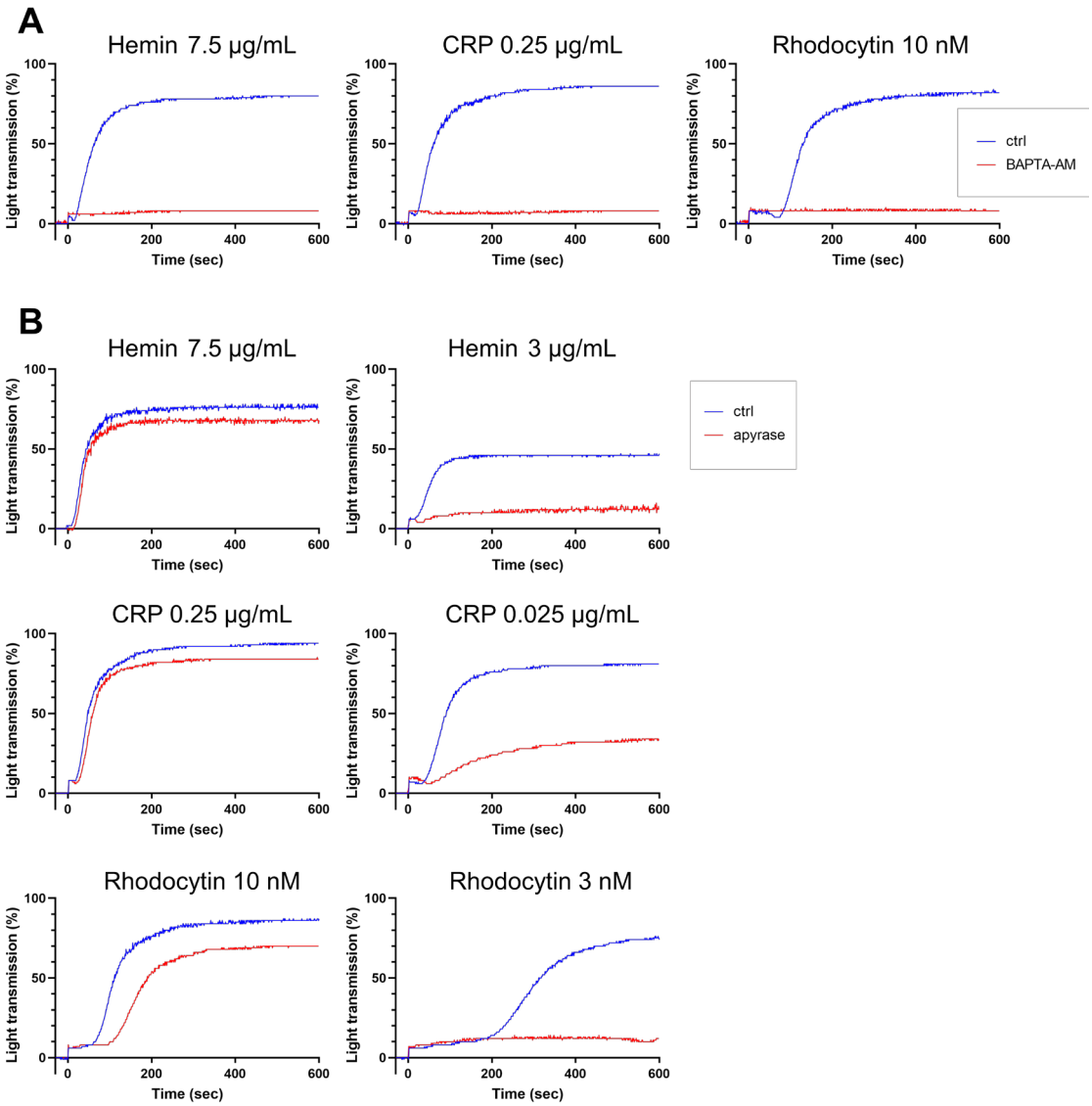
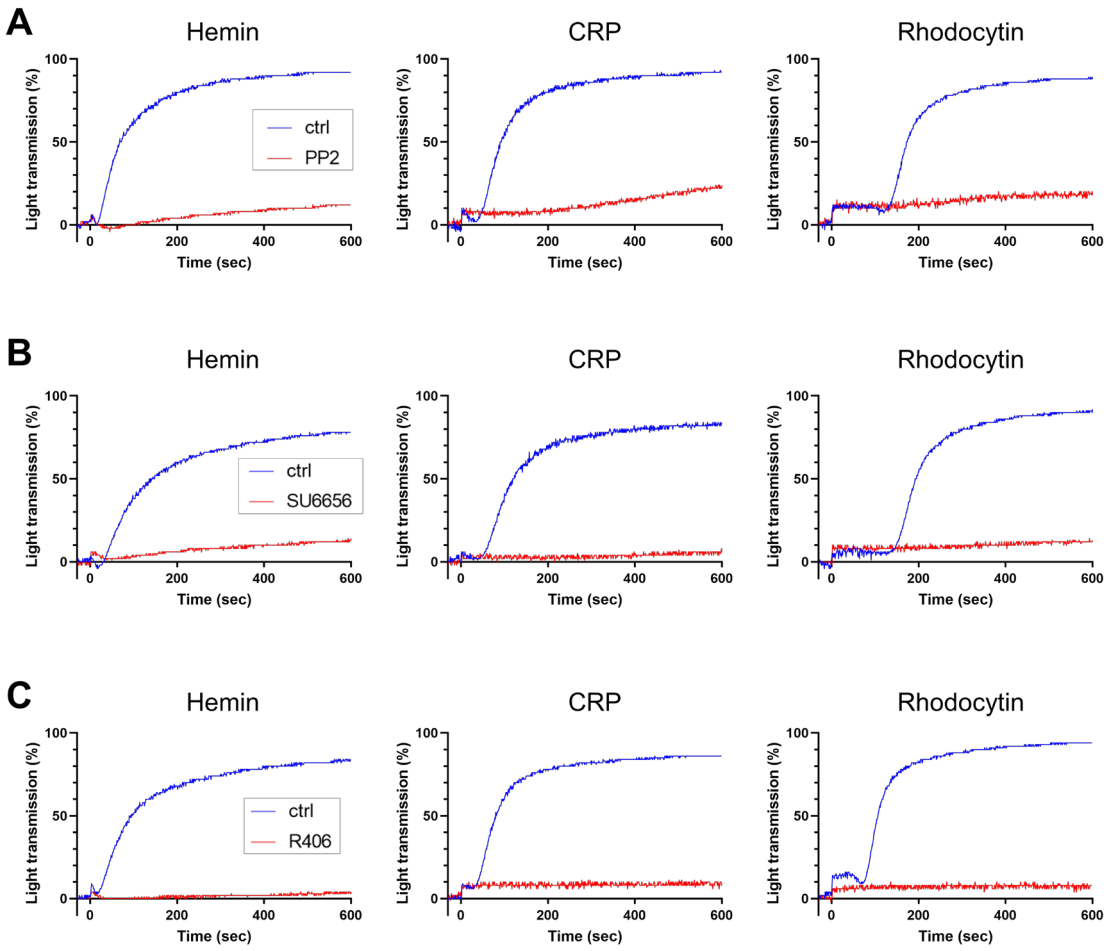


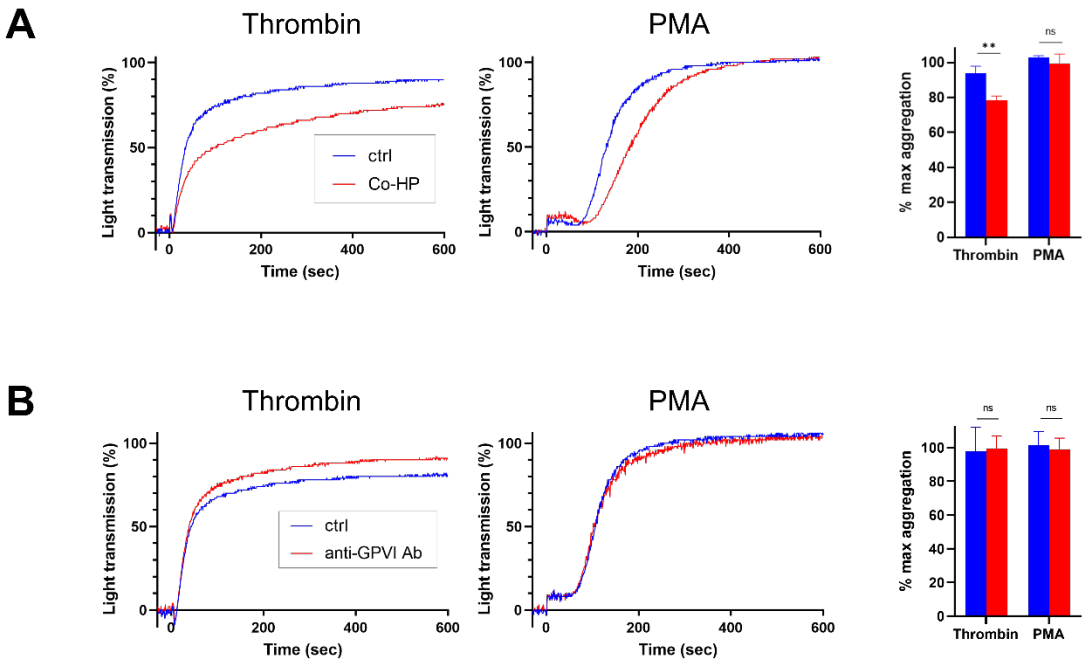
Supplemental Figure 1.

Aggregation assay of washed human platelets. (A) Blocking effect of 20 µM BAPTA-AM on hemin (7.5 µg/mL)-, CRP (0.25 µg/mL)-, and rhodocytin (10 nM)-induced platelet aggregation. The representative curves are shown. (B) Blocking effect of 1 U/mL apyrase on hemin (7.5 and 3 µg/mL)-, CRP (0.25 and 0.025 µg/mL)-, or rhodocytin (10 and 3 nM)-induced platelet aggregation. The representative curves are shown.



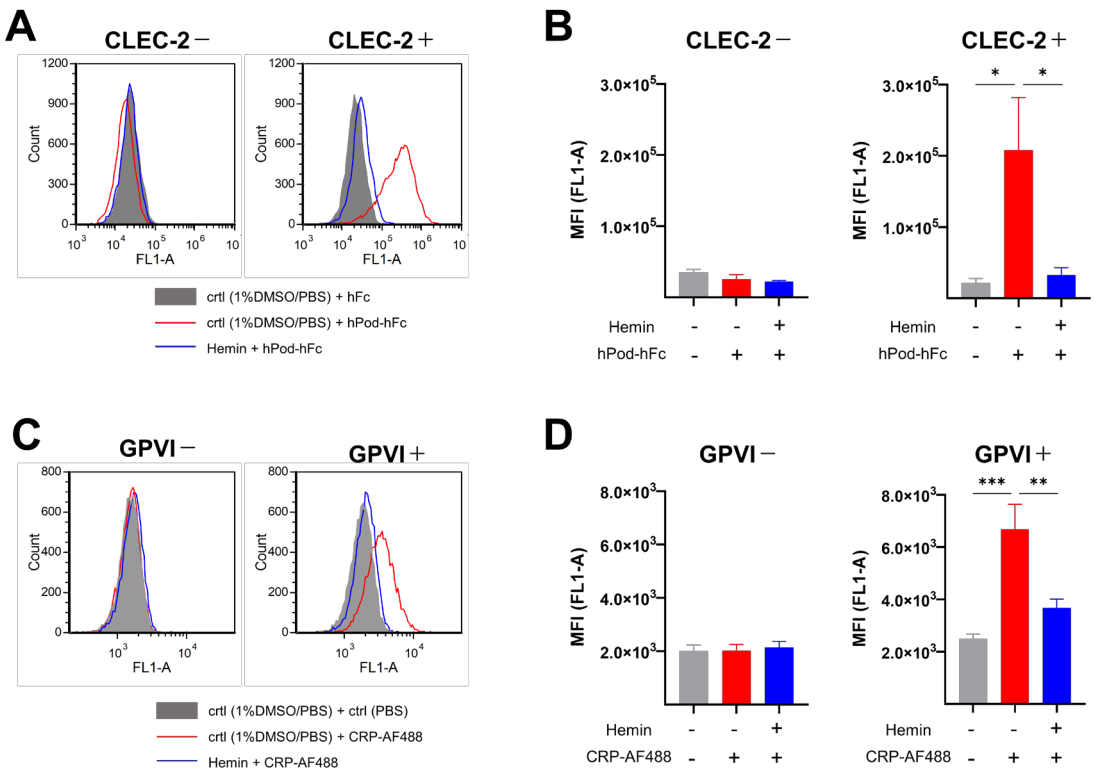
Supplemental Figure 2.

Aggregation assay of wild-type murine platelets. (A-C) Blocking effect of (A) 50 μM PP2, (B) 10 μM SU6656, and (C) 1 μM R406 on hemin (7.5 μg/mL)-, CRP (0.125 μg/mL)-, and rhodocytin (5 nM)-induced platelet aggregation. The representative curves are shown.



Supplemental Figure 3.

(A) Aggregation assay of FcRγ-deficient murine platelets. Blocking effect of 0.8 µg/mL Co-HP or 1% DMSO on thrombin (0.25 U/mL)- and PMA (250 nM)-induced platelet aggregation. (B) Aggregation assay of CLEC-2-depleted murine platelets. Blocking effect of 10 µg/mL anti-GPVI antibody or control rat IgG on thrombin (0.25 U/mL)- and PMA (250 nM)-induced platelet aggregation. (A and B) The representative curves (left) and the quantifications of maximum light transmission (right) are shown. Data are presented mean ± SD; n = 3. $^{**}P < 0.01$; ns: not significant; Student's *t*-test was used.



Supplemental Figure 4.

(A and B) Cell-based competitive binding assay for detecting the inhibitory effect of hemin on podoplanin binding to T-REx-293 cells with or without CELC-2 expression. (A) Representative histograms. Fill: 1% DMSO + hFc, red: 1% DMSO + hPod-hFc, blue: hemin + hPod-hFc. (B) Mean fluorescence intensity (MFI) for each condition. Gray: 1% DMSO + hFc, red: 1% DMSO + hPod-hFc, blue: hemin + hPod-hFc. Bar graphs represent mean ± SEM; n = 3 (CLEC-2−) and n = 6 (CLEC-2+); $*P < 0.05$. Tukey's multiple-comparison test was used. (C and D) Cell-based competitive binding assay for detecting the inhibitory effect of hemin on CRP binding to Jurkat cells with or without GPVI expression. (C) Representative histograms. Fill: 1% DMSO + PBS, red: 1% DMSO + 0.1 µg/mL CRP-AF488, blue: hemin + CRP-AF488. (D) MFI for each condition. Gray: 1% DMSO + PBS, red: 1% DMSO + CRP-AF488, blue: hemin + CRP-AF488. Bar graphs represent mean ± SEM; n = 3 (GPVI−) and n = 6 (GPVI+); $*P < 0.05$, $**P < 0.01$, $***P < 0.001$; Tukey's multiple-comparison test.