Corrections

Prothrombin Is a Cofactor for the Binding of Factor XI to the Platelet Surface and for Platelet-Mediated Factor-XI Activation by Thrombin, by Frank A. Baglia and Peter N. Walsh* , Volume 37, Number 8, February 24, 1998, pages 2271-2281.

Dr. Peter N. Walsh, corresponding author, retracts this paper. The following narrative written by Dr. Walsh provides a chronology of events underlying his decision to retract this paper which concluded that activated platelets provide a surface for receptor-mediated factor XI activation by thrombin. Activated platelets provide a surface for initiation of intrinsic blood coagulation (*1*−*3*), by promoting the activation of factor XI by both factor XII-dependent and factor XII-independent mechanisms, thus providing a potential explanation for the requirement of factor XI for normal hemostasis (*4*−*6*), whereas the so-called "contact factors" (factor XII, prekallikrein, and high-M_r kininogen or HK) are not required for normal hemostasis (*7*). This contribution of ADP- or collagen-activated platelets to the promotion of factor XI activation by factor XIIa was shown to require the exposure of specific, high-affinity, saturable receptors for the zymogen, factor XI, on the activated platelet plasma membrane (*8*, *9*). A major advance to our understanding of the physiological mechanism of the initiation of the intrinsic coagulation pathway was the seminal observations of Naito and Fujikawa (*10*) and Gailani and Broze (*11*) that the protease, thrombin, generated via the factor VIIa/tissue factor pathway, was able to activate factor XI by cleaving the same scissile bond (R369−I370) cleaved by factor XIIa. However, the only surface shown to promote this factor XI activation at physiologically relevant rates by physiologically achievable concentrations of thrombin was dextran sulfate, hardly a physiologically relevant substance. Moreover, physiological concentrations of HK or fibrinogen were shown to abrogate factor XI activation by thrombin (*12*, *13*).

In an attempt to define physiologically relevant conditions and cellular surfaces for rate enhancements of factor XI activation by thrombin, we examined platelets and endothelial cells and concluded from our studies that PAR-1-activated platelets (*14*, *15*), but not endothelium (*16*), promoted rate enhancements of factor XI activation by picomolar thrombin concentrations that were similar to those obtained with dextran sulfate. Moreover, compared with factor XIIa and factor XIa, both of which activate factor XI, thrombin appeared to be the preferred activator in the presence of PAR-1-activated platelets (*15*). These studies, all of which were carried out by Dr. Frank A. Baglia in my laboratory, supported the attractive hypothesis that activated platelets provide a surface for receptor-mediated assembly of coagulation complexes, initiated by thrombin activation of factor XI, a conclusion reached independently by Oliver et al. (*17*) on the basis of results obtained under different experimental conditions.

It was therefore a source of considerable dismay when I learned, well after the publication of these two papers (*14*, *15*), that Dr. Dipali Sinha in my laboratory was unable to reproduce some of Dr. Baglia's experimental results. Subsequently, in September 2005, I received a personal communication from Dr. Earl Davie indicating that he and Drs. Daniel Greenberg and Kazuo Fujikawa (Department of Biochemistry, University of Washington, Seattle, WA) had also been unable to reproduce these results. In January 2007, I received yet another personal communication from Dr. Theo Lindhout (Department of Biochemistry, Maastricht University, Maastricht, The Netherlands) indicating similar difficulties. Since both groups of highly esteemed scientists asked me for suggestions about the potential sources of experimental variability, I provided a detailed response with a list of technical details, including concentrations of metal ions (e.g., zinc and calcium), platelet isolation and activation procedures, and other experimental details, that might potentially affect the results. Following my initial correspondence with Dr. Davie, I also asked Dr. Baglia and three other colleagues in my laboratory (Sergei Shikov, Dr. Wenman Wu, and Dr. Syed Ahmad) to repeat the original experiments. Dr. Baglia presented to me numerous experiments over a period of several months, confirming his original observations, utilizing both amidolytic assays of factor XIa generation and proteolytic activation assays employing SDS−PAGE, to demonstrate profound rate enhancements by activated platelets of factor XI activation by thrombin. In contrast, Sergei Shikov and Drs. Wu and Ahmad have so far been consistently unable to demonstrate significant rate enhancements attributable to activated platelets on the time scale and at thrombin concentrations reported by Dr. Baglia.

I have therefore come to the conclusion that our original observations (*14*, *15*) were incorrect. A fundamental principle utilized by all scientists in arriving at scientific validity is the act of confirmation by other scientists. On the basis of this principle, our original observations fail to meet the standard of scientific veracity, and for that reason, I am retracting these papers (without the concurrence of Dr. Baglia) and the conclusions drawn from them.

On a personal note, I wish to express my profound gratitude to my colleagues (Dipali Sinha, Sergei Shikov, Wenman Wu, Syed Ahmad, Kazuo Fujikawa, Dan Greenberg, Earl Davie, and Theo Lindhout) for their honest forthrightness in helping to point out and correct these errors. Finally, I wish to apologize to the Editor and readers of *Biochemistry* and to all my colleagues and fellow scientists for publishing these erroneous data.

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Molecular Understanding of Aβ Peptide Interaction with Isoflurane, Propofol, and Thiopental: NMR Spectroscopic Study Pravat K. Mandal,* John P. Williams, and Ratna Mandal, Volume 46, Number 3, January 23, 2007, pages 762−771.

Dr. Pravat Mandal, corresponding author, acting on behalf of all authors of this published work, retracts this paper. His rationale follows.

The anesthetic concentration of our paper was misrepresented, and we have decided to retract this paper. The reported anesthetic concentration was 6 times higher than a clinically relevant concentration; however, the actual concentration of isoflurane was 8−10 times higher than that reported in the paper.

We are continuing studies to determine if a clinically relevant concentration of isoflurane has interactions with specific residues of the Aβ peptide.

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Structure and Sodium Channel Activity of an Excitatory I_1-Superfamily Conotoxin, by Olga Buczek, Daxiu Wei, Jeffrey J. Babon, Xiaodong Yang, Brian Fiedler, Ping Chen, Doju Yoshikami, Baldomero M. Olivera, Grzegorz Bulaj, and Raymond S. Norton,* Volume 46, Number 35, September 4, 2007, pages 9929−9940.

Page 9937. In Figure 6, ι-RXIA is depicted in the right panels and ι-RXIA[L-Phe44] in the left panels.

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