Abstract

Oxidative stresses are considered to play an important role in the induction of cell adhesion molecules and proinflammatory cytokines implicated in inflammatory processes. Heme oxygenase (HO)-1 and suppressors of cytokine signaling (SOCS)-3 exert several biological functions, including antiapoptotic and anti-inflammatory effects. Here, we report that HO-1 and SOCS-3 were induced in A549 cells and human pulmonary alveolar epithelial cells (HPAEpiCs) treated with (−)-epigallocatechin-3-gallate (EGCG). EGCG protected against tumor necrosis factor (TNF)-α-mediated lung inflammation by down-regulation of oxidative stress and intercellular adhesion molecule (ICAM)-1 expression in A549 cells or HPAEpiCs and the lungs of mice. EGCG inhibited TNF-α-induced ICAM-1 expression, THP-1 cells adherence, pulmonary hematoma and leukocyte (eosinophils and neutrophils) count in bronchoalveolar lavage fluid in mice. In addition, EGCG also attenuated TNF-α-induced oxidative stress, $p47^{phox}$ translocation, MAPKs activation, and STAT-3 and activating transcription factor (ATF)2 phosphorylation. EGCG also reduced the formation of a TNFR1/TRAF2/Rac1/$p47^{phox}$ complex. Moreover, in this study, the observed suppression of TNF-α-stimulated ICAM-1 expression and reactive oxygen species (ROS) generation by EGCG was abrogated by transfection with siRNA of SOCS-3 or HO-1. These results suggested that HO-1 or SOCS-3 functions as a suppressor of TNF-α signaling, not only by inhibiting adhesion molecules expression but also by diminishing intracellular ROS production and STAT-3 and ATF2 activation in A549 cells or HPAEpiCs and the lungs of mice.