Finding better targets for the treatment of thrombosis

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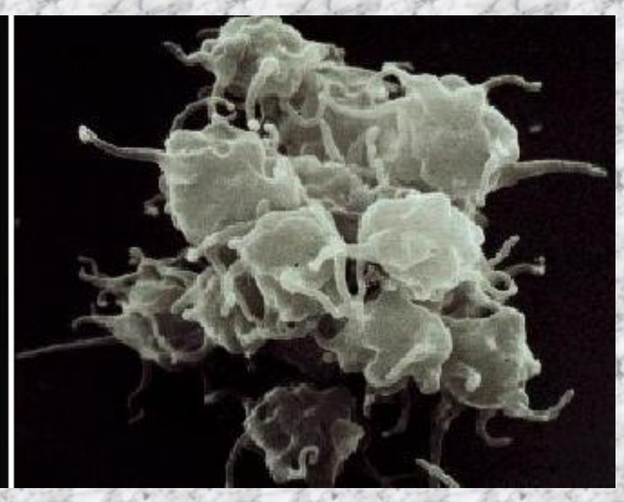
PLATELETS

- smallest of our blood cells
- prevents blood loss by creating a blood clot
- involved in atherothrombosis

Unactivated platelets



Activated platelets

ATHEROTHROMBOSIS

A ruptured atherosclerotic plaque

→ activates platelets

→ formation of a plug *inside* the vessel

→ ↓blood flow ↓oxygen delivery

→ possible tissue death / heart attack

PAR1 & PAR4

PAR1 and PAR4:

- receptors for thrombin – a protein in our circulation that activates platelets
- potential therapeutic targets

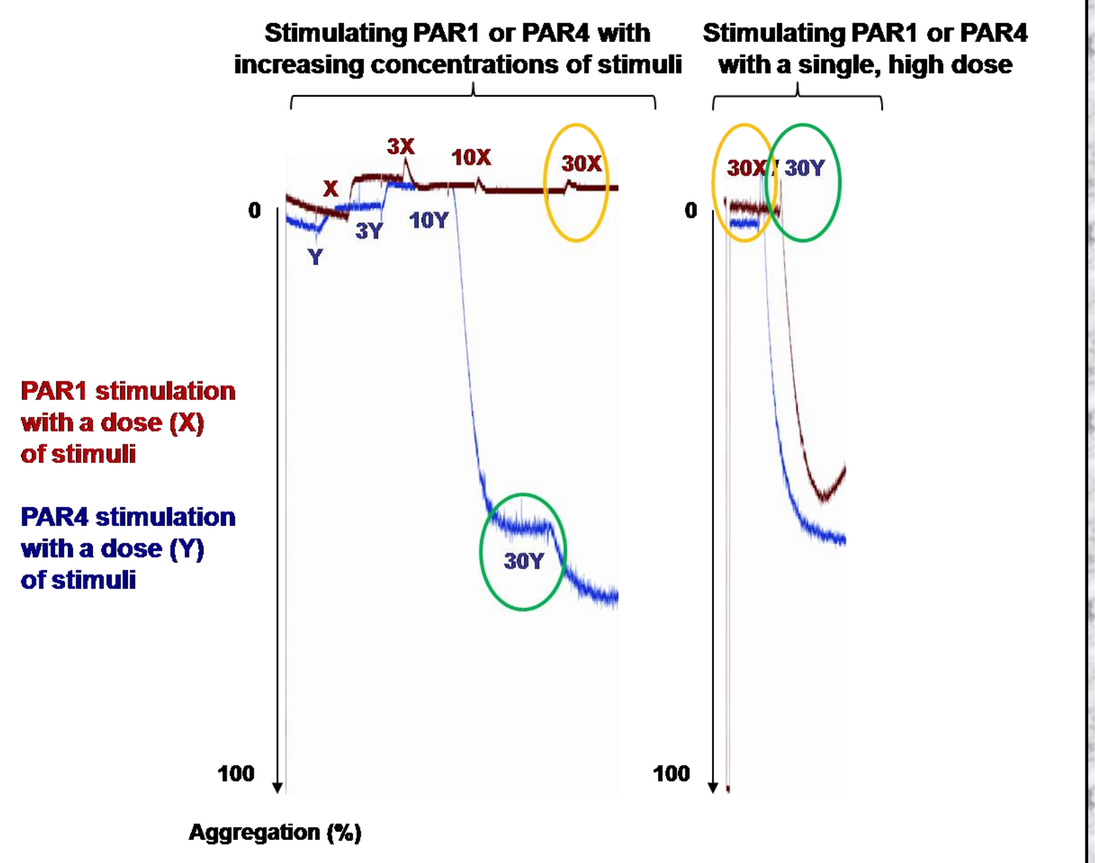
AIM & HYPOTHESIS

AIM
Clarify differences between PAR1 and PAR4

HYPOTHESIS
PAR1 and PAR4 differ in their abilities to undergo desensitization*

*** when the receptors no longer responds to stimulation**

RESULT



(Left figure): Platelets were stimulated with increasing concentrations of stimuli (X or Y), activating PAR1 (X) or PAR4 (Y). Aggregation was measured.
→ PAR1 did not respond to stimulation.
As controls (right figure), PAR1 or PAR4 were stimulated with one, high, dose of stimuli (30X or 30Y).

CONCLUSION

PAR1 is desensitized when re-exposed to stimuli. PAR4 is not

PAR4 might be a more suitable therapeutic target than PAR1

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