A 227 ARG A 231		(1;9)
Gly168Arg	LQTS1	S2, near to crossing point with S3 and partially oriented towards S3	oriented away from helical bundle towards solvent	yes/yes	TYR A 171 VAL A 172	PHE A 167 TYR A 171 VAL A 172		(1;10;11)
Val172Met	LQTS1	S2, oriented towards solvent	near end of S2, oriented towards solvent	yes/yes	GLY A 168 TYR A 171 VAL A 173	GLY A 168 TYR A 171 VAL A 173		(7)

					TRP A 176	TRP A 176	
Val173Asp	LQTS1	S2, located near bottom (C-terminus) of S2, oriented towards solvent	located near bottom (C-terminus) of S2, oriented towards solvent	yes/yes	THR A 169 VAL A 172 ARG A 174 SER A 177	THR A 169 VAL A 172 ARG A 174 SER A 177	(3)
Arg174Cys	LQTS1	S2, located near bottom, oriented towards center of sensor domain	oriented towards beginning of S1, but no contact	partial/yes	TYR A 125 GLU A 170 VAL A 173 SER A 177 ARG A 243	GLU A 170 VAL A 173 LEU A 175	When expressed alone or with E1: complete loss of function. When co-expressed with E1 and WT, observed channel properties match that of WT. (12) Misfolds/mistrafficks prior to co-assembly with WT. (1;11;12)
Arg174His	LQTS1	S2, located near bottom, oriented towards center of sensor domain	oriented towards beginning of S1, but no contact	partial/yes	TYR A 125 GLU A 170 VAL A 173 SER A 177 ARG A 243	GLU A 170 VAL A 173 LEU A 175	(9)
Arg174Pro	LQTS1	S2, located near bottom, oriented towards center of sensor domain	oriented towards beginning of S1, but no contact	partial/yes	TYR A 125 GLU A 170 VAL A 173 SER A 177 ARG A 243	GLU A 170 VAL A 173 LEU A 175	(3)
Ala178Thr	LQTS1	S2-S3, located at beginning of S2-S3 connector helix	located at beginning of S2-S3 connector	yes/yes	SER A 177 ARG A 181 SER A 182	ARG A 181	(13)
Ala178Pro	LQTS1	S2-S3, located at beginning of S2-S3 connector helix	located at beginning of S2-S3 connector	yes/yes	SER A 177 ARG A 181 SER A 182	ARG A 181	(14)
Gly179Ser	LQTS1	S2-S3, located at beginning of S2-S3 connector helix, oriented towards end of S2	located at beginning of S2-S3 connector	yes/yes	LEU A 175 SER A 182	SER A 182 TRP A 188	(9)
Tyr184Ser	LQTS1	S2-S3, in S2-S3 helix oriented away from sensor domain	in extended loop in S2-S3 connector, solvent exposed	yes/yes	CYS A 180 LYS A 183 VAL A 185 LEU A 187 TRP A 188	GLY A 186 PHE A 193 LYS A 196	(15)
Gly189Arg	LQTS1	S2-S3, near end of S2-S3 helix, oriented towards end of S3	in extended loop in S2-S3 connector, solvent exposed	yes/yes	GLY A 186 ARG A 192 PHE A 193 LYS A 196	TRP A 188 ARG A 190 LEU A 191	Loss of function, but no DN effect on WT in presence or absence of E1. (16) Misfolds/mistrafficks. (14;16)
Arg190Gln	LQTS1 RWS	S2-S3, near end S2-S3 helix, side chain fills nook bounded by loop and end of S3	in extended loop in S2-S3 connector, solvent exposed	yes/yes	LEU A 187 LEU A 191 LYS A 196 SER A 199	GLY A 189	When expressed alone, sharply reduced current relative to WT., No DN effect on WT in presence or absence of E1. (16) Complete loss of function when expressed in presence or absence of E1. When co-

							expressed in presence of WT, no perturbation of WT channel properties. (17) Misfolds/mistrafficks.	
Arg190Trp	LQTS1	S2-S3, near end S2-S3 helix, side chain files nook bounded by loop and end of S3	in extended loop in S2-S3 connector, solvent exposed	yes/yes	LEU A 187 LEU A 191 LYS A 196 SER A 199	GLY A 189		(3)
Leu191Pro	LQTS1	S2-S3, located at end of S2-S3 helix, oriented away from sensor domain	in extended loop in S2-S3 connector, solvent exposed	yes/yes	LEU A 187 TRP A 188 ARG A 190 ARG A 192	CYS A 180 TRP A 188 GLY A 189 PHE A 193		(18)
Arg192Pro	LQTS1	S2-S3, located at end of S2-S3 helix, oriented away from sensor domain	in extended loop in S2-S3 connector, solvent exposed, could possibly interact with S4-S5 connector	yes/yes	LEU A 187 TRP A 188 ARG A 190 ARG A 192	CYS A 180 TRP A 188 GLY A 189 PHE A 193		(3)
Phe193Leu	LQTS1 (mild)	S2-S3, located in loop connecting S2-S3 to S3, oriented towards solvent	in extended loop in S2-S3 connector, nested interactions with other loop residues	yes/partial	GLY A 189 ARG A 192 ARG A 195	TYR A 184 GLY A 186 TRP A 188 LEU A 191 ARG A 195 LYS A 196	When expressed alone or with E1 only it is similar to WT, except that current is reduced, activation kinetics are somewhat slowed and $V_{1/2}$ is shifted to a more positive potential. (Not co-expressed with WT) (19) Favors closed state in a largely KCNE1-independent manner.	(19)
Ala194Pro	LQTS1	S2-S3, in loop before S3, oriented towards S4-S5 linker	in extended loop in S2-S3 connector, nested interactions with other loop residues	yes/partial	ARG A 195	ARG A 181 ARG A 192 ARG A 195 ILE A 198		(9)
Asp202Asn	JLNS	S3, located near beginning of S3, at interface with S2	located in S3, modest interaction with S2	partial/partial	TYR A 171 ILE A 198 VAL A 206	TYR A 171 ARG A 195 ILE A 201 VAL A 206		(20)
Asp202His	LQTS1	S3, located near beginning of S3, at interface with S2	located in S3, modest interaction with S2	partial/partial	TYR A 171 ILE A 198 VAL A 206	TYR A 171 ARG A 195 ILE A 201 VAL A 206		(3)
Ile204Phe	LQTS1	S3, in S3 at interface with C-terminal end of S4	S3, in S3 at interface with S4	partial/slightly	ILE A 200 LEU A 203 VAL A 205 LEU A 239 HIS A 240 ASP A 242 TRP A 248	ILE A 200 ILE A 201 LEU A 203 VAL A 205 GLN A 234 ARG A 237 VAL A 241		(1)
Ile204Met	LQTS	S3, in S3 at interface with C-terminal end of S4	S3, in S3 at interface with S4	partial/slightly	ILE A 200 LEU A 203 VAL A 205 LEU A 239	ILE A 200 ILE A 201 LEU A 203 VAL A 205		(3)

					HIS A 240 ASP A 242 TRP A 248	GLN A 234 ARG A 237 VAL A 241		
Ser209Phe	LQTS	near middle of S3, at interface with S2	modest interface with S2	partial/yes	VAL A 164 PHE A 167 VAL A 205 LEU A 213	VAL A 205 VAL A 206 ALA A 208 LEU A 213	(3)	
Val215Met	LQTS	at C-terminus of S3, partly at interface with beginning of S4	at end of S3, interacts with S3-S4 loop and S4	yes/partial	VAL A 212 CYS A 214 ILE A 230 LEU A 233	VAL A 211 CYS A 214 GLY A 216 GLY A 219 ALA A 223 ALA A 226 ILE A 227	(3)	
Ser225Leu	LQTS1	S4, located near beginning of S4, oriented towards S3-S4 loop	interacting with end of S1 from same subunit and at interface with S4 from another subunit	yes/slightly	VAL A 221 THR A 224	VAL A 221 ARG A 228 LEU B 282 LYS B 285 TYR B 299	When expressed only with E1, current is reduced and $V_{1/2}$ is shifted towards more positive potential. Trafficks normally. When co-expressed with WT, exerts DN effect to reduce current. (21) Favors closed state, at least in presence of KCNE1.	(22) (21)
Ala226Val	LQTS1	S4, located near beginning of S4, oriented towards S3-S4 loop and S3	near beginning of S4 at interface with S5 from another subunit, some interaction with S3 of same subunit	yes/slightly	VAL A 221 ILE A 227 ILE A 230	VAL A 211 VAL A 215 ALA A 223 ILE A 227 PHE B 279 LEU B 282	(23)	
Arg231Cys	LQTS1	S4, located at interface with S5 from another subunit	located at interface between S1 and S2 of the same subunit	partial/no	ILE A 227 ARG A 228 PHE A 232 ILE A 235 PHE B 279 LEU B 282 ALA B 283	CYS A 136 SER A 140 MET A 159 GLU A 160 LEU A 163 VAL A 164 ALA A 208 VAL A 212 ILE A 227 ILE A 230 GLN A 234	(24)	
Arg231His	LQTS1	S4, located at interface with S5 from another subunit	located at interface between S1 and S2 of the same subunit	partial/no	ILE A 227 ARG A 228 PHE A 232 ILE A 235 PHE B 279 LEU B 282 ALA B 283	CYS A 136 SER A 140 MET A 159 GLU A 160 LEU A 163 VAL A 164 ALA A 208 VAL A 212 ILE A 227 ILE A 230 GLN A 234	Non-disease mutants R231A and R237A result in constitutive activation of the channel in both the presence and absence of KCNE1.(25) Mutation of this key residue in the voltage sensor to Ala favor the open state relative to the closed state in a KCNE1-independent manner.	(3) (25)

Ile235Asn	LQTS1	S4, , located at interface with S5 from another subunit	at interface with S1 from same subunit	partial/slightly	ARG A 231 PHE A 232 GLN A 234 LEU A 236 PHE B 275 TYR B 278 PHE B 279 LEU B 282	VAL A 133 CYS A 136 LEU A 137 SER A 140 PHE A 232 GLN A 234 LEU A 236 MET A 238 PHE B 275	(1;26)	
Leu239Pro	LQTS1	located near end of S4 , where it interacts with both S3 and S4-S5 linker	a little interaction with S5 from a different subunit	partial/partial	ILE A 204 LEU A 236 MET A 238 HIS A 240 ASP A 242 TRP A 248 LEU B 271	LEU A 236 HIS A 240 ASP A 242 ARG A 243 LEU B 271	(3)	
Asp242Asn	LQTS1	located at end of S4 and interacts with S4-S5	surface exposed	no/yes	ILE A 200 ILE A 201 ILE A 204 LEU A 239 ARG A 243 TRP A 248 ARG A 249	MET A 238 LEU A 239 ARG A 243	(1;27)	
Arg243Cys	LQTS1	located at S4 connector to S4-S5 helix, oriented towards middle of S1-S4 helical bundle	interface with S5 of a different subunit	partial/partial	HIS A 126 VAL A 129 GLU A 170 ARG A 174 ILE A 201 ASP A 242 GLN A 244	LEU A 239 HIS A 240 ASP A 242 THR B 264 TYR B 267 ILE B 268 LEU B 271	(1;28)	
Arg243His	JLNS	located at S4 connector to S4-S5 helix, oriented towards middle of S1-S4 helical bundle	interface with S5 of a different subunit	partial/partial	HIS A 126 VAL A 129 GLU A 170 ARG A 174 ILE A 201 ASP A 242 GLN A 244	LEU A 239 HIS A 240 ASP A 242 THR B 264 TYR B 267 ILE B 268 LEU B 271	R243H plus E1 channel exhibits only minimal current. R243H plus E1 plus WT exhibits ca 40% reduced current relative to WT, V _{1/2} shifted to more positive potentials, and more rapid deactivation. (29) When expressed alone it is similar to WT. When co-expressed with KCNE1, exhibits much lower current than WT and a V _{1/2} shifted to more positive values. When expressed with WT and E1, current is reduced to about 50% of WT/WT, V _{1/2} is shifted to higher values, and deactivation I is more rapid. (17) When expressed alone, slightly reduced current, slowed activation and increased V _{1/2} . When expressed with WT only, current similar to WT, but slowed activation and increased V _{1/2} . (28) Does show some trafficking deficiency. (30) This site is believed to be involved in PIP ₂ , which is defective for this mutant. (31)	(17;29;31;32) (28) (30)

Trp248Arg	LQTS1	in S4-S5 helix, at interface with S4 from same subunit and S5 from a different subunit	interface with S3 from same subunit, and with S5 and S6 from another subunit	slightly/slightly	ILE A 200 ILE A 204 LEU A 239 ASP A 242 ARG A 249 LEU A 251 TYR B 267 LEU B 271	PRO A 197 ILE A 198 GLN A 244 GLY A 245 THR A 247 ARG A 249 LEU A 251	Defect is KCNE1-dependent. Favors closed state. Modest tendency to misfold/mistraffick. Involved in PIP ₂ binding. When expressed alone, reduced current, slowed activation and increased V _{1/2} . When expressed with WT only, current is somewhat lower than WT, slowed activation and increased V _{1/2} . (28) Favors closed state in a KCNE1 independent manner.	(28)
Leu250His	LQTS1	in S4-S5 at interface with bottom of S6 from same subunit	in S4-S5 at interface with bottom of S6 from same subunit	slightly/partial	THR A 247 ARG A 249 VAL A 254 PHE A 351 LYS A 354 VAL A 355 LYS A 358	SER A 253 VAL A 254 LYS A 354		(27)
Leu251Pro	LQTS1	in S4-S5 at interface with S6 from same subunit and S5 and S6 from another subunit	at interface with S6 from both same and different subunit	slightly/no	THR A 247 TRP A 248 GLY A 252 VAL A 254 VAL A 255 PHE A 351 ILE B 268 LEU B 271 PHE B 339 LEU B 342	THR A 247 TRP A 248 GLY A 252 VAL A 254 VAL A 255 ARG A 259 LEU A 262 ILE A 346 LEU A 347	Complete loss of function with or without KCNE1. DN reduction of WT current with no other affects on channel properties. (33) Misfolds/mistrafficks	(33;34)
Val254Met	LQTS1	in S4-S5 interacting with S6 from some subunit and S6 from adjacent subunit	at interface with S6 from both same and different subunit	slightly/slightly	LEU A 250 LEU A 251 SER A 253 VAL A 255 HIS A 258 LEU A 347 GLY A 350 PHE A 351 LYS A 354 LEU B 342	LEU A 250 LEU A 251 SER A 253 VAL A 255 HIS A 258 ARG A 259 LEU A 353		(1;14)
Val254Leu	LQTS1	in S4-S5 interacting with S6 from some subunit and S6 from adjacent subunit	at interface with S6 from both same and different subunit	slightly/slightly	LEU A 250 LEU A 251 SER A 253 VAL A 255 HIS A 258 LEU A 347 GLY A 350 PHE A 351 LYS A 354 LEU B 342	LEU A 250 LEU A 251 SER A 253 VAL A 255 HIS A 258 ARG A 259 LEU A 353	Loss of function when expressed alone. When co-expressed with WT, DN effect on channel current. When co-expressed with WT and E1, DN effect on channel current and increase in the V _{1/2} for channel activation. (16) Favors closed state in KCNE1-independent manner.	(3) (16)

His258Asn	LQTS1	located at turn connector between S4-S5 helix and S5, at interface with S6 from same subunit	at interface with S6 from both same and different subunit	partial/partial	VAL A 254 ILE A 257 GLU A 261 ILE A 346 LEU A 347 GLY A 350	VAL A 254 ILE A 257 ARG A 259 LEU A 353 VAL D 355 LYS D 358		(3)
His258Arg	LQTS1	located at turn connector between S4-S5 helix and S5, at interface with S6 from same subunit	at interface with S6 from both same and different subunit	partial/partial	VAL A 254 ILE A 257 GLU A 261 ILE A 346 LEU A 347 GLY A 350	VAL A 254 ILE A 257 ARG A 259 LEU A 353 VAL D 355 LYS D 358		(3)
Arg259Cys	LQTS1	in S5 facing outwards into solvent from channel domain	at interface with S6 from both same and different subunit	yes/no	PHE A 256 LEU A 262 ILE A 263	LEU A 251 VAL A 254 VAL A 255 HIS A 258 GLU A 261 LEU A 262 ILE A 346 SER A 349 PHE D 351 LYS D 354 VAL D 355 LYS D 358	When expressed alone it is WT-like except that current is reduced. When expressed alone with E1 or both E1 and WT Q1, current is reduced and voltage-dependence of activation is shifted to more positive potentials. (35) Favors closed state in KCNE1-dependent manner.	(1;35)
Arg259Leu	LQTS1	in S5 facing outwards into solvent from channel domain	at interface with S6 from both same and different subunit	yes/no	PHE A 256 LEU A 262 ILE A 263	LEU A 251 VAL A 254 VAL A 255 HIS A 258 GLU A 261 LEU A 262 ILE A 346 SER A 349 PHE D 351 LYS D 354 VAL D 355 LYS D 358		(26) (1)
Glu261Asp	JLNS	in S5, interacting with S6 from both same subunit and close to S6 from adjacent subunit	interacts with S6 from both same and different subunit, also interacts with S4-S5 linker from different subunit	partial/slightly	HIS A 258 GLN A 260 THR A 264 THR A 265 PRO A 343 ILE A 346 LEU A 347	ARG A 259 GLN A 260 LEU A 262 THR A 265 LEU A 342 ILE A 346 THR D 247 PHE D 351 LYS D 354	E261E plus E1 channel exhibits minimal current. E261E plus E1 plus WT also exhibits only minimal current—strong DN effect. (29) Severe mistrafficking with or without E1 or WT. Also causes mistrafficking of co-expressed WT. (30) Misfolds/mistrafficks in KCNE1 independent manner. Also causes mistrafficking of co-expressed WT.	(1;30;36) (29)
Glu261Lys	LQTS1	in S5, interacting with S6 from both same subunit and close to S6 from adjacent	interacts with S6 from both same and different subunit, also interacts with S4-S5	partial/slightly	HIS A 258 GLN A 260 THR A 264 THR A 265	ARG A 259 GLN A 260 LEU A 262 THR A 265	In absence or presence of E1, complete loss of function. Upon co-expression with WT, channel has WT properties. (28) Severe mistrafficking with or without E1 or	(11;28;29) (30)

		subunit	linker from different subunit		PRO A 343 ILE A 346 LEU A 347	LEU A 342 ILE A 346 THR D 247 PHE D 351 LYS D 354	WT. Also causes mistrafficking of co-expressed WT. (30) Mistrafficks/misfolds.	
Leu262Val		in S5 at interface with S6 from adjacent subunit	interacts with S6 from both same subunit, interacts with S4-S5 linker from same subunit	partial/slightly	VAL A 255 ARG A 259 ILE A 263 THR A 265 LEU A 266 PHE B 335	LEU A 251 VAL A 255 ARG A 259 GLU A 261 ILE A 263 LEU A 266 PHE A 339 LEU A 342 ILE A 346	(3)	
Leu266Pro	LQTS1	in S5 at interface with S6 from adjacent subunit	Interacts with S6 from same subunit	partial/partial	LEU A 262 THR A 265 PHE A 270 VAL B 334	LEU A 262 ILE A 263 TYR A 267 PHE A 339		(1;9)
Gly269Ser	LQTS1	S5, located near end of pore helix and S6 of same subunit	at interface with S6 from same subunit	no/no	ILE A 268 LEU A 273 VAL A 310 PHE A 339 PHE A 340	ILE A 268 GLY A 272 PHE A 332	When expressed with E1 only: complete loss of function. When expressed with WT and E1, the channel exhibits normal WT properties, but current is 50% relative to WT/WT case. This mutant most likely misfolds/mistrafficks.(37) Mistrafficks/misfolds.	(1) (37)
Gly269Asp	LQTS1	S5, located near end of pore helix and S6 of same subunit	at interface with S6 from same subunit	no/no	ILE A 268 LEU A 273 VAL A 310 PHE A 339 PHE A 340	ILE A 268 GLY A 272 PHE A 332	When expressed alone or with E1: complete loss of function. When co-expressed with E1 and WT, observed channel properties match that of WT. Likely misfolds/mistrafficks prior to co-assembly with WT. (12) Mistrafficks/misfolds.	(1;11;12)
Gly272Asp	JLNS	S5, located at interface with S6 from same subunit	located at interface with S6 from same subunit	slightly/no	LEU A 271 PHE A 275 PHE A 332 PHE A 339	GLY A 269 PHE A 275 PHE A 332 PHE A 335		(3;38)
Leu273Phe	LQTS1	S5, located at interface with pore helix from same subunit, with some contact to S6 from both same another subunit	located at interface with S6 from same subunit; close to S4 from another subunit	slightly/slightly	GLY A 269 PHE A 270 ILE A 274 SER A 276 SER A 277 LEU A 303 GLY A 306 VAL A 307 VAL A 310 PHE A 332 SER B 330	PHE A 270 ILE A 274 SER A 276 SER A 277 LEU A 303 GLY A 306 VAL A 307 VAL A 310 PHE A 332	L273F exhibits inactivation even in the presence of KCNE1, which normally suppresses inactivation (39) Exhibits some degree of trafficking deficit. (40) Restores inactivation to KCNQ1 in presence of KCNE1. Some tendency to misfold/mistraffick.	(1;14;39;40)
Ile274Val	SIDS	S5, located at interface between S1 and S4 of another	a little interaction with S6 from same subunit	partial/yes	PHE A 270 LEU A 273 TYR A 278	PHE A 270 LEU A 273 SER A 277	Similar to WT in the absence of E1. In presence of E1 exhibits higher current than WT, faster activation kinetics, and slow	(41)

		subunit			TYR A 299 LEU D 137 MET D 238	TYR A 278 LEU A 303 PHE D 232 LEU D 236	deactivation, although no significant change in $V_{1/2}$. (TE Rhodes, AF George et al., unpublished) Favors open state in KCNE1-specific manner.	
Phe275Ser	LQTS1	in S5 located in gap between S5 of same subunit and S4 of another, contacting both	interacts with S6 segment of same subunit and with S4 from a different subunit	partial/slightly	LEU A 271 GLY A 272 SER A 276 PHE A 279 ILE A 328 PHE A 335 ILE D 235 LEU D 236	GLY A 272 SER A 276 ILE A 328 CYS A 331 PHE A 332 LEU D 233 LEU D 236 ARG D 237	(18)	
Ser277Leu	LQTS1	in S5, located at interface with P-helix	in S5, located at interface with P-helix	no/slightly	LEU A 273 SER A 276 TYR A 299 ALA A 302 LEU A 303 GLY A 306	LEU A 273 ILE A 274 SER A 276 TYR A 278 ALA A 302 LEU A 303	(1;42)	
Ser277Trp	LQTS	in S5, located at interface with P-helix	in S5, located at interface with P-helix	no/slightly	LEU A 273 SER A 276 TYR A 299 ALA A 302 LEU A 303 GLY A 306	LEU A 273 ILE A 274 SER A 276 TYR A 278 ALA A 302 LEU A 303	(3)	
Tyr278His	LQTS1	S5, at interface with both S1 and S4 from another subunit in open state; some interaction with pore helix of same subunit	at interface with S4 segment different subunit, some interaction with pore helix of same subunit	no/partial	ILE A 274 TYR A 281 LEU A 282 TYR A 299 LEU D 137 SER D 140 VAL D 141 THR D 144 ILE D 235 ARG D 237	ILE A 274 SER A 277 PHE A 279 LEU A 282 TYR A 299 GLY D 229 PHE D 232 LEU D 233 LEU D 236	(1;26)	
Val280Glu	LQTS1	in top of S5 at interface with P-helix and S6	at interface with S6 and P-helix	no/no	TYR A 281 GLU A 284 ALA A 302 TRP A 305 PRO A 320 GLY A 325 ILE A 328	SER A 276 PHE A 279 TYR A 281 PHE A 296 ALA A 302 TRP A 305 PRO A 320 GLY A 325 ILE A 328	(3)	
Tyr281Cys	LQTS1	in top of S5, interacts with S6 in same subunit and with top of S1 from another subunit in open state	at interface with S6 and P-helix	slightly/slightly	TYR A 278 VAL A 280 LEU A 282 GLU A 284 LYS A 285 PHE A 296	VAL A 280 LEU A 282 GLU A 284 LYS A 285 PHE A 296 GLY A 297	When expressed only with E1, complete loss of function. However, trafficks normally. When co-expressed with WT, exerts DN effect to reduce current. (21) Favors closed state or reduces conductance of open state.	(21;22)

					GLY A 297 TYR A 299 ALA A 302 THR D 144 GLN D 147	TYR A 299 ALA A 302		
Glu284Lys	LQTS1	located in S5-P connector, interacts with top ends of S5 and S6 under connector segment	located in S5-P connector, interacts with top ends of S5 and S6 under connector segments	slightly/slightly	VAL A 280 TYR A 281 ALA A 283 PHE A 296 PRO A 320 GLN A 321 THR A 322 GLY A 325	TYR A 281 ALA A 283 ALA A 287 GLY A 292 ARG A 293 PHE A 296 PRO A 320 GLN A 321 THR A 322 GLY A 325	(7)	
Glu290Lys	LQTS1	located in 3-10 helix of S5-P connector, at interface with P-S6 connecting strand	located in extended loop of S5-P connector, solvent exposed	partial/yes	ALA A 287 ASN A 289 ARG A 293 GLU A 295 PHE A 296	VAL A 288 ASN A 289 SER A 291	(1)	
Gly292Asp	LQTS1	S5-P, located at end of 3-10 helix, oriented away from channel	located in middle of loop connector of S5-P; in contact with filter-S6 connector	yes/slightly	none	GLU A 284 ALA A 287 GLN A 321	(1;43)	
Arg293Cys	LQTS1	S5-P, located at end of 3-10 helix, oriented toward central pore axis, but no interactions	located in towards end of S5-P connector, oriented towards central axis and interacts with filter-S6 connector	yes/yes	ASN A 289 GLU A 290 GLU A 295	GLU A 284 GLU A 295 PHE A 296 LYS A 318 VAL A 319 GLN A 321 ASP D 317	(1;26)	
Ala300Thr	reported as LQTS1 but may be AF	at beginning of P-helix, oriented towards S6 of another subunit	interacts with top of S6 from different subunit	yes/yes	SER A 298 TRP A 304	SER A 298 TYR A 299 ASP A 301 LYS B 326	When expressed only with E1, current is reduced and V _{1/2} is shifted towards more NEGATIVE potential and activation is accelerated. Trafficks normally. When co-expressed with WT, no loss of WT current. (21) Favors open state.	(21;44)
Ala302Val	LQTS1	P-helix, at interface with S5 from same subunit	at interface with S5 from the same subunit	no/no	SER A 277 VAL A 280 TYR A 281 TYR A 299	SER A 277 VAL A 280 TYR A 281 PHE A 296 TYR A 299 LEU A 303 TRP A 305	(1;26)	
Ala302Thr	LQTS1	P-helix, at interface with S5 from same subunit	at interface with S5 from the same subunit	no/no	SER A 277 VAL A 280 TYR A 281	SER A 277 VAL A 280 TYR A 281	(3)	

					TYR A 299	PHE A 296 TYR A 299 LEU A 303 TRP A 305		
Trp304Arg		P-helix, in direct contact with selectivity filter of the same subunit and the filter-S5 connector from another subunit	interaction with filters from same and different subunits, interaction with S6 from different subunit	partial/partial	ALA A 300 ASP A 301 LEU A 303 LYS A 318 TRP B 323 LYS B 326	ASP A 301 TRP A 305 VAL A 308 TYR A 315 ASP A 317 LYS A 318 VAL B 319 PRO B 320 LYS B 326	(1)	
Trp305Ser	JLNS	P-helix, interacts with filter, filter-S6 connector, and S6, all from same subunit and also filter from adjacent subunit	interacts with S6, P-helix and filter, all from same subunit and also filter from adjacent subunit	no/no	SER A 276 VAL A 280 GLY A 306 THR A 309 LYS A 318 VAL A 319 PRO A 320 ILE A 328 ALA A 329 PHE A 332 TYR D 315	SER A 276 VAL A 280 PHE A 296 ALA A 302 TRP A 304 GLY A 306 THR A 309 LYS A 318 VAL A 319 PRO A 320 ILE A 328 ALA A 329 PHE A 332 TYR D 315	When expressed alone or with E1: complete loss of function. When co-expressed with E1 and WT, observed channel properties match that of WT. (12) Misfolds/mistrafficks.	(1;12;45)
Gly306Val	LQTS1	P-helix, located at interface between S5 and S6 from same subunit	at interface with S5 and S6 from same subunit	no/no	LEU A 273 SER A 277 LEU A 303 TRP A 305 THR A 309 PHE A 332	LEU A 273 SER A 276 TRP A 305 THR A 309 PHE A 332		(18)
Gly306Arg	LQTS1	P-helix, located at interface between S5 and S6 from same subunit	at interface with S5 and S6 from same subunit	no/no	LEU A 273 SER A 277 LEU A 303 TRP A 305 THR A 309 PHE A 332	LEU A 273 SER A 276 TRP A 305 THR A 309 PHE A 332	Loss of function when expressed alone. When co-expressed with WT and E1, DN effect on channel current and increase in the V _{1/2} for channel activation. (16) Favors closed state.	(14) (16)
Val307Leu	Short QT syndrome (gain-of-function)	P-helix at interface with S6 from another subunit, also some contact with S5 from same subunit	at interface with S6 from a different subunit also some contact with S5 from same subunit	slightly/slightly	LEU A 273 LEU A 303 VAL A 308 VAL A 310 SER B 330	LEU A 273 LEU A 303 VAL A 308 THR A 311 LYS B 326 SER B 330	Expression with E1 and in presence or absence of WT leads to more rapid channel activation and a shift to more negative V _{1/2} . (46). When expressed in absence of E1 or WT, similar current to WT, slightly delayed activation, and no inactivation (unlike WT-only). (39) Favors open state in a partially KCNE1-dependent manner.	(46) (39)

Val308Asp	LQTS1	in P-helix at interface with selectivity filter	in P-helix at interface with selectivity filter	no/no	VAL A 307 ILE A 313 GLY A 314 TYR A 315 ASP A 317 LYS B 326 TYR D 315	TRP A 304 VAL A 307 THR A 309 ILE A 313 GLY A 314 TYR A 315 TYR D 315	(3)	
Thr309Arg	LQTS1	in P-helix at interface between selectivity filter and S6, both from same subunit	in P-helix at interface between selectivity filter and S6, both from same subunit	no/no	TRP A 305 GLY A 306 VAL A 310 PHE A 332 SER A 333 ILE D 313 TYR D 315	TRP A 305 GLY A 306 VAL A 308 ALA A 329 PHE A 332 SER A 333 ILE D 313 TYR D 315	(11)	
Thr309Ile	LQTS1	in P-helix at interface between selectivity filter and S6, both from same subunit	in P-helix at interface between selectivity filter and S6, both from same subunit	no/no	TRP A 305 GLY A 306 VAL A 310 PHE A 332 SER A 333 ILE D 313 TYR D 315	TRP A 305 GLY A 306 VAL A 308 ALA A 329 PHE A 332 SER A 333 ILE D 313 TYR D 315	(47)	
Val310Ile	LQTS1	P-helix, at interface with S5 and S6 from same subunit	P-helix, at interface with S5 and S6 from same subunit	slightly/slightly	GLY A 269 LEU A 273 VAL A 307 THR A 309 THR A 311 PHE A 332 ALA A 336 PHE A 340	LEU A 273 THR A 311 PHE A 332 ALA A 336 PHE A 339 PHE A 340	V310I is similar to WT in absence of KCNE1. In presence of WT KCNQ1 and KCNE1, V310I exerts a DN reduction of WT current amplitude, but little other effect. Based on data for V310A, V310G, and other mutants, it was proposed that this site participates in interactions with Leu273 and F340 that stabilize the open state relative to the closed state. V310A and V310G close more rapidly than WT. (48) Favors closed state in a KCNE1-dpendent manner. Proposed to be close to Leu273 and F340.	(9) (48)
Thr311Ile	LQTS1	P-helix, at interface between S6 and bottom of filter from another subunit and bottom of filter from same subunit	P-helix, at interface between S6 and bottom of filter from another subunit and bottom of filter from same subunit	partial/slightly	VAL A 310 ILE A 313 PHE A 340 THR B 312 SER B 333 VAL B 334 ILE B 337	VAL A 307 VAL A 310 ILE A 313 PHE A 340 THR B 312 SER B 333 VAL B 334 ILE B 337	(49)	
Thr312Ile	LQTS1	Filter, forms contacts with itself right at 4-fold symmetry axis	Filter, forms contacts with itself right at 4-fold symmetry axis	yes/no	SER A 333 ILE A 337 THR B 312 THR C 312 THR D 311 THR D 312	SER A 333 ILE A 337 PHE A 340 THR B 312 THR C 312 THR D 311	(1;14;32)	

					ILE D 313	THR D 312 ILE D 313		
Ile313Met	LQTS1	Filter, forms contacts with P-helix from same subunit, same residue in other subunits, and S6 in adjacent subunit	Filter, forms contacts with P-helix from same subunit, same residue in other subunits, and S6 in adjacent subunit	no/no	VAL A 308 THR A 311 TYR A 315 THR B 309 THR B 312 GLY B 314 SER B 333	VAL A 308 THR A 311 TYR A 315 THR B 309 THR B 312 GLY B 314 SER B 333 ILE B 337		(13)
Gly314Ser	LQTS1	Filter, forms contacts with itself right at 4-fold symmetry axis	Filter, forms contacts with itself right at 4-fold symmetry axis	slightly/slightly	VAL A 308 ILE D 313 TYR D 315	VAL A 308 ILE D 313 TYR D 315	Induces DN reduction in current when co-expressed with native levels of WT Q1 and E1. (50) When expressed alone or with E1: complete loss of function. When co-expressed with E1 and WT, observed channel properties match that of WT. (12) Misfolds/mistrafficks.	(12;32;51) (50)
Gly314Cys	LQTS1	Filter, forms contacts with itself right at 4-fold symmetry axis	Filter, forms contacts with itself right at 4-fold symmetry axis	slightly/slightly	VAL A 308 ILE D 313 TYR D 315	VAL A 308 ILE D 313 TYR D 315		(52)
Gly314Arg		Filter, forms contacts with itself right at 4-fold symmetry axis	Filter, forms contacts with itself right at 4-fold symmetry axis	slightly/slightly	VAL A 308 ILE D 313 TYR D 315	VAL A 308 ILE D 313 TYR D 315		(1)
Gly314Asp	LQTS1	Filter, forms contacts with itself right at 4-fold symmetry axis	Filter, forms contacts with itself right at 4-fold symmetry axis	slightly/slightly	VAL A 308 ILE D 313 TYR D 315	VAL A 308 ILE D 313 TYR D 315		(1;26)
Gly314Ala	LQTS1	Filter, forms contacts with itself right at 4-fold symmetry axis	Filter, forms contacts with itself right at 4-fold symmetry axis	slightly/slightly	VAL A 308 ILE D 313 TYR D 315	VAL A 308 ILE D 313 TYR D 315		(23)
Tyr315Ser	LQTS1	Filter, interacts with pore helix from same subunit and S6 from adjacent subunit	Filter, interacts with pore helix from same subunit and S6 from adjacent subunit and with S5-P connector	partial/slightly	VAL A 308 ILE A 313 ASP A 317 TRP B 305 VAL B 308 THR B 309 GLY B 314 GLY B 316 VAL B 319 PRO B 320 ALA B 329	TRP A 304 VAL A 308 ILE A 313 ASP A 317 TRP B 305 VAL B 308 THR B 309 GLY B 314 GLY B 316 VAL B 319 PRO B 320 ALA B 329	When expressed alone or with E1: complete loss of function. When co-expressed with E1 and WT, observed channel properties match that of WT. (12) Misfolds/mistrafficks.	(11;12)
Tyr315Cys	LQTS1	Filter, interacts with pore helix from same subunit and S6 from adjacent subunit	Filter, interacts with pore helix from same subunit and S6 from adjacent subunit and with S5-P connector	partial/slightly	VAL A 308 ILE A 313 ASP A 317 TRP B 305 VAL B 308	TRP A 304 VAL A 308 ILE A 313 ASP A 317 TRP B 305	When expressed alone with E1, little or no channel function detected. When co-expressed with both WT Q1 and E1, it exerts a DN affect on the WT current and also shifts V _{1/2} to more positive potentials, suggesting	(1;10) (21;53)

					THR B 309 GLY B 314 GLY B 316 VAL B 319 PRO B 320 ALA B 329	VAL B 308 THR B 309 GLY B 314 GLY B 316 VAL B 319 PRO B 320 ALA B 329	stabilization of the closed state relative to the open state.(53); When expressed only with E1, complete loss of function. However, trafficks normally. When co-expressed with WT, exerts DN effect to reduce current. (21) Favors closed state.
Gly316Arg	LQTS1	Filter, forms contacts with itself right at 4-fold symmetry axis	Filter, forms contacts with itself right at 4-fold symmetry axis	partial/partial	VAL A 319 TYR D 315	VAL A 319 TYR D 315	(1;54)
Gly316Glu		Filter, forms contacts with itself right at 4-fold symmetry axis	Filter, forms contacts with itself right at 4-fold symmetry axis	partial/partial	VAL A 319 TYR D 315	VAL A 319 TYR D 315	(3)
Asp317Gly	LQTS1	top of filter, interacting with filter-S6 connector from another subunit, and P-helix from same subunit	top of filter, interacting with filter-S6 connector from another subunit, and P-helix from same subunit, and the S4-P connector from a different subunit	partial/partial	VAL A 308 TYR A 315 LYS A 318 VAL B 319 GLN B 321 LYS B 326	TRP A 304 TYR A 315 LYS A 318 VAL B 319 GLN B 321	(55)
Asp317Asn	LQTS1	top of filter, interacting with filter-S6 connector from another subunit, and P-helix from same subunit	top of filter, interacting with filter-S6 connector from another subunit, and P-helix from same subunit, and the S4-P connector from a different subunit	slightly/partial	VAL A 308 TYR A 315 LYS A 318 VAL B 319 GLN B 321 LYS B 326	TRP A 304 TYR A 315 LYS A 318 VAL B 319 GLN B 321	(32;56)
Lys318Asn	LQTS1	located in filter-S6 connector, interacts with P-helix and S5-P connector, both from same subunit	located in filter-S6 connector, interacts with P-helix and S5-P connector, both from same subunit	partial/slightly	VAL A 294 PHE A 296 ASP A 301 TRP A 304 TRP A 305 ASP A 317	ARG A 293 GLU A 295 PHE A 296 SER A 298 ASP A 301 TRP A 304 TRP A 305 ASP A 317	(10)
Pro320Ala	LQTS1	located in filter-S5 connector, interacts with P helix from both same and adjacent subunit and S6 from same subunit, also interacts with S5-P connector	located in filter-S5 connector, interacts with P helix from both same and adjacent subunit and S6 from same subunit, also interacts with S5-P connector	no/no	VAL A 280 GLU A 284 TRP A 305 VAL A 319 GLY A 325 LYS A 326 ALA A 329 TRP D 304 TYR D 315	VAL A 280 GLU A 284 PHE A 296 TRP A 305 VAL A 319 GLY A 325 ALA A 329 TRP D 304 TYR D 315	(11)
Thr322Ala	LQTS1	at beginning of S6, interacts with top of S5 and S5-P connector from same	at beginning of S6, interacting with S5-P-helix connector from the same subunit	yes/partial	ALA A 283 GLU A 284 GLN A 321 VAL A 324	ALA A 283 GLU A 284 ALA A 287 GLN A 321	(1;2)

		subunit			GLY A 325	TRP A 323 VAL A 324 GLY A 325		
Thr322Met	LQTS	S6, located at interface with S5 of same subunit	at beginning of S6, interacting with S5-P-helix connector from the same subunit	yes/partial	ALA A 283 GLU A 284 GLN A 321 VAL A 324 GLY A 325	ALA A 283 GLU A 284 ALA A 287 GLN A 321 TRP A 323 VAL A 324 GLY A 325	(3)	
Gly325Arg	LQTS1	S6, located at interface with S5 of same subunit	at interface with S5 from the same subunit	no/no	VAL A 280 ALA A 283 GLU A 284 PRO A 320 THR A 322 VAL A 324 ILE A 328	VAL A 280 ALA A 283 GLU A 284 PRO A 320 THR A 322 VAL A 324 ILE A 328	(13)	
Ala341Glu	LQTS1	S6 (inside vestibule), located near the same position in adjacent subunits	at interface with other S6 subunits	yes/no	ILE A 337 LEU A 342 ALA D 344	ILE A 337 PRO D 343 ALA D 344 LEU D 347	Loss of function when expressed alone. When co-expressed with WT, DN effect on channel current. When co-expressed with WT and E1, DN effect on channel current and increase in the V _{1/2} for channel activation. (16) Favors closed state.	(14) (16)
Ala341Val	LQTS1	S6 (inside vestibule), located near the same position in adjacent subunits	at interface with other S6 subunits	yes/no	ILE A 337 LEU A 342 ALA D 344	ILE A 337 PRO D 343 ALA D 344 LEU D 347	Loss of function, but no DN effect on WT in presence or absence of E1. Almost certainly misfolds/mistrafficks. (16); Induces DN reduction in current when co-expressed with native levels of WT Q1 and E1. (50) Conflicting results.	(1;14;16) (50)
Leu342Phe	LQTS1	S6, located at interface with S6 from adjacent subunit	at interface with S5 from same subunit and S6 from a different subunit	slightly/slightly	ILE A 268 PHE A 339 ALA A 341 PRO A 343 LEU D 251 VAL D 254 LEU D 347 GLY D 348 PHE D 351	GLU A 261 LEU A 262 THR A 265 PHE A 339 PRO A 343 ILE A 346 LEU D 347 PHE D 351	When expressed alone or with E1: complete loss of function. When co-expressed with E1 and WT, observed channel properties match that of WT. (12) Misfolds/mistrafficks.	(11;12)
Pro343Ser	LQTS1	S6, at interface with S5 from same subunit	interacts with the same side chain at central 4-fold axis	no/partial	GLU A 261 THR A 264 THR A 265 ILE A 268 PHE A 340 LEU A 342 LEU A 347	PHE A 340 LEU A 342 ALA B 341	When expressed alone, shows reduced current, activates slowly and exhibits no tail current. When expressed with E1 only, exhibits complete loss of function. When expressed with WT Q1 only or with both E1 and Q1, exhibits DN effect on current and no tail current.(57) Favors closed state or lower conductance of open state.	(1;57)

Pro343Arg	LQTS1	S6, IBID	interacts with the same side chain at central 4-fold axis	no/partial	GLU A 261 THR A 264 THR A 265 ILE A 268 PHE A 340 LEU A 342 LEU A 347	PHE A 340 LEU A 342 ALA B 341		(3)
Pro343Leu	LQTS1	S6, IBID	at interface with S6 from different subunit	no/partial	GLU A 261 THR A 264 THR A 265 ILE A 268 PHE A 340 LEU A 342 LEU A 347	PHE A 340 LEU A 342 ALA B 341		(3)
Ala344Glu	LQTS1	S6 (inside vestibule)	interacts with the same side chain at central 4-fold axis	partial/no	ILE B 337 ALA B 341	ALA B 341 ALA B 344 ALA C 344 ALA D 344		(1;23)
Ala344Val	LQTS1	S6, at interface with S6 from other subunit	interacts with the same side chain at central 4-fold axis	partial/no	ILE B 337 ALA B 341	ALA B 341 ALA B 344 ALA C 344 ALA D 344	Trafficks normally and has near-normal max current. In absence of E1, induces voltage-induced inactivation and shifts voltage dependence of activation to more positive potentials. With E1 only, exhibits near-WT current, but increased V _{1/2} . Co-expression with WT and E1 leads to properties intermediate between WT/E1 and this mutant/E1. (58) Favors closed state in KCNE1-independent manner.	(1;11) (58)
Gly345Glu	LQTS1	S6, at interface with S6 from other subunits	interacting with other S6 segments	yes/no	GLY A 348 SER A 349	GLY A 348 LEU D 347 GLY D 348 PHE D 351	Loss of function when expressed alone. When co-expressed with WT, DN effect on channel current. When co-expressed with WT and E1, DN effect on channel current and increase in the V _{1/2} for channel activation. (16) Favors closed state in KCNE1-independent manner.	(1;14;16)
Gly345Arg	LQTS1	S6, at interface with S6 from other subunits	interacting with other S6 segments	yes/no	GLY A 348 SER A 349	GLY A 348 LEU D 347 GLY D 348 PHE D 351		(59)
Ser349Trp	LQTS1	S6, oriented towards center of pore, exposed to solvent	interacting with other S6 segments	yes/no	GLY A 345 ILE A 346	ARG A 259 ILE A 346 GLY D 348 PHE D 351 ALA D 352 VAL D 355		(1;9)

Ser349Pro	LQTS1	S6, oriented towards center of pore, exposed to solvent	interacting with other S6 segments	yes/no	GLY A 345 ILE A 346	ARG A 259 ILE A 346 GLY D 348 PHE D 351 ALA D 352 VAL D 355	(3)
Gly350Arg	LQTS1	S6 oriented towards center of pore, exposed to solvent	at interface with S4-S5 linker from same subunit	partial/partial	VAL A 254 HIS A 258 LEU A 353 LYS A 354	PHE A 351 LEU A 353	(3)
Phe351Ser	LQTS1	S6, at interface with S4-S5 linker of same subunit and with S5 and S6, both of a different subunit	located at interface between S5 and S6 of a different subunit	slightly/slightly	THR A 247 LEU A 250 LEU A 251 VAL A 254 GLY A 348 VAL A 355 GLU B 261 THR B 264 ILE B 268 LEU B 342 PRO B 343	THR A 247 LEU A 347 GLY A 348 GLY A 350 LYS A 354 VAL A 355 ARG B 259 GLU B 261 LEU B 342 GLY B 345 ILE B 346 SER B 349	(3)
Leu353Pro	LQTS1	S6, aligned towards solvent	interacts with both other S6 segments and S4-S5 linker on same subunit	yes/slightly	GLY A 350 ALA A 352 LYS A 354 GLN A 356 GLN A 357	VAL A 254 HIS A 258 GLY A 350 LYS A 354 GLN A 356 GLN A 357 VAL D 355 GLN D 359	(1;10)
Gln357Arg	LQTS1	S6, exposed to solvent, oriented towards S4-S5 linker of the same subunit	S6, exposed to solvent, oriented towards S4-S5 linker of the same subunit	yes/yes	LEU A 353 LYS A 354 GLN A 356	LEU A 353 LYS A 354 GLN A 356 LYS A 358	Q357R alone shows slightly reduced current, $V_{1/2}$ shifted in more positive direction and delayed activation. In presence of E1, similar trends, but also faster tail current decay (faster deactivation). In presence of both E1 and WT, properties are intermediate between WT/E1-only and mutant/E1-only. Q357R is more mistrafficking prone than WT. (60) Favors closed state. Modest trafficking defect.

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