

Table S2. Percent identity matrix for human TRP channels from the same multiple sequence alignment described in Table S1. In this case, the color intensity from white to red illustrates increasing sequence conservation.

	TRPM1	TRPM3	TRPM6	TRPM7	TRPM4	TRPM5	TRPM8	TRPM2	TRPC6	TRPC3	TRPC7	TRPC1	TRPC4	TRPC5	TRPA1	TRPN1	TRPV5	TRPV6	TRPV3	TRPV4	TRPV1	TRPV2	TRPML1	TRPML2	TRPML3	TRPP5	TRPP2	TRPP3
TRPM1	100.0	64.6	47.1	49.5	30.1	29.4	29.2	31.3	19.4	17.6	17.8	17.0	17.9	16.7	12.7	15.6	14.6	13.3	15.4	13.4	14.5	16.0	8.9	9.3	8.8	12.4	14.0	14.4
TRPM3	64.6	100.0	48.2	53.5	29.8	29.4	29.9	30.7	18.7	16.5	17.8	17.2	17.7	17.8	13.1	15.0	14.5	12.9	15.4	13.4	15.6	16.5	8.6	9.4	8.3	12.4	13.3	12.6
TRPM6	47.1	48.2	100.0	57.1	28.3	28.3	26.7	28.4	19.5	17.7	18.8	15.8	18.6	17.1	12.6	14.2	13.2	12.8	15.3	12.3	13.0	14.6	9.9	8.7	9.1	11.6	12.9	12.0
TRPM7	49.5	53.5	57.1	100.0	28.3	26.9	28.3	29.5	18.8	16.3	17.3	16.0	17.4	17.4	11.9	14.7	13.0	12.3	13.5	11.9	13.0	15.0	11.0	9.6	10.5	12.3	12.5	11.1
TRPM4	30.1	29.8	28.3	28.3	100.0	46.4	34.0	37.7	18.3	18.6	17.9	17.8	19.6	18.8	13.0	16.4	13.2	13.8	15.2	13.8	13.8	14.8	10.2	8.3	10.0	10.6	14.3	11.1
TRPM5	29.4	29.4	28.3	26.9	46.4	100.0	35.6	39.5	18.3	17.9	17.9	16.4	19.3	19.1	12.8	15.6	13.2	12.7	14.0	14.8	12.9	14.0	10.0	8.3	10.8	10.9	11.7	11.7
TRPM8	29.2	29.9	26.7	28.3	34.0	35.6	100.0	42.6	18.0	18.3	18.0	17.5	20.3	19.3	13.6	15.0	12.7	13.1	14.3	13.6	14.3	15.7	10.2	8.0	9.7	11.9	14.3	12.5
TRPM2	31.3	30.7	28.4	29.5	37.7	39.5	42.6	100.0	21.2	20.8	20.8	19.9	18.6	19.2	12.7	16.4	12.8	11.7	14.1	13.3	12.3	14.4	9.5	8.1	8.8	11.2	12.9	13.4
TRPC6	19.4	18.7	19.5	18.8	18.3	18.3	18.0	21.2	100.0	74.7	74.9	36.2	40.8	39.5	16.2	21.7	13.5	14.0	14.0	14.6	14.2	14.9	11.5	12.1	12.9	17.4	16.7	17.2
TRPC3	17.6	16.5	17.7	16.3	18.6	17.9	18.3	20.8	74.7	100.0	81.4	35.7	42.0	42.1	15.0	22.8	13.1	13.1	14.5	14.4	14.4	14.5	12.7	12.9	13.5	16.5	15.1	17.7
TRPC7	17.8	17.8	18.8	17.3	17.9	17.9	18.0	20.8	74.9	81.4	100.0	34.8	41.6	40.5	14.4	21.1	12.8	13.0	14.0	14.3	13.9	14.0	12.0	12.3	13.4	16.3	16.5	17.8
TRPC1	17.0	17.2	15.8	16.0	17.8	16.4	17.5	19.9	36.2	35.7	34.8	100.0	46.5	45.5	12.2	20.2	12.8	13.5	14.1	12.4	14.3	13.6	11.5	11.7	10.4	10.9	10.0	11.9
TRPC4	17.9	17.7	18.6	17.4	19.6	19.3	20.3	18.6	40.8	42.0	41.6	46.5	100.0	68.3	15.1	21.7	16.2	16.4	16.3	14.4	16.6	16.0	12.8	10.9	11.7	13.4	13.5	15.9
TRPC5	16.7	17.8	17.1	17.4	18.8	19.1	19.3	19.2	39.5	42.1	40.5	45.5	68.3	100.0	13.5	21.6	15.0	15.2	16.5	14.4	16.0	16.3	13.0	12.5	11.9	12.7	13.5	15.1
TRPA1	12.7	13.1	12.6	11.9	13.0	12.8	13.6	12.7	16.2	15.0	14.4	12.2	15.1	13.5	100.0	22.9	18.2	19.2	18.5	18.5	18.4	18.2	15.7	13.6	14.7	16.7	16.4	15.8
TRPN1	15.6	15.0	14.2	14.7	16.4	15.6	15.0	16.4	21.7	22.8	21.1	20.2	21.7	21.6	22.9	100.0	20.3	19.7	19.2	18.5	20.0	20.4	12.4	12.7	13.0	15.1	14.1	13.1
TRPV5	14.6	14.5	13.2	13.0	13.2	13.2	12.7	12.8	13.5	13.1	12.8	12.8	16.2	15.0	18.2	20.3	100.0	74.7	28.3	29.5	28.2	27.5	15.1	15.6	16.5	13.4	15.4	14.6
TRPV6	13.3	12.9	12.8	12.3	13.8	12.7	13.1	11.7	14.0	13.1	13.0	13.5	16.4	15.2	19.2	19.7	74.7	100.0	27.8	29.4	28.4	28.0	15.6	15.4	16.5	13.5	14.3	13.7
TRPV3	15.4	15.4	15.3	13.5	15.2	14.0	14.3	14.1	14.0	14.5	14.0	14.1	16.3	16.5	18.5	19.2	28.3	27.8	100.0	41.5	41.9	38.2	13.7	14.4	13.5	13.8	14.4	15.7
TRPV4	13.4	13.4	12.3	11.9	13.8	14.8	13.6	13.3	14.6	14.4	14.3	12.4	14.4	14.4	18.5	18.5	29.5	29.4	41.5	100.0	45.6	43.2	13.7	14.4	14.6	16.9	15.8	17.0
TRPV1	14.5	15.6	13.0	13.0	13.8	12.9	14.3	12.3	14.2	14.4	13.9	14.3	16.6	16.0	18.4	20.0	28.2	28.4	41.9	45.6	100.0	46.8	14.3	13.7	13.0	13.1	13.4	13.5
TRPV2	16.0	16.5	14.6	15.0	14.8	14.0	15.7	14.4	14.9	14.5	14.0	13.6	16.0	16.3	18.2	20.4	27.5	28.0	38.2	43.2	46.8	100.0	16.1	16.0	15.6	11.2	12.7	14.0
TRPML1	8.9	8.6	9.9	11.0	10.2	10.0	10.2	9.5	11.5	12.7	12.0	11.5	12.8	13.0	15.7	12.4	15.1	15.6	13.7	13.7	14.3	16.1	100.0	48.7	56.4	17.6	17.9	18.9
TRPML2	9.3	9.4	8.7	9.6	8.3	8.3	8.0	8.1	12.1	12.9	12.3	11.7	10.9	12.5	13.6	12.7	15.6	15.4	14.4	14.4	13.7	16.0	48.7	100.0	57.1	18.0	17.1	17.6
TRPML3	8.8	8.3	9.1	10.5	10.0	10.8	9.7	8.8	12.9	13.5	13.4	10.4	11.7	11.9	14.7	13.0	16.5	16.5	13.5	14.6	13.0	15.6	56.4	57.1	100.0	19.2	19.6	17.3
TRPP5	12.4	12.4	11.6	12.3	10.6	10.9	11.9	11.2	17.4	16.5	16.3	10.9	13.4	12.7	16.7	15.1	13.4	13.5	13.8	16.9	13.1	11.2	17.6	18.0	19.2	100.0	47.0	46.9
TRPP2	14.0	13.3	12.9	12.5	14.3	11.7	14.3	12.9	16.7	15.1	16.5	10.0	13.5	13.5	16.4	14.1	15.4	14.3	14.4	15.8	13.4	12.7	17.9	17.1	19.6	47.0	100.0	50.8
TRPP3	14.4	12.6	12.0	11.1	11.1	11.7	12.5	13.4	17.2	17.7	17.8	11.9	15.9	15.1	15.8	13.1	14.6	13.7	15.7	17.0	13.5	14.0	18.9	17.6	17.3	46.9	50.8	100.0

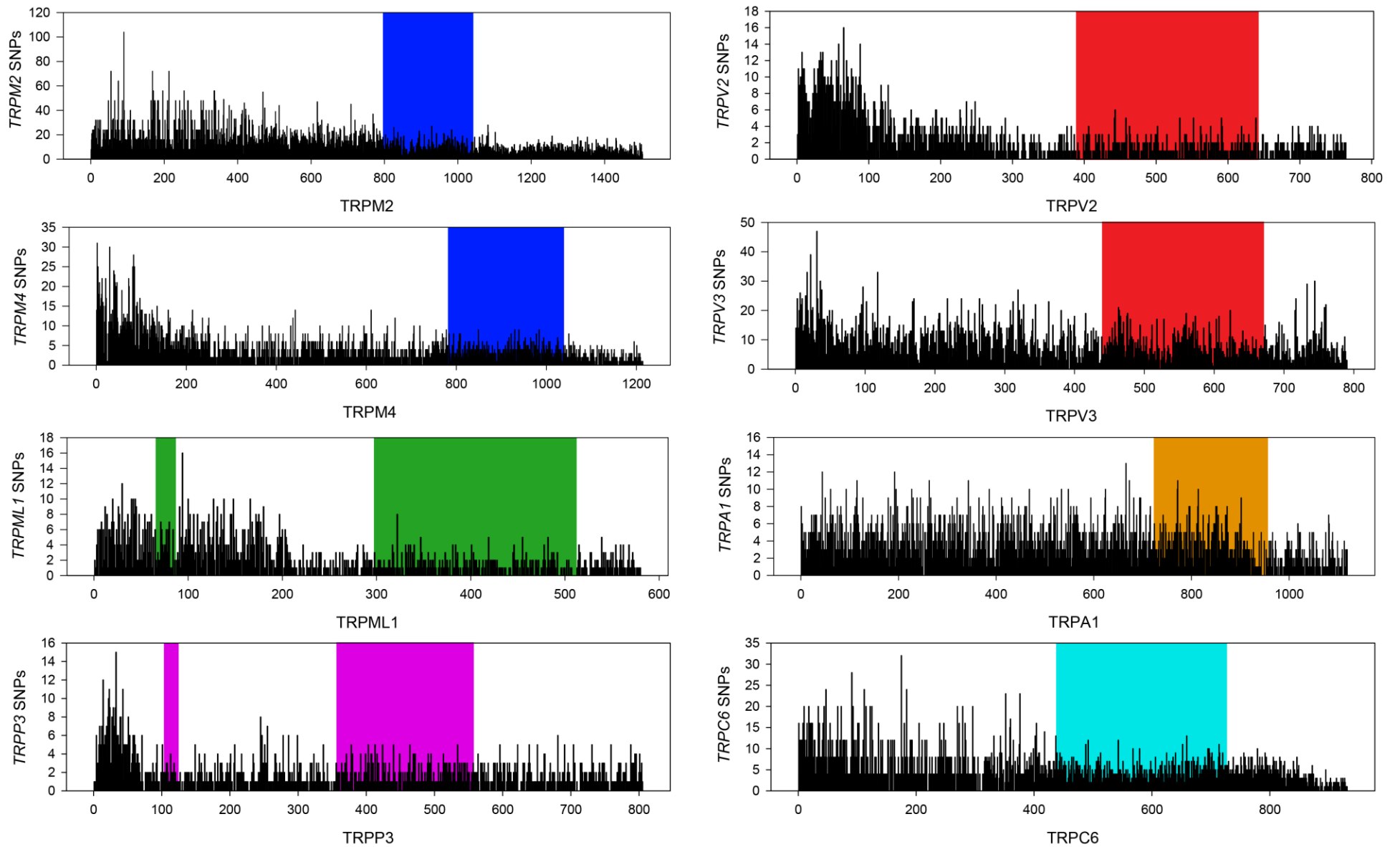


Figure S1. SNP frequencies by residue position in representative TRP channels. Exonic SNP data was downloaded from the Ensembl database (<https://www.ensembl.org>). Raw data was processed in Linux to count unique SNPs at each residue number. Color shading indicates transmembrane regions of the channels and corresponds to the colors of subfamilies shown in Figure 1. Note that TRPML and TRPP channels have an extended extracellular segment between the S1 helix and the rest of the transmembrane region.