**Supporting Information**

# Evidence that polyphenols do not inhibit the phospholipid scramblase TMEM16F

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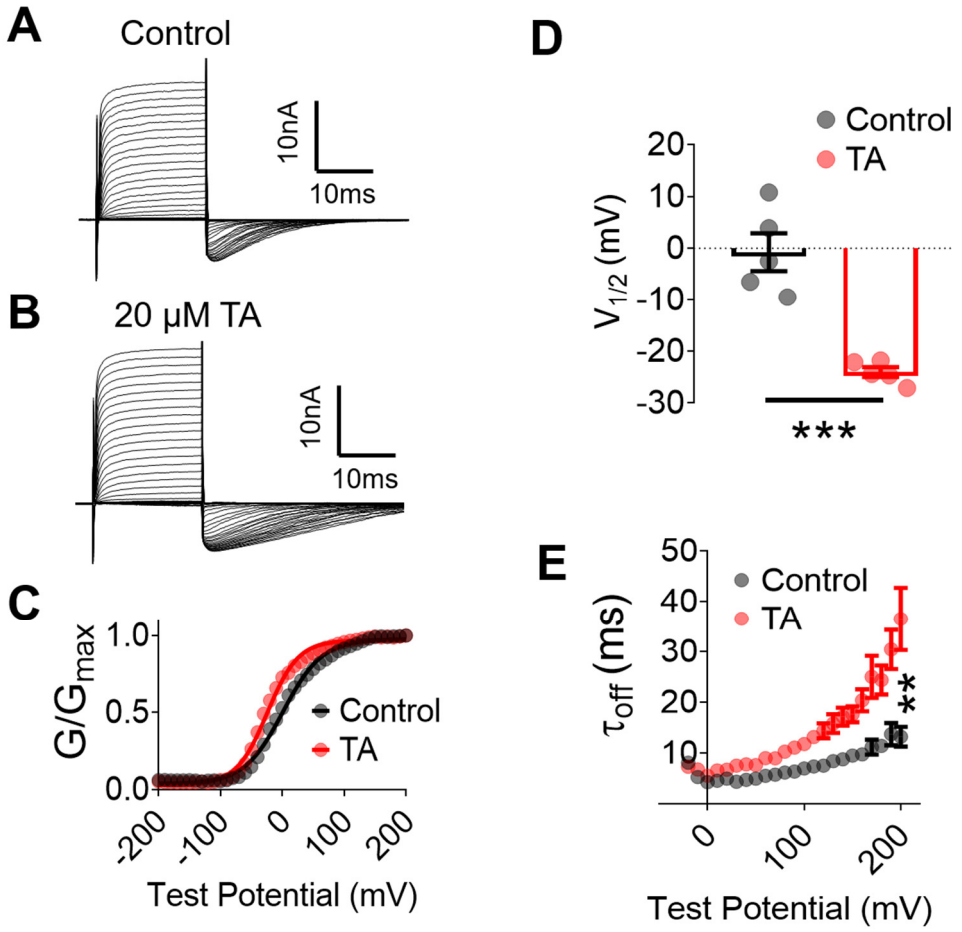


**Figure S1. TA activates BK channels.** *A*, representative BK currents recorded from HEK-293T cells overexpressed BK-α subunit under outside-out configuration. Intracellular solution contained 100 μM $Ca^{2+}$. Currents were evoked by steps from −200 to +200 mV with 10 mV increments and holding potential was set at -60 mV. *B*, representative BK currents recorded from outside-out patches containing 100 μM $Ca^{2+}$ in the pipette and 20 μM TA from extracellular side. *C*, mean *G-V* relations of the BK channels with and without TA. Relative conductance was determined by measuring the amplitude of tail currents 400 μs after repolarization to a fixed membrane potential (−60 mV). The smooth curves represent Boltzmann fits $G/G_{max}=1/(1+exp(-ze(V-V_{1/2})/kT)$. $G_{max}$ represents tail current amplitude in response to depolarization to +200 mV. Error bars represent SEM (N=5). *D*, $V_{1/2}$ obtained from C. $V_{1/2}$ in the absence and presence of TA were -0.77±3.7 mV and -24.0±1 mV, respectively. Student's t-test was performed and *** represents $p<0.001$(N=5). *E*, $\tau_{off}$ obtained from single exponential fitting of the tail currents for both control and in the presence of TA. Average $\tau_{off}$ at 200mV were 13.2±2.0 ms and 36.5±6.2 ms, respectively. Student's t-test was performed and ** represents $p<0.01$(N=5).

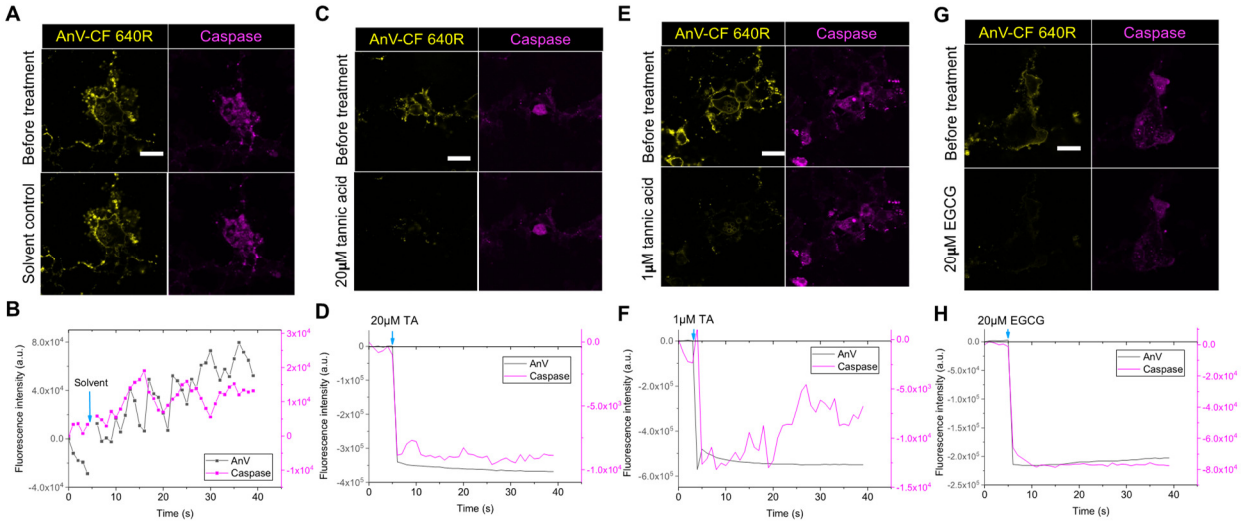


**Figure S2. TA and EGCG instantaneously suppress fluorescence signal from AnV-CF640R that are bound to PS on the surface of apoptotic cells**. *A, C, E* and *G,* representative images showing the effect of control (A), 20 μM TA (C), 1 μM TA (E), and 20 μM EGCG (G) on AnV-CF640R signal (yellow) on membrane surface of STS-induced apoptotic cells, which are labeled by caspase 3/7 dye (magenta). Scale bars = 25 μm. *B, D, F* and *H*, plots show the quantification of AnV and caspase dye fluorescence intensity before and after treatments of control (B), 20 μM TA (D), 1 μM TA (F) and 20 μM EGCG (H) of each cell in A, C, E and G, respectively. All images are representatives of at least three independent biological replicates.

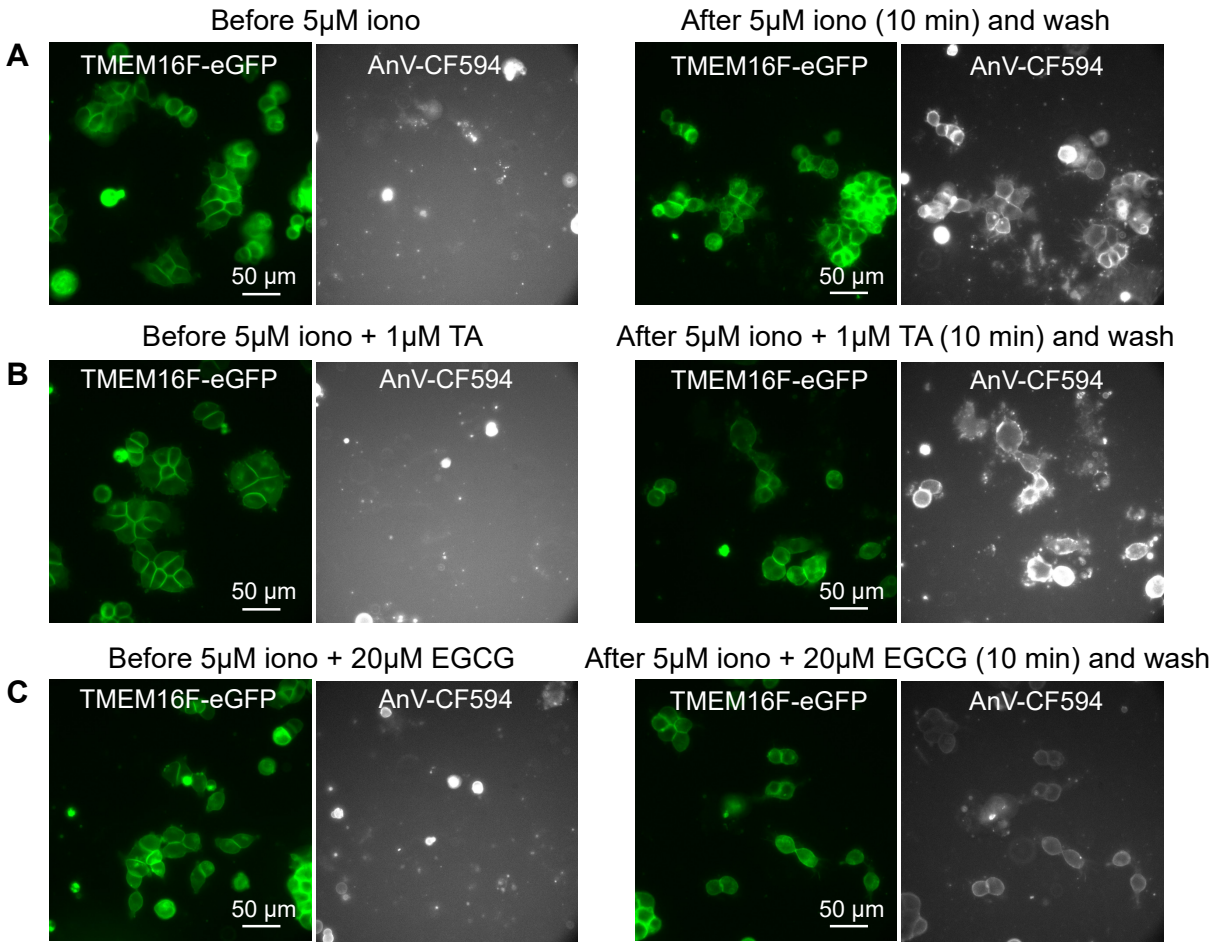


**Figure S3. TA and EGCG do not prevent TMEM16F phospholipid scrambling**. Left columns, representative images showing the AnV-CF594 staining of the HEK293 cells stably expressing mouse eGFP-tagged-TMEM16F (TMEM16F-eGFP) before treatment. The viable cells were AnV negative. The coverslips were subsequently transferred to new imaging chambers with either 5 μM ionomycin (iono) alone (A), 5 μM iono with 1 μM TA (B), or 5 μM iono with 20 μM EGCG (C) to stimulate TMEM16F activation for 10 minutes. Right columns, after stimulation, the cells were washed rigorously with HBSS twice and then AnV-CF594 was reintroduced to stain PS-exposed cells. All images are representatives of at least three independent biological replicates.