

# Deciphering glycoprotein VI signalling in platelet activation

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## Deciphering Glycoprotein VI Signalling in Platelet Activation: Integration of Functional and Computational Modelling Data

**Yam Fung Hilaire Cheung**

1. Ion chromatography-coupled mass spectrometry allow to separate the positional isomers of phosphoinositide in platelets, particularly PtdIns(3,4)P<sub>2</sub> and PtdIns(4,5)P<sub>2</sub>. (*This thesis*)
2. Mathematical models are useful to simulate the phosphoinositide metabolism of glycoprotein VI-activated platelets, and to predict a contribution of PtdIns(4,5)P<sub>2</sub> resynthesis to sustained signalling. (*This thesis*)
3. Platelet disaggregation depends on the choice of agonist and the presence of shear. (*This thesis*)
4. Platelet-produced secondary mediators play an important role in the Ca<sup>2+</sup> entry by weak agonists, and extend the role of the ORAI1 Ca<sup>2+</sup> channel and Na<sup>+</sup>/Ca<sup>2+</sup> exchange proteins in the Ca<sup>2+</sup> entry process. (*This thesis*)
5. The integration of platelet functional data with mathematical modelling is of additive value for the discovery and valorisation of new antiplatelet drugs. (*Valorisation*)
6. Because glycoprotein VI deficiency is linked to only mild bleeding incidents, this platelet receptor represents a potential anti-platelet candidate. (*Matus et al. 2013, and Jandrot-Perrus et al. 2019*)
7. Multiplex measurements of Ca<sup>2+</sup> mobilisation in platelets using a high throughput assay is effective for the profiling of signal transduction and platelet activation. (*Fernández et al. 2022*)
8. Mathematical modelling of platelet activation sheds light on negative-feedback signalling mechanisms and agonist potency, offering a unique and complementary approach to traditional reductionist methods in platelet biology. (*Diamond et al. 2008*)