Angiotensin II Stimulates Hypoxia-Inducible Factor 1{alpha} Accumulation in Glomerular Mesangial Cells

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摘要

Abstract

Hypoxia increases hypoxia-inducible factor 1alpha (HIF-1alpha) protein levels by inhibiting ubiquitination and degradation of HIF-1alpha, which regulates the transcription of many genes. Recent studies have revealed that many ligands can stimulate HIF-1alpha accumulation under nonhypoxic conditions. In this study, we show that angiotensin II (Ang II) increased HIF-1alpha protein levels in a time- and dose-dependent manner under normoxic conditions. Treatment of mesangial cells with Ang II (100 nM) increased production of reactive oxygen species (ROS). Ang II (100 nM) increased the phosphorylation of PDK-1 and Akt/PKB in glomerular mesangial cells. Ang II-stimulated HIF-1alpha accumulation was blocked by the phosphatidylinositol 3-kinase (PI-3K) inhibitors, Ly 294001, and wortmannin, suggesting that PI-3K was involved. Because increased ROS generation by Ang II may activate the PI-3K-PKB/Akt signaling pathway, these results suggest that Ang II may stimulate a ROS-dependent activation of the PI-3K-PKB/Akt pathway, which leads to HIF-1alpha accumulation

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