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K2P1 Assembles with K2P3 or K2P9 to Form Sumo-Regulated Task Background Channels

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TASK subunits K2P3 and K2P9 form homo- and hetero-dimeric channels in neurons with varied sensitivities to anesthetics, flavors and pH (Berg et al. J Neurosci. 2004. 24:6693-702; Bautista et al. Nat. Neurosci. 2008. 11:772-9). Here, K2P1 subunits (Rajan et al. 2005. Cell 121, 37-47) are shown to confer SUMO-regulation on TASK channels in rat cerebellar granule neurons (CGN). First, CFP (C) or YFP (Y)-tagged subunits studied in CHO cells by donor-decay Forster resonance energy transfer (FRET) confirm biochemical evidence for assembly of K2P2 and its native isoform (Thomas et al., Neuron 2008 58:859-70). Next, FRET shows association of C-K2P1 and Y-K2P1, Y-K2P3 or Y-K2P9 but not Y-K2P2 or Kv2.1. As expected from Rajan et al, FRET registers association of Y-SUMO and C-K2P1 but not C-K2P3 or C-K2P9. In contrast, Y-SUMO and C-K2P3 or C-K2P9 FRET when untagged K2P1 is co-expressed. Consistent with electrophysiological studies (EP) showing one SUMO per channel is sufficient to silence K2P channels (Plant et al. this meeting), channels with two linked K2P1 subunits (WT-WT), WT and SUMO-insensitive K2P1 (WT-K274Q), WT and K2P3 (WT-K2P3) or WT and K2P9 (WT-K2P9), pass currents when membrane patches are exposed to SUMO-protease (SENP1) and silenced by SUMO1. In contrast, K2P3-K2P3, K2P9-K2P9, K2P3-K274Q or K2P9-K274Q are constitutively active and insensitive to SENP1 and SUMO1. Finally, in CGN, immunochemistry shows K2P1, K2P3, K2P9, SUMO, SUMO E1 conjugase and SUMO E2 ligase in plasma membrane; EP reveals IK_{SO} regulation by SENP1 and SUMO, and transfection with mutant subunits demonstrate assembly of K2P1 with K2P3 or K2P9 by FRET and EP.