

Extended action of FIX for improving the lifestyle of Hemophiliacs

Darrel W. Stafford

University of North Carolina at Chapel Hill, USA

Several pharmaceutical companies are in the process of developing Factor IX (FIX) molecules with a longer half-life. The goal of this is to improve the lifestyle of patients with hemophilia by decreasing their frequency of injection of coagulation FIX. Biogen IDEC has developed a FIX molecule with a Fc terminal extension that is purported to be re-cycled via the Fc receptor. NovoNordisk developed a new FIX that has had PEG added to one of its N-Glycosylation sites in its activation peptide. Behring has developed a longer lasting FIX molecule that has albumin added to its C-terminus. The albumin has a FXI cleavage site and is cleaved when FIX is activated.

All of these molecules are considerably larger than normal FIXWT, and may not be distributed normally into the extravascular space where much of FIX normally resides. FIX has been shown to bind tightly and reversibly to type IV collagen which underlies all endothelial cells. This binding is correlated with the observation that much of FIX seems to be located extravascularly. We have recently shown that normal FIX can protect hemophilia B mice for up to 7 days after infusion, well after the FIX has disappeared from circulation. Therefore, extravascular FIX plays an important role in hemostasis and may be the most relevant compartment for coagulation. The distribution of these new longer lasting factor IX molecules needs to be established.

Biography

Darrel W. Stafford completed his Ph.D. at the age of 29 years from the University of Miami. He attended Albert Einstein Medical School in New York for his post-doctoral work. He is currently a professor of Biology and Pathology at the University of North Carolina at Chapel Hill. He has published ~198 peer-reviewed papers in many reputable journals. His laboratory is known for having purified and cloned both VKOR and gamma-glutamyl carboxylase of the vitamin K cycle.

dws@email.unc.edu