**Table I. Proposed mechanisms of histone-mediated cytotoxicity, inflammatory and procoagulant effects**

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| **Cytotoxicity**   * Membrane disruption causing calcium influx and overload * Toll-like receptor (mainly TLR 2, 4 and 9) signalling |
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| **Inflammatory effects**   * NFκB activation * NLRP inflammasome activation * Cytokine release |
|  |
| **Procoagulant effects**   * Vascular endothelial damage * Enhanced release of ultra-large multimers of von Willebrand factor * Enhanced tissue factor expression on endothelial cells * Increased thrombin generation * Suppression of thrombomodulin-mediated protein C activation * Enhanced platelet aggregation and disruption * Enhanced polyphosphate release from platelets * NETosis * Increased clot resistance to fibrinolysis |