Editorial

A closer look at hypoxia inducible factor

Oxygen availability is vital for cellular metabolism. Low oxygen tension, or hypoxia in cells will lead to the induction of many genes in angiogenesis, metabolism and cell proliferation.[1,2]

Hypoxia inducible factor (HIF) is a known important mediator in the process of cells and tissues adaptation to hypoxia.[1] HIF is responsible for the induction of genes that facilitate adaptation and survival of cells and the whole organism from normoxia (≈21% O_2) to hypoxia (≈1% O_2),[3] by activating genes essential to cellular adaptation to low oxygen conditions.[1] These genes include the vascular endothelial growth factor (VEGF), erythropoietin, and glucose transporter-1.[2] HIF also plays an important role in the proper cellular response to changes in oxygen tension in pathological processes such as cardiovascular disease, neurological disease and cancer.[4]

In cardiovascular diseases, HIF-1 activities were studied in animal models of myocardial ischemia and ischemic preconditioning. Myocardial ischemia induces VEGF expression and the extent to which VEGF induction is correlated with the degree of coronary collateralization. HIF-1 mRNA and protein expression are induced, precede VEGF expression during acute ischemia and early infarction in the human heart.[5]

In cerebral ischemia conditions, studies showed that the overexpression of HIF-1α, followed by co-localization of HIF-1 and VEGF expressions are associated with neuro-vascularization and reduced cell death in response to oxygen and glucose deprivation.[5] In acute tubular necrosis (ATN) caused by ischemia/ reperfusion during renal transplantation model, it was found that HIF-1 is stabilized in proximal tubule cells during ischemia and even in late reperfusion, when oxygen tension comes back to normal.[6]

In cancer cells, hypoxia is commonly found in solid tumors of various origins. Severe and prolonged hypoxia may initiate apoptosis, whereas cells often adapt to acute and mild hypoxia and survive. Key regulator of hypoxia-induced apoptosis is HIF-1, which can induce or inhibit apoptosis.[7]

To date, deep understanding of the process that control HIF-1 activity is still under intensive investigations, some of which are published in the present edition of MJI. Prijanti et al[8] showed that there is a strong correlation of HIF-1α with renin mRNA in animal model of hypoxia induced by cobalt chloride. In physiological exercise, Flora et al[9] showed that in animal model of anaerobic physical activity, stronger correlation between the vascular endothelium growth factor (VEGF) and HIF-1α were found than that in aerobic physical activity.

In the future, in-depth understanding about the mechanism of HIF-1 activity and control will be crucial for the development of new diagnostic and therapeutic strategies in many clinical manifestations.

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