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HIF1 α PLAYS AN ESSENTIAL ROLE IN ENDOTHELIAL CELL HYPOXIC RESPONSE

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Hypoxia in wound healing, cardiovascular and cerebral ischemia, inflammatory disorders and solid tumor formation is an important regulator of angiogenesis and blood vessel structure. Hypoxia-inducible transcription factor-1 α (HIF-1 α) acts as a master switch to induce the expression of several hypoxia inducible genes. At normoxia, HIF-1 α is rapidly degraded through targeted ubiquitination by direct binding of its oxygen dependent domain to VHL. In response to hypoxia, HIF-1 α protein goes to nucleus and dimerizes with HIF-1 β . Then this dimer binds to a hypoxia-response element and induces the transcription of several angiogenic factors. In adult organisms, vascular endothelial cells (ECs) remain quiescent unless ischemia or hypoxic conditions stimulate the secretion of angiogenic factors. It is shown that HIF-1 α regulates many factors in endothelial cells that could control vasoconstriction and proliferation. To understand how HIF-1 α control ECs hypoxic responses, we specifically delete the double-floxed (DF) HIF-1 α alleles in mouse endothelial cells by using Tie2-Cre recombinase transgenic mice. Although HIF-1 α DF-Tie2-Cre mice seems have normal development, *in vivo* wound healing experiment and matrigel plug implantation experiment all show these null mice have angiogenesis defects. *In vitro*, loss of HIF-1 α in ECs causes loss of tube-forming ability on matrigel even in the presence of exogenous VEGF. HIF-1 α null ECs, but not VEGF null ECs, show motility defects toward VEGF. By realtime quantitative PCR, we find that selected VEGF receptor expressions are reduced in HIF-1 α null ECs. The results here show HIF-1 α is an important factor for isolated endothelial cell hypoxic responses by regulating VEGF receptors on endothelial cells. The interactions of tissue and endothelial cell during hypoxia likely depend on coordinated hypoxic response. *Nan Tang is a trainee in environmental sciences supported by Superfund/NIEHS grant.