Tumor Metabolism, from Sugar to Lipids

State Key Laboratory of Chemical Resource Engineering

报告人：Deliang Guo , Ph.D.

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个人简介：

Deliang Guo, assistant Professor of Department of Radiation Oncology, The Ohio State University James Comprehensive Cancer Center and College of Medicine, Columbus.

Awards / Honors

Aug 2015, SNO Young Investigator Award for Basic/Translational Research, Society of Neuro-Oncology (SNO) www.soc-neuro-onc.org

Dec 2009, Scholar-in-Training Aflac Award for AACR Special Conference in "Genetics and Biology of Brain Cancers", American Association of Cancer Research (AACR)

Apr 2009, Scholar-in-Training Aflac Award For AACR 100th Annual Meeting, American Association of Cancer Research (AACR)

Nov 2008, Scholar-in-Training Aflac Award for AACR Special Conference in Cancer Research "Targeting the PI3-Kinase Pathway in Cancer", American Association of Cancer Research (AACR)

报告摘要:

Abstract:

Metabolic reprogramming emerges as a new hallmark of malignancies. Understanding the molecular mechanisms underlying metabolic alteration in tumor cells provides new opportunity for cancer treatment. Our laboratory focuses on understanding the role and regulation of lipid metabolism in tumorigenesis. Recently, we found that sterol regulatory element-binding protein-1 (SREBP-1), an endoplasmic reticulum (ER)-bound transcription factor with central roles in lipid synthesis and uptake, is highly upregulated in human cancer. Our data showed that oncogenic EGFR/PI3K/Akt signaling upregulates SREBP-1 activation and low-density lipoprotein receptor (LDLR) expression to promote lipogenesis and cholesterol uptake for tumor growth. More recently, we further found that SREBP-cleavage activating protein (SCAP), a key transporter for SREBP trafficking from the ER to the Golgi, is a critical glucose-responsive protein that integrates oncogenic signaling and fuel availability to SREBP-dependent lipogenesis. Our data showed that glucose-mediated N-glycosylation of SCAP is a prerequisite step for SCAP/SREBP trafficking and subsequent SREBP activation. This process is greatly upregulated by EGFR signaling in human cancer. Xenograft studies revealed that blocking SCAP N-glycosylation significantly ameliorates tumor growth. Moreover, we identified a novel negative feedback loop in SCAP/SREBP pathway mediated by miRNA-29.

In summary, our studies demonstrated that SCAP/SREBP-1, the central machinery of lipid metabolism, are upregulated in human cancer to promote tumor rapid growth. Our studies also showed that targeting SCAP/SREBP-1 signaling represents a promising therapeutic strategy to treat malignancies.

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