

Figure S1. Comparison of fluorescence intensities of K-Kv1.3 and K-ΔKv1.3 expressed in membrane of HEK293 cells. Intensities were measured with confocal microscopy using the same parameters and treated with Image J software as described in the Results section. Data were averaged (mean \pm SD, $n = 20$; $p = 0.47$) for each channel.

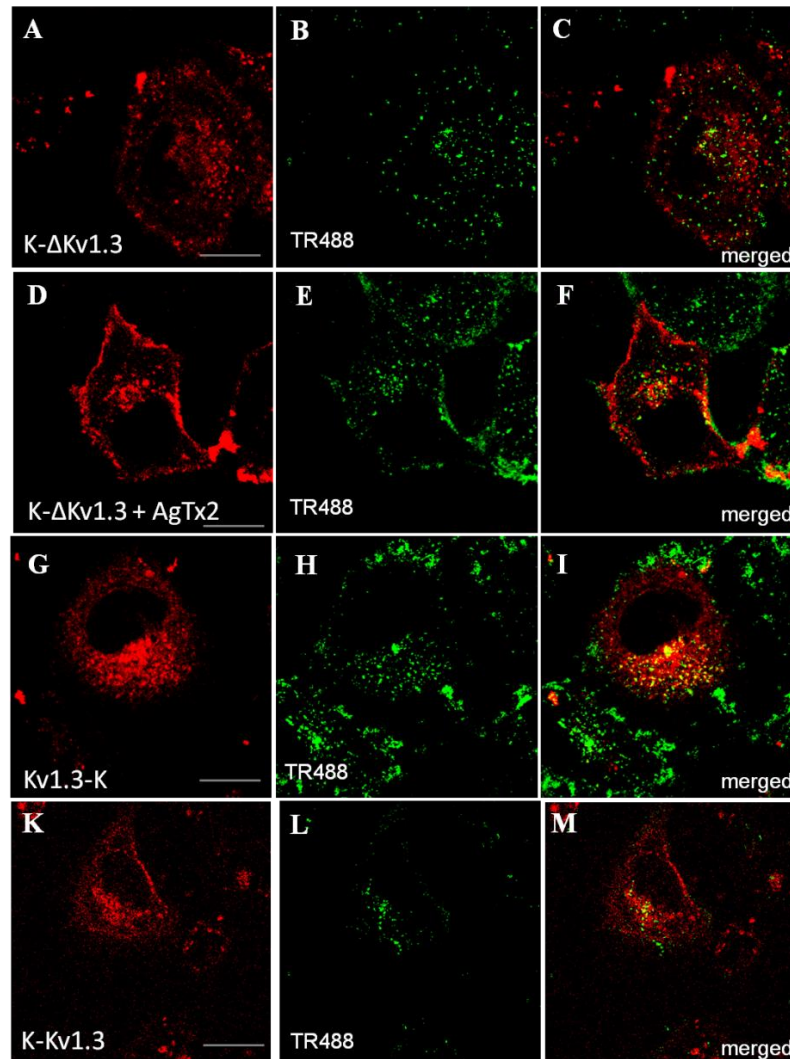


Figure S2. Distribution of mKate2-tagged Kv1.3 (red) and the endosome marker TR488 (green) in living HEK293 cells. (A-C), (D-F) Cells expressing K-ΔKv1.3. (D-F) Cells were co-incubated with agitoxin 2 (AgTx2, 100 nM, 30 min) and TR488. (G-I) Cells expressing Kv1.3-K. (J-M) Cells expressing K-Kv1.3. (C,F,I,M) Merged images of mKate2-tagged Kv1.3 and TR488 fluorescence. Yellow color indicates co-localization of the channels and ERTG in endosomes. Scale bar: 20 μ m.

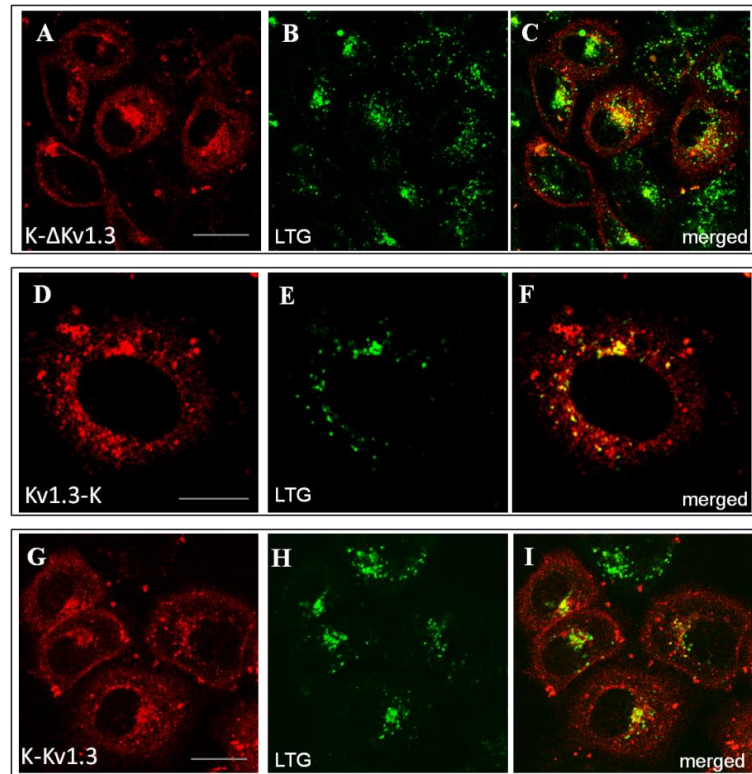


Figure S3. Distribution of mKate2-tagged Kv1.3 (red) and the lysosome marker LTG (green) in living HEK293 cells. (A-C) Cells expressing K-ΔKv1.3. (D-F) Cells expressing Kv1.3-K. (G-I) Cells expressing K-Kv1.3. (C,F,I) Merged images of mKate2-tagged Kv1.3 and LTG fluorescence. Yellow color indicates co-localization of the channels and LTG in lysosomes. Scale bar: 20 μ m.

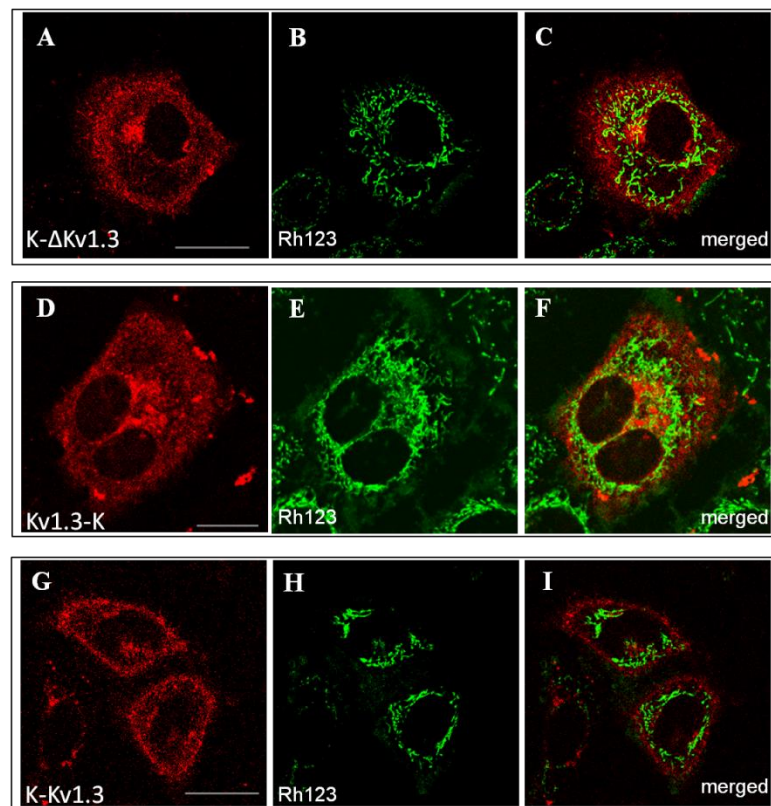


Figure S4. Distribution of mKate2-tagged Kv1.3 (red) and the mitochondrion marker Rh123 (green) in living HEK293 cells. (A-C) Cells expressing K-ΔKv1.3. (D-F) Cells expressing Kv1.3-K. (G-I) Cells expressing K-Kv1.3. (C,F,I) Merged images of mKate2-tagged Kv1.3 and Rh123 fluorescence. Scale bar is 20 μ m.

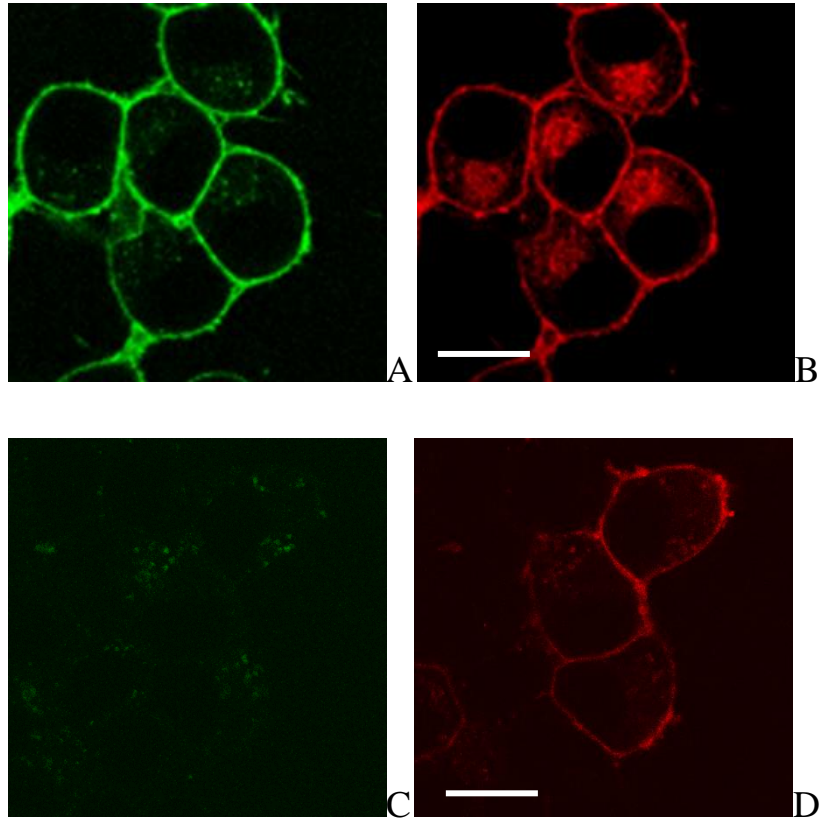


Figure S5. Confocal imaging of A-HgTx interactions with K-ΔKv1.3 channels transiently expressed in Neuro-2A cells. (A, B) Distribution of A-HgTx (2 nM) bound at the membrane of cells expressing K-ΔKv1.3. (C,D) Displacement of A-HgTx (2 nM) with HgTx (20 nM) from the complexes with K-ΔKv1.3 at the membrane of cells. Scale bar is 20 μm . Green and red colors – fluorescence of A-HgTx and K-ΔKv1.3, respectively.

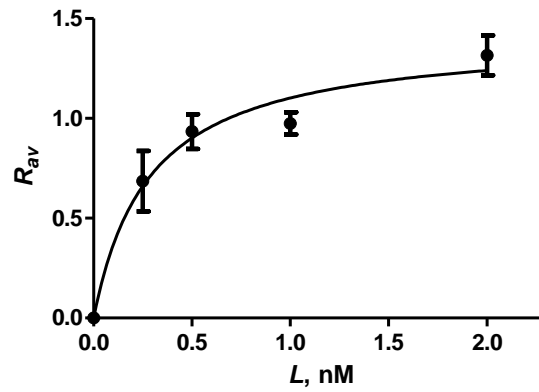


Figure S6. Concentration dependence of A-HgTx binding to K-Kv1.3 on a cell membrane that was measured as the dependence of R_{av} on the concentration L of A-HgTx added to HEK293 cells transiently transfected with K-Kv1.3.