Blood clotting begins when platelets adhere at a lesion site in the cut wall of an injured blood vessel. In a cascade of enzymatically regulated reactions, soluble fibrinogen molecules are converted by the enzyme thrombin to insoluble strands of fibrin that hold the platelets together in a thrombus. At each step in the cascade, a protein precursor is converted to a protease that cleaves the next protein precursor in the series. Co-factors are required at most of the steps.

Quantitative or qualitative deficiency in FVIII results in a bleeding disorder called hemophilia A (Scandella et al., 1998; Rick et al., 2003). Severe hemophiliacs number about 17,000 in the United States. These patients can suffer uncontrolled internal bleeding that may result in serious symptoms ranging from inflammatory reactions in joints to early death. These patients can be treated with human FVIII, which will restore the blood’s normal clotting ability if administered with sufficient frequency and concentration. Hemophiliacs require daily replacement of factor VIII to prevent bleeding and the resulting deforming hemophilic arthropathy.

The invention provides highly sensitive immunoassays and antibodies capable of accurate detection of FVIII concentration in the plasma of normal human subjects and those with hemophilia. This assay detects FVIII concentrations significantly below 1% normal physiological concentration which is important for management of hemophilia and in FVIII replacement therapy. Levels of detection exhibited by particular embodiments greatly exceed those of previously described assays. This assay works between 1-4000 pM (0.001-4 nM, 3 orders of magnitude range). The enhanced sensitivity of the assays is contributed in part by using a combination of two antibodies that can bind human FVIII protein in plasma with high affinity and selectivity following treatment with an agent that causes the FVIII to dissociate from FVIII-binding molecules to which it is bound, such as Von Willebrand factor (vWF).

Advantages

- Detects FVIII protein between about 0.001 nM and 1000 nM.
- Quantifies FVIII in healthy individuals, hemophiliacs
- Quantifies FVIII in patients with anti-coagulant antibodies

Applications

- Pharmaceutical companies manufacturing products for blood coagulation disorders
- Medical settings where patients are being treated for blood coagulation disorders such as hemophilia

I.P. Status

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Learn more about Dr. Mann’s research at: http://bit.ly/18jJlSm

For more information and licensing opportunities, contact us at: Ph: 802-656-8780 or email: innovate@uvm.edu