INNOVATION PARTNERSHIPS
UNIVERSITY OF MICHIGAN

Modified Tissue Factor with Increased Clotting Activity

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OVERVIEW

A newly discovered baboon tissue factor more active than human tissue factor

- Discovery of mutations in tissue factor capable of increasing clotting two-fold
- Applicable to the use of clotting factors for diagnosis or treatment of illnesses

BACKGROUND

Tissue factor (TF), or platelet tissue factor, is a protein present in subendothelial tissue and leukocytes which initiates thrombin formation during the clotting process. TF begins the pathway which causes activation of factor X (FX), a vitamin-K dependent serine protease zymogen that stimulates the first common step of the intrinsic and extrinsic pathways of blood coagulation. The means by which TF facilitates this pathway involves its secondary binding to the precursor of factor VII (FVIIa), a serine protease which activates both factors IX and X. Recombinant human tissue factor has multiple existing and potential uses as a diagnostic and a therapeutic, though the need exists to define a more active TF with the goal of improving testing and treatment of multiple diseases.

INNOVATION

Researchers at the University of Michigan have discovered that baboon tissue factor is more active than human tissue factor, leading to faster clotting times. Baboon TF shows an increased ability to support FX activation by FVIIa and a greater ability to trigger the clotting of human plasma. The scientists identified mutations that can be made in the human tissue factor sequence which increases its procoagulant activity up to twofold. Almost all of the increased procoagulant activity results from a single amino acid difference between human and baboon

TF which results in the insertion of an arginine residue between amino acids 196 and 197 of the human TF sequence. This new agent could provide improvements to existing prothrombin time (PT) clotting tests, either through increased TF activity or a decrease in the amount of recombinant TF required as a reagent. There is also ongoing research in using tumor-targeted tissue factor as a method of inducing tumor infarction, as well as investigation of the use of relipidated, recombinant tissue factor as a hemostatic agent to control surgical bleeding. The enhanced activity of TF should therefore provide opportunities to improve diagnostic and therapeutic uses of this discovery.