

Letter: In response to a recent letter by Prior et al.

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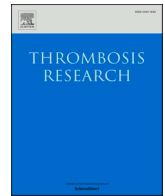
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Letter to the Editors-in-Chief

Letter: In response to a recent letter by Prior et al.

Dear Sir/Madam,

Within this letter, kindly find below our response to the letter submitted by Prior and Butenas [1]. First and foremost, we would like to apologise for raising the suggestion that we had overlooked previous contributions to the development of FXIa assays. We would like to clarify our work and point of view in relation to the comments made by Prior and Butenas.

In their letter Prior and Butenas highlight several studies in which factor XIa (FXIa) and tissue factor (TF) were quantified using a newly developed assay based on prolongation of plasma clotting time upon addition of monoclonal antibodies against FXIa or TF [2]. This assay was later improved upon, and the same principle could be used to quantify FXIa in plasma and whole blood via a thrombin generation assay [3–5]. These studies have repeatedly shown correlations between procoagulant phenotype and increased FXIa concentration in circulation. We acknowledge the importance of these assays and their clinical impact, which emphasizes the importance of FXIa quantification in general.

The sample preparation of these assays, however, is similar to studies done by Loeffen et al., and is therefore susceptible to time-dependent FXIa-inactivation [6,7]. Stability experiments of FXIa in plasma showed a significant decrease in activity after 30 min (11%), up to 38% after 120 min [6]. The instability of FXIa in plasma requires swift processing and analysis of samples for accuracy. This makes quantification of a large group of patients (>1000) logistically challenging. The main focus of our proof-of-concept study is the development of an FXIa-assay that is independent of serpin inhibition and auto-inactivation. In our assay, a multivalent inhibitor is used to bind, protect and isolate FXIa from fresh blood samples [8].

Ultimately, optimization of this assay will allow direct addition of the multivalent construct to the blood collection tube with subsequent instantaneous binding and protection of FXIa from serpin inhibition and auto-inactivation during blood drawing. In the end a FXIa determination procedure is achieved that is independent of blood work-up and storage time.

It is evident that we and Prior and Butenas share similar goals. It is likely that this will result in a better understanding of FXIa and its role in cardiovascular diseases. However, the instability of FXIa in plasma due to serpin-inhibition and auto-inactivation creates the need for a different and more dependable quantification strategy.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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