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Thioredoxin reductase attenuates vascular inflammatory responses during oxidative stress

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Overall selenium (Se) nutritional status of the host will influence endothelial cell integrity and consequently impact the development of certain pathological conditions including atherosclerosis. The importance of Se to health may be related to selenoprotein activities, including glutathione peroxidase (GPX) and thioredoxin reductase (TrxR1) that have diverse biological roles. These enzymes can function as potent antioxidants by directly reducing pro-atherogenic reactive oxygen species (ROS) to less reactive metabolites[1]. There is a growing body of evidence to suggest that hydroperoxides also can influence vascular signalling cascades by redox modification of various protein kinases, protein phosphatases and transcription factor activities[2]. Therefore, it follows that both GPX and TrxR1 also may impact the repertoire of pro-inflammatory gene expression following oxidant challenge by controlling intracellular redox environment[3]. Increased intercellular adhesion molecule 1 (ICAM-1) expression and enhanced leucocyte recruitment to the endothelium are critical steps in the early development of atherosclerosis. The establishment and resolution of vascular inflammatory responses, including the expression of adhesion molecules, can be regulated to a large extent by oxidative stress. Therefore, the goal of this study was to define the regulatory role of individual selenoproteins in modulating the adhesive properties using an oxidative stress model based on selenium deficiency in bovine aortic endothelial cells (BAEC), we sought to determine whether TrxR1 activity may contribute to the differential regulation of ICAM-1 during pro-oxidant challenge. Selenium supplementation reduced ICAM-1 expression and leucocyte adhesion to BAEC. Furthermore, ICAM-1 expression increased proportionately when selenium-deficient BAEC were challenged with a pro-oxidant fatty acid hydroperoxide. Subsequent results using TrxR1 siRNA showed that this selenoprotein is at least partially responsible for controlling ICAM-1 expression during oxidative stress. Finally, restoring intracellular levels of the reduced substrate thioredoxin (Trx) in selenium-deficient BAEC was sufficient to reduce ICAM-1 expression during oxidative stress. These data provide evidence for the involvement of the Trx/TrxR1 system in the regulation of ICAM-1 expression in BAEC during pro-oxidant challenge.

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