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Insulin-like growth factor-1 regulates glutathione peroxidase expression and activity in vascular endothelial cells: Implications for atheroprotective actions of insulin-like growth factor-1.

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Abstract

Oxidative stress promotes endothelial cell senescence and endothelial dysfunction, important early steps in atherogenesis. To investigate potential antioxidant effects of IGF-1 we treated human aortic endothelial cells (hAECs) with 0-100ng/mL IGF-1 prior to exposure to native or oxidized low-density lipoprotein (oxLDL). **IGF-1 dose- and time- dependently reduced basal- and oxLDL-induced ROS generation**. IGF-1 did not alter superoxide dismutase or catalase activity but **markedly increased activity of glutathione peroxidase (GPX), a crucial antioxidant enzyme, via a phosphoinositide-3 kinase dependent pathway.** IGF-1 did not increase GPX1 mRNA levels but increased GPX1 protein levels by 2.6-fold at 24h, and altered selenocysteine-incorporation complex formation on GPX1 mRNA. Furthermore, **IGF-1 blocked hydrogen peroxide** induced premature cell senescence in hAECs. In conclusion, **IGF-1 upregulates GPX1 expression in hAECs via a translational mechanism**, which may play an important role in the ability of IGF-1 to reduce endothelial cell oxidative stress and premature senescence. Our findings have major implications for understanding vasculoprotective effects of IGF-1.