Pathophysiology of von Willebrand factor in bleeding and thrombosis

Pagliari, M.T.

Stellingen
behorende bij het proefschift getiteld

PATHOPHYSIOLOGY OF VON WILLEBRAND FACTOR IN BLEEDING AND THROMBOSIS

1. The diagnosis of von Willebrand disease (VWD) benefits from combining biochemical and genotype testing (this thesis).

2. Despite the already reported limitations, *in vitro* studies based on heterologous systems remain the most accessible instrument to prove the pathogenetic effect of *novel* von Willebrand factor (VWF) variants (this thesis).

3. The capacity to detect the presence of VWF inhibitors strongly relies on the type of assay performed (this thesis).

4. Understanding of the pathophysiological mechanisms underlying type 3 VWD may contribute to explain patients' bleeding phenotype and provide novel insight to treat this condition.

5. Even small alterations of ADAMTS13-VWF equilibrium contribute to increase the risk for deep vein thrombosis (this thesis).

6. Next-generation sequencing approaches have greatly contributed to the diagnostic and gene discovery studies of inherited bleeding and thrombotic disorders. However, additional advances in high-throughput screening assays required for variant validation are still needed (Adapted Ver Donck F et al; RPTH 2021).

7. The heterogeneous nature of VWD implies that the development of treatments based on a "one-size-fits-all" approach will never have the potential to address all the patient's needs, although the management of VWD patients currently follows such a trend (adapted from Denis CV et al; Blood 2021).

8. Endothelial colonies forming cells (ECFCs) have been used to investigate cellular and molecular defects in endothelial cells from patients with VWD. Nevertheless, several issues remain that prevent their widespread use—most notably, the lack of consensus with regard to the methods used to quantify, culture and evaluate ECFCs (Adapted from Smadja DM et al; JTH 2019).

9. The dual role of VWF in hemostasis and thrombosis makes it a candidate target for the development of novel therapeutical approaches.

10. From 2021 to 2022, the number of universities reporting performance indicators on gender equality and women's empowerment increased. However, universities should also monitor and compare the success rates and outcomes of women and men to improve gender equality.

11. Researchers and publishers must lay down ground rules about using large language models (LLM) ethically (adapted from Nature editorials; January 2023).