

Supplementary Information for

GAIN-OF-FUNCTION DUE TO INCREASED OPENING PROBABILITY BY TWO KCNQ5 PORE VARIANTS CAUSING DEVELOPMENTAL AND EPILEPTIC ENCEPHALOPATHY

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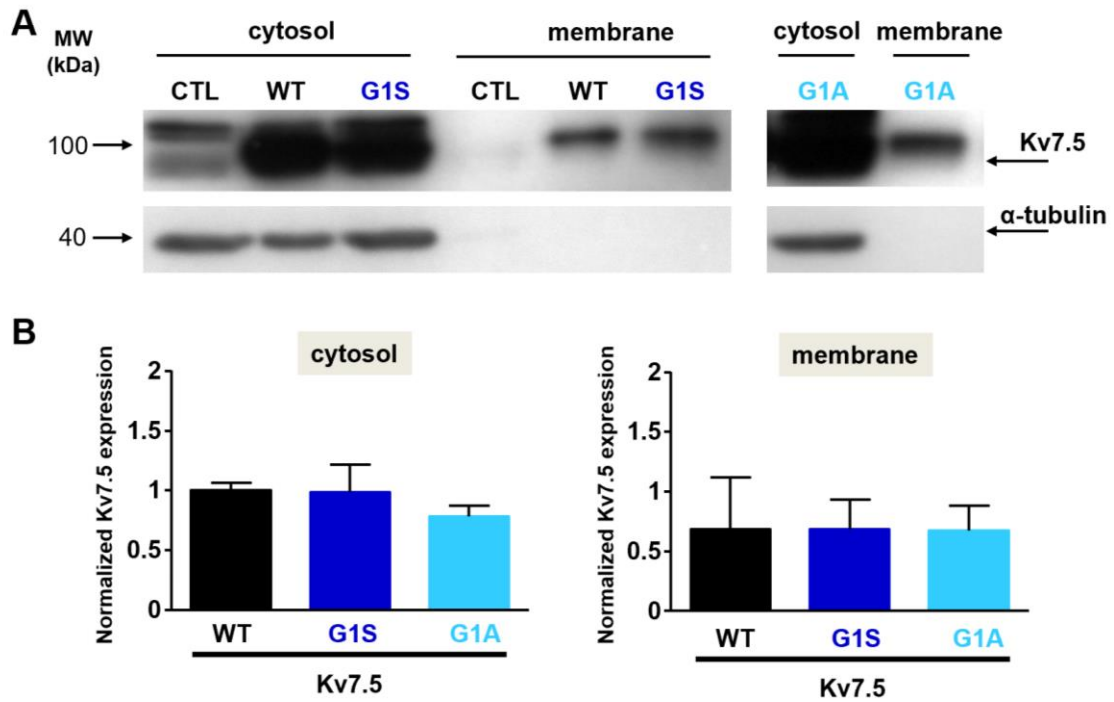


Figure S1. Subcellular fractionation of Kv7.5, Kv7.5 G1S or Kv7.5 G1A subunits. (A) Representative Western blot analysis of proteins from cytosol- or plasma membrane-fractions (membrane) from CHO cells transfected with pcDNA3.1 (empty vector, CTL), Kv7.5 (WT), Kv7.5 G1S or Kv7.5 G1A subunits. Lysates were incubated with anti-Kv7.5 antibody (top panels) or anti- α -tubulin antibody (lower panels), as indicated. (B) Quantification of cytosol and membrane Kv7.5 proteins from CHO cells transfected with pcDNA3.1 (empty vector, CTL), Kv7.5 (WT), Kv7.5 G1S or Kv7.5 G1A subunits. Data are expressed as Mean \pm S.E.M. n=4.

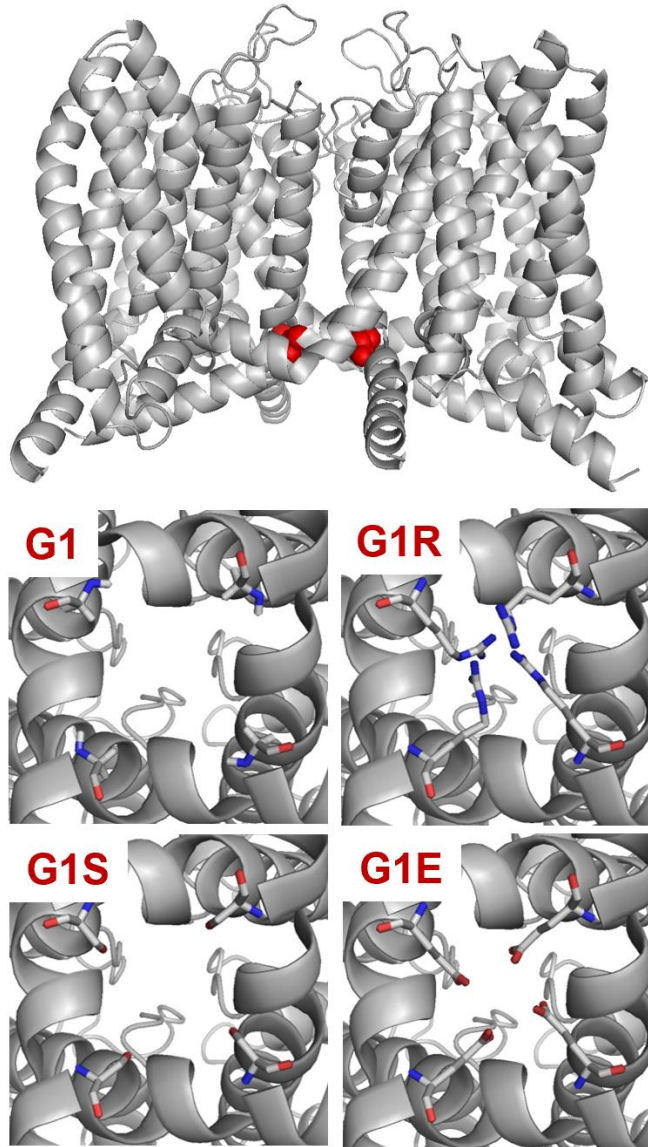


Figure S2. Modelling the effects of G1 variants in Kv7.5. The top panel shows a homology model of a Kv7.5 channels, using as template the coordinates of human Kv7.1 in the Activated/Open (AO) state; the G1 residue in the top panel is colored in red using a space-filling model. For clarity only two of the four subunits are shown (top panel). In the bottom panels, enlarged views showing a bottom view of the pore domain of four Kv7.5 subunits in which the residue at position 347 is G (wild-type, G1), S (G1S), R (G1R), or E (G1E).

Table S1. Available estimates of opening probabilities (P_o) and i single-channel current (i) for Kv7.2 and Kv7.5 channels

Kv7.2				
Opening probability (P_o)	Single channel current (i; pA)	Membrane voltage (mV)	Method	Reference
0.17	0.55	0	Patch-clamp recordings of unitary events	1
0.29	0.75	+20	Patch-clamp recordings of unitary events	2
0.25	0.65	+20	Patch-clamp recordings of unitary events	3
0.13	0.51	0	Patch-clamp recordings of unitary events	4
0.11	0.57	0	Patch-clamp recordings of unitary events	5
0.27	0.8	Not indicated	Nonstationary noise analysis	6
0.27	0.4	+20	Nonstationary noise analysis	Present work
Kv7.5				
0.17	0.19	0	Patch-clamp recordings of unitary events	1
0.25	0.25	+20	Nonstationary noise analysis	Present work

SI References

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