

## Supplementary Information

Human EAG channels are directly modulated by PIP<sub>2</sub> as revealed by electrophysiological and optical interference investigations

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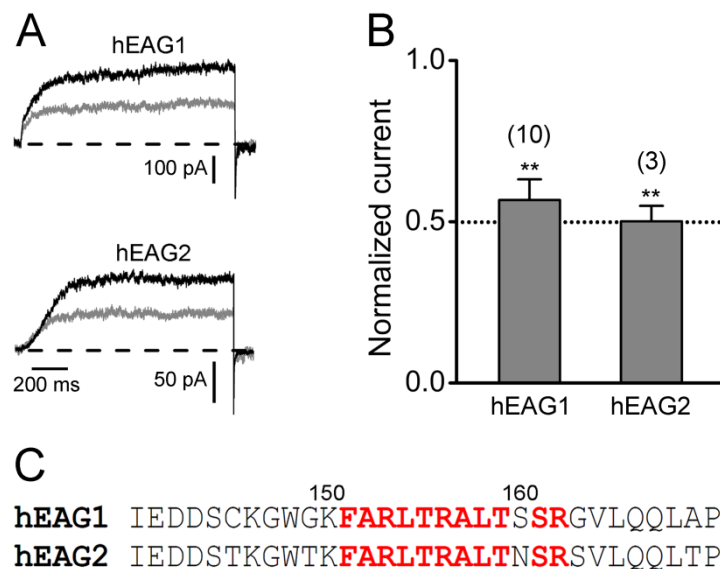
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**Figure S1: Both hEAG2 and hEAG1 channels are inhibited by PIP<sub>2</sub>.** (A) Representative current traces of hEAG1 and hEAG2 channels before and 30 s

following application of 3  $\mu$ M PIP2. The currents were elicited by pulses to 40 mV from a holding potential of  $-80$  mV. **(B)** Normalized hEAG1 channel peak current before and after PIP2 (3  $\mu$ M) application.  $P < 0.01$  compared to the control level before PIP2 applications (Statistical significances were evaluated by one-way ANOVA with Student-Newman-Keuls's multiple comparisons test). **(C)** Sequence alignment of the N termini of hEAG1 and hEAG2 channels using ClustalW (<http://www.ebi.ac.uk/Tools/msa/clustalw2/>). The residues shown in red indicate the conserved residues that are key determinants of PIP2 inhibition on hEAG1 channels as shown in Figure 6.