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Rescuing Platelet Function in the Cold: The Role of GPCRs in Calcium Homeostasis and Coagulation

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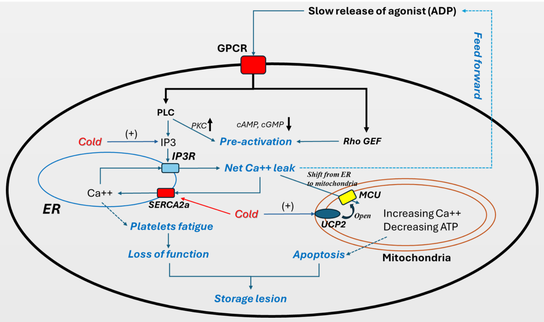
Introduction

- Cold-stored platelets are critical for hemorrhage control in trauma medicine, but they rapidly develop “cold storage lesions”—including premature activation and phosphatidylserine (PS) exposure—which limits their operational viability.
- This study investigates whether targeting G-coupled receptors using Cangrelor can mitigate these storage lesions to extend platelet shelf life without compromising fundamental platelet function.

Hypothesis

We hypothesize that targeting G-coupled receptors with Cangrelor will mitigate cold-induced phosphatidylserine exposure without impairing baseline metabolic functions, thereby improving clot integrity and extending the operational shelf-life of cold-stored platelets.



Methods

- Platelet-rich plasma from healthy donors (n=10) was stored at 4-6°C for three days and allocated to either a control group or a group pre-treated with a reversible GPCR inhibitor (GCRI).
- On Day 0 (baseline) and Day 2, we assessed a comprehensive panel of parameters, including CRC, phosphatidylserine exposure (+PS), platelet count and volume, coagulation function (ROTEM), and metabolic profiles.
- CRC was the maximal ER calcium release following stimulation with high-dose thrombin (0.05 U/mL) and convulxin (0.5 µg/mL)

Results

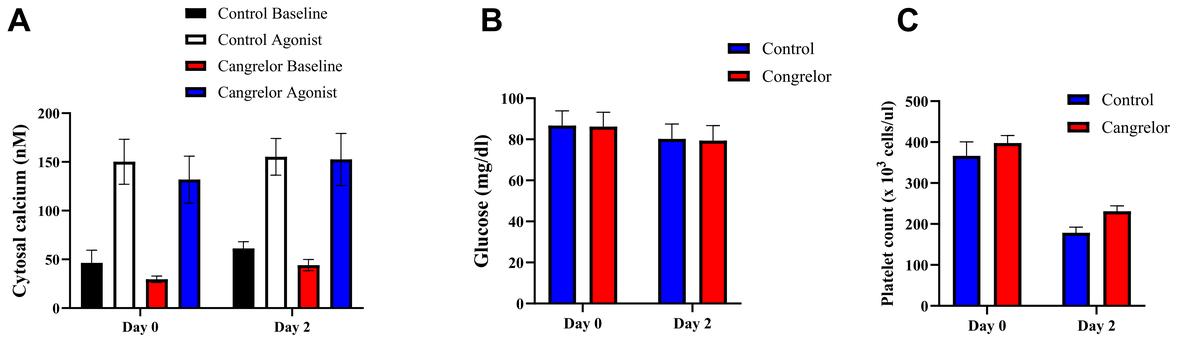


Figure 1. The effect of Cangrelor on platelet function. The figure displays three sets of bar charts demonstrating that Cangrelor does not inhibit key platelet functions. (A) Platelet calcium release capacity, (B) platelet glucose usage, and (C) platelet count are shown. The different colored bars represent different experimental conditions or treatment groups. Data are presented as mean values, with error bars likely indicating standard error or standard deviation. The sample size for each group was n=6. Overall, the data suggests that Cangrelor has no significant impact on these measured platelet parameters.

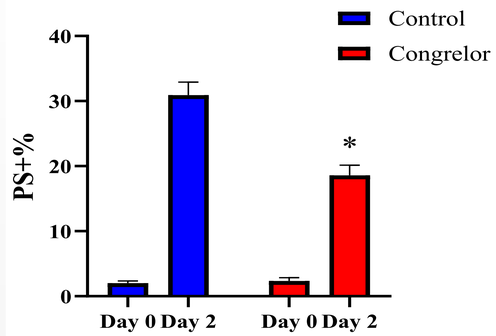


Figure 3. Cangrelor reduces phosphatidylserine (PS) exposure. Cangrelor-treated group exhibits a significantly lower percentage of PS+ cells on Day 2 compared to the control group. *P < 0.01 control vs. Cangrelor groups on Day 2. n=6 for each group.

Baseline (day 0)

	Clot Formation time	A10	A20
Control	32 ± 3 s	73 ± 2 mm	77 ± 1 mm
Cangrelor	33 ± 3 s	74 ± 1 mm	77 ± 1 mm

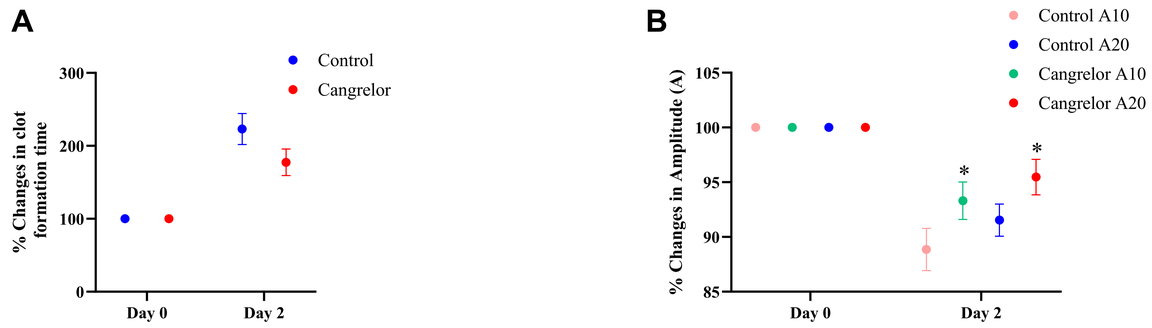


Figure 2. Effects of Cangrelor on clot formation parameters measured by ROTEM intrinsic pathway. (Table) Baseline measurements on Day 0 showed no significant differences between the groups. (A) Percentage (%) changes in clot formation time. The difference between the control and Cangrelor groups was not statistically significant (P = 0.06). (B) Percentage (%) changes in A10 and A20 parameters. A statistically significant difference between the control and Cangrelor groups is denoted by *P < 0.05. n=6 for each group

Summary

- Cangrelor does not disrupt fundamental platelet homeostasis.
- While the initiation of clotting (clot formation time) is not definitively delayed (trending at P=0.06), Cangrelor significantly alters the kinetic development and ultimate structural firmness of the clot via the intrinsic pathway.
- The marked reduction in phosphatidylserine (PS+) exposure by Day 2 suggests that Cangrelor specifically inhibits procoagulant surface activity or platelet apoptotic pathways.
- The G-coupled receptor may be a potential target for the shelf-life extension of cold storage platelets.

Conclusion

Targeting G-coupled receptors preserves essential baseline platelet functions while significantly mitigating procoagulant phosphatidylserine exposure, highlighting its potential as a viable strategy for extending the shelf-life of cold-stored platelets.

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