

# Novel platelet glycoprotein VI and CLEC-2 targeting strategies

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Propositions belonging to the dissertation:

**Novel platelet glycoprotein VI and CLEC-2 targeting strategies: studies in humanized mouse models**

by Stefano Navarro

1. The JAQ1-binding epitope on human and mouse glycoprotein VI (GPVI) has diverged during evolution, resulting in different functions. (*This thesis*)
2. In shear-dependent thrombus formation, human platelet thrombin receptors have a more persistent contribution than the collagen receptor GPVI. (*This thesis*)
3. In transgenic mice, in vivo immune depletion of the human GPVI receptor by JAQ1 from the platelet surface results in a low GPVI phenotype. (*This thesis*)
4. The platelet CLEC-2 receptor has distinct roles in mouse disease models. Functional targeting of this receptor is still a challenge. (*This thesis*)
5. Under high shear flow conditions, GPVI acts in concert with GPIIb $\alpha$  to tether platelets to the subendothelial matrix. The fast off-rate of these receptor interactions prevents stable platelet adhesion. (*Bernhard Nieswandt, Steve Watson, Blood, 2003*)
6. Platelet activation and blood coagulation are complementary, mutually dependent processes in haemostasis and thrombosis. (*Johan Heemskerk et al, Thromb Haemost; 2002*)
7. The scaled or complete immune-depletion of GPVI is a promising therapeutic approach for the reduction of arterial thrombotic events. (*Impact, this thesis*)
8. Despite technological and medical advances of the last decades, cardiovascular diseases are still leading causes of death globally. Platelet research is fundamental for achieving further disease reduction and better treatment. (*Impact, this thesis*)
9. The good thing about science is that it's true whether or not you believe in it. (*Neil de Grasse Tyson*)
10. Science should not judge on ethnicity, religion or gender. Empirical science needs to be objective and not rely on prejudice or believe.
11. Ho perso un po' la vista, molto l'udito. Alle conferenze non vedo le proiezioni e non sento bene. Ma penso più adesso di quando avevo vent'anni. Il corpo faccia quello che vuole. Io non sono il corpo: io sono la mente. (*Rita Levi Montalcini*)

April 25<sup>th</sup>, 2023