

# Supplementals of “Small-molecule cyclophilin inhibitors potently reduce platelet procoagulant activity”

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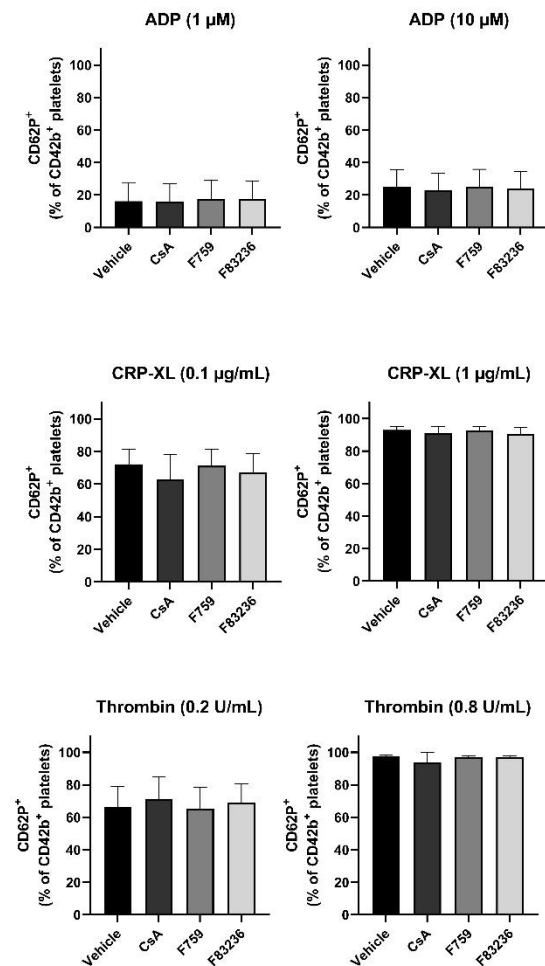
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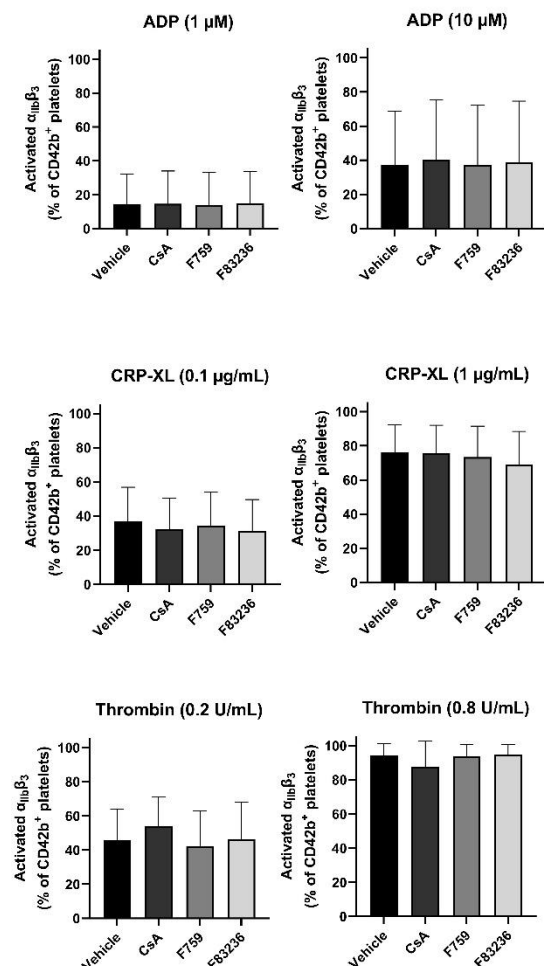
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**Supplemental Figure A1:** SMCyplIs do not affect platelet activation. Washed platelets were incubated with 125  $\mu$ M F759 or F83236, or 4  $\mu$ M CsA. Platelets were then activated with either ADP (1 or 10  $\mu$ M), CRP-XL (0.1 or 1  $\mu$ g/mL) or thrombin (0.2 or 0.8 U/mL). During activation, platelets were labeled with anti-CD42b, anti-CD62P and anti-activated  $\alpha_{IIb}\beta_3$  (PAC-1 clone). CD42b<sup>+</sup>/CD62P<sup>+</sup>/activated  $\alpha_{IIb}\beta_3$ <sup>+</sup> platelets were analyzed using flow cytometry. **(a)** Percentages of CD42b<sup>+</sup>/CD62P<sup>+</sup> platelets. **(b)** Percentages of CD42b<sup>+</sup>/activated  $\alpha_{IIb}\beta_3$ <sup>+</sup> platelets. Data are represented as mean  $\pm$  SD of 4 separate experiments. SMCyplIs, small-molecule cyclophilin inhibitors; CsA, Cyclosporin A; ADP, adenosine 5'-diphosphate; CRP-XL, collagen related peptide.

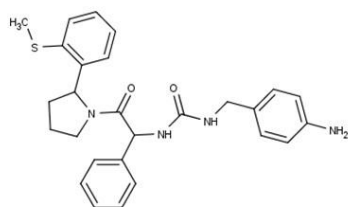
**A**



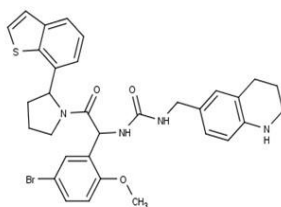
**B**



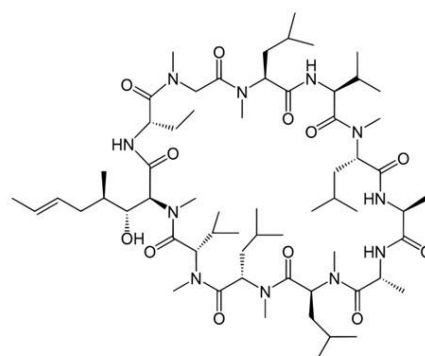
**Supplemental Figure A2:** Chemical structures of the SMCypIs and CsA



F759



F83236



Cyclosporine A

**Supplemental Video A3:** SMCypIs inhibit coagulation induced by procoagulant platelets. Whole blood was incubated with 125  $\mu$ M F759 or F83236, 4  $\mu$ M CsA before perfusion over a Horm collagen coated surface, in the presence of 6.6 mM  $\text{CaCl}_2$  and 3.08  $\text{MgCl}_2$ . Shown are representative videos of: (i) top row: DIC images of platelet aggregates; (ii) middle row: anti-GpIb-VhH Alexa647 indicating platelets and (iii) bottom row: tPA-Alexa488 binding to fibrin. SMCypIs, small-molecule cyclophilin inhibitors; CsA, Cyclosporin A; tPA, tissue plasminogen activator.

**Supplemental Data A4:** Informed consent form.

Informed consent form of clinical study (S64328) to obtain blood from healthy individuals.