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[\[BioChemistry\] Academia Sinica's Biochemists Discover Protein that Plays Key Role in Tumor Progression under Low Oxygen Conditions](#)

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Academia Sinica Newsletter (2011/08/24) A research team led by Dr. Ruey-Hwa CHEN, Research Fellow and Deputy Director of Institute of Biological Chemistry has discovered a protein called KLHL20 that plays a key role in tumor progression under hypoxic (low oxygen) conditions. The research was published in the leading cancer journal Cancer Cell on August 16.

Tumor cells often encounter low oxygen conditions because their rapid growth rate exceeds the rate of blood vessel formation. In response to hypoxia, tumor cells induce a protein called HIF-1. HIF-1 regulates a large panel of genes that promote tumor cell survival in hypoxia, inducing cancer cell migration (metastasis) and contributing to resistance to chemotherapy and radiotherapy. Understanding how tumor cells control HIF-1 synthesis is therefore an attractive topic in cancer research.

Dr. CHEN's research team, including PhD student Wei-Chien YUAN and postdoctoral fellow Yu-Ru LEE found that a protein named KLHL20 is induced by HIF-1 under low oxygen conditions. They further found that KLHL20 forms a complex with proteins Cullin 3 and Roc1 and this complex is responsible for the degradation of the protein PML. PML is a well-known tumor suppressor protein that is decreased in many types of tumors. Interestingly, PML itself inhibits HIF-1. Thus, the HIF-1-induced PML degradation successfully relieves the inhibitory effect of PML on HIF-1. Tumor cells exploit this double negative mechanism to amplify HIF-1 production in the early phase of hypoxia, thereby aiding tumor progression.

Another highlight of the study is the discovery of how tumor cells decrease PML expression. Furthermore, this research team found that the KLHL20-mediated PML degradation is abnormally activated in human prostate cancer tissues, and this phenomenon is more prominent in late-stage than early-stage patients. HIF-1 is currently considered as a target for pharmaceutical intervention in cancer therapy. This study suggests that KLHL20 may also be a new drug target for aggressive tumors.

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