The HMGB1/RAGE axis triggers neutrophil-mediated injury amplification following necrosis

Peter Huebener, …, Daniel J. Antoine, Robert F. Schwabe


**Expression of concern**


Citation for this expression of concern: *J Clin Invest.* 2019;129(4):1802. https://doi.org/10.1172/JCI126976

An investigative committee at the University of Liverpool recently identified evidence of data fabrication relating to the mass spectrometry data contributed by Daniel J. Antoine for Supplemental Figure 6 of this paper. The Editorial Board is issuing this Expression of Concern to alert readers to this problem. No issues have been raised in regard to any of the other data in this manuscript.

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Corrigendum

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The Editors posted an Expression of Concern for this article following notification that an investigative committee at the University of Liverpool had data integrity concerns regarding the mass spectrometry data contributed by Daniel J. Antoine for Supplemental Figure 6 of this paper. The authors have provided a corrected version of this article and a description of changes below.

In our published work, we reported that hepatocyte-derived HMGB1 triggers neutrophil-driven injury amplification following liver necrosis. We based our conclusions on extensive animal studies, including models of LPS-induced shock as well as models of hepatocyte apoptosis or necrosis in mice with cell-specific knockouts of HMGB1 and knockout of its main receptor, RAGE. Mice harboring bone marrow– and hepatocyte-specific deletion of HMGB1 showed vulnerability to endotoxemia and apoptotic liver injury equal to that of their wild-type littermates. However, in contrast to their floxed littermates, mice with hepatocyte-specific deletion of HMGB1 were protected from injury induced by acetaminophen intoxication or ischemia/reperfusion. While hepatocyte-specific HMGB1 deletion did not reduce initial injury in these models, it attenuated postnecrotic inflammation and neutrophil-mediated exacerbation of tissue damage. Accordingly, we found that these inflammatory and damage-exacerbating effects of HMGB1 were mediated by RAGE on bone marrow–derived cells, as demonstrated by studies in mice lacking neutrophil elastase in bone marrow and our finding that neutrophil migration required HMGB1 release from necrotic tissue and RAGE expression on neutrophils.

Supplemental Figure 6 shows data from an analysis of HMGB1 isoforms by mass spectrometry that was undertaken in a separate laboratory by Daniel J. Antoine. In September 2018, we learned that these data were compromised. We contacted the journal, and the Editorial Board agreed to publish an updated online version of the article. In the corrected version, all conclusions based on Supplemental Figure 6 have been removed, and the journal has published an online version of the original article and supplemental file with the unreliable statements and Supplemental Figure 6 crossed out (Supplemental File, Redaction) and the modified text highlighted in red. Daniel J. Antoine’s name was removed from the author list. The investigative committee at the University of Liverpool did not have any concerns in regard to the contributions and research activities of Rosalind E. Jenkins. Her name was removed from this publication solely because of a lack of contribution to the corrected manuscript. We affirm that the major conclusions of the study are accurate and that the corrected paper is reliable.