Treatment of Bleeding Disorders with Novel Pro-coagulant Compounds

A novel approach for direct coagulation activation which bypasses the intrinsic & extrinsic pathway.

Reference: Bleeding Disorders Treatment

Seeking

Development partner, Commercial partner

About University of Liverpool

By facilitating access to our expertise, facilities and networks, the University of Liverpool offers the means to transform ideas into creative solutions, improved performance, new technologies, strategies, applications, products or skills.
Background

The coagulation system is a haemostatic response to injury that prevents excessive bleeding. There are two main pathways, Intrinsic and Extrinsic (Figure 1), that converge at the common pathway.

Thrombin (IIa) generation is central to coagulation activation and leads to clot formation. Subsequent FVIII or FIX deficiency in the amplification pathway causes a heightened bleeding risk in individuals with haemophilia. Current pro-coagulant therapy uses factor replacement.

This treatment is used to treat a range of bleeding disorders, including:

- Haemophilia A and B
- Factor V, VII, X, or XII deficiencies (bleeding disorders related to blood clotting or abnormal bleeding problems)
- Von Willebrand’s disease (most common inherited bleeding disorder, develops when the blood lacks von Willebrand factor which helps the blood to clot)

Tech Overview

Researchers at the University of Liverpool have developed a novel approach for direct coagulation activation which bypasses the intrinsic & extrinsic pathway where factors are deficient (Figure 2).

This works through the use of synthesized functional peptides that can promote coagulation by targeting prothrombin. The physiological relevance has been determined in vitro (Figure 3), and the translational relevance has been determined ex vivo using FVIII deficient human plasma (Figure 4) and in vivo animal models (Figure 5).

Opportunity

The researchers are seeking expertise in the development of the pro-coagulant molecules to make them more drug-like and eventually resulting in a lead compound.

This work has been carried out by a multidisciplinary team including clinicians and basic scientists with strong clinical links within the NHS allowing access to clinical samples, and the ability to comprehensively undertake bench-to-bedside research.
Appendix 3

Figure 3

(A) Binding studies and functional assays to characterize biological mechanism.

Pro-coagulant effects (B) Prothrombin cleavage & (C) thrombin generation demonstrated in purified systems.
Appendix 4

Figure 4

Restores thrombin generation & clot formation in FVIII and FIX-deficient human plasma.
Appendix 5

Figure 5

In vivo administration enables clotting of plasma from FVIII-deficient mice, without causing dissemination of coagulation.