Abstract

Air pollution exposure is associated with cardiovascular events triggered by clot formation. Endothelial activation and initiation of coagulation are pathophysiological mechanisms that could link inhaled **air** pollutants to vascular events. Here we investigated the underlying mechanisms of increased endothelial cell procoagulant activity following exposure to soluble components of ultrafine particles (soluble UF). Human coronary artery endothelial cells (HCAEC) were exposed to soluble UF and assessed for their ability to trigger procoagulant activity in platelet-free plasma. Exposed HCAEC triggered earlier thrombin generation and faster fibrin clot formation, which was abolished by an anti-tissue factor (TF) antibody, indicating TF-dependent effects. Soluble UF exposure increased TF mRNA expression without compensatory increases in key anticoagulant proteins. To identify early events that regulate TF expression, we measured endothelial H2O2 production following soluble UF exposure and identified the enzymatic source. Soluble UF exposure increased endothelial H2O2 production, and antioxidants attenuated UF-induced upregulation of TF, linking the procoagulant responses to reactive oxygen species (ROS) formation. Chemical inhibitors and RNA silencing showed that NOX-4, an important endothelial source of H2O2, was involved in UF-induced upregulation of TF mRNA. These data indicate that soluble UF exposure induces endothelial cell procoagulant activity, which involves de novo TF synthesis, ROS production, and the NOX-4 enzyme. These findings provide mechanistic insight into the adverse cardiovascular effects associated with **air pollution** exposure.