SUPPLEMENTARY MATERIALS

Markov I_{Ks} Models

The I_{Ks} Markov model paradigm was based on the work of Silva and Rudy. Figure 1 was reproduced from reference with permission [1].

Using experimental data, we changed transition rates equations from WT for V141M KCNQ1 of heterozygous expression. Because experiments were conducted at room temperature, model validation for I_{Ks} was set at room temperature (T=298). The transition rates equations for WT and V141M KCNQ1 I_{Ks} Markov model were listed in the Table 1.

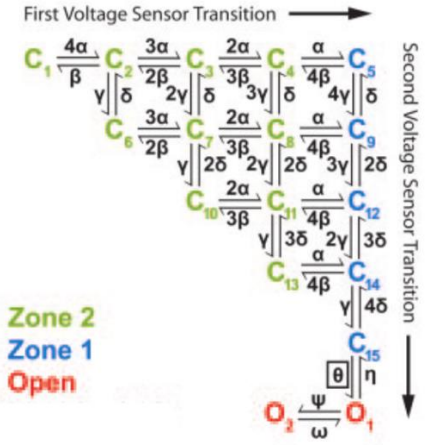

Figure 1. The I_{Ks} Markov model. The model of I_{Ks} contains 15 closed (C_1 to C_{15}) states to account for 2 transitions of each of the 4 voltage sensor domains before channel opening and 5 open states (O_1 to O_5).

Table 1. **Equations of transition rates for WT and V141M KCNQ1 I_{Ks} Markov models**

Transition rates	WT	V141M KCNQ1
α	0.0025*exp(0.301*Vm*F/(R*T))	0.002875*exp(0.301*Vm*F/(R*T))
β	0.0006*exp(-0.0964*Vm*F/(R*T))	0.000525*exp(-0.0964*Vm*F/(R*T))
γ	0.0126*exp(0.8622*Vm*F/(R*T))	0.0283*exp(0.8622*Vm*F/(R*T))
δ	0.0089*exp(-0.3692*Vm*F/(R*T))	0.00825*exp(-0.3692*Vm*F/(R*T))
η	0.0668*exp(-0.3494*Vm*F/(R*T))	0.0574*exp(-0.3494*Vm*F/(R*T))
θ	0.0011	0.011
ω	0.011*exp(-0.3356*Vm*F/(R*T))	0.00975*exp(-0.3356*Vm*F/(R*T))
ψ	0.02*exp(1.0348*Vm*F/(R*T))	0.03*exp(1.0348*Vm*F/(R*T))

*Symbols indicating transition rates are illustrated in Figure 1. Vm= membraneous potential [1].

1. Silva, J. and Y. Rudy, Subunit interaction determines I_{Ks} participation in cardiac repolarization and repolarization reserve. Circulation, 2005. 112(10): p. 1384-91.