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Hypoxia not only is a major driving force in oncogenesis but presents a main cause of drug resistance in cancer treatment. Hypoxia inducible factor-1 (HIF1) has a pivotal role in the regulation of cell and tissue responses to oxygen deficiency. We recently discovered a molecular switch that activates oxygen-independent degradation of HIF1. This molecular switch is consisted of human rhomboid family-1 (RHBD1), the receptor of activated protein-C kinase-1 (RACK1), and heat shock protein 90 (HSP90). Our data also show that inhibition of RHBD1 activity results in sensitisation of cancer cells to anticancer drugs under hypoxic conditions. In addition, vascular endothelial growth factor (VEGF) as a key target gene of HIF1 plays a critical role in tumor angiogenesis. We found that tumor necrosis factor superfamily-15 (TNFSF15), a cytokine predominantly produced by endothelial cells, is able to regulate the activities of VEGF receptors-1 and -2. TNFSF15 action on VEGFR1 changes the latter from an angiogenesis promoter to an angiogenesis inhibitor. TNFSF15 action on VEGFR2 leads to inhibition of VEGF-induced VEGFR2-phosphorylation and thus diminished VEGFR2-mediated enhancement of vascular permeability. These findings provide a foundation to address two issues. One is the role of HIF1 in oncogenesis, including the selection of cancer cells capable of glycolysis and the activation of cancer stem cells. The other is the management of the vicious cycle of angiogenesis which generates dysfunctional, poorly structured blood vessels in malignant tumors, driving tutor growth and metastasis. These two issues are also of great importance to the understanding of the mechanism of resistance to anti-cancer drugs in clinical settings.

Luyuan Li obtained a BS degree in Biochemistry from Sichuan University, Chengdu, China, in 1982, and a PhD degree from Cornell University, New York, the United States in 1988, also in Biochemistry. Having completed his postdoctoral training at Pennsylvania State University, he joined American Cyanamid Company in New York in 1991 as a Senior Scientist. He moved back to academia to join the faculty of Georgetown University Medical Center, Washington, DC, in 1995, as an Assistant Professor of Biochemistry and Molecular Biology, and a Member of the Lombardi Cancer Center. He moved to University of Pittsburgh School of Medicine in 2002 as an Associate Professor of Pathology, Member of the University of Pittsburgh Cancer Institute, and Member of McGowan Institute for Regenerative Medicine. He moved his laboratory to China in 2008 and joined the faculty of Nankai University, Tianjin. He is currently a Professor of Pharmacology in the College of Pharmacy, and Director of the State Key Laboratory of Medicinal Chemical Biology at Nankai University.