Deciphering glycoprotein VI signalling in platelet activation

Propositions belonging to the dissertation

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_2 and PtdIns(4,5)P_2. *(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_2 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^{2+} entry by weak agonists, and extend the role of the ORAI1 Ca^{2+} channel and Na^{+}/Ca^{2+} exchange proteins in the Ca^{2+} 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^{2+} 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)*

Yam Fung Hilaire Cheung, 27th September 2023