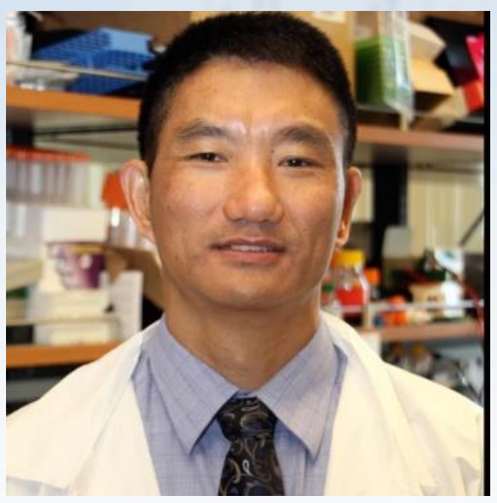
巴斯德讲坛-资深系列
Pasteur Colloquium-Senior

TLR4-Mediated Inflammation Promotes Oncogenesis:Complex Interactions of Host,KSHV and Microbiome



[Speaker] Prof. Shoujiang Gao

[Time] 10:00-11:30AM, November 2, 2017

[Host] Prof. Xiaozhen Liang

[Venue] A0201, Life Science Research Building

[Speaker Introduction]

2011, 7- Professor, Department of Molecular Microbiology and Immunology, University of Southern California (USC) Keck School of Medicine, Los Angeles, CA
2011, 7- Member, USC Norris Comprehensive Cancer Center
2011, 7- Member, USC Institute for Emerging Pathogens and Immune Diseases
2011, 8- Faculty member, Graduate Programs in Biomedical and Biological Sciences (PIBBS), USC

[Abstract]

Aerobic glycolysis is essential for supporting the fast growth of a variety of cancers. However, its role in the survival of cancer cells under stress conditions is unclear. We have previously reported an efficient model of gammaherpesvirus Kaposi's sarcoma-associated herpesvirus (KSHV)-induced cellular transformation of rat primary mesenchymal stem cells. KSHV-transformed cells efficiently induce tumors in nude mice with pathological features reminiscent of Kaposi's sarcoma tumors. Here, we report that KSHV promotes cell survival and cellular transformation by suppressing aerobic glycolysis and oxidative phosphorylation under nutrient stress. Specifically, KSHV microRNAs and vFLIP suppress glycolysis by activating the NF-κB pathway to downregulate glucose transporters GLUT1 and GLUT3.Mechanistically, GLUT1 and GLUT3 inhibit constitutive activation of the AKT and NF-κB pro-survival pathways. Strikingly, GLUT1 and GLUT3 are significantly downregulated in KSHV-infected cells in human KS tumors. Furthermore, we have detected reduced levels of aerobic glycolysis in several KSHV-infected primary effusion lymphoma cell lines compared to a Burkitt's lymphoma cell line BJAB, and KSHV infection of BJAB cells reduced aerobic glycolysis. These results reveal a novel mechanism by which an oncogenic virus regulates a key metabolic pathway to adapt to stress in tumor microenvironment, and illustrate the importance of fine-tuning the metabolic pathways for sustaining the proliferation and survival of cancer cells, particularly under stress conditions.

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