

Coagulation factor XII contributes to hemostasis when activated by soil in wounds

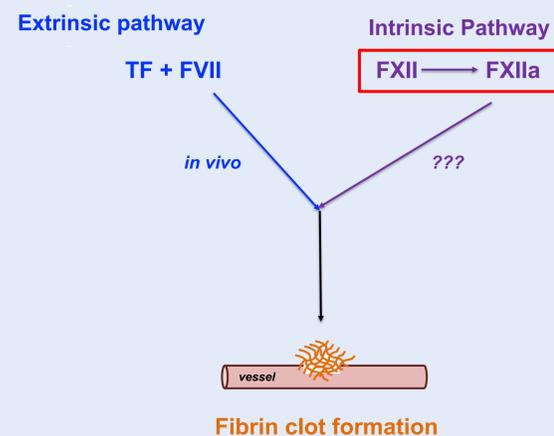


Lih Jiin Juang^{1,2}, Nima Mazinani^{1,2}, Stefanie Novakowski^{1,2}, Emily Prowse²,
Martin Haulena³, David Gailani⁴, Leslie Lavkulich⁵, Christian Kastrup^{1,2*}

Michael Smith Laboratories¹, Department of Biochemistry and Molecular Biology² and Department of Soil Science⁵, The University of British Columbia. Vancouver Aquarium³ Department of Medicine and Department of Pathology, Microbiology and Immunology, Vanderbilt University Medical Center.⁴

Introduction

Clotting occurs through the intrinsic (FXII) or the extrinsic pathway (TF+VII) *in vitro*.



It is believed that FXII does not contribute to clotting *in vivo* because FXII deficient individuals do not have compromised hemostasis.¹

FXII remains conserved in humans despite being implicated in pathological conditions. In contrast, birds and marine mammals do not have FXII.²

Clays are known to be powerful activators of FXII and are naturally found in the environment as a major component in soil.³ Soil can enter wounds and contact blood during injury.

Hypothesis

When wounded in the presence of soil, FXII will activate and contribute to clotting.

Results

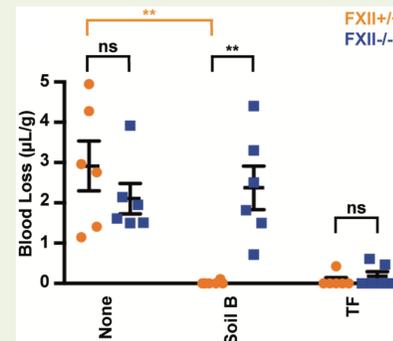


Fig. 1. Soils are hemostatic in tail wounds of FXII+/+ but not FXII-/- mice.⁴

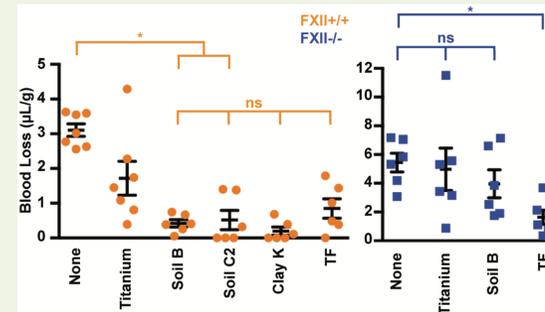


Fig. 2. Soils are hemostatic in tail wounds of FXII+/+ but not FXII-/- mice on aspirin.⁴

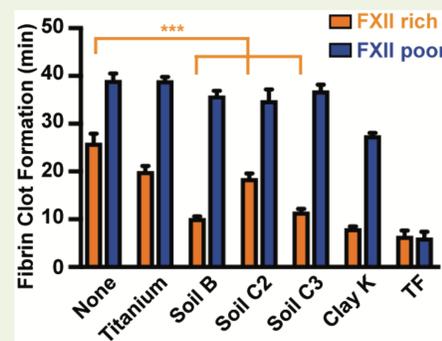


Fig. 3. Soils induce faster clotting in normal but not FXII depleted plasma.⁴

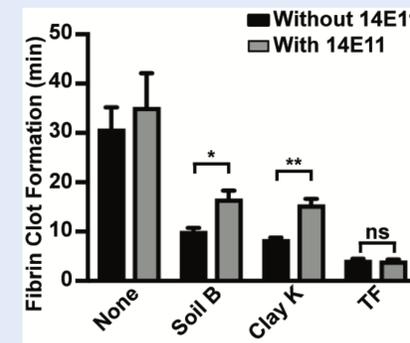


Fig. 4. Inhibiting FXI activation by FXIIa with an antibody prolonged clot times with soil.⁴

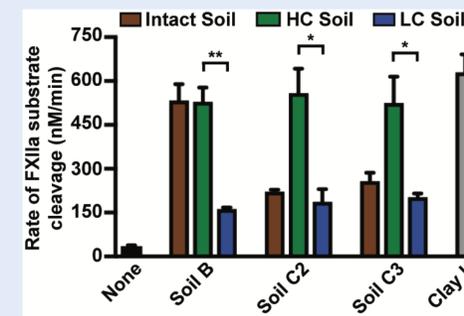


Fig. 5. Soil high clay (HC) fractions activate more FXII than low clay (LC) fractions.⁴

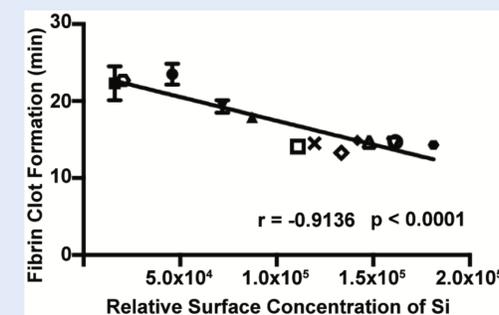


Fig. 6. Concentration of silicon (Si) at the soil surface, measured by TOF-SIMS, strongly predicts clot times with soil.⁴

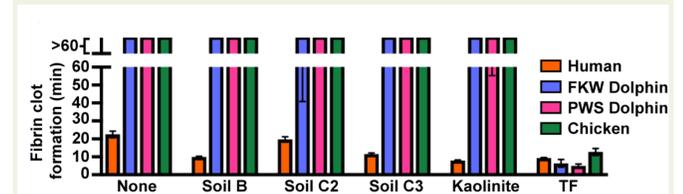


Fig. 6. Soils induce faster clotting in plasma from human than a dolphin or a bird.⁴

Conclusion

- This is the first study to describe a conclusive role of FXII in hemostasis: blood of terrestrial mammals respond to soil silicates in wounds to trigger FXII-dependent clotting to minimize blood loss.⁴
- Plasma from cetaceans, and birds, who do not come in regular contact with soil, do not respond to soil.⁴

Future Directions

- Role of FXII in wound healing and inflammatory response at the wound site.
- Can extra-terrestrial soils also trigger FXII-dependent coagulation and minimize blood loss?

Acknowledgements



References

- Renne et al. *Blood*. (2012)
- Doolittle. *J Innate Immun*. (2011)
- Ito & Wagai. *Sci Data* (2017)
- Juang et al. *Blood Advances* (2020)