

Zinc induces normoxic accumulation of transcriptionally active hypoxia-inducible factor 1-alpha in mammary epithelial cells

ABSTRACT

Both zinc and the α -subunit of hypoxia-inducible factor (HIF-1 α) play important roles in the remodelling of mammary gland tissues. In the present study, we examined the level and the transcriptional activity of HIF-1 α in mammary cells upon zinc treatment. In MCF-7 mammary adenocarcinoma and MCF-10A mammary epithelial cell lines, the toxicity levels of zinc differ. Interestingly, both cell lines overexpress HIF-1 α following zinc treatment. As it was evident from an up-regulation of its specific target gene CA9 that encodes carbonic anhydrase IX, the stabilized HIF-1 α translocated to the nucleus and was transcriptionally active. Hence, we conclude that zinc causes normoxic accumulation of transcriptionally active HIF-1 α by interfering with its post-translational regulation.

Keyword: Hypoxia-inducible factor; Mammary epithelial cells; Zinc