

Novel mechanisms of platelet activation and sustained signalling through GPVI and PAR1

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Propositions belonging to the dissertation:

**Novel mechanisms of platelet activation and sustained signalling through
GPVI and PAR1**

by Ilaria De Simone

1. The effect of a stimulus on platelet activation is determined by whether it is soluble or immobilized on a surface. (This thesis)
2. Coagulation factor XIIIa and activated protein C support platelet activation via GPVI and PAR1, respectively. (This thesis)
3. Depending on the concentration and type of the initial trigger, platelet activation is reversible, whereafter platelets can be reactivated by a second stimulus. (This thesis)
4. Previously activated, reversed platelets can contribute to thrombus formation. (This thesis)
5. Because of the large inter-individual variation among patients, the use of flow cytometric panels, as well as population studies, can contribute to better patient stratification and tailored antiplatelet therapy. (This thesis, impact)
6. The challenge in improving antithrombotic strategies, is to inhibit a receptor which has a great role in the pathophysiology of thrombosis, but a minor role in haemostasis. For this reason, GPVI is an extremely interesting target. (Lecut, J Thromb Haemost 2003; Zahid, J Thromb Haemost 2012)
7. The 'dual-pathway' approach, a combination of antiplatelet and anticoagulant drugs, provides net benefit in the secondary prevention of cardiovascular complications in patients with atherosclerotic disease. (Olie Res Pract Thromb Haemost 2018)
8. When identifying novel interactions between platelets and ligands, platelet activation can be studied best after platelet isolation from whole blood, while studying these effects in whole blood is physiologically more relevant.
9. As a scientist, you have to do the thing that everyone said you should not do when you were little: ask a lot of questions.
10. By doing a PhD, we are pushing ourselves to extend the limits of human knowledge. This process knows its ups and downs.
11. Nothing in life is to be feared, it is only to be understood. Now is the time to understand more, so that we may fear less. (Marie Skłodowska-Curie)

Ilaria De Simone, 26th April 2023