

**OVERLAPPING BINDING SITES OF STRUCTURALLY DIFFERENT  
ANTIARRHYTHMICS FLECAINIDE AND PROPAFENONE IN THE SUBUNIT  
INTERFACE OF POTASSIUM CHANNEL Kv2.1\***

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**Supplementary Data**

**Table S1. Nucleotide composition of the Kv1/2/K2.1 chimeras used in the study.**

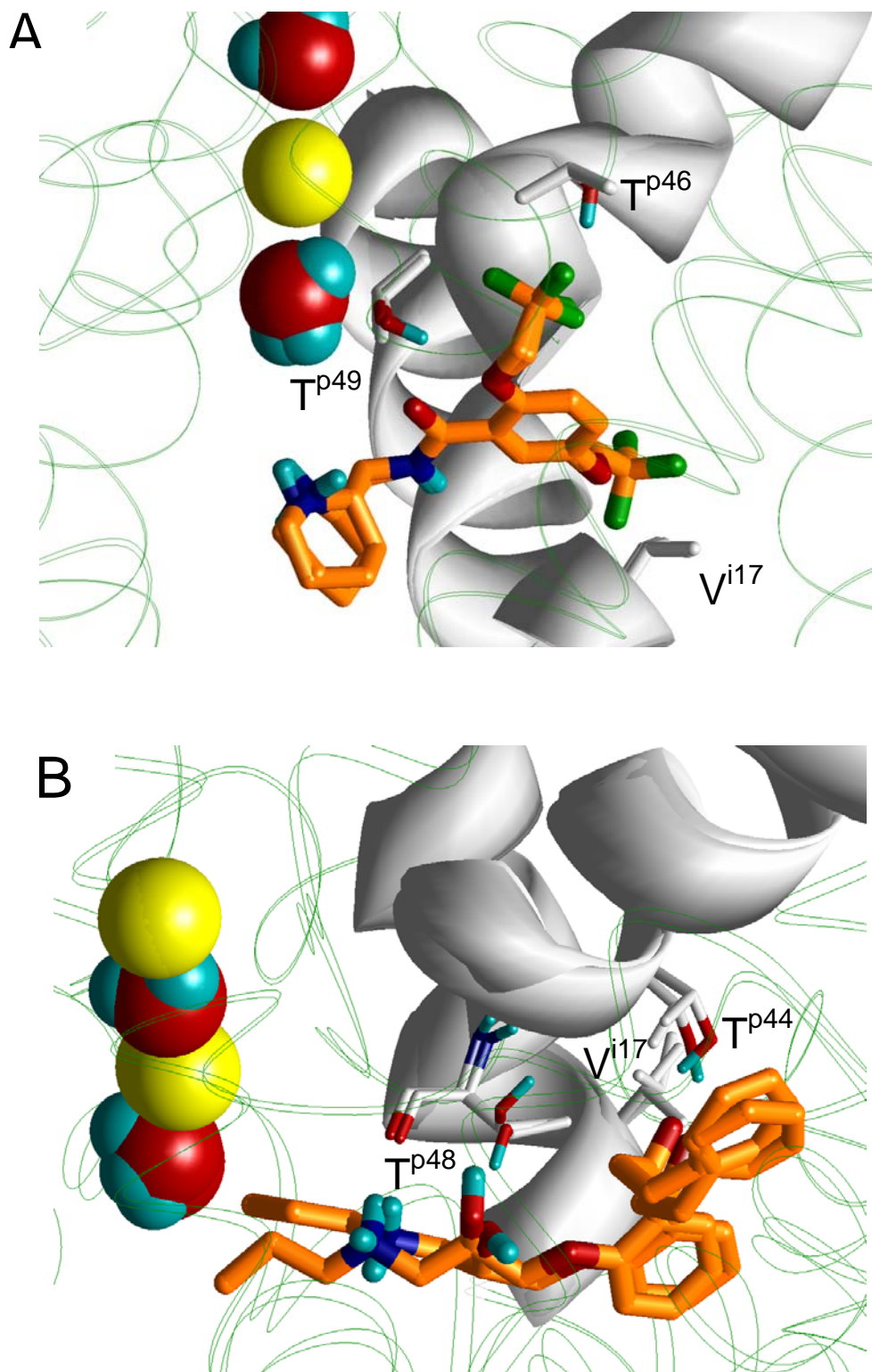
Chimera	Nucleotide composition
Kv2.1 N-Term	nt 1-492 of Kv1.2, nt 571-Stop of Kv2.1
Kv2.1 S1	nt 1-555 of Kv2.1, nt 480-546 of Kv 1.2, nt 627-Stop of Kv2.1
Kv2.1 LS1/S2	nt 1-624 of Kv2.1, nt 547-663 of Kv1.2, nt 685-Stop of Kv2.1
Kv2.1 S2	nt 1-684 of Kv2.1, nt 664-735 of Kv1.2, nt 757-Stop of Kv2.1
Kv2.1 LS2/S3	nt 1-750 of Kv2.1, nt 730-759 of Kv1.2, nt 781-Stop of Kv2.1
Kv2.1 S3	nt 1-774 of Kv2.1, nt 754-843 of Kv1.2, nt 862-Stop of Kv2.1
Kv2.1 LS3/S4	nt 1-840 of Kv2.1, nt 820-879 of Kv1.2, nt 889-Stop of Kv2.1
Kv2.1 S4	nt 1-882 of Kv2.1, nt 874-936 of Kv1.2, nt 946-Stop of Kv2.1
Kv2.1 LS4/S5	nt 1-954 of Kv2.1, nt 946-996 of Kv1.2, nt 1006-Stop of Kv2.1
Kv2.1 S5	nt 1-1005 of Kv2.1, nt 997-1035 of Kv1.2, nt 1042-Stop of Kv2.1
Kv2.1 LS5/S6	nt 1-1059 of Kv2.1, nt 1051-1164 of Kv1.2, nt 1171-Stop of Kv2.1
Kv2.1 LP	nt 1-1059 of Kv2.1, nt 1051-1077 of Kv1.2, nt 1087-1155 of Kv2.1, nt 1147-1164 of Kv1.2, nt 1174-Stop of Kv2.1
Kv2.1 S6	nt 1-1182 of Kv2.1, nt 1174-1230 of Kv1.2, nt 1240-Stop of Kv2.1
Kv2.1 C-Term	nt 1-1239 of Kv2.1, nt 1231-Stop of Kv1.2
Kv2.1 AS <sup>39</sup> → DA	nt 1-1095 of Kv2.1, nt 1087-1092 of Kv1.2, nt 1102-Stop of Kv2.1
Kv2.1 TIT <sup>p46</sup> → VVS	nt 1-1113 of Kv2.1, nt 1105-1113 of Kv1.2, nt 1123-Stop of Kv2.1
Kv2.1 IY <sup>p56</sup> → MV	nt 1-1146 of Kv2.1, nt 1138-1143 of Kv1.2, nt 1153-Stop of Kv2.1
Kv2.1 GLCC <sup>i11</sup> → SLCA	nt 1-1182 of Kv2.1, nt 1174-1176 of Kv1.2, nt 1186-1191 of Kv2.1, nt 1183-1185 of Kv1.2, nt 1195-Stop of Kv2.1
Kv2.1 V <sup>i17</sup> → T	nt 1-1209 of Kv2.1, nt 1201-1203 of Kv1.2, nt 1213-Stop of Kv2.1
Kv2.1 IPIIVN <sup>i27</sup> → VPVIVS	nt 1-1224 of Kv2.1, nt 1216-1218 of Kv1.2, nt 1228-1230 of Kv2.1, nt 1222-1224 of Kv1.2, nt 1234-1239 of Kv2.1, nt 1231-1233 of Kv1.2, nt 1243-Stop of Kv2.1
Kv2.1 SE <sup>i31</sup> → NY	nt 1-1248 of Kv2.1, nt 1240-1245 of Kv1.2, nt 1255-Stop of Kv2.1
Kv1.2 VVS → TIT <sup>p46</sup>	nt 1-1104 of Kv1.2, nt 1102-1110 of Kv2.1, nt 1114-Stop of Kv1.2
Kv1.2 MV → IY <sup>p56</sup>	nt 1-1137 of Kv1.2, nt 1135-1140 of Kv2.1, nt 1144-Stop of Kv1.2
Kv1.2 T → V <sup>i17</sup>	nt 1-1200 of Kv1.2, 1198-1200 of Kv2.1, nt 1204-Stop of Kv1.2
Kv1.2 VVS → TIT <sup>p46</sup> + T → V <sup>i17</sup>	Nt 1-1104 of Kv1.2, 1102-1110 of Kv2.1, nt 1114-1120 of Kv1.2, nt 1198-1200 of Kv2.1, nt 1204-Stop of Kv1.2

The numbers refer to the open reading frame of the respective channel. nt: nucleotide.

**Table S2. Electrophysiological properties of chimeras used in the study under control and with 200  $\mu\text{mol/l}$  flecainide**

Channel	Control			Flecainide			
	$G_{\text{max}}$	$V_{1/2}$ (mV)	$s$ (mV)	$G_{\text{max}}$	$V_{1/2}$ (mV)	$s$ (mV)	
Kv1.2 wildtype	0.97 ± 0.00	-10.2 ± 1.3	10.2 ± 1.1	0.86 ± 0.02	-11.8 ± 1.3	9.6 ± 1.2	13
Kv2.1 wildtype	0.98 ± 0.00	3.5 ± 1.1	12.7 ± 0.4	0.44 ± 0.03	-1.7 ± 1.1	11.4 ± 0.4	16
Kv2.1 N-Term	1.00 ± 0.00	4.0 ± 1.8	10.7 ± 0.6	0.53 ± 0.02	1.3 ± 2.0	8.8 ± 0.5	12
Kv2.1 S1	0.98 ± 0.00	-5.4 ± 0.8	19.4 ± 0.2	0.39 ± 0.01	-12.4 ± 1.0	17.8 ± 0.3	6
Kv2.1 LS1/LS2	1.24 ± 0.04	14.4 ± 3.5	35.1 ± 1.1	0.66 ± 0.02	27.4 ± 4.2	39.2 ± 1.8	11
Kv2.1 S2	1.02 ± 0.01	6.7 ± 0.9	18.6 ± 0.4	0.31 ± 0.02	-7.1 ± 0.8	18.5 ± 1.3	6
Kv2.1 LS2/LS3	1.02 ± 0.00	18.0 ± 0.9	14.7 ± 0.3	0.43 ± 0.03	14.3 ± 1.2	14.1 ± 0.6	6
Kv2.1 S3	1.12 ± 0.01	28.5 ± 0.8	15.8 ± 0.4	0.46 ± 0.04	25.2 ± 0.9	16.3 ± 0.3	6
Kv2.1 LS3/LS4	1.06 ± 0.01	9.3 ± 1.4	22.6 ± 0.6	0.46 ± 0.03	9.4 ± 1.9	20.3 ± 2.0	10
Kv2.1 S4	1.04 ± 0.00	19.0 ± 0.6	15.7 ± 0.2	0.54 ± 0.05	13.8 ± 1.1	14.4 ± 0.2	6
Kv2.1 LS4/LS5	1.04 ± 0.01	21.8 ± 1.3	10.0 ± 0.5	0.50 ± 0.03	20.4 ± 2.5	16.5 ± 2.5	6
Kv2.1 S5	0.99 ± 0.01	15.1 ± 0.6	12.3 ± 0.2	0.41 ± 0.02	6.4 ± 0.6	10.4 ± 0.3	6
Kv2.1 LS5/LS6	0.99 ± 0.01	6.4 ± 1.4	15.8 ± 0.4	0.96 ± 0.01	6.0 ± 1.2	16.0 ± 0.4	11
Kv2.1 LP	0.97 ± 0.01	-9.5 ± 1.5	9.8 ± 0.4	0.48 ± 0.01	-15.5 ± 1.4	11.3 ± 0.5	7
Kv2.1 S6	0.93 ± 0.02	-26.8 ± 0.6	13.8 ± 0.6	0.86 ± 0.01	-28.5 ± 0.6	13.0 ± 0.5	6
Kv2.1 C-Term	0.96 ± 0.01	8.0 ± 1.1	10.4 ± 0.2	0.47 ± 0.04	4.3 ± 1.3	9.2 ± 0.5	6
Kv2.1 AS <sup>39</sup> →DA	0.99 ± 0.01	6.8 ± 1.0	11.7 ± 0.5	0.40 ± 0.03	-12.3 ± 1.1	12.4 ± 0.4	7
Kv2.1 TIT <sup>p46</sup> →VVS	1.03 ± 0.01	14.6 ± 0.7	15.7 ± 0.6	0.74 ± 0.02	11.3 ± 1.3	14.7 ± 0.4	6
Kv2.1 IY <sup>p56</sup> →MV	1.01 ± 0.01	9.1 ± 1.4	15.3 ± 0.6	0.86 ± 0.03	6.3 ± 1.6	14.6 ± 0.6	7
Kv2.1 GLCC <sup>i11</sup> →SLCA	0.98 ± 0.00	-1.3 ± 1.3	4.6 ± 0.5	0.34 ± 0.03	-11.8 ± 1.1	12.8 ± 0.5	5
Kv2.1 V <sup>i17</sup> →T	1.01 ± 0.01	10.4 ± 0.9	16.4 ± 0.6	0.94 ± 0.02	11.2 ± 0.7	16.5 ± 0.6	6
Kv2.1 IPIIVN <sup>i27</sup> →VPVIVS	1.06 ± 0.00	11.6 ± 0.4	19.5 ± 0.3	0.63 ± 0.02	9.9 ± 0.8	20.5 ± 0.6	7
Kv2.1 SE <sup>i31</sup> →NY	0.96 ± 0.00	-7.6 ± 2.7	11.6 ± 0.4	0.32 ± 0.02	-15.1 ± 2.6	10.6 ± 0.8	6
Kv1.2 VVS→TIT <sup>p46</sup>	0.94 ± 0.00	-14.5 ± 0.9	5.9 ± 0.8	0.69 ± 0.03	-16.5 ± 1.6	5.5 ± 1.0	5
Kv1.2 MV→IY <sup>p56</sup>	0.96 ± 0.02	15.3 ± 2.1	11.4 ± 3.6	0.86 ± 0.03	-13.3 ± 2.4	12.1 ± 4.0	5
Kv1.2 T→V <sup>i17</sup>	0.95 ± 0.02	-18.3 ± 1.7	5.7 ± 0.6	0.55 ± 0.07	-20.0 ± 2.0	5.7 ± 0.3	6
Kv1.2 VVS→TIT <sup>p46</sup> +T→V <sup>i17</sup>	0.90 ± 0.02	22.6 ± 1.7	4.7 ± 0.9	0.60 ± 0.04	-24.2 ± 1.2	4.0 ± 0.6	7

$G_{\text{max}}$  is the normalized maximal conductance,  $V_{1/2}$  is the potential of the half-maximal conductance,  $s$  is the slope factor, and  $n$  is the number of experiments.



**Figure S1.** Superposition of MC-minimized complexes of Kv2.1 with enantiomers of FLEC (A) and PROP (B). Atoms  $K^+$ , O, N, F, and H are colored yellow, red, blue, green, and cyan, respectively. Carbon atoms are gray in the channel and orange in the ligands. Only polar hydrogens are shown for clarity.