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Transcriptional reprogramming in cancer cells triggered by glucose or glutamine starvation

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Cancer cell proliferation depends on increased supply of nutrients including carbon sources and molecular oxygen. However, solid tumors frequently outgrow the blood supply, resulting in insufficient supply of oxygen, glucose and glutamine. Particularly, carbon sources are critical for the generation of ATP and building blocks, and for the maintenance of intracellular redox. Two metabolic features of cancers are the Warburg effect and glutaminolysis, underlines the importance of carbon utilization. While hypoxic adaptation of cancer cells has been well studied, how cancer cells respond to lack of carbon sources remain elusive. Using microarray technology, we compared the gene expression profiles of Hep3B cells under a series of defined culture conditions. Data analysis reveals that depletion of glucose and depletion of glutamine have dramatically different effects on transcriptional reprogramming. This observation suggests that glucose and glutamine are two different types of carbon sources, each having some specific metabolic roles in cell proliferation. Analysis of differentially expressed genes and their functional networks reveals that lack of either glucose or glutamine may lead to inhibition of multiple anabolic pathways and cell growth. Considering metabolite homeostasis in cancer cells, we are trying to validate and interpret the data, expecting to eventually establish a systemic view of the sensing, signaling, transcription reprogramming and metabolic reprogramming of cancer cells in response to carbon source insufficiency. A better understanding of the molecular mechanisms that link the carbon source sensing, signaling, transcriptional reprogramming and adaptive metabolic reprogramming may pinpoint novel targets for drug development and cancer prevention.

Biography

Dr. Sang completed his medical school and clinical training in Fudan University Shanghai Medical College in 1992. He received research training in Molecular Biology in Fels Institute for Cancer Research, Temple University School of Medicine (1992-1994), and then continued his Ph.D. research in Kimmel Cancer Center, Thomas Jefferson University (1994-1997). He received postdoctoral training in University of Pennsylvania (1997-1999) and Cardeza Foundation for Hematological Research (1999-2003) prior to his appointment to the faculty of Jefferson Medical College in 2003. Since 2008, he has relocated his group to Drexel University where his research and teaching focus on Molecular Biology and Biochemistry.