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Lipid Regulation Signaling in Cancer

Deliang Guo
The Ohio State University, USA

Dysregulated lipid metabolism is emerging as a new hallmark in malignancies. Understanding lipid biology in cancer cells is important to identify the key player in regulating lipid reprogramming and develop an effective therapeutic strategy to treat cancer. Our studies have characterized that sterol regulatory element-binding protein (SREBP-1), an endoplasmic reticulum-bound transcription factor with central roles in lipid metabolism, is highly upregulated in glioblastoma (GBM), a most common primary brain tumor with a median survival only 12-15 months even after advanced therapies. Furthermore, we found that EGFR/PI3K/Akt signaling via SREBP-1 upregulates low-density lipoprotein receptor (LDLR) for elevated cholesterol uptake. These data demonstrate that SREBP-1 plays a central role in mediating oncogenic signaling-driven lipid metabolism reprogramming in cancer cells. Recently, we found that lipid droplets (LD) are prevalent in GBM and inversely correlated with patient overall survival. Blocking LD formation via inhibition of ACAT1 significantly suppressed GBM tumor growth via inhibition of SREBP-1-dependent de novo fatty acid synthesis. Taken together, our studies demonstrate that SREBP-1 is a central player in cancer lipid metabolism, and suggest that targeting SREBP-1 and LD formation is a promising therapeutic strategy to treat malignancies.

Biography

Deliang Guo is an Assistant Professor at Ohio State University Comprehensive Cancer Center. His major research interests are tumor metabolism, autophagy and oncogenic signaling. His research is supported by multiple grants from NIH, American Cancer Society and American Brain Tumor Association.

Deliang.Guo@osumc.edu

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