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[Physiology] NCKU Landmark Project: Systematic Investigation of Roles of Hypoxia Inducible Factor in Diseases: Searching for a Common Cause of Multiple Malignancies

[Physiology] NCKU Landmark Project: Systematic Investigation of Roles of Hypoxia Inducible Factor in Diseases - Searching for a Common Cause of Multiple Malignancies (Chinese Version)

NCKU Research Express (2011/05/13) Hypoxia plays key roles in critical developmental and physiological processes including angiogenesis, erythropoiesis, glucose transport, glycolysis, iron transport, cell survival, and proliferation. More importantly, clinical and laboratory studies have demonstrated that hypoxia-regulated genes involve in numerous human diseases such as myocardial and cerebral ischemia, pulmonary hypertension, preeclampsia, intrauterine growth retardation, and cancer. Hypoxia inducible factor-1 (HIF-1) is the master transcription factor controls gene expression under hypoxia. Experimental data further indicate that overexpression of HIF-1α is linked to poor prognosis in human cancer and is associated with treatment failure and increased mortality. The NCKU Landmark Project conducted by the principal investigator Professor Shaw-Jenq TSAI, Department of Physiology, College of Medicine, has identified numerous HIF-1 targeted genes by using the in-house bioinformatic platform, the Binding Element Searching Tools (the BEST). Wet-bench experimental validations using both in vitro and in vivo methodologies demonstrate such information-driven approach is a useful tool for systematic identification of hypoxia responsive genes that normally would be missed if one only relies on large-scale “omic” approaches. Furthermore, results from functional study revealed many novel findings related to hypoxia-regulated human diseases. To name a few, the project identified that 1) hypoxia suppresses human cad gene resulting in decreased pyrimidine biosynthesis may account for hypoxia-regulated cell cycle arrest; 2) induction of leptin expression by HIF-1 may contribute to the development of endometriosis; 3) suppression of CD151 by HIF-1 reduces cell-cell and cell-matrix adhesion may increase cancer metastasis; and 4) induction of pyruvate dehydrogenase kinase-3 by HIF-1 regulates the metabolic switch from aerobic metabolism to glycolysis in cancer cell, which ultimately increases malignancy of cancer. In sum, the project has taken an integrated, genome-wide approach that combines informative and molecular biological techniques to define complex gene regulatory patterns directed by HIF-1. Such integrative approach should be broadly applicable to the identification of gene regulatory networks of other transcription factors.

Further Information:
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