A Novel Therapeutic Approach to Restore Haemostasis in Individuals with Inherited and Acquired Bleeding Disorders

RCSI UNIVERSITY OF MEDICINE AND HEALTH SCIENCES

RCSI has developed a novel therapeutic approach to restore haemostasis in individuals with haemophilia and other bleeding disorders by the inhibition of the initiation and activity of anticoagulant pathways mediated by Activated Protein C (APC).

BACKGROUND

The majority of patients with inherited and acquired bleeding disorders are under-served by existing haemostatic agents. There is an unmet clinical need for novel haemostatic drugs that are efficacious and not associated with increased thrombotic risk. Emerging therapies such as Gene therapy will only ever be useful for a minority of male patients with severe haemophilia. In addition, none of the currently available therapies address the key role played by inflammation in driving clinical bleeding. At RCSI, we have developed a novel treatment to prevent and manage bleeding in patients with all types of inherited and acquired bleeding disorders by re-balancing haemostasis by effectively attenuating the Protein C anticoagulant pathway.

VALUE PROPOSITION

The global haemophilia treatment market is valued at US$ 10,042.7 Million in 2016, and is expected to reach US$ 15,124.7 Million by 2025, expanding at a CAGR of 4.5% from 2017 to 2025. Individuals with severe haemophilia A exhibit an increased tendency to bleed uncontrollably after injury due to mutation of a gene that encodes an important clotting protein (FVIII). Current therapy for individuals with severe haemophilia involves prophylactic recombinant FVIII administration which in individuals with severe Haemophilia A leads to the generation of antibodies that block the function of the administered rFVIII. ProtX, a recombinant, soluble form of an endogenous protein developed by RCSI is able to restore clotting activity in haemophilia A plasma. Furthermore, given that the mode of action is not directly tied to the correction of defective intrinsic tenase activity caused by missing or dysfunctional FVIII; ProtX may also have utility as a general haemostatic agent in other clinical contexts.

TECHNOLOGY

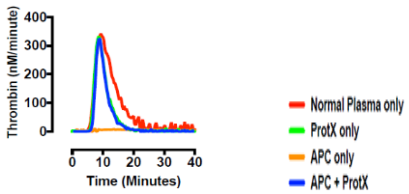
ProtX can stimulate blood coagulation in FVIII deficient plasma, therefore has the potential to correct bleeding in individuals with severe haemophilia A. Furthermore, as ProtX restores clotting activity via an approach orthogonal to restoration of intrinsic tenase activity, it is anticipated to have utility as a haemostatic agent for non-haemophilia patients in which bleeding management is otherwise challenging, including those with other inherited bleeding disorders, and patients with uncontrolled bleeding caused by traumatic injury, surgery or childbirth.

As ProtX is based on a naturally occurring protein and not deficient in haemophilia patients, it would also not be recognised as foreign to the recipient's immune system so is unlikely to provoke an immune response upon administration.

Applications

- A novel therapeutic for Haemophilia/rare bleeding disorders
- A novel haemostatic agent to prevent bleeding after trauma/surgery

Fig 1. ProtX potently suppresses APC anticoagulant activity to correct thrombin generation in normal plasma



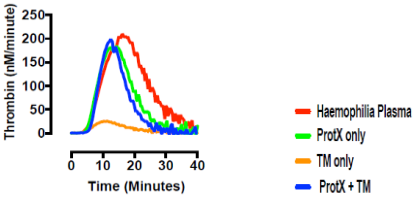


Fig 2. ProtX suppresses APC anticoagulant activity, restores thrombin generation in Haemophilia A plasma

FEATURES	BENEFITS
Novel Haemophilia therapeutic	Efficacious in restoring Thrombin generation in ex vivo blood samples from Haemophilia patients
Natural Endogenous Protein	Non-immunogenic so will not raise antibody inhibitors like recombinant Factor VIII
Platform Technology	Potential wider application as haemostatic agent to prevent bleeding following trauma or surgery,

TECHNOLOGY READINESS LEVEL

- Proof of Concept Achieved
- Patent Protected

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