Lessons from snake venom: new insights into the structural and functional aspects of factor V and factor X

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STELLINGEN

behorende bij het proefschrift

Lessons from snake venom: New insights into the structural and functional aspects of factor V and factor X

1. The unique biochemical characteristics of chimeric factor X-C (aka VMX-C001) enable restoration of blood clotting in the presence of factor Xa-DOACs without the risk of thrombotic side effects *(this thesis)*.

2. The A-domain trimer of human factor V(a) supports selectivity for negatively charged phospholipid membranes by reinforcing conformational flexibility of the C-domain pair via allosteric crosstalk between the A-domain trimer and C-domain pair *(this thesis)*.

3. The non-conserved disulfide bond between the A2- and A3-domain of Pseudonaja textilis venom FV obstructs conformational flexibility of the A-domain trimer and impedes high affinity phospholipid binding by the C-domains of Pseudonaja textilis venom factor V *(this thesis)*.

4. Rabbit, rat, and mouse plasma are characterized by a high anticoagulant threshold resulting, at least in part, from elevated rates of factor Xa inhibition relative to human plasma *(this thesis)*.

5. The truncated B-domain of snake factor V has evolved as a host-defense mechanism to counter the effects of procoagulant snake toxins by serving as a binding partner to tissue factor pathway inhibitor *(Vincent et al., J Clin Invest, 2013)*.

6. Andexanet-alpha interacts with tissue factor pathway inhibitor in a similar fashion as human factor Xa, resulting in sequestering of free tissue factor pathway inhibitor and increasing the risk of thrombotic complications in patients *(Lu et al., Nat Med, 2013)*.

7. Murine models of coagulation are not appropriate for studying the effects of factor Xa-DOACs and human coagulation factors that are associated with prothrombinase function, such as factor V, factor X and tissue factor pathway inhibitor *(von Drygalski et al., Blood Adv, 2020)*.

8. The crystal structure of the lipid-independent prothrombinase complex from the venom of Pseudonaja textilis closely represents the lipid-bound conformation of human prothrombinase *(Lechtenberg, B.C., et al., Blood, 2013)*.

9. An appropriate answer brings joy to a person, and a well-timed word is a good thing *(Proverbs, 15:23)*.

10. Als dit universum in zijn miljoenvoudige orde en precisie het resultaat van een blind toeval zou zijn, dan is dat net zo geloofwaardig als wanneer een drukkerij explodeert en alle druklettertjes weer op de grond terecht komen in de voltooide en foutloze vorm van het woordenboek *(Albert Einstein)*.

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