ID 4551 - Circulating neutrophil extracellular traps contribute to endothelial dysfunction in preeclampsia

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Background and aim: Preeclampsia is a pregnancy pathology characterized by hypertension, proteinuria, endothelial dysfunction and complement dysregulation. Recent studies demonstrate that neutrophil extracellular traps (NETs) play a pathogenic role in other complement mediated pathologies. NETs formation is triggered by innate immune receptors and induced in response to microbial cues and endogenous danger signals (i.e. cytokines) and must be tightly regulated to prevent excessive tissue damage. We aimed to study the contribution of NETs in preeclampsia.

Methods: Sera samples from 8 preeclampsia and 6 normotensive pregnancies were pooled in 3 preeclampsia pools and 1 control pool. NETs were obtained from the incubation of donor preactivated neutrophils with preeclampsia and control sera. To evaluate endothelial damage, endothelial cells in culture were incubated (48h) with preeclamptic or control sera in the presence or absence (depleted) of NETs. Then, changes in endothelial biomarkers (VCAM-1, ICAM-1), von Willebrand factor (VWF) expression and reactive oxygen species (ROS) production were assessed. The results were expressed as the average fold increase versus control.

Results: VCAM-1, VWF and ROS were significantly higher in cells exposed to preeclamptic versus control sera [fold change of 5.4, 3, and 1.3, respectively, $p<0.05$]. VCAM-1, VWF and ROS were significantly lower in depleted preeclamptic sera compared to non-depleted sera [fold change of 5.0 vs 0.7 for VCAM-1, 4.3 vs 2.8 for VWF, and 1.3 vs 1.2 for ROS, $p<0.05$]. Cells incubated with preeclamptic NETs showed a significantly increased VCAM-1, ICAM-1 and ROS expression compared to control NETs [fold change of 3.5, 1.2, and 2, respectively, $p<0.05$].

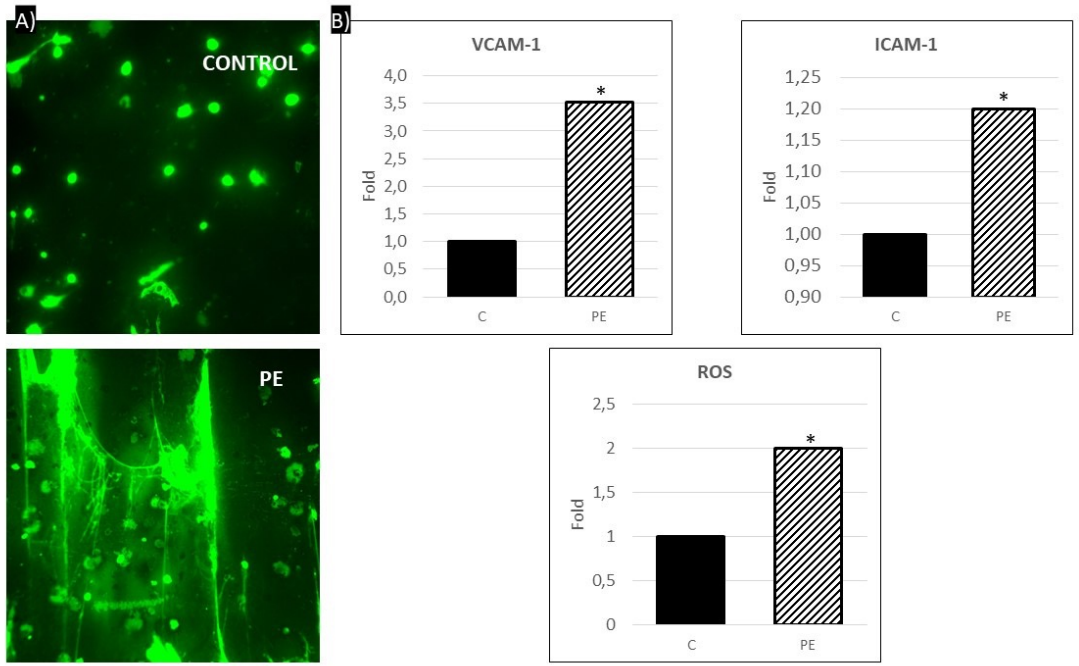

Figure 1. A) Representative microphotographs of neutrophils extracellular traps (green) on donor neutrophils preactivated with TMA. B) Endothelial damage markers induced by incubation with control and PE NETs. The results were expressed as the average fold increase versus control. The vertical bars indicate the standard deviation. * $p<0.05$ versus control.

Conclusions: Circulating NETS are potentially pathogenic in endothelial damage associated with PE triggering an oxidative, prothrombotic and proinflammatory state.