

Supplementary Materials

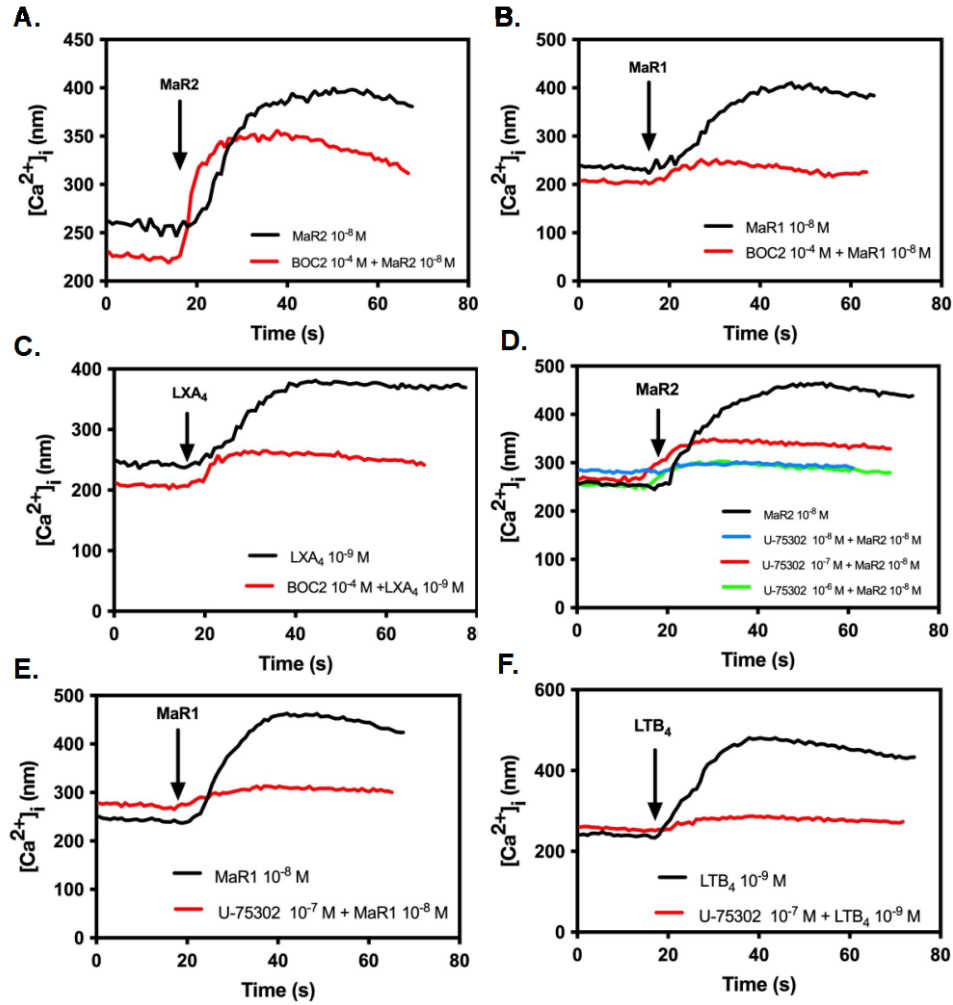


Figure S1: Inhibition of the ALX/FPR2- and the BLT1 receptors acts on stimulation of $[Ca^{2+}]_i$ by $MaR2$ at 10^{-8} M. A, B, and C show changes in $[Ca^{2+}]_i$ with time treated with the ALX/FPR2 receptor inhibitor $BOC2$ (10^{-4} M) and then stimulated with $MaR2$ 10^{-8} M, $MaR1$ 10^{-8} M, and LXA_4 10^{-9} M. D, E and F show changes in $[Ca^{2+}]_i$ with time treated with the BLT1 receptor inhibitor $U-75302$ (10^{-8} – 10^{-6} M) and then stimulated with $MaR2$ 10^{-8} M, $MaR1$ 10^{-8} M, and LTB_4 10^{-9} M. Data are mean \pm SEM of five (A, B, and C) and six (D, E, and F) experiments.

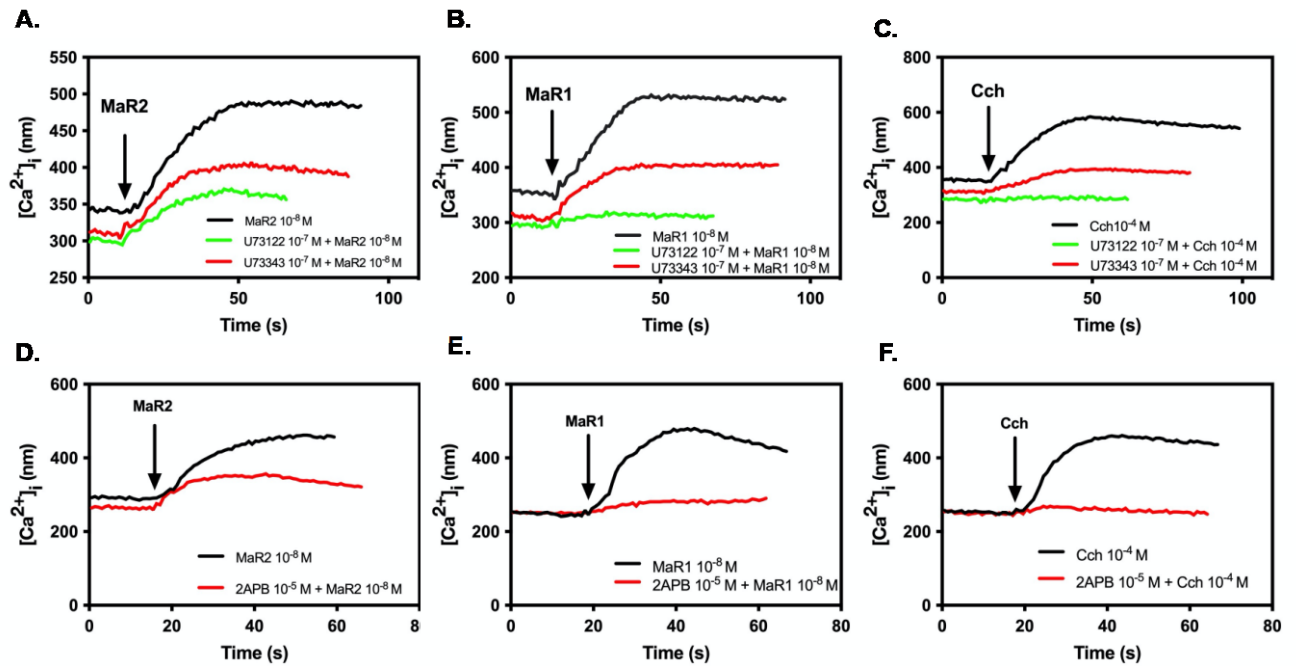


Figure S2: Maresin 2 increase in $[Ca^{2+}]_i$ is independent of the PLC-pathway in rat conjunctival goblet cells. Changes in $[Ca^{2+}]_i$ with time are shown. In A, B and C, goblet cells were treated with vehicle, the active PLC inhibitor U-73122 or the inactive PLC inhibitor U-73343 both at 10^{-7} M for 30 minutes and stimulated with MaR2 (10^{-8} M), MaR1 (10^{-8} M) or Cch (10^{-4} M). In D, E and F, goblet cells were treated with vehicle or 2APB (10^{-5} M) and stimulated with MaR2 (10^{-8} M), MaR1 (10^{-8} M) or Cch (10^{-4} M). Data are mean \pm SEM of four (A, B, and C) and five (D, E, and F) experiments.

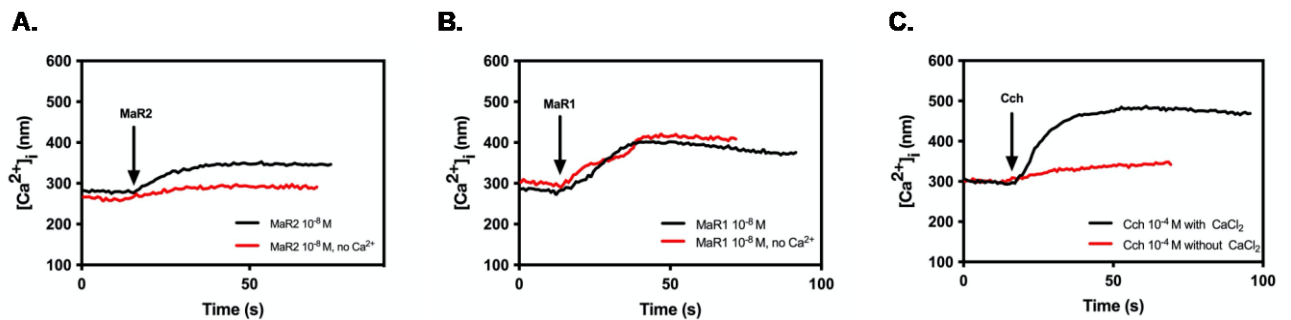


Figure S3: Maresin 2 stimulated increase in $[Ca^{2+}]_i$ is independent of extracellular Ca^{2+} in rat conjunctival goblet cells. Changes in $[Ca^{2+}]_i$ with time are shown in goblet cells incubated with KRB with or without $CaCl_2$ and then stimulated with (A) MaR2 (10^{-8} M), (B) MaR1 (10^{-8} M) or (C) Cch (10^{-4} M). Data are mean \pm SEM of four experiments in each panel.

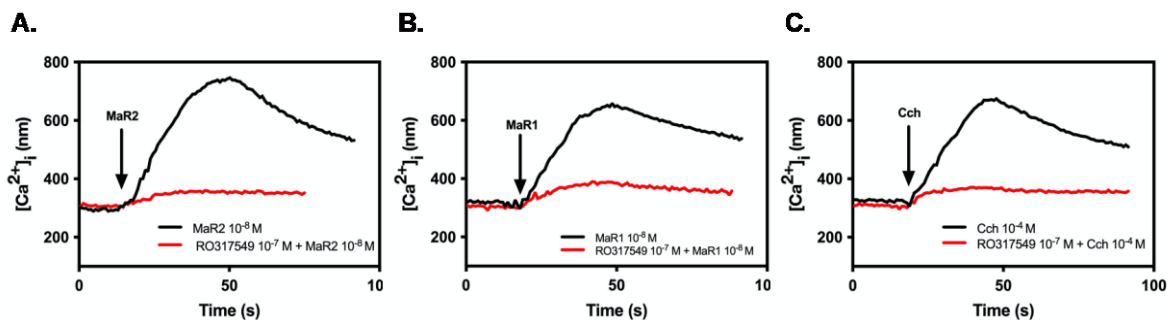


Figure S4: Maresin 2 increases $[Ca^{2+}]_i$ by activation of protein kinase C (PKC). Changes in $[Ca^{2+}]_i$ with time are shown in goblet cells incubated with RO317549 (10^{-7} M) for 30 minutes and then stimulated with (A) MaR2 (10^{-8} M), (B) MaR1 (10^{-8} M) or (C) Cch (10^{-4} M). Data are mean \pm SEM of three experiments in each panel.

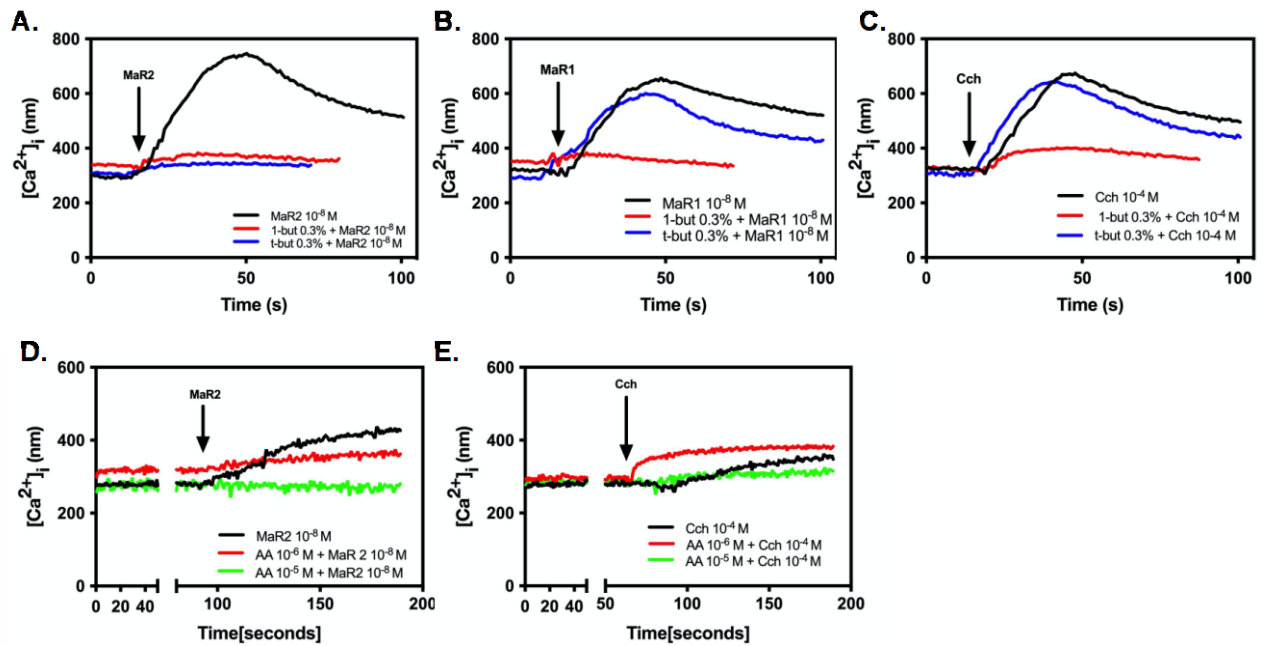


Figure S5: Maresin 2 has different dependency than MaR1 and Cch on Phospholipase D (PLD) and Phospholipase A₂ (PLA₂) to increase $[Ca^{2+}]_i$ and stimulate secretion in rat conjunctival goblet cells. Changes in $[Ca^{2+}]_i$ with time are shown. Goblet cells were preincubated with the PLD inhibitor 0.3% 1-butanol or the inactive analog 0.3% t-butanol for 15 minutes and then stimulated with (A) MaR2 (10^{-8} M), (B) MaR1 (10^{-8} M) or (C) Cch (10^{-4} M). Goblet cells were preincubated with the PLA₂ inhibitor aristolochic acid 10^{-5} M or 10^{-6} M for 30 minutes and stimulated with (D) MaR2 (10^{-8} M) or (E) Cch (10^{-4} M). Data are mean \pm SEM of three (A, B, and C) and four (D and E) experiments.

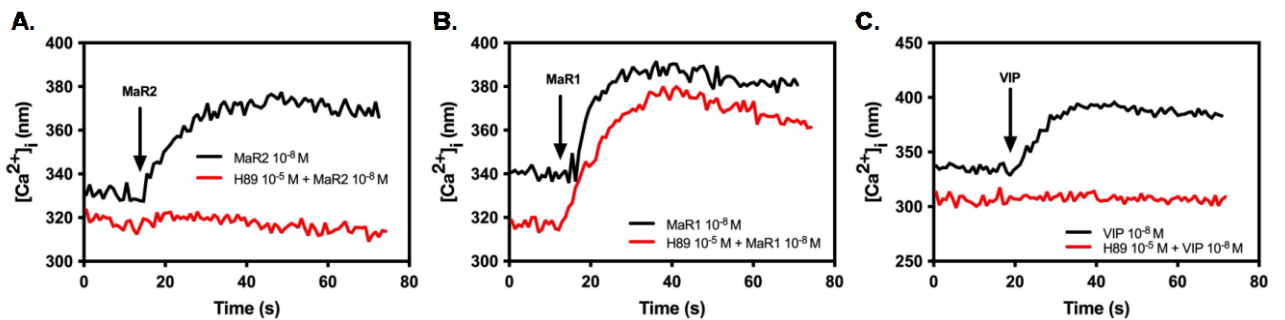


Figure S6: Maresin 2 uses protein kinase A to increase $[Ca^{2+}]_i$ and stimulate secretion in rat conjunctival goblet cells. Goblet cells were incubated with the protein kinase A (PKA) inhibitor H89 (10^{-5} M) for 30 minutes and then stimulated with (A) MaR2 (10^{-8} M), (B) MaR1 (10^{-8} M) or (C) VIP (10^{-8} M) to measure $[Ca^{2+}]_i$ over time. Data are mean \pm SEM of five experiments in each panel.

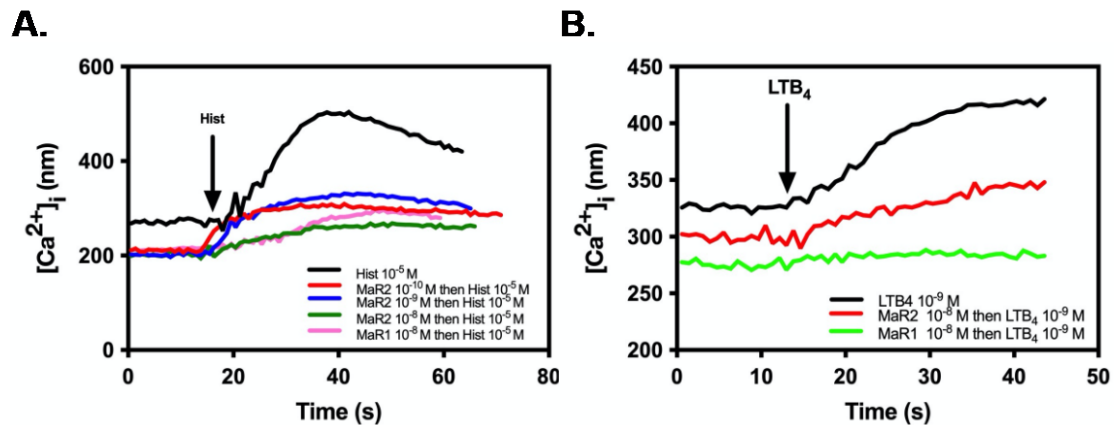


Figure S7: Maresin 2 inhibits histamine-, but not LTB₄-stimulated increase in [Ca²⁺]_i and histamine-stimulated glycoconjugate secretion in rat conjunctival goblet cells. Changes in [Ca²⁺]_i with time are shown. (A) Goblet cells were incubated with MaR2 (10⁻¹⁰ to 10⁻⁸ M) or MaR1 (10⁻⁸ M) for 30 minutes, then stimulated with histamine (10⁻⁵ M) and (B) goblet cells were incubated with MaR2 (10⁻⁸ M) or MaR1 (10⁻⁸ M) for 30 minutes, then stimulated with LTB₄ 10⁻⁹ M. Data are mean ± SEM of three (A) and four (B) experiments.